

# **<sup>18</sup>F DOPA PET/CT in Neuroendocrine Tumours and in Presynaptic Dopaminergic Deficits**

KP Koopmans, Martini Ziekenhuis, Groningen  
SA Eshuis, Medical Centre Leeuwarden  
AH Brouwers, University Medical Centre Groningen

## **1. Introduction**

- a. The use of Fluoro-18-L-Dihydroxyphenylalanine (<sup>18</sup>F-FDOPA) in PET was developed in the 80's for the visualisation of the dopaminergic system in patients with degenerative disorders, such as Parkinson's Disease (PD) and related disorders. The first publication on the use of <sup>18</sup>F-FDOPA PET for brain imaging was in 1983, which was followed by many others on the use of <sup>18</sup>F-FDOPA PET for the diagnosis of Parkinson's disease. Years later, in 1999 the first publication on the use of <sup>18</sup>F-FDOPA PET for imaging of neuroendocrine tumour tumours appeared. The value of <sup>18</sup>F-FDOPA PET has now been proven for the diagnosis and staging of many neuroendocrine tumour tumours, brain tumours and congenital hyperinsulinaemia of infants. The increased use of <sup>18</sup>F-FDOPA PET has led to commercial availability of this tracer in several countries. In the Netherlands, availability is still limited to centres which have a cyclotron.
- b. The 2013 Dutch guidelines for neuroendocrine tumours, suggest <sup>18</sup>F-FDOPA PET for patients suspected of neuroendocrine tumours which are negative on somatostatin receptor scintigraphy.

## **2. Methodology**

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

## **3. Indications**

- a. Patients suspected of a presynaptic dopaminergic deficiency such as Parkinson's Disease (PD), Multi System Atrophy (MSA), Progressive Supranuclear Palsy (PSP) and Cortico Basal Degeneration (CBD) or dementias e.g. Diffuse Lewy Body Disease (DLB).
- b. The detection and staging of primary neuroendocrine tumours and their metastases.
  - Carcinoid tumours
  - Medullary thyroid carcinoma
  - Paragangliomas
  - Pheochromocytomas
- c. <sup>18</sup>F-FDOPA PET can be of benefit for the detection of:
  - Pancreatic Isletcell tumours
  - Merkelcell tumours
  - Brain tumours
- d. Congenital Hyperinsulinaemia

#### 4. Relation to other diagnostic procedures

##### a. Parkinson's Disease and related disorders

- <sup>123</sup>I-FP-CIT SPECT can also be used to diagnose presynaptic dopaminergic deficits. <sup>18</sup>F-F-DOPA PET scans assess striatal DOPA decarboxylase activity and storage capacity of <sup>18</sup>F-dopamine, whereas <sup>123</sup>I-FP-CIT SPECT binds to the dopamine transporter. In Parkinson's Disease, MSA, PSP and CBD, the number of dopamine transporters are reduced. The sensitivity and specificity of <sup>123</sup>I-FP-CIT SPECT is approximately equal to <sup>18</sup>F-FDOPA PET scan. A disadvantage of <sup>123</sup>I-FP-CIT SPECT is the longer scanning time compared to <sup>18</sup>F-FDOPA PET, which can be a problem in this patient group.
- Post synaptic imaging is reported to be reduced in MSA but not in PD. Therefore postsynaptic imaging may possibly be used to differentiate between PD and related disorders. The postsynaptic dopaminergic system can be visualized with either SPECT or PET, e.g. <sup>123</sup>I-IBZM SPECT or <sup>11</sup>C-raclopride PET. However, it is difficult to differentiate between iPD, MSA, PSP and CBD, due to an overlap in binding potential of both <sup>123</sup>I-IBZM and <sup>11</sup>C-raclopride. Postsynaptic DOPA imaging cannot be used for differentiating between healthy individuals on the one hand and PD and related disorders on the other hand.
- By combining <sup>18</sup>F-FDG PET and <sup>18</sup>F-FDOPA PET, it is possible to distinguish between Parkinson's Disease, MSA, PSP and CBD. With this combination, the sensitivity and specificity rise above 90%.

