# Updates to QIBA Amyloid PET Profile

In preparation for Technical Confirmation decision

April 15, 2022

The following updates have been made to the Amyloid PET Profile in order to:

- Increase compatibility with the New Profile Template provided by process committee
- Address Technical Conformance Questionnaire feedback and subsequent discussion and input from working group members
- Complete outstanding or unfinished sections
- Address other items noted upon review

This version could be "final", but will benefit from:

- reviewing /editing the way in which the PET scanner specifications were updated based Technical Conformance feedback, as there was a fairly significant reorganization of content to address this feedback and to be clearer for users
- additional checks of numbering
- insertion of the QIBA url link to access the DRO
- review of the DRO description, with any further edits needed
- decisions regarding which specifications should be left within the checklists
    - several are noted to be "low impact" or "done anyway"
    - several within the Image Acquisition Device are standard on a wide range of manufacturers and models and could be covered by a list of acceptable scanners and software versions

| Section | Change |
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| Title page | Added "and Technical Conformance Questionnaire Comments" to "Version with Public Comments… considered"<br>Updated date |
| Table of contents | Updated |
| Change Log | Inserted |
| Open and Closed Issues | Updated per the updated template format |
| All sections | The word "SPECIFICATIONS" has been added in bold prior to each table containing one or more Specifications, consistent with the updated Profile template.<br>The word "DESCRIPTION" has not been added (after initially doing this) because there are many sections of description and by default they are not the Specifications, which are labeled as such. |
| Various sections | Section numbering has been corrected |

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| Header and Footer | Updated because this version incorporates the newest Profile template as well as the prior 2014 template (which was indicated in the header), and the document generator that was cited in the footer is also not as applicable |
| 1. Executive Summary | The text and format provided in the updated Profile template have been incorporated as the beginning of this section, and blended with the content that was previously present. Some sentences from the original content were reorganized to prevent redundancy.<br>The figure has been given a number (as have all figures in the body) |
| 2. Clinical Context | In this section and all sections, the section number references have been linked to their numbering with the aim of maintaining correct numeric referencing.<br>Sub-section headers were added.<br>Figure numbers and legends were added. |
| 3. Profile Activities | The introductory table of Actors, Activities, and Sections that is used in the updated Profile template was added, along with the updated template text that describes it. |
| 3.2 Amyloid PET activity process flow | Figure number was updated. Step numbers were inserted into the figure, as they are referenced in the text.<br>The text below the figure was updated although the amount of red-lining suggests that more content was changed than was actually the case. Some of the legend content was moved into the body text. |
| Old number 3.2.1.4; adjusted number 3.4.1.4.2 CT Acquisition | Per public comment and working group discussion (prior to Technical Conformance questionnaire) two Specifications pertaining to using lowest dose of radiation possible for CT scan were removed |
| 3.3.3.1.2 Radiotracer Activity Calculation and Schedule | Phrase added “which includes tracers approved by the FDA to date”. Table label added “Tracer reference table” since it is called out in the text. |
| 3.4.1.1 Timing of Image Data Acquisition | Title “Tracer acquisition parameter example table (Refer to manufacturer label for actual use in case of changes)” added to the tracer acquisition parameter table. |
| 3.4.1.1 Timing of Image Data Acquisition | The test “as closely as possible and not more than” was added in front of +/- 5 minutes for the tolerance regarding start of emission following tracer injection. |
| 3.4.1.2 Subject Positioning | Figure 6 added to illustrate the quantitative error caused by translational and rotational motion between emission and transmission scan for several target regions of interest and reference regions. |
| 3.4.1.2 Subject Positioning | Two items added into the Specifications (Actor = Technologist) pertaining to ensuring subject comfort and instructing subject to hold as still as possible during the scan. These were in the description but not specified; despite their qualitative nature, they are important elements in preventing head motion, a major source of error relevant to the Claim. Otherwise, specifications merely required the Technologist to document when the subject did not hold still. |
| 3.5.1 Image Data Reconstruction | Specifications are shown as changed but it was primarily due to consolidation of tables and change of order with descriptive text. |

