J of Nuclear Medicine Technology, first published online December 24, 2020 as doi:10.2967/jnmt.120.258491

Pitfalls and Artifacts of DaTscan Imaging in Parkinsonian Syndromes

A quality improvement teaching tool

Cristiane A. Tuma Santos[1], M.D., M.Sc.

William David Wallace[1], MD

Sanghun Kim[1], MD

Vani Vijayakumar[1]. M.D.

[1]Department of Radiology, Nuclear Medicine Division, University of Mississippi Medical Center,

Jackson, MS 39216

The authors have no conflict of interest.

Corresponding Author:

Vani Vijayakumar, MD

Professor of Nuclear Medicine

Department of Radiology

University of Mississippi Medical Center

2500 N State Street

Jackson, MS 39216

601-984-2575

vvijayakumar@umc.edu

The authors have no conflict of interest.

Abstract:

Methods: The aim of the current article is image quality improvement and a teaching tool on ^{123}I Ioflupane SPECT (DaTscan). The imaging uses the radiopharmaceutical ^{123}I Ioflupane (^{123}I–FP-CIT) to visualize the nigrostriatal pathway. Parkinson's disease and Parkinsonian syndromes are movement disorders that exhibit nigrostriatal degeneration, with a decreased Dopamine transporter level in the pathway and thus a decreased ^{123}I Ioflupane distribution. Other non-Parkinson's movement disorders, such as essential tremor, will have intact dopaminergic neurons and exhibit a normal distribution of the radiopharmaceutical throughout the striata. Parkinson's disorders are usually diagnosed clinically. However, DaTscan (GE Healthcare) can be a valuable tool when the clinical features are not sufficiently clear. Results: DaTscan image interpretation is not always straightforward. Many pitfalls, including biological factors, technical factors, medications, and various other factors, including age, race, ethnicity, body habitus, can make the interpretation challenging. Conclusion: The technologist and nuclear radiologist must identify the expected imaging findings to avoid the most common mistakes related to artifacts. Our main goal is to improve image quality by reviewing the most common pitfalls and artifacts of DaTscan that can compromise an accurate diagnosis and lead to misinterpretation.

Keywords:

Parkinson Disease, Ioflupane, SPECT, Artifacts, Striatum, Image Quality

Materials and Methods:

To accomplish an optimal image, quality review and teaching exercise of DaT scans are utilized. Parkinson's Disease and Parkinsonian syndromes' diagnosis is mainly based on clinical signs that include bradykinesia, rigidity, tremor, and postural instability *(1)*. Clinical symptoms and the evaluation of response to levodopa are usually sufficient to diagnose Parkinson's Disease. However, some patients can present with incomplete signs and an unclear clinical picture. This is particularly true in the early stages of the disease. Others may represent a mixed pattern with overlap between different concurrent conditions. Clinical diagnosis alone fails to recognize these patients fully. Conventional imaging is also not sensitive and not used to differentiate these disorders. Functional imaging with dopamine transporter analog (DaT) comes into play in these circumstances, being remarkably useful in diagnosing Parkinson's disease and other Parkinsonian syndromes with equivocal signs and symptoms and debatable responses to treatment *(2)*.

^{123}I Ioflupane is a radio-iodinated cocaine analog used to visualize the dopamine transporters in the presynaptic membrane. A decreased amount of DaT in the dopaminergic nigrostriatal pathway is seen with presynaptic Parkinsonian syndromes. Patients with essential tremor have an intact nigrostriatal pathway. As a result, the DaTscan can differentiate a patient with essential tremor from a patient with presynaptic Parkinson Syndrome, as evidenced by nigrostriatal pathway degeneration*(3)*. DaTscan can also help differentiate Alzheimer's disease (AD) and Lewy Body Dementia, with normal uptake in AD and decreased uptake in Lewy Body Dementia. DaTscan image interpretation, however, is not always straightforward. Many pitfalls that make the interpretation challenges have been identified. These pitfalls include but are not limited to technical artifacts and interference of certain medications and several other human and patient factors. This article reviews the most common artifacts related to ^{123}I Ioflupane SPECT imaging and how it will affect the quality of imaging and interpretation.

Results:

Image quality depends on several factors, which are described in detail below.

Technical Artifacts

Strict adhesion to imaging protocol is fundamental to avoid technical errors. DaT-SPECT imaging should be performed with the energy window (10%) centered on 159 keV, with a dual-headed camera, an image head with an 11–15–cm radius, low energy high resolution/low energy ultra-high-resolution parallel hole or fan-beam collimators, full 360° sampling, 120 projections total, 128/128 matrix. It is essential to block the thyroid gland with potassium iodide (Lugol solution) using approximately 100 mg of iodine or 400 mg of potassium perchlorate. After administration of 3–5 mCi (111-185 MBq) ^{123}I IFP-CIT intravenous injection, imaging should be acquired within 3–6 hours after injection, with a SPECT scan duration of approximately 30–45 minutes *(4)*.