##### b. Neuroendocrine tumours

- For a long time, <sup>111</sup>In-pentetreotide has played a primary role in the diagnosis and staging of neuroendocrine tumours. The <sup>111</sup>In-pentetreotide scan can also be used to assess whether patients are suitable for PRRT.
- Recently, <sup>68</sup>Ga labelled somatostatin analogues have become available for PET imaging. The size of the synthesis units and the accessibility of raw materials needed for this synthesis, make this tracer easily available for widespread use in PET. <sup>68</sup>Ga labelled somatostatin analogues are a good alternative to <sup>18</sup>F-FDOPA PET in neuroendocrine tumours.
- In patients with neuroblastoma, MIBG scintigraphy is still the method of choice. There is evidence that <sup>18</sup>F-FDG PET, <sup>18</sup>F-FDOPA PET and <sup>18</sup>F-Dopamine PET are good alternatives for the diagnosis of neuroblastomas. However, <sup>18</sup>F-FDG PET, <sup>18</sup>F-FDOPA PET and <sup>18</sup>F-Dopamine PET should be considered experimental for this indication.
- MIBG has long been used in the diagnostic work-up for adrenal pheochromocytomas. However, <sup>18</sup>F-FDOPA PET seems to have a higher sensitivity for the detection of metastasized disease.
- <sup>18</sup>F-FDOPA PET seems to have a better sensitivity for the detection of paragangliomas, as compared to <sup>111</sup>In-pentetreotide. This has been published only in small studies. Both <sup>18</sup>F-dopamine and <sup>18</sup>F-FDOPA PET seem to be a good first choice for the detection of paragangliomas, but in patients with SDHB gene mutations, <sup>18</sup>F-FDG PET is preferable.
- For neuroendocrine tumours, <sup>11</sup>C-5-HTP can be used as an alternative. <sup>11</sup>C-5-HTP is a precursor in the serotonin pathway, which is active in many neuroendocrine tumours. Very few publications are available on this topic, and due to the

complex synthesis, its use seems limited to pancreatic islet cell tumours.

- The use of <sup>18</sup>F-FDG PET is limited to patients in whom dedifferentiation of neuroendocrine tumour lesions is suspected. Generally, <sup>18</sup>F-FDG PET has a low sensitivity for the detection of neuroendocrine tumour lesions.

### **5. Medical information necessary for planning**

- Any signs or symptoms relating to a presynaptic dopaminergic defect (PD, MSA, PSP, CBD, DLB), including use of medication, lateralisation of symptoms and duration of symptoms
- Symptoms associated with neuroendocrine tumours
- Biochemical findings, biomarkers indicative of a neuroendocrine tumour
- Possible localisation of tumour, based on previous imaging
- Use of COMT inhibitors, chemotherapy, radiotherapy or somatostatin analogs as treatment? If so, until when?

### **6. Radiofarmaceutical**

Tracer: <sup>18</sup>F-fluorodihydroxyphenylalanine (<sup>18</sup>F-FDOPA)

Nuclide: Fluorine-18

Activity: Parkinsonism 200 MBq, Neuroendocrine tumours standard 200MBq or > 1,5 MBq/kg, minimum 80 MBq

Administration: Intravenous

### **7. Radiation safety**

- The effective dose equivalent for adults ranges from 0,025 mSv/MBq
- Clinical information is necessary to compare the benefits to the possible harm of carrying out any procedure in patients known or suspected to be pregnant
- According to ICRP 106 there is no need to interrupt breastfeeding

### **8. Patient preparation/essentials for procedure**

- For diagnosis of PD, related disorders and DLB, patients have to stop using COMT inhibitors 5 half-lives before scanning. Other drugs used for PD can be continued.
- For the diagnosis of neuroendocrine tumours, all medication can be continued.
- For the diagnosis of congenital hyperinsulinemia, diazoxide, octreotide and glucagon should be stopped 48 h before injection of <sup>18</sup>F-DOPA.
- Theoretically, a higher tracer uptake could be realised by patients fasting 2-6 h before this procedure. However, thus far, there is no evidence to support/disprove this theory. All studies of <sup>18</sup>F-FDOPA PET and Parkinsonism have been performed in a fasting state, therefore, it seems fit to follow this guideline.
- Patients should not take any amino-acid containing foods 6 h prior to this procedure. Prehydration by drinking up to 1 liter of water prior to the injection of <sup>18</sup>F-FDOPA is important to decrease the <sup>18</sup>F-FDOPA urinary concentration.
- All patients, excluding patients suspected of pancreatic problems, should be premedicated with 2 mg/kg carbidopa 60 min prior to injection of <sup>18</sup>F-FDOPA. Carbidopa inhibits the peripheral conversion of <sup>18</sup>F-FDOPA to <sup>18</sup>F-FDopamine. <sup>18</sup>F-FDopamine is excreted actively by the kidneys, therefore, premedication with carbidopa results in increased availability of <sup>18</sup>F-FDOPA for striatal or tumoural