| Section | Change |
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| 3.5.1 Image Data Reconstruction | The specification regarding the voxel size for reconstruction previously stated <4.5 mm for slice thickness (z-direction). However, this seemed to suggest that this was acceptable for newer scanners, whereas their reconstruction specs are on the order of 2.37mm in ADNI or similar trials. The Profile language was changed to indicate <2.5mm with a parenthetical mention that older scanners (e.g. GE Advance or Discovery LS) may require up to 4.25mm. Although the older GE scanners are still listed for ADNI 3, these scanners are progressively being phased out in favor of newer models. |
| 3.5.2.1 Ensure image orientation | Actor was changed to Technologist from PET Technologist to be consistent with other uses of the Actor term |
| 3.5.2.2.1 Intra-scan inter-timeframe assessment and alignment | In Specification parameter 'Inter-timeframe Consistency", changed "Consistency" to "Spatial alignment" for clarity |
| Old number 3.6.3 Amyloid-PET Acquisition Scanner | The Specification "Shall, on a daily basis, check gantry covers in tunnel and subject handling system" was removed based upon Technical Performance Questionnaire feedback.<br>The Specification immediately following it was moved further down into what is now section 3.8.4.3, Routine Quality Control Schedule. |
| Old number 3.6.3.1 Ancillary equipment | Ancillary equipment (e.g. Radionuclide Calibrator, Scales, Clocks) was previously located within PET scanner in between two PET scanner specification blocks and has been moved to its own section below PET scanner. |
| 3.6.3.2.2 Determine Reference Region | Subheadings added in bold for each different reference region discussed |
| 3.6.3.2.2 Determine Reference Region | "of florbetaben" added to clarify that this was the tracer for which cerebellar cortex was found to be optimal by Villemagne et al |
| 3.6.3.3.1 Generate SUVR image | Introductory sentences were added to be more clear regarding generation of SUVR image vs. measuring and dividing by reference region value |
| 3.8.1.1 Imaging Facility | Actor term was changed to Imaging Facility Coordinator to be consistent with other uses of the term |
| 3.8.3.1 PET scanner models | Descriptive text was added regarding minimizing variability across scanners and using scanners that are well supported and likely to be in use for the duration of a clinical trial. |
| 3.8.3.2 Use of same scanner for longitudinal scans | A subsection 3.8.3.2 was created to focus on the need to use the same scanner for longitudinal scans. Previously, this point was made in multiple places but somewhat buried in other text. Two specifications were added relating to this requirement. |
| 3.8.4 PET Scanner Quality Control | This section has undergone the most updates with the aim of addressing the following issues:<br>(a) multiple responses to the Technical Confirmation Questionnaire raised a concern with the requirement for a Hoffman phantom or equivalent that most sites do not have |

