Comparative Nigrostriatal Dopaminergic Imaging with Iodine-123-βCIT-FP/SPECT and Fluorine-18-FDOPA/PET

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SPECT imaging of the dopamine transporter is now an alternative to PET in the quantification of nigrostriatal dopaminergic function. We compared [^{123}I]βCIT-FP/SPECT and [^{18}F]FDOPA/PET in the assessment of nigrostriatal dopaminergic function in Parkinson's disease (PD) and normal aging. **Methods:** We studied 12 mildly affected PD patients (mean age: 61.0 ± 13.2 yr; H&Y Stage I-II) with both [^{123}I]βCIT-FP and [^{18}F]FDOPA. Fifteen normal volunteers (mean age: 45.5 ± 22.1 yr) served as controls for both tracers. We measured the striato-occipital ratio (SOR) for both tracers at approximately 100 min postinjection. **Results:** We found a highly significant correlation between SOR measures obtained for both tracers ($r = 0.79$, $p < 0.0001$). In normal volunteers a significant age-related decline in striatal uptake was noted with [^{123}I]βCIT-FP ($r = -0.56$, $p < 0.04$) but not with [^{18}F]FDOPA. SOR values for both tracers discriminated PD patients from controls with comparable accuracy ($F[1,25] = 52.1$ and 53.0, $p < 0.0001$ for [^{123}I]βCIT-FP and [^{18}F]FDOPA, respectively). UPDRS motor ratings correlated with SOR values obtained by both imaging techniques ($r = -0.69$ and -0.60, $p < 0.04$ for [^{123}I]βCIT-FP and [^{18}F]FDOPA, respectively). **Conclusion:** These results indicate that [^{123}I]βCIT-FP/SPECT can provide quantitative descriptors of presynaptic dopaminergic function comparable to those obtained with [^{18}F]FDOPA/PET.

Key Words: dopamine transporter; SPECT; PET; Parkinson's disease

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6-[^{18}F]fluoro-L-dopa (FDOPA) has been used with PET for the quantitative assessment of presynaptic nigrostriatal dopaminergic function in life. Specifically, FDOPA/PET has become a useful diagnostic imaging tool for the early diagnosis of Parkinson's disease (PD) (*1–5*) and for the objective assessment of disease severity in this condition (*3–5*). Although simple noninvasive data analytical strategies have been developed, the widespread application of FDOPA/PET in clinical assessment has been limited by the availability of PET instruments and the radiochemical demands of FDOPA synthesis (*1,3*).

The cocaine analog, 2β-carbomethyl-3β-(4-idophenyl)tropane (βCIT), has a high affinity for the dopamine (DA) transporter. When labeled with ^{123}I, βCIT is a useful radiotracer for imaging the striatal DA transporter with SPECT (*6,7*). This compound is characterized by high striatal uptake with slow binding kinetics, reaching equilibrium between 20 and 30 hr after injection (*8*). Striatal [^{123}I]βCIT binding has been found to correlate with subject age in normal volunteers scanned with this tracer (*9*). Moreover, PD patients were found to have significantly lower striatal binding than normal controls (*6*) which also correlated with quantitative measures of disease severity (*10*).

In spite of these attributes, [^{123}I]βCIT/SPECT imaging has the disadvantage of requiring a second day for imaging and potentially prolonged dynamic acquisitions for kinetic analysis (*6,7*). By contrast, the N-ω-fluoroalkyl analogs of βCIT (*11,12*), particularly the fluoropropyl methyl ester (βCIT-FP), has faster uptake than βCIT. After injection of [^{123}I]βCIT-FP, the striatal-to-occipital ratio counts plateaus at approximately 100 min (*13*). Given the comparable kinetics of this compound, βCIT-FP/SPECT may provide a simple quantitative imaging alternative to FDOPA/PET in the study of the nigrostriatal dopaminergic system in PD and normal aging. To examine this possibility, we studied 15 normal subjects and 12 PD patients with both FDOPA/PET and βCIT-FP/SPECT. We assessed the comparative power of both imaging techniques in the early stage diagnosis of PD and in the correlation of dopaminergic function with clinical severity and subject age.

MATERIALS AND METHODS

Subjects

We recruited 12 classical PD patients without dementia (9 men, 3 women; mean age 61.0 ± 13.2 yr) from the Movement Disorders Services of North Shore University Hospital and New York Hospital-Cornell Medical Center. A diagnosis of PD was made if the patient had "pure" parkinsonism without a history of known causative factors such as encephalitis or neuroleptic treatment; did not have early dementia, supranuclear gaze palsy or ataxia and did have a convincing response to levodopa. In all patients, family history was negative for neurodegenerative illnesses. This group was selected with mild clinical involvement [Hoehn and Yahr Stages I and II (*14*) see Table 1]. Permission was obtained from the Institutional Review Board of North Shore University Hospital to perform the studies. Written consent for all subjects was obtained after a detailed explanation of the scanning procedures.