uptake. Additionally, this premedication lowers the radiation exposure of bladder and kidneys. However, in patients with congenital hyperinsulinaemia and pancreatic neuroendocrine tumours, premedication with carbidopa lowers <sup>18</sup>F-FDOPA uptake by pathological processes in the pancreas. This can result in a false negative scan.

- In patients with extensive neuroendocrine disease and extensive liver metastases it is advised to administer <sup>18</sup>F-FDOPA slowly in 2 min. This reduces the possibility of the development of a carcinoid crisis in these patients.

a. *Schematically:*

- PD, related disorders and DLB
- no amino-acid intake 2-6 h prior to <sup>18</sup>F-FDOPA injection
- 90 min prior to <sup>18</sup>F-FDOPA injection 2 mg/kg carbidopa (max 150mg) orally, start prehydration.
- 90 min after <sup>18</sup>F-FDOPA injection (200MBq), start scanning.

b. *Neuroendocrine tumours*

- no amino-acid intake 2-6 h prior to <sup>18</sup>F-FDOPA injection
- 1 h prior to <sup>18</sup>F-FDOPA injection 2 mg/kg carbidopa (max 150mg) orally (however, no carbidopa in patients with pancreatic pathology), start prehydration.
- 1h after <sup>18</sup>F-FDOPA injection, start scanning.

## 9. Acquisition and processing

- The patient should be placed in a comfortable position with the head fixed, using the orbitomeatal line as a reference
- State of the art PET-CT scanner with full ring detectors LSO/LYSO/BGO/GSO crystal. Acquisitions should not start earlier than 30 min after injection and may start up to several hours after injection for detection of tumours. For imaging the brain, acquisition should start 90 min after the injection of the tracer
- Acquisition-time 6 min (3D-mode)
- CT-based attenuation correction with low-dose CT scan if only for attenuation purposes
- Image reconstruction in the form of trans axial images with a matrix of at least 128x128
- The reconstruction methods and choices of iterations, subsets and smoothness depend on the type of camera and recommendations of the manufacturer
- Use a continuous colour scale for displaying the images
- Absolute quantification is not possible with static FDOPA images. Only dynamic data acquisition with arterial sampling allows for absolute quantification. (These protocols are beyond the scope of this document. See European Association of Nuclear Medicine and Society of Nuclear Medicine guidelines.)
- However for static imaging, various software programs for voxel based quantification and brain mapping with or without normal databases are available

## 10. Interpretation

### a. Visual interpretation <sup>18</sup>F-FDOPA PET

- Normally, after carbidopa pre-treatment, a moderately increased uptake is seen in the striata as compared to other brain regions. Also, low intensity uptake in the heart, liver, and bowels can be noted. Pancreatic uptake can be inhomogeneous due to the tissue composition of the pancreas. The uptake in the pancreatic head seems more intense as there is more tissue present in the head compared to the tail.
- Increased <sup>18</sup>F-FDOPA uptake is seen in the kidneys, ureters and bladder.
- Lightly asymmetrical uptake can occur in the adrenal glands. However, when there is intense uptake on one side, a neuroendocrine tumour should be considered.
- Normally, no bone marrow uptake is seen on <sup>18</sup>F-FDOPA PET scans.
- The <sup>18</sup>F-FDOPA uptake in the gallbladder is usually intense. Gallstones may lead to inhomogeneous uptake. Correlation with CT is warranted for superficial liver lesions.
- Female patients, may show low intensity uptake in the areolas. This is physiological.

