

ACR–ACNM–SNMMI PRACTICE PARAMETER FOR THE PERFORMANCE OF DOPAMINE TRANSPORTER (DaT) SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) IMAGING FOR MOVEMENT DISORDERS

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PREAMBLE

This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care¹. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents 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 practitioner considering all the circumstances presented. Thus, an approach that differs from the guidance in this document, 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 this document when, in the reasonable judgment of the practitioner, such course of action is indicated by variables such as the condition of the patient, limitations of available resources, or advances in knowledge or technology after publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document may consider documenting in the patient record information sufficient to explain the approach taken.

The practice of medicine involves the science, and 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 the guidance in this document 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 purpose of this document is to assist practitioners in achieving this objective.

¹ *Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing*, 831 N.W.2d 826 (Iowa 2013) Iowa Supreme Court refuses to find that the "ACR Technical Standard for Management of the Use of Radiation in Fluoroscopic Procedures (Revised 2008)" sets a national standard for who may perform fluoroscopic procedures in light of the standard's stated purpose that ACR standards are educational tools and not intended to establish a legal standard of care. See also, *Stanley v. McCarver*, 63 P.3d 1076 (Ariz. App. 2003) where in a concurring opinion the Court stated that "published standards or guidelines of specialty medical organizations are useful in determining the duty owed or the standard of care applicable in a given situation" even though ACR standards themselves do not establish the standard of care.

I. INTRODUCTION

This practice parameter has been developed collaboratively by the American College of Radiology (ACR), the American College of Nuclear Medicine (ACNM), and the Society of Nuclear Medicine and Molecular Imaging (SNMMI).

Application of this practice parameter should be in accordance with the [ACR–ACNM–SNMMI–SPR Practice](#)

[Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures](#) [1].

Parkinsonian syndromes (PSs) consist of a group of neurodegenerative diseases including Parkinson disease (PD), progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD), some cases of vascular PD, drug/environmental toxicity-induced PS, and dementia with Lewy bodies (DLB) [2,3]. Most patients with a PS have movement disorders such as bradykinesia or akinesia, extrapyramidal rigidity, resting tremor, and postural imbalance. PD is the second most common neurodegenerative disorder, with a prevalence in industrialized countries of 0.3% in the entire population and approximately 1% in people older than 60 years and an incidence of 8 to 18 per 100,000 person-years [2,4-6]. PS is associated with a twofold increase in the risk of death and is expected to impose an increasing social and economic burden on society as the population ages [7].

Accurate diagnosis of a PS is critical for clinical management. Until recently, the diagnosis was based mainly on clinical presentation and often proven incorrect with further clinical follow-up. Even movement disorder specialists misdiagnose PS in up to 10% of cases [8,9]. Misdiagnosis can result in either a lack of effective treatment, leading to unnecessary disability, or inappropriate treatment and procedures that may expose patients to potential side effects [10]. An important diagnostic dilemma is the differentiation of PS and non-neurodegenerative disorders such as essential tremor (ET), psychogenic parkinsonism, or drug-induced parkinsonism, due to the overlap of clinical symptoms [11]. The management approach to these conditions is distinctly different. In ET, there may be asymmetry, rest tremor, cogwheeling, or subtle parkinsonian signs that are particularly common in the elderly [7,12,13]. In a study of 502 patients with presumed PD [14], 103 (26%) were found not to have a neurodegenerative PS, whereas 50 of the 103 patients (29%) met criteria for ET. Therefore, there is a need for a more accurate test that supports accurate clinical diagnosis in these patients to ensure appropriate management.

Although the exact pathological mechanism of neurodegenerative PSs is largely unknown, an important feature of these diseases is the progressive loss of dopaminergic neurons in the nigrostriatal pathway. The dopamine transporter (DaT) is expressed exclusively on the presynaptic terminals of dopaminergic neurons and is responsible for the reuptake of dopamine from the synaptic cleft [15]. DaT plays a critical role in the maintenance of the presynaptic neuron. In neurodegenerative PS, there is progressive degeneration of the presynaptic terminals, resulting in reduction of DaT. In non-neurodegenerative disorders, such as ET, there is no nigrostriatal DaT loss.

