

**Conformance Checklist**

QIBA Profile: Quantifying Dopamine Transporters with 123Iodine Labeled Ioflupane in Neurodegenerative Disease

(Short Title: SPECT dopamine transporters)

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# 3. Profile Activities

The Profile is documented in terms of “Actors” performing “Activities”. Equipment, software, staff or sites may claim conformance to this Profile as one or more of the “Actors” in the following table.

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Conformant Actors shall support the listed Activities by conforming to all requirements in the referenced Section.

## 3.1. Pre-delivery

### 3.1.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Release Testing | Manufacturer | The gamma camera (and any replacements parts) must pass all manufacturing in-process and release testing criteria |
| Non-OEM parts supplier | All parts and accessories must meet or exceed OEM specifications and pass all release testing criteria |
| DICOM format | Manufacturer | Shall meet the Conformance Statement written by manufacturer of each system |
| Computer workstations | Vendor | All workstations used to process images must be validated, able to support the image file type generated by the gamma camera and able to perform the image reconstruction and analysis requirements detailed in Sections 3.7 and 3.10. |
| Camera System | Owned by imaging center; placed by technologist | A camera system should be used that meets the requirements detailed under Image Data Acquisition in Section 3.6. This includes specific requirements for the collimator, projection bin (pixel) size, head-holder, etc. |

### **3.2 INSTALLATION AND Acceptance tests**

### 3.2.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Acceptance tests | Physicist or other trained, qualified personnel | Perform recommended tests at prescribed intervals. |
| Scanner | Must pass initial acceptance tests and perform within prescribed parameters for duration of study. |

## 3.3. Periodic QA

### 3.3.2 Specification

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| Parameter | Actor | Requirement |
| Planar Uniformity | Imaging Site | Uniformity of response to a uniform flux of radiation from a I-123 point source should be measured intrinsically every quarter. On a daily basis planar uniformity with collimators used for I-123 imaging should be performed using a Tc-99m or Co-57 source. The result should be 4 % in CFOV. |

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| --- | --- | --- |
| System Uniformity | Physicist | Performed to check all commonly used collimators for defects that might produce artifacts in planar and tomographic studies. Test should be conducted semiannually. Value should be within manufacturers’ specifications. |
| System Spatial Resolution | Physicist | Tests the resolution of the system in terms of the FWHM of its point spread function. Test should be conducted semiannually with the collimators routinely used with 123I ioflupane studies. The result of the test should be less than 8 mm at 10 cm. |
| Center-of-Rotation (COR) | Physicist | Tests the COR offset, alignment of camera Y-axis, and head tilt with respect to the scanner center of rotation. Mean value of the COR offset should not exceed1/2 pixel (typically 2 mm) when measured at the center and edges of the FOV. Position of Y=0 axis and the Y gain should be the same for all heads in a multi-head system. |
| Photon Energy Analyzer | Physicist | The accuracy of the photon energy analyzer should be within manufacturer specifications. Verifying this is typically part of daily QC. |
| CT Attenuation map registration | Medical physicist | Shall confirm that the attenuation maps are registered to the SPECT images within the manufacturer specifications. This is typically performed using manufacturer-provided phantoms and procedures. |

## 3.4. Subject Selection

### 3.4.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Subject Selection | Referring health care provider | For the cross sectional claim, shall establish a differential diagnosis that includes Parkinson’s disease versus other causes of parkinsonism, such as essential tremor. |
| For the longitudinal claim, shall refer eligible subjects |
| Health care provider (nurse, physician, or technologist) | Shall take a history of allergies to iodine;Shall perform a pregnancy test in women of childbearing potential |

