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NLM Citation: Leung K. 2-[18F]Fluoroacetate. 2007 Mar 22 [Updated 2008 Jun 24]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.
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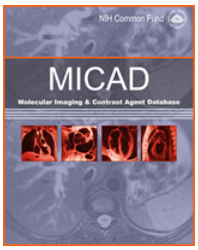


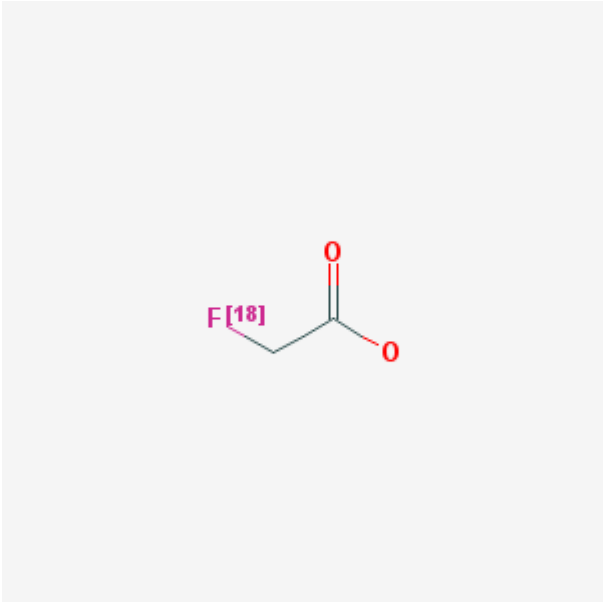
2-[18F]Fluoroacetate

[18F]FAC

Kam Leung, PhD[1]

Created: March 22, 2007; Updated: June 24, 2008.

Chemical name:	2-[18F]Fluoroacetate
Abbreviated name:	[18F]FAC
Synonym:	2-[18F]Fluoroacetic acid
Agent Category:	Compound
Target:	TCA cycle, acetyl-CoA synthetase
Target Category:	Trapped as [18F]fluorocitrate
Method of detection:	PET
Source of signal:	18F
Activation:	No
Studies:	• Rodents • Non-human primates



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Background

[PubMed]

Acetate is readily taken up by cells and is activated to acetyl-CoA in both the cytosol and mitochondria by acetyl-CoA synthetase. Acetyl-CoA is a common metabolic intermediate for synthesis of cholesterol and fatty acids, which are then incorporated into membrane (1). Acetyl-CoA is also oxidized in mitochondria by the tricarboxylic acid (TCA) cycle to CO_2 and water. Some of the acetate is converted to amino acids. In normal myocardium, acetate is metabolized to CO_2*via* the TCA cycle as the dominant pathway. In contrast, tumor cells convert most of the acetate into fatty acids by a key enzyme fatty acid synthetase, which is overexpressed in cancer cells (2). Acetate is predominantly incorporated into intracellular phosphatidylcholine membrane microdomains that are important for tumor growth and metastasis (3).

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[^{11}C]Acetate ([^{11}C]ACE) has been used as a positron emission tomography (PET) tracer for studying myocardial oxidative metabolism and regional myocardial blood flow (4) and for imaging renal, pancreatic, and prostate tumors (5). However, the potential for widespread use of [^{11}C]ACE is limited by the short half-life of ^{11}C (20 min). Fluoroacetate, an analog of acetate (6), is metabolized to fluoroacetyl-CoA and then fluorocitrate, which cannot be further metabolized to CO_2 and water (7). Therefore, fluorocitrate is trapped in the cell in proportion to oxidative metabolism. [^{18}F]Fluoroacetate ([^{18}F]FAC) is being evaluated as a PET agent for imaging prostate cancer.

