

Objectives for Call

- Voting Explanation
- Recap of Profile Updates
- Transition to Feasibility Testing
- Next Steps

Voting



Susan Stanfa <sstanfa@rsna.org>

Susan Stanfa

Monday, May 7, 2018 at 4:13 PM

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Dear QIBA PET Amyloid BC Voting Members:

The PET Amyloid BC would like to vote to establish that the Profile has attained [CONSENSUS](#) status (Stage 2 of Profile development).

Please visit the eBallot at: <https://tinyurl.com/y8ynokmy> and vote by **EOB** on **Monday, May 21**. For reference, the [PET Amyloid Profile](#) is available on the QIBA wiki.

Working documents are posted on the Biomarker Committee's page: http://qibawiki.rsna.org/index.php/PET_Amyloid_Biomarker_Ctte

If you have questions, please contact the PET Amyloid BC Co-Chairs, [Ms. Matthews](#), [Dr. Anne Smith](#), [Dr. Satoshi Minoshima](#), and NM Scientific Liaison, [Dr. Paul Kinahan](#).

Best Regards,

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Voting

Stage 2 Consensus	The wider community has read the profile and believe it to be practical and expect it to achieve the claimed performance
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Voting: Consensus Stage

Stage 2: Consensus

Meaning:

- The Profile is widely believed to be practical.
- The Profile is expected to achieve the claimed performance.
- The Profile is ready for Feasibility testing.
- The Profile claim and requirements may change based on Feasibility testing results.

Criteria:


- All public comments have been addressed
- All open issues necessary for conformant deployment have been resolved
- Few, if any, groundwork projects remain active
- All recommended procedures have been tested in one or more groundwork project(s) or referenced studies. (Reasonable deviations from Profile details may exist.)
- Requirement specifications include requirements and assessment procedures for the statistical assumptions underlying the Profile Claims (e.g. assessment procedure includes sample sizes, details of phantoms and data collection methods, metric computation, requirement specified thresholds).

Posted documents

Priority (L, M, H)	Line #	Section #	Issue	Proposal	Resolution	Modification entered in red line version
M	357		Other health professionals, such as nurses, can also administer radiotracers, with appropriate training.		Modify actor for this box to read "Technologist, Physician, Nurse, or c	x
M	1013-1014	3.6.2	Definition of qualifications of physicians overseeing amyloid brain PET CT in United States.	The physician should either be boarded by ABNM and/or ABR.	Add under qualifications that "the physician should have board certification by the American Board of Nuclear Medicine (ABNM)	x
L	1194	4.1	Duties of Medical Physics not completely listed	Sentence could be completed with "...address issues of quantification such as attenuation maps movement, etc."	Add "and to address issues relating to quantification such as attenuat	x
H	143		Threshold change metric of 8% when data shows 1% per year is expected. Will this be interpreted to mean that a trial should not be considered appropriately powered if the change is less than 8%? The implication of this 8% number needs further explanation in the text, esp since NIH typically only funds studies for 5 years.		Addressed by stating a Coefficient of Variation that can be tied to published studies aligned with profile guidelines, tightening the guidelines and adding caveats, and then explaining in the Clinical Interpretation section how this information can be applied to study design for the calculation of required numbers of subjects, as well as implications for individual longitudinal measurements.	x
H	130ff		The 2 claims: "A measured change in SUVR of Δ % indicates that a true change has occurred if Δ > 8 %, with 95% confidence" and "Y1 and Y2 are the SUVR measurements at two time points, then the 95% confidence interval for the true course of disease (initial increase of amyloid-burden, later plateau-	It should be explained on which assumptions these claims are based and references need to be added (e.g. changes greater than test-retest variability?). Also, it may be important to consider which time frame these claims are referring to (% change in a year?). Also, the natural course of disease (initial increase of amyloid-burden, later plateau-	Addressed by stating a Coefficient of Variation that can be tied to published studies aligned with profile guidelines, tightening the guidelines and adding caveats, and then explaining in the Clinical	x
H	130					x
H	181					x