A radioiodinated cocaine analogue, iodine-123 ioflupane, or iodine-123 FP-CIT (N-[omega]-fluoropropyl-1-2[beta]-carbomethoxy-3[beta] [4-iodophenyl] nortropane), binds with high affinity to presynaptic DaT in the striatum (caudate nucleus and putamen) [16]. Iodine-123 ioflupane was developed for single-photon emission computed tomography (SPECT) imaging to visualize the distribution and density of DaT in the striatum. Therefore, iodine-123 ioflupane SPECT imaging can be used for the objective confirmation of nigrostriatal pathway degeneration and to distinguish neurodegenerative PSs from non-neurodegenerative disorders with suspicious clinical symptoms as described above [11,17]. In addition, iodine-123 ioflupane SPECT is valuable to differentiate between Alzheimer disease (AD) and DLB, with normal uptake in AD and decreased DaT uptake in DLB, although this indication is not yet approved by the FDA.

Iodine-123 ioflupane was approved by the US Food and Drug Administration (FDA) in 2011 for striatal DaT visualization using SPECT brain imaging to assist in the evaluation of adult patients with suspected PS. Although this radiopharmaceutical is an adjunct to other diagnostic tools, it was not designed to distinguish among PD, MSA, and PSP. The effectiveness of the DaT scan as a screening test and for monitoring disease progression or response to therapy has not been established [18,19]. Abnormal iodine-123 ioflupane SPECT scans demonstrate decreased striatal uptake, specifically involving at least the putamen, often asymmetric, which suggests a diagnosis of a neurodegenerative PS. A normal scan suggests ET or a nondegenerative parkinsonism [2,20,21].

II. INDICATIONS AND CONTRAINDICATIONS

A. Clinical indications for DaT SPECT imaging include, but are not limited to:

1. Differentiating a neurodegenerative PS from a non-neurodegenerative disorder such as ET
2. Differentiating a neurodegenerative PS from neuroleptic or other drug-induced parkinsonism
3. Differentiating a neurodegenerative PS from psychogenic tremors
4. Differentiating DLB or Parkinson Disease Dementia (PDD) from AD in patients with dementia
5. Identifying early neurodegenerative PS in patients with nonmotor symptoms, including REM sleep

behavior disorder and autonomic dysfunction among others [22-24]

B. Contraindications

Pregnancy and known allergy to iodine-123 ioflupane are contraindications. Breastfeeding is a relative contraindication as it is not known whether iodine-123 ioflupane is excreted in breast milk. Patients should cease or interrupt nursing and should pump and discard the milk for 6 days after iodine-123 ioflupane administration [18,25].

For information on radiation risks to the fetus, see the [ACR–SPR Practice Parameter for Imaging Pregnant or Potentially Pregnant Patients with Ionizing Radiation](#) [26].

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A. Physician

Iodine-123 ioflupane SPECT examinations of the brain should be performed under the supervision of and interpreted by a physician who meets qualifications outlined in the [ACR–ACNM–SNMMI–SPR Practice Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures](#) [1].

Continuing Education and Experience

For continuing education and experience, please see the [ACR–ACNM–SNMMI–SPR Practice Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures](#) [1] and the [ACR Practice Parameter for Continuing Medical Education \(CME\)](#) [27].

B. Qualified Medical Physicist

For Qualified Medical Physicist qualifications, see the [ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of SPECT-CT Equipment](#) [28].

C. Radiologic and Nuclear Medicine Technologist

See the [ACR Practice Parameter for Performing and Interpreting Diagnostic Computed Tomography \(CT\)](#) [29] and the [ACR–ACNM–SNMMI–SPR Practice Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures](#) [1].

D. Radiation Safety Officer

The radiation safety officer must meet applicable requirements of the Nuclear Regulatory Commission (NRC) for training as specified in 10 CFR 35.50 or equivalent state regulations.

IV. SPECIFICATIONS OF THE EXAMINATION

The written or electronic request for a DaT SPECT imaging should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance and interpretation.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). Additional information regarding the specific reason for the examination or a provisional diagnosis would be helpful and may at times be needed to allow for the proper performance and interpretation of the examination.