## 3.5. Subject Handling

### 3.5.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Pre-injection | Nuclear pharmacy | Shall provide a system that is capable of receiving, dispensing and administering non-radioactive potassium iodide and 123I ioflupane. |
| Health care provider (nurse, physician, or technologist) | Shall perform a formal “time out” identification procedure; |
| Shall administer about 120 mg of Iodine in the form of Lugol’s solution or supersaturated potassium iodide (SSKI) at least 60 minutes prior to administration of ioflupane, and monitor subjects for adverse events and allergic reactions , such as nausea, vomiting, stomach ache, diarrhea, metallic taste in the mouth, fever, headache, runny nose, or sneezing. |
| Shall establish an intravenous line and prove its patency by showing the rate of a saline drip can be easily altered with an inclined roller. |
| Post-injection | Technologist | Shall ensure the subject voids prior to placement on the table |
| Shall place the subject on the table in such a way that maximizes comfort, minimizes the risk of motion, and positions the basal ganglia as close to the center of the field of view as feasible. |
| Shall select the proper acquisition protocol of 123I ioflupane |
| Shall begin image acquisition at 4 hours +/- 15 minutes post intravenous administration of ioflupane |

## 3.6. Image Data Acquisition

### 3.6.2 Specification

| **Parameter** | **Actor** | **Requirement** | **DICOM Tag** |
| --- | --- | --- | --- |
| Imaging device | imaging center and its derivatives standard operating procedures | The acquisition device shall be selected to produce comparable results regardless of the scanner make and model. **Camera:** Multi detector SPECT or SPECT/CT cameras shall be used.**Collimator:** A collimator that provides planar system resolution of < 8 mm FWHM (in ‘air’ at 10 cm distance) shall be used.Head Holder: An off-the-bed head holder (with appropriate cushioning) to achieve an acquisition radius of 12-15cm must be used.  |  |
| Technologist | Shall be certified by local authorities to operate the instrument in compliance with this profile. |  |

| **Parameter** | **Actor** | **Requirement** | **DICOM Tag** |
| --- | --- | --- | --- |
| SPECT Acquisition mode | Imaging center and its applicable standard operating procedures | The key SPECT acquisition mode parameters shall be specified in a manner that is expected to produce comparable results regardless of the scanner make and model. The key parameters are:**Rotational radius**: shall be fixed at 11 – 15 cm (circular orbit) or smallest possible. An off the table head rest is usually needed to achieve this.**Matrix and pixel size**: A matrix size and zoom factor that gives a pixel size of one-third to one-half the expected spatial resolution shall be used. Typically, a 128 x 128 matrix and pixel size of no larger than 4 mm.**Angular sampling:** 360 degree coverage of the head with angular sampling of not less than 120 views shall be used (<= 3 degree increments). Step-and-shoot is typically used, but continuous mode can be used to provide shorter total scan time.**Total counts:** The scan time shall be adjusted to obtain > 1.5 million total counts detected in the photopeak window. Typically, this requires a 25 – 45 min scan.**Energy windows:** The photopeak window shall be set at 159 keV +- 10% (143 – 175 keV). If triple energy-window based scatter correction is to be used, two additional narrow windows (typically 7%) adjacent to the photopeak or as recommended by the system manufacturer shall be used.  |  |
| Technologist | The technologist shall set up the acquisition, acquire the data, and store the data. |  |

**CT Acquisition**

| **Parameter** | **Actor** | **Requirement** | **DICOM Tag** |
| --- | --- | --- | --- |
| CT Acquisition mode | Imaging center and its applicable standard operating procedures | The key CT acquisition mode parameters (kVp, mAs, pitch, and collimation) shall be specified in a manner that is expected to produce comparable results regardless of the scanner make and model, and with the lowest radiation doses consistent for the role of the CT scan: correction for attenuation and for localization. The CT acquisition mode shall utilize the protocol that delivers the lowest possible amount of radiation dose to the subject (e.g. a relatively low dose protocol) that retains the quantitative accuracy of corrections for attenuation.  |  |
| Technologist | The key CT acquisition mode parameters (kVp, mAs, pitch, and collimation) shall be set as specified by study protocol and used consistently for all subject scans.  |  |

| **Parameter** | **Actor** | **Requirement** | **DICOM Tag** |
| --- | --- | --- | --- |
| CT Technique: Protocol Design  | Technologist / Physician / Medical Physicist  |  A team comprising a Technologist / Physician / Medical Physicist shall ensure that CT techniques protocols are designed such that dose exposure is the lowest radiation dose necessary to achieve the objective. Protocols defined by Image Gently and Image Wisely should be used where feasible. The protocol shall be recorded and documented.  |  |
| Technologist | The technologist shall ensure that the CT dose conforms to the dose prescribed by the supervising physician or protocol.  |  |

