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The SNM will periodically define new procedure guidelines for nuclear medicine practice to help advance the science of nuclear medicine and to improve the quality of service to patients throughout the United States. Existing procedure guidelines will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.

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THE SNM PRACTICE GUIDELINE FOR $^{123}$I-FP-CIT SPECT 1.0

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the Society of Nuclear Medicine (SNM) cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology subsequent to publication of the guidelines.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.
I. INTRODUCTION

\(^{123}\)I-Fluoropropyl-2-beta-carbomethoxy-3-beta(4-iodophenyl) nortropane (FP-CIT) is a molecular imaging agent used to demonstrate the location and concentration of dopamine transporters in the synapses of striatal dopaminergic neurons. This agent has shown efficacy for detection of the degeneration of the dopaminergic nigrostriatal pathway, allowing better separation of patients with essential tremor (ET) from those with presynaptic Parkinsonian syndromes (PS), as well as differentiating between some causes of parkinsonism.

PS is a group of diseases that share similar cardinal signs of parkinsonism, characterized by bradykinesia, rigidity, tremor at rest, and postural instability. While the neurodegenerative condition Parkinson’s disease (PD) is the most common cause of parkinsonism, numerous other etiologies can lead to a similar set of symptoms, including: multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), drug-induced parkinsonism (DIP), vascular parkinsonism (VP) and psychogenic parkinsonism (PP). The tremor with ET typically occurs during voluntary movement rather than at rest; however, some patients with ET can demonstrate resting tremor, rigidity, or other isolated parkinsonian features, mimicking other etiologies. Clinical diagnosis of parkinsonism is often straightforward, obviating the need for additional tests in many cases. However when faced with incomplete syndromes, or overlap between multiple concurrent conditions, particularly early on, an improvement in diagnostic accuracy may be possible using a test for dopamine transporter (DaT) visualization. (1-3)

The dopaminergic neurotransmitter system plays a vital role in parkinsonism. The nigrostriatal dopaminergic pathway can be analyzed at the striatal level where the nigrostriatal neurons end and connect to the postsynaptic neurons using dopamine as the neurotransmitter. Dopamine is produced in the presynaptic nerve terminals and transported into vesicles by the vesicular monoamine transporter 2 (VMAT-2, an integral membrane protein that transports neurotransmitters such as dopamine from the cytosol into vesicles). Upon excitation, the dopamine from these vesicles is released into the synapse and binds to the predominantly postsynaptic dopamine receptors. On the presynaptic side, the dopamine transporters move dopamine out of the synaptic cleft and back into the nigrostriatal nerve terminals for either storage or degradation (figure 1).

Imaging the integrity of the nigrostriatal dopaminergic system can improve the accuracy of diagnosing movement disorders. The DaT concentrations are lower in presynaptic PS, which includes PD, MSA and PSP, and are also lower in dementia with Lewy bodies (DLB). In these cases, the decrease in DaT density is probably even greater than the decrease in intact synapses, due to compensatory down-regulation of DaT in an attempt to increase synaptic dopamine concentration. Conversely, the DaT concentrations will generally be normal in parkinsonism without presynaptic...
dopaminergic loss, which includes ET, DIP and PP. And in contrast to DLB, DaT concentrations are usually normal in Alzheimer’s disease (AD). (3-18)

Anatomical imaging is of little help when determining the integrity of this system, but both pre- and postsynaptic levels can be targeted by PET and SPECT tracers. There are several PET tracers (e.g. $^{18}$F-DOPA for L-DOPA decarboxylase activity; $^{11}$C-DTBZ for VMAT-2) but their use is largely limited to scientific research. For SPECT, most of the tracers are cocaine analogs and target the DaT. (19, 20) In Europe two of these tracers, $^{123}$I-FP-CIT and $^{123}$I-β-CIT, have been approved and have been commercially available since 2000 and 2002 respectively. (21) In the United States, $^{123}$I-FP-CIT has been FDA approved recently at the time of this writing and has become commercially available. (22) This guideline covers the indications, technical aspects, interpretation and reporting of DaT SPECT scans with $^{123}$I-FP-CIT and considers the work of the European Association of Nuclear Medicine (EANM). (23)

II. GOALS

The purpose of this information is to assist health care professionals in performance, interpretation, and reporting the results of dopamine transporter imaging with $^{123}$I-FP-CIT SPECT.

