QIBA PET Amyloid BC Meeting

August 12, 2016

Agenda

- Round 6 Projects that received funding
- Image Analysis Workstation Conformance – Draft Protocol
- Next Steps/Closing Remarks

Round 6 Funded Projects

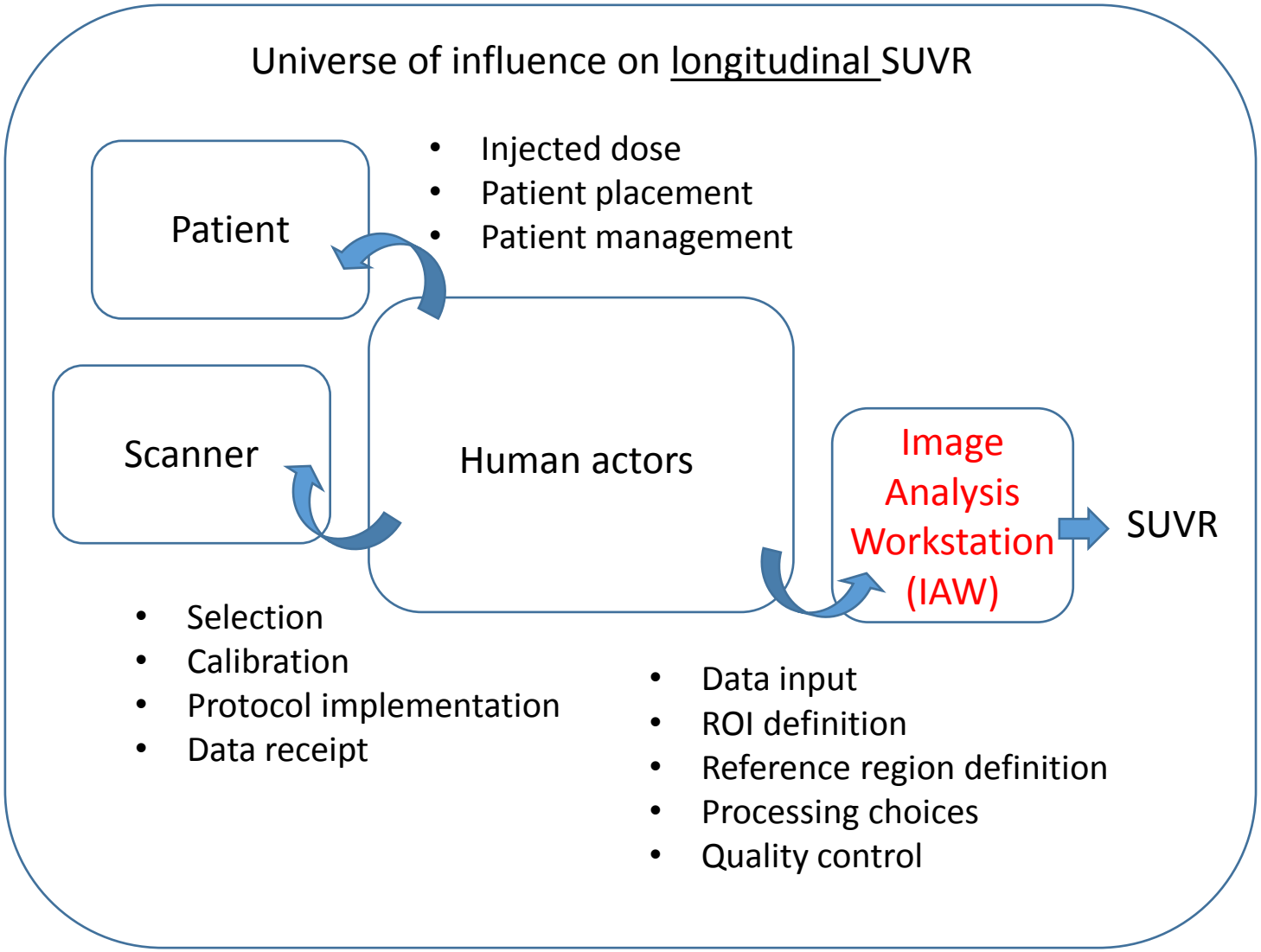
Proj ID	BC	Project Description	PI
1	FDG-PET	SUV Quantification with Point Spread Function PET Reconstruction	Martin Lodge, PhD Johns Hopkins University Co-PI: R Boellaard, PhD
19	CT Vol	Methodology and Reference Image Set for Lesion Characterization in Terms of Texture and Morphology	Ehsan Samei, PhD Duke University
11	DTI	Measurements of Reproducibility of DTI Metrics on Clinical MR scanners using a DTI Phantom	James Provenzale, MD Duke University
20	Lung Density	CT Lung Density Biomarker: Translating Phantom Harmonization to Clinical Practice	Stephen Humphries, PhD, National Jewish Health
3	SPECT	Multi-Center Phantom Study to Characterize Bias and Precision of Quantitative ^{123}I SPECT	Yuni Dewaraja, PhD, University of Michigan Co-PI: J Dickson, PhD
15	VBF	Examination of Flow Phantom as Reference Standard for Validation of Ultrasound Volume Blood Flow Measurement	Oliver Kripfgans, PhD U of Michigan
2	SPECT	I-123 DAT Scan Digital Reference Object Development	Robert Miyaoka, PhD U of Washington
13	QIDW / PDF: DSC	A Web-Based Tool for Creating DSC Digital Reference Objects	Bradley Erickson, MD, PhD Mayo Clinic
12	DCE	Evaluation of RF transmit calibration options for quantitative DCE-MRI	Krishna Nayak, PhD U of Southern California
7	Amyloid	Matched Digital and Physical Amyloid Phantom for Software and Scanner Validation: Digital Component	Paul E. Kinahan, PhD U of Washington
16	SWS	Establishing Acceptable Variance Limits for Healthy, F1 and ≥F2 Fibrosis Shear Wave Speed Values Across Systems and Between Operators for the QIBA Profile	Manish Dhyani, MD MGH
5	FDG-PET	Simple Variability Estimates in PET	Timothy Turkington, PhD Duke University
4	Amyloid	Quantification of Reconstruction Method Impact on Measured Amyloid Load	Dawn Matthews ADM Diagnostics, LLC

