IMPLEMENTATION OF A NEW REFERENCE VALUES DATABASE FOR SEMIQUANTIFICATION IN ^{123}I-FP- CIT BRAIN SINGLE EMISSION TOMOGRAPHY

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INTRODUCTION

Brain dopamine transporters imaging by Single Emission Tomography (SPECT) with 123I-FP-CIT (DaTScan^{TM}) has become an important tool in the diagnosis and evaluation of Parkinson syndromes[1,2].This diagnostic method allows the visualization of a portion of the *striatum* –where healthy pattern resemble two symmetric commas - allowing the evaluation of dopamine pre-synaptic system, in which dopamine transporters are responsible for dopamine release into the synaptic cleft, and their reabsorption into the nigrostriatal nerve terminals, in order to be stored or degraded.[1-3]

In daily practice for assessment of DaTScan ^{TM}, it is common to rely only on visual assessment for diagnosis. However, this process is complex and subjective as it depends on the observer's experience and it is associated with high variability intra and inter observer[4].

Studies have shown that semiquantification can improve the diagnosis of Parkinson syndromes[4]. For semiquantification, analysis methods of image segmentation using regions of interest (ROI) are necessary[3]. ROIs are drawn, in specific - *striatum* - and in nonspecific – background – uptake areas. Subsequently , specific binding ratios are calculated[3-4].

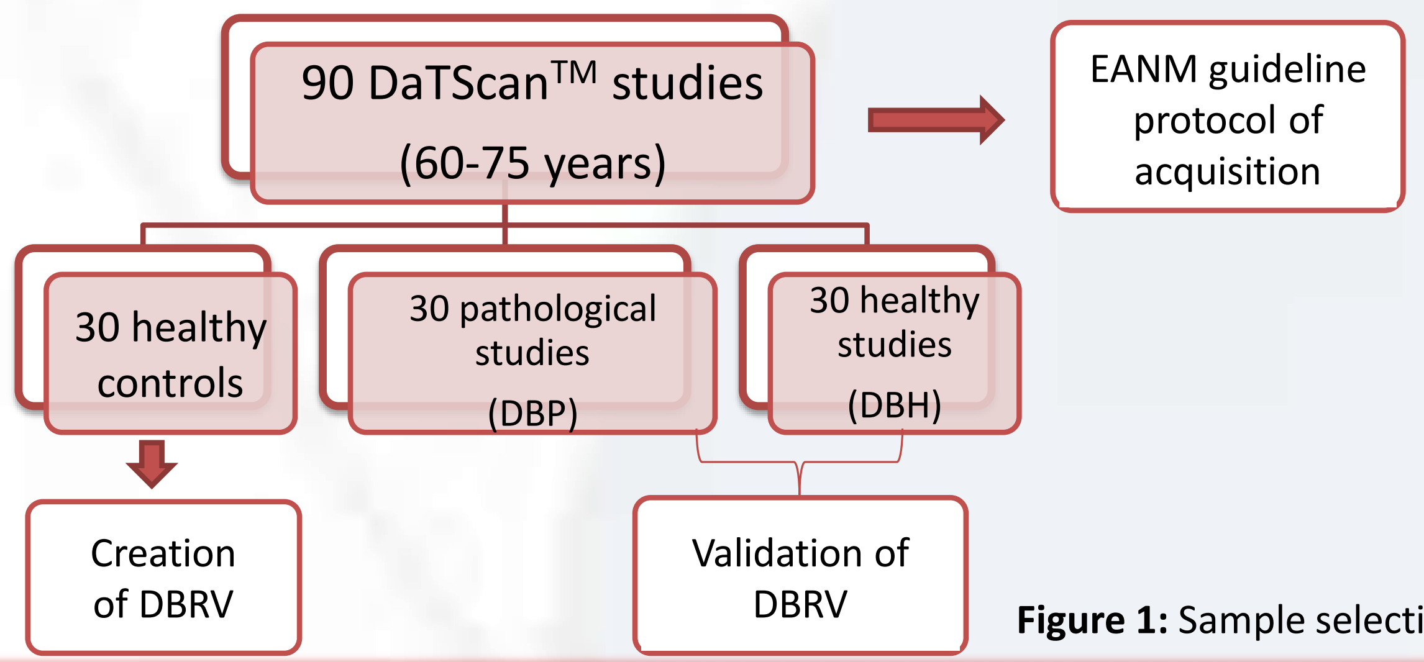
Low adherence of semiquantification for diagnosis of Parkinson syndromes is related, not only with the associated time spent, but also with the need of an adapted database of reference values for the population concerned, as well as, the examination of each service protocol[3]. Studies have concluded, that this process increases the reproducibility of semiquantification[3].

The aim of this investigation was to create and validate a database of healthy controls for Dopamine transporters with DaTScan^{TM} named DBRV. The created database has been adapted to the Nuclear Medicine Department's protocol, and the population of Infanta Cristina's Hospital located in Badajoz, Spain.

SUBJECTS & METHODS

1 - Sample Selection

A sample of 90 DaTScan^{TM} tests, divided into 3 groups of 30 tests each was used. These were acquired according EANM guideline[2]. The first Group of 30 Healthy controls was used for calculation of reference values, therefore, creating a database of reference values (DBRV). The Second group of 30 pathological (DBP) studies, and Third group of 30 healthy studies were used to validate the DBRV. Figure 1 shows the sample selection process.



90 DaTScan^{TM} studies (60-75 years)

EANM guideline protocol of acquisition

30 healthy controls

30 pathological studies (DBP)

30 healthy studies (DBH)

Creation of DBRV

Validation of DBRV

Figure 1: Sample selection process

2 - Reconstruction and segmentation of DaTScan^{TM} studies (DBRV, DBH and DBP)

Each DaTScan^{TM} was reconstructed by Filtered Back Projection and processed three times by the same operator. In the summed image of 3 transaxial slices, that identify the full extent of *striatal* tissue,[5]the average uptake of left and right caudate nucleus (LC and RC), left and right putamens (LP and RP) and occipital (OC) was determined through semiautomatic ROIs.

3- Reference Values Formulas

After segmentation, for each DaTScan^{TM} the Binding Ratios[3] were calculated from the formulas shown in Table 1.

Table 1: Calculation formulas of DaTScan^{TM} semiquantification Binding Ratios

Binding Ratio		Code
$\frac{\mathbf{Caudate\ Nucleous}}{\mathbf{Occipital}}$	$\frac{Left\ Caudate}{Occipital}$	A
	$\frac{Right\ Caudate}{Occipital}$	B
$\frac{\mathbf{Putamen}}{\mathbf{Occipital}}$	$\frac{Left\ Putamen}{Occipital}$	C
	$\frac{Right\ Putamen}{Occipital}$	D
$\frac{\mathbf{Striatum}}{\mathbf{Occipital}}$	$\frac{\frac{Right\ Putamen\ +Left\ Putamen\ +\ Right\ Caudate\ +Left\ Caudate}{4}}{Occipital}$	E
$\frac{\mathbf{Left\ Striatum}}{\mathbf{Occipital}}$	$\frac{\frac{Left\ Putamen\ +Left\ Caudate}{2}}{Occipital}$	F
$\frac{\mathbf{Right\ Striatum}}{\mathbf{Occipital}}$	$\frac{\frac{Right\ Putamen\ +Right\ Caudate}{2}}{Occipital}$	G
$\frac{\mathbf{Putamen}}{\mathbf{Caudate\ Nucleous}}$	$\frac{Right\ Putamen+Left\ Putamen}{Right\ Caudate+Left\ Caudate}$	H

4 – Creation of the Database Reference Values (DBRV)

The mean ± standard deviation ($\bar{x} \pm \delta$) for each binding ratio (A-H) of all DaTScan^{TM} studies composing the 30 healthy controls of the first group was calculated . The resulting values for each ratio formed the Database Reference Values.

5 – Validation of Database Reference Values (DBRV)

For validation of DBRV control charts[6-9] (figure 2-9) were created. An analysis of the distribution of the results obtained for the binding ratios A-H of the DBP and DBH around the reference values was done. For accuracy issues, the value of mean less standard deviation ($\bar{x} - \delta$) of each reference value was used to differentiate healthy of pathological individuals. Thus the binding ratios A-H from semiquantification of DBH should be above the line $\bar{x} - \delta$, and the DBP below this same line.

RESULTS

The reference values that comprise the DBRV, semiquantification result of the healthy controls, are shown in Table 2.

Table 2: Database of reference values($x \pm \delta$) *Binding ratios (BR)A-H*

Binding Ratios	Refrence Values ($\bar{x} \pm \delta$)
A	2,60 ± 0,40
B	2,57±0,36
C	2,29± 0,36
D	2,31±0,35
E	2,44±0,35
F	2,44±0,37
G	2,44±0,34
H	0,89±0,07

The following figures (figure 2-9) represent the control charts of the Binding Ratios A-H, used for validation of the DBRV.

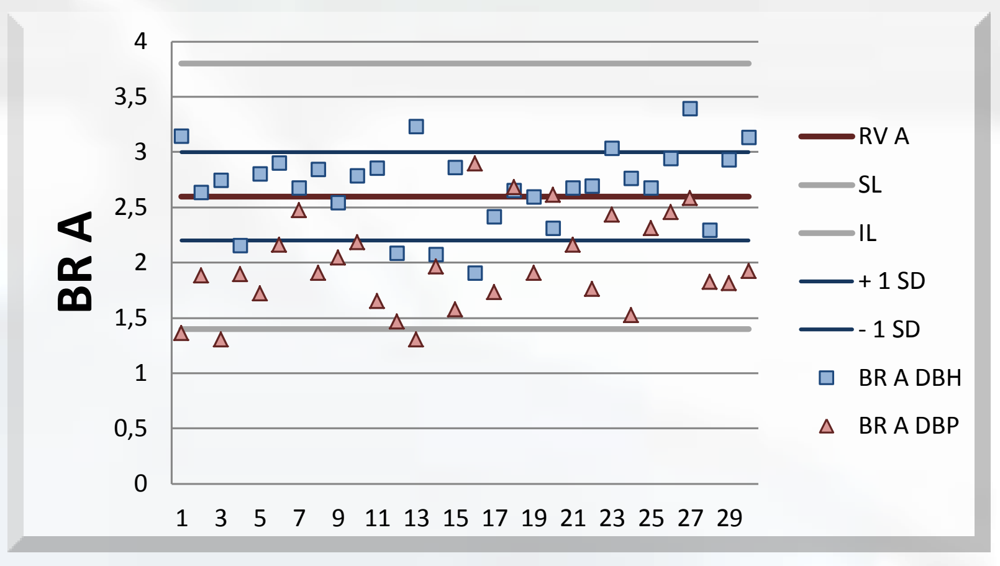


Figure 2: Control Chart DBH and DBP BR A

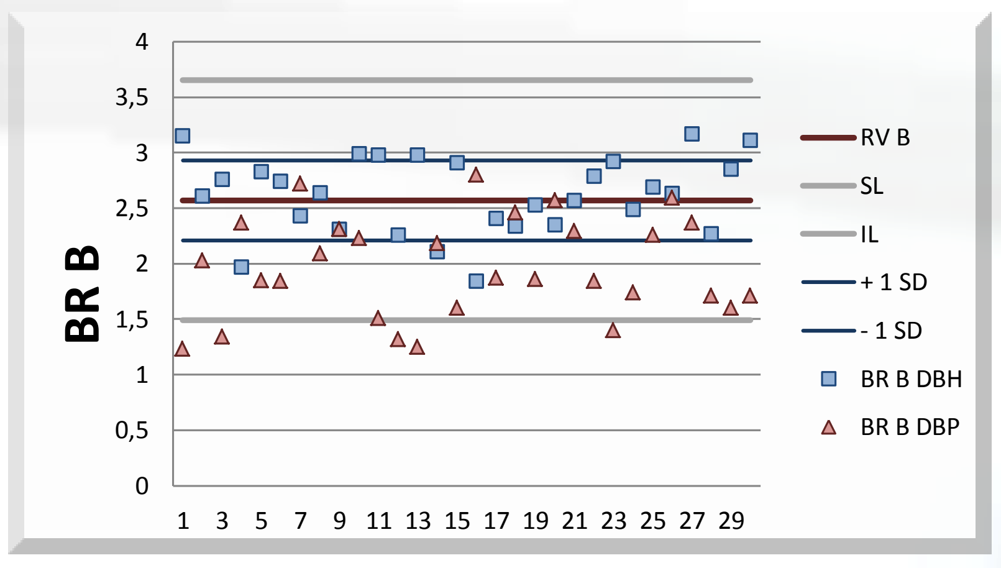


Figure 3: Control Chart DBH and DBP BR B

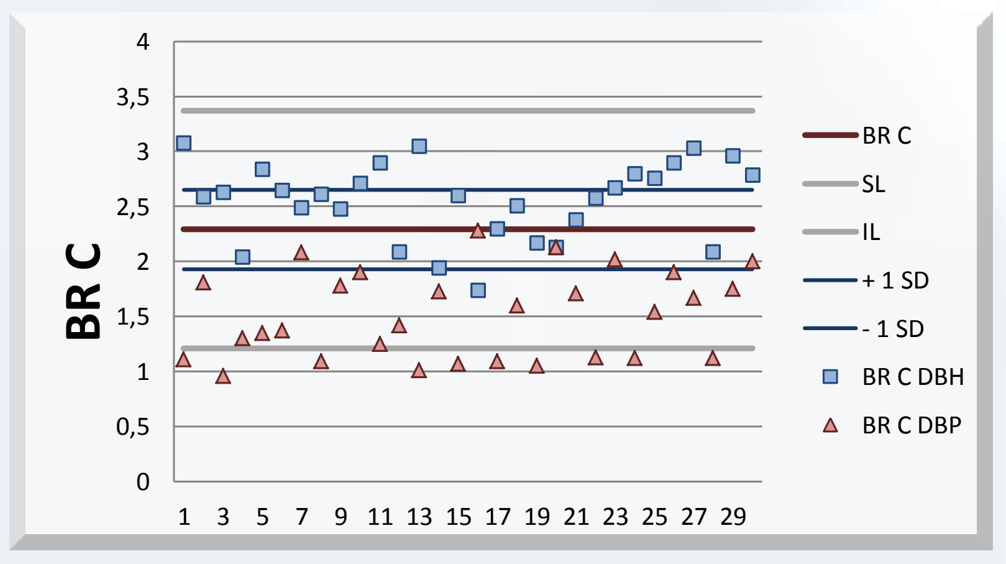


Figure 4: Control Chart DBH and DBP BR C

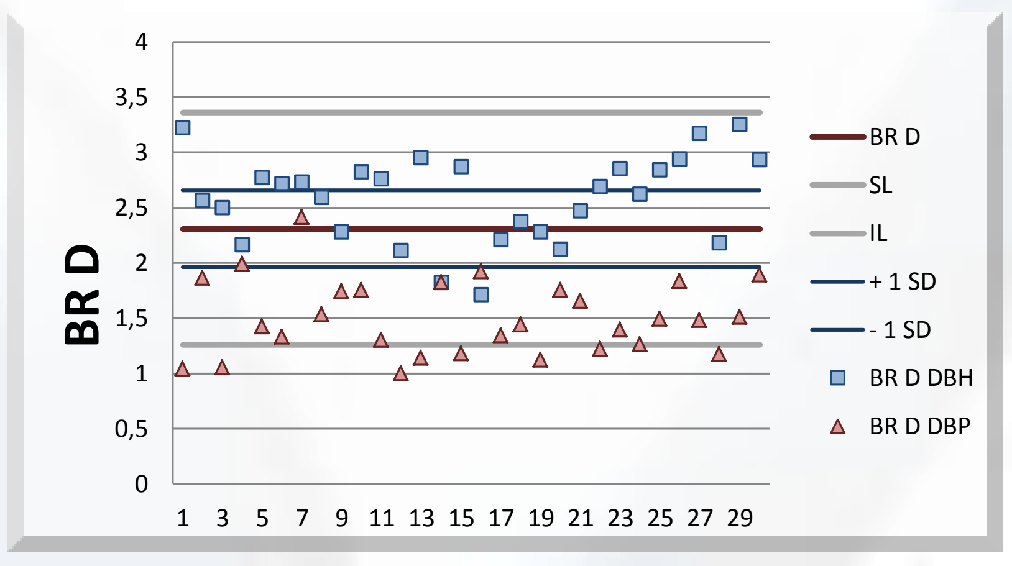


Figure 5: Control Chart DBH and DBP BR D

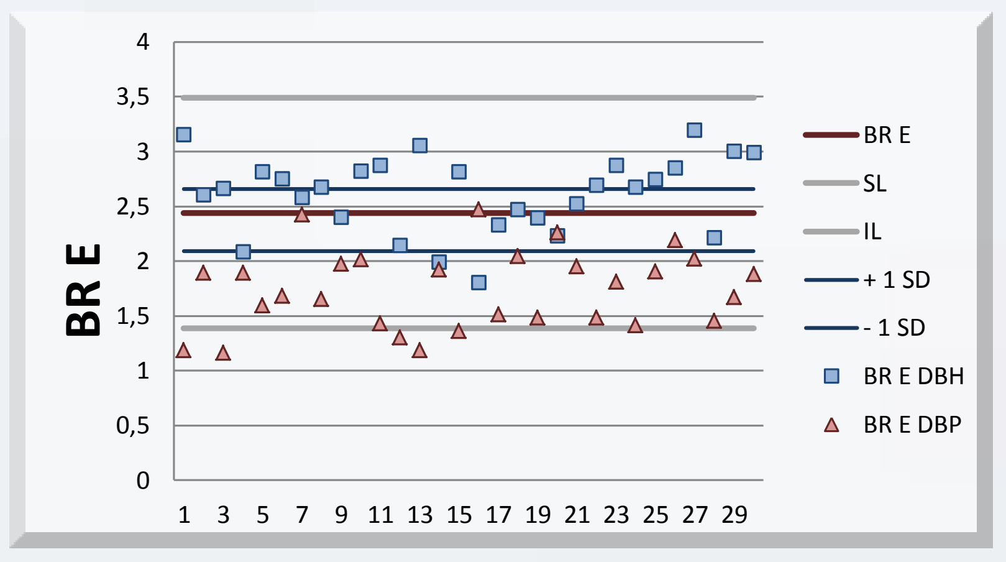


Figure 6: Control Chart DBH and DBP BR E

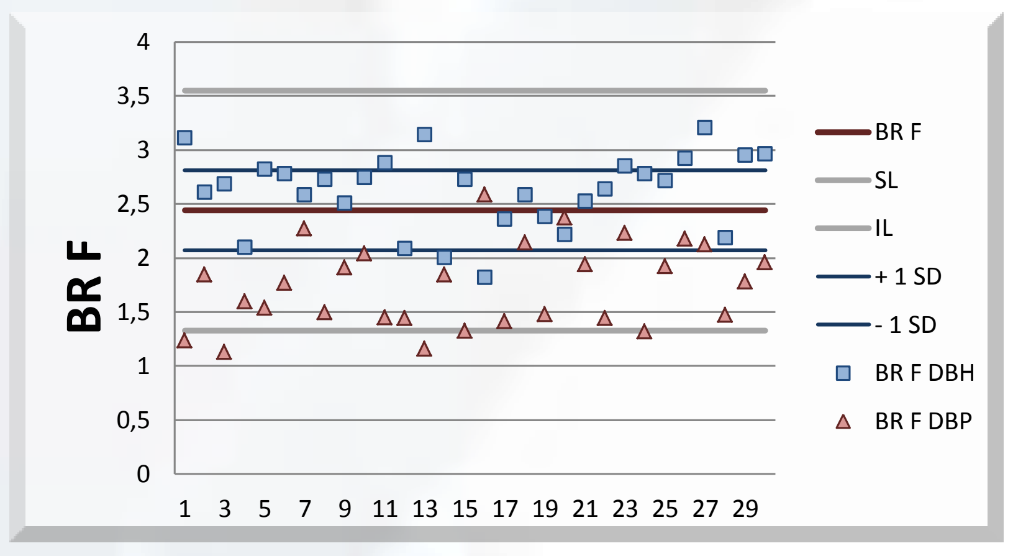


Figure 7: Control Chart DBH and DBP BR F

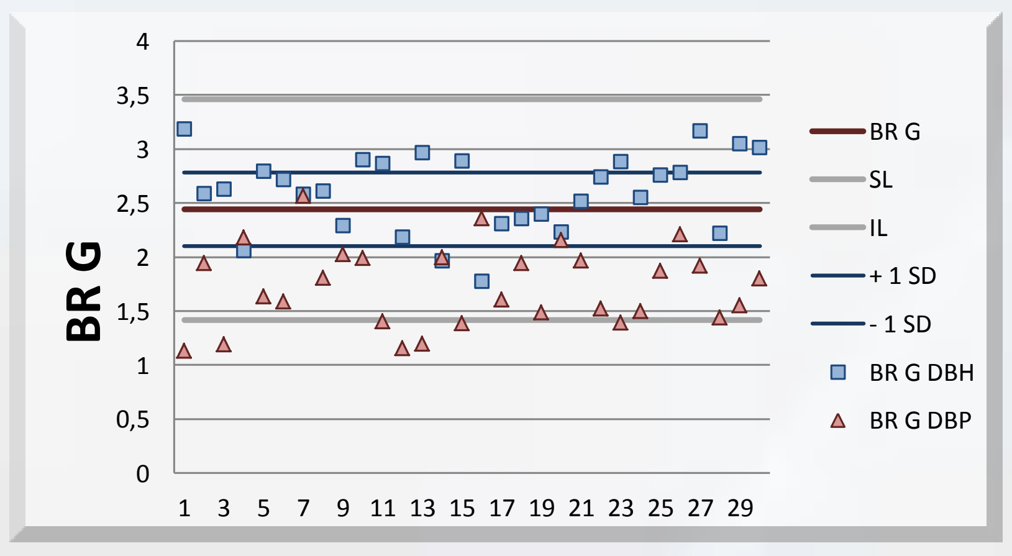


Figure 8: Control Chart DBH and DBP BR G

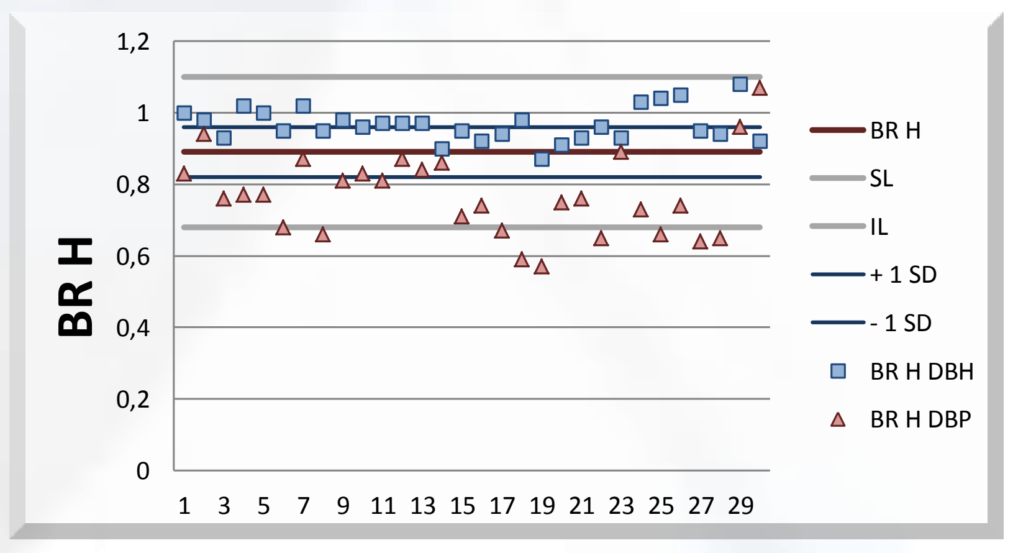


Figure 9: Control Chart DBH and DBP BR H

Legend: — Binding Ratio A-H (BR) ; — Superior Limit (SL); — Inferior Limit (IL);
— $x + \delta$ (+1 SD); — $x - \delta$ (- 1 SD); □ Binding Ratio (BR) A-H DBH ; △ Binding Ratio (BR) A-H DBP

DISCUSSION/CONCLUSION

In DBRV, the binding ratios A-B, C-D and F-G are similar due to their *striatal* homologous symmetrical structures. The binding ratios F and G are an average value between left and right caudate nucleus and putamen respectively.

Through analysis of control charts[8,9], (Figures 2-9) according to the criteria established previously, for diagnostic determination, it was found that 93% of DBH patients are located above the limit ($\bar{x}$- δ) and 80% of DBP patients are below the same limit, as a consequence of a decrease in *striatal* uptake visible in pathological cases.

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