

Importance of ^{123}I -ioflupane SPECT and Myocardial MIBG Scintigraphy to Determine the Candidate of Deep Brain Stimulation for Parkinson's Disease

Takashi ASAHI,¹ Daina KASHIWAZAKI,¹ Tatsuya YONEYAMA,²
Kyo NOGUCHI,² and Satoshi KURODA¹

Departments of Neurosurgery¹ and Radiology,² University of Toyama, Sugitani, Toyama

Abstract

^{123}I -ioflupane SPECT (DaTscan) is an examination that detects presynaptic dopamine neuronal dysfunction, and has been used as a diagnostic tool to identify degenerative parkinsonism. Additionally, myocardial ^{123}I -metaiodobenzyl guanidine (MIBG) scintigraphy measures the concentration of cardiac sympathetic nerve fibers and is used to diagnose Parkinson's disease (PD). These exams are used as adjuncts in the diagnosis of parkinsonism, however, the relationship of these two examinations are not well-known. We investigated the relationship of these two scanning results specifically for determining the use of deep brain stimulation therapy (DBS). Subjects were Japanese patients with suspected striatonigral degeneration, including PD; DaTscans and myocardial MIBG scintigraphy were performed. The mean values of the left-right specific binding ratios (SBRs) from the DaTscan, and the early/delayed heart-to-mediastinum ratios (HMRs) from the MIBG scintigraphy were calculated. Using simple linear regression analysis, we compared the SBR and early/delayed HMR values. Twenty-four patients were enrolled in this study. Twenty-one patients were positive via the DaTscan, and the MIBG scintigraphy results showed 14 patients were positive. SBR and both early and delayed HMR were positively correlated in cases of PD, but negative in non-PD cases. A mean SBR value less than 3.0 and a delayed HMR value less than 1.7 indicated a Hoehn-Yahr stage 3 or 4 for PD, which is commonly regarded as a level appropriate for initiating DBS therapy. Our results indicate that performing both DaTscan and MIBG scintigraphy is useful for the evaluation of surgical intervention in PD.

Key words: DaTscan, ^{123}I -metaiodobenzyl guanidine scintigraphy, Parkinson's disease, deep brain stimulation

Introduction

^{123}I -ioflupane SPECT (DaTscan) is a radionuclide scanning that detects presynaptic dopamine neuronal dysfunction, and has been used as a diagnostic tool for degenerative parkinsonism.^{1–3)} Similarly, myocardial ^{123}I -metaiodobenzyl guanidine (MIBG) scintigraphy, which reflects the concentration of cardiac sympathetic nerve fibers, is also used for diagnosing Parkinson's disease (PD).^{4,5)} Both examinations are utilized during the differential diagnosis of parkinsonism. However, the differences and relationship between the conclusion or results of the two examinations are controversial.^{6–8)} Deep brain stimulation (DBS) is a well-known and established treatment for advanced PD.^{9,10)} A precise diagnosis is important for successful treatment with DBS, however, it is not uncommon that the final diagnosis will often change

to something other than PD, even in cases referred by neurology specialists.¹¹⁾ We examined patients with parkinsonism and analyzed the relationship between the results of these two scanning methods, and evaluated the importance of both examinations in determining the need for treatment with DBS.

Materials and Methods

Subjects: Patients suspected of striatonigral degeneration, including PD, were referred to our department, and were diagnosed by neurology specialists.

Imaging: All subjects received DaTscan and MIBG scintigraphy within 6 months, for diagnostic purposes.

DaTscan: The images were taken 3 h after injection of ^{123}I -ioflupane (167 MBq). The images were taken with a GCA-9300A SPECT system (TOSHIBA, Tokyo). Specific binding ratios (SBRs) from the DaTscan were calculated using specialized software (DaTView,

Aze Ltd., Tokyo). The SBR was estimated using a volume of interest technique that accounts for the partial volume effect by deriving the “specific” count concentration in the striatum from a measure of the total counts. The whole brain accumulation concentration was used as a reference.¹²⁾ The mean values of the left-right SBRs were calculated. Radiology specialists diagnosed the results.