### b. Semiquantitative interpretation of <sup>18</sup>F-FDOPA PET

- Thus far there is no evidence that the SUV (standard uptake value) gives any indication of response to therapy in neuroendocrine tumours.
- For brain imaging, a standard template with ROIs should be positioned around the caudate nucleus, the striatum and the occipital cortex as the reference region. The striato-occipital ratio (striatal uptake divided by non-specific brain uptake) should be calculated and compared to normal values, obtained within each department.

## 11. Report

### a. <sup>18</sup>F-FDOPA PET brain scans

- Scans must be interpreted visually. The uptake pattern in the striatum must be noted. This is symmetrical in the normal population. Also, compare the different areas of the striatum. Quantitative analysis of the scans is also possible by means of a standard template of ROIs. ROIs should be positioned around the caudate nucleus, the putamen and the occipital cortex as a reference region. The striato-occipital ratio (striatal uptake divided by non-specific brain uptake) should be calculated and compared to normal values, obtained within the department. This data helps to determine whether the uptake pattern fits with a presynaptic dopaminergic defect. <sup>18</sup>F-FDOPA PET scans cannot differentiate between PD, MSA, PSP, CBD or LBD and these specific diagnoses can thus not be made based on <sup>18</sup>F-FDOPA PET imaging solely.

### b. <sup>18</sup>F-FDOPA PET whole body scans

- Reconstructed images must be analysed from the computer monitor. Both attenuation corrected and non-corrected images should be evaluated, thereby paying attention to physiological uptake in the brain, adrenal glands, kidneys, urethra, urinary bladder, gall bladder and bile ducts. Abnormal, focal uptake of <sup>18</sup>F-FDOPA must be described, noting both size and intensity. With regards to

the adrenal glands, special attention should be paid to symmetry of uptake. Asymmetrical uptake can point to a neuroendocrine tumour in one of the adrenal glands.

- Uptake can be quantified using SUV. However to date there is no evidence that the SUV of neuroendocrine tumours has a relation to therapy response.

## 12. Literature

- Garnett ES, Firnau G, Nahmias C. Dopamine visualized in the basal ganglia of living man. *Nature*. 1983;305:137-8.
- Antonini A, Vontobel P, Psylla M et al. Complementary positron emission tomographic studies of the striatal dopaminergic system in Parkinson's disease. *Arch Neurol*. 1995;52:1183-90.
- Leenders KL, Herold S, Brooks DJ et al. Pre-synaptic and post-synaptic dopaminergic system in human brain. *Lancet*. 1984;2:110-1.
- Leenders KL, Palmer AJ, Quinn N et al. Brain dopamine metabolism in patients with Parkinson's disease measured with positron emission tomography. *J Neurol Neurosurg Psychiatry*. 1986;49:853-60.
- Hu XS, Okamura N, Arai H et al. 18F-fluorodopa PET study of striatal dopamine uptake in the diagnosis of dementia with Lewy bodies. *Neurology*. 2000;55:1575-7.
- McKeith I, O'Brien J, Walker Z et al. Sensitivity and specificity of dopamine transporter imaging with 123I-FP-CIT SPECT in dementia with Lewy bodies: a phase III, multicentre study. *Lancet Neurol*. 2007;6:305-13.
- Walker Z, Costa DC, Walker RW et al. Differentiation of dementia with Lewy bodies from Alzheimer's disease using a dopaminergic presynaptic ligand. *J Neurol Neurosurg Psychiatry*. 2002;73:134-40.
- Walker Z, Jaros E, Walker RW et al. Dementia with Lewy bodies: a comparison of clinical diagnosis, FP-CIT single photon emission computed tomography imaging and autopsy. *J Neurol Neurosurg Psychiatry*. 2007;78:1176-81.
- Firnau G, Sood S, Chirakal R, Nahmias C, Garnett ES. Metabolites of 6-[18F]fluoro-L-dopa in human blood. *J Nucl Med*. 1988;29:363-9.
- Becherer A, Szabo M, Karanikas G et al. Imaging of advanced neuroendocrine tumours with (18) F-FDOPA PET. *J Nucl Med*. 2004;45:1161-7.
- Hoegerle S, Althoefer C, Ghanem N et al. Whole-body 18F dopa PET for detection of gastrointestinal carcinoid tumours. *Radiology*. 2001;220:373-80.
- Koopmans KP, de Vries EG, Kema IP et al. Staging of carcinoid tumours with 18F-DOPA PET: a prospective, diagnostic accuracy study. *Lancet Oncol*. 2006;7:728-34.
- Koopmans KP, Neels OC, Kema IP et al. Improved staging of patients with carcinoid and islet cell tumours with 18F-dihydroxy-phenyl-alanine and 11C-5-hydroxy-tryptophan positron emission tomography. *J Clin Oncol*. 2008;20(26):1489-95.
- Nanni C, Rubello D, Fanti S. 18F-DOPA PET/CT and neuroendocrine tumours. *Eur J Nucl Med Mol Imaging*. 2006;33:509-13.
- Beuthien-Baumann B, Strumpf A, Zessin J, Bredow J, Kotzerke J. Diagnostic impact of PET with 18F-FDG, 18F-DOPA and 3-O-methyl-6-[18F]fluoro-DOPA in recurrent or metastatic medullary thyroid carcinoma. *Eur J Nucl Med Mol Imaging*. 2007;34:1604-9.
- Hoegerle S, Althoefer C, Ghanem N et al. 18F-DOPA positron emission tomography for tumour detection in patients with medullary thyroid carcinoma and elevated calcitonin levels. *Eur J Nucl Med*. 2001;28:64-71.
- Koopmans KP, de Groot JW, Plukker JT et al. 18F-dihydroxyphenylalanine PET in patients with biochemical evidence of medullary thyroid cancer: relation to tumour differentiation. *J Nucl Med*.

