

DaTscans: *When should we order them and how are they interpreted?*

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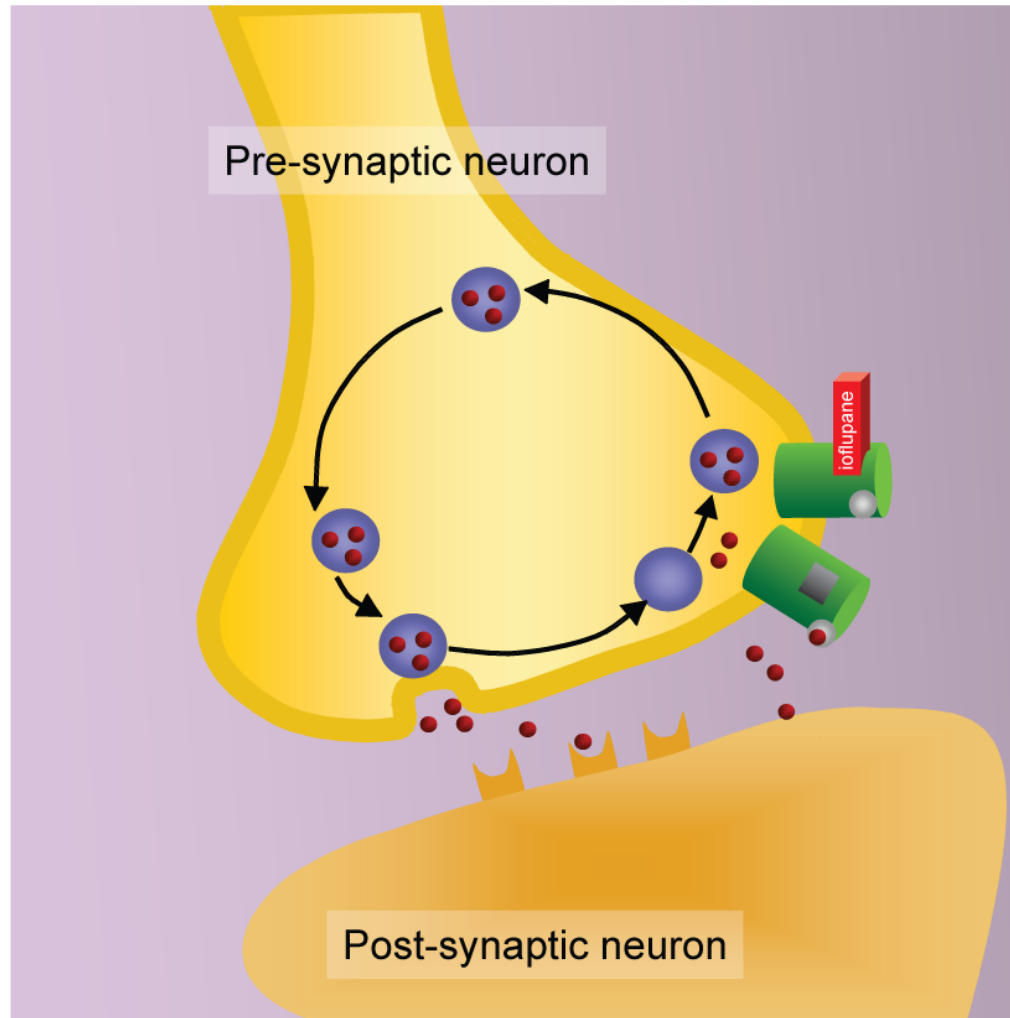
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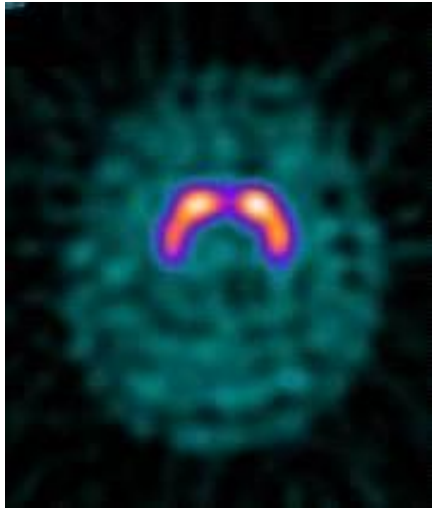
The Dopamine Transporter



Courtesy of D. Brooks

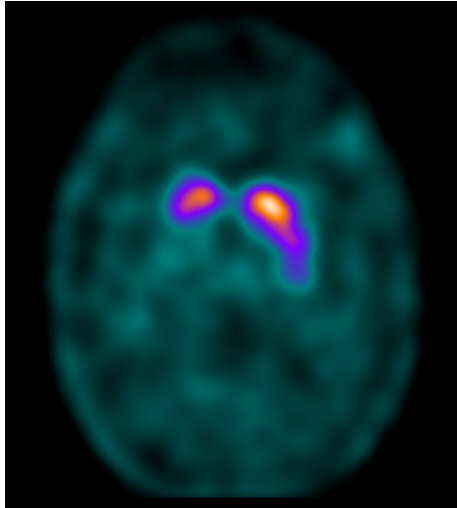
Stages of DaT loss in PD

Normal



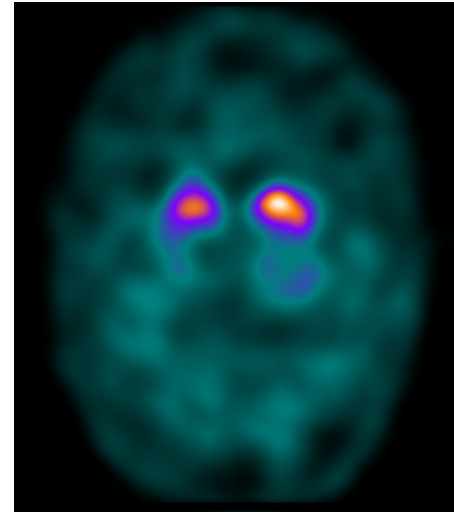
Signal evident in both right and left putamen and caudate; signal largely symmetrical about midline with ~equal signal bilaterally, forming roughly crescent shaped regions

Stage 1



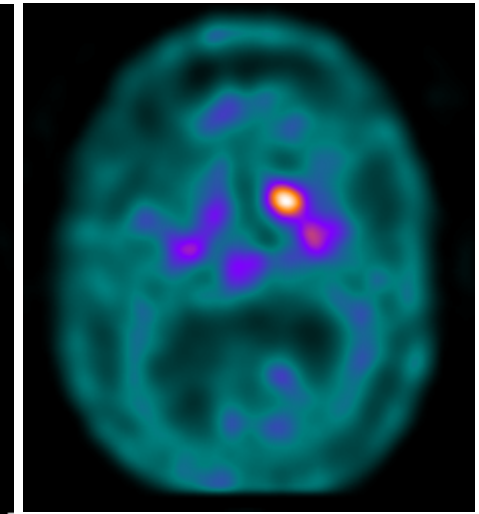
Signal asymmetric with normal or almost normal putamen in one hemisphere and more marked change in the other

Stage 2



Signal significantly reduced in both putamens. Signal only in caudate, appearing as two symmetrical, circular areas