Myocardial MIBG scintigraphy: After injection of MIBG (111 MBq), early phase images were taken after 15 min, and then delayed phase images were taken after 3 h and 15 min. The images were taken with an e.cam Signature 180 (Siemens AG, Munich, Germany). Early and delayed heart-to-mediastinum ratios (HMRs) were calculated using specialized software (smart MIBG, FUJIFILM RI Pharma, Tokyo).

The results were adjusted to standard values by using a phantom, in order to standardize the data to even out inter-institutional differences.¹³⁾

Statistical analyses: Using simple linear regression analysis, SBRs were compared with both early and delayed HMRs in patients with and without PD.

This study was reviewed and then approved by our institutional ethics committee.

Results

Participants

This prospective study included 24 patients (14 men and 10 women; mean age, 67.4 years; age range, 27–78 years). Table 1 lists characteristics of the patients, and Table 2 shows the distribution

Table 1 Patient's characteristics of 24 cases performed DaTscan and myocardial MIBG scintigraphy

	Age	Gender	Diagnosis	H-Y stage	DAT scan	Mean SBR	MIBG	Early HMR	Delayed HMR
1	74	F	PD tremor dominant	I	+	4.5	–	3.1	2.8
2	73	M	PD tremor dominant	I	+	2.5	+	2.1	1.8
3	73	M	PD tremor dominant	II	+	3.2	–	2.5	2.3
4	71	M	PD	III	+	2.8	+	1.4	1.3
5	73	M	PD	III	+	2.5	+	1.5	1.4
6	56	F	PD	III	+	2.5	+	1.8	1.3
7	67	F	PD	III	+	2.5	+	2.1	1.5
8	74	F	PD	III	+	1.8	+	1.5	1.2
9	72	M	PD	III	+	1.5	+	1.6	1.4
10	55	M	PD	III	+	1.4	+	1.3	1.1
11	71	F	PD	III	+	0.7	+	1.7	1.2
12	70	F	PD	III	+	0.5	+	1.4	1.2
13	72	F	PD	IV	+	2.8	+	1.5	1.2
14	70	F	PD	IV	+	1.3	+	1.6	1.2
15	69	M	PD	IV	+	1.0	+	1.8	1.4
16	71	M	iNPH		+	3.0	+	1.2	1.0
17	72	F	PSP-P		+	2.0	–	2.7	4.1
18	78	M	CBD		+	2.7	–	2.2	1.9
19	47	F	Hemi-moyamoya disease		+	4.2	–	2.1	2.3
20	77	M	Post-stroke tremor		+	5.0	–	2.2	2.0
21	68	M	iNPH		+	5.6	–	2.7	3.0
22	63	M	Vascular parkinsonism		–	4.1	–	3.1	3.7
23	75	M	iNPH		–	5.6	–	2.7	2.7
24	27	M	Cervical dystonia		–	7.6	–	2.6	3.0

CBD: corticobasal degeneration, F: female, HMR: heart-to-mediastinum ratio, iNPH: idiopathic normal pressure hydrocephalus, M: male, MIBG: ¹²³I-metaiodobenzyl guanidine, PD: Parkinson's disease, PSP-P: progressive supranuclear palsy-parkinsonism, SBR: specific binding ratio.

Table 2 Distribution and diagnoses of the cases divided by the results of DaTscan and MIBG scintigraphy

		Myocardial MIBG scintigraphy			
		Positive	Negative	Total	
DaTscan	Positive	14	7	21	
		PD 12	PD tremor dominant phenotype 2		
	PD tremor dominant phenotype 1	PSP-P 1			
Negative	0	iNPH 1	CBD 1		3
			Hemi-moyamoya disease 1		
			Post-stroke tremor 1		
Total	14		iNPH 1		24
			3		
			Cervical dystonia 1		
		iNPH 1			
		Vascular parkinsonism 1			

iNPH: idiopathic normal pressure hydrocephalus, MIBG: ¹²³I-metaiodobenzyl guanidine, PD: Parkinson's disease, PSP-P: progressive supranuclear palsy-parkinsonism.

of the patients and their diagnoses as divided by the results of the examinations. Fourteen patients were positive for PD in both examinations, and 13 were diagnosed with PD. One patient out of 13 was diagnosed with a tremor dominant phenotype of PD with Hoehn-Yahr (H-Y) stage 1. Seven out of 21 patients who were diagnosed positive for PD with the DaTscan were diagnosed negative with the MIBG scintigraphy. Two of them were tremor dominant

phenotypes of PD. There were no PD patients with genetic abnormalities. No patients were diagnosed with cardiac failure or myocardial infarction.