QIBA PET Amyloid Claim 1

A measured change in SUVR of Δ % indicates that a true change has occurred if $\Delta > 8\%$, with 95% confidence.

QIBA PET Amyloid Image Analysis Workstation Needs Based on Claim

- Only have longitudinal claim
  - No need to measure bias, as long as:
    - Same patient, same scanner, same protocol, same analysis, etc.
    - Note: major offsets or constant error still unacceptable and detected by linearity tests (under what conditions)
  - Linearity
    - Is our system linear for a range of SUVRs?
  - Repeatability
    - Can we get the same SUVR multiple times if nothing has changed?



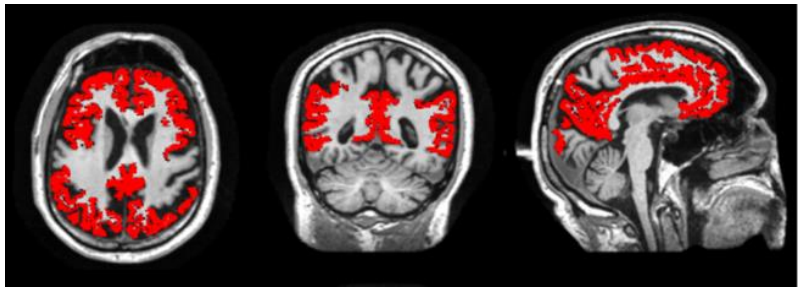
Key Points

- Unknown how each component contributes to overall system variance
- We are focusing only on IAW for this section of conformance testing

Analysis methods (two approaches of several)

ADNI (Jagust Lab)

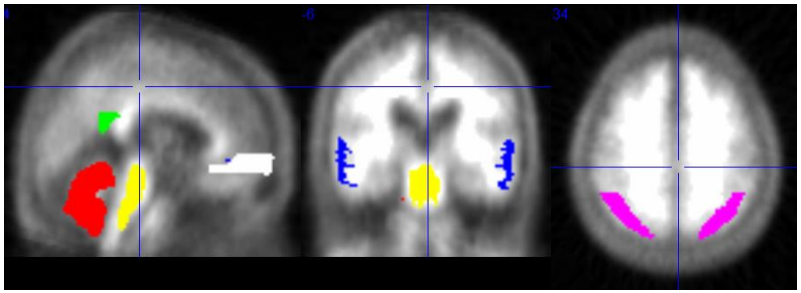
- PET image motion corrected, frames averaged, intensity normalized, smoothed
- PET coregistered to MRI
- Gray matter ROIs defined using Freesurfer
- Signal intensity measured
- Cortical average = frontal, AC, PC, lateral temporal, lateral parietal
- SUVRs calculated
    - Ref regions: Whole cer, brainstem, subcortical white matter, composite