III. DEFINITIONS

See also the SNM Guideline for General Imaging

$^{123}$I-FP-CIT is an abbreviation for $[^{123}\text{I}]\text{N-ω-fluoropropyl-2β-carbomethoxy-3β-(4 iodophenyl)nortropane}$, generic name $^{123}$I-oflupane.

DaT: dopamine transporter, a transmembrane protein in the presynaptic membrane of the dopaminergic synapse that transports dopamine from the synaptic cleft back into the presynaptic neuron.

DaT SPECT with $^{123}$I-FP-CIT is a radionuclide imaging study that evaluates the integrity of nigrostriatal dopaminergic synapses by visualizing the presynaptic dopamine transporters (DaTs). (4, 6, 9, 19, 20)

PS: Parkinsonian syndromes
PD: Parkinson’s disease
MSA: multiple system atrophy
CBD: corticobasal degeneration
DIP: drug-induced parkinsonism
PP: psychogenic parkinsonism
ET: essential tremor
AD: Alzheimer’s dementia
DLB: dementia with Lewy bodies
IV. COMMON CLINICAL INDICATIONS

Indications for $^{123}$I-FP-CIT SPECT include, but are not limited to the following:

1. Main indication:
   Striatal DaT visualization in the evaluation of adult patients with suspected PS. In these patients, this test may be used to help differentiate ET from tremor due to presynaptic PS, which includes PD, MSA and PSP. However, the pattern of $^{123}$I-FP-CIT uptake cannot discriminate between these latter disorders with any high degree of accuracy. (5-9, 22)

2. Other indications:
   a. Early diagnosis of presynaptic PS. (12, 13)
   b. Differentiation of presynaptic PS from parkinsonism without presynaptic dopaminergic loss, such as DIP or PP. (14, 15)
   c. Differentiation of DLB from AD. (16, 17)

3. Contraindications:
   a. Pregnancy.
   b. Inability to cooperate with SPECT or SPECT/CT brain imaging.
   c. A known hypersensitivity to the active substance or to any of its excipients. An iodine allergy is, however, not a contraindication to receiving this tracer.

4. Relative contraindication:
   Breastfeeding; it is not known if $^{123}$I-FP-CIT is excreted into human milk. For caution, if the test remains indicated, nursing women may consider pumping and discarding breast milk for at least 1 day, and perhaps up to 6 days after tracer administration. (22, 23)

V. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See SNM Guideline for General Imaging

VI. PROCEDURE/SPECIFICATIONS OF THE EXAMINATION

See also SNM Guideline for General Imaging

A. Request/history

The requisition should include a brief description of symptoms and the clinical question. Information should be obtained regarding:

1. Past or current drug use, head trauma, stroke, psychiatric illness, epilepsy, or tumor.

2. Neurological symptoms: kind, duration, left or right sidedness.

3. Current medications and when last taken.

4. Patient’s ability to lie still for approximately 30-45 minutes.

5. Prior brain imaging studies (e.g. CT, MRI, PET and SPECT).
B. Patient preparation and precautions

1. Pre-arrival
   a. Check for medication/drugs that may alter tracer binding, and (if possible) stop such medication for at least five half-lives.
   b. Cocaine, amphetamines and methylphenidate severely decrease $^{123}$I-FP-CIT binding to DaT. The central nervous system stimulants ephedrine and phentermine may decrease $^{123}$I-FP-CIT, particularly when used as tablets.
   c. Bupropion, Fentanyl and some anesthetics (ketamine, phencyclidine (PCP), isoflurane) may decrease $^{123}$I-FP-CIT binding to DaT.
   d. Selective serotonin reuptake inhibitors (SSRIs) may increase binding to DaT somewhat but should not interfere with visual interpretation. (24)
   e. Cholinesterase inhibitors and neuroleptics probably do not interfere significantly with $^{123}$I-FP-CIT binding to DaT. (24)
   f. Antiparkinsonian drugs (e.g. L-DOPA, dopamine agonists, MAO-B inhibitors, NMDA receptor blockers, amantadine, and COMT inhibitors in standard dosages) do not interfere with $^{123}$I-FP-CIT binding to DaT to any significant degree. (24, 25)
   g. An extensive overview of drug influences on DaT SPECT imaging can be found in the article by Booij and Kemp. (24)

2. Pre-injection
   To protect the thyroid from free $^{123}$I, administer a single dose of 400mg potassium perchlorate or a single dose of Potassium Iodide Oral Solution or Lugol’s Solution (equivalent to 100 mg iodide) at least one hour prior to the tracer injection. Avoid the use of any of these products in patients with known sensitivities. (22)

C. Radiopharmaceuticals

1. In Europe two DaT SPECT tracers labeled with $^{123}$I, have been approved, $^{123}$I-FP-CIT and $^{123}$I-β-CIT. (23) In the United States $^{123}$I-FP-CIT, is the only FDA approved DaT SPECT tracer. $^{123}$I-FP-CIT is a cocaine analog substance, and in the United States it is classified as a Schedule II controlled substance under the Controlled Substances Act. Registration with the DEA using form #222 will be required to order the tracer. Alternatively, it can be ordered electronically through the DEA’s Controlled Substance Ordering System (CSOS) system (more info at: www.deaecom.gov).

2. Appropriate physician licensure and clinic registration, in addition to secure storage, handling and destruction practices in keeping with a Schedule II compound are mandatory for $^{123}$I-FP-CIT. Failure to keep accurate records or to follow proper security controls for a controlled substance may result in DEA violations and compulsory fines.

3. $^{123}$I-FP-CIT is delivered ready for use, although the calibrated amount of activity may need to be adjusted.

4. The recommended dosage of $^{123}$I-FP-CIT is 111-185 MBq (3-5 mCi), typically 185 MBq (5 mCi).

5. The effect of renal or hepatic impairment upon $^{123}$I-FP-CIT imaging has not been established. It is excreted by the kidney, so patients with severe renal
impairment may have increased radiation exposure and altered $^{123}$I-FP CIT images.

6. $^{123}$I-FP-CIT is not indicated for use in children. The safety and efficacy of $^{123}$I-FP-CIT have not been established in pediatric patients.

7. $^{123}$I-FP-CIT should be administered as a slow intravenous injection (over approximately 20 seconds), followed by saline flush.

8. Hypersensitivity and injection site reactions have been reported. In clinical trials, the most common adverse reactions were headache, nausea, vertigo, dry mouth or dizziness, and occurred in less than 1% of subjects.

9. It would be reasonable to instruct the patient to increase hydration within reasonable limits and to void frequently for 48 hours following tracer administration to reduce the radiation dose. (22, 23)

D. Protocol/Image acquisition

1. Timing
   a. SPECT imaging should be started when striatal and occipital $^{123}$I-FP-CIT binding is stable, between 3 and 6 hours after injection of the radiotracer. (12, 27)
   b. It is recommended that each center use a fixed time interval between tracer injection and image acquisition to optimize reproducibility and to limit inter- and intrasubject variability. Patients do not have to be kept in a dim or quiet environment.