Figs. 1 and 2 show the relationship between mean values of the left-right SBR and HMR for each patient. In the PD cases, there was a significant relationship between the mean SBRs and HMRs (early: $P = 0.015$, delayed: $P < 0.001$), however, there was no significant relationship between the SBR and HMR values

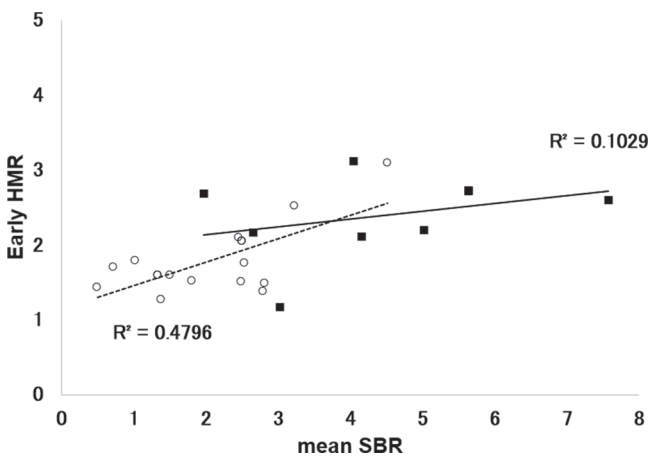


Fig. 1 Relationship between mean SBR and early HMR. There was a significant relationship between SBR and early HMR in PD cases ($P = 0.015$); however there was no significance in non-PD cases ($P = 1.99$). *Circles*: PD cases, *filled rectangles*: non-PD cases. HMR: heart-to-mediastinum ratio, PD: Parkinson's disease, SBR: specific binding ratio.

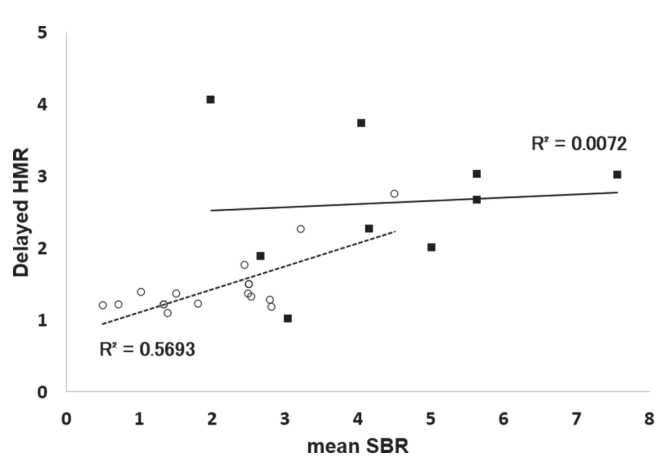


Fig. 2 Relationship between mean SBR and delayed HMR. There was a significant relationship between SBR and delayed HMR in PD cases ($P < 0.001$); however there was no significant difference in the non-PD cases ($P = 0.412$). *Circles*: PD cases, *filled rectangles*: non-PD cases. HMR: heart-to-mediastinum ratio, PD: Parkinson's disease, SBR: specific binding ratio.

in the non-PD cases (early; $P = 1.99$, delayed; $P = 0.412$) (Figs. 1, 2). The cases of H-Y stage 3 or 4 were distributed across mean SBR values less than 3.0 and mean delayed HMR values less than 1.7 (Fig. 3).