Technical artifacts are again mainly related to issues during acquisition (1). These include errors from a few technologists' inabilities to follow standard practice parameters. These so-called inconsistency errors can result from a change in acquisition parameters, reconstruction parameters, use of inconsistent color scale, and change in display normalization (Table 1). These can easily be avoided by the ability to follow specific procedures with consistent adherence to standardized protocols. The Society of Nuclear Medicine practice guidelines is an invaluable resource that sets practice parameters for dopamine transporter imaging *(3).* Although the protocol is not a fixed rule, it serves as an educational tool to assist health care professionals in providing high-quality patient care. Also, the protocol can be tailored to an individual to ensure the most accurate results. The most common technical artifacts, however, are related to patient positioning *(1).* It is important to emphasize that DaTscan imaging relies on visualizing tiny anatomical structures, the caudate and putamen nuclei, known as the striatum. The caudate measures 3.4 cm^3 and the putamen 4.3 cm^3, making DaTscan images particularly susceptible to significant position and motion artifacts *(4).*

Patient preparation and position are cornerstones of optimal imaging. Improper position of the head causes the forward tilt and the well-known semicolon sign *(4).* This causes the caudate and putamen

to be seen on separate axial slices, which gives the impression that DaT activity in the putamen is decreased or absent. To avoid false interpretation of this artifact, the interpreting physician can scroll the full dataset of images to ensure there is, in fact, normal putamen activity. Confirmation with age-matched quantitative data analysis using several available software tools is helpful. Technologists should strictly follow the imaging protocol to correctly position each patient's head and not exceed the SPECT diameter to minimize the head tilt artifact on DaT scan images. Orientation artifacts can be avoided or at least minimized by proper head positioning. The correct position of each patient's head on DaTscan images is part of the quality control, which should happen before image acquisition. If the artifact is recognized after image acquisition, while the patient is still on the table, the technologist can potentially rescan the patient in a more optimal position *(4).* A head and neck holder should be utilized to ensure proper positioning. The head should rest entirely within the holder, with the vertex of the head reaching the superior edge of the holder. The identification of the canthomeatal line provides an additional aid. This imaginary line coursing from the lateral canthus, the corner of the eye, to the external auditory canal should be oriented as vertically as possible. The position of the chin should also be verified. The chin must lie in a neutral position, neither up nor down in relation to the head (Figure 1).

Lateral head tilt can give the false impression of asymmetry. The apparent lack of activity in the caudate and putamen on one side can be just a result of an incorrect head position (Figure 2).

Motion artifacts may also lead to quantification and interpretation errors. Assessment for motion should be done before the submission of images. The lateral rotation of the head can cause blurring, which gives the false impression of added activity to the ipsilateral striatum. The artifact that results from lateral head rotation during SPECT acquisition is described as the pinwheel artifact, an analogy with the rotatory motion and subsequent blurring of the pinwheel (5). The acquired images should always be checked for quality before interpretation. Movement artifacts are easier to spot in the raw projection images in cine mode than in reconstructed SPECT slices. When detected before interpretation, motion artifacts will prompt the utilization of motion-corrected algorithms or even rescanning if necessary *(3).* Another motion artifact that

can occur during image acquisition is the kissing caudate sign. This is demonstrated when the left and right caudate appear as fused anteriorly without the normal gap seen between them *(1)*.

Medication artifacts

Artifacts may result from interactions of various medications with the striatal binding of ^{123}I Ioflupane. If the medication increases the uptake, the result will be a "false-negative" mimicking a degenerative disorder. On the other hand, if the medication competing with ^{123}I Ioflupane decreases the radiotracer's uptake in the synaptic cleft, a "false-positive" result will entail. The aforementioned demonstrates the importance for every patient to be screened for medication usage before image acquisition, so drug interactions can be accounted for before rendering an examination abnormal *(1)*. Table 2 summarizes the most common effects of drugs on DaTscan results. Table 3 shows Drugs that alter DaT uptake in more than 20% need to be discontinued if clinically safe *(6)*. For example, the use of some antidepressants that increase the dopamine transporter uptake of ^{123}I Ioflupane can significantly increase the background uptake and render the exam nondiagnostic (Figure 3).

If possible, any medications or drugs that might interfere with the radiopharmaceutical's binding mechanism must be stopped for at least five half-lives *(3)*. Interestingly, dopamine products used for the treatment of Parkinsonian syndromes do not compete with ^{123}I Ioflupane. Thus, medications such as levodopa, dopamine agonists, and monoamine oxidase B inhibitors do not need to be discontinued prior to a DaTscan *(1)*.