| Section | Change |
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| | (b) some specifications were redundant as basic evaluations were called for followed by evaluations in a separate section with a specialized phantom that focused on the same spec<br>(d) alternative methods to measure performance specifications (vs. the Hoffman phantom) had been mentioned but needed clarification<br>(d) responses to the Technical Conformance Questionnaire indicated the need for 1-2 corrections of testing frequency.<br>In addressing the above issues, all attempts were made to retain the very useful information that existed regarding the Hoffman phantom while also including alternatives. Therefore, much of the Hoffman text, though redline, is not newly written but rather reorganized.<br>The time points or circumstances for which each test should be performed is now located with the test description and specifications rather than in the introduction section. |
| 3.8.4.2 Phantoms for quality control | While retaining the descriptions provided for the Hoffman phantom, the section has been organized in a manner to fit with the discussion of other phantoms, allow that it is an option, and provide a more cohesive or orderly discussion of phantoms followed by tests to be performed. A description of the PAT uniformity software offered through SNMMI (Lodge et al, 2009) has now been included, with example report output added as Appendix J. |
| Old number 3.6.4.1, adjusted number 3.8.4.4 Uniformity and Calibration | An explanation and illustrations relating to the importance of scanner uniformity, as well as notes regarding edge effects, have been added. These provide a quantified rationale for specifications regarding uniformity and head positioning. Thanks to J Sunderland for providing the examples of uniformity results using the PAT Uniformity software.<br>There was mixed feedback regarding the first Uniformity QC check listed in this section. It has been kept in but the comparison to prior scans may need to be required by protocol or performed by a central imaging CRO. |
| Old number 3.6.4.1, adjusted number 3.8.4.4 Uniformity and Calibration | Multiple specifications at different places in the Profile were unified and updated per feedback to adjust frequency, method, and acceptable range.<br>*Previous:* "The transaxial (within plane) uniformity as specified in NEMA NU2 1994 is measured; uniformity is < 10 % for each qualified axial slice (see method below)" and "The scanner calibration is tested using a NIST-traceable (or equivalent) simulated 18F source object, e.g. a uniform cylinder, large enough to avoid partial volume effects or other resolution losses" and "Method: Axial uniformity is measured by placing a circular ROI that is at least 1 cm in diameter less than the active diameter of the cylinder phantom, centered on each of the axial planes. Calculate the COV (std dev/mean * 100) of each ROI. Axial planes whose COV is < 1 % qualify for use (e.g. some of the end planes may not qualify). Please specify if another method is used" and statement that it can be measured with Hoffman phantom.<br>*Revised: "*Axial uniformity shall be measured at least monthly by placing a circular ROI that is at least 1 cm in diameter less than the active diameter of the cylinder phantom, centered on each of the axial planes. The phantom image is |

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| | to be corrected for attenuation, scatter, and decay. Mean axial concentrations in ROIs in the central 80% of planes shall be within ±3% of the overall average for each qualified axial slice within sufficient distance from the axial edge of the field of view (2-4 cm as available). A method and software such as the PAT Uniformity software available from SNMMI may be used for measurement" and "Uniformity across planes against a gold standard reference can also be measured using a Hoffman phantom as described in Appendix H."<br>The uniformity requirement for +/-3% was discussed within the QIBA working group and determined to be feasible (although close to 0 is optimal). Examples acquired by J Sunderland using the PAT software across numerous scanners were useful in determining feasibility; a good example and not as good example are included in the Profile. |
| 3.8.4.5 Resolution | Definition of spatial resolution added at beginning of section.<br>There was some recommendation to remove the reference to a qualitative verification of gross anatomy as it was somewhat confusing as stated and was sometimes interpreted as requiring a Hoffman phantom. This specification remains but wording was adjusted to indicate "either a clinical image or representative brain phantom". This is a simple qualitative check and should not be difficult to implement although it may be superseded by the quantitative test. The Actor has been updated to be either the Nuclear Medicine Physician or the Image Analyst, as this type of check could be performed by an Imaging CRO.<br>Resolution was previously specified in two locations – one where a variety of phantoms were listed, and another that was focused on the Hoffman or equivalent (which resulted in concerns). The resolution specification has been consolidated and alternatives have been clarified: 1) Hoffman phantom, 2) Modified procedure by Lodge et al/PAT uniformity software (previously listed as a grayed out specification for future use), 3) Other published methods since FWHM resolution is a fundamental acceptance test for PET scanners. |
| Old number 3.6.4.3; adjusted number 3.8.4.6 Noise | Same but Actor for frequency specification updated to Medical physicist |
| 3.8.4.7 Contrast | This was previously described as using the Hoffman phantom (and still includes it), but alternative approaches have been added. The required contrast ratio is left to the phantom that is used and its associated QC spec. |
| 3.8.4.8 Accuracy | Allows for use of multiple methods including the SNMMI PAT uniformity software or the Hoffman phantom. |
| Old number 3.6.3.1.1; adjusted number 3.8.5.1 | 'Constancy is evaluated daily (or after any radionuclide calibrator event) using a NIST-traceable (or equivalent) simulated 18F, Cs-137, or Co-57 radionuclide calibrator standard and confirmed that net measured activity differs by no greater than ±2.5 % from the expected value." No change except that "net" was removed and starts out "Shall evaluate daily…" since the actor is the Technologist. |