Stage 3



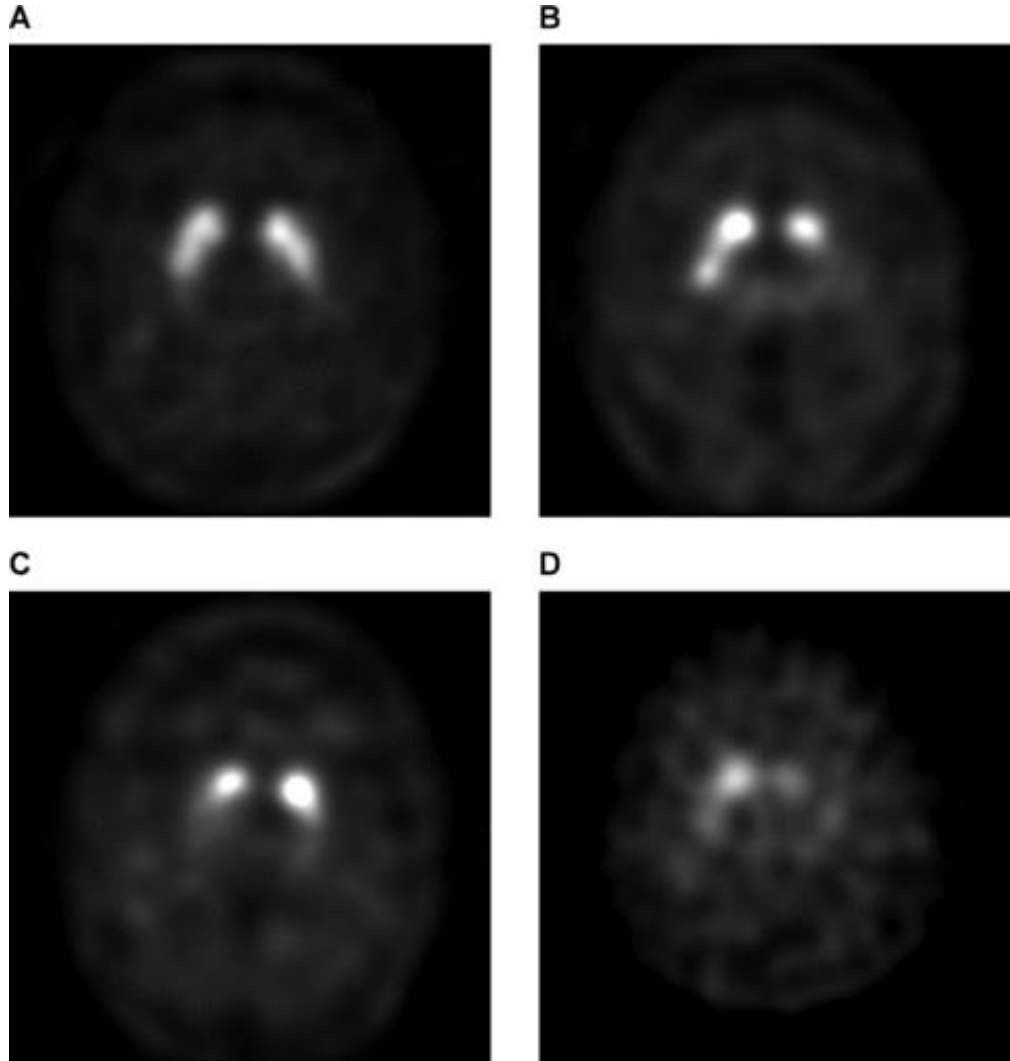
Signal nearly or virtually absent from both striata leading to reduction in contrast and visualization of background activity in rest of image

Loss of DaT significantly correlates with loss of nigrostriatal neurons in Parkinson's disease ($r = 0.635, p < 0.01$) Piggott MA 1998

DaTscan Indication

- “to assist in the evaluation of adult patients with suspected Parkinsonian syndromes (PS). In these patients, DaTscan may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson’s disease, multiple system atrophy and progressive supranuclear palsy). DaTscan is an adjunct to other diagnostic evaluations.”

[123I]FP-CIT (DaTscan) SPECT Brain Imaging in Patients with Suspected Parkinsonian Syndromes



Early DaTscan studies in ET and PD

- 93-100% specific, 95-97% sensitive
- But mostly fully established PD and ET

A multicenter assessment of dopamine transporter imaging with DOPASCAN/SPECT in parkinsonism

Parkinson Study Group*

November (2 of 2) 2000 NEUROLOGY 55 1541

Movement Disorders
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© 2000 Movement Disorder Society

Accurate Differentiation of Parkinsonism and Essential Tremor Using Visual Assessment of [¹²³I]-FP-CIT SPECT Imaging: The [¹²³I]-FP-CIT Study Group

Writing Committee: Hani T. S. Benamer, MRCP (UK), Jim Patterson, PhD,
Donald G. Grosset, BSc, MD, FRCP

Original article

The clinical benefit of imaging striatal dopamine transporters with [¹²³I]FP-CIT SPET in differentiating patients with presynaptic parkinsonism from those with other forms of parkinsonism

Jan Booij¹, Johannes D. Speelman², Martin W.I.M. Horstink³, Erik C. Wolters⁴

European Journal of Nuclear Medicine Vol. 28, No. 3, March 2001

What about clinically uncertain cases?

- Patients with tremor of uncertain etiology
 - Parkinsonian tremor with action component
 - Essential tremor with resting component or asymmetry
 - Possible psychogenic tremor
 - Parkinsonian tremor vs. dystonic tremor
- Neurodegenerative vs. secondary causes of Parkinsonism
 - PD vs. vascular Parkinsonism
 - PD vs. drug-induced Parkinsonism
- Idiopathic vs. atypical causes of PD

Comparing clinical exam and DaTscan in clinically uncertain cases

- 99 patients with clinically uncertain Parkinsonism
- DaTscan at baseline, then assessment at 36 months with blinded consensus clinical diagnosis using all clinical data and videotaped exam – 66 probable PD, 5 possible PD and 28 non-PD
- Initial Datscan: 78% sensitive, 96.6% specific
- Initial clinical exam: 93% sensitive, 46.4% specific
- DaTscan was highly consistent across exams : only one patient converted from normal to abnormal and one from abnormal to normal

TABLE 4. *T = 36 Video gold standard diagnosis versus T = 0 baseline [¹²³I]FP-CIT SPECT*

	Probable PD	Possible PD*	Non-PD**
T = 36 Video gold standard diagnosis	66	5	28
T = 0 [¹²³ I]FP-CIT SPECT Abnormal:Normal	56 : 10	0 : 5	1 : 27

TABLE 5. *T = 0 clinical on-site diagnosis versus T = 0 baseline [¹²³I]FP-CIT SPECT*

	Abnormal	Normal
T = 0 [¹²³ I]FP-CIT SPECT	57	42
T = 0 On-site clinical diagnosis PD: Non-PD	55 : 2	26 : 16

CUPS f/u Study – 2 years

- 85 of 118 patients in initial study re-examined at 2 years
- In 77/85 clin dx established at follow-up
 - In 69/77, this agreed with initial DaTscan result (90%, NPV 96%, PPV 87%)
 - 8 still had inconclusive dx – 2nd DaTscan helped dx in 7/8
 - 6 patients had discordance between initial DaTscan and final clinical dx – 2nd DaTscan confirmed clinical dx in 4/6 and remained discordant in 2/6

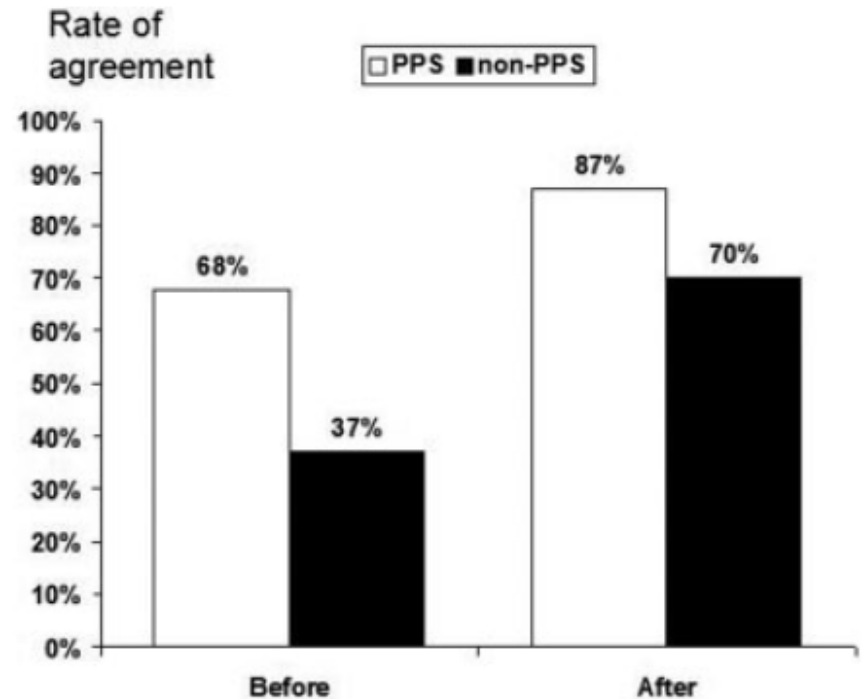


FIG. 2. Rate of agreement between clinical diagnosis at 2 years follow-up and diagnosis at baseline before and after initial DaTSCAN SPECT (PPS, presynaptic Parkinsonian syndrome).