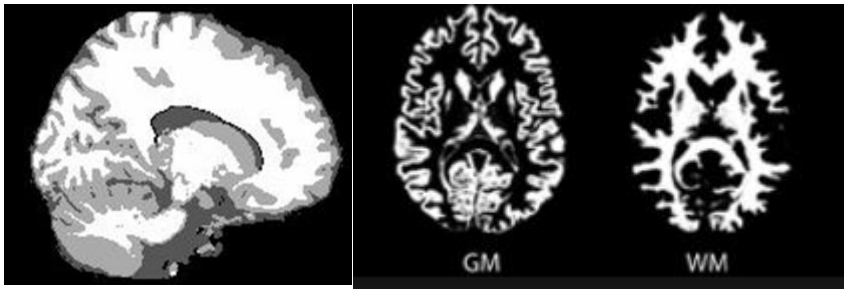
ADNI_UCBERKELEY_AV45_Methods_12.03.15.pdf

Avid (not on label)

- PET preprocessed
- PET spatially warped to PET template
- Probabilistic template ROIs applied
- Signal intensity measured
- SUVRs calculated
    - Ref regions: Whole cer, pons, subcortical white matter



IAW Conformance Testing – Draft Protocol



DRO has 3 regions

- GM – variable Bq/ml
- WM – fixed Bq/ml
- Reference Region e.g. Cerebellum GM– fixed Bq/ml

Planning to use Paul Kinahan's

Protocol will simulate 6 different "subjects" tested 5 "times"

- 6 different "subjects" simulated using variable (GM)/(Reference Region) ratios
  - The SUVR range should cover healthy controls to advanced amyloid plaques
  - e.g. SUVR of target GM-only regions = 0.9, 1.0, 1.1, 1.2, 1.3, 1.4
  - Note: since not all target regions are GM only, the actual target SUVR ratios will vary within a subject. How best to handle this? Explicitly state which target regions should be tested?
- 5 different "times" tested using different noise realizations and transformation parameters
  - Use representative patient images to measure typical noise level for each region
  - Generate 5 different noise realizations for each "subject", using typical noise level found above
    - Transform each noise realization in a clinically realistic way (e.g. 2 mm translation, 2 degree rotation)
- Final DRO dataset will be a 30 volume series
- Sites should analyze these 30 volumes using same IAW and protocol they use for patients

Typical Regions Used for Target and Reference

Target

- Frontal
- Anterior cingulate
- Posterior cingulate
- Lateral temporal
- Inferior parietal regions
- Occipital cortex