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| Old number 3.6.3.1.1; adjusted number 3.8.5.1 Radionuclide Calibrator Accuracy | Changed from at least monthly to at least annually, and use of other long-lived NIST standards are acceptable. It was noted during Technical Conformance discussions that because SUVRs and DVRs are ratiometric, accuracy would likely not impact the claim; however, this is a fundamental PET QA step and was recommended to be retained. |
| Old number 3.6.3.1.1; adjusted number 3.8.5.1 | Specification that stated "The scanner calibration is tested using a NIST-traceable (or equivalent) simulated 18F source object, e.g. a uniform cylinder, large enough to avoid partial volume effects or other resolution losses." Was moved because it was a scanner specification, not a calibrator specification. |
| Old number 3.6.3.1.1; adjusted number 3.8.5.1 Radionuclide Calibrator Linearity | Changed from annually to quarterly. "Concentric sleeve method is acceptable" also added. |
| Old number 3.6.3.1.2 Scales and stadiometers | "Scales and stadiometers are confirmed that error is less than +/- 2.5% from expected values using NIST-traceable or equivalent standards" was removed as it does not impact SUVR or DVR. |
| Old number 3.6.4.1 Uniformity and Calibration | "2. The standard deviation of a large central 2D ROI (3D when drawn on multiple slices) shall be compared with similar previous scans to check for measurable differences" was removed from this section as Noise properties are handled in a section below that (old number 3.6.4.3) |
| 4.1 Performance Assessment: Image Acquisition Site | Changed from "Shall perform daily water equivalent phantom analysis; ensure that output is acceptable and manually enter on form /electronic database" to "Follow manufacturer's recommendations" |
| 4.2 Performance Assessment: PET Acquisition Device | Updated PET Scanner calibration specification for uniformity to be consistent with specifications in the PET scanner quality control section. These requirements can also be stated explicitly but they need to be aligned with the quality control section if so. |
| REFERENCES | Two references were added (Lodge, Gong) |
| APPENDICES | A list of Appendices has been added at the beginning of this section. |
| APPENDIX A | Some names have been added to include in recognition. |
| APPENDIX D | Section 6.4.1 had been incomplete and now has a paragraph stating that PET acquisition parameters have been optimized through large multi-site studies such as ADNI, etc. Rather than attempting to include scanner specific protocols in this profile, it refers to these large studies as scanners and protocols will continue to evolve. |
| APPENDIX E | "SUVs" changed to "SUVRs" |
| APPENDIX F | Description of the DRO was updated. Images of the DRO at three different gray/white levels were added. The fact that the image data is deidentified was stressed further. A note was added regarding the fact that the slope of the line for Truth vs. SUVR does not need to be 1, but that the slope should be taken into account when calculating study power based upon expected performance. *The link for the QIDW is needed.* |

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| APPENDIX J | An example report from the SNMMI PAT Uniformity Software report was included. This is a potentially very useful tool that is now referenced in some of the PET scanner specifications and which was developed and is being used by QIBA members (M Lodge, J Sunderland). |
| APPENDIX K | Checklists added per updated Profile template, organized by Actor: Site, Imaging Facility Coordinator, Nuclear Medicine Physician/Radiologist, Medical Physicist, Technologist, Acquisition Device and Reconstruction Software, Image Analyst/Tool checklists<br>Since the Profile has gone through the Technical Conformance Questionnaire stage, the column on the right was used to indicate High impact, Low impact, or Done anyway to aid in consideration as to whether to include these in the checklist. In some cases, a note was also included. Once decisions are made regarding which specifications to include in the checklist, the column could be used for notes regarding impact on Profile Claim (which was mentioned during the presentation of the FDG Profile checklist and its testing in Europe.). |