CUPS f/u Study – 2 years

- In 6/14 patients, results of 1st and 2nd DaTscans were discordant
 - In 1 patient with PPS initial scan was read as normal and follow-up scan was read as abnormal
 - So you can have early PS with a normal scan, rarely
 - In 7/8 patients with Non-PPS, initial scan was read as ABNORMAL and follow-up scan was read as NORMAL
 - Blinded re-evaluation of all scans suggested all were normal – early studies were read as abnormal for minor putaminal uptake deficits

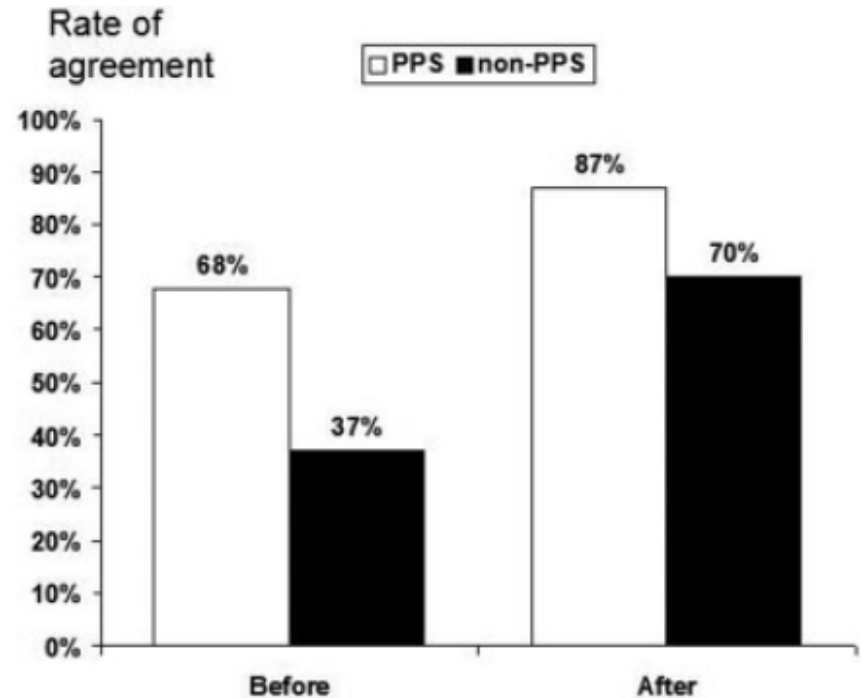
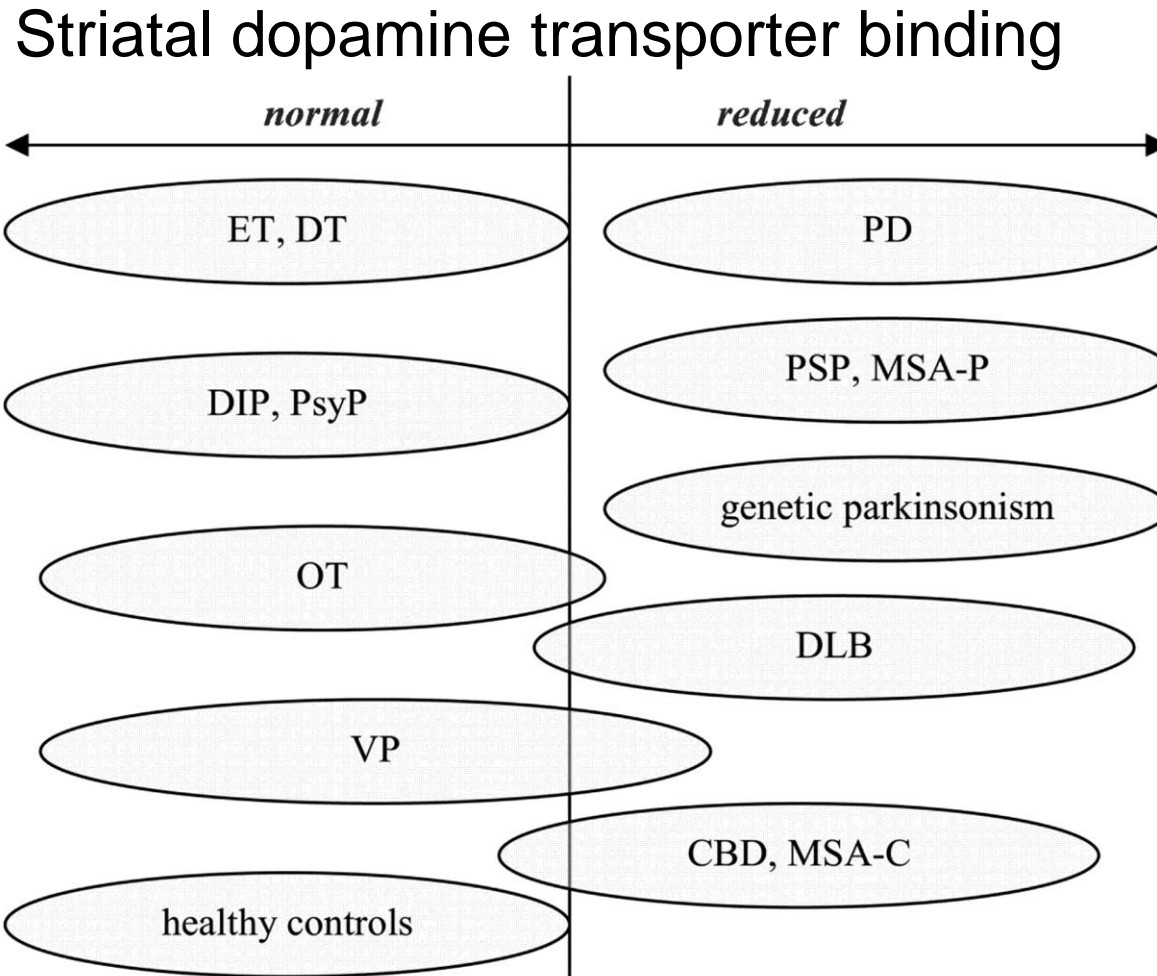


FIG. 2. Rate of agreement between clinical diagnosis at 2 years follow-up and diagnosis at baseline before and after initial DaTSCAN SPECT (PPS, presynaptic Parkinsonian syndrome).

Does a DaTscan change management, diagnosis and confidence of diagnosis?

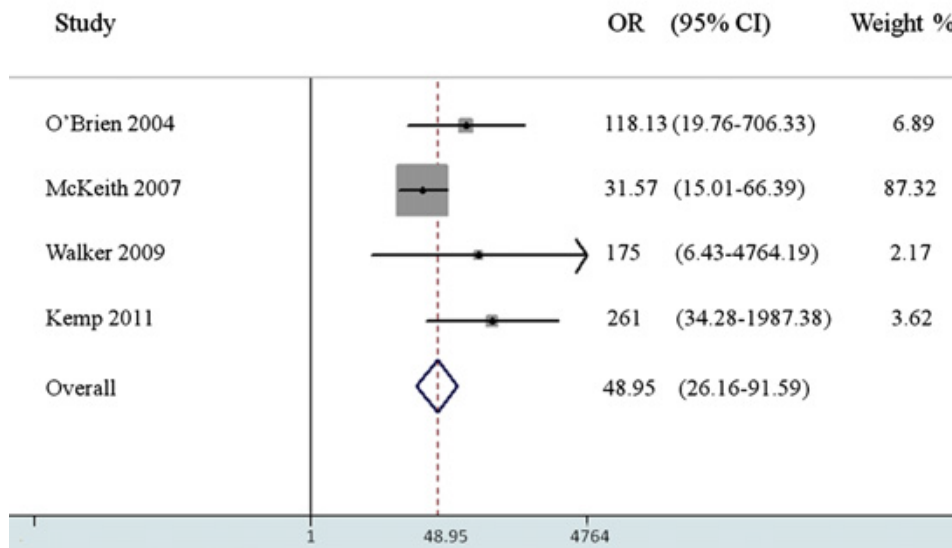
- 215 patients (165 PS, 63 non-PS, 31 inconclusive) randomized to get DaTscan (113) or not (102) and then followed for 1 year
- DaTscan group more likely to have change in management (50%) than controls (21%)
- DaTscan group more likely to have change in diagnosis (45%) than controls (9%)
- DaTscan improved confidence of diagnosis but not quality of life

What about other causes of Parkinsonism?



DaTscan in dementia with Lewy bodies

- Meta-analysis of 4 studies
- 419 total patients
- Pooled results for DLB vs. non-DLB dementia:
 - 93.6% specificity
 - 86.5% sensitivity



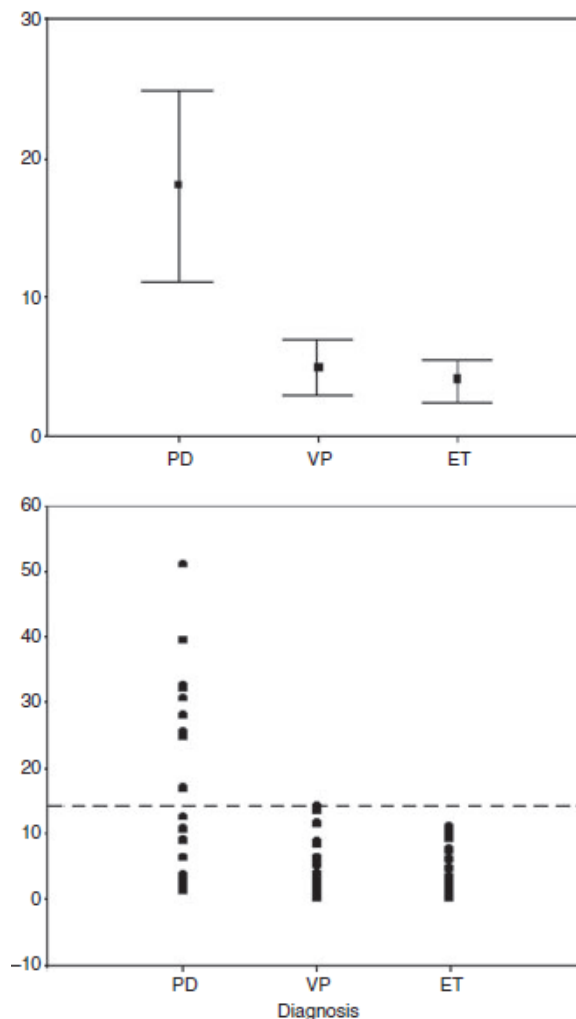
[¹²³I]-FP/CIT SPECT Imaging for Distinguishing Drug-Induced Parkinsonism From Parkinson's Disease