2. Positioning
   a. Patients should be encouraged to void prior to scanning to avoid disturbance during image acquisition.
   b. Patients should be instructed to remain still during SPECT acquisition.
   c. Position the patient lying supine, with head centered and straight as much as possible.
   d. Although proper alignment with no head tilt would be preferable, patient comfort is more important than the actual orientation of the head, as long as the striatum and occipital cortex are in the field of view. If necessary, images can be re-oriented after acquisition.
   e. An off-the-table headrest or a flexible head restraint such as a strip of tape across the chin or forehead may be used to minimize movement.
   f. Patients who prefer to lie with the knees slightly bent may need supporting cushions. Binding the shoulders (e.g. with a sheet) may also help to prevent movement as well as to reduce the orbital radius of the camera heads.
   g. If a patient is not able to remain still, and if the referring physician and patient’s legal representative agreed, sedation with short acting benzodiazepines could be used (and would not affect scan quality). If sedation is used and the patient travelled to the clinic by car, there should be an accompanying person to drive the patient home. (22, 23)

3. Image acquisition
   a. Field of view: should include the entire brain.
   b. Rotational radius: it is stressed that the smallest possible radius should be used. The typical radius is 11-15 cm.
c. Energy window: photopeak should be set to 159 keV ± 10%. Additional energy windows may be used for scatter correction purposes.

d. Matrix: 128x128 is recommended.

e. Experimental studies with a striatal phantom suggest that optimal images are obtained with matrix size and zoom factors selected to give a pixel size of 3.5 to 4.5 mm. Slices should be 1 pixel thick.

f. Detector movement: step-and-shoot with angle increments of 3 degrees is recommended. Alternatively, continuous rotation may be used. Full 360 degree coverage of the head is required (i.e. 180 degrees for each head of a dual head camera). The number of seconds per position depends on the sensitivity of the system, but usually 30-40s is required.

g. Segmentation of the data is not necessary but may allow for correction of some types of motion artifacts.

h. Total counts: Collect a minimum of 1.5 million counts for optimal images.

i. Acquisition time: varies with the specifications of the camera. It often is in the range of 30-45 minutes. (22, 23)

4. Image Processing

a. Review of projection data in cine mode and sinograms is helpful for an initial determination of scan quality, patient motion and artifacts. Motion correction algorithms, if available, may be used prior to reconstruction for minor movements but rescanning is necessary if there is substantial head motion.

b. Reconstruction method: iterative reconstruction is preferred, but filtered back-projection may be used. Reconstructed pixel size should be 3.5 to 4.5 mm with slices 1 pixel thick.

c. Filtering: a low pass filter (e.g. Butterworth) is recommended. Other types of filters can introduce artifacts, may affect the striatal binding ratio and should be used with caution. The employed filter should preserve the linearity of the count rate response.

d. Filtering includes either a two-dimensional pre-filtering of the projection data or a three-dimensional post-filtering to the reconstructed data.

e. Attenuation correction is recommended. An attenuation map can be measured from a simultaneously or sequentially acquired transmission or CT scan, or can be calculated, as with a correction matrix according to Chang. The broad-beam attenuation coefficient is typically assumed to be 0.11 cm⁻¹. Some variance may occur with fan-beam collimators. Consider verifying accuracy with an appropriate ¹²³I phantom. (28)

f. Images are reformatted into slices in 3 planes (axial, coronal, sagittal). Correct re-orientation makes visual interpretation easier and is crucial when semi-quantification is used. Transverse slices should be parallel to a standard and reproducible anatomic orientation, such as the anterior commissure-posterior commissure (AC-PC) line as used for brain MRI. This can be approximated by orientating the brain such that the inferior surface of the frontal lobe is level with the inferior surface of the occipital lobe. The canthomeatal plane, as routinely used for CT, is also acceptable. Activity in the striatum and the parotid glands, and the contours of the brain and the head can usually be seen and can be used to assist re-alignment. A simultaneously acquired CT scan will allow more precise re-alignment of the head.
5. Semi-quantification
   a. With semi-quantification, striatal binding ratios are calculated by comparing the activity in the structure of interest with the activity in a reference region (with a very low DaT concentration, usually the occipital area), using the following formula:

   \[
   \text{Striatal binding ratio} = \frac{\text{mean counts of striatal ROI} - \text{mean counts of background ROI}}{\text{mean counts of background ROI}}
   \]

   Alternatively volumes of interest can be used (in 3D analysis).