Reference

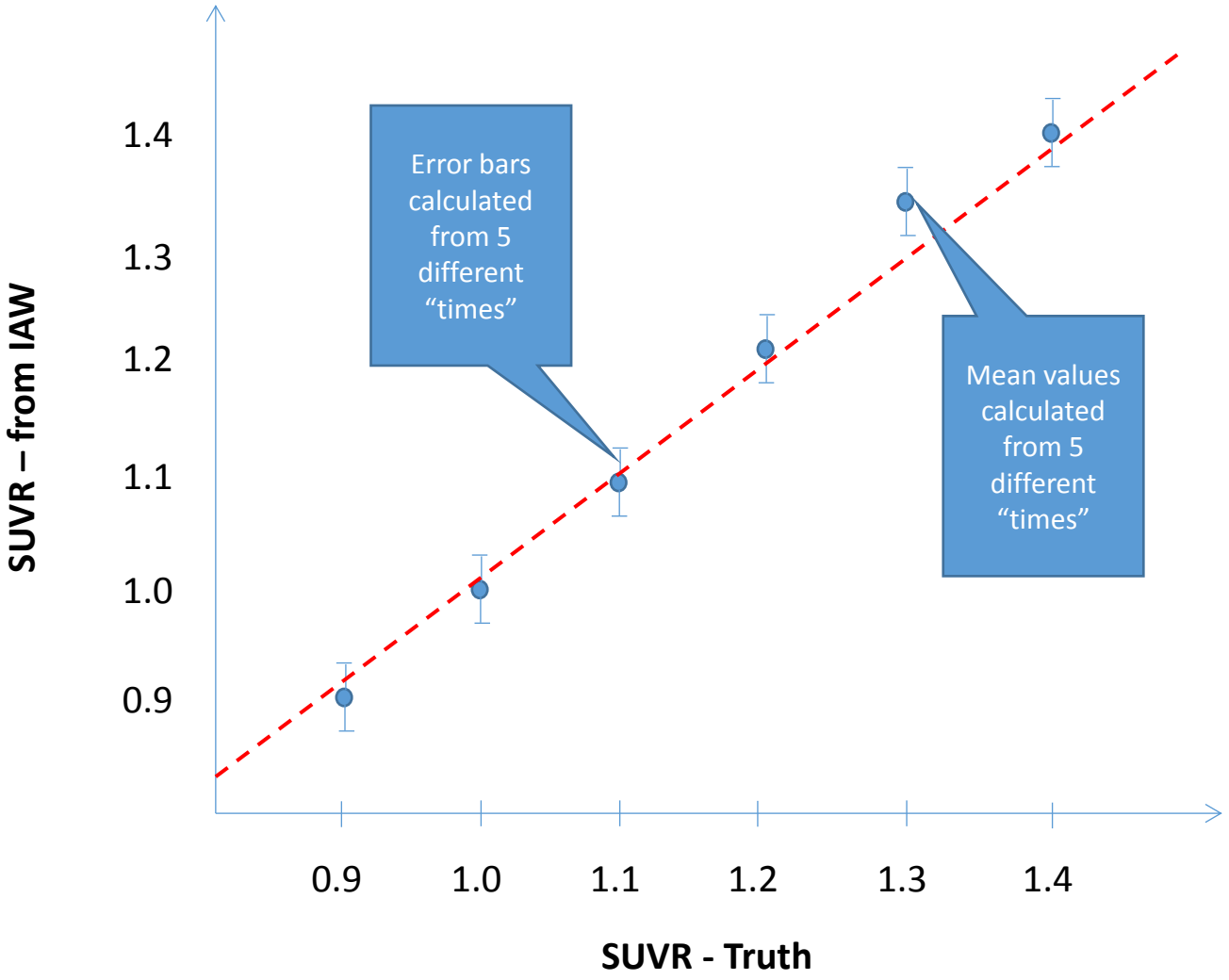
- Whole cerebellum
- Cerebellar gray matter
- Pons
- Brainstem
- Eroded subcortical white matter
- Composite

Specify regions that are GM only for this conformance test?

Example Output – For Single Target Region

Will be one graph for each Target Region if single reference region is used
If multiple reference regions, then total graphs = (number of target regions) x (number of reference regions)

IAW Conformance – Target Region 1



Key Points

- Linearity: Profile will state accepted linearity measures (e.g. quadratic term, slope, R^2, etc.)
- Repeatability: Profile will state acceptable error bars for data points

The Profile would tell the IAW actor to:

1. Fit an ordinary least squares (OLS) regression of the Y_i's on X_i's (blue data points on previous graph). A quadratic term is first included in the model: $Y = \beta_0 + \beta_1 X + \beta_2 X^2$.
2. Re-fit a linear model: $Y = \beta_0 + \beta_1 X$ (red dotted line on previous graph). R-squared (R^2) shall be >0.90.
3. The estimate of β_1 and of B_2 shall be reported as part of the assessment record. – see Compliance Statistics Template

4. At each measurand (e.g. SUVR) value, calculate the mean and SD.
5. Calculate the %RC (formula).
6. The %RC shall be ≤4%.

Sample Size Considerations for Testing RC:

Assumption (due to our Claim): The IAW's RC needs to be ≤4%.

- With 6 SUVR values ("subjects"), and 5 realizations ("times") at each, an actor would need to have their RC<2.6% in order to meet the Profile criterion (80% power to show that their RC is ≤4%)

Options:

# of Subjects (SUVRs)	# of Realizations (Tests per subject)	RC Threshold
6	5	2.6%
7	5	2.8%
9	5	2.9%
11	5	3.0%
6	10	3.1%

Other Notes/Questions from Dawn:

- clarify what aspects of IAW the conformance approach will and will not test
  - need to be realistic limits on just how many aspects of the software should be tested

- The proposed approach will specify the anatomical regions that should be included in the SUVR. We will give a table of all anatomical regions that will be used for target and reference regions with the "true" SUVR listed for each.