Figs. 4 and 5 show illustrative cases of the examinations. Fig. 4 shows a typical case of PD. Both examinations were positive, with a mean SBR value of 0.72, an early HMR of 1.40, and a delayed HMR value of 1.12. Fig. 5 indicates a variation of a case of progressive supranuclear palsy—parkinsonism (PSP-P). Lack of accumulation of ^{123}I -ioflupane in the striatum in DaTscan was observed, and the mean SBR was 1.99. However, the accumulation of heart was normal in MIBG scintigraphy, and

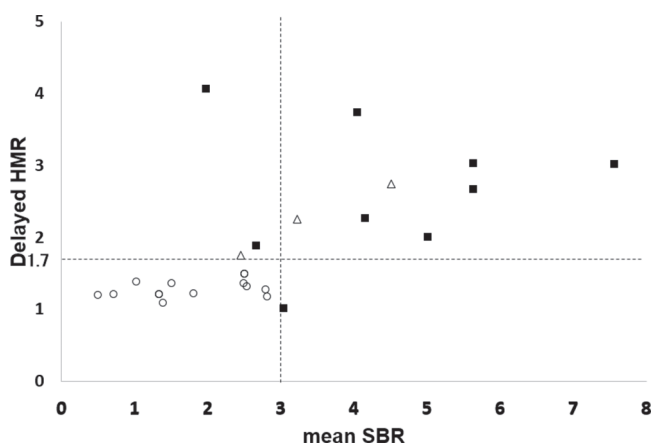


Fig. 3 Relationship between mean SBR and delayed HMR. The cutoff level for PD with 3 or 4 in the H-Y stage was 3.0 in the mean SBR, and 1.7 in the delayed HMR. *Circles*: PD cases, *triangle*: tremor dominant subtype of PD with stage 1 and 2 in H-Y scale, *filled rectangles*: non-PD cases. HMR: heart-to-mediastinum ratio, PD: Parkinson's disease, SBR: specific binding ratio.

the early and delayed HMRs were 2.21 and 2.74, respectively. There was a discrepancy between the two method results. Typical MRI findings of PSP (humming bird appearance and atrophy of midbrain tegmentum lesions) were observed.

Discussion

The DaTscan method reflects the number of dopaminergic neurons and reveals dopaminergic function. The examination is important for differentiating non-PD cases, referred to as SWEDDs (scans without evidence of dopaminergic deficit), from PD cases.^{14,15} The diagnosis was performed visually after identifying a laterality, or partial lack, of accumulation of ^{123}I -ioflupane. The criteria for positive diagnoses from DaTscans may be different depending on the implementation. SBR is one of the tools to digitalize the decrease of accumulation of ^{123}I -ioflupane within dopaminergic neurons. However, the measuring algorithm of SBR is not unified, and the manual detection of the range of interest (ROI) results in low reproducibility across different facilities. Some choose to set the ROI around part of the striatum.^{16,17} Similarly, the occipital lobe is often adopted as a reference ROI, however, the location and shape of the ROI varies.^{6,17} It is, therefore, difficult to set an exact universal cutoff value for PD. In this study, SBR was standardized with an algorithm using whole-brain uptake as a reference, which is commonly utilized in Japan, because it generates a simple ROI and stable data may be automatically obtained using specific software.^{12,13}

Myocardial MIBG scintigraphy reveals autonomic function, and was originally designed to evaluate cardiac function.¹⁸ Reduced accumulation of the

