QIBA SPECT Biomarker Committee: Overview and Status Update

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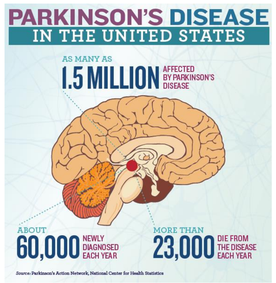
Quantitative Imaging Biomarkers Alliance RSNA

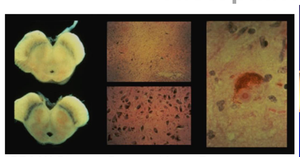
Parkinson's Disease

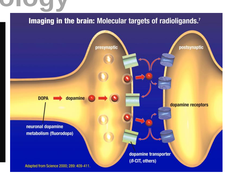
Facts & Societal Impact



Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive bradykinesia, rigidity, tremor, and loss of balance. A significant minority of patients with idiopathic PD will become demented. There are an estimated 1-1.5 million Americans with PD, with approximately 60,000 new diagnoses per year. Men are 1.5 times more likely to develop PD than women. The average age of onset is 61 years old, although 4% who develop PD are younger than age 50. There have been significant advances in the scientific understanding of the pathophysiology of the disease, but there is yet much to learn. The pathologic hallmark of the disease is the α-synuclein-containing Lewy body.

Histopathology





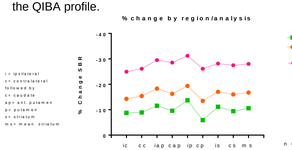
BRAAK Staging- Spread of Lewy Bodies

Stage 1: Dorsal motor nucleus of the vagal nerve; anterior olfactory structures
Stage 2: Lower raphe nuclei; locus coeruleus
Stage 3: Substantia nigra; amygdala; nucleus basilis of Meynert (clinical diagnosis made at this stage)
Stage 4: Temporal mesocortex
Stage 5: Temporal neocortex; sensory association and premotor areas
Stage 6: Neocortex; primary sensory and motor areas

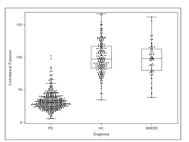
The primary neuropathic event in PD is the progressive accumulation of synuclein containing inclusions called Lewy bodies. By Braak stage 3 these involve nigrosrtriatal dopamine pathways resulting in motor symptoms Neuronal loss results in decreased presynaptic markers projecting to striatum, like the dopamine transporter, DaT.

Imaging Biomarkers- PPMI Study

The Parkinson Progression Marker Initiative (PPMI) is an international, multicenter, naturalistic study of de novo PD (n=423) and Healthy Volunteers (n=196) providing data on longitudinal change of clinical and biological biomarkers, including ioflupane SPECT, over 5 y. SPECT procedures for acquisition, reconstruction, and analysis are very similar to the QIBA profile.



PPMI STUDY Percent Change in DaT Binding in PD Over 4 Years

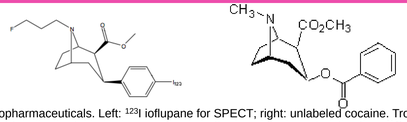


PPMI STUDY Baseline contralateral putamen SBR in PD and Controls

Ioflupane SPECT is used in clinical trials to confirm eligibility and monitor rates of DaT signal loss in treatment cohorts. From the perspective of powering a study, DaT SPECT provides a more robust outcome measure than clinical motor assessments.

RSNA 2018. Various QIBA projects and activities have been funded in whole or in part with Federal funds from the National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, Department of Health and Human Service, under Contracts Nos. HHSN268201000050C, HHSN268201300071C and HHSN268201500021C

Clinical Use Cases for Ioflupane

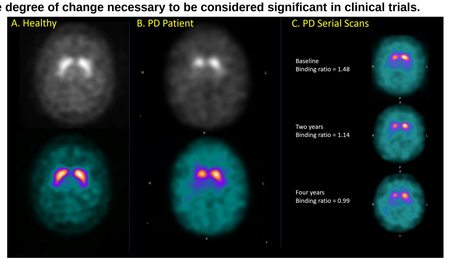


DaT Radiopharmaceuticals. Left: ^{123}I ioflupane for SPECT; right: unlabeled cocaine. Tropanes like ioflupane are more metabolically stable in vivo resulting in better imaging characteristics than ^{11}C radiolabeled cocaine.

DaT SPECT Imaging Interpretation

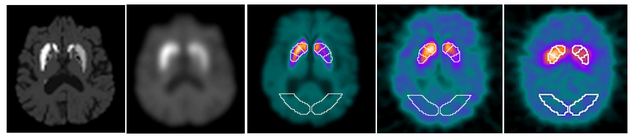
Radiotracers are currently used to estimate DaT density in patients with movement disorders. The QIBA group is defining technical performance requirements to use ioflupane quantitatively. The current Claim will be used to help assess new patients during their initial presentation, as well as across time points (longitudinal claim) to assess the degree of change necessary to be considered significant in clinical trials.

Axial images to the right show the distribution of DaT in a 66 y old healthy volunteer (A) and 65 y old PD patient (B). The PD image reveals asymmetric uptake in the striata. Panel C is a different PD patient imaged over 4 y with decreasing striatal signal with time.



Groundwork: Digital Reference Objects

Goal: Design and construct a brain Digital Reference Object (DRO) phantom with properties appropriate for testing software used to characterize SPECT DaT uptake patterns in a quantitative fashion.



T2w MRI image converted to a DRO SPECT DaT uptake image by defining uptake values in segmented regions (i.e., caudate, putamen, CSF and reference region). Various levels of processing were applied to the unblurred DRO. From left to right: unblurred DRO, 10 mm Gaussian blur; blurred DRO with ROI placement; 3M count DRO Monte Carlo simulation reconstructed with FBP no corrections; 3M count experimental image reconstructed with FBP no corrections.

Table 1. SBR Results from different DaT quantitation analysis software.

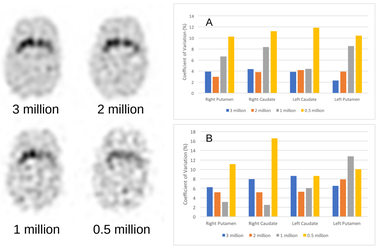
Analysis Software	Striatum SBR		Caudate SBR		Putamen SBR	
	Right	Left	Right	Left	Right	Left
Truth	4.5	4.5	4.5	4.5	4.5	2.25
Vendor 1 (no blur)	2.9	2.05	3.36	2.76	2.7	1.69
Vendor 2 (no blur)	3.19	1.87				
Vendor 3 (no blur)	2.53	1.81	2.4	2.33	2.56	1.43
Vendor 4 (no blur)			3.6	3.05	2.76	1.7
Vendor 1 (6 mm blur)	2.59	1.8	3.02	2.34	2.4	1.52
Vendor 2 (6 mm blur)	3.23	1.86				
Vendor 3 (6 mm blur)	2.13	1.53	2.3	1.99	2.05	1.2
Vendor 4 (6mm blur)			3.19	2.61	2.2	1.39
Vendor 1 (10 mm blur)	2.17	1.52	2.57	1.9	2	1.32
Vendor 2 (10 mm blur)	3.23	1.86				
Vendor 3 (j10 mm blur)	1.72	1.21	1.92	1.61	1.66	0.91
Vendor 4 (10 mm blur)			2.67	2.11	1.71	1.12

True SBR for right and left caudate was 4.5; for right putamen 4.5 and for left putamen 2.25. DRO was analyzed using a variety of vendor packages (e.g., DaTView, DaTQuant, PPMI and MIM). Results (Table 1) illustrate variability of SBR for the same DRO using different analysis packages (results randomized to preserve vendor anonymity).

Groundwork: Acquisition & Recon

Objective: Using two popular contemporary gamma cameras (Scanner A & Scanner B), groundworks were performed to determine the best acquisition and reconstruction parameters for measuring Specific Binding Ratio (SBR) in ^{123}I Ioflupane SPECT.

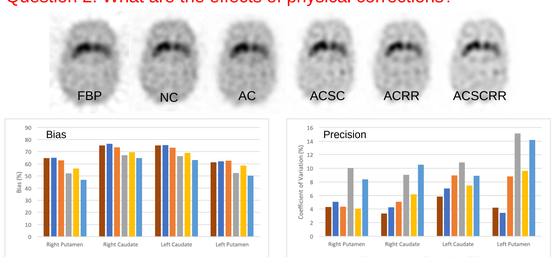
Question 1: How many acquired counts are required for quantification?



Bias is relatively unaffected by the number of acquired counts.

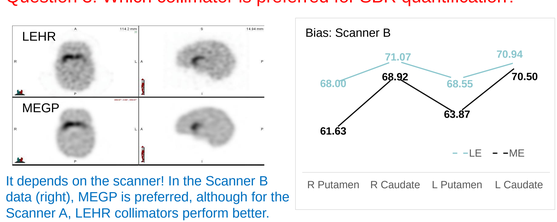
However, precision (CoV) worsens between 2 and 1 million acquired counts on the Scanner A system while Scanner B data showed 1 million acquired counts to be sufficient for quantification.

Question 2: What are the effects of physical corrections?



Bias is reduced after the application of more corrections e.g. attenuation (AC), scatter (SC) and resolution modelling (RR). Precision is optimal with no corrections.

Question 3: Which collimator is preferred for SBR quantification?



It depends on the scanner! In the Scanner B data (right), MEGP is preferred, although for the Scanner A, LEHR collimators perform better.

Planned Activities 2019 ioflupane

Profile: Version 1.0 was released for public comment. Each suggested revision was addressed by the BC and resolved. The committee's new goal is to provide an updated Version 2 by the end of 1Q 2019.

Checklist: Each of the performance requirements in the Profile has been compiled as a set of checklists. These lists have been developed as tools to help actors and imaging sites evaluate their work for conformance with the Profile.

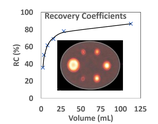
Feasibility Testing: The checklists are being used as quality control tools to assess the ability (or practicality/willingness) of actors to perform each of the Profile's performance specifications. The results of these feasibility tests will then be used to streamline and tighten the Profile performance requirements.

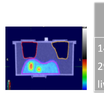
Planned Activities 2019 Technetium-99m

Use cases: (1) quantitation of volumes that are 30 mL or greater; and (2) changes in volumes. Use cases can be applicable to transarterial radioembolization by interventional radiology as shown below; pulmonary surgery; radiation therapy planning for lung cancer; pharmacokinetics of large molecules; theranostics; etc.

Quantification of 'lesions' in liver and liver background

Sphere phantom RCs ~ 68% and 78% at these volumes, hence PVC with RCs will give close to 100% quantification accuracy for these 'lesions'

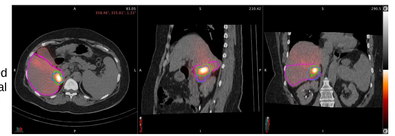




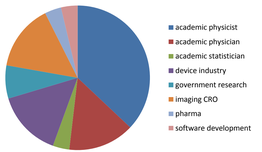
	Activity Recovery (%)	
	physical size VOI	small VOI
14 mL sphere in liver	70.0	82.5
29 mL ovoid in liver	76.7	92.1
liver background	114.7	

Activity recovery above is from using CT-based physical size of VOI and smaller VOI at center. Recon para: 48i, 1 ss (10mm Gaussian filter) of OSCG

Tc-MAA SPECT/CT. Lesion-to-liver uptake ratio ~ 3:1. Radiologist defined (on co-registered baseline CT) manual lesion outline in blue and outline from SPECT thresholding (30%) in green.



SPECT Biomarker Committee in collaboration with QIBA-Japan



The DaT SPECT Biomarker Committee is composed of volunteers who work together in a pre-competitive, international forum. The current composition of the group is indicated by stakeholder category in the pie chart at left. Membership is open to qualified and interested individuals. Questions or comments about QIBA or regarding material on this poster should be addressed to qiba@rsna.org.

The SPECT Biomarker Committee is deeply grateful for all the help and support from the professional staff at the RSNA who made this work possible by mediating about 4 meetings each month for over a year, among many other things that were essential for any success that results. The Committee would also like to thank the many contributions from QIBA Japan.