Tumors, infarcts, trauma affect the putamen can obscure the striatum and mislead the reader to an inaccurate diagnosis of Parkinsonian Syndromes. Decreased to absent uptake in the caudate and putamen due to involvement from prior MCA territory infarct or tumor involvement of the midbrain can cause Parkinson-like symptoms, thus mimicking Parkinson's Syndrome (Figures 4 and 5). A careful review of a patient's history and available prior imaging, including CT and MRI of the head, is paramount.

Discussion:

This is a review article on image quality and as per our institutional IRB, presenting just the images performed for routine clinical purpose can be used without any approvals or waivers since this is not a research paper and no human subject exists in the research as no identifiers, or identifiable data is present.

Patient-related pitfalls: Biological Factors - Gender, Age, Body Habitus, Ethnicity, Smoking (Table1):

In clinical practice, potential factors influencing DaT density like gender, age, body habitus, ethnicity smoking, and are of importance *(7, 8)*.

Although the sensitivity and specificity of ^{123}I Ioflupane are high among all groups, potential factors influencing DaT density like age and gender must be taken into consideration, as they may impact the performance of ^{123}I Ioflupane in detecting movement disorders. According to some, the sensitivity of DaTscan was higher in males *(8)*. Females were reported as having a 16% higher Ioflupane binding than males, and a lower sensitivity of the test at earlier stages of the disease, defined as disease onset and first ten years of follow-up. The clinical symptoms are also different among the genders, with females having a milder course, which could explain differences in uptake patterns. Later in the disease, however, the sensitivity in females approximated that in males, what brings the conclusion that age also plays a significant role in ^{123}I Ioflupane binding. Another important factor to note is that dopamine transporter concentration in the striate decreases with age by up to 65%–75%, and this decrease is linear and symmetrical in both the caudate and putamen. Besides, advanced age may cause a decrease in striatum size secondary to age-related brain atrophy (Figure 6). Thus, it is crucial to evaluate CT or MR imaging concurrently *(7)*. In older subjects (> 75 years), the sensitivity of DaTscan was lower for Parkinson's Disease and higher for Lewy Body Dementia. It is not clear how relevant these differences are in clinical practice, yet those can potentially affect the diagnostic performance of DaTscan *(8)*. Finally, head circumference for SPECT imaging must be within 11-15 cm as increased circumference can cause blurring of the images in patients with increased body habitus (Fig 7).

Racial disparities in the prevalence of neurodegenerative diseases are well documented. For instance, Parkinson's Disease and Essential tremors are more common among Caucasians. However, studies comparing the accuracy of DaTscan both among Caucasians and non-Caucasians and Hispanics and non-Hispanics failed to demonstrate a statistically significant difference in DaTscan accuracy among these racial groups *(9, 10)* .

There is evidence for lower dopamine transporter availability with a moderate to large effect size but normal D2 dopamine receptor availability in smokers. These findings identify dopamine transporter abnormalities as either involved in the pathophysiology of tobacco dependence or as a biological response to long-term exposure to tobacco. Further studies are needed to determine the nature of alterations in other aspects of the dopamine system and whether there are longitudinal changes in dopamine transporter levels during the acquisition of a smoking habit *(11)* .

The interpretation of DaTscans is based mainly on visual reads. SBRquant is an automated method that measures the striatal binding ratio (SBR) in DaTscans but has yet to be optimized *(12)*. Many factors influence quantification, such as the type of camera, calibration, collimators, acquisition procedure, and corrections (attenuation, scatter, and partial-volume effect) *(3)*. Following the recently updated EANM /SNMMI guidelines and thoroughly understanding the various artifacts of SBR will improve the quality of DaTscan and [18F]fluorodopa PET imaging *(13)*.

Finally, comparing with other studies on the DaTscan artifacts(*4-6)*, our primary focus is on improving the quality of imaging, continuing education, and promoting professional development of technologists and interpreting physicians. Understanding how medications affect image quality is crucial and discussed in detail above. Referring physicians need an accurate diagnosis, particularly in clinically difficult cases. If DaTscan imaging is nondiagnostic due to artifacts and needs to be repeated, it will be unsatisfactory to all parties with unnecessary waste of time, resources and additional radiation exposure.

Conclusion

DaTscan has proved to be very useful in diagnosing Parkinsonian Syndromes when the clinical features are not sufficiently clear. However, DaTscan image interpretation can be riddled with many pitfalls, which can make the interpretation challenging. The technologist must identify the most common artifacts and pitfalls during imaging and processing to avoid the most common artifacts and unreliable results. We hope that this review is useful for the technologists who perform DaTscans to provide optimal imaging, avoiding the technical and processing errors.

