^{18}F fluorodopa

^{18}F -FDOPA, ^{18}F-L-Dihydroxyphenylalanine

1. Indications

^{18}F-FDOPA was originally developed as a positron emitting radiopharmaceutical for the *in vivo* imaging of functional dopaminergic neuron terminals in the striatum. Recently its applications shifts more towards the imaging of neuroendocrine tumours (NET). NETs exert the unique property of producing and secreting various substances which requires the uptake of metabolic precursors, such as ^{18}F-FDOPA.

Neurology

PET with ^{18}F-fluorodopa is indicated for detecting loss of functional dopaminergic neuron terminals in the striatum in patients with clinically uncertain parkinsonian syndromes. It can be used to differentiate essential tremor from parkinsonian syndromes related to degenerative diseases affecting the nigrostriatal system (Parkinson disease (PD), multisystem atrophy and progressive supranuclear palsy). PET with ^{18}F-fluorodopa, on its own, is unable to discriminate between different parkinsonian syndromes related to degenerative diseases affecting the nigrostriatal system. It is also unable to discriminate between PD with and without tremor.

Oncology

From imaging studies, PET with ^{18}F-fluorodopa allows a functional approach to pathologies, organs or tissues in which an increase of intracellular transport and of decarboxylation of the amino acid dihydroxyphenylalanine is sought. The following indications were particularly documented:

Diagnosis

- Diagnosis and localisation of an insulinoma in case of hyperinsulinism in infants and children
- Diagnosis and localisation of glomus tumours in patients with a mutation of the succinate dehydrogenase subunit D gene
- Localisation of pheochromocytomas and paragangliomas

Staging

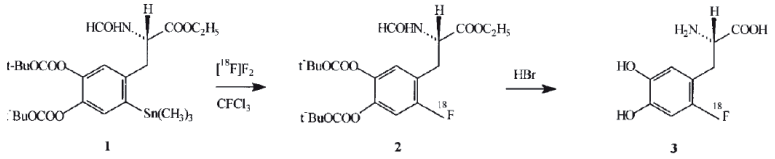
- Pheochromocytomas and paragangliomas
- Well-differentiated carcinoid tumours of the intestinal tract

Detection in case of reasonable suspicion of recurrent or residual disease

- Primary brain tumours restricted to high grade gliomas (grade III and IV)
- Pheochromocytomas and paragangliomes
- Medullary thyroid carcinoma with elevated serum calcitonin level
- Well-differentiated carcinoid tumours of the intestinal tract
- Other endocrine digestive tumours when somatostatin receptors scintigraphy is negative

2. Preparation

Carrier added ^{18}F-DOPA is produced via electrophilic substitution method as described by de Vries et al.



3. Quality control

^{18}F-FDOPA is described in the European Pharmacopeia.

4. Interactions

Carbidopa, inhibitors of the enzyme catechol-O-methyl transferase (COMT) such as entacapone or nitecapone: the bioavailability of fluorodopa in the brain can be increased by pre-treatment with either inhibitors of the enzyme aromatic amino acid decarboxylase (AAAD) such as carbidopa which block peripheral conversion of fluorodopa to fluorodopamine, or inhibitors of the enzyme catechol-O-methyl transferase (COMT) such as entacapone and nitecapone which decrease peripheral degradation of fluorodopa to 3-O-methyl-6-fluorodopa.

Carbidopa: a case of congenital hyperinsulinism has been reported where fluorodopa uptake in the pancreas was no longer detectable after carbidopa administration.

Glucagon: Glucagon affects fluorodopa (^{18}F) uptake in pancreas by interacting with pancreatic beta-cell function.

Haloperidol: an increase in intracerebral dopamine caused by haloperidol may increase the accumulation of fluorodopa (^{18}F) in the brain.

Reserpine: Reserpine can empty the contents of intraneuronal vesicles and thus prevent the retention of fluorodopa (^{18}F) in the brain.

5. Adverse reactions

No serious adverse reactions have been observed so far. Pain on injection site was reported to have disappeared in a few minutes, without treatment. A case of carcinoid crisis related to an injection administrated too fast has been reported in the literature. Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 7 mSv when the maximal recommended activity of 280 MBq (for an individual of 70 kg) is administered these adverse events are expected to occur with a low probability.

6. Biodistribution & pharmacokinetics

Distribution: Studies in healthy subjects after administration of fluorodopa (^{18}F) showed an ubiquitous distribution of activity in all body tissues.

Organ uptake: Fluorodopa (^{18}F) is an analogue of an aromatic amino acid rapidly accumulated by target tissues, especially in the striatum of the human brain, and converted into dopamine, neurotransmitter of the

catecholamines family.

Elimination: Fluorodopa (^{18}F) is eliminated by the kidney, 50% is removed after 0,7 h, and 50% after 12 h.

Half-Life: Fluorodopa (^{18}F) is eliminated by a bi-exponential kinetics with a biological half-life of 12 h (67-94%) and a physical half-life of 1,7-3,9 h (6-33%). These two half-lives seem to depend on age.

7. Stability

Physical half-life of ^{18}F-FDOPA is 110 min. The injection takes place as soon as possible after production. The stability of the product has been investigated and the product is stable for at least 8 h after production in the current formulation up to 200-900 MBq/ml. This allows transportation of the product to other hospitals for clinical use in those hospitals within the product's expiry time.

8. Literature

- de Vries, E. F., Luurtsema, G., Brüssermann, M., Elsinga, P. H., & Vaalburg, W. (1999). Fully automated synthesis module for the high yield one-pot preparation of 6-[^{18}F] fluoro-L-DOPA. *Applied Radiation and Isotopes*, 51(4):389-94.