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state's scope of practice requirements. (ACR Resolution 35 adopted in 2006 – revised in 2016, Resolution 12-b)

A. Nuclear Medicine Examination Request

Relevant patient data should be obtained for optimal interpretation of the examination. The data should include patient history, including the results of recent imaging examinations (eg, CT or MRI) and current medications/drugs, including when last taken.

B. Radiopharmaceutical

Iodine-123 ioflupane is the nonproprietary name for N-v-fluoropropyl-2b-carbomethoxy-3b-(4-123 I-iodophenyl) nortropane (123I-FP-CIT). Iodine-123 ioflupane binds with high affinity to striatal presynaptic DaT. DaT is a sodium chloride-dependent transmembrane transport protein on the presynaptic dopaminergic nerve terminals.

The recommended dosage of iodine-123 ioflupane is 111 to 185 MBq (3-5 mCi). It should be administered as a slow intravenous injection (over approximately 20 seconds), followed by a saline flush. The most common adverse reactions are headache, nausea, vertigo, dry mouth, and dizziness and have been observed in fewer than 1% of patients.

C. Patient Preparation

1. Prearrival

Patients should be instructed by the referring provider to stop any medications or drugs (if possible) that might interfere with the binding mechanism of the radiopharmaceutical for at least 5 half-lives of the medication or drug [30,31].

Drugs that may decrease striatal iodine-123 ioflupane binding:

- Opioid: fentanyl
- Eugeroic: modafinil
- Antidepressants: bupropion, mazindol, radafaxine [32]
- Anticholinergic: benztropine
- Amphetamines: d-amphetamine, methamphetamine, methylphenidate
- Anesthetics: isoflurane, ketamine, phencyclidine (PCP) (the latter 2 are of interest particularly for animal SPECT studies, although ketamine and PCP may be used illicitly)
- Central nervous system (CNS) stimulants: cocaine, ephedrine, phentermine

Drugs that may increase striatal iodine-123 ioflupane binding:

- Adrenergic agonists: norepinephrine, phenylephrine
- Antidepressants: venlafaxine, paroxetine [33]

Drugs that do not increase or decrease striatal iodine-123 ioflupane binding and do not need to be stopped:

- Antiparkinsonian medication: levodopa (L-DOPA) (however, it is possible that chronic use of L-DOPA will downregulate the expression of DaT) [34]
- Dopamine agonists
- N-methyl-d-aspartate (NMDA) receptor blockers
- Monoamine oxidase type B (MAO-B) inhibitors
- Catechol-o-methyl transferase (COMT) inhibitors

2. Preinjection

- a. Evaluate the patient for the ability to cooperate.
- b. To minimize the uptake of free iodine-123 by the thyroid gland (expecting cases of prior thyroidectomy), administer a single dose of potassium iodide solution (SSKI) or Lugol solution (equivalent to 100 mg iodide) or potassium perchlorate (4600 mg) at least 1 hour before radiopharmaceutical injection (<http://us.datascan.com/staging/wp-content/uploads/2014/06/prescribing-information.pdf>).
- c. To minimize bladder radiation exposure, encourage patients to be well hydrated prior to and for 48 hours after the examination.

D. Image Acquisition

1. Timing

- a. SPECT imaging should be performed 3 to 6 hours following the intravenous administration of iodine-123 ioflupane.

2. Patient Positioning

- a. Place the patient's head in an off the table head holder, which is positioned in the center of

- the detector's field-of-view.
- b. Inform the patient of the importance of remaining still throughout the scan [35].
- c. A head holder minimizes motion artifacts and may help with more optimal positioning if used properly [36]
- 3. Image Protocol
 - a. Camera: Dual- or triple-detector gamma cameras are recommended.
 - b. Collimators: Low-energy high-resolution (LEHR) collimator centered on 159 keV with a $\pm 10\%$ energy window or per manufacturer's recommendations
 - c. Flexible head restraints with off-the-table headrest
 - d. Use a circular orbit (360° rotation) with the smallest possible radius (typically 11-15 cm).
 - e. Suggested matrix size is 128×128 with a zoom of 3.5 to 4.5 mm.
 - f. Step-and-shoot acquisition mode is preferred. However, continuous mode can also be used.
 - g. Collect a minimum of 1.5 million counts.
 - h. Duration of the scan depends on the camera and the imaging technique used. Imaging typically requires 30 to 45 minutes.