An early and accurate diagnosis of neurodegenerative parkinsonian syndromes is vital in improving the patients' quality of life and overall outcomes. Clinical diagnosis can be difficult as several neurodegenerative conditions have similar presentations and anatomic changes on conventional radiologic examinations (6). That is why we believe that the interpreting physician should be aware of these imaging pitfalls and artifacts to avoid misinterpretations and render an accurate diagnosis. The study may need to be rescheduled when the patient is not adequately screened and medications are not discontinued promptly. Awareness of the above-described artifacts helps avoid misdiagnosis and most of all, prevents unnecessary treatment, reducing health care costs and decreasing the burden on the patient and family members. Also, interpreting physicians must be aware of age-related changes in striatal uptake and anatomic variations and compare them with available anatomic imaging. The ultimate goal is to avoid misinterpretation and improve the confidence level for an accurate report. The semiquantitative analysis may help in difficult to interpret cases but has yet to be optimized with different available software programs.

Acknowledgments

We would like to thank Ms. Maribeth E Borrello, CNMT for her help in posing for the picture in Figure 1.

References:

1. Banks KP, Peacock JG, Clemenshaw MN, Kuo PH. Optimizing the Diagnosis of Parkinsonian Syndromes With (123)I-Ioflupane Brain SPECT. AJR Am J Roentgenol. 2019;213(2):243-53.
2. Booth TC, Nathan M, Waldman AD, Quigley AM, Schapira AH, Buscombe J. The role of functional dopamine-transporter SPECT imaging in parkinsonian syndromes, part 1. AJNR Am J Neuroradiol. 2015;36(2):229-35.
3. Djang DS, Janssen MJ, Bohnen N, Booij J, Henderson TA, Herholz K, et al. SNM practice guideline for dopamine transporter imaging with 123I-ioflupane SPECT 1.0. J Nucl Med. 2012;53(1):154-63.
4. Covington MF, McMillan NA, Avery RJ, Kuo PH. The semicolon sign: dopamine transporter imaging artifact from head tilt. J Nucl Med Technol. 2013;41(2):105-7.
5. Janicek AK, Avery RJ, Kuo PH. The pinwheel sign: artifact from head rotation during SPECT acquisition for dopamine transporter imaging. J Nucl Med Technol. 2014;42(1):75-6.
6. Kägi G, Bhatia KP, Tolosa E. The role of DAT-SPECT in movement disorders. J Neurol Neurosurg Psychiatry. 2010;81(1):5-12.
7. Chaudhry AA, Gul M, Gupta R, Chaudhry A, Sheikh M, Peyster R. et al. Pearls and Pitfalls of DaT-SPECT Imaging in Neurodegenerative Disorders: What the Radiologists and Clinicians Need to Know. Neurographics. 2016;July/August; 6(4):219 –228.
8. Grosset DG, O'Brien JT, Ortel WH, McKeith IG, Walker Z, Tatsch K, et al. Age, gender, and diagnostic performance of Ioflupane I123 injection (DaTscan™) brain Imaging in patients with movement disorders and/or dementia". J Neurol Stroke. 2014;1(2): 42-58.
9. Ahmed A, Huang J, Chen K, Zubeldia JM, Booij J, Vijayakumar V. [(123)I]Ioflupane imaging in Caucasians and non-Caucasians: Are there any differences? J Neurol Sci. 2018;395:159-63.
10. Lundeen TF, Covington M, Krupinski EA, Avery R, Lei H, Sherman SJ, et al. Accuracy of Dopamine Transporter Imaging with (123)I-Ioflupane in Hispanic and Non-Hispanic Patients. J Nucl Med Technol. 2020;48(2):154-7.
11. Ashok AH, Mizuno Y, Howes OD. Tobacco smoking and dopaminergic function in humans: a meta-analysis of molecular imaging studies. Psychopharmacology (Berl). 2019;236(4):1119-29.
12. Tinaz S, Chow C, Kuo PH, Krupinski EA, Blumenfeld H, Louis ED, et al. Semiquantitative Analysis of Dopamine Transporter Scans in Patients With Parkinson Disease. Clin Nucl Med. 2018;43(1):e1-e7.
13. Morbelli S, Esposito G, Arbizu J, Barthel H, Boellaard R, Bohnen NI, et al. EANM practice guideline/SNMMI procedure standard for dopaminergic imaging in Parkinsonian syndromes 1.0. Eur J Nucl Med Mol Imaging. 2020;47(8):1885-912.