2008;49:524-31.

- Hoegerle S, Ghanem N, Altehoefer C et al. 18F-DOPA positron emission tomography for the detection of glomus tumours. *Eur J Nucl Med Mol Imaging*. 2003;30:689-94.
- Ledezma CJ, Chen W, Sai V et al. 18F-FDOPA PET/MRI fusion in patients with primary/recurrent gliomas: initial experience. *Eur J Radiol*. 2009;71:242-8.
- Fiebrich HB, Brouwers AH, van Bergeijk L, van den Berg G. Image in endocrinology. Localization of an adrenocorticotropin-producing pheochromocytoma using 18F-dihydroxyphenylalanine positron emission tomography. *J Clin Endocrinol Metab*. 2009;94:748-9.
- Fiebrich HB, Brouwers AH, Kerstens MN et al. 6-[F-18]Fluoro-L-dihydroxyphenylalanine positron emission tomography is superior to conventional imaging with (123I)-metaiodobenzylguanidine scintigraphy, computer tomography, and magnetic resonance imaging in localizing tumours causing catecholamine excess. *J Clin Endocrinol Metab*. 2009;94:3922-30.
- Hoegerle S, Nitzsche E, Altehoefer C et al. Pheochromocytomas: detection with 18F DOPA whole body PET—initial results. *Radiology*. 2002;222:507-12.
- Imani F, Agopian VG, Auerbach MS et al. 18F-FDOPA PET and PET/CT accurately localize pheochromocytomas. *J Nucl Med*. 2009;50:513-9.
- Taieb D, Tessonnier L, Sebag F et al. The role of 18F-FDOPA and 18F-FDG-PET in the management of malignant and multifocal pheochromocytomas. *Clin Endocrinol (Oxf)*. 2008;69:580-6.
- Peloschek P, Novotny C, Mueller-Mang C et al. Diagnostic imaging in Merkel cell carcinoma: Lessons to learn from 16 cases with correlation of sonography, CT, MRI and PET. *Eur J Radiol*. 2008.
- Talbot JN, Kerrou K, Missoum F et al. 6-[F-18]fluoro-L-DOPA positron emission tomography in the imaging of Merkel cell carcinoma: preliminary report of three cases with 2-deoxy-2-[F-18]fluoro-D-glucose positron emission tomography or pentetreotide-(111In) SPECT data. *Mol Imaging Biol*. 2005;7:257-61.
- Becherer A, Karanikas G, Szabo M et al. Brain tumour imaging with PET: a comparison between [18F] fluorodopa and [11C]methionine. *Eur J Nucl Med Mol Imaging*. 2003;30:1561-7.
- Chen W, Silverman DH, Delaloye S et al. 18F-FDOPA PET imaging of brain tumours: comparison study with 18F-FDG PET and evaluation of diagnostic accuracy. *J Nucl Med*. 2006;47:904-11.
- Schiepers C, Chen W, Cloughesy T, Dahlbom M, Huang SC. 18F-FDOPA kinetics in brain tumours. *J Nucl Med*. 2007;48:1651-61.
- Kauhanen S, Seppanen M, Minn H et al. Fluorine-18-L-dihydroxyphenylalanine (18F-DOPA) positron emission tomography as a tool to localize an insulinoma or beta-cell hyperplasia in adult patients. *J Clin Endocrinol Metab*. 2007;92:1237-44.
- Barthlen W, Blankenstein O, Mau H et al. Evaluation of [18F]fluoro-L-DOPA positron emission tomography-computed tomography for surgery in focal congenital hyperinsulinism. *J Clin Endocrinol Metab*. 2008;93:869-75.
- Hardy OT, Hernandez-Pampaloni M, Saffer JR et al. Accuracy of [18F]fluorodopa positron emission tomography for diagnosing and localizing focal congenital hyperinsulinism. *J Clin Endocrinol Metab*. 2007;92:4706-11.
- Kapoor RR, Flanagan SE, James C et al. Hyperinsulinaemic hypoglycaemia. *Arch Dis Child*. 2009;94:450-7.
- Mohnike K, Blankenstein O, Minn H et al. [18F]-DOPA positron emission tomography for preoperative localization in congenital hyperinsulinism. *Horm Res*. 2008;70:65-72.
- Otonkoski T, Nanto-Salonen K, Seppanen M et al. Noninvasive diagnosis of focal hyperinsulinism of infancy with [18F]-DOPA positron emission tomography. *Diabetes*. 2006;55:13-8.
- Psylla M, Gunther I, Antonini A et al. Cerebral 6-[18F]fluoro-L-DOPA uptake in rhesus monkey:

