Quantification and Image Analysis Task Group

QIBA Quantitative SPECT Committee

12 Jan 2016

Agenda

- Lessons learned from PPMI- camera standardization, measurand, VOI strategy
- Writing the Profile

Definition of Measurands

- Striatial binding ratio
- Ratio of putamen to caudate
- Asymmetry of caudate and putamen
- % injected dose/gram tissue

System Variance Sources Model – Ioflupane SPECT

Each source contributes variance to final measureand and ideally should be measured/controlled

Equipment QC

- Time synchronization
- Dose calibrator
- SPECT calibrations & QC
  - •Uniformity
  - •Alignment
  - •Sensitivity
- CT calibrations* & QC
  - •HU accuracy
  - •Uniformity

Acquisition Protocol

- CT acquisition*
- Injected dose
- Uptake time
- Head position
- Data statistics
- Detector/Collimator response
- Data sampling
  - •Framing
  - •Time sampling
  - •Angular sampling

Patient

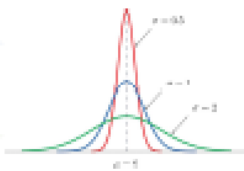
- Size
- Motion
- Tracer kinetics
- Brain condition
  - •Age
  - •Atrophy
  - •Pathology

Image Reconstruction

- Attenuation correction
- Scatter correction
- Gantry response correction
- Reconstruction algorithm and settings
- Detector/collimator response corrections

Image Analysis

- Partial volume correction
- Spatial normalization to template
- Target VOIs
- Reference region
- Age correction



*if SPECT/CT or CT image used for attenuation correction

Parkinson's Progression Marker Initiative (PPMI)

Study synopsis

Study population	400 *de novo* PD subjects (newly diagnosed and unmedicated) 200 age- and gender-matched healthy controls Subjects will be followed for a minimum of 3 years and a maximum of 5 years
Assessments/ Clinical data collection	• Motor assessments • Neuropsychiatric/cognitive testing • Olfaction • DaTSCAN imaging •DTI, resting state MRI •AV-133
Biologic collection/ Verification studies	• DNA collected at baseline • Blood collected at each visit; CSF collected at 6mo and then annually • Samples aliquoted and stored in central biorepository • Lead biologic candidates potential to be tested: alpha-synuclein, DJ-1, urate
PD treatment	• De novo for 6 months • Can participate in clinical trials after 12 months

PPMI Study Sites

Northwestern Univ
IND- New Haven
Johns Hopkins
Federico II - Naples
Parkinson's Institute- Sunnyvale
Univ Pennsylvania
Univ Rochester
APDC- Sun City, Az
Baylor
London
Univ Cincinnati
Univ Alabama-Birmingham
Boston University
Portland
Innsbruck
Marburg
Tübingen
Univ Washington
Tampa
Emory Univ
San Diego
Cleveland Clinic
Boca Raton
Sydney

Technical Challenges in Multicenter Imaging Trials

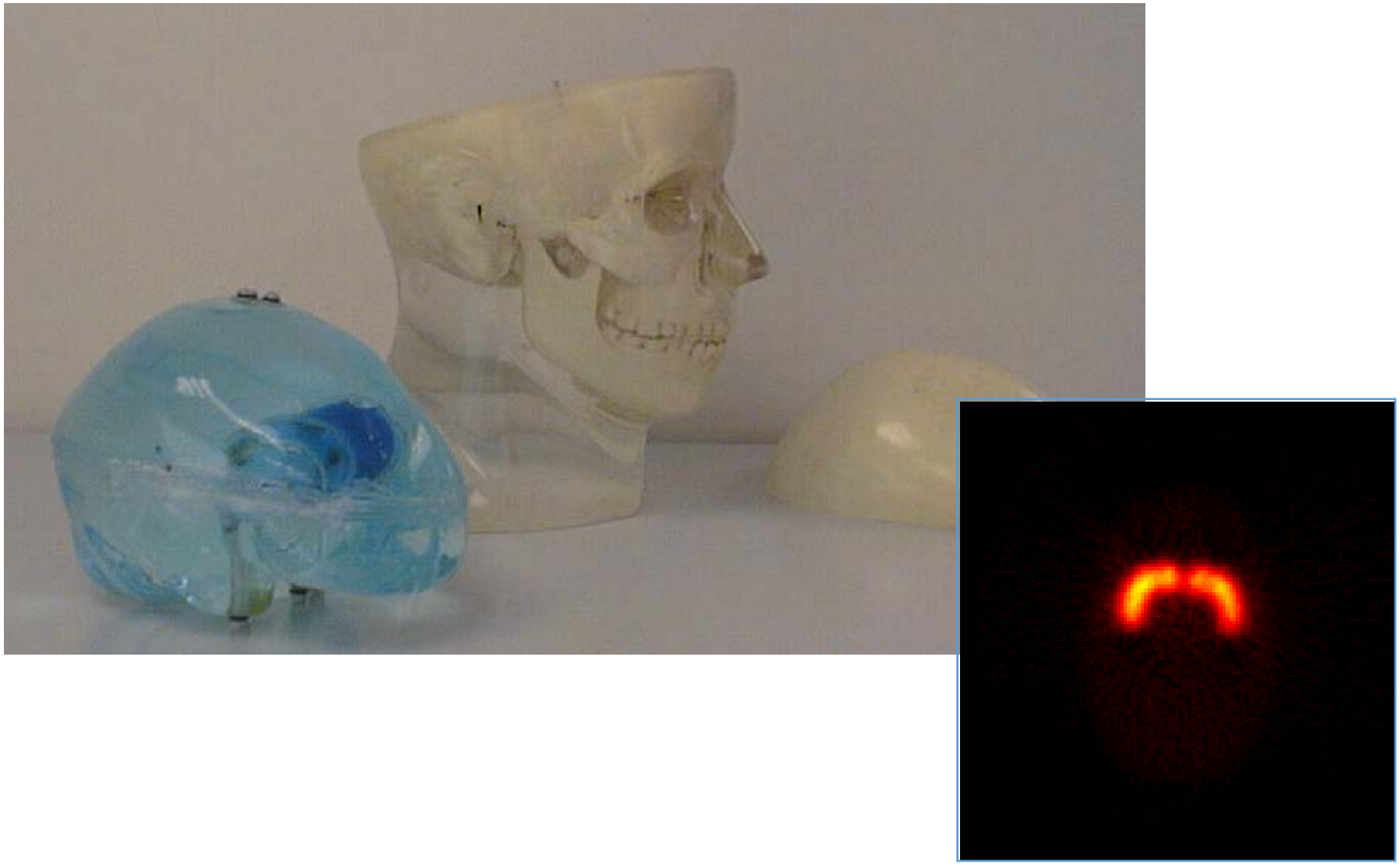
- Different cameras have different physical characteristics
- Image reconstruction and filtration
- Post hoc processing: attenuation correction, spatial normalization,
- VOI strategies
- Normal controls: what's normal, how heterogeneous
- Camera drifts, especially over long studies
- Other sources of increased variance:
  - updates in reconstruction
  - software
  - ambient changes in background radiation levels

Factors Which Influence the Specific Binding Ratio

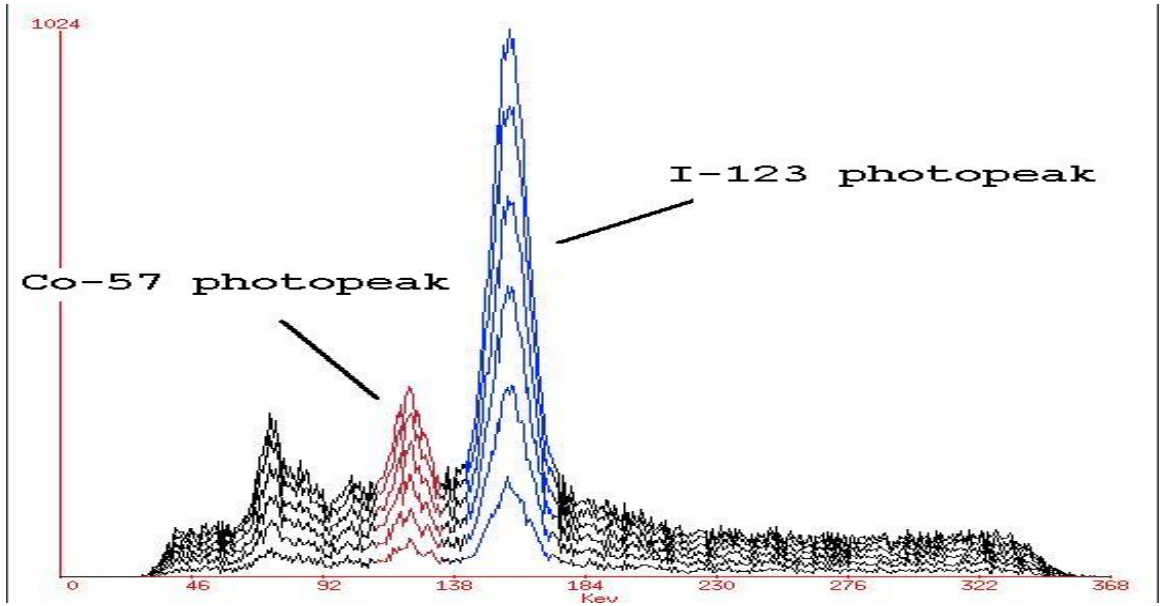
- **Biological factors**
  - **Dopamine transporter density**
  - **Age**
  - **Pharmacokinetic factors- rate of uptake, metabolism and elimination of tracer**
  - **Genetic: allelic variants of DAT**
  - **Drugs competing with DATScan for DAT binding**
  - **Patient ability to remain motionless in the camera**

- **Technical factors**
  - **Equipment: Resolution and sensitivity of selected camera, collimator**
  - **Performance drifts over time**
  - **Photon flux- counts in image**
  - **Reconstruction/filtration**
  - **Size and placement of regions of interest**

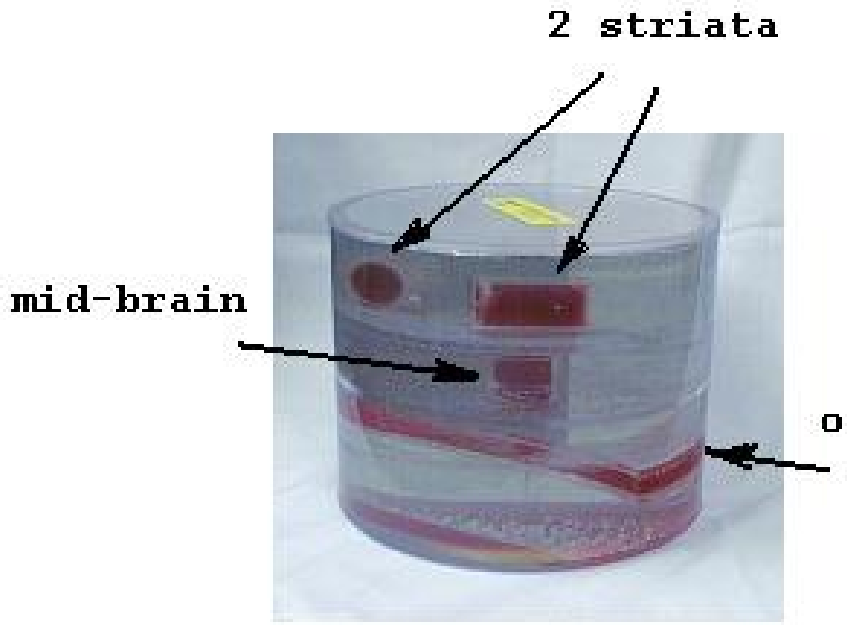
Anthropomorphic Striatal Phantom for Set-up Calibration

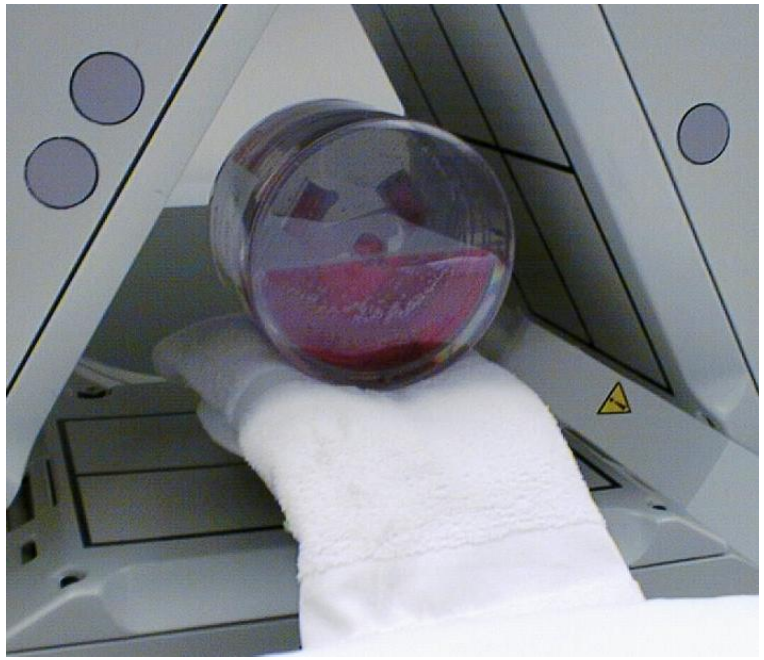


Dual Energy Window Acquisition Protocol for both 57Co phantom and PD patient



57-Co Striatal Phantom



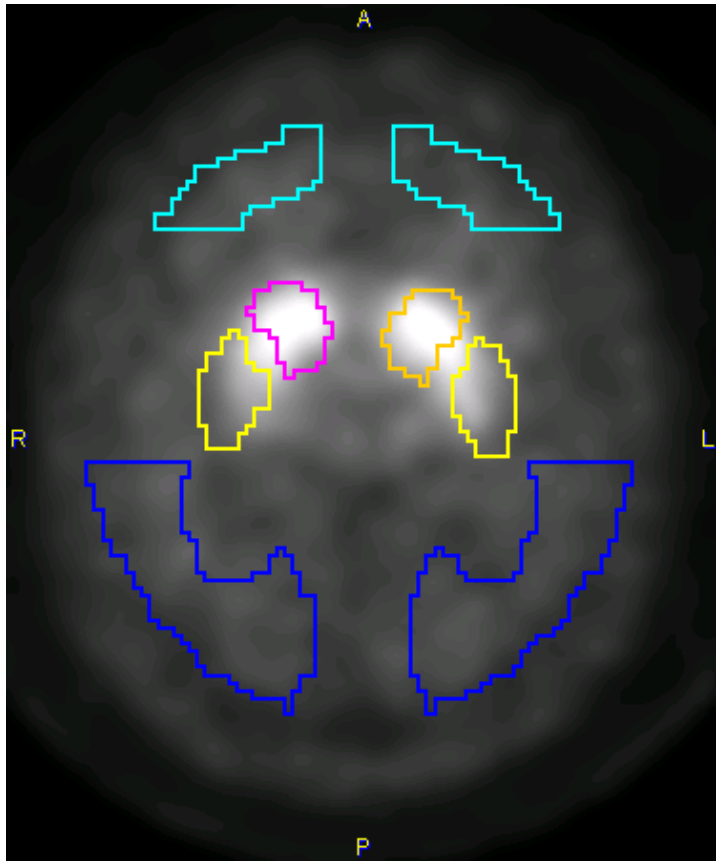


Striatal sampling strategy

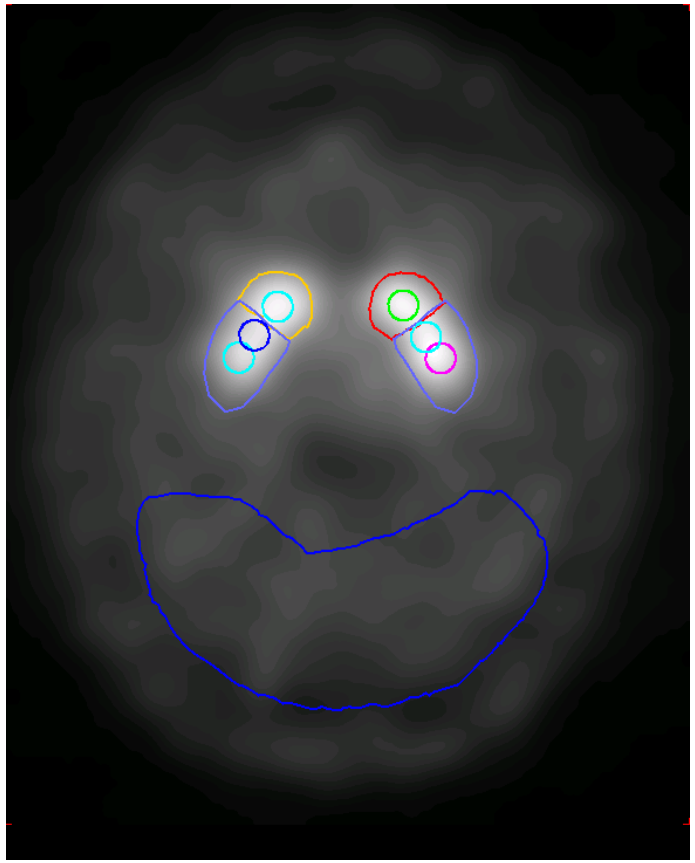
- Different region of interest sampling strategies are needed for within subject longitudinal sampling vs. cross-sectional separation of populations to assess the presence or absence of DAT deficit.
- Changes in putamenal DAT density in PD: reductions extend from posterior to anterior

Volume of Interest Strategies

A



B

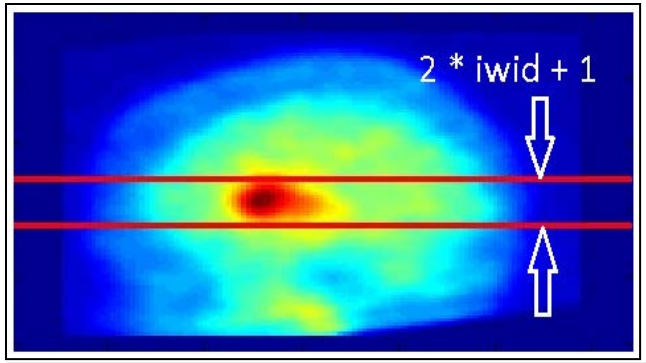


Caudate
Ant putamen
Post putamen

DAT Analyses

- On spatial normalized SPECT image volumes the transaxial slice with the highest striatal uptake is identified and the 8 hottest striatal slices around it were averaged in to generate a single slice image.
- Regions of interest (ROI) were then place on the of left and right caudate, the left and right putamen, and the occipital cortex (reference tissue).
- Count densities for each region were extracted and used to calculate specific binding ratios (SBRs) for each of the striatal regions. SBR is calculated as (target region/reference region)-1.

OSA: Automated Objective Striatal Analysis



Summed sagittal slices view of brain volume showing selection of transverse slices (between red lines); total slices added for analysis is 2*iwid*+1.

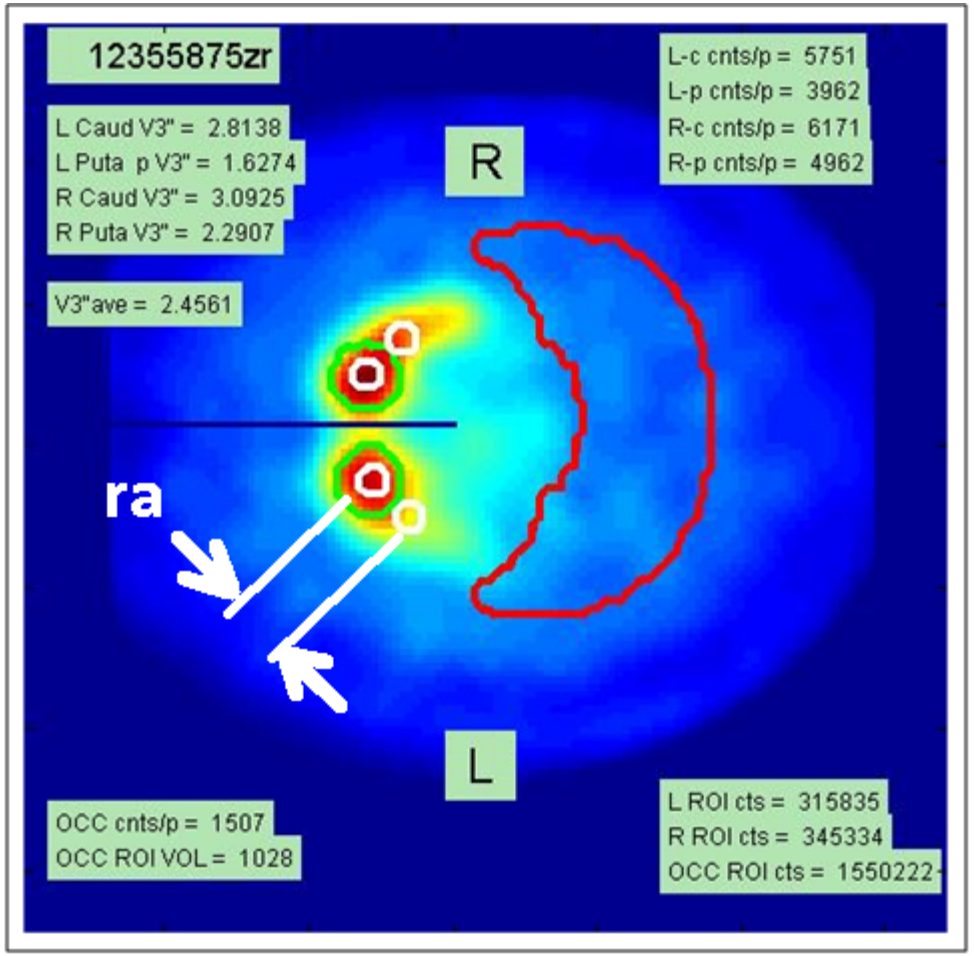
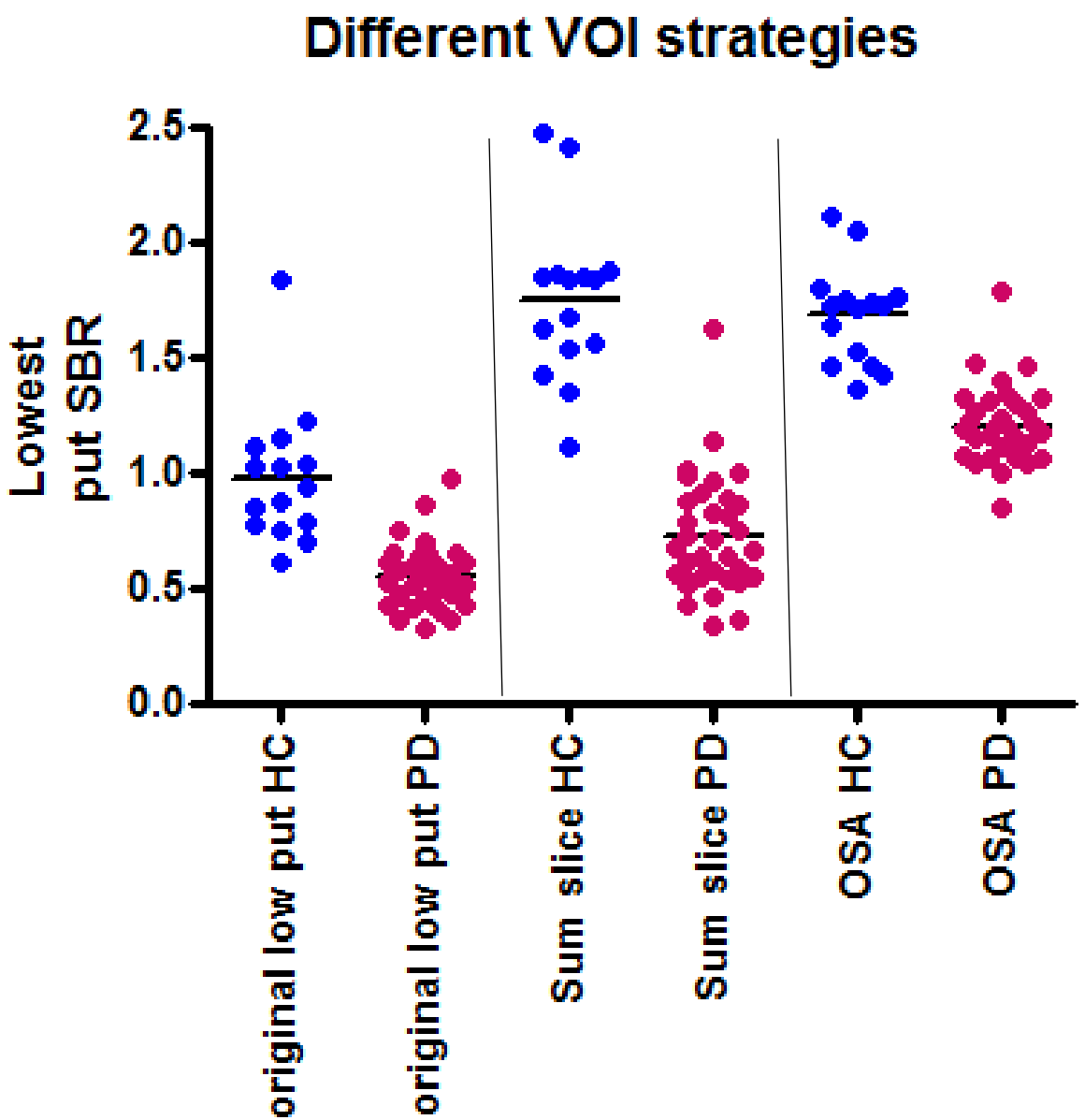
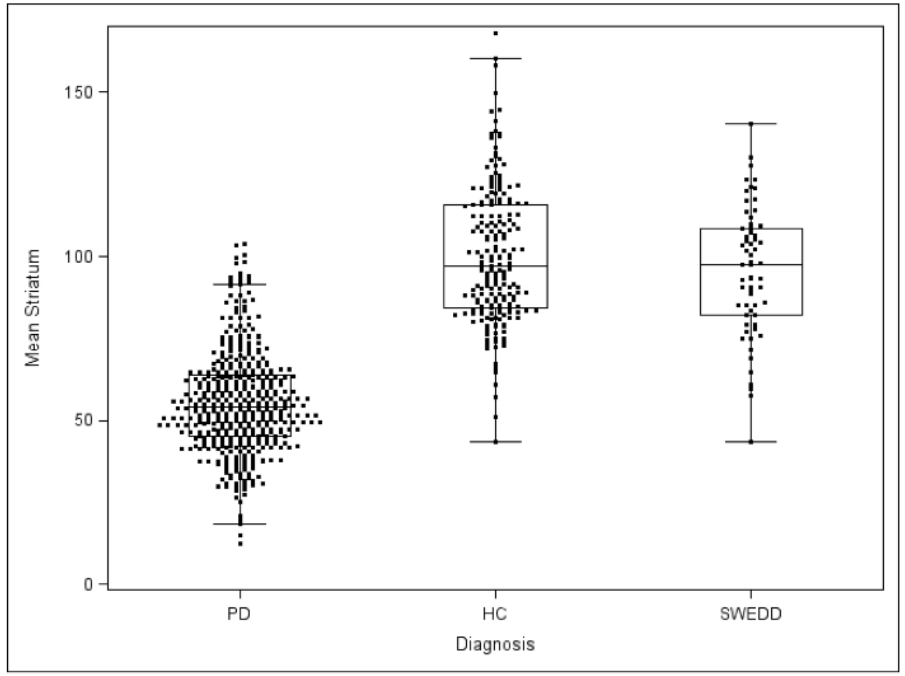


Figure 3: Summed transverse slice showing ROI placement and region statistics for calculating the Striatal Binding Ratios (referred to as V3" in the image).

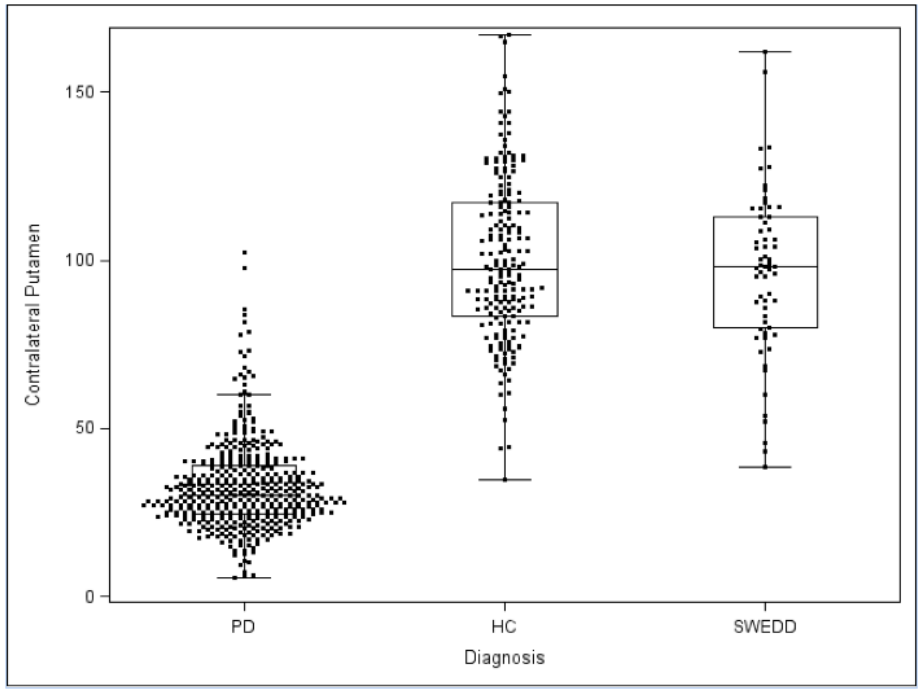

Different VOI strategies
Lowest put SBR
2.5
2.0
1.5
1.0
0.5
0.0
original low put HC
original low put PD
Sum slice HC
Sum slice PD
OSA HC
OSA PD

Baseline DAT SBR, Age-corrected

Mean Striatal SBR



Contralateral Putamen SBR



PD n= 423
HC n= 196
SWEDD = 64

Baseline DAT Data

Striatal Binding Ratio	PD Subjects (n=423)	Healthy Volunteers (n=196)	P-value
Lowest caudate	1.83	2.87	<0.001
Lowest putamen	0.67	2.03	<0.001
Mean caudate	1.99	2.98	<0.001
Mean putamen	.87	2.15	<0.001
Mean striatum	1.41	2.57	<0.001