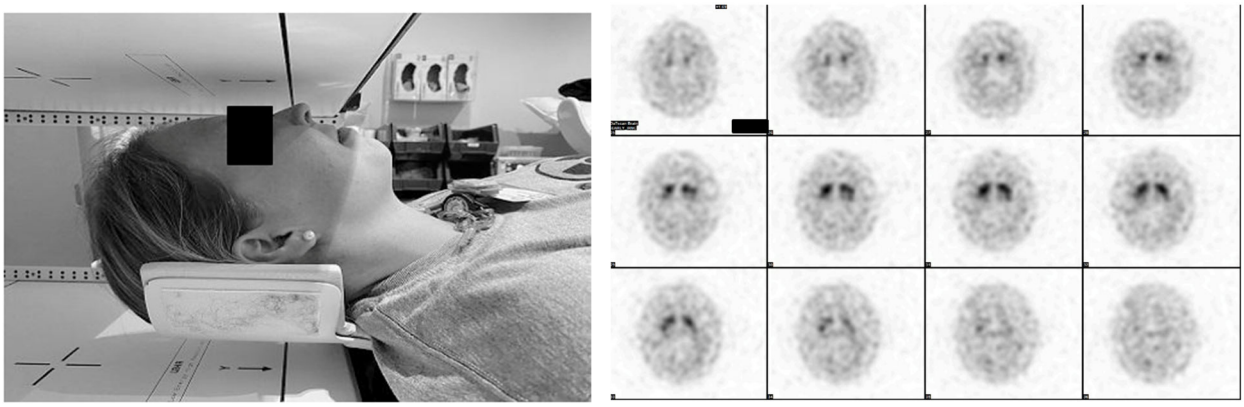

FIGURE 1. 1a. Correct position with the head resting in the head and neck holder and the chin in neutral position. 1b. Normal axial brain SPECT without head tilt.

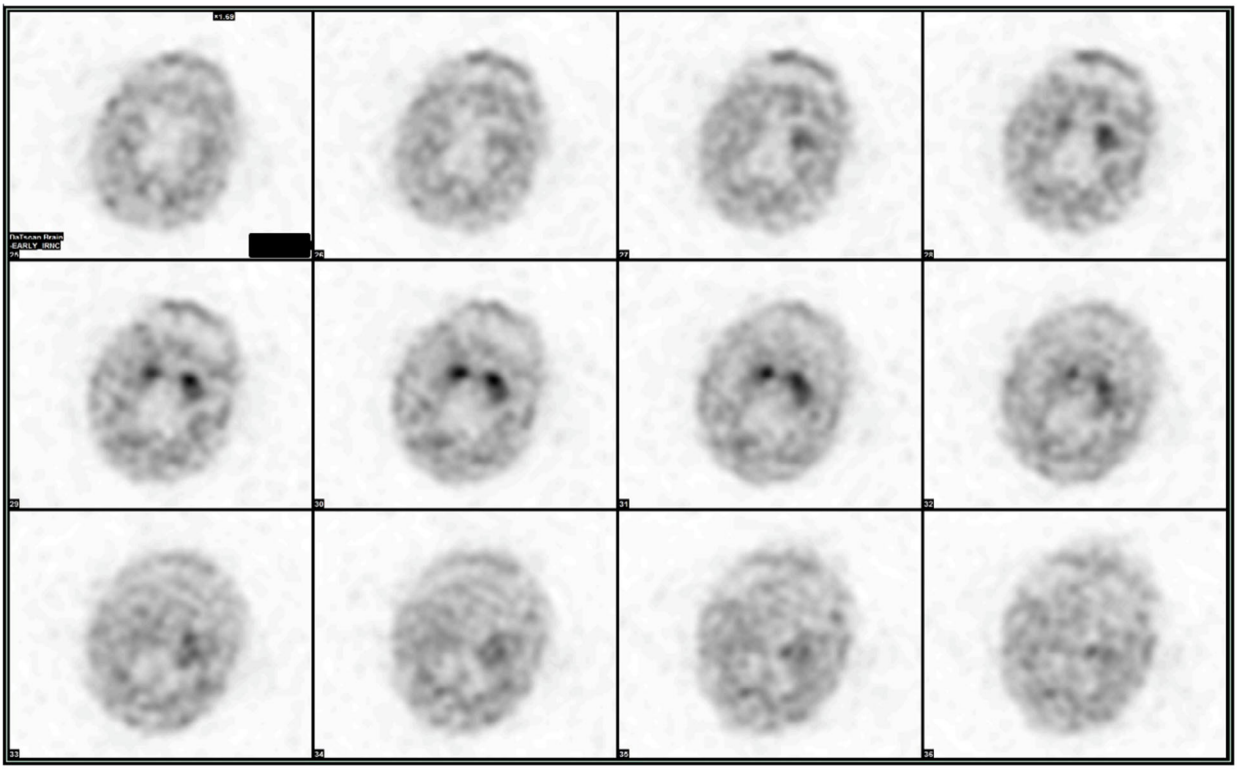

FIGURE 2. 87-year-old female with parkinsonian features, left-sided weakness, dysarthria, and generalized weakness. Axial brain SPECT showing head tilt, normal comma shape on the left, decreased uptake in the right putamen, and dilated ventricles.