E. Data Processing

1. Reconstruction

Iterative reconstruction using ordered-subset expectation maximization (OSEM) with 4 iterations with 8 subsets is recommended over filtered backprojection (FBP). OSEM demonstrates reliable quantification of DaT binding [37]. Software motion correction is not recommended. It is better to reimage after repositioning the patient to improve comfort and reduce the likelihood of motion.
2. Filtering
 - a. 2-D prefiltering should be applied prior to reconstruction or 3-D postfiltering to reconstructed images.
 - b. A low-pass filter such as a Butterworth filter is recommended, as it provides the most acceptable balance between noise and smoothing compared to other filters such as Hanning and Hamming [38]. Resolution recovery may create artifacts and is not recommended [39].
3. Attenuation

Attenuation correction has a significant effect on quantitative analysis, but not for visual interpretation, which is the FDA-approved method [40]. The use of attenuation correction is recommended, either through low-dose CT or through software using linear or a zeroth-order algorithm (such as Chang's). If software attenuation correction is applied, the attenuation correction coefficient may be determined using phantoms. Alternatively, the normal value of 0.11 cm^{-1} can be used [40,41].
4. Quantification [42,43]

Semiquantitative method uses the ratios of a region of interest (ROI) of highly binding DaT structures (striatum) compared with regions of low-binding DaT structures (occipital lobe) using the following formula: Specific binding ratio = [mean counts of striatal ROI - mean counts of occipital ROI]/mean counts of occipital ROI, which is algebraically equivalent to [mean counts of striatal ROI/mean counts of occipital ROI] - 1. This ratio represents an estimate of the binding potential. However, ROI determination may be achieved by a variety of methods to calculate different volumes of interest (VOI) [43-45].

 - a. Manual ROIs: Manual drawing of ROI around the striatum and occipital lobe to define areas of high and low DaT bindings. To minimize inter- and intraobserver variability, the use of ROI templates is suggested.
 - b. Semimanual: ROIs are drawn using coregistered anatomical imaging templates, such as CT, MRI, or normal functional SPECT, or PET brain imaging templates. Alternatively, ROI templates may be used based on normal anatomical templates.
 - c. Semiautomated and automated systems: Software packages offer different reconstructions and attenuation corrections with auto-quantification that are based on different mathematical algorithms to calculate VOI. Some software uses MRI and normal DaT scan maps for ROI templates.

F. Image Interpretation

1. Qualitative

- a. Allows the determination of whether there is imaging evidence of nigrostriatal neurodegeneration (abnormal scan) or a lack of evidence for nigrostriatal neurodegeneration (normal scan).
- b. Images should be reviewed on a computer screen. Automated brain analysis software packages provide a comprehensive platform for image review, including reorientation of the brain in a standard, consistent position for proper interpretation.
- c. Examinations should be interpreted only with knowledge of the clinical data such as the patient's age, sex, and results of correlative morphological examinations such as MRI and CT scans. Image interpretation should be performed after confirmation that the image quality is adequate. Interpretation is done in softcopy with a software platform that allows review in grayscale and color scales, including a "cool" color scale that facilitates qualitative interpretation. Level of contrast and background subtraction should be used with the knowledge of the specific reconstruction software used and the scale-normal database. Inappropriate color map or scaling may result in incorrect interpretation of the examination.
- d. Unprocessed projection images should be reviewed in a cinematic display to assess for the presence and degree of patient motion, target-to-background ratio, and potential artifacts. Specific attention should be given to maintaining straight head positioning, as head tilt or head movement may result in artifactual appearance of striatal asymmetry [35,36]. Technologists should constantly monitor the patients for motion, which can be more reliable than the cinematic display, particularly for rotation motion.

