

QIBA PET Amyloid Biomarker Committee (BC) Call

09 February 2018 at 9:00 AM CT

Call Summary

Additional notes provided by Ms. Matthews

In attendance:			RSNA
Anne Smith, PhD (Co-Chair)	Rachid Fahmi, MSc, PhD	Nancy Obuchowski, PhD	Joe Koudelik
Dawn Matthews, MS, MBA (Co-Chair)	Adriaan Lammertsma, PhD	John Sunderland, PhD	Julie Lisiecki
Satoshi Minoshima, MD, PhD (Co-Chair)	Martin Lodge, PhD	Jean-Luc Vanderheyden, PhD	
Ronald Boellaard, PhD			

Moderator: Dr. Smith

Addressing Profile Public Comments Update:

- Drs. Smith and Lodge met to discuss and prioritize some of the open physics questions earlier in the week
- A few physics points remain for discussion with the entire BC:
 1. One reviewer wanted to include PET/MR scanners to perform PET Amyloid imaging
 - In the current version of the Profile, it would be difficult to include PET/MR parameters
 - Dr. Boellaard suggested that it may be possible to include PET/MR with some additional requirements; some scanner manufacturers already have PET/MR protocol templates in place
 - Although attenuation correction in the brain is considered under control, some questions remain regarding statistical corrections
 - It will be necessary to review the available literature with Dr. Obuchowski to determine the possible impact of attenuation correction on the claim, with a CT-based attenuation correction
 - It will be necessary to evaluate the scanners in a longitudinal study
 - Consensus reached that PET/CT and PET/MR were not interchangeable for base and follow-up scans; the same techniques must be used for both scans
 - Wash U may have a data set for florbetapir similarities and differences, which may be helpful
 - Another ad hoc PET Physics call will be scheduled with PET/MR physicists to sort out these few remaining questions
 - Dr. Smith to contact Dr. LaForest (Wash U) to join the physics call and provide a list of invitees to RSNA staff
 2. The Profile uses the Hoffman 3-D Brain Phantom for quality control
 - A significant roadblock to the use of this phantom is that there is no specific analysis package available; sites typically use a variety of analysis software which makes cross comparisons difficult
 - There is no publicly available open-source software analysis program to use with the phantom
 - Dr. Boellaard has created his own template for use with the Hoffman phantom; however, he too advocates for a standard analysis package to be identified/ made available for use with this Profile
 - As it may not be possible to develop such a package without adequate lead time, the group agreed to add this as a caveat for a future version of the Profile
- Updated documents will be posted by Ms. Matthews to the QIBA wiki on the BC page for review including:
 1. The public comment Excel spreadsheet including proposed BC resolution responses and comments
 2. A PDF version of the original Profile sent out for public comment which contains line numbers that correspond to the resolution spreadsheet
 3. A Word version of the Profile with tracked changes that no longer matches the line numbers due to editsA related document is [Dr. Obuchowski's Statistical Planning for a Clinical Trial Guidance document](#), which explains how the Profile Claims are translated into meaningful statistical numbers, e.g. confidence intervals. (accessible on the wiki through the underlined link in this sentence)

Gap Analysis in comparison to ADNI amyloid PET protocol

- Ms. Matthews conducted a gap analysis comparing the QIBA PET Amyloid BC Profile to the ADNI Amyloid PET Technical Procedure Manual (January 2011)
- Based upon an inquiry to W. Jagust (ADNI PET Core head) the ADNI amyloid data acquisition protocol has remained the same between ADNI 2 and ADNI 3, with the exception that floretaben has been added as an amyloid tracer
- The gap analysis is a two page document that itemizes each aspect of the QIBA Profile compared to the ADNI Protocol.
- The gap analysis identified many similarities, including an emphasis on proper subject positioning and prevention of subject motion
- There are a few inconsistencies, shown in red font on the gap analysis document. One more notable item is that there is some potentially conflicting wording in the ADNI manual regarding the post-tracer injection time window allowed if a re-scan is required. Neither the public comment version of the Profile nor the ADNI protocol had addressed the impact of different head placement and/or scanner axial variability in longitudinal scans.
- ADNI protocols do not address image processing and analysis.
- This [gap analysis report](#) has been posted on the QIBA wiki (accessible through the link associated with “gap analysis” in this bullet point).

Proposals Regarding the Claims

- Propose to leave the technical performance claim as the prominent claim, but adjust the value for the within subject coefficient of variation based upon the updated selection of reference literature
- The second section that follows the claim is very important
- The discussion regarding the impact of blood flow changes will be modified to be clearer as a point of note within this section, followed by further detail in a separate section. This will include the following topics:
 - Changes in blood flow may create false changes in amyloid SUVR, but can be separated from changes in amyloid burden using kinetic modeling
 - Changes in blood flow and clearance can be caused by certain drugs, making this analysis important in the evaluation of therapeutic agents
 - While random changes in blood flow or clearance are already “embedded” as noise accounted for in the SUVR parameters, unidirectional blood flow or clearance changes arising from disease progression or drug effect can become most problematic if they are systematic, biasing amyloid results rather than increasing variability

Alternatives for addressing blood flow and clearance factors that will be described in the profile section:

- Exploratory full dynamic studies
- Dual frame acquisition has been gaining Pharma interest
- Bolus (more difficult to implement consistently)

NM WebEx Schedule

03/02	FDG-PET BC
03/09	PET Amyloid BC
03/16	SPECT BC
03/23	NM Coordinating Cttee