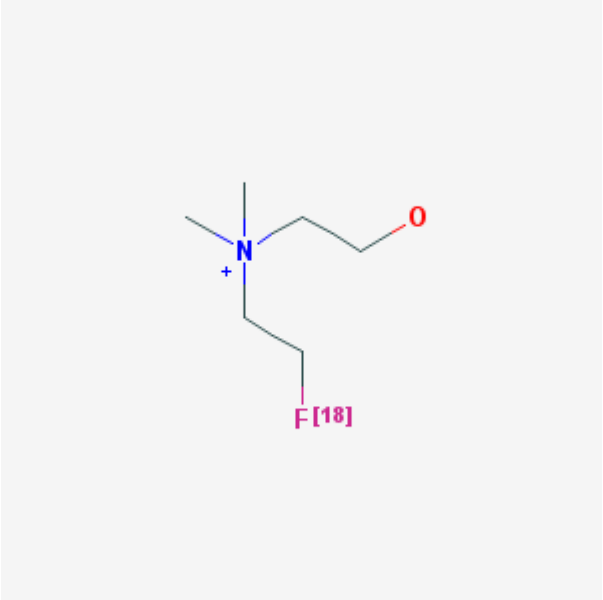
[^{18}F]Fluoroethylcholine

[^{18}F]FECh

Kam Leung, PhD[1]

Created: March 1, 2011; Updated: June 23, 2011.

Chemical name:	[^{18}F]Fluoroethylcholine
Abbreviated name:	[^{18}F]FECh
Synonym:	2-[^{18}F]Fluoroethylcholine
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]

Choline is an important component of phospholipids in cell membranes. Increased metabolism in tissues will lead to an increased uptake of choline. Choline is phosphorylated by choline kinases (CHK) to phosphorylcholine within cells and, after

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

Corresponding author.

NLM Citation: Leung K. [^{18}F]Fluoroethylcholine. 2011 Mar 1 [Updated 2011 Jun 23]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.

several biosynthetic processes, is finally integrated into phospholipids (1). Because tumor cells have a high metabolic rate, choline uptake is high in order to keep up with the demands of 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 the liver, kidney, and spleen. An ^{18}F-labeled choline analog was initially synthesized as [^{18}F]fluoroethylcholine ([^{18}F]FECh) to replace [^{11}C]choline as a PET tracer due to the short physical half-life of ^{11}C (20 min) (4). Although ^{18}F has a longer half-life (110 min), [^{18}F]FECh exhibited 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]FECh (5). PET studies with FCH showed high uptake in malignancies in patients with prostate cancer, breast carcinoma, and brain tumors (6, 7). Choline is also metabolized by choline oxidase in competition with CHK to choline betaine (8), which cannot be phosphorylated by CHK.

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]

An automated method of [^{18}F]FECh synthesis was achieved with two-step reactions (9). 2-[^{18}F]fluoroethyl tosylate was first prepared by reaction of [^{18}F]fluoride with 1,2-bis(tosyloxy)ethane in the presence of tetrabutylammonium carbonate for 8 min at 100°C. 2-[^{18}F]Fluoroethyl tosylate was reacted with dimethylethanolamine for 10 min at 100°C. [^{18}F]FECh was eluted from a sterile cation-exchange cartridge with saline. The total time required for obtaining the finished chemical was 65 min from the end of bombardment. The radiochemical yield (decay-corrected) was ~40%, with a radiochemical purity of >98%. The specific activity of [^{18}F]FECh chloride was 74 MBq/nmol (2 mCi/nmol).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

[^{18}F]FECh was rapidly consumed by yeast choline kinase and bacterial choline oxidase *in vitro* to form phosphoryl-[^{18}F]FECh and [^{18}F]FECh betaine (9), respectively. Ehrlich ascites tumor cells converted ~18% of [^{18}F]FECh to phosphoryl-[^{18}F]FECh with no

detectable [^{18}F]FECh betaine for 30 min at 37°C. Phosphatidyl-[^{18}F]FECh was identified in the tumor cellular membrane homogenates.

Animal Studies

Rodent Studies

[PubMed]

[^{11}C]Choline and [^{18}F]FECh PET scans were compared in an animal model of hepatocellular carcinoma (HCC) in woodchucks (n = 6) (10). The size of HCC foci in the liver was 1.0–1.6 cm, with mean tumor/background contrast values of 1.3 ± 0.2 with [^{18}F]FECh and 1.5 ± 0.2 with [^{11}C]choline at 50 min after injection. The tracers show similar patterns of accumulation immediately after injection, and both radioactivities plateaued at 10 min after injection.

Other Non-Primate Mammal Studies

[PubMed]

No publication is currently available.

Non-Human Primate Studies

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

Hara et al. (9) performed a preliminary PET study in one prostate cancer patient after injection of 370 MBq (10 mCi) [^{18}F]FECh. [^{18}F]FECh was cleared from blood within 5 min after administration. The highest radioactivity was found in the urinary bladder, followed by the kidney and liver. Little radioactivity was found in the bones. The standard uptake values (SUV) were 2.87 at 1.5 min and 4.43 at 55 min after injection. In another study, PET static scans with [^{18}F]FECh and [^{11}C]choline were performed in 16 patients with untreated primary prostate cancer. The tumor SUV was 3.84 ± 1.25 at 30 min and 4.02 ± 1.46 at 60 min after injection of [^{18}F]FECh. For [^{11}C]choline, the tumor SUV was 4.03 ± 1.38 at 5 min and 4.50 ± 1.56 at 20 min after injection. PET with [^{18}F]FECh showed sharper images of the tumors than did PET with [^{11}C]choline. However, a urinary catheter was used to remove urine during the time of PET scanning with [^{18}F]FECh.

Steuber et al. (11) performed PET/CT scans with [^{18}F]FECh for the detection of lymph node metastasis in 20 high-risk prostate cancer patients prior to radical prostatectomy. Overall, 31 lymph nodes (0.8–12 mm) were identified as positive out of 285 lymph nodes

examined after dissection. However, PET/CT scans with [^{18}F]FECh did not detect a single positive lymph node before radical prostatectomy.

NIH Support

R01 CA095307

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. Ueland P.M. *Choline and betaine in health and disease.* J Inherit Metab Dis. 2011;34(1):3–15. PubMed PMID: 20446114.
9. Hara T., Kosaka N., Kishi H. *Development of (18)F-fluoroethylcholine for cancer imaging with PET: synthesis, biochemistry, and prostate cancer imaging.* J Nucl Med. 2002;43(2):187–99. PubMed PMID: 11850483.
10. Kolthammer J.A., Corn D.J., Tenley N., Wu C., Tian H., Wang Y., Lee Z. *PET imaging of hepatocellular carcinoma with (18)F-fluoroethylcholine and (11)C-choline.* Eur J Nucl Med Mol Imaging. 2011;38(7):1248–56. PubMed PMID: 21344223.
11. Steuber T., Schlomm T., Heinzer H., Zacharias M., Ahyai S., Chun K.F., Haese A., Klutmann S., Kollermann J., Sauter G., Mester J., Mikecz P., Fisch M., Huland H., Graefen M., Salomon G. *[F(18)]-fluoroethylcholine combined in-line PET-CT scan for detection of lymph-node metastasis in high risk prostate cancer patients prior to radical prostatectomy: Preliminary results from a prospective histology-based study.* Eur J Cancer. 2010;46(2):449–55. PubMed PMID: 19969447.