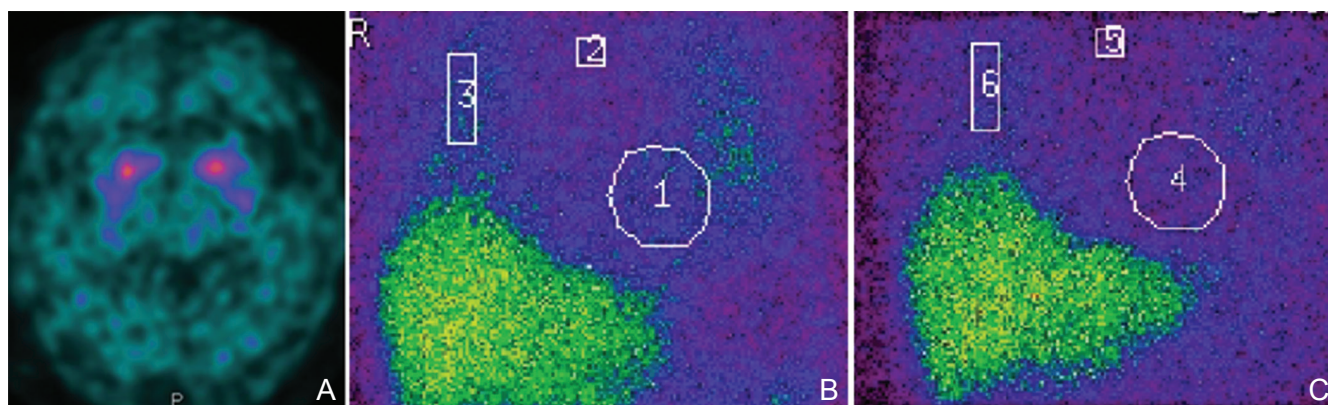


Fig. 4 Radiological illustrative case of PD. The patient is a 71-year-old woman with typical findings of PD. A: DaTscan; the striatal accumulation of the isotope decreased in both sides (SBR; right = 1.02, left = 0.43, average = 0.72). B, C: MIBG scintigraphy; the HMR decreased in both the early (B) and delayed (C) phase (HMR; early 1.40, delayed 1.12). Circle: ROI (region of interest) of the heart, HMR: heart-to-mediastinum ratio, PD: Parkinson's disease, rectangle 2, 5: ROI of the mediastinum, SBR: specific binding ratio.

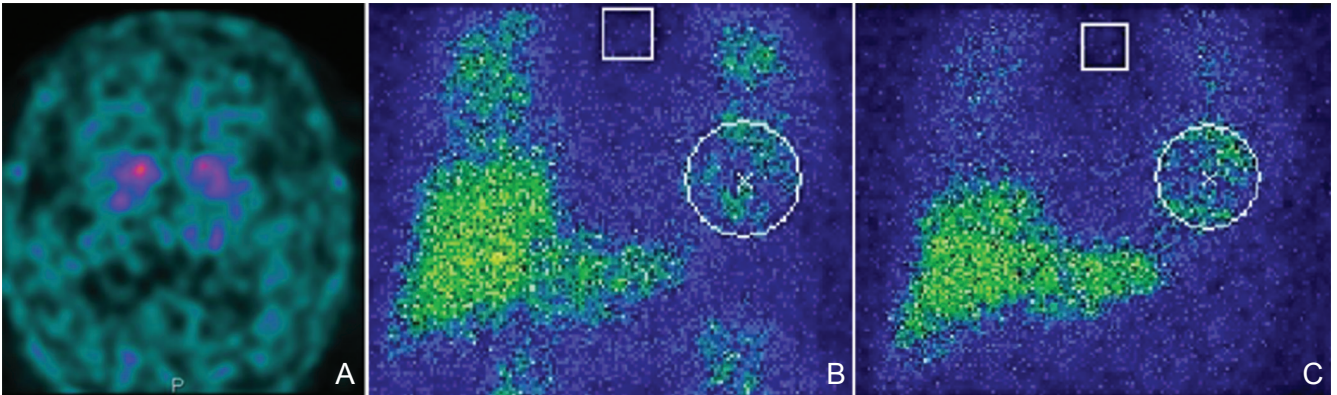


Fig. 5 Radiological illustrative case of non-PD. The patient is a 72-year-old woman with progressive supranuclear palsy-parkinsonism (PSP-P). **A:** DaTscan; the striatal accumulation of the isotope decreased in both sides (SBR; right = 1.68, left = 2.29, average = 1.99). **B, C:** MIBG scintigraphy; the HMR did not decrease in the early (**B**) or delayed (**C**) phase (HMR; early 2.21, delayed 2.74). Circle: ROI (region of interest) of the heart, HMR: heart-to-mediastinum ratio, PD: Parkinson's disease, rectangle: ROI of the mediastinum, SBR: specific binding ratio.