   Semi-quantification techniques roughly fall into four categories: the classic manual regions of interest (ROIs), manual volumes of interest (VOIs), more advanced automated systems using VOIs, and voxel-based mathematical systems. (29)

   b. The classic and most widely-used method applies ROIs manually on to one or more slices with the highest striatal activity. This is a simple method, but interobserver variability is considerable. For this method it is recommended to:
      i. Reduce interobserver variability by rigorously standardizing realignment and using predefined ROIs.
      ii. Use ROI size of at least twice the full width at half maximum (FWHM). (30)
      iii. Use the sum of at least three consecutive slices. Choose the slices with the highest activities in the target regions. Within the same center, it is recommended to be consistent with the number of slices chosen. (31)

   c. Manual VOI strategies stress accurate characterization of the putamen as the most sensitive region for distinguishing normals from PS. For sampling the putamen, consider a small VOI not encompassing the whole structure. Ensure the VOI is neither too anterior so as to avoid the caudate, nor too posterior to avoid partial volume errors. Mid-putamenal VOIs probably offer the most accurate manual results. Automated VOI systems incorporating the whole striatum using individualized VOIs, either based on the \(^{123}\)I-FP-CIT SPECT data or on a co-registered anatomical scan, produce more objective, observer-independent results, and are faster, though are not widespread. (32-35) Examples of automated systems are QuantiSPECT, NEUROTRANS 3D, EXINI DAT, and a modified version of the Brain Analysis Software (BRASS).

   d. For interpretation of both manual and automated semi-quantification:
      i. Left and right striatum should be quantified separately.
      ii. Caudate and putamen should be quantified separately.
      iii. Known anatomic lesions may influence the location of the striatal or background ROIs.

   The voxel-based systems often use Statistical Parametric Mapping (SPM) that runs on a MATLAB platform. These are widely used for scientific
purposes but seem impractical for use in routine clinical practice and will not be discussed here. (35, 36)

E. Interpretation

1. Image quality

   It is important to routinely check the quality of the acquired images before interpretation.
   a. The raw projection images should be watched in cine mode or in sinogram mode to check for movement. This may be difficult to recognize in the reconstructed SPECT slices.
   b. The alignment of the head should be checked. Misalignment may create artificial asymmetry and may lead to misinterpretation of the scan.
   c. Use of medications known to interfere with $^{123}$I-FP-CIT binding, if present, should be taken into account when interpreting the images. (See list above VI. B. pre-arrival.)

2. Visual interpretation

   Because patients usually do not become symptomatic before a substantial amount of striatal synapses have degenerated, visual evaluation of the scan is usually sufficient for clinical evaluation. Several studies show excellent results with trained readers using visual interpretation only. (5, 37, 38, 39)

Recommendations for visual interpretation:
   a. Striatal shape, extent, symmetry and intensity differentiate normal from abnormal.
   b. In transaxial images, the normal striata should look crescent or “comma” shaped and should have symmetric well-delineated borders. In an abnormal scan, the striata will have reduced intensity on one or both sides, often shrinking to a circular or oval shape.
   c. Assess the level of striatal activity in comparison to the background activity. Both the orthogonal slices and the multiple intensity projection images can be used. The head of the caudate and the putamen should have high contrast to the background in all scales and for patients of all ages.
   d. Some decrease in striatal binding, in both the caudate and putamen, occurs with normal aging, approximately 5-7% per decade. This is small in comparison to the decreases caused by disease and should not normally interfere with interpretation. (40)
   e. Look for significant asymmetry. The left and right striata should be rather symmetric in the healthy state; mild asymmetry may occur in normals. Often disease first becomes visible in the putamen contralateral to the neurological signs. (37)
   f. Compare the activity in the caudate nucleus to the activity in the putamen. The putamen is usually more severely affected than the caudate nucleus. (37)
   g. Common patterns for abnormalities emerge: for example, in PD there is usually a decrease in $^{123}$I-FP-CIT binding in the dorsal putamen contralateral to the side of the neurological symptoms, in time progressing anteriorly, and ipsilaterally, whereas atypical parkinsonian syndromes tend to be more symmetrical, and with relatively more involvement of the
caudate nucleus. However, there is too much overlap between the disease patterns to allow for adequate discrimination between PD, MSA, PSP and CBD. (5-9)