## 3.7. Image Data Reconstruction

### 3.7.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| SPECT Image Reconstruction | Study Sponsor and Medical Physicist and imaging center and its applicable standard operating procedures | The key SPECT reconstruction parameters (algorithm, iterations, smoothing, field of view, voxel size) shall be specified in a manner that is expected to produce comparable results regardless of the scanner make and model. The key SPECT image reconstruction parameters shall be specified according to pre-determined harmonization parameters.  |
| Technologist | The key SPECT reconstruction parameters (algorithm, iterations, smoothing, field of view, voxel size) shall be followed and set as specified in order to produce comparable results regardless of the scanner make and model.  |
| SPECT Matrix/Voxel size | Technologist | The Technologist shall perform the image reconstruction such that the matrix, slice thickness, and reconstruction zoom shall yield a voxel size of < 4 mm (same as projection bin size) in all three dimensions, although not necessarily isotropic. The final size shall not be achieved by re-binning, etc., of the reconstructed images.  |
| Correction: Attenuation | Technologist | Uniform or non-uniform attenuation correction shall be included in the reconstruction. For uniform correction a narrow beam attenuation coefficient of 0.148 cm-1 shall be used when scatter correction is included while a broad beam attenuation coefficient of 0.11 cm-1 shall be used when scatter correction is not included.For non-uniform attenuation correction the attenuation map shall be obtained by a transmission measurement or x-ray CT (preferred). |
| Estimated Attenuation Map (if used) | Technologist | Shall be defined so that it conforms to the outline of the head as closely as possible. |
| Reconstructed image | Technologist | Shall be reconstructed in such a way as to compensate for attenuation and scatter. Optimal reconstruction depends on the image analysis method used (see Section 3.10).**Whole striatum VOI method**: the reconstruction should be implemented to reduce partial volume effects, e.g., using CDR and partial volume compensation. Controlling voxel-level noise is less important, so post-reconstruction filtering is not recommended, though may be used for visual interpretation.**Small VOI method:** the reconstruction should be implemented to control the effects of voxel-level artifacts such as noise spikes and ringing, including the use of 3-dimensional low-pass post-reconstruction filtering (with 8 – 10 mm FWHM).The reconstructed image should have sufficient spatial resolution to allow reliable independent estimates of the SBR in the Caudate and Putamen.  |
| Stored Reconstructed Image | Camera Manufacturer | Reconstructed images should be stored in such a way as to preserve the image dynamic range. |

## 3.8. Image QA/QC

### 3.8.2 Specification

The normative list below is based on the recommendations from several national and international guidance document and should be applied as appropriate.

| **Parameter** | **Actor** | **Specification** |
| --- | --- | --- |
| Phantom tests: Frequency | Imaging Site | Shall perform and document results of all tests no less than quarterly, and always after scanner upgrades, and repairs or recalibration of the gamma camera motions and/or detectors |
| Phantom tests:Planar Uniformity | Imaging Site | Uniformity of response to a uniform flux of radiation from a I-123 point source shall be measured intrinsically every quarter. On a daily basis planar uniformity with collimators used for I-123 imaging should be performed using a Tc-99m or Co-57 source |
| System Spatial Resolution | Physicist | Tests the resolution of the system in terms of the FWHM of its point spread function. Test should be conducted semiannually with the collimators routinely used with 123I ioflupane studies. The result of the test should be less than 8 mm at 10 cm. |
| Phantom tests: transaxial uniformity measurement | Imaging Site | Using a uniform cylinder filled with I-123, obtain a within slice variability of less than 5%. |
| Phantom tests:suitability for basal ganglia imaging | Imaging Site | Using an anthropomorphic phantom with basal ganglia and reference region background compartments filled at a homogeneous striatal ratio of 4.5:1, to distinguish the caudate nuclei and putaminal, and also with a caudate/putamen gradient of 4.5:1 caudate, 2.25:1 putamen to assess systems ability to determine an uptake gradient across the striata |
| Phantom test: | Imaging Site | Voxel noise in the reference region/background compartment. The COV of the volume of interest thus determined should be recorded and should be below 15%.  |
| Phantom test: data acquisition | Imaging Site | Shall acquire according to Section 3.6 |
| Phantom test: data reconstruction | Imaging Site | Shall reconstruct according to Section 3.7 |
| Phantom test: data analysis | Imaging Site  | Shall ensure noise is less than specified above. |

## 3.9. Image Distribution

This activity describes criteria and procedures related to distributing images that are necessary to reliably meet the Profile Claim.