Table 3 Typical findings of DaTscan and MIBG scintigraphy in major degenerative diseases

	DaTscan	MIBG scintigraphy
Parkinson's disease	+	+*
Dementia with Lewy bodies	+	+
Multiple sclerosis	+	-
Progressive supranuclear palsy	+	-
Corticobasal degeneration	+	-
Essential tremor	-	-
Alzheimer's dementia	-	-

*Early stage disease, tremor dominant phenotype, and certain abnormal Parkinson's disease genotypes may show negative results. MIBG: ^{123}I -metaiodobenzyl guanidine.

isotope in the heart was found in patients with PD and subsequently applied as a differential diagnostic tool for parkinsonism.⁵⁾ The accumulation is reduced in most PD cases; however, it should be noted that some PD cases show general normal patterns, e.g., during the early stage of PD (particularly within the first year of the disease), and for tremor dominant phenotypes, along with some abnormal PD genotypes, such as PARK2 or PARK8.^{19–21)} The standardization of HMR is proceeding. Nakajima et al. developed a standardization method for HMR calibration to minimize institutional differences, and the present data were standardized using this method.¹³⁾ Generally, the diagnostic value of delayed HMRs is higher than that of early HMRs. The cutoff value for detecting PD in MIBG scintigraphy is determined by a meta-analysis, with a value of 1.77 in delayed HMRs.⁸⁾

The present data show that the cutoff value for the DaTscan SBR data from patients with H-Y stage 3 or 4 was 1.7, and 3.0 for the MIBG scintigraphy delayed HMR values. Consequently, if patients are not of the tremor dominant type, or in an early stage of PD, or have specific gene abnormalities, and their values are not within the cutoff levels, their diagnoses should be reconfirmed before surgical treatment. Both dopaminergic and autonomic functions are impaired in patients with PD. The typical results of DaTscan and MIBG scintigraphy in major degenerative diseases are summarized in Table 3. The sensitivity of DaTscan and MIBG scintigraphy is 95% and 80%, respectively, and the specificities are 21% and 75%, respectively.²²⁾ DaTscan has more false positives than the MIBG scintigraphy method, and the MIBG scintigraphy has more false negatives than the DaTscan method. The results of our study indicated that the final diagnosis might not be PD if the DaTscan is positive and the MIBG scintigraphy is negative. Some studies have compared the relationship between DaTscan and myocardial MIBG scintigraphy results. Specifically, Chiaravalloti et al. showed no statistical relationships between the striatal uptake found with the DaTscan and the early or delayed HMRs in myocardial MIBG in patients with PD.⁶⁾ Additionally, Spiegel et al. examined putamen uptake in DaTscan and myocardial MIBG uptake in patients with PD, and found that the myocardial MIBG uptake values correlated significantly with putamen uptake values from the DaTscan at each H-Y stage.¹⁶⁾ Cases of dementia with Lewy bodies, which show similar radiological characteristics as PD, show a positive correlation between SBR and HMR values after the evaluations.⁷⁾ Each study used occipital uptake as a reference, however the evaluation methods were different. Thus, whether the dopaminergic and

autonomic functions in PD are correlated remains controversial. We found correlations between the SBRs and HMRs as measured by reliable methods. The positive correlation means that both SBR and HMR are getting decrease as the disease progresses. If only one value decreases in patients considering DBS in the case without gene abnormality, the diagnosis should be re-considered. For these reasons, this study is significant from the perspective of decision of DBS indication for PD.

Indication of DBS therapy should be decided considering the neurological symptoms and past history. However, clinical overdiagnosis of PD is not rare.^{14,15} Nowadays, two radionuclide scanning methods are available. The combination of these radiological scanning methods is useful for evaluating the need for DBS treatment. To our knowledge, our study is the first showing the relationship between SBR and HMR results for the purpose of surgical intervention.

Conclusion

There were significant correlations between the mean SBRs from the DaTscan and the early/delayed HMRs from the MIBG scintigraphy. Cases with SBR values less than 3.0 and delayed HMR values less than 1.7 indicated PD with H-Y stages 3 or 4, which is the common indication of DBS. Although, the number of patients in this study is small, we believe that the combination of DaTscan and MIBG scintigraphy methods is necessary to evaluate the need for DBS treatment before invasive surgery, and may affect the detection of non-PD cases, including SWEDDs. Further research with a greater number of participants will be necessary to validate our results.