2. Quantitative

- a. Quantitative analysis and comparison with a normal database should be performed on images created using the recommended reconstruction algorithms (additional details in section IV.E.4).
- b. Primary interpretation is a qualitative review of the images, but this may be supported by quantification. Several software platforms support quantification, but it is important to recognize that multiple medications and drugs affect quantification [46]. Quantification may be most useful when qualitative interpretation is inconclusive [47], FDA-approved quantitative analysis software must be used.
- c. At its simplest, quantification software may document differences between left and right basal ganglia and anterior-posterior gradients. Comparison against a database of normal patients adds another level of sophistication, but it may introduce errors if the patient does not match the demographics used to create the database. An important feature of quantitative software programs displays the results for a given patient as a quantitative value, which can be compared with the normal patient dataset, thereby allowing statistical comparison as is performed in bone densitometry (DXA).
- d. The use of quantification for monitoring response to therapy or tracking disease progression remains a subject of research and is not recommended at this time [19,43].

V. DOCUMENTATION

Reporting should be in accordance with the [ACR Practice Parameter for Communication of Diagnostic Imaging Findings](#) [48].

The report should include the radiopharmaceutical, administered activity, and route of administration, as well as any other pharmaceuticals administered, also with dosage and route of administration.

VI. EQUIPMENT SPECIFICATIONS

A. Hardware

1. Imaging may be done with SPECT or SPECT/CT equipment that supports the imaging protocol (IV.D.3).

1. The equipment must also support reconstruction using either FBP or iterative reconstruction algorithms with appropriate filters. Iterative reconstruction algorithms such as OSEM are preferred because they may result in improved image quality [37].

If SPECT/CT is performed, all additional relevant quality control procedures should be used. It is important to be aware that misregistration can cause attenuation correction artifacts.

Equipment performance monitoring should be in accordance with the [ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of SPECT-CT Equipment](#) [28].

VII. RADIATION SAFETY IN IMAGING

Radiologists, medical physicists, non-physician radiology providers, radiologic technologists, and all supervising physicians have a responsibility for safety in the workplace by keeping radiation exposure to staff, and to society as a whole, "as low as reasonably achievable" (ALARA) and to assure that radiation doses to individual patients are appropriate, taking into account the possible risk from radiation exposure and the diagnostic image quality necessary to achieve the clinical objective. All personnel who work with ionizing radiation must understand the key principles of occupational and public radiation protection (justification, optimization of protection, application of dose constraints and limits) and the principles of proper management of radiation dose to patients (justification, optimization including the use of dose reference levels). https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1775_web.pdf

Facilities and their responsible staff should consult with the radiation safety officer to ensure that there are policies and procedures for the safe handling and administration of radiopharmaceuticals in accordance with ALARA principles. These policies and procedures must comply with all applicable radiation safety regulations and conditions of licensure imposed by the Nuclear Regulatory Commission (NRC) and by applicable state, local, or other relevant regulatory agencies and accrediting bodies, as appropriate. Quantities of radiopharmaceuticals should be tailored to the individual patient by prescription or protocol, using body habitus or other customized method when such guidance is available.

Nationally developed guidelines, such as the [ACR's Appropriateness Criteria](#)®, should be used to help choose the most appropriate imaging procedures to prevent unnecessary radiation exposure.

Additional information regarding patient radiation safety in imaging is available from the following websites – Image Gently® for children (www.imagegently.org) and Image Wisely® for adults (www.imagewisely.org). These advocacy and awareness campaigns provide free educational materials for all stakeholders involved in imaging (patients, technologists, referring providers, medical physicists, and radiologists).

Radiation exposures or other dose indices should be periodically measured by a Qualified Medical Physicist in accordance with the applicable ACR Technical Standards. Monitoring or regular review of dose indices from patient imaging should be performed by comparing the facility's dose information with national benchmarks, such as the ACR Dose Index Registry and relevant publications relying on its data, applicable ACR Practice Parameters, NCRP Report No. 172, Reference Levels and Achievable Doses in Medical and Dental Imaging: Recommendations for the United States or the Conference of Radiation Control Program Director's National Evaluation of X-ray Trends; 2006, 2009, amended 2013, revised 2023 (Res. 2d).

VIII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education appearing under the heading *Position Statement on Quality Control & Improvement, Safety, Infection Control, and Patient Education* on the ACR website (<https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Quality-Control-and-Improvement>).

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