

Impact of reconstruction method on quantitative parameters of ^{99m}Tc -TRODAT-1 SPECT

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ABSTRACT

Introduction: Quantitative evaluation is recommended to improve diagnostic ability and serial assessment of dopamine transporter (DAT) density scans. We decided to compare the ordered subsets expectation maximization (OSEM) with filtered backprojection (FBP), and to investigate the impact of different iteration and cut-off frequencies on SBR values.

Methods: We retrospectively examined 27 consecutive patients. SPECT reconstruction was performed using OSEM and FBP with fixed 10 subsets and different subsets including 5, 10 and 15 with fixed 6 iterations. Reconstruction with FBP were performed with different cut-off frequencies of 0.3, 0.4 and 0.5.

Results: Comparing SBR derived by OSEM reconstruction with 10 subsets but different iterations revealed statistically significant intraclass correlation (ICC) in both right and left side. There is also no significant difference between OSEM reconstruction with different subsets and ICC was excellent in all patients. ICC for FBP reconstruction with different cut-off frequency revealed good ICC in all patients. However, lower degree of SBR showed higher decrease in ICC with insignificant and poor correlation in patients with $\text{SBR} < 0.2$. While comparing OSEM and FBP, good correlation was observed in total patients, there was poor correlation between these reconstruction methods in lower SBR values.

Conclusion: Our study showed that change in FBP reconstruction parameters can greatly impact the SBR value of TRODAT-1, especially in patients with more severe disease. However, OSEM reconstruction revealed better reproducibility for SBR using different iterations.

Key words: SPECT reconstruction, ^{99m}Tc -TRODAT-1; Ordered subsets expectation maximization; Filtered backprojection

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INTRODUCTION

Imaging of striatal dopamine transporter density with single-photon emission computed tomography (SPECT) was developed to evaluate movement disorders including differentiation of Parkinson's disease from essential tremor and Alzheimer's disease from dementia with Lewy bodies [1, 2]. Interpretation of DAT-SPECT is mainly based on visual assessment by an expert reader; however, quantitative evaluation is also recommended to improve diagnostic ability and serial assessment of DAT density during follow up or evaluation of response to therapy [2, 3].

The main quantitative parameters of DAT-SPECT is specific binding ratio (SBR) which is defined as the ratio of striatal uptake to background activity [2]. There are different methods of manual or automated quantification of this parameter including different region-of-interest (ROI) analysis, partial volume effect reduction and method of attenuation correction (AC) [3].

Impact of different method reconstructions on the quantitative result of DAT-SPECT was studied by several authors [4]. Although it was stated that SBR by iterative reconstruction and filtered-back-projection method were similar [5], some authors found them to be different according to the method of quantification and AC or when details of each reconstruction method such as number of iterations changed [4, 6]. However, almost all of these studies worked on [^{123}I]N- ω -fluoropropyl-2- β -carbomethoxy-3- β -(4-iodophenyl)nortropane (^{123}I -FP-CIT), which is the most widely used radiotracer, while the latest radiotracer of this category ^{99m}Tc -TRODAT-1 has been also accepted to be used in clinical settings [7]. The SBR in normal individuals, reported in studies with ^{123}I -FP-CIT, ranging from 1.9 to 5.5 [1, 8, 9], which was higher than the SBR value reported by studies using this radiotracer ^{99m}Tc -TRODAT-1 (with values usually <1) [10, 11]. Considering the lower value of SBR obtained by ^{99m}Tc -TRODAT-1 SPECT, we decided to compare ordered subsets expectation-

maximization (OSEM) with filtered back-projection (FBP) reconstruction in order to study the impact of different iteration and cut-off frequencies on SBR values amongst patients with different stages of DAT reduction upon visual assessment.

METHODS

Patients

We retrospectively examined 27 (11 women and 13 men) consecutive patients who were clinically suspected of Parkinson's disease. The patients were referred for ^{99m}Tc -TRODAT-1 to verify or exclude the diagnosis of Parkinson's disease or other Parkinsonian syndromes.

SPECT acquisition and processing

Four hours after IV injection of 740 MBq ^{99m}Tc -TRODAT-1, data were acquired using a dual-head SPECT system (Infinia Hawkeye, GE Healthcare) equipped with a low-energy high-resolution collimator. SPECT acquisition was performed using a 180° non-circular orbit, with 60 projection angles for each detector, a 64×64 matrix size was applied with 1 mm pixel size (1 zoom) for all acquisitions. A symmetrical 10% wide energy window for the acquisition was centered at 140 keV.

SPECT data reconstruction was performed using OSEM and FBP with Chang's AC (threshold:5; coefficient:0.11). Iterative reconstruction parameters were used with various combination of iterations and subsets. Different iterations ranging from 2, 4, 6, 8, and 10 with fixed 10 subsets and different subsets including 5, 10 and 15 with fixed 6 iterations were processed and compared together. A Butterworth post-filter (critical cut-off frequency= 0.4, power=10) was applied to all OSEM reconstructions. The EM-equivalent iterations (= number of iterations \times number of subsets) for all OSEM reconstructions are shown in Table 1.

Table 1: Mean \pm SD of right and left SBR value in all patients according to OSEM reconstruction with different EM-equivalent iterations.

Number of EM-equivalent iterations (subsets:10)	Right SBR (mean \pm SD)	Left SBR (mean \pm SD)
20	0.33 \pm 0.16	0.34 \pm 0.16
30	0.33 \pm 0.17	0.35 \pm 0.17
40	0.33 \pm 0.16	0.35 \pm 0.15
60	0.33 \pm 0.16	0.35 \pm 0.16
80	0.32 \pm 0.16	0.34 \pm 0.16
90	0.32 \pm 0.17	0.34 \pm 0.17
100	0.33 \pm 0.17	0.34 \pm 0.17

SD: standard deviation, OSEM: ordered subsets expectation-maximization, SBR: specific binding ratio.

For OSEM reconstruction, combination of iterations and subsets systematically varied between 20 and 100 EM-equivalent iterations.

Reconstruction with FBP was performed using a tenth-power Butterworth filter with different critical cut-off frequencies of 0.3, 0.4 and 0.5.

After reconstruction and reorientation, 3 transverse slices with maximum striatal activity in visual assessment were selected from each patient and applied for all reconstructed images of the same patient. Composite of these three slices were used for quantitative analysis of each reconstruction set.

Quantitative analysis

Manually, Rectangle's region of interest (ROI) for left and right striatum (176 mm²) were drawn as a mean normal ROI derived from 3 normal CT images and then copied the ROI on all 270 reconstructed images. A circular background ROI with 103 mm² area was also placed on the occipital region of the brain images. To compare quantitative results, the specific binding ratios (SBRs), defined as [mean count of the striatal region (Cs) – mean counts of background (Cb)] / Cb was calculated for each patients. The quality of the reconstructed images was visually evaluated by a nuclear medicine physician.

Statistical analysis

The statistical analysis was performed with SPSS and Medcalc software. To evaluate the effect of OSEM and FBP reconstruction parameters on SBR, we computed two-way random effect intra-class correlation coefficient (ICC) for absolute agreement and its 95% confidence interval (95% CI) because each reconstruction subset was selected as different samples of each reconstruction method and we intended to generalize these reliability results to any reconstruction parameters with OSEM or FBP. This analysis was performed for three sets of data including different orders in OSEM, different subsets in OSEM and different cut-offs in FBP. To evaluate the difference between OSEM and FBP, the reconstruction parameters with best visual quality were selected from each dataset and then compared. To compare these two methods, Bland-Altman plots were also generated. The comparisons were also repeated in three subgroups with different stages of striatal DAT density including patients with mild to normal, moderate and severe degree of the disease. The ICC values (with consideration of their 95%CI) less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 indicate poor, moderate, good, and excellent reliability, respectively. In addition, repeated measure test was also used to assess the trend of SBR changes along with change in EM-

equivalent iterations in OSEM reconstruction and with change in cut-off frequency in FBP reconstruction. P value less than 0.05 was considered to be statistically significant.

RESULTS

OSEM reconstruction using different parameters

Total of 27 patients with different degrees of striatal uptake were consecutively selected. Table 1 shows the mean SBR value of each side calculated for each set of OSEM reconstruction.

Comparison of SBR derived by OSEM reconstruction with 10 subsets, using different iterations revealed statistically significant ICC in both right and left side in all 27 patients (Table 2). The ICC for bilateral SBR in each SBR group was generally good, except for right SBR in patients with moderate SBR values.

In comparison between OSEM reconstructions with different subsets with fixed number of iterations (6), no significant difference was found for SBR, and ICC was excellent in all patients (Table 3). However, ICC of subgroup with moderate degree of disease showed moderate correlation for both sides.

Repeated measure analysis for comparison of trend between changes in EM-equivalent iterations and changes in SBR, showed no significant relationship (Figure 1).

FBP reconstruction using different parameters

The mean±SD of right and left SBR values derived from each set of FBP reconstruction in all patients are shown in Table 4.

ICC for FBP projection with different cut-off frequency revealed good ICC in all patients. However, in subgroup analysis, lower degree of SBR showed higher decrease in ICC with insignificant poor correlation in patients with SBR<0.2 (Table 5).

Repeated measure analysis for comparison of trend between changes in cut-off frequencies and changes in SBR, showed no significant relationship (Figure 2).

Comparison of OSEM and FBP reconstruction

For the comparison of OSEM and FBP we selected the results of OSEM reconstruction with subset: 6 and order: 6 and FBP with cut-off: 0.4 for Butterworth filter. Although in total sample good correlation was observed, there was insignificant poor correlation between these reconstruction methods in lower SBR values (Table 6). The Bland-Altman plot also shows higher values of SBR by FBP as compared to OSEM reconstruction with wide range of difference in lower mean SBR values (left side of the diagram) in both left and right striatum (Figure 3).

Table 2: ICC for absolute agreement between OSEM reconstruction with different iterations in three groups and all patients for right and left SBR.

		ICC	95% confidence interval for ICC		P value
			Lower bound	Upper bound	
SBR<0.2	Right SBR	0.773	0.547	0.932	<0.001
	Left SBR	0.925	0.822	0.980	<0.001
0.2<SBR<0.4	Right SBR	0.607	0.318	0.868	<0.001
	Left SBR	0.802	0.591	0.942	<0.001
SBR>0.4	Right SBR	0.985	0.961	0.996	<0.001
	Left SBR	0.958	0.898	0.989	<0.001
Total	Right SBR	0.974	0.956	0.987	<0.001
	Left SBR	0.973	0.954	0.989	<0.001

P value<0.05 was considered to be significant.

ICC: intraclass correlation coefficient, OSEM: ordered subsets expectation-maximization, SBR: specific binding ratio.

Table 3: ICC for absolute agreement between OSEM reconstruction with different subsets in three groups and all patients for right and left SBR.

		ICC	95% confidence interval for ICC		P value
			Lower bound	Upper bound	
SBR<0.2	Right SBR	0.804	0.527	0.946	<0.001
	Left SBR	0.846	0.601	0.959	<0.001
0.2<SBR<0.4	Right SBR	0.626	0.226	0.888	0.002
	Left SBR	0.684	0.312	0.909	0.001
SBR>0.4	Right SBR	0.943	0.803	0.986	<0.001
	Left SBR	0.939	0.829	0.984	<0.001
Total	Right SBR	0.955	0.917	0.977	<0.001
	Left SBR	0.944	0.897	0.972	<0.001

P value<0.05 was considered to be significant.

ICC: intraclass correlation coefficient, OSEM: ordered subsets expectation-maximization, SBR: specific binding ratio.

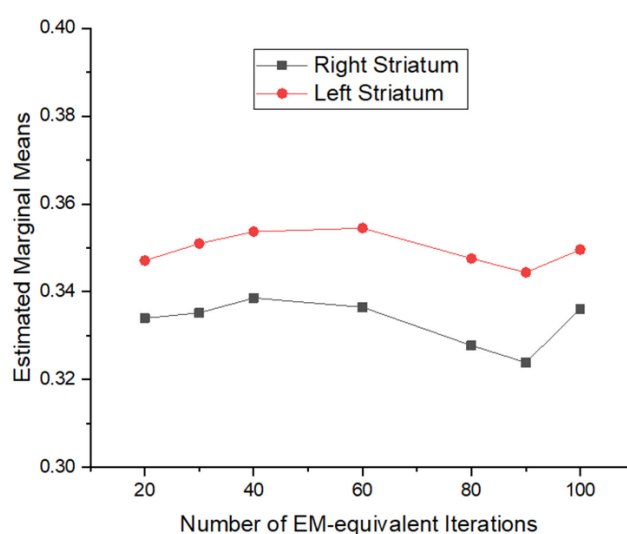
**Fig 1.** A repeated measures ANOVA with a Greenhouse-Geisser correction revealed that mean SBR value in both right and left sides was not statistically significant between OSEM reconstructions with different EM-equivalent iterations in all patients. (P value: 0.607 in right side; P value; 0.839 in left side).

Table 4: Mean \pm SD of right and left SBR value in all patients according to FBP reconstruction with different cut-off frequency.

Cut-off frequency	Right SBR (mean \pm SD)	Left SBR (mean \pm SD)
0.3	0.34 \pm 0.17	0.35 \pm 0.16
0.4	0.37 \pm 0.20	0.38 \pm 0.18
0.5	0.40 \pm 0.22	0.41 \pm 0.21

SD: standard deviation, FBP: filtered back projection, SBR: specific binding ratio.

Table 5: ICC for absolute agreement between FBP reconstruction with different cut-off in three groups and all patients for right and left SBR.

		ICC	95% confidence interval for ICC		P value
			Lower bound	Upper bound	
SBR<0.2	Right SBR	-0.068	-0.373	0.467	0.591
	Left SBR	-0.022	-0.348	0.512	0.511
0.2<SBR<0.4	Right SBR	0.544	0.163	0.851	0.003
	Left SBR	0.510	0.118	0.836	0.001
SBR>0.4	Right SBR	0.628	0.262	0.886	0.001
	Left SBR	0.696	0.355	0.911	<0.001
Total	Right SBR	0.787	0.641	0.888	<0.001
	Left SBR	0.777	0.625	0.882	<0.001

P value<0.05 was considered to be significant

ICC: intraclass correlation coefficient, FBP: filtered back projection, SBR: specific binding ratio.

Table 6: ICC for absolute agreement between OSEM (order:10, iteration:6) with FBP (cut-off frequency :0.4) reconstruction in three groups and all patients for right and left SBR

		ICC	95% confidence interval for ICC		P value
			Lower bound	Upper bound	
SBR<0.2	Right SBR	0.515	-0.190	0.866	0.071
	Left SBR	0.682	0.132	0.916	0.014
0.2<SBR<0.4	Right SBR	0.359	-0.335	0.806	0.156
	Left SBR	0.534	-0.126	0.871	0.058
SBR>0.4	Right SBR	0.908	0.309	0.982	<0.001
	Left SBR	0.873	0.330	0.973	<0.001
Total	Right SBR	0.866	0.721	0.937	<0.001
	Left SBR	0.914	0.803	0.961	<0.001

P value<0.05 is considered significant

ICC: intraclass correlation coefficient, OSEM: ordered subsets expectation-maximization, FBP: filtered back projection, SBR: specific binding ratio.

Figure 4 shows composite transverse slices of a patient reconstructed by OSEM (subset: 6 and order: 6) and FBP (cut-off: 0.4 for Butterworth filter).

DISCUSSION

OSEM reconstruction with different parameters

This study revealed that different range of SBR value remain almost similar upon different EM-equivalent iteration (different subsets and orders) of OSEM reconstruction when other acquisition variables were

unchanged. We also found that in images with lower SBR value, the variability of reconstruction parameters led to lower ICC with wider 95% CI. This effect can potentially lead to misinterpretation, especially when SBR value trend should be assessed in serial imaging. Previous studies with the other radiotracer of DAT imaging, ^{123}I -FP-CIT showed different results according to impact of reconstruction method on SBR values. In a phantom study, Dickson et al. studied the impact of reconstruction method on different striatal to background ratios.

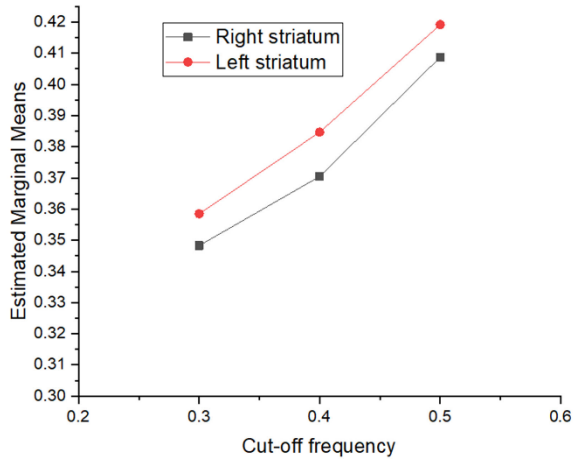


Fig 2. A repeated measures ANOVA with a Greenhouse-Geisser correction revealed that mean SBR value in both right and left sides has no statistically significant difference between FBP reconstructions with different cut-off frequency in all patients. (P value: 0.077 in right side; P value; 0.069 in left side).

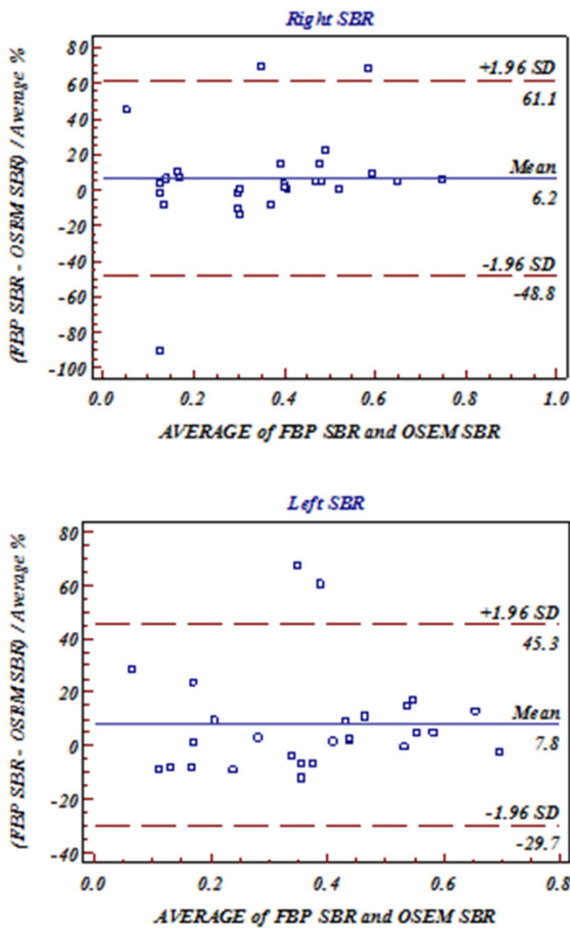


Figure 3. Bland-Altman plot for comparison of OSEM reconstruction (order: 10, iteration: 6) with FBP (cut-off frequency: 0.4) in all patients for right SBR (above) and left SBR (below). The mean difference/average percentage was 6.2% higher with FBP in the right side and 7.8% higher in the left side.

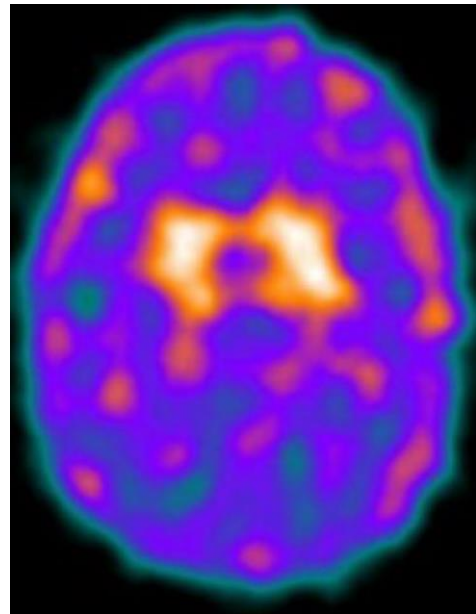
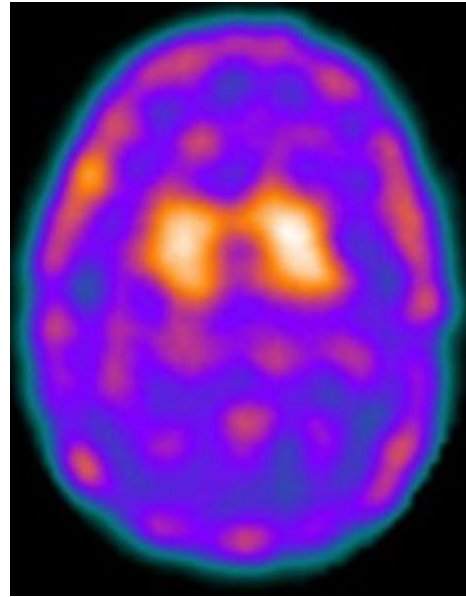


Fig 4. Composite image of 3 transverse slices of a ^{99m}Tc-TRODATSPECT reconstructed by (above) OSEM (subset: 6 and order: 6) and (below) FBP (cut-off: 0.4 for Butterworth filter).

They showed that SBR values derived by OSEM reconstruction was higher than values with FBP [12]. When comparing different iterations (20-200), significant convergence of SBR was observed, which was close to 100 EM-equivalent iterations [12]. Matsutomo et al. also evaluated the effect of OSEM reconstruction with different EM-equivalent iterations by setting the subset number at 6 and changing iteration number from 1 to 10 [6]. They found that SBR increased with increase in update number (subset *iteration) and converged over update number of 90 [6]. Although we did not use a phantom to evaluate the best EM-equivalent iteration, the non-significant

difference between these different subsets and iterations indicates enough similarity of SBR derived by different OSEM reconstruction.

FBP reconstruction using different parameters

Our study showed that with FBP reconstruction, when different cut-off frequency is used, there is lower ICC with a wide range of 95% CI. In comparison of FBP-AC reconstruction with different cut-off frequency for Butterworth filter, the ICC was lower than that of different OSEM reconstructions. This finding indicates more reliability of OSEM reconstruction, especially in serial imaging. Since, there was a significant difference between different FBP reconstruction, necessity of a local-based normal databases and cut-off points will be highlighted in centers where FBP is being used for reconstruction of ^{99m}Tc -TRODAT-1 SPECT. These results indicate the inferiority of FBP reconstruction for an accurate quantitative evaluation and comparison of ^{99m}Tc -TRODAT-1 SPECT, especially in diseased patients with lower SBR values.

Comparison of OSEM and FBP reconstruction

In the current study, we also found a moderate to good agreement between a sample OSEM and a sample FBP reconstruction that were selected upon visual assessment as best quality images of each reconstruction method. In a phantom study by Maebatake, OSEM reconstruction without resolution recovery (RR) was equal to FBP reconstruction, though OSEM revealed better image quality [13]. The difference in the accuracy of the two methods was not statistically significant, the authors stated that the image quality was significantly higher with OSEM reconstruction [6]. Winz et al. evaluated 18 patients with different degrees of DAT binding in ^{123}I -FP-CIT SPECT and compared visual and quantitative results of three reconstruction methods including FBP, 2D-OSEM and 3D-OSEM [14]. They revealed that specific binding uptake was higher with 2D-OSEM and 3D-OSEM reconstruction in comparison with FBP [14]. However, our study showed higher SBR value (mean 6-7% difference/average) with FBP reconstruction when compared to OSEM, but the difference was not significant. Koch et al. also estimated 6% lower SBR value with OSEM reconstruction [15]; however, Winz et al. suggested that this difference might have been due to lower EM-equivalent iteration (24 iterations) [14]. On the other hand, our study showed that mean SBR calculated from FBP reconstruction with cut-off frequency of 0.4 and 0.5 for Butterworth filter was higher than mean SBR values derived from different EM-equivalent iterations from 20-100, while FBP with cut-off frequency of 0.3 has similar mean SBR value. It seems that the difference between studies is more likely due

to variability in FBP reconstruction methods rather than OSEM reconstruction. In contrast to OSEM reconstruction, variation in FBP reconstruction parameters leads to larger changes in SBR values.

To the best of our knowledge, this is the first study to evaluate the effect of different reconstruction parameters on quantitative parameters of ^{99m}Tc -TRODAT-1 SPECT. The reported SBR value of ^{99m}Tc -TRODAT-1 SPECT by different studies amongst normal subjects or non-parkinsonian patients is lower than that of ^{123}I -DAT tracers. By comparison of the two tracers, Van Laere et al. estimated putamen binding index of 1.9 vs. 4.2 for ^{99m}Tc -TRODAT-1 vs. ^{123}I -FP- β -CIP, respectively, in 10 normal patients [16]. In a study by Bor-Seng-Shu, SBR cut-off point of 0.9 was suggested for differentiation of normal from abnormal DAT density by ^{99m}Tc -TRODAT-1, reconstructed by FBP [17]. In another study by Fallahi et al. mean SBR value of 0.65 was achieved in essential tremor patients who were supposed to have normal striatal DAT density [11]. However, studies by ^{123}I -FP-CIT showed higher mean value of SBR, even with different reconstruction and quantification methods [4]. Koh et al. calculated a reference value for SBR by ^{123}I -FP-CIT in a control group of adult Japanese population and estimated a mean SBR value of 6.84 by AC-OSEM [8]. In the current study, the range of SBR values was closer to other previous ^{99m}Tc -TRODAT-1 SPECT studies, and lower than what was reported by ^{123}I -DAT tracers. This main difference between these tracers (^{99m}Tc -based vs ^{123}I -based) can explain the more impact of reconstruction method on ^{99m}Tc -TRODAT-1 SPECT in our study as compared to previous similar studies using other radiotracers. In fact, the lower target to background ratio and higher noise ratio that leads to lower contrast and image quality of ^{99m}Tc -TRODAT-1 SPECT studies, make this scan more vulnerable to be easily affected by different reconstruction methods.

The main limitation of our study was the small number of cases in each group. Nonetheless, our study showed that change in FBP reconstruction parameters can greatly impact the SBR value of ^{99m}Tc -TRODAT-1, especially in patients with severer disease.

CONCLUSION

OSEM reconstruction revealed better reproducibility for SBR by different iterations. In addition, quantitative results of FBP and OSEM were not well correlated; hence, should not be compared directly for different patients or same patient in different times. It is suggested that in case of quantitative comparison between the two ^{99m}Tc -TRODAT-1 SPECT studies, OSEM reconstruction is the preferred method of reconstruction. However, further phantom studies with larger sample sizes are warranted in order to

evaluate the best reconstruction method for ^{99m}Tc -TRODAT-1 SPECT.

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