Mordechai Lorberboym, MD,¹ Therese A. Treves, MD,² Eldad Melamed, MD,² Yair Lampl, MD,³
Mark Hellmann, MD,² and Ruth Djaldetti, MD^{2*}

- 20 patients with presumed drug-induced Parkinsonism scanned
- 9 patients had normal scans and 11 had abnormal scans
- No clinical features distinguished the two groups

Can DaTscan asymmetry help to differentiate causes of Parkinsonism?

- Two studies have compared a DaTscan striatal asymmetry index (SAI) in PD vs. vascular Pism (VP)
- Largest - 20 PD, 20 VP, 20 ET
- Suggests that high SAI scores are very specific for PD compared to both VP and ET
- Further studies needed in both VP and atypical Pism



VA Guidelines for the Use of Dopaminergic Functional Imaging

- Dopaminergic functional imaging has been shown to be a useful adjunct to the clinical diagnosis of movement disorders in some settings.
- In general, the risk of functional imaging is justified when the outcome of the examination will help to dictate clinical management.
- Accurate diagnosis can prevent exposure to inefficacious treatments, improve prognostic abilities and improve cost efficiency.

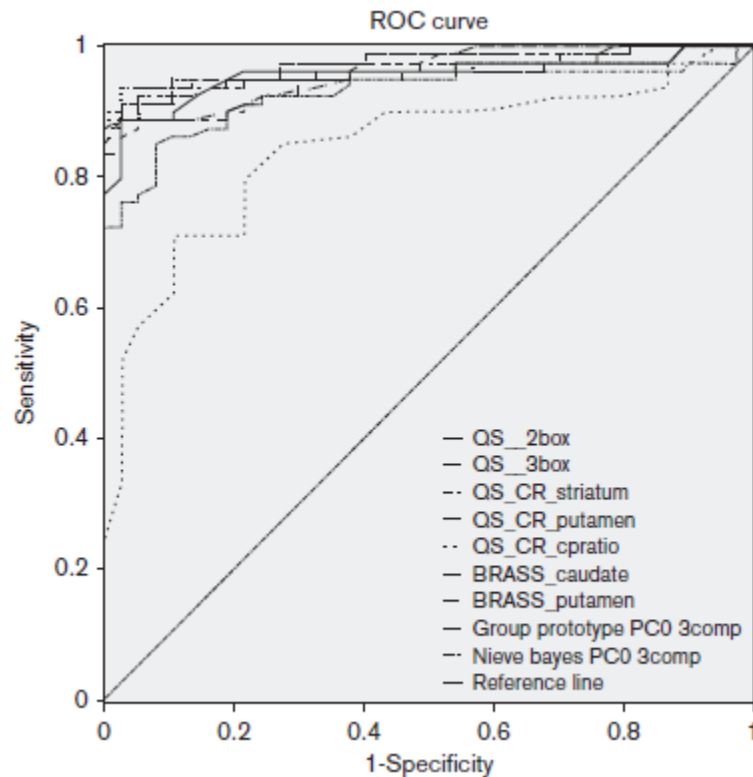
VA Guidelines for the Use of Dopaminergic Functional Imaging

- Dopaminergic functional imaging has not been shown to be helpful in differentiating between different Parkinsonian syndromes (e.g. Parkinson's disease, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration).
- Decisions on whether or not to conduct scans for a given clinical scenario should also be guided by relevant sensitivity and specificity data as well as the recognition that there is some inter-rater variability in the interpretation of scans.

VA Guidelines for the Use of Dopaminergic Functional Imaging

- Scenarios in which the result of dopaminergic functional imaging may prove helpful in determining therapeutic interventions include:
 - Patients with tremor that is not clearly differentiated into either essential tremor or Parkinsonian tremor.
 - Patients with tremor or other features of Parkinsonism in the context of treatment with dopamine-blocking medications known to induce Parkinsonism to determine if the Parkinsonism is likely to be purely drug-induced or if there is an underlying neurodegenerative condition.
 - Patients with possible psychogenic Parkinsonism.
 - Patients with tremor of unclear etiology that is not responsive to dopaminergic replacement therapies and who are being considered for deep brain stimulation therapy to help guide target selection.

Automated quantification of DaTscans

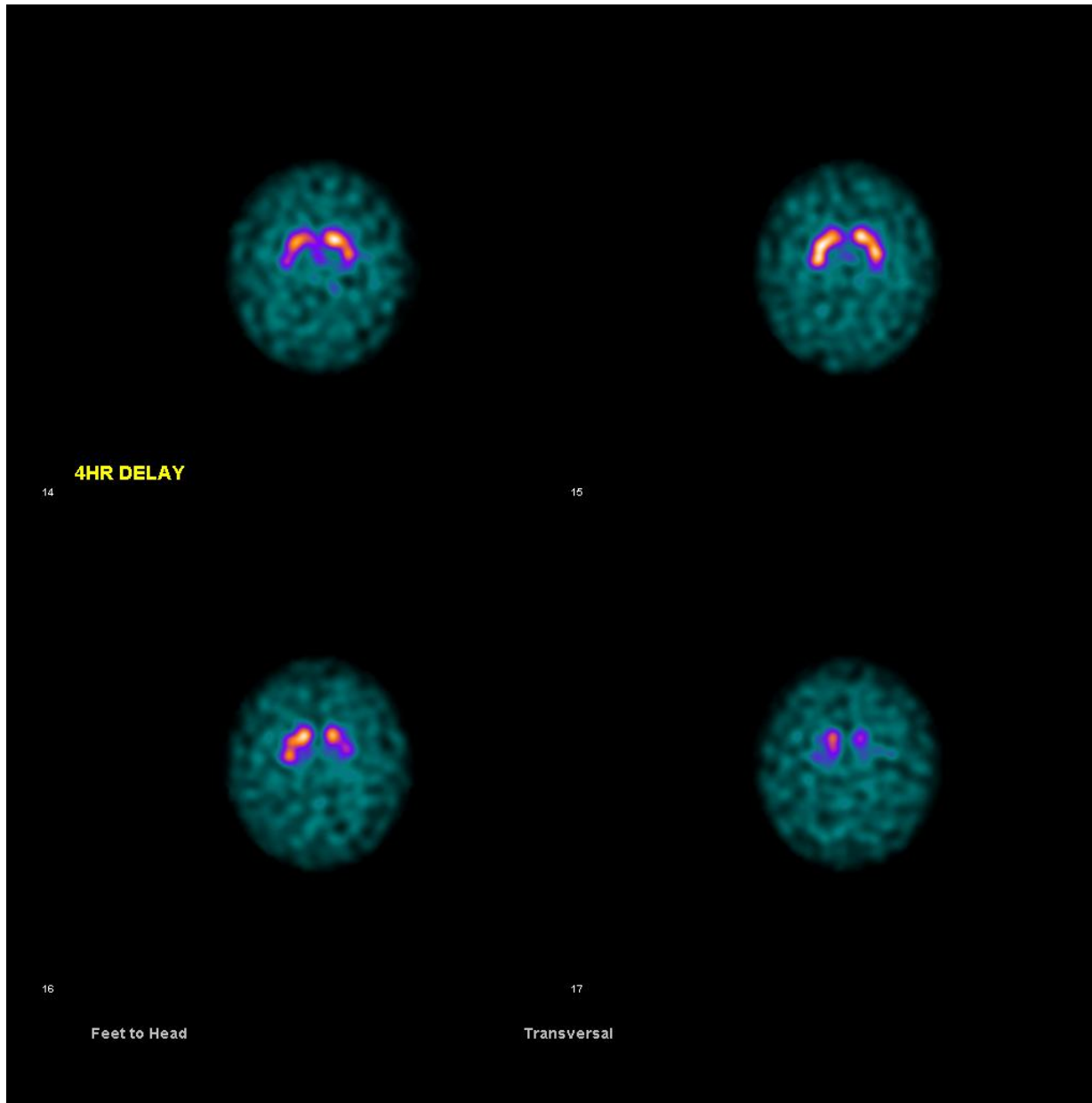


- 79 PS patients, 27 non-PS patients
- Compared 4 commercial assessments and several of their own
- Best methods correctly identified 110/116 patients (94.8%); 93.7% sensitivity, 97.3% specificity