Excel spreadsheet with (deidentified) public comments, pdf line number references, and proposed responses

QIBA Profile Format 20140221



1
2
3 **QIBA Profile. ¹⁸F-labeled PET tracers targeting**
4 **Amyloid as an**
5 **Version with PUBLIC COMMENT**
6 **02May2018**
7

Pdf version of the profile as updated

224 **2.1. Claim**
225
226 If Profile criteria are met, then:
227
228 Claim 1: Brain amyloid burden as reflected by the SUVR is measurable from 18F amyloid tracer PET with a
229 within-subject coefficient of variation (wCV) of <=1.94%.
230
231 This technical performance claim is to be interpreted in the context of the considerations stated below.
232
233 **2.2. Considerations for claim**
234
235 The following important considerations are noted:
236 1. The technical performance claim was derived from a review of the literature summarized in Appendix
237 B, where 18F amyloid PET tracers were used and data acquisition and processing procedures were
238 considered to be adequately aligned with the recommendations in this profile. The constraint of a
239 sixty day period (or less) for test-retest was applied in order to avoid the possible contribution of actual
240 changes in amyloid burden. The wCV cited is the highest ("worst case") of these short term test-retest
241 studies, where wCV values ranged from 1.15% in healthy controls using a cerebellar cortex reference
242 region to 1.94% in AD patients using a whole cerebellum reference region. A limitation is that only two

Red-lined Word version of profile as updated

Public Comments and Responses

Category	Number
Acquisition parameters	5
Analysis methods	6
Centiloid	5
→ Claim	5
Clinical context	4
→ Full dynamic modeling	1 (3)
Patient prep/positioning	6
Personnel qualifications	3
→ PET/MR	1
Radiotracer	10
Reconstruction	2
→ References (ref region)	9
Reporting	1
Scanner QC	4
→ Terminology, numberings	26
Total	87

Claim

Category	Number
Acquisition parameters	5
Analysis methods	6
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- Reference literature updated to align with guidelines
- Citing one Technical Performance Claim
- Updated Claim Considerations; strongly stated caveats
- Developed Clinical Trial Examples using wCV and assumptions for literature
- See Profile group meeting slides from:
 - Oct 12, 2017
 - Feb 9, 2018
 - April 13, 2018

Full Dynamic Modeling

Category	Number
Acquisition parameters	5
Analysis methods	6
Centiloid	5
Claim	5
Clinical context	4
→ Full dynamic modeling	1 (3)
Patient prep/positioning	6
Personnel qualifications	3
PET/MR	1
Radiotracer	10
Reconstruction	2
References (ref region)	9
Reporting	1
Scanner QC	4
Terminology, numberings	26
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- Claim considerations revised to make more clear
- Appendix I added on Kinetic Modeling
- See Profile group meeting slides from:
March 9, 2018
April 13, 2018

PET-MR

Category	Number
Acquisition parameters	5
Analysis methods	6
Centiloid	5
Claim	5
Clinical context	4
Full dynamic modeling	1 (3)
Patient prep/positioning	6
Personnel qualifications	3
→ PET/MR	1
Radiotracer	10
Reconstruction	2
References (ref region)	9
Reporting	1
Scanner QC	4
Terminology, numberings	26
Total	87

- PET-MR is now included
- Text updates implemented
- See Profile group meeting slides from:
March 9, 2018

References

Category	Number
Acquisition parameters	5
Analysis methods	6
Centiloid	5
Claim	5
Clinical context	4
Full dynamic modeling	1 (3)
Patient prep/positioning	6
Personnel qualifications	3
PET/MR	1
Radiotracer	10
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- Numerous references added
- Primary categories:
 - Reference region
 - Kinetic modeling
- In reference section, retained by-topic grouping but stated and ordered by first author last name