h. In essential tremor, $^{123}$I-FP-CIT binding is normal. (14, 39)

i. In drug-induced parkinsonism, $^{123}$I-FP-CIT binding is normal (unless the drugs are unmasking underlying neurodegenerative disease). (14)

j. In vascular parkinsonism, $^{123}$I-FP-CIT binding is normal or only slightly diminished, except when an infarct directly involves a striatal structure. Even then, a deficit from an infarct often gives a “punched-out” appearance, differing in morphology and quality from a typical presynaptic PS deficit. If clarification were needed, a recent MRI should be reviewed. (3, 41, 42)

k. Current evidence suggests that $^{123}$I-FP-CIT binding is normal in psychogenic parkinsonism. (7, 15)

l. $^{123}$I-FP-CIT binding differentiates between AD and DLB with a high degree of accuracy. Striatal binding is usually normal or very mildly diminished in AD, and should be significantly decreased in DLB. (16, 17)

m. Image interpretation should be performed on the computer screen rather than a hard copy since adjustment may be needed for alignment, scaling and color.

n. Scans should be analyzed in both gray scale and color. It is recommended that readers select one color scale with which to become familiar, consistent and well-versed.

o. Review of any available CT head or MRI brain may give additional information. Known anatomic lesions may alter location of shape of the striatal structures. A side-by-side read with an MRI might assist equivocal scans to exclude or estimate vascular co-morbidity.

**Examples of visual interpretation**

**Figure 1. Normal $^{123}$I-FP-CIT of a 62 year old healthy volunteer. In transaxial images, normal striatal binding is characterized by two symmetric crescent- or comma-shaped regions of activity. Excellent distinction from the surrounding brain tissue background.**
Figure 2. Abnormal $^{123}$I-FP-CIT of an 80 year old male with newly diagnosed PD. Some early cases will demonstrate an abnormality on only one side. This individual demonstrates decreases in both putamina, worse on the left side. Almost normal activity in the right caudate nucleus, mildly decreased activity in the left caudate nucleus. The overall striatal shape on the left is more circular/oval and less crescent- or comma-shaped.

Figure 3. Abnormal $^{123}$I-FP-CIT of a 79 year old male with 7 year history of PD. Very little tracer binding in the putamina as compared to background. The caudate nuclei show decreases as well, worse on the right. Striatal shape is roughly circular/oval.

Figure 4. Abnormal $^{123}$I-FP-CIT of a 76 year old female with 12 year history of PD. Essentially absent putaminal activity. Markedly decreased activity in the caudate nuclei, worse on the left. Small rounded foci are all that remain of the striatal activity.

Images and clinical information courtesy of John Seibyl, MD, Institute for Neurodegenerative Disorders, New Haven, CT.
3. Semi-quantitative analysis
   a. Good results have been reported for diagnosis based solely on semi-quantitation. (6, 37, 43) Therefore, it has been suggested that it yields more objective results and perhaps could benefit the inexperienced reader.
   However, semi-quantification in the aforementioned studies was done by experienced readers, and it has not been validated that inexperienced readers can reproduce these results. Despite the fact that semi-quantification seems straightforward, there can be considerable interobserver variation and errors in the placement of the ROIs, or in the re-orientation of the brain, that may lead to false interpretations. (31) This variability may be reduced by using automated systems analyzing volumes of interest in raw data. (29)