Patient 1

- Patient assessed for possible PD, with very mild/subtle symptoms
- Patient was interested in any test to assess whether his symptoms were actually the result of early PD or not

Patient 1



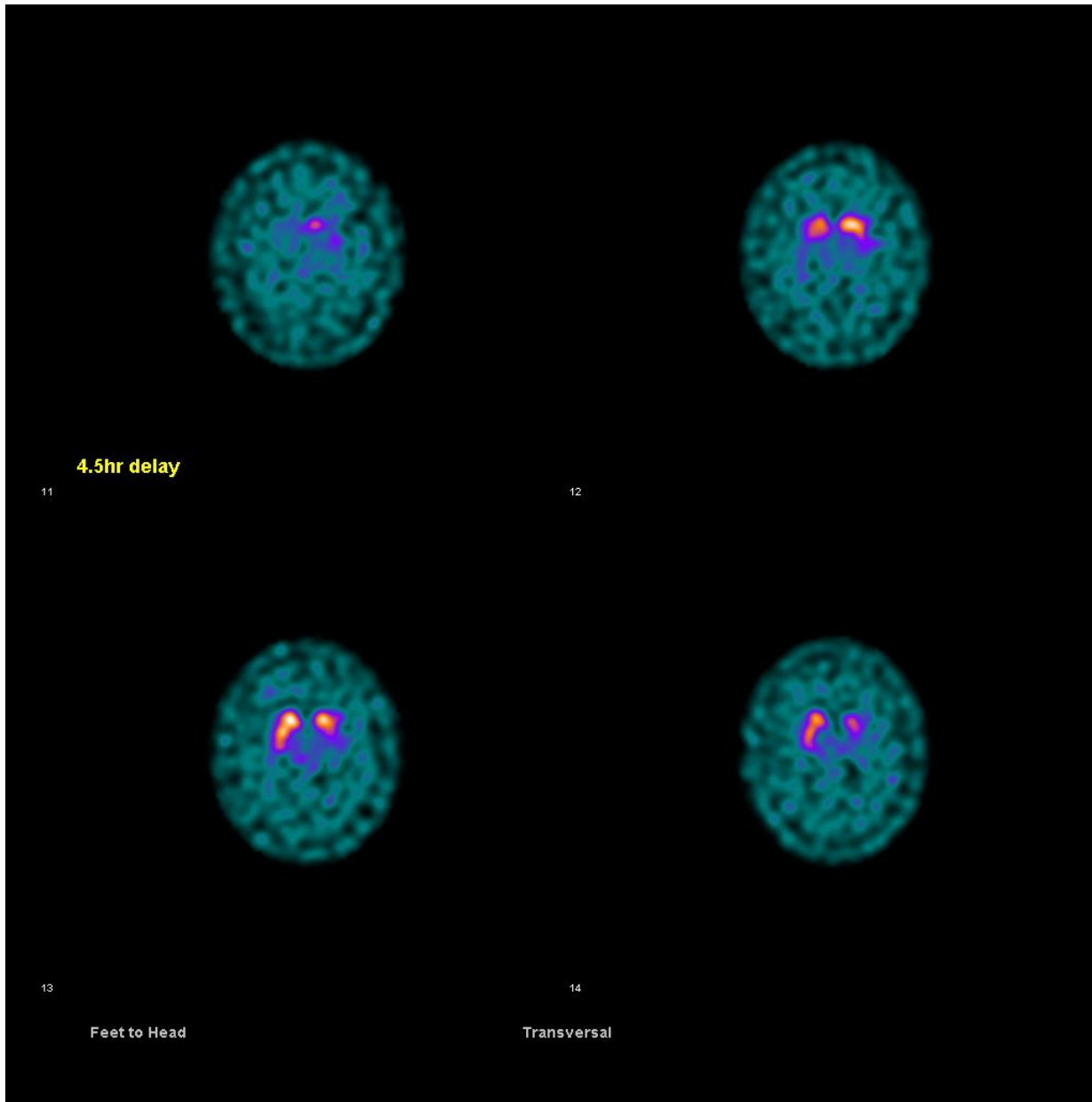
Patient 1

- This DaTscan was read as being normal
- Is this a valid reason to order a DaTscan?
- What if he was an Agent Orange exposed Vietnam Veteran seeking service connection?

Patient 2

- Patient had history of REM-sleep behavior disorder, but no evidence of Parkinsonism on exam
- Patient was interested in any test to assess whether his RBD was actually the result of early PD or not

Patient 2

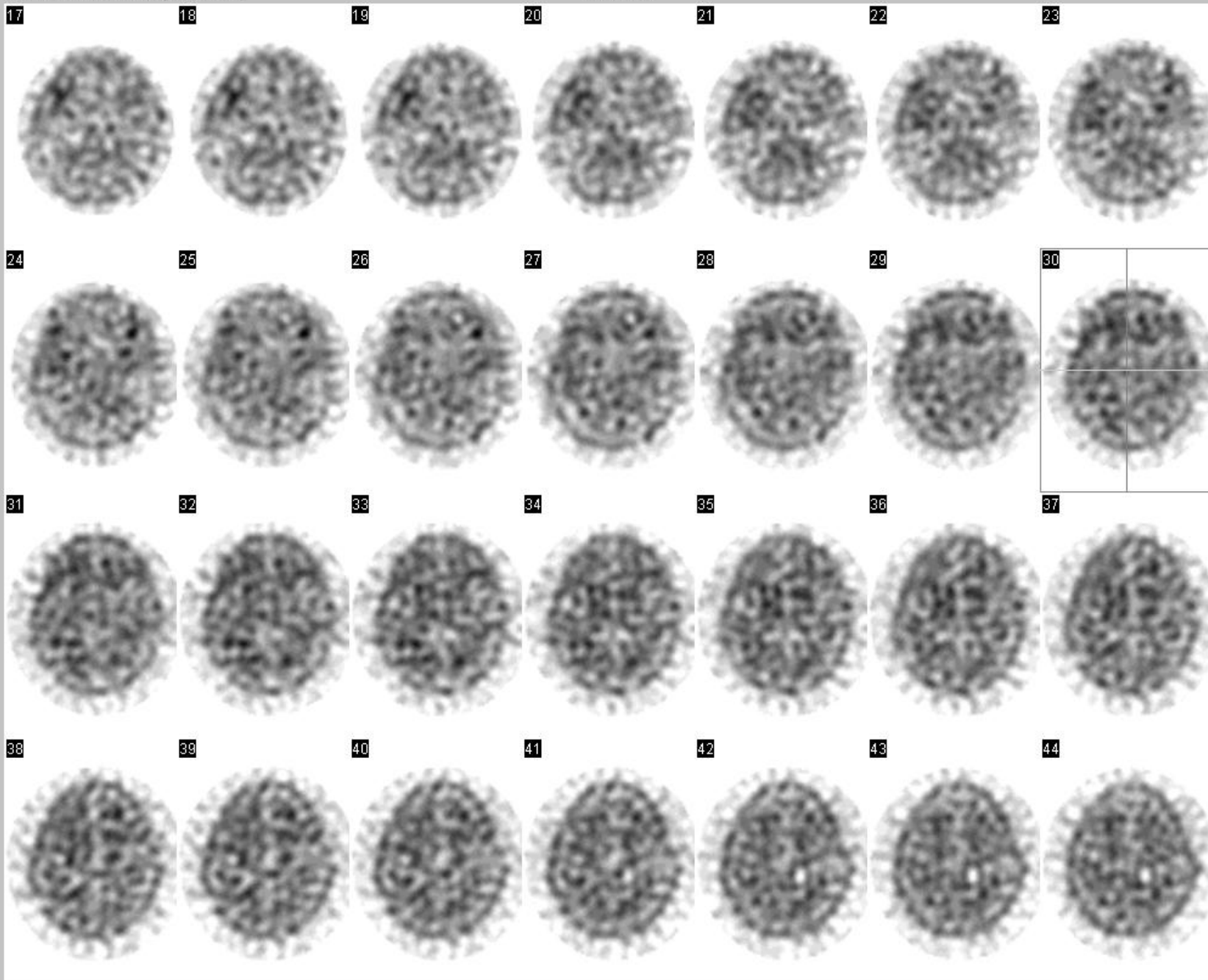


Patient 2

- This DaTscan was read as being abnormal
- Is this a valid reason to order a DaTscan?