References

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- Numerous references added
- Primary categories:
 - Reference region
 - Kinetic modeling
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Other

Category	Number
Acquisition parameters	5
Analysis methods	6
Centiloid	5
Claim	5
Clinical context	4
Full dynamic modeling	1 (3)
Patient prep/positioning	6
Personnel qualifications	3
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Radiotracer	10
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- Uniformity in axial field of view
- 10% variability allowance is automatic recipe for longitudinal SUVR error
 - Reference region dependent
- Narrowed variability guidance
 - Less issue in new scanners

Notes regarding variability

ADNI PET procedures have a similar focus to profile on motion avoidance

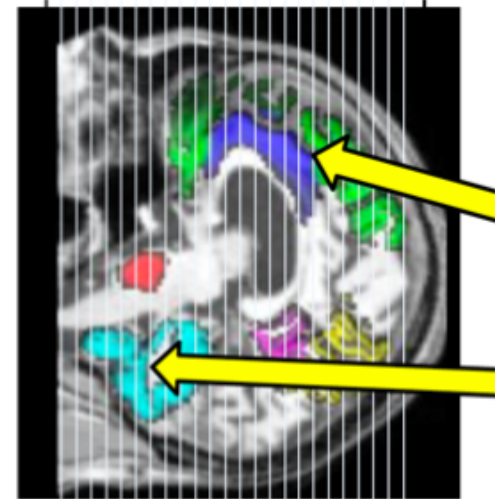
Participant Positioning

Proper patient positioning is a key aspect of the successful completion of the PET exam. It is important to take the time necessary to ensure not only that the patient is properly positioned but can comfortably maintain that position throughout the duration of the scanning session. **Excessive motion and in particular a difference in the subjects' position between the emission scan and the transmission (or CT) scan used for attenuation correction is the single most common cause of failed studies.**

- However, cautions against subject motion do not preclude motion from occurring
 - Subject motion occurs, despite precautions
 - Other sources of variability occur
 - Thus, reference region definition has impact as evidenced in the literature (e.g. Chen, 2015; Brendel 2015; others cited in profile); Groundwork projects showed that different reference and target regions have differing vulnerabilities to factors such as subject motion