   Furthermore, in order to interpret the semi-quantitative data they must be compared with a suitable database of normal values, preferably age-matched. Because many details of the camera system, the acquisition protocol, and the quantification system influence semi-quantification, there is no universal cut-off value for normal vs. abnormal. (44, 45) Each site needs to establish their own normal range by scanning a population of healthy controls, or needs to calibrate their procedure with another center that has a normal database. The latter can be done by using an anthropomorphic phantom filled with different concentrations of activity. By means of this phantom the (usually linear) relationship between the measured uptake ratio and the true activity can be established. If the same is done in another center the results can be compared by calculating the true uptake ratios from the measured uptake ratios. (45)

   Results from a large European database of $^{123}$I-FP-CIT scans of healthy subjects of all ages are expected to be published soon and would be useful as a reference. A similar database may soon be available from the Parkinson’s Progression Markers Initiative.

   Overall, there is no evidence-based answer as to whether the inexperienced reader in routine clinical setting does better with visual reading alone, with semi-quantification alone, or with the combination of both. Properly performed semi-quantification, with use of an extensive cross-validated age-matched set of normal values, may aid visual diagnosis. Ideally, visual interpretation and semi-quantification would be complementary. When they yield varied results the differences should be analyzed to reach a conclusion.

   b. Potential advantages of semi-quantification:
      i. More objective measurement of striatal binding ratios.
      ii. Providing a quantitative result that correlates with loss of presynaptic dopaminergic neurons.

   c. And if a reference database of age-matched normal values is available:
      i. Possibly earlier detection of disease, by detecting very subtle changes.
      ii. Strengthening the interpretation in patients that are difficult to classify visually.
iii. Useful for research purposes and multicenter studies.

d. Limitations of semi-quantification:
i. With manual ROI based semi-quantification interobserver variability
   tends to be high, and is highest with inexperienced readers. This is
   largely caused by differences in re-alignment of the head, leading to
   artificial asymmetry or wrong placement of the reference ROI. The
   more slices are used in quantification, the better the reproducibility.
   (31)

ii. Automated 3D VOI or voxel-based systems have better reproducibility
   and are faster but may not be available. They may be hampered by the
   lack of anatomical information in the images, especially in advanced
   disease, and in patients with abnormal anatomy. The automated VOI
   placement should therefore be checked manually. (29, 32-34) Of
   course, patients with advanced deficits should not pose a diagnostic
   challenge, and automated results can be verified visually.

iii. Many factors influence quantification, e.g. camera, calibration of the
   camera, collimators, acquisition procedure, corrections (attenuation,
   scatter and partial volume effect), etc. Therefore, comparison with
   normal databases from other centers, or the use of published control
   values only yields valid results when the reference values were
   obtained with exactly the same technique or when these centers were
   cross-calibrated using a phantom. (44, 45) Age-matched controls are
   preferred for interpreting quantitative results.

   e. Advice:
      i. Visual interpretation is generally sufficient for clinical interpretation. (5,
         22, 37, 38, 39)

      ii. Semi-quantitative interpretation may aid visual interpretation, and, if
          performed rigorously, may increase diagnostic accuracy. (46)

      iii. For manual semi-quantification, employ standardized re-alignment of
          the head and use the sum of at least three consecutive slices with
          standardized ROIs of at least twice the FWHM size. Within the same
          center, choose a consistent number of slices. (31)

      iv. If available, automated 3D VOI semi-quantitation is preferred,
          especially for inexperienced readers, for higher reproducibility.
          Placement of the VOIs should be checked visually, especially in
          patients with abnormal anatomy or with very low uptake in the
          striatum.

      v. To interpret the semi-quantitative results, values of a normal reference
         population, preferably age-matched, are essential. Consider reporting
         the striatal binding ratio as a percentage of age-matched normal uptake.
         When using an external reference database the scanner, scanning
         protocol, and quantitation procedure should be calibrated with those
         used for the reference database with an anthropomorphic phantom with
         known activity concentrations. (45)

VII. DOCUMENTATION/REPORTING

See also the SNM Guideline for General Imaging
Items specific to $^{123}$I-FP-CIT SPECT that should be included in the report are:

A. History
1. State whether the patient used interfering drugs, and if so which drugs.
2. If sedation had to be performed, describe the route, dosage and timing in relation to the scan.