### 3.9.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Image Distribution | Technologist | The original projections (sinogram) images (scanner raw data), shall always be archived at the local site.The reconstructed SPECT images (image raw data), along with all required corrections, and CT images shall always be archived at the local site.If processed SPECT images are required, they shall be archived as separate secondary datasets. If scanner raw data need to be archived for future reprocessing, this should be defined prospectively in the Protocol. |

## 3.10. Image Analysis

This activity describes criteria and procedures related to producing quantitative measurements from the images that are necessary to reliably meet the Profile Claim.

### 3.10.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Specific Binding Ratio | Image Analyst | Analysis WorkstationShall 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 analysisImage 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 plus and minus up to two adjacent slices spanning an axial extent of 2 cm or less are averaged to generate a single slice image. |
| VOI software analysis toolsUsing analysis workstation tools, volumes of interest are placed on the left and right caudate, the left and right putamen, and the 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 shall 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. |

## 3.11. Image Certification and Interpretation

This activity describes criteria and procedures related to clinically interpreting the measurements and images that are necessary to reliably meet the Profile Claim.

### 3.11.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| count sufficiency | nuclear medicine specialist or nuclear radiologist | Shall confirm sufficient counts have been acquired to reconstruct the images properly |
| clear, conspicuous margins | Shall confirm the margins are sufficiently conspicuous and have not been degraded by excessive patient motion. |
| Excessive motion | Shall confirm that image quality has not been degraded by excessive patient motion. |
| Proper positioning in FOV | Shall confirm that basal ganglia are in the field of view by assessing where the top of the head is. |
| artifacts | Shall ensure assessment is not confounded by ring artifacts, artifacts related to too large a radius for COR (i.e., should be <15 cm, or edge artifacts |
| Mis-registration of SPECT/CT or discordance of Chang’s | Shall ensure that the attenuation map is visually registered to the CT map within one reconstructed voxel dimension. |

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Place VOI | Technologist or image analysis specialist | For SBR, shall cause to have placed volumes of interest (VOI) on structures of interest and appropriate reference tissue. VOIs include caudate, anterior putamen, and posterior putamen on each side of brain. |
| Calculate measurand | Technologist or image analysis specialist | Shall calculate time-point measurand (SBR or %dose/mL) |
| Certify VOI | Qualified physician | Shall either (1) agree with region boundaries, (2) reject boundaries and return for reprocessing, or (3) make revisions “on the fly” as indicated. |
| Certify measurand | Qualified physician | Shall either (1) agree with region boundaries, (2) reject boundaries and return for reprocessing, or (3) make revisions “on the fly” as indicated. |
| classification | Qualified physician | Claim 1: interpret measurand as consistent with, or not consistent with, Parkinson’s disease.Claim 2: interpret measurand a consistent with a value of X +/- y, where x is the measured value, and y is the confidence interval described in Section 2 under Claim 2Claim 3: interpret the measurand as consistent with, or not diagnostic of, change greater than the Repeatability Coefficient (RC) described above |

# 4. Assessment Procedures

## 4.2.5 Assessment Procedure: Voxel noise in the reference/background compartment

| **Parameter** | **Entity/Actor** | **Requirement** |
| --- | --- | --- |
| Planar Uniformity QC | Technologist | At least quarterly and following detector changes, calibrations and/or software upgrades the uniformity of detector response to a uniform flux of radiation of Iodine-123 should be assessed.Daily, or at least on the day of a trial subject, the collimated uniformity of the detectors using collimators to be used for Iodine-123 imaging should be assessed using a Tc-99m or Co-57 source.For both measurements, uniformity should be measured and assessed in accordance with local regulatory requirements. |
| SPECT uniformity QC | Technologistor Medical Physicist | At least quarterly and following detector changes, calibrations and/or software upgrades, the SPECT uniformity should be measured using acquisition parameters defined in the clinical protocol trial. |

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