pharmacological influence of aromatic amino acid decarboxylase (AAAD) and catechol-O-methyltransferase (COMT) inhibition. *Brain Res.* 1997;767:45-54.

- Mohnike K et al, Proposal for a Standardized Protocol for 18F-DOPA-PET (PET/CT in Congenital Hyperinsulinism. *Horm Res.* 2006; 66:40-2.
- Jager PL. Improving amino acid imaging: hungry or stuffed? *J Nucl Med.* 2002;43:1207-9.
- Lahoutte T, Caveliers V, Franken PR et al. Increased tumour uptake of 3-(123I)-Iodo-L-alpha-methyltyrosine after preloading with amino acids: an in vivo animal imaging study. *J Nucl Med.* 2002;43:1201-6.
- Leenders KL, Poewe WH, Palmer AJ, Brenton DP, Frackowiak RS. Inhibition of L-[18F]fluorodopa uptake into human brain by amino acids demonstrated by positron emission tomography. *Ann Neurol.* 1986;20:258-62.
- Brown WD, Oakes TR, DeJesus OT et al. Fluorine-18-fluoro-L-DOPA dosimetry with carbidopa pretreatment. *J Nucl Med.* 1998;39:1884-91.
- Orlefors H, Sundin A, Lu L et al. Carbidopa pretreatment improves image interpretation and visualisation of carcinoid tumours with 11C-5-hydroxytryptophan positron emission tomography. *Eur J Nucl Med Mol Imaging.* 2006;33:60-5.
- Hoffman JM, Melega WP, Hawk TC et al. The effects of carbidopa administration on 6-[18F]fluoro-L-dopa kinetics in positron emission tomography. *J Nucl Med.* 1992;33:1472-7.
- Kema IP, Koopmans KP, Elsinga P.J., Brouwers AH, Jager PL, de Vries EG. Correspondence. *J.Clin. Oncol.* 2008;26(32), 5308-9.
- Nataf V, Balard M, De Beco V et al. Safety of 18F-DOPA injection for PET of carcinoid tumour. *J Nucl Med.* 2006;47:1732.
- Koopmans KP, Brouwers AH, De Hooge MN et al. Carcinoid crisis after injection of 6-18F-fluorodihydroxyphenylalanine in a patient with metastatic carcinoid. *J Nucl Med.* 2005;46:1240-3.
- Dhawan V, Ma Y, Pillai V et al. Comparative analysis of striatal FDOPA uptake in Parkinson's disease: ratio method versus graphical approach. *J Nucl Med.* 2002;43:1324-30.
- Morrish PK, Sawle GV, Brooks DJ. Regional changes in [18F]dopa metabolism in the striatum in Parkinson's disease. *Brain.* 1996;119 ( Pt 6):2097-103.
- Antonini A, Leenders KL, Vontobel P et al. Complementary PET studies of striatal neuronal function in the differential diagnosis between multiple system atrophy and Parkinson's disease. *Brain.* 1997;120(Pt 12):2187-95.
- Balan KK. Visualization of the gall bladder on F-18 FDOPA PET imaging: a potential pitfall. *Clin Nucl Med.* 2005;30:23-4.
- Eshuis SA, Maguire RP, Leenders KL, Jonkman S, Jager PL. Comparison of FP-CIT SPECT with F-DOPA PET in patients with de novo and advanced Parkinson's disease. *Eur J Nucl Med Mol Imaging.* 2006;33:200-9.
- Eshuis SA, Jager PL, Maguire RP et al. Direct comparison of FP-CIT SPECT and F-DOPA PET in patients with Parkinson's disease and healthy controls. *Eur J Nucl Med Mol Imaging.* 2009;36:454-62.
- Ishikawa T, Dhawan V, Kazumata K et al. Comparative nigrostriatal dopaminergic imaging with iodine-123-beta CIT-FP/SPECT and fluorine-18-FDOPA/PET. *J Nucl Med.* 1996;37:1760-5.
- Kim YJ, Ichise M, Ballinger JR et al. Combination of dopamine transporter and D2 receptor SPECT in the diagnostic evaluation of PD, MSA, and PSP. *Mov Disord.* 2002;17:303-12.
- Eidelberg D, Takikawa S, Moeller JR et al. Striatal hypometabolism distinguishes striatonigral degeneration from Parkinson's disease. *Ann Neurol.* 1993;33:518-27.
- Ghaemi M, Hilker R, Rudolf J, Sobesky J, Heiss WD. Differentiating multiple system atrophy from Parkinson's disease: contribution of striatal and midbrain MRI volumetry and multi-tracer PET imaging. *J*