Synthesis

[PubMed]

Synthesis of [^{18}F]FAC was reported by several groups with a long synthesis time (>60 min) and a low radiochemical yield (<34%) (8, 9). Sun et al. (10) and Ponde et al. (11) recently reported an automated synthesis of [^{18}F]FAC with a commercial 2-[^{18}F]fluoro-2-deoxy-2-D-glucose ([^{18}F]FDG) synthesizer. [^{18}F]FAC was prepared by nucleophilic substitution of ethyl-O-mesyl-glycolate with K[^{18}F]F/Kryptofix 2.2.2 for 5 min at 100–105°C to form ethyl-[^{18}F]FAC, which was hydrolyzed by NaOH to form [^{18}F]FAC. This method produced [^{18}F]FAC with radiochemical yields of 55 ± 5% in 35 min and radiochemical purity of >99%, decay-corrected to the end of bombardment. The average specific activity of [^{18}F]FAC was 74–130 GBq/μmol (2.0–3.5 Ci/μmol) at the end of synthesis.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

No publication is currently available.

Animal Studies

Rodents

[PubMed]

Ponde et al. (11) performed a biodistribution study in mature male rats (n = 5 per group) with [^{11}C]ACE at 20 and 60 min after injection and with [^{18}F]FAC at 20, 60, 120, and 240 min after injection. Biodistribution data of [^{11}C]ACE showed a rapid clearance (30–60%) at 60 min from most of the organs studied. However, radioactivity from the pancreas did not clear after 60 min. [^{18}F]FAC cleared significantly more slowly from the organs investigated, including the pancreas ($P < 0.001$). After injection of [^{18}F]FAC, the radioactivity in bone increased significantly over time ($P < 0.001$), which suggests defluorination. There was no significant difference in uptake in the normal prostate between [^{18}F]FAC and [^{11}C]ACE at 60 min (0.28 ± 0.05% injected dose/g (ID/g) vs. 0.28 ± 0.04% ID/g, respectively). There was a slight but significant decrease in [^{18}F]FAC uptake in the normal prostate over time (0.30 ± 0.05% ID/g at 20 min, 0.28 ± 0.05% ID/g at 1 h, 0.23 ± 0.01% ID/g at 2 h, and 0.20 ± 0.03% ID/g at 4 h; $P = 0.002$).

Ponde et al. (11) also a performed biodistribution study in 4- to 6-week-old nude mice bearing CWR22 human prostate carcinoma xenografts (n = 4 per group) with [^{11}C]ACE at 30 min after injection and with [^{18}F]FAC at 30 and 120 min after injection. The uptake in normal prostate at 30 min was significantly higher for [^{18}F]FAC compared with [^{11}C]ACE (2.60 ± 0.50% ID/g vs. 0.60 ± 0.17% ID/g, respectively; $P < 0.001$). In contrast, [^{18}F]FAC uptake in the tumor at 30 min was ~4 times higher than [^{11}C]ACE uptake at 30 min (4.01 ± 0.32% ID/g vs. 0.78 ± 0.06% ID/g, respectively; $P < 0.001$). The uptake of [^{18}F]FAC was significantly higher than the uptake of [^{11}C]ACE in all organs studied with exception of the spleen. There was also a notable increase of

radioactivity in the bone from 30 min to 120 min. On the basis of [18F]FAC microPET imaging data obtained at 30, 60, and 120 min after injection, the tumor was clearly delineated in the mice (n = 2) with tumor/muscle ratios of 1.40–1.44.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

Ponde et al. (11) reported that there was no extensive defluorination in a PET study with one male baboon, as indicated by [18F]FAC standardized uptake values (SUVs): SUVs of iliac bones and femurs were 0.26 and 0.3 at 60 min and 0.22 and 0.4 at 120 min, respectively). The organs with greatest uptake were the kidneys and liver with SUVs of 3.7 and 1.3, respectively. The brain and muscle exhibited SUVs <1.0. Further evaluation of [18F]FAC as a prostate cancer imaging agent and its mechanism of action are needed.

Human Studies

[PubMed]

No publication is currently available.

NIH Support

HL27970, NS15654, NS20867, NH37916, CA83060

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