Patient 3

- 80yo Veteran with Parkinsonism that appeared while on risperidone
- Diagnosed with possible drug-induced Parkinsonism and risperidone withdrawn
- Parkinsonism not resolved 11 months later so question of underlying Parkinson's disease raised
- Reluctance to start carbidopa/levodopa with history of psychosis



%

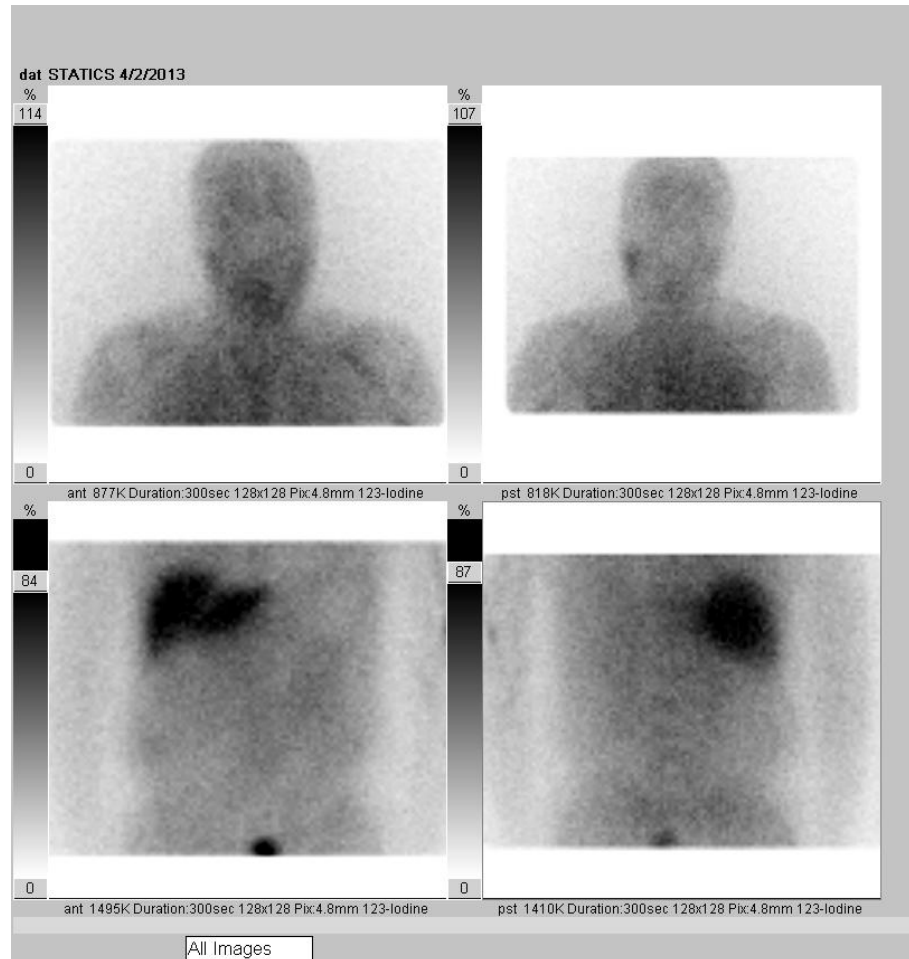
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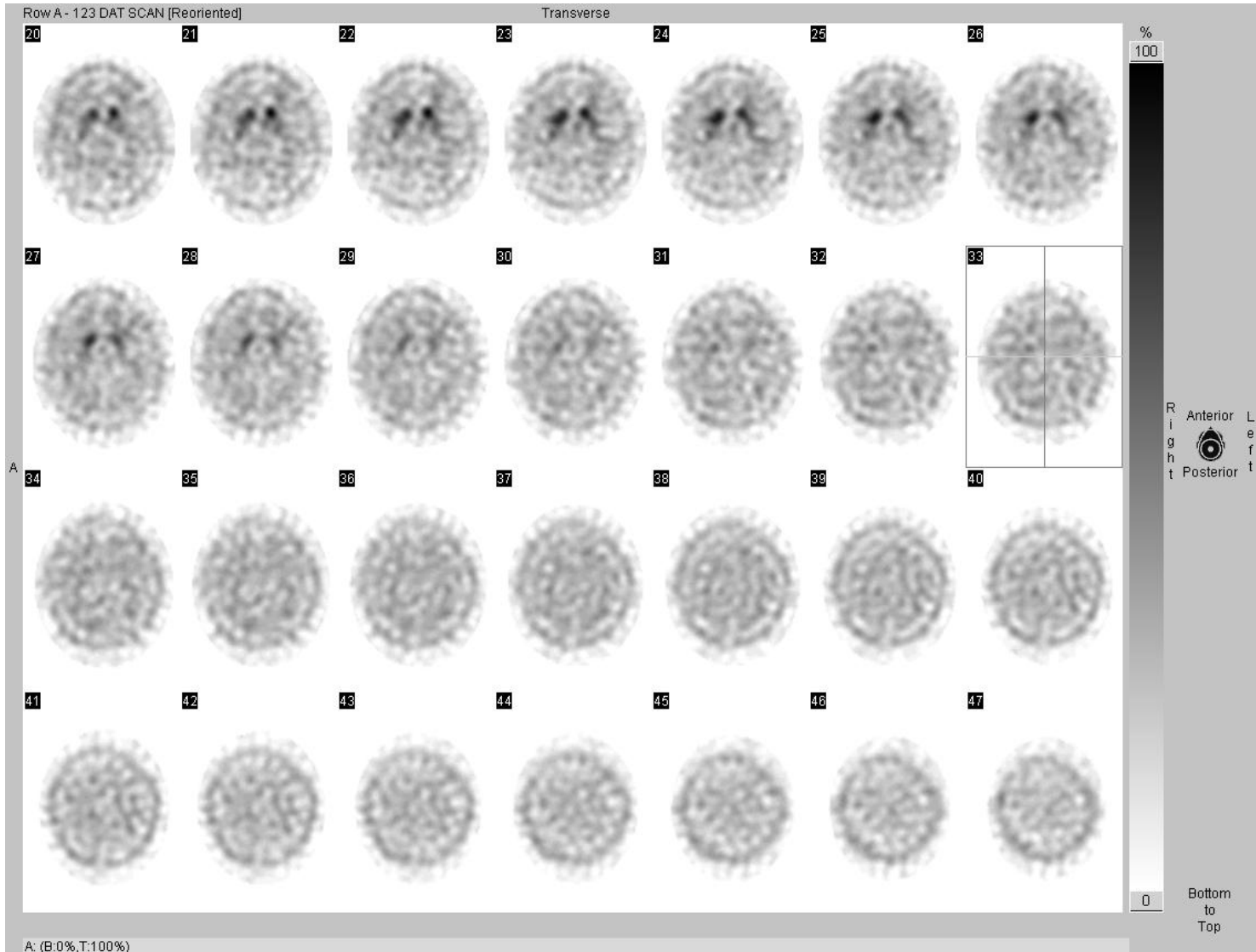
Given lack of cerebral uptake, normal hepatic uptake assessed



Patient 3

- This DaTscan was read as being abnormal
- Further review of history revealed patient was also taking methylphenidate
- Methylphenidate held for 3 days and DaTscan repeated

Repeat DaTscan is abnormal



DaTscan drug interactions

Table 1 Relevant drug interaction with dopamine transporter single photon emission computed tomography (DAT-SPECT)

Minor* effect on DAT-SPECT	To be stopped prior to DAT-SPECT	Significant† effect on DAT-SPECT	To be stopped prior to DAT-SPECT
Citalopram	8 days	Cocaine	2 days
Fluoxetine	45 days	Amphetamine	7 days
Paroxetine	5 days	Methylamphetamine	3 days
Venlafaxine	3 days	Methylphenidate	1 days
Duloxetine	3 days	Methylphenidate	2 days
Escitalopram	8 days	Dexamphetamine	7 days
Fluvoxamine	5 days	Mazindol	3 days
Sertraline	6 days	Phentermine	14 days
Imipramine	5 days	Modafinil	3 days
Clomipramine	21 days	Bupropion or amfebutamone	8 days
Pimozide	28 days	Benzatropine	5 days
Ziprasidone	2 days		
Memantine	5 days		
Amantadine	6 days		
Budipine	6 days		
Ephedrine, epinephrine	6–10 h		
Phenylephrine			
Pseudoephedrine			
Xylometazoline			

*May have a small effect on uptake (at most 15%). This is acceptable for routine DAT-SPECT but not for research.

†All of these drugs are likely to alter (usually decrease) radioligand uptake by at least 20% and often substantially more, and therefore have to be stopped prior to routine DAT-SPECT.