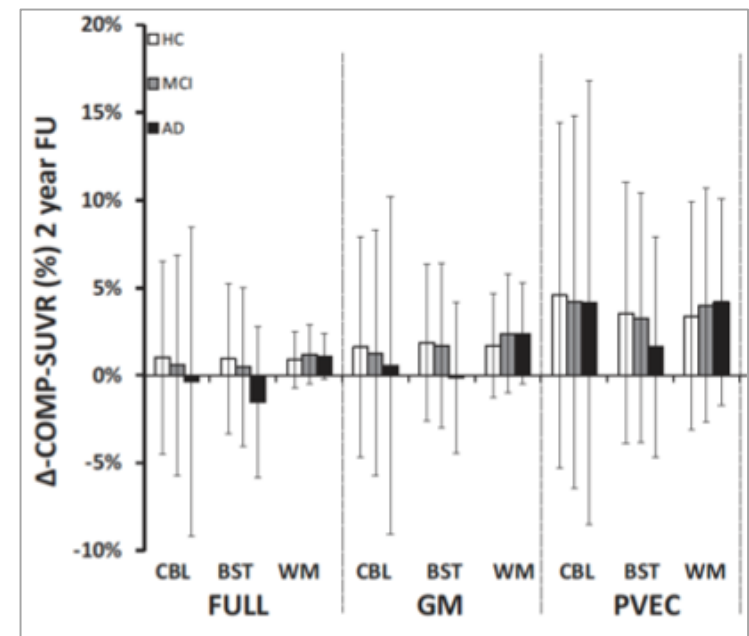
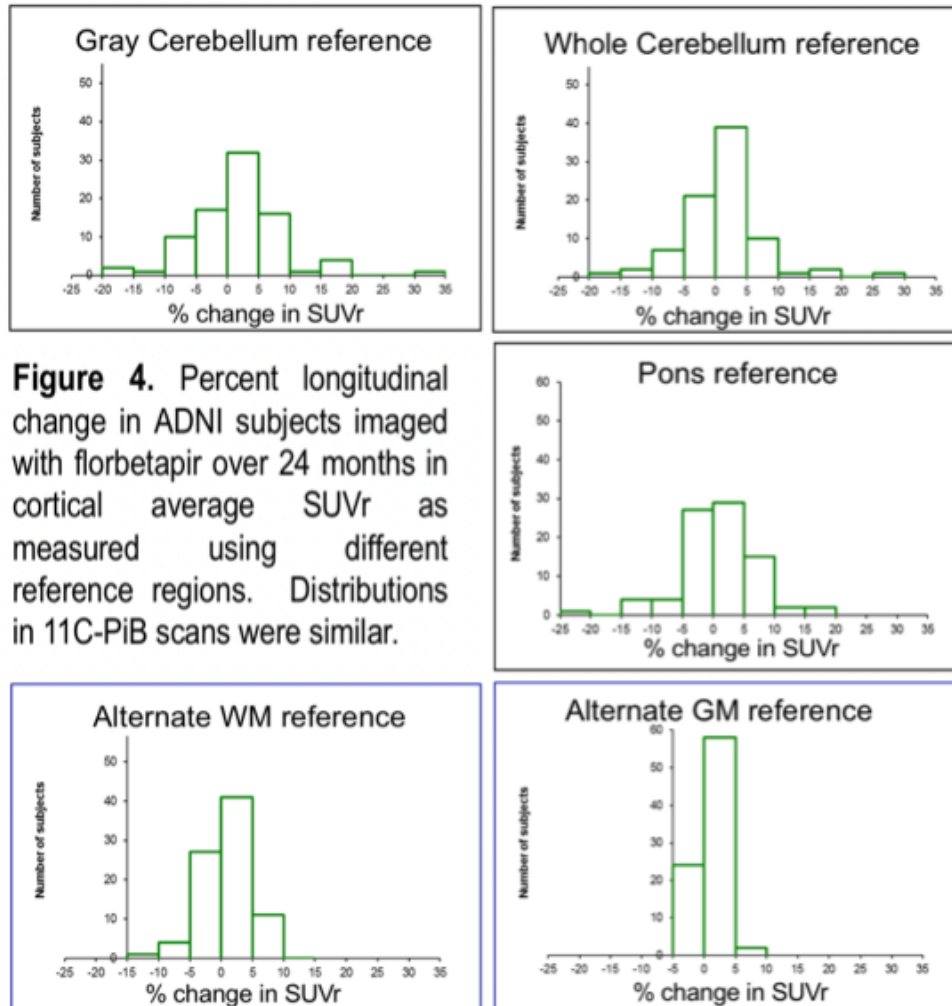
Notes regarding variability

- Scanner axial variability is historically “within 10%”, which is a “recipe” for longitudinal variation in SUVR
- The axial uniformity guideline was tightened in the profile update
- However, the profile claim is based on reference literature that did not constrain axial variability to a more rigid standard than within 10% (so a “worst case”, even though the profile recommends a tighter constraint)
- This is one reason that reference region selection makes a difference (see explanation at right)



If scanner axial uniformity varies, then depending upon subject position from scan to scan, differences in SUVR will be introduced not because of amyloid changes, but rather due to differences in scanner sensitivity across axial slices. Impact on SUVR only cancels out when the target region and reference region are in the same axial slice.

Note regarding variability



Brendel et al 2015

Matthews et al, HAI 2014

Next Steps

Vote

If not passed:

Address concerns, remaining items

If passed (and regardless):

Feasibility testing

Follow up on Hoffman file, script