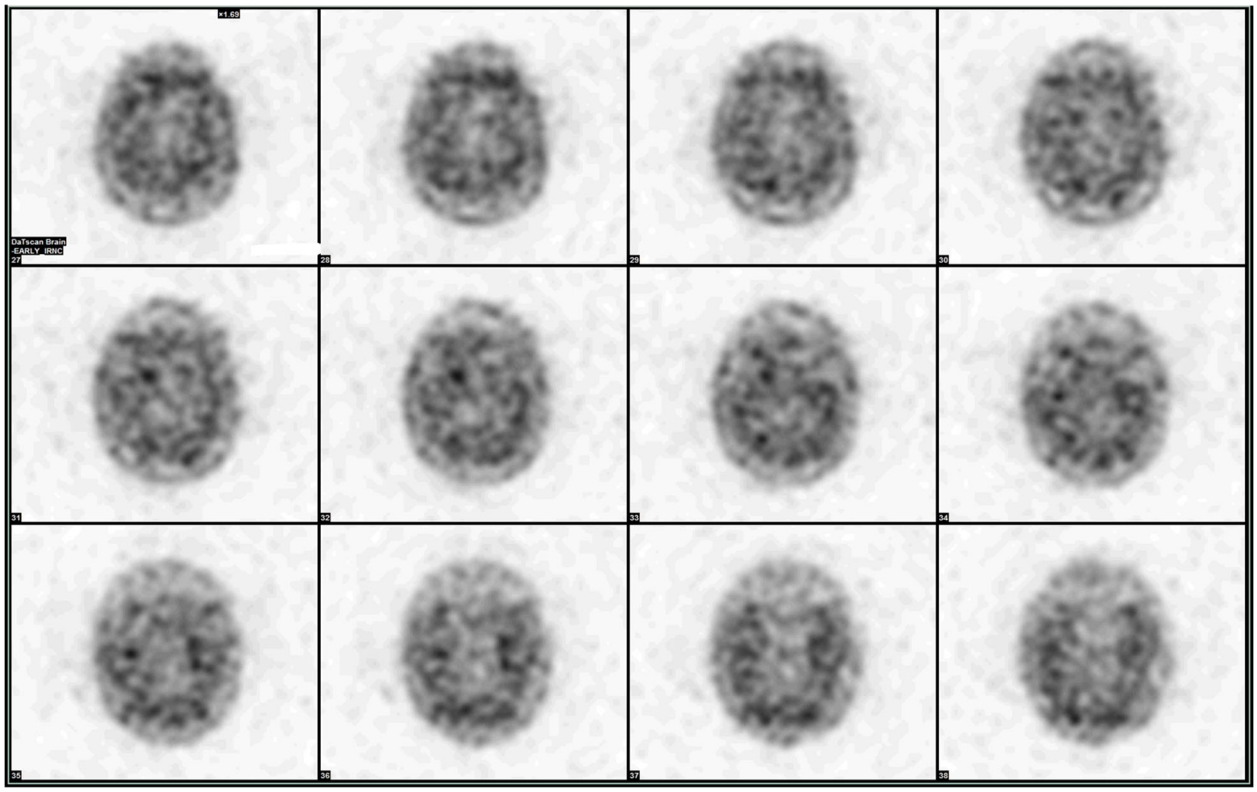

FIGURE 3. 67-year-old female on bupropion and citalopram presented for evaluation of progressive gait instability with falls, micrographia, depth perception, and vertical gaze palsy. Nondiagnostic study due to increased background uptake from patient's medications, citalopram and bupropion.

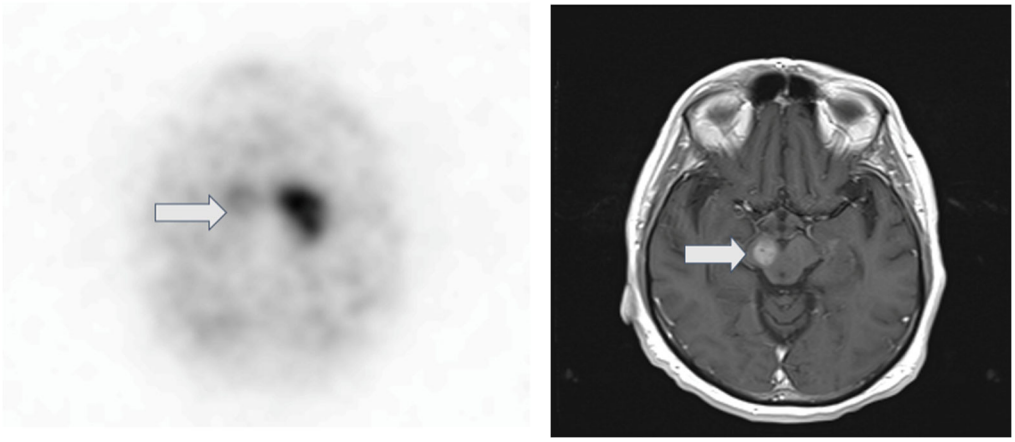

FIGURE 4. 65-year-old male with history of low-grade glioma in right midbrain evaluation for right arm rigidity and tremor. 4a. Axial brain SPECT showing decreased uptake in the right caudate and absent uptake in the right putamen due to right midbrain glioma (arrow). Normal comma shaped activity in the left caudate and putamen. 4b. MRI Brain T1 with contrast showing enhancing lesion in the right midbrain consistent with history of low-grade glioma.