Patient 4

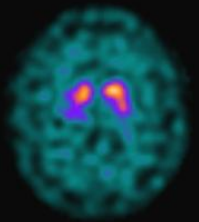
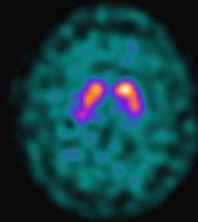
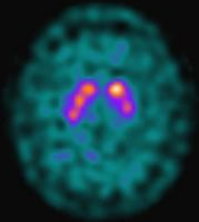
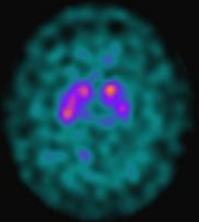
- Mildly symptomatic subject
- UPDRS 6

Patient 4

19

20

21



25

26

27

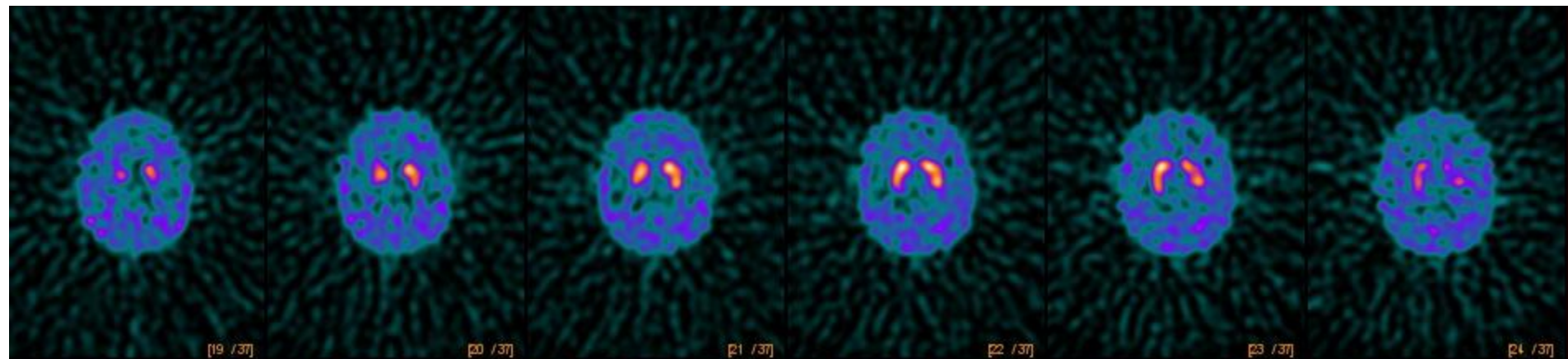
Patient 4

- Read as normal by nuclear medicine
- Read as abnormal by treating physician
- What do you tell the patient?

Patient 5

- 67 yo with 2 year history of tremor, mild rigidity and bradykinesia
- Prior history of acute loss of smell
- Started on olanzapine around the onset of symptoms

Patient 5



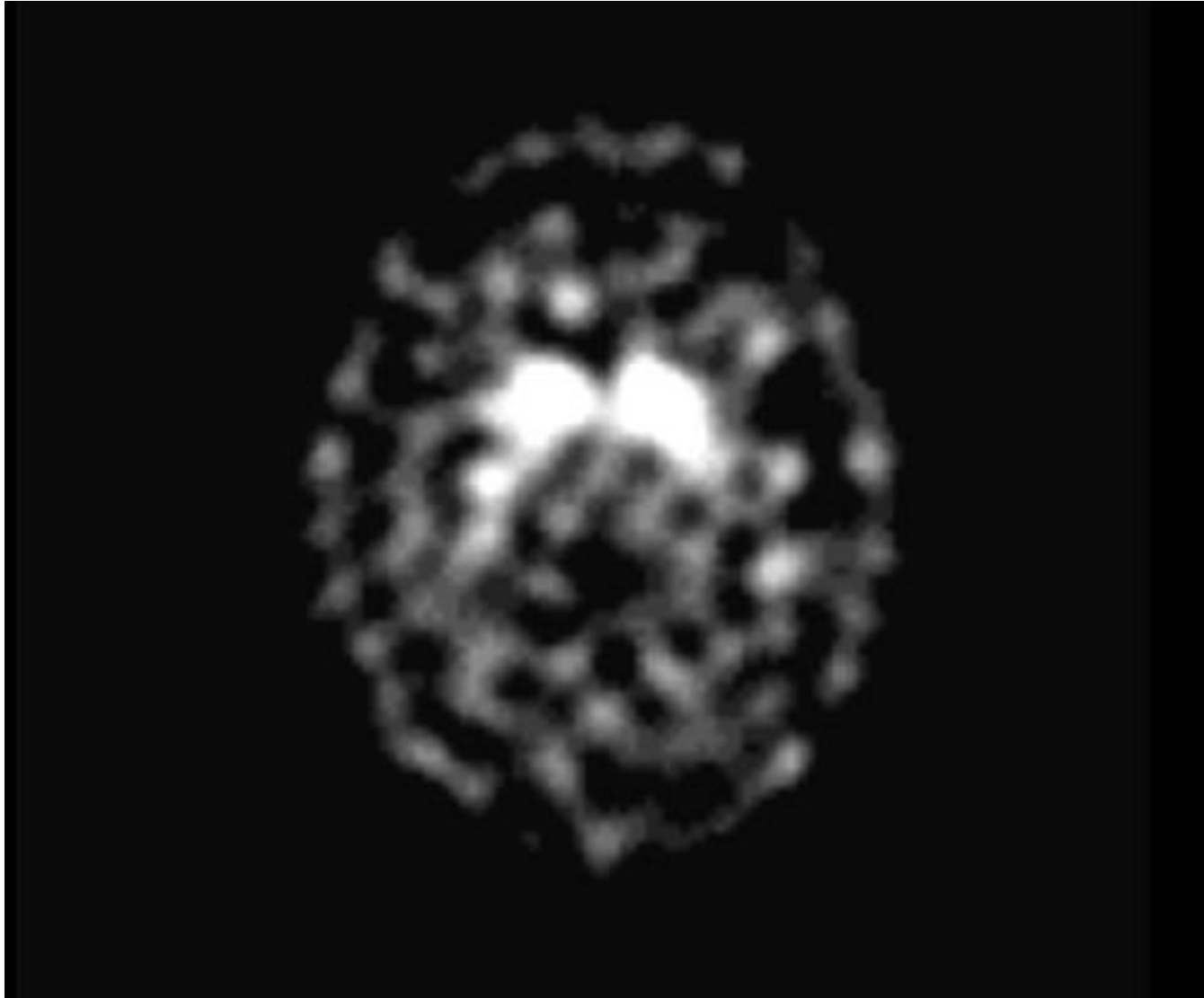
Patient 5

- Read as normal
- Diagnosed with drug-induced Parkinsonism
- Switch from olanzapine to quetiapine attempted

Patient 6

- 78yo Veteran with history of essential tremor who has developed a resting component and possible rigidity (vs. paratonia) and mild non-decrementing bradykinesia
- History of psychotic depression in past

