2-(2-Nitro-1*H*-imidazol-1-yl)ethyl 2-[^{18}F]fluoroacetate

[^{18}F]NEFT

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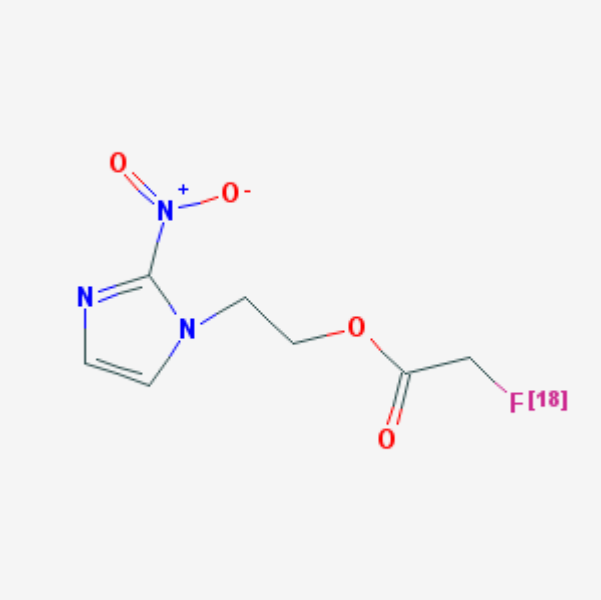
Chemical name:	2-(2-Nitro-1*H*-imidazol-1-yl)ethyl 2-[^{18}F]fluoroacetate
Abbreviated name:	[^{18}F]NEFT, [^{18}F]8
Synonym:	
Agent Category:	Compound
Target:	Hypoxic tissue
Target Category:	Hypoxia
Method of detection:	Positron emission tomography (PET)
Source of signal / contrast:	^{18}F
Activation:	No
Studies:	• Rodents



Click on the above structure for additional information in PubChem.

Background

[PubMed]

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Hypoxia is found in a variety of solid tumors and leads to tumor progression and the resistance of tumors to chemotherapy and radiotherapy (1-3). Tumor oxygenation is heterogeneously distributed within human tumors (4). It would be beneficial to assess tumor oxygenation before and after therapy to provide an evaluation of tumor response to treatment and an insight into new therapeutic treatments (5). Tumor oxygenation is measured invasively using computerized, polarographic, oxygen-sensitive electrodes, which is regarded as the gold standard (6). Functional and non-invasive imaging of intratumoral hypoxia has been demonstrated to be feasible for the measurement of tumor oxygenation (7).

Chapman proposed the use of 2-nitroimidazoles for hypoxia imaging in 1979 (8). 2-Nitroimidazole compounds are postulated to undergo a reduction in hypoxic conditions, forming highly reactive oxygen radicals that subsequently bind covalently to macromolecules inside the cells (9). In normoxic conditions, the reduced molecule is rapidly reoxidized and transported from the cell. [^{18}F]Fluoromisonidazole ([^{18}F]FMISO) is the most widely used positron emission tomography (PET) tracer for imaging tumor hypoxia (7). However, it has slow clearance kinetics and high lipophilicity, resulting in substantial background signal in PET scans. [^{18}F]Fluoroazomycinarabinofuranoside ([^{18}F]FAZA) is a 2-nitroimidazole with a sugar addition (10) and has been studied as a hypoxia-imaging agent, showing promising results in various tumor models in rats and mice (11, 12). Zha et al. (13) reported a new [^{18}F]-labeled 2-nitroimidazole derivative, 2-(2-nitro-1*H*-imidazol-1-yl)ethyl 2-[^{18}F]fluoroacetate ([^{18}F]NEFT, which contains a hydrolyzable ester group for *in vivo* hypoxic tissue imaging.

Related Resource Links:

- Chapters in MICAD (Hypoxia)
- Gene information in NCBI (Hypoxia-inducible factor 1, alpha subunit)
- Articles in Online Mendelian Inheritance in Man (OMIM) (Hypoxia)
- Clinical trials (Hypoxia imaging)

Synthesis

[PubMed]

[^{18}F]NEFT was readily synthesized by ^{18}F-fluorination of 2-(2-nitro-1*H*-imidazol-1-yl)ethyl2-bromoacetate ([^{18}F]KF/18-crown-6/$KHCO_3$, 10 min at 90°C) in dimethyl sulfoxide (13). [^{18}F]NEFT was purified with solid-phase extraction. Overall yield was 9%–10% at the end of synthesis, with a radiochemical purity of >98%. Total synthesis time was ~60 min. The specific activity of [^{18}F]NEFT was not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

No publication is currently available.

Animal Studies

Rodents

[PubMed]

Ex vivo biodistribution studies of [^{18}F]NEFT were performed in mice (n = 3) bearing EMT-6 tumors at 30 min after injection (13). The tumor accumulation was 2.45 ± 0.08% injected dose/gram (ID/g). The bone (6.29% ID/g) had the highest accumulation, followed by the lung (2.54% ID/g), blood (2.50% ID/g), heart (2.46% ID/g), kidney (2.38% ID/g), liver (2.23% ID/g), muscle (1.74% ID/g), spleen (1.71% ID/g), and brain (1.24% ID/g). The tumor/blood, tumor/liver, and tumor/muscle ratios were 0.98, 1.10, and 1.41, respectively. These ratios for [^{18}F]FMISO were 0.91, 0.59, and 1.74, respectively. The authors suggested that enzymatic or chemical hydrolysis of [^{18}F]NEFT would yield [^{18}F]fluoroacetate. It is difficult to determine if the hypoxia or the trapping of [^{18}F]fluoroacetate or both is more important for tumor accumulation. No blocking study was performed.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

NIH Support

AG 022559-01

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