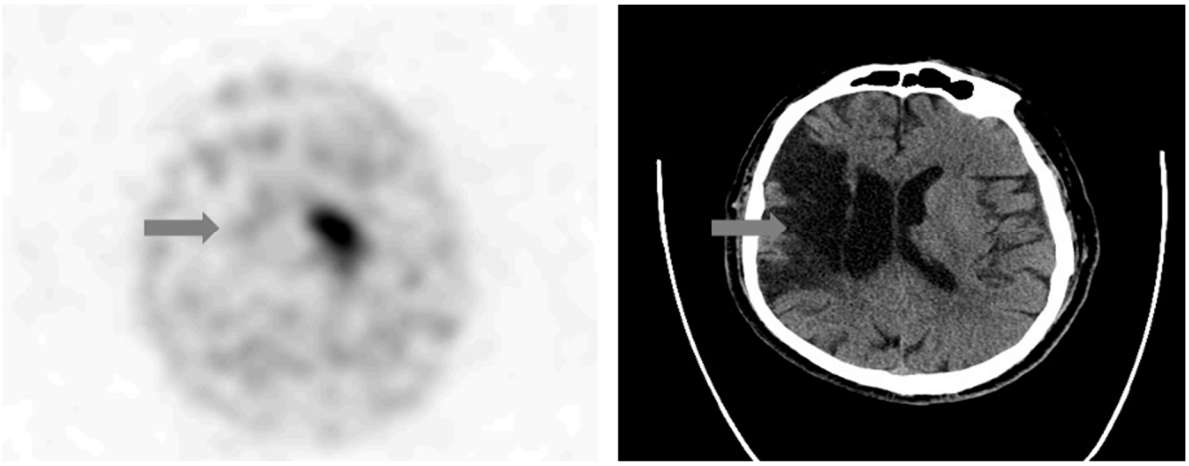

FIGURE 5. 61-year-old male with history of right MCA territory infarct evaluation for RUE tremors for 2-4 months. 5a. Axial brain SPECT showing decreased to absent uptake in the right caudate and putamen (arrow) due to prior right MCA territory infarct. 5b. Axial CT head without contrast showing right MCA territory infarct (arrow).

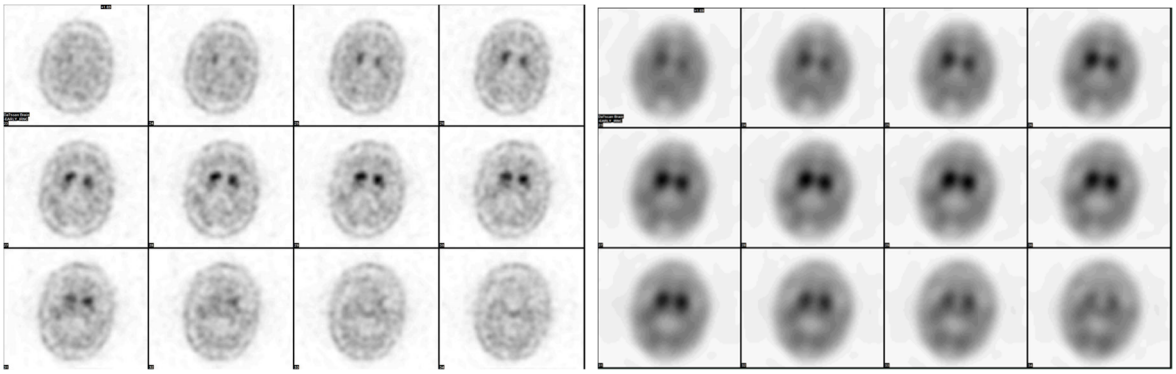

FIGURE 6. 80-year-old male on Sinemet without improvement of tremors, shuffling gait, bradykinesia for 2-3 months. 6a. Axial brain SPECT showing decreased uptake in the bilateral putamina and loss of normal comma shape, scintigraphic evidence of presynaptic deficit Parkinsonian Syndromes with probably age associated changes due to no improvement with Sinemet. 6b. Axial brain SPECT with oversmoothing artifact.