B. Technique
1. State the time elapsed between tracer injection and acquisition.
2. State the injected radiopharmaceutical dose.
3. State what criteria are used for the report interpretation (visual assessment, semi-quantitative analysis, comparison to normal database, etc.).

C. Diagnostic findings
1. Mention any significant scan quality limitations, such as patient motion.
2. Describe the subjective visual impression of the striatal binding as compared to background activity. Examine both the caudate nuclei and putamina for decreased activity; note which region(s), if any, appear decreased. Note any significant asymmetries; mild asymmetry may occur in normals.
3. If abnormalities are present, report the location and intensity of the area(s) of decreased activity.
4. If semi-quantitative analysis is performed, report the values and the normal range. An age-matched normal range would be preferable.
5. A comparison with any of the individual’s previous $^{123}$I-FP-CIT SPECT studies should be made, if available.
6. Correlation with any relevant anatomic changes displayed on CT or MRI or abnormal FDG PET pattern may be helpful if available.

D. Report conclusion
The conclusion should state:
1. Whether a presynaptic dopaminergic deficit is present or absent. An abnormal scan indicates a presynaptic striatal dopaminergic deficit, which is consistent with a variety of diagnoses, including: PD, PSP, MSA and DLB. A normal scan could suggest: ET, DIP, PP, AD or a state of health.
2. For the properly selected patient within the approved indication in the US, an abnormal scan would be consistent with tremor due to presynaptic PS rather than ET.
3. To aid the referring clinician, descriptors such as “mild”, “moderate” or “severe” can be used to characterize any deficits.
4. When appropriate, follow-up or additional studies (FDG PET, perfusion SPECT, MRI, or cardiac $^{123}$I-MIBG) can be recommended to clarify or confirm the suspected diagnosis. Postsynaptic D2 receptor SPECT or PET may be helpful for the differential diagnosis of PS, but may have to be performed within an IRB-approved clinical trial.

VIII. EQUIPMENT SPECIFICATION
Multi-detector SPECT gamma camera is advised for image acquisition. A single detector camera may provide less than optimal resolution. (32) Low Energy High Resolution (LEHR) or Low Energy Ultra High Resolution (LEUHR) parallel-hole
Collimators are most commonly used for brain imaging, and provide acceptable images of diagnostic quality. Medium energy collimators or all-purpose collimators are less suitable. Dedicated brain SPECT systems, collimator sets specifically adapted to the characteristics of $^{123}$I, or fan-beam collimators may be preferred if available. For extrinsic uniformity calibrations, the use of an $^{123}$I flood source may be more rigorous than $^{99m}$Tc or $^{57}$Co flood sources.

**IX. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS**

See SNM Guideline for General Imaging

**X. RADIATION SAFETY IN IMAGING**

See also the SNM Guideline for General Imaging

Radiation Dosimetry in Adults

<table>
<thead>
<tr>
<th>Administered Activity MBq (mCi)</th>
<th>Organ receiving the largest radiation dose mGy/MBq (rad/mCi)</th>
<th>Effective dose mSv/MBq (rem/mCi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>111-185 (3-5)</td>
<td>Urinary bladder wall: 0.054 (0.20)</td>
<td>0.021-0.024 (0.078-0.09)</td>
</tr>
<tr>
<td>Typical dose: 185 (5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Effective Dose resulting from $^{123}$I-FP-CIT administration with an administered activity of 185 MBq (5 mCi) is 3.89 - 4.44 mSv in an adult.

[Table adapted from sources 22, 23, 47]

**XI. ACKNOWLEDGEMENTS**

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XI. BOARD OF DIRECTORS APPROVAL DATES

Version 1.0