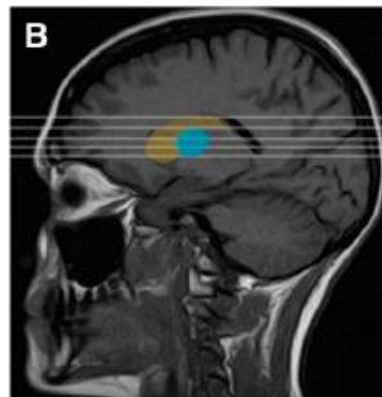
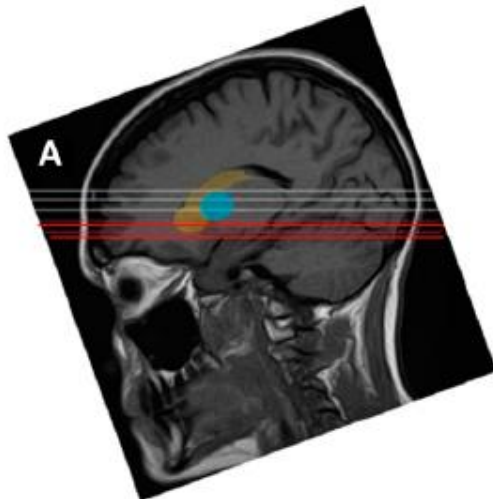
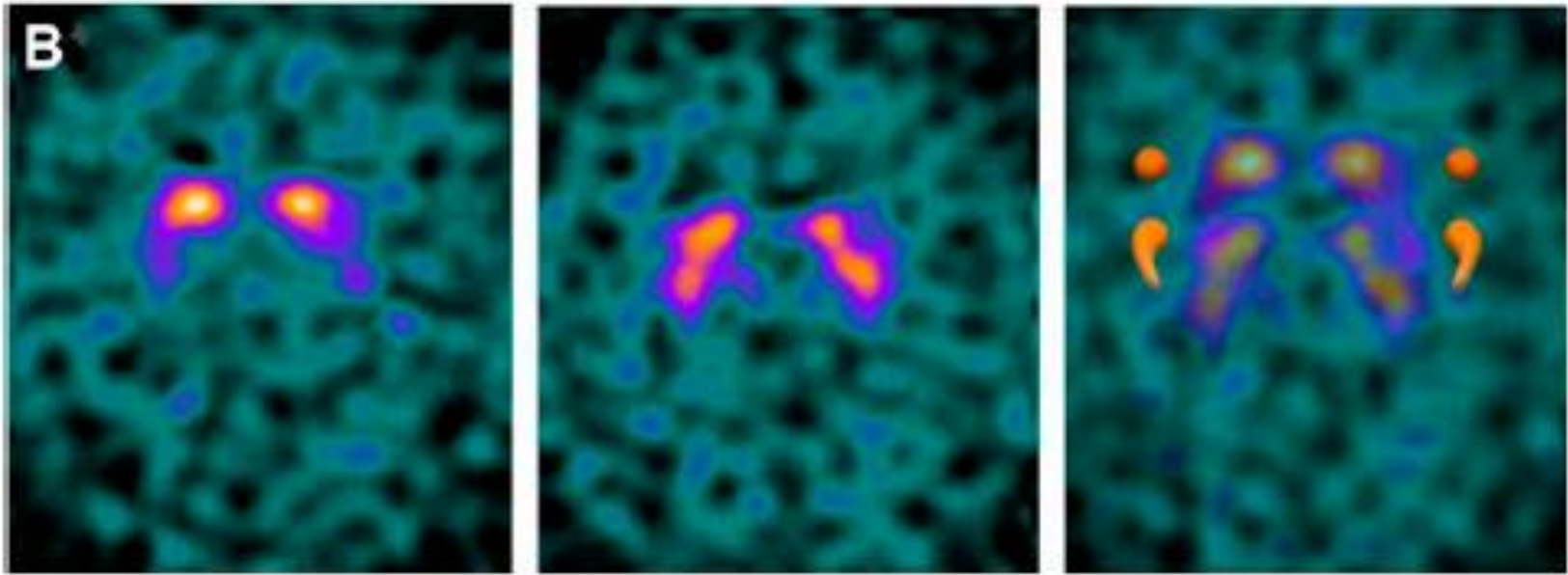
Is this abnormal?



Patient 6

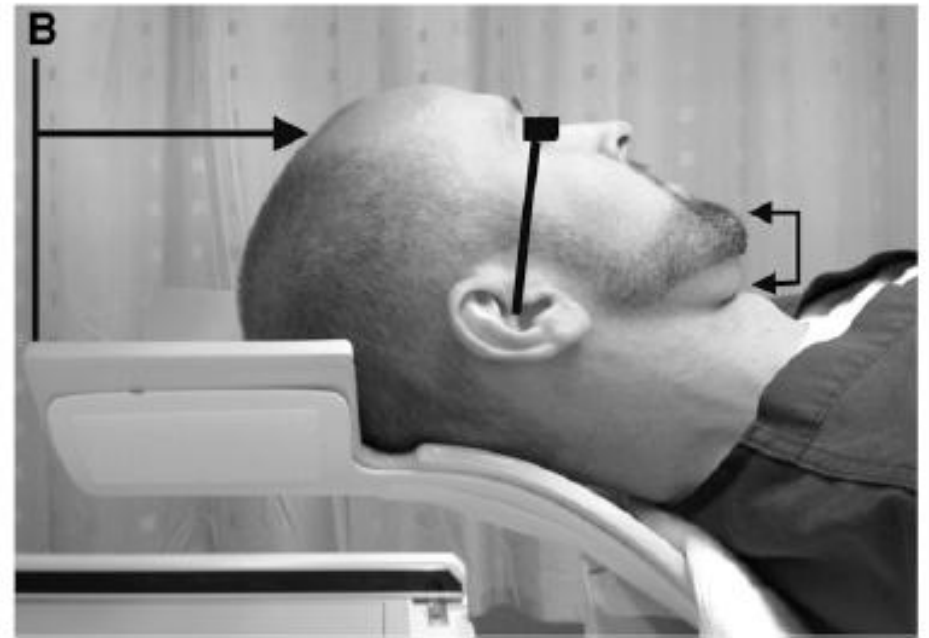
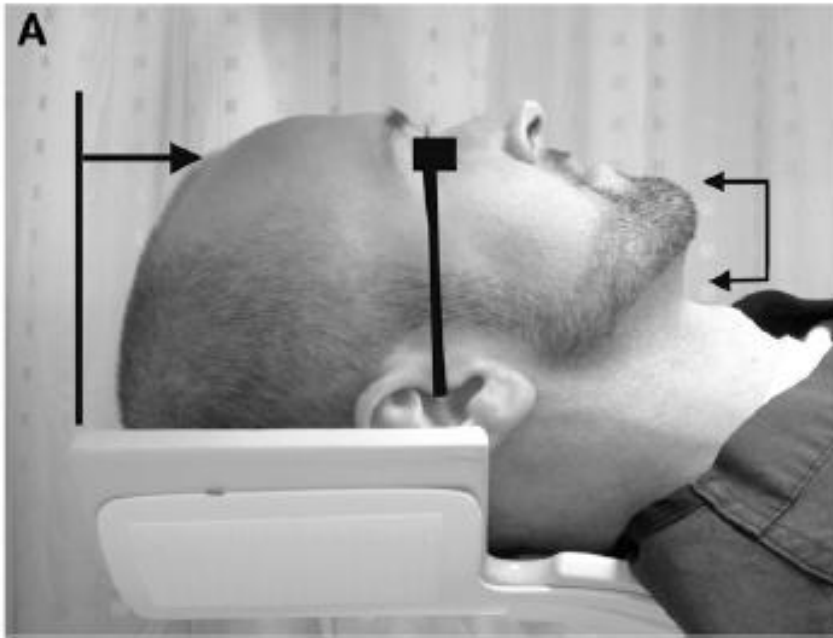
- DaTscan read as abnormal
- However, imaging technique may have contributed to appearance of DaTscan

The 'Semicolon sign'



Covington, et al. J Nucl
Med Technol (2013);41:1-3

Proper patient positioning avoids appearance of 'Semicolon sign'

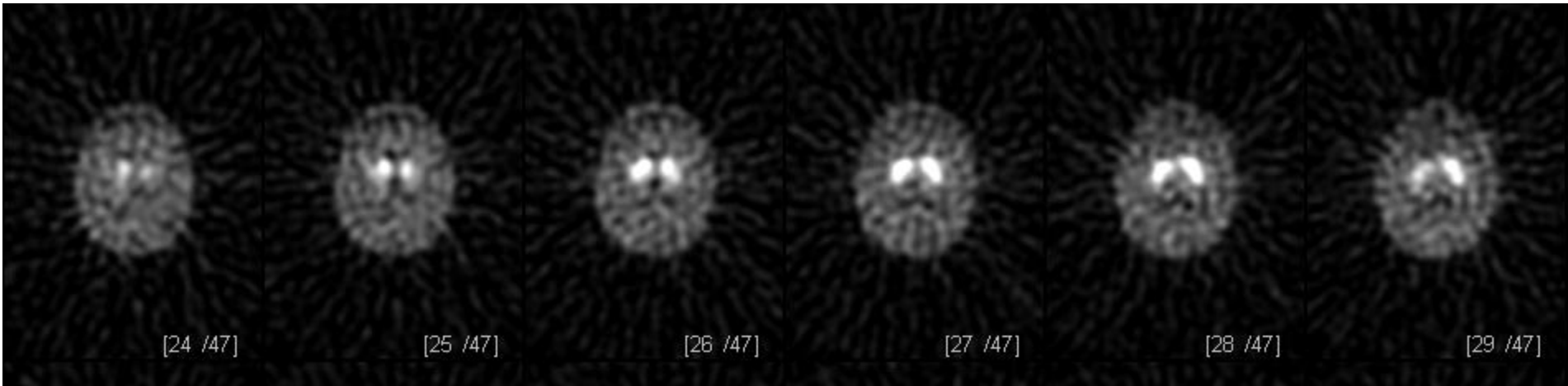


Covington, et al. J Nucl
Med Technol (2013);41:1-3

Patient 7

- 59 yo with tremor of LUE that progressed to RUE and LLE
- Sinemet was tried, which benefitted tremor by history but made him more stiff so he stopped it
- On exam, LUE pill-rolling tremor, normal tone, non-decrementing hypokinesia L>R, but question of psychogenic gait

Patient 7



Patient 7

- Read as being normal, and not consistent with any Parkinsonian syndrome.
- Good quality scan, excellent levels of background noise.
- Possible psychogenic Parkinsonism

Conclusions

- DaTscan can be helpful in some appropriately selected patients
- Keep in mind medication effects
- Thought to be the Gold Standard, but there are exceptions and no pathology confirmation studies in Parkinsonism to date
- Make sure you check scans yourself