Conflicts of Interest Disclosure

There are no potential conflicts of interest, or direct financial and funding sources associated with this research.

References

- 1) Asenbaum S, Pirker W, Angelberger P, Bencsits G, Pruckmayer M, Brücke T: [123I]beta-CIT and SPECT in essential tremor and Parkinson's disease. *J Neural Transm (Vienna)* 105: 1213–1228, 1998
- 2) Brücke T, Asenbaum S, Pirker W, Djamshidian S, Wenger S, Wöber C, Müller C, Podreka I: Measurement of the dopaminergic degeneration in Parkinson's disease with [123I] beta-CIT and SPECT. Correlation with clinical findings and comparison with multiple system atrophy and progressive supranuclear palsy. *J Neural Transm Suppl* 50: 9–24, 1997
- 3) Tatsch K, Poepperl G: Nigrostriatal dopamine terminal imaging with dopamine transporter SPECT: an update. *J Nucl Med* 54: 1331–1338, 2013
- 4) Hakusui S, Yasuda T, Yanagi T, Tohyama J, Hasegawa Y, Koike Y, Hirayama M, Takahashi A: A radiological analysis of heart sympathetic functions with meta-[123I]iodobenzylguanidine in neurological patients with autonomic failure. *J Auton Nerv Syst* 49: 81–84, 1994
- 5) Yoshita M, Hayashi M, Hirai S: Decreased myocardial accumulation of 123I-meta-iodobenzyl guanidine in Parkinson's disease. *Nucl Med Commun* 19: 137–142, 1998
- 6) Chiaravalloti A, Stefani A, Di Biagio D, Pierantozzi M, Tavolozza M, Di Pietro B, Stanzione P, Schillaci O: Cardiac sympathetic denervation is not related to nigrostriatal degeneration in Parkinson's disease. *Ann Nucl Med* 27: 444–451, 2013
- 7) Camacho V, Marquí M, Lleó A, Alvés L, Artigas C, Flotats A, Duch J, Blesa R, Gómez-Isla T, Carrió I, Estorch M: Cardiac sympathetic impairment parallels nigrostriatal degeneration in Probable Dementia with Lewy Bodies. *Q J Nucl Med Mol Imaging* 55: 476–483, 2011
- 8) King AE, Mintz J, Royall DR: Meta-analysis of 123I-MIBG cardiac scintigraphy for the diagnosis of Lewy body-related disorders. *Mov Disord* 26: 1218–1224, 2011
- 9) Krack P, Batir A, Van Blercom N, Chabardes S, Fraix V, Ardouin C, Koudsie A, Limousin PD, Benazzouz A, LeBas JF, Benabid AL, Pollak P: Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. *N Engl J Med* 349: 1925–1934, 2003
- 10) Deuschl G, Schade-Brittinger C, Krack P, Volkmann J, Schäfer H, Bötzel K, Daniels C, Deuschländer A, Dillmann U, Eisner W, Gruber D, Hamel W, Herzog J, Hilker R, Klebe S, Kloss M, Koy J, Krause M, Kupsch A, Lorenz D, Lorenzl S, Mehdorn HM, Moringlane JR, Oertel W, Pinsker MO, Reichmann H, Reuss A, Schneider GH, Schnitzler A, Steude U, Sturm V, Timmermann L, Tronnier V, Trottenberg T, Wojtecki L, Wolf E, Poewe W, Voges J; German Parkinson Study Group, Neurostimulation Section: A randomized trial of deep-brain stimulation for Parkinson's disease. *N Engl J Med* 355: 896–908, 2006
- 11) Hughes AJ, Daniel SE, Kilford L, Lees AJ: Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatr* 55: 181–184, 1992
- 12) Tossici-Bolt L, Hoffmann SM, Kemp PM, Mehta RL, Fleming JS: Quantification of [123I]FP-CIT SPECT brain images: an accurate technique for measurement of the specific binding ratio. *Eur J Nucl Med Mol Imaging* 33: 1491–1499, 2006
- 13) Nakajima K, Okuda K, Yoshimura M, Matsuo S, Wakabayashi H, Imanishi Y, Kinuya S: Multicenter cross-calibration of I-123 metaiodobenzylguanidine heart-to-mediastinum ratios to overcome camera-collimator variations. *J Nucl Cardiol* 21: 970–978, 2014

