QIBA PET Amyloid BC March 11, 2016 - Agenda

1. QIBA Round 6 Funding
   a. Deadlines
   b. What projects can be funded, what cannot
   c. Discussion of projects
      - Mechanical phantom and DRO – Paul & John ?
      - Any Profile gaps left to fill with a project?

2. QIBA Round 5 Project awarded to Dawn: subject motion

3. Status of Profile feedback
   a. Next steps

Round 6 Funding Details

- Project proposal due April 15th
  - Send to RSNA Staff: qiba@rsna.org
  - Funding cannot support human studies
- Note new focus - for all Round-6 projects:
  - All projects must support the NIBIB contract objectives
  - Support the completion/advancement of a Profile and/or conformance procedures/checklists.
    - BC leadership are charged with approving preliminary projects.
    - Final selection in July

Project Ideas

- Continue work on DRO and Phantom (Paul and John)
- Current knowledge gaps in Profile
  - Tracer uptake time differential between measurement time points
    - Acceptable level of difference
    - Ronald Boellaard will develop a draft project
      - Dr. Vanderhayden will support, perhaps radiopharm vendors?
  - Conformance testing project
    - Sites, scanner vendors, analysis vendors
  - Reader variability project
  - Scanner/reconstruction harmonization project
    - Ex: PET/CT scanner model is changed, is there a way to harmonize the SUVR values between the old and new scanners?

Quantitative Imaging Biomarkers Alliance

RSNA

PET Amyloid BC

QIBA Round 5 Funding

Analyses to Support Amyloid Imaging Profile Development:

Quantify the Effect of Misalignment and Subject Motion

Anne M. Smith, PhD Technical Support

Siemens Molecular Imaging

Dawn Matthews Principal Investigator

ADMdx

Profile Gaps We Want to Fill With This Work

- Characterize the effect of patient motion on SUVRs
  - How significant is movement between CT and PET acquisitions
  - How significant is movement during PET acquisitions
    - Make recommendations for "how much is too much" motion
  - Does the distribution of an 18-F amyloid tracer matter

- (If time) Effect of PET image reconstruction algorithm on SUVRs
  - Determine if significant differences for these algorithms
  - Reconstructed voxel size 1 mm x 1 mm x 2 mm (zoom=2)
    - OSEM3D (2i24s, 5 mm Gaussian)
    - OSEM3D + TOF (2i21s, 5 mm Gaussian)
    - OSEM3D + PSF (3i24s, 5 mm Gaussian)
    - OSEM3D + TOF +PSF (2i21s, 5 mm Gaussian)

Project Workhorse

PET/CT Scanner

- Siemens mCT 4 Ring Scanner
  - 22.1 cm axial FOV
  - 70 cm transaxial FOV
  - 4.1 nsec coincidence window
  - ≤12% FWHM Energy Resolution
  - 540 psec TOF
  - 33% scatter fraction @ low act
  - 10.2 cps/kBq Sensitivity
  - NEMA Pt Source FWHM Resolution

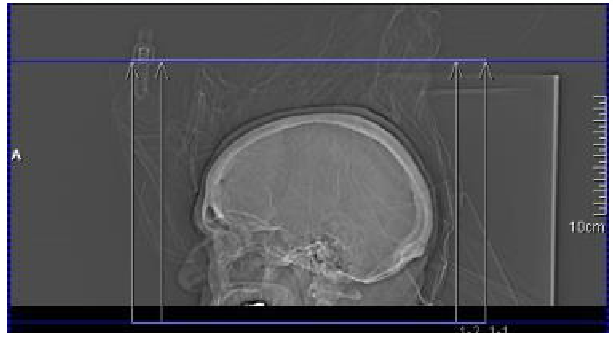
400x400 (2mmx2mmx2mm)	@1 cm	@10 cm
Transaxial	4.5 mm	5.2 mm
Axial	4.7 mm	6.1 mm

PET/CT Amyloid Data

- Avid Florbetapir Clinical Trial at University of Tennessee Medical Center
  - Selected three datasets with minimal motion/misalignment
    - Healthy Control, amnestic MCI, early AD
  - 10 mCi of Florbetapir injected with 50 min uptake time
  - 120 kVp 50 mAs non-diagnostic quality CT acquired, with Care Dose
    - Used for PET attenuation and scatter corrections
    - 30 cm transaxial FOV
  - Subject’s head secured with a bean bag Vac bag
  - PET data
    - Single bed position
    - 10 minute listmode acquisition
  - Reconstruction
    - 400x400 matrix
    - Matched axial slices of CT volume
    - Reconstructed voxel size 1 mm x 1 mm x 2 mm (zoom=2)
    - Multiple recon algorithms/parameters used (previous slide)

Topogram – Patient Prep & Scan Planning

Healthy Control (HC)
- Female
- 75 years old
- 73 kg
- