QIBA SPECT BIOMARKER COMMITTEE: Quantitative / Image Analysis Task Force

12 July 2016

Agenda

1. Profile Development/Writing (Section 3.10)
2. AOB

3.10 Image Analysis

3.10.1 DISCUSSION

The Image Analyst using computer workstation analysis tools shall perform the specified measurements. The main quantitative data analysis task is to determine the Specific Binding Ratios (SBR) of Ioflupane DaTscan for the right and left caudate and putamen. The derived results are then compared to an age-normalized database to provide a reference for the SBR versus age-matched normals. The profile describes the data analysis methodology.

Quantitative Specific Binding Ratio (SBR) of Ioflupane DaTscan will be based upon patient SBR and compared to an age normalized database (or striatal phantom or digital reference object as the case may be). Qualified systems will be able to achieve a SBR within a certain range (i.e., ±15%* of reference value) for quantitative imaging of I-123 Ioflupane for the DaTscan phantom (described in this profile). Further, the coefficient of repeatability (RC) should be <15%** for repeat studies of VOIs that are the size of the whole striatum. The profile seeks to provide the methodology for data analysis and also for qualification of systems and processing for I-123 Ioflupane DaTscan data analysis.

May need to adjust this value.

I have data suggesting that ±10% is more realistic than ±5%, but still could be challenging.

We must go out on a limb because we have a discriminatory claim.

- in previous version was ±10%
- ** in previous version was 20%

3.10 Image Analysis

Input Data:

The output images from Image Reconstruction are considered the input for Image Analysis. Once stored on the analysis workstation the image data will be processed for region of interest image analysis as described below. The original input data will be maintained as a separate file and will be stored along with the processed data for image analysis. In addition to output images from Image Reconstruction, digital reference object images may also be used as input for Image Analysis to validate the Image Analysis and workstation tools. Two types of digital reference objects will be considered. The first will represent the actual I-123 Ioflupane tracer distribution without any of the effects associated with the data acquisition and image reconstruction process. The second object will be a digital representation of first object including all physical effects and image reconstruction. Both digital reference objects will have known SBR's that can be used to assess the data analysis tools and workstation. The SBR for one half of the DRO will represent healthy control and the other side a patient with Parkinson's disease.

How much information do we want to provide about the DRO. For example:

The SBR for one half of the DRO will represent healthy control and the other side a patient with Parkinson's disease. The true binding ratio of for the healthy control side is 4.5 and 2.25 for the diseased patient. The Caudate to background binding ratio after image reconstruction is 2.5 (note will need to determine this) for the healthy control and 1.25 for the diseased patient.

numbers from section 4.1 are background 5 and right striatum 40 (ratio 7) and left striatum 20 (ratio 3)

3.10 Image Analysis

Methods to be Used:
Uptake in the striatum (i.e., caudate, anterior putamen and posterior putamen) and background region (e.g., cerebellum or occipital region) is characterized by defining a region-of-interest (ROI). The measurand is the specific binding ratio and is determined from the following equation:

$$\frac{striatum_{VOI} - backgrnd_{VOI}}{backgrnd_{VOI}} \qquad \text{(eq 1)}$$

where the background $(backgrnd)_{ROI}$ counts are normalized to the same ROI volume as the striatal ROI (i.e., caudate or anterior putamen or posterior putamen).

Volumes of interests will be drawn on preprocessed images as described below.

3.10 Image Analysis

Two volume of interest analysis strategies are described. The first method is referred to as the Small VOI approach. The second method is referred to as the whole striatum VOI approach.

The small VOI approach is described as follows. On spatial normalized SPECT image volumes the transaxial slice with the highest striatal uptake is identified and the adjacent hottest slices spanning an axial extent of 2 cm or less* are averaged to generate a single slice image. VOIs are then placed on the left and right caudate, the left and right putamen, and the occipital cortex (reference tissue), as shown in Figure 3.10.1. It should be clear which values belong to which striatal structures. This can be done by capturing DICOM coordinates along with VOI values or secondary screen capture of the VOI for identification. MRI anatomical images can be used for VOI drawing if they exist. VOIs maybe placed according to VOI template or using semi-automated or automated placement tools. Count densities for each region are extracted and used to calculate specific binding ratios (SBRs) for each of the striatal regions. SBR is calculated as ((target region – reference region)/reference region), as described above in eq 1.

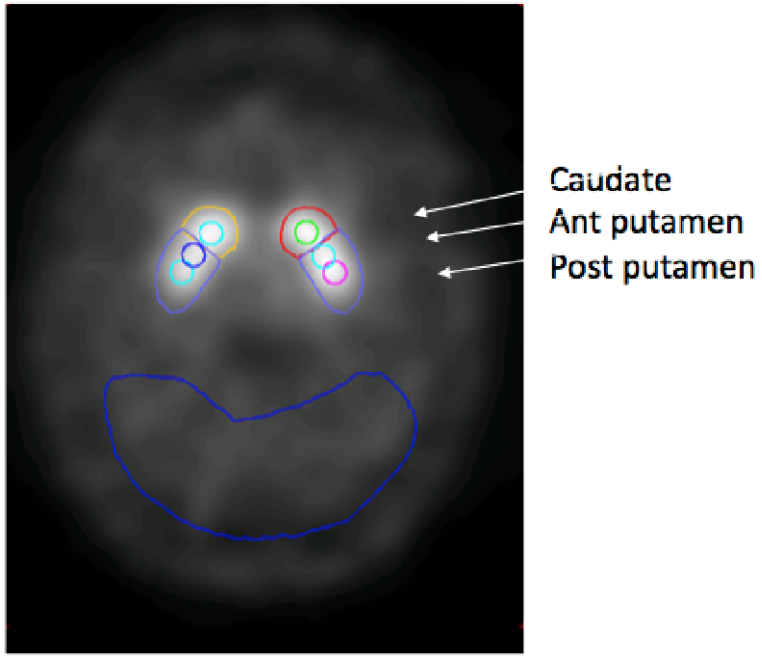
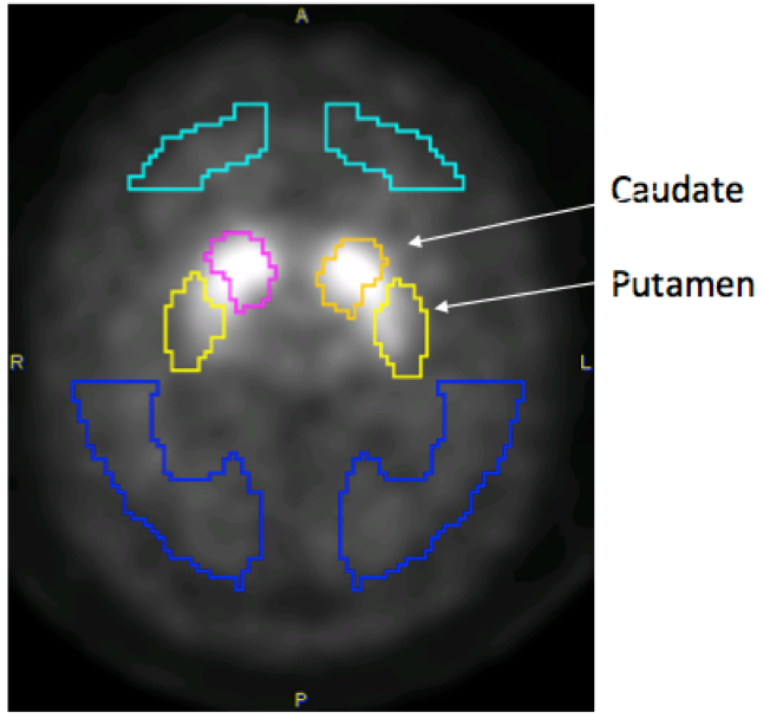


Figure 3.10.1. Illustration of Small VOI placement on summed slice image.

* suggest defining as 75% of axial extent. suggestion to move blue text to paragraph below

3.10 Image Analysis

The whole striatum VOI approach is similar to the Small VOI approach but uses larger volumes of interest (VOIs) and does not separate the putamen into two regions. The whole striatum VOI approach is implemented in many commercial software packages. The reconstructed image is spatially normalized to a SPECT template. Volumes of interest sampling most of the right and left caudate and putamen are drawn on the image as illustrated in Figure. 3.10.2. Background VOIs are drawn on the occipital cortex, as shown. VOIs can be systematically placed or semi-automatically or automatically defined over the caudate nucleus and putamen to assess specific tracer binding and over the occipital cortex to assess non-specific binding. The striatal specific binding ratios are calculated using equation 1.



3.10 Image Analysis

Required characteristics of resulting data:

The specific trial protocol shall prospectively define the SBR parameter that is required for the striatum and the caudate and putamen, specifically. Some studies may also compare different metrics (e.g., right to left asymmetry or caudate to putamen ratio) and will require recording multiple parameters. SBR measures (and the analysis tools used to obtain them, including software version) shall be used consistently across all subjects and across all sequential SBR measurements.

SBR's are intended as a measure of relative uptake and in that sense, can be regarded as dimensionless (unitless)

It should be clear which values belong to which structures (e.g., the whole striatum, left – right caudate, left – right putamen). This can be done by capturing DICOM coordinates along with the SBR or secondary screen captures of the VOI for identification. It should be reported what background region was used for normalization (e.g., occipital cortex or cerebellum).

For data analysis of the digital reference objects, the actual activity distribution and range of acceptable SBR values after data analysis will be provided in the digital reference object users manual. This seems to repeat what is said a few paragraphs above. I suggest deleteing it above. It is worth its own paragraph for emphasis.

Parameter	Actor	Requirement
Specific Binding Ratio	Image Analyst	Analysis Workstation Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.
		Post processed image for data analysis Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.7. If needed, image is spatially normalized. If using the Small VOI approach, the transaxial slice with the highest striatal uptake is identified and the adjacent hottest slices spanning an axial extent of 2 cm or less* are averaged to generate a single slice image
		VOI software analysis tools Using analysis workstation tools, volumes of interest are placed on the left and right caudate, the left and right putamen, and the occipital cortex (reference tissue). Count densities for each region are extracted to calculate SBRs for each of the striatal regions and for the striatum as a whole. VOIs may be systematically placed by the image analyst or by the image analysis software.
Certify VOI	Qualified professional	Shall either (1) agree with region boundaries, (2) reject boundaries and return for reprocessing, or (3) make revisions "on the fly" as indicated.

3.10 Image Analysis

should we include blue text

define at 75% axial extent

comments from John Seibyl

Profile section assignments (first draft/next iteration/last check before public review)

- Executive Summary: Mozley/Seibyl/whole committee
- 3.1-3.2 (Pre-delivery, Installation) Device manufacturers/Cella
- 3.3 (Periodic QA) Dickson/Zimmerman, et al.
- 3.4 -3.5 (Subject selection, Subject Handling) Mozley/Seibyl
- 3.6 (Acquisition) Dewaraja
- 3.7 (Reconstruction) Frey/Dewaraja
- 3.8 (Image QA) Dickson/Zimmerman
- 3.9 (Image Distribution) ?Klein/Pierre
- **3.10 (Image Analysis) Miyaoka/Seibyl**
- 3.11 (Image Interpretation) Seibyl, et al.
- 4 Assessment procedures – assignments?

Wrap-up

Review action Items

Any other business

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