- Add a step where IAW will show the template regions it found super-imposed on the DRO

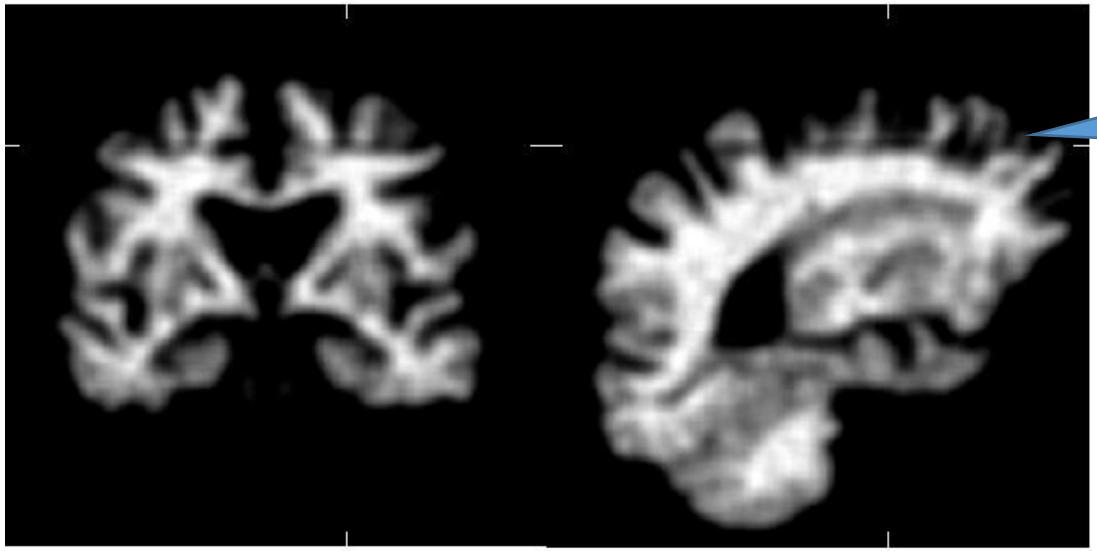
- The proposed approach does not specify the VOI boundaries to be applied. Should it?

- Currently each subject will have multiple orientations by transforming each replication differently. Is this worthwhile?

- An approach of using a single morphology will only test the software's ability to accurately transform or segment that morphology. Should we change DRO morphology for the higher SUVR "subjects" (i.e. segment an advanced AD patient's MRI for DRO)?

- Unless an MRI is provided along with the "PET" scan, software that uses a coregistration with MRI and segmentation of the MRI to produce VOIs for sampling will not be testable. Do we need to supply the corresponding MRI with our DRO?

Details of Paul Kinahan's PET Amyloid DRO



Segmentation artifact that Paul will correct

DRO Steps:

1. Used MRI images from a patient
2. Segmented needed regions
3. Assigned appropriate values to segmented regions
4. Add typical PET levels of blurring and noise
   - Anne can transform volumes using tools developed for motion characterization project
5. Save DROs in DICOM format to an "IAW DRO Conformance Series" (e.g. a set of 30 volumes)

Paul willing to vary Steps 3 and 4 to mimic "subjects" and "times"

Profile: Next Steps and Milestones

- Have current version of DRO read by radiologist (Rathan?)
- Make requested changes to DRO based on radiologist feedback
- Hold task group meeting and write up IAW Conformance section, based on limited knowledge and knowing it will be changed later
    - Constrain what DRO tests in optimal way
        - Single Gaussian filter value for smoothing? (currently set at 6 mm FWHM)
        - Only one patient morphology will be tested (no time to segment another MRI volume)
        - Decide if anatomical regions will be specified
        - Decide if region boundaries will be specified
        - Decide if test needs to report an overlay of the target and reference regions on the DRO
        - Should MRI be provided with DRO series?
        - Should multiple realizations include simulation of patient movement?
- Develop limited initial series of DROs and test on IAWs
- Based on feedback, updated DRO series and Profile IAW Conformance section of Profile