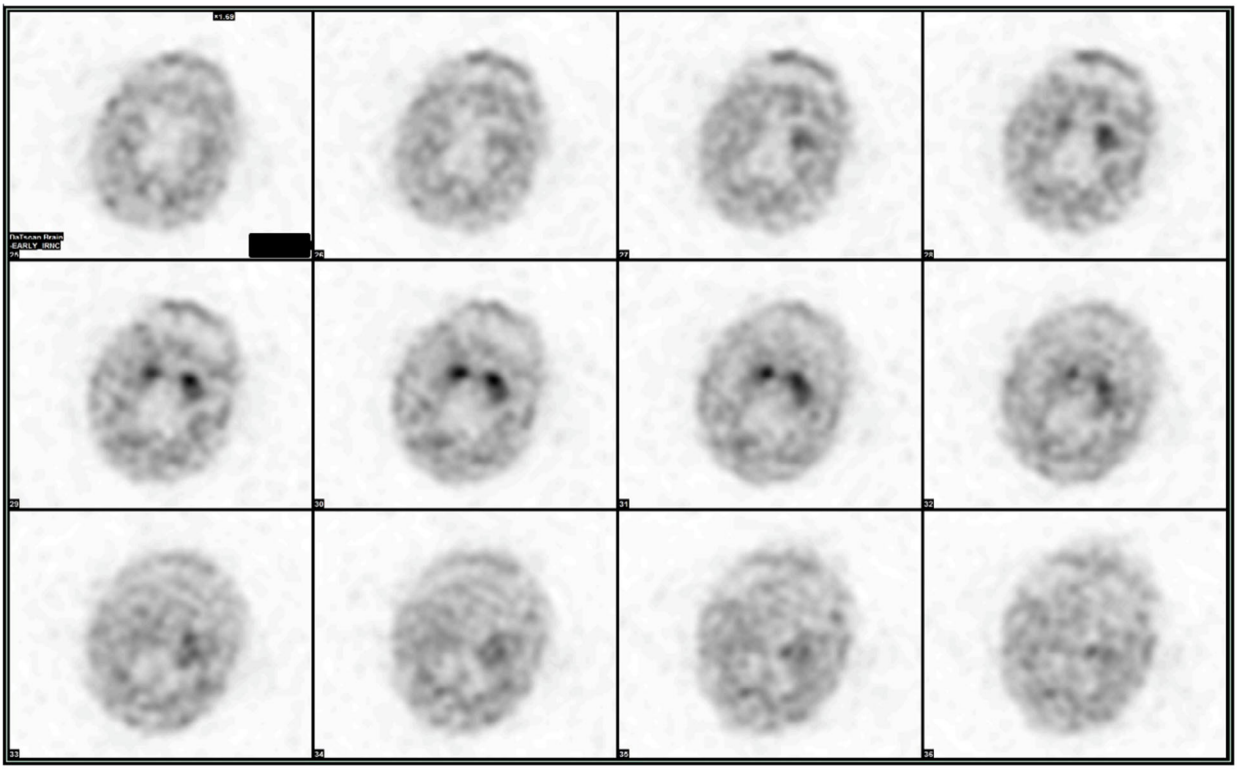

FIGURE 7. 76-year-old male on primidone with history of resting and action tremors, cogwheel rigidity for 5 years. Axial brain SPECT showing decreased uptake in bilateral putamina and right caudate with loss of normal comma shape on the right and scintigraphic evidence of probable presynaptic deficit Parkinsonian Syndrome. Limited study due to patient's body habitus and inability to perform closer to head with the required diameter.

Tables:

Table 1. Pitfalls in DaTscan imaging

Biological Factors	**Technical Factors**
Dopamine Transporter Density	Patient motion
Age	Patient position
Gender	Patient orientation
Body Habitus	Equipment resolution
Ethnicity	Equipment collimator
Genetic: allelic variants	Dose extravasations
Medications: drugs competing with DAT	Time post-injection
Striatal infarct	Photopeak
Brain tumors	Filtration, Oversmoothing
Trauma	Attenuation correction
Surgery	Size and placement of regions of interest

Adapted from Morbelli S and collaborators *(13)*.

Table 2. Drugs that increase, decrease, or do not interfere with iodine-123 Ioflupane

Drugs that may increase striatal ^{123} I Ioflupane binding
Opioid: fentanyl
Eugeroic: modafinil
Antidepressants: bupropion, mazindol, radafaxine
Anticholinergic: benztropine
Anesthetics: isoflurane, ketamine, phencyclidine
Central nervous system stimulant: cocaine
Drugs that may increase or decrease striatal ^{123} I Ioflupane binding
Adrenergic agonists: norepinephrine, phenylephrine
Amphetamines: d-amphetamine, methamphetamine, methylphenidate
Central nervous system stimulants: ephedrine, phentermine
Drugs that do not interfere with ^{123} I Ioflupane binding and do not need to be stopped
Dopamine agonists
NMDA receptor blockers
MAO-B inhibitors
COMT inhibitors

Adapted from Djang and collaborators *(3)*.

Table 3. Relevant drug interactions with DAT-SPECT

Significant Effect on DAT- SPECT	To be stopped before DAT-SPECT
Amphetamine	7 days
Benztropine	5 days
Bupropion	8 days
Cocaine	2 days
Dexamphetamine	7 days
Mazindol	3 days
Methylamphetamine	3 days
Methylphenidate	1-2 days
Modafinil	3 days
Phentermine	14 days

Adapted from Kägi and collaborators (*6)*.

Graphical Abstract