Neurol Neurosurg Psychiatry. 2002;73:517-23.

- Klein RC, de Jong BM, de Vries JJ, Leenders KL. Direct comparison between regional cerebral metabolism in progressive supranuclear palsy and Parkinson's disease. *Mov Disord.* 2005;20:1021-30.
- Sawle GV, Brooks DJ, Marsden CD, Frackowiak RS. Corticobasal degeneration. A unique pattern of regional cortical oxygen hypometabolism and striatal fluorodopa uptake demonstrated by positron emission tomography. *Brain.* 1991;114 ( Pt 1B):541-56.
- Eckert T, Barnes A, Dhawan V et al. FDG PET in the differential diagnosis of parkinsonian disorders. *Neuroimage.* 2005;26:912-21.
- Sharp SE, Shulkin BL, Gelfand MJ, Salisbury S, Furman WL. 123I-MIBG scintigraphy and 18F-FDG PET in neuroblastoma. *J Nucl Med.* 2009;50:1237-43.
- Shore RM. Positron emission tomography/computed tomography (PET/CT) in children. *Pediatr Ann.* 2008;37:404-12.
- Bayer M, Kuci Z, Schomig E et al. Uptake of mIBG and catecholamines in noradrenaline- and organic cation transporter-expressing cells: potential use of corticosterone for a preferred uptake in neuroblastoma- and pheochromocytoma cells. *Nucl Med Biol.* 2009;36:287-94.
- Timmers HJ, Chen CC, Carrasquillo JA et al. Comparison of 18F-Fluoro-L-DOPA, 18F-Fluoro-Deoxyglucose, and 18F-Fluorodopamine PET and 123I-MIBG Scintigraphy in the Localization of Pheochromocytoma and Paraganglioma. *J Clin Endocrinol Metab.* 2009.
- Orlefors H, Sundin A, Garske U et al. Whole-body (11)C-5-hydroxytryptophan positron emission tomography as a universal imaging technique for neuroendocrine tumours: comparison with somatostatin receptor scintigraphy and computed tomography. *J Clin Endocrinol Metab.* 2005;90:3392-400.