- 14) Utiumi MA, Felício AC, Borges CR, Braatz VL, Rezende SA, Munhoz RP, Bressan RA, Ferraz HB, Teive HA: Dopamine transporter imaging in clinically unclear cases of parkinsonism and the importance of scans without evidence of dopaminergic deficit (SWEDDs). *Arq Neuropsiquiatr* 70: 667–673, 2012
- 15) Marshall VL, Reininger CB, Marquardt M, Patterson J, Hadley DM, Oertel WH, Benamer HT, Kemp P, Burn D, Tolosa E, Kulisevsky J, Cunha L, Costa D, Booij J, Tatsch K, Chaudhuri KR, Ulm G, Pogarell O, Höffken H, Gerstner A, Grosset DG: Parkinson's disease is overdiagnosed clinically at baseline in diagnostically uncertain cases: a 3-year European multicenter study with repeat [123I]FP-CIT SPECT. *Mov Disord* 24: 500–508, 2009
- 16) Spiegel J, Hellwig D, Jost WH, Farmakis G, Samnick S, Fassbender K, Kirsch CM, Dillmann U: Cerebral and Extracranial Neurodegeneration are Strongly Coupled in Parkinson's Disease. *Open Neurol J* 1: 1–4, 2007
- 17) Walker Z, Costa DC, Walker RW, Shaw K, Gacinovic S, Stevens T, Livingston G, Ince P, McKeith IG, Katona CL: Differentiation of dementia with Lewy bodies from Alzheimer's disease using a dopaminergic presynaptic ligand. *J Neurol Neurosurg Psychiatr* 73: 134–140, 2002
- 18) Kawai T, Yamada T, Tamaki S, Morita T, Furukawa Y, Iwasaki Y, Kawasaki M, Kikuchi A, Kondo T, Takahashi S, Ishimi M, Hakui H, Ozaki T, Sato Y, Seo M, Sakata Y, Fukunami M: Usefulness of cardiac meta-iodobenzylguanidine imaging to identify patients with chronic heart failure and left ventricular ejection fraction <35% at low risk for sudden cardiac death. *Am J Cardiol* 115: 1549–1554, 2015
- 19) Tomiyama H, Li Y, Funayama M, Hasegawa K, Yoshino H, Kubo S, Sato K, Hattori T, Lu CS, Inzelberg R, Djaldetti R, Melamed E, Amouri R, Gouider-Khouja N, Hentati F, Hatano Y, Wang M, Imamichi Y, Mizoguchi K, Miyajima H, Obata F, Toda T, Farrer MJ, Mizuno Y, Hattori N: Clinico-genetic study of mutations in LRRK2 exon 41 in Parkinson's disease patients from 18 countries. *Mov Disord* 21: 1102–1108, 2006
- 20) Orimo S, Amino T, Yokochi M, Kojo T, Uchihara T, Takahashi A, Wakabayashi K, Takahashi H, Hattori N, Mizuno Y: Preserved cardiac sympathetic nerve accounts for normal cardiac uptake of MIBG in PARK2. *Mov Disord* 20: 1350–1353, 2005
- 21) Spiegel J, Hellwig D, Samnick S, Jost W, Möllers MO, Fassbender K, Kirsch CM, Dillmann U: Striatal FP-CIT uptake differs in the subtypes of early Parkinson's disease. *J Neural Transm (Vienna)* 114: 331–335, 2007
- 22) Treglia G, Cason E, Cortelli P, Gabellini A, Liguori R, Bagnato A, Giordano A, Fagioli G: Iodine-123 metaiodobenzylguanidine scintigraphy and iodine-123 ioflupane single photon emission computed tomography in Lewy body diseases: complementary or alternative techniques? *J Neuroimaging* 24: 149–154, 2014

Address reprint requests to: Takashi Asahi, MD, PhD,
Department of Neurosurgery, University of Toyama,
2630 Sugitani, Toyama 930-0194, Japan.
e-mail: takashi-tym@umin.ac.jp