We also recruited 15 normal subjects (11 men, 4 women; mean age 45.5 ± 22.1 yr) by soliciting hospital personnel of North Shore University Hospital and the spouses of the PD patients in local support groups. The following exclusion criteria were used: (a) past history of neurological or psychiatric illness, (b) prior exposure to neuroleptic agents or drug use, (c) past medical history of hypertension, cardiovascular disease and diabetes mellitus and (d) abnormal neurological examination.

FDOPA/PET Imaging

All patients and normal volunteers fasted overnight before PET scanning. All antiparkinsonian medications were discontinued at least 12 hr before the PET studies. At the time of the PET study, all PD patients were rated quantitatively according to the Hoehn and Yahr (H&R) Scale (*14*) and the Unified Parkinson Disease Rating

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Scale (UPDRS 3.0) (*15*). PET studies were performed using a whole-body, high-resolution PET scanner (Advance, General Electric Medical Systems, Milwaukee, WI). This 18-ring bismuth germanate tomograph produces 35 slices with 4.2 mm resolution in all directions (FWHM). The performance characteristics of this instrument have been described elsewhere (*16*).

Subjects were positioned in the scanner in a Laitinen steroadaptor with three- dimensional laser alignment (*17*). The gantry angle of the tomograph was adjusted to be parallel to the orbitomeatal line. All studies were performed with eyes open in a dimly-lit room and minimal auditory stimulation. FDOPA was produced according to the radiochemical synthesis of Luxen et al. (*18*) and was >95% radiochemically pure (specific activity approximately 400 mCi/mmole). All subjects received 200 mg carbidopa 1.5 hr before the study to inhibit decarboxylation. 185–370 MBq (5–10 mCi) of FDOPA in 25 ml saline was injected into an antecubital vein over 45 sec with an automated infusion pump. Emission scan data were acquired between 40 and 100 min postinjection. PET reconstructions were also corrected for random coincidences, electronic deadtime and scatter effects. Attenuation correction was made using orbiting ^{68}Ge rod sources. The plasma FDOPA time-activity curve was determined by radial arterial blood sampling with a population-derived metabolite correction (*3*).

Region of interest (ROI) analysis was performed on 256 × 256 PET reconstructions. ROIs were identified in the striatum and occipital cortex by visual inspection with reference to coplanar MR images. Elliptical ROIs were placed interactively on composite (40–100 min) PET brain slices (slice thickness 15.2 mm) to outline the whole striatum (mean 3.7 cm^2). Irregular occipital ROIs (12–18 cm^2) were also defined on the same composite slices. Occipital counting rates were assumed to represent background activity referable to nonspecific FDOPA uptake in extrastriatal tissues and to untrapped metabolites. Occipital activity concentrations were subtracted from striatal ^{18}F-activity concentrations measured in each of seven 8-min scans, acquired approximately between 40 and 100 min postinjection to obtain the time profile for specific striatal activity for FDOPA.

Kinetic measures for striatal FDOPA uptake were calculated graphically by the multiple time graphical approach (MTGA) (*19*) using the time course of radioactivity in the whole striatum and the plasma FDOPA input function (*3*). The time course of specific (background subtracted) striatal concentration divided by plasma FDOPA activity was plotted against the ratio of the plasma time-integral to the plasma FDOPA concentration. In the MTGA, the slope of the this line represents the rate constant of FDOPA uptake into the striatum (K_i^{FD}). In all patient and control scans, we additionally calculated the ratio of target to occipital activity (SOR^{FD}) by dividing counting rates in each ROI by occipital counting rate measured in the last 8 min scan (approximately 90–100 min postinjection).

βCIT-FP/SPECT

The mean interval between the PET and SPECT imaging sessions was 29.2 ± 25.4 days. Two days before SPECT imaging, all subjects received potassium iodide orally to block thyroid uptake of free radioactive iodine. For PD patients, deprenyl was withdrawn 2 days before the study, while other antiparkinsonian medication, including L-dopa, were continued (*7*). βCIT-FP was produced from the corresponding trimethylstannyl precursor as described previously (*11,12*) and was >95% radiochemically pure (specific activity > 500 mCi/mmole); 185–333 MBq (5–9 mCi) of this tracer were injected intravenously as described above. SPECT imaging was performed on a tomograph with a resolution of 7.7 mm FWHM measured by a point source in the air. To assume compatibility with the PET studies, SPECT scanning was conducted using the Laitinen stereoadaptor with settings identical to those used in the PET studies. Tomographic images were acquired for 60-min beginning approximately 70 min after the injection. In eight subjects, a second 60 min scan was obtained beginning approximately 220 min postinjection. Images were acquired with the energy window set at 159 keV, reconstructed with a ramp filter and displayed in 128 × 128 matrix (pixel size 2.8 × 2.8 mm with an interslice distance of 2.8 mm). Attenuation correction was performed with reslicing parallel to the orbitomeatal line. We determined striatal and occipital ROIs of size and configuration analogous to those used in the PET studies. To reduce partial volume effects, 55% of pixels with the highest counts were used to determine the striatal concentration of ^{123}I activity within each ROI (*20*). We calculated the striatal-occipital ratio ($SOR^{\beta CIT}$) in each subject by dividing striatal by occipital counting rates.

Statistical Analysis

βCIT-FP/SPECT—Scan Stability. In the eight subjects who underwent two sequential βCIT-FP/SPECT scans, we compared the $SOR^{\beta CIT}$ values for the first and second scans using Student's t-test.

Normal Aging. In the normal subjects, we correlated subject age with the mean of left and right values for each parameter (K_i^{FD}, SOR^{FD} and $SOR^{\beta CIT}$) by computing Pearson product-moment correlation coefficients.

Disease Discrimination. Discriminant analysis for PD and normal subjects was performed for each parameter (K_i^{FD}, SOR^{FD} and $SOR^{\beta CIT}$) using a stepwise procedure with the *F*-test associated with Wilk's λ (*21*). We used the mean of left and right striatal values for the normal control subjects. For the PD patients, we used striatal values for the side contralateral to the more affected limbs. Because of potential aging effects with βCIT and related tracers (*9*) we corrected $SOR^{\beta CIT}$ by dividing the measured values by normal values calculated for the subject's age (*10*). Discriminant analysis for the age-corrected values [$SOR^{\beta CIT}$(COR)] was performed in the same manner as described above.

Disease Severity Assessment. In the PD group, we independently correlated mean values for striatal K_i^{FD}, SOR^{FD}, $SOR^{\beta CIT}$ and $SOR^{\beta CIT}$(COR) with off-state UPDRS composite motor scores by computing Pearson product-moment correlation coefficients.

Correlation between FDOPA/PET and βCIT-FP/SPECT. We correlated individual left and right striatal K_i^{FD} and SOR^{FD} values with corresponding striatal $SOR^{\beta CIT}$ values for all subjects using

TABLE 1
Parkinson's Disease Patients

Patient no.	Age	Sex	Disease duration (yr)	H&Y*	UPDRS ratings† BK	T	R	Composite
1	44	F	4	1	1	0	1	2
2	46	M	3	1	1	3	1	5
3	54	M	5	1	4	1	1	8
4	71	M	5	1	1	1	2	4
5	72	M	1.5	1	2	0	1	3
6	69	M	10	1	2	1	0	3
7	72	M	1.5	1	0	0	1	2
8	59	F	8	2	5	0	1	8
9	42	F	10	2	5	1	1	9
10	80	M	9	2	1	1	4	9
11	51	M	9	2	3	4	5	15
12	70	M	12	2	7	1	2	12

*Hoehn and Yahr score in the "off" state.

†Summed United Parkinson's Disease Rating Scale scores for bradykinesia (BK), tremor (T) and rigidity (R) in the affected limbs.

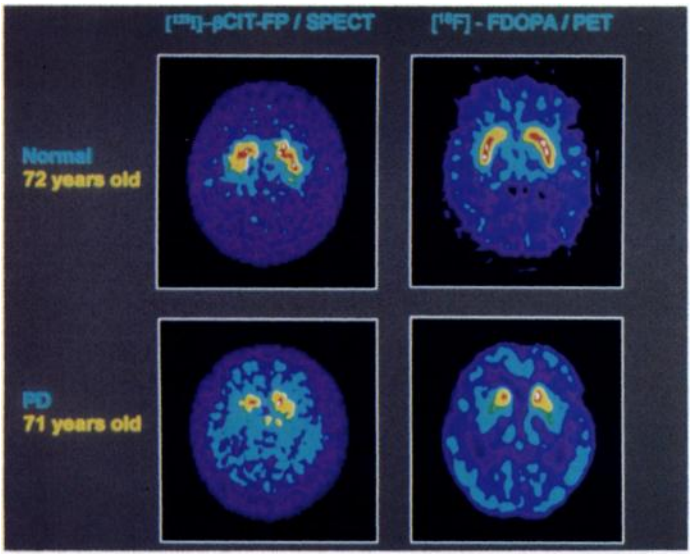

FIGURE 1. Left: βCIT-FP SPECT images from a 72-yr-old normal volunteer (top) and a 71-yr-old patient with H&Y Stage I PD (bottom). Right: FDOPA PET images from the same subjects. In the parkinsonian patient, both PET and SPECT show a comparable 55% reduction in striatal radiotracer uptake localized primarily to the left putamen.

Pearson product-moment correlation analysis. These correlations were also computed separately in the normal volunteer and PD patient subgroups.

RESULTS

βCIT-FP/SPECT. Comparative FDOPA/PET and βCIT-FP/SPECT images in a normal volunteer and a H&Y Stage I patient are given in Figure 1. The mean absolute difference between $SOR^{\beta CIT}$ values calculated in the initial and delayed scans was 5% ± 4% (range: 0%-13%). This difference was not statistically significant.

Normal Aging. We found a significant age-dependent decline in $SOR^{\beta CIT}$ of approximately 3.3% per decade ($r = -0.56$, $p < 0.04$; Fig. 2). Neither K_i^{FD} nor SOR^{FD} values correlated with age ($r = 0.08$, and 0.24, respectively; $p > 0.40$).

Disease Discrimination. Mean values of K_i^{FD}, SOR^{FD}, $SOR^{\beta CIT}$ and $SOR^{\beta CIT}$(COR) for normals and PD patients are given in Table 2. These parameters significantly discriminated the two subject groups with comparable accuracy ($F[1,25] = 42.2, 53.0, 58.9$ and 52.1, $p < 0.0001$ for K_i^{FD}, SOR^{FD}, $SOR^{\beta CIT}$ and $SOR^{\beta CIT}$(COR), respectively). Likewise, when the analysis was restricted to H&Y Stage I patients and normals comparable discrimination was achieved with both tracer methods ($F[1,20] = 21.1, 26.6, 32.9, 31.7$; $p < 0.0005$ for K_i^{FD}, SOR^{FD}, $SOR^{\beta CIT}$ and $SOR^{\beta CIT}$(COR), respectively). A discriminant line based on SOR correctly classified 26 out of 27 (96%) subjects with both techniques (Fig. 3).

TABLE 2
Striatal K_i^{FD}, SOR^{FD}, $SOR^{\beta CIT}$ and $SOR^{\beta CIT}$ (COR)

		K_i^{FD}	SOR^{FD}	$SOR^{\beta CIT}$	$SOR^{\beta CIT}$ (COR)
Normal (n = 15)	Mean	0.0180	2.27	3.78	100%
	s.d.	0.0046	0.27	0.58	12.6%
	COV	25%	12%	15%	13%
PD (n = 12)	Mean	0.0095	1.70	2.33	65.9%
	s.d.	0.0027	0.18	0.52	15.9%
	COV	28%	11%	22%	24%

PD = Parkinson's disease; s.d. = standard deviation; COV = coefficient of variation defined as (s.d./mean) × 100 (%).
K_i^{FD} is expressed as ml/min/g; SOR values are unitless.
See text for definitions of K_i^{FD}, SOR^{FD}, $SOR^{\beta CIT}$ and $SOR^{\beta CIT}$ (COR).

Disease Severity Assessment. $SOR^{\beta CIT}$ correlated significantly with composite UPDRS scores with accuracy comparable to SOR^{FD} and K_i^{FD} ($SOR^{\beta CIT}$: $r = -0.69$, $p < 0.02$; SOR^{FD} and K_i^{FD}: $r = -0.60$, $p < 0.04$; Fig. 4). $SOR^{\beta CIT}$(COR) correlation with UPDRS ratings was comparable with uncorrected $SOR^{\beta CIT}$ values ($r = -0.67$, $p < 0.02$).

Correlation between FDOPA/PET and βCIT-FP/SPECT. In the combined population of normals and PD patients, $SOR^{\beta CIT}$ correlated significantly both with K_i^{FD} and SOR^{FD} ($r = 0.74$, $p < 0.0001$; $r = 0.77$, $p < 0.0001$, respectively; Fig. 5). In the PD patient subgroup, $SOR^{\beta CIT}$ correlated significantly both with K_i^{FD} and SOR^{FD} ($r = 0.73$, $p < 0.0001$; $r = 0.72$, $p < 0.0001$, respectively). In the normal volunteer subgroup, however, there was no significant correlation between $SOR^{\beta CIT}$ and K_i^{FD} or SOR^{FD} values ($|r| < 0.24$, $p > 0.2$ for both correlations).

DISCUSSION

In this study, we demonstrated the comparability of FDOPA/PET and βCIT-FP/SPECT as quantitative imaging markers of presynaptic nigrostriatal dopaminergic function in parkinsonism. We observed that a simple SPECT measure of striatal dopamine transporter binding, $SOR^{\beta CIT}$, correlated significantly with analogous FDOPA/PET parameters. We found that both PET and SPECT methods discriminated early stage PD patients from normals with similar sensitivity. Additionally, the two techniques were found to be fully comparable in their capacity to quantify the extent of nigrostriatal dysfunction in parkinsonism. Thus, βCIT-FP/SPECT imaging may be a useful

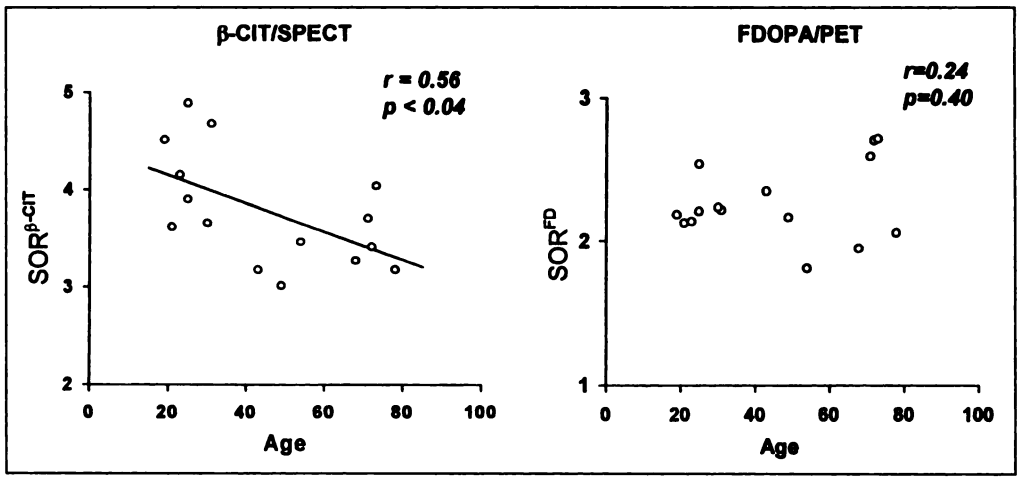

FIGURE 2. Respective correlations of the striato-occipital ratio (SOR) for βCIT-FP (left) and FDOPA (right) with subject age in 15 normal volunteers. A significant aging effect of 3.3% per decade was found with βCIT-FP/SPECT but not with FDOPA/PET.

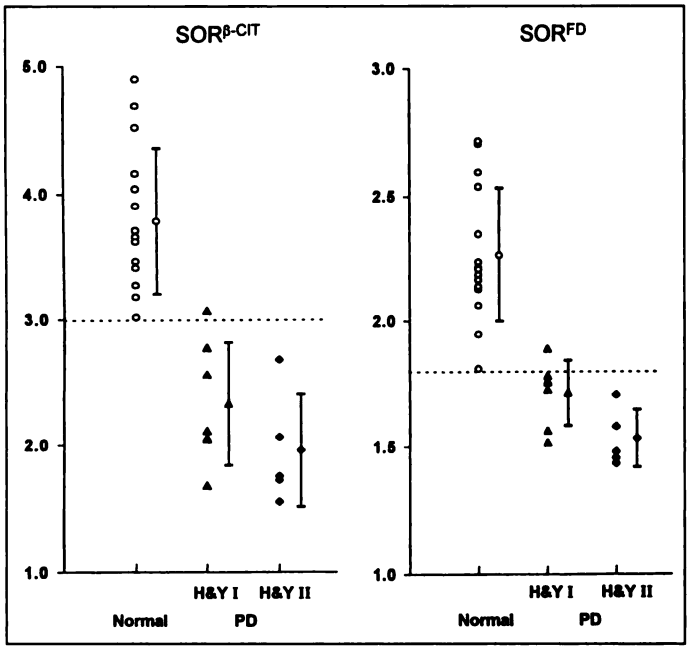

FIGURE 3. Discriminant analysis of early stage PD patients and normals using the striato-occipital ratio (SOR) for βCIT-FP (left) and FDOPA (right). Significant between-group separation was obtained with both tracers ($p < 0.0001$). A discriminant line (dots) based on SOR for each tracer correctly identified all normals and 11 out of 12 PD patients (▲ and ◆ refer to H&Y Stage I and II patients, respectively).

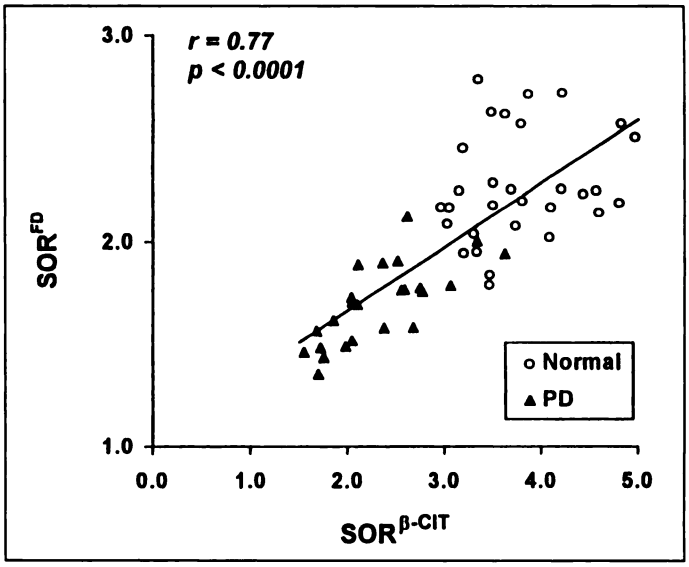

FIGURE 5. Correlation between the striato-occipital ratios (SORs) for βCIT-FP and FDOPA in normal subjects (○) and PD patients (▲). A highly significant ($p < 0.0001$) within subject correlation was evident for the two tracers in the whole population and in the PD patient subgroup. SOR values for the two tracers were not significantly correlated in the normal volunteer subgroup.

alternative to FDOPA/PET in a number of relevant clinical-research settings.

We found that nigrostriatal dopaminergic defects in early stage PD patients can be accurately discerned with both βCIT-FP/SPECT and FDOPA/PET. In accordance with our previous studies with FDOPA/PET (*2–4*), SOR^{FD} provided a straightforward, readily obtained imaging parameter for discriminating mildly affected patients from normal controls. Indeed, kinetic determinations of striatal K_i^{FD} appear not to be necessary for purposes of early stage diagnosis. Our findings with βCIT-FP/SPECT reveal that an analogous static SPECT measure, $SOR^{\beta CIT}$, can discriminate early stage patients with accuracy comparable to SOR^{FD}. Because of the relatively low resolution of our SPECT system, we compared the PET and SPECT technique using measurements obtained from the *whole striatum*, although superior discrimination may be achieved with putamen values alone (*2,22,23*). It is possible that comparatively similar improvements in discrimination can be achieved with the development of high resolution SPECT systems (FWHM < 5 mm) which can allow for accurate quantification of βCIT-FP binding within striatal subnuclei. Nonetheless, in spite of the current limitations, we found that whole striatal measures proved to be effective in discriminating PD patients at the earliest clinical stages of disease.

We also found that $SOR^{\beta CIT}$ was comparable to both static and dynamic PET measures of striatal FDOPA uptake. In our previous studies, we observed that graphically estimated striatal FDOPA uptake rate constants (K_i^{FD}) correlated significantly with quantitative clinical motor ratings (*3–5*) as well as with kinetic PET estimates of striatal dopa decarboxylase activity (DDC) (*4,24*). By contrast, in those investigations, SOR^{FD} values did not correlate with independent disease severity measures. In the current study, conducted using a PET instrument of higher resolution and sensitivity, we found a significant correlation between SOR^{FD} and UPDRS motor ratings over a relatively narrow range of clinical disability. It is likely that measurement errors in the final scan attributable to low counting rates were reduced on the newer high sensitivity instrument, providing improved estimates of SOR^{FD} and more accurate clinical correlations. The observation that comparable clinical correlations can be achieved with SOR values obtained with either FDOPA/PET or βCIT-FP/SPECT indicates the potential for the use of simple noninvasive methods in the quantification of dopaminergic defects by functional imaging. The current studies also suggest that longitudinal imaging studies of disease progression in parkinsonism can be effectively conducted with βCIT-FP/SPECT.

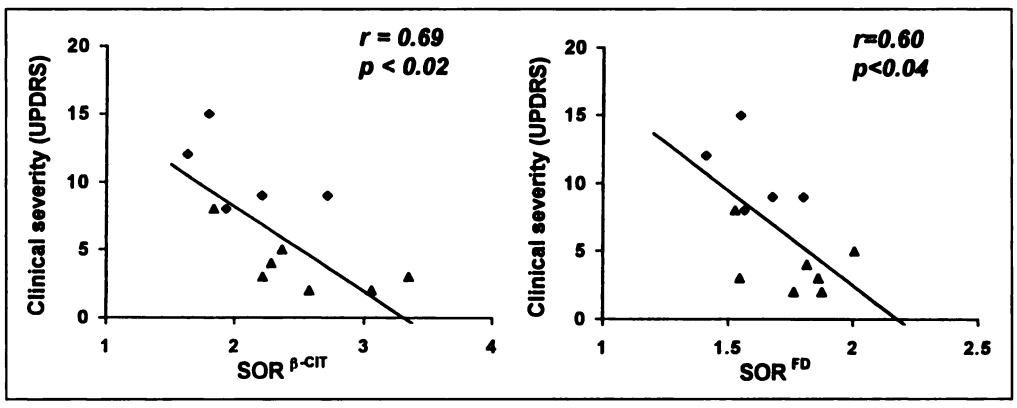

FIGURE 4. Correlations between clinical severity ratings measured according to the Unified Parkinson Disease Rating Scale (UPDRS) and striato-occipital ratios (SOR) for βCIT-FP (left) and FDOPA (right). Comparably significant ($p < 0.05$) clinical correlations with SOR were found with both tracers (▲ and ◆ refer to Hoehn and Yahr Stage I and II patients, respectively).

Our observations are based on measurements of $SOR^{\beta CIT}$ obtained in single 60- min SPECT scans beginning approximately 70 min postinjection. We found no significant difference in $SOR^{\beta CIT}$ values obtained in this time frame with those obtained in a second acquisition approximately 4-hr postinjection. This finding is compatible with dynamic human SPECT studies conducted with this tracer (*11*) and suggests that stable $SOR^{\beta CIT}$ values can be obtained beginning 70–80 min after injection. We note, however, that in normals the mean striatal specific to nonspecific count ratio was 4.6 ± 1.6 for βCIT-FP (*11*), whereas we measured this value as 2.8 ± 0.6. This difference may stem from the lower sensitivity of our camera compared to the brain dedicated annular SPECT instrument used in the other study. Additionally, specific-to-nonspecific count ratio for βCIT-FP is less than that reported for unconjugated βCIT (*6–8*).

While striatal βCIT binding may be higher in normal brain, βCIT-FP has the clinical advantage of rapid equilibration, thereby permitting imaging shortly after radiotracer injection. Moreover, the uptake kinetics of this compound make it potentially useful as a radiofluorinated tracer for high resolution kinetic PET studies. The comparative utility of βCIT and its various fluoroalkyl derivatives in quantifying presynaptic nigrostriatal dopaminergic function is a subject for further investigation.

While FDOPA/PET and βCIT-FP/SPECT were found to be comparable in our studies of parkinsonism, the two methods diverged in their relationships to the normal aging process. A significant aging effect of approximately 3.3% per decade was evident with βCIT-FP/SPECT which was not discerned in the FDOPA/PET studies conducted in the same subjects. Indeed, correlations between $SOR^{\beta CIT}$ and striatal FDOPA uptake parameters attained significance only in the PD patient subgroup, but not in the normal controls. Our demonstration of a normal aging effect is compatible with postmortem studies documenting a decrease of 4.7% per decade in nigrostriatal neurons in normal brain (*25*). Recent imaging studies have demonstrated significant losses of striatal DA transporter binding at a similar or greater rate. Respective aging decrements of 7.0%, 6.6% and 10% per decade has been reported with [^{11}C]cocaine, [^{11}C]d-threo-methylphenidate and [^{123}I]βCIT (*9,26,27*).

The current βCIT-FP data support prior findings of an aging decrement in striatal DA transporter binding, albeit of lower magnitude than that reported with βCIT. This disparity may stem from differences in the binding characteristics of the two compounds as well as differences in instrumentation and data analytical approaches. Indeed, the true extent of this aging effect can be determined only with the implementation of three dimensional MRI coregistration methods with a correction for striatal atrophy (*28*). In any event, our data indicate that age-related decrements in striatal DA transporter binding are relatively small. Adjusting $SOR^{\beta CIT}$ for age did not alter the accuracy of this parameter in assessing nigrostriatal dysfunction in PD patients.

In contrast to βCIT-FP/SPECT, no aging effect was demonstrated with striatal FDOPA/PET. Age-related declines in striatal FDOPA uptake have been reported in some studies (*29,30*) but not in others (*4,31,32*). Potential reasons for these disparities have been discussed elsewhere (*33*). In accordance with our earlier findings, we did not detect an aging effect in SOR^{FD} and K_i^{FD} in the current group of 15 normal volunteers scanned on the newer PET tomograph. Nonetheless, a significant aging effect was evident in the same subjects when imaged with βCIT-FP. Striatal FDOPA uptake is determined to a large degree by local DDC activity (*24,34*) which may be modulated differently than the DA transporter under physiological conditions. It is conceivable that as dopaminergic neurons decline in normal senescence, FDOPA uptake can be maintained at a relatively constant level by the upregulation of DDC activity (*4*). This possibility is supported by the postmortem studies indicating little or no decline in striatal DDC activity with age (*35*). On the other hand, striatal DA transporter binding may be somewhat more sensitive to the attrition of nigral dopaminergic cells with advancing age.

These findings, however, do not exclude the possibility of DA transporter upregulation in the early stages of disease. The onset of clinical parkinsonism is associated with approximately 70% loss of nigral dopaminergic cell bodies (*25*). By contrast, previous FDOPA/PET studies have demonstrated an approximately 50% decline in striatal tracer uptake at early disease stages (*1–4*). We also found a parallel βCIT-FP decrement of similar magnitude in these patients, suggesting the possibility of DA transporter upregulation at clinical presentation. We interpret these observations with caution given the technical limitations of our SPECT system. Indeed, localized reductions in DA transporter binding of greater magnitude may be appreciated with PET (*36*) and perhaps with higher resolution SPECT imaging (*10*). Although the radiotracer uptake decrements associated with early parkinsonism are smaller than those expected from histochemical studies, FDOPA and βCIT-FP imaging parameters still accurately discriminated mildly affected patients. Indeed, the presence of only modest decrements in radiotracer accumulation at clinical onset may actually be advantageous in that a wider dynamic range remains for the longitudinal assessment of disease progression. This consideration is especially relevant in the implementation of imaging agents with diminishing specific uptake with advancing disease.

CONCLUSION

Our studies indicate that βCIT-FP is a useful tracer for the quantification of nigrostriatal dopaminergic deficits in parkinsonism. $SOR^{\beta CIT}$ is an easily computed noninvasive measure which can discriminate PD patients at early stage from their normal counterparts. This SPECT parameter is also sufficiently sensitive to small decrements in nigrostriatal function to predict quantitative motor ratings over a fairly narrow range of disease severity. The accuracy of early stage diagnosis and disease severity assessment with βCIT/SPECT was comparable to that obtained with established FDOPA/PET methods. The additional presence of an aging effect with βCIT-FP may be advantageous in the study of the dopaminergic correlates of the normal aging process as well as in validating mathematical models of disease progression in parkinsonism (*37*). By contrast, the decline in $SOR^{\beta CIT}$ with age is not sufficiently large as to require a specific correction in the assessment of parkinsonism with this radiotracer.

Because of the wider availability of SPECT, βCIT-FP/SPECT may become an acceptable alternative to FDOPA/PET in imaging studies of parkinsonism and related disorders. It should be emphasized, however, that in spite of the demonstrated comparability of whole striatal values obtained with PET and SPECT methods, critical regional changes within the striatum may not be reliably ascertained with SPECT. Indeed, small biologically relevant changes in dopaminergic function localized to the caudate, putamen, or substantia nigra cannot be accurately quantified with currently available SPECT instruments. In this regard, quantitative PET imaging will continue to serve an important role in scientific investigations of the degeneration of the dopamine system in normal aging and parkinsonism.

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ERRATUM

In the human studies article by Juweid et al. (September 1996 issue of *JNM*, pages 1504–1510), tumor volumes in the Abstract and Results Section were printed incorrectly. In the Abstract, the correct statement is "Targeting of all tumor lesions >0.5 cm in diameter, not 70.5 cm in diameter] was possible in nine patients etc.". The same applies to the statement in Results under "Targeting", "All disease sites >0.5 cm in diameter [not 0.5 cm] were visualized in 9 of 13 patients studied". Also, in Table 2, the information on Patients 1125 and 1318 was transposed. The corrected table is printed below.

TABLE 2
Therapeutic Results in Initial Assessable Patients

Patient no.	No. of treatments	Initial red marrow dose (cGy)	Anti-tumor effects (duration)
1142	1	55	Progression
1063	1	55	Stable disease (1 mo)
1124	1	108	Progression
775	4	150*	Stabilization of disease (7 mo) (Regression of small pulmonary nodules and stable adrenal and bony metastases)
1125	1	191	Progression
1318	2	194†	Stabilization of disease (5 mo) [25% reduction in left cervical and stable right cervical adenopathy. Stable CEA and calcitonin (11 mo)]
1047	1	250	Progression
991	2	450	Stabilization of disease (3.5 mo)
1014	3	450	Stabilization of disease (5 mo)
1036	3	450	Stabilization of disease (6.5 mo)
1217	3	450	Stabilization of disease (7 mo)
1156	1	450	Progression
1186	1	450	Progression

*Patient received two additional RAIT cycles in 2-mo intervals, delivering a total red marrow dose of 501 cGy.

†Red marrow dose after the second RAIT, 10 mo after the first RAIT, delivering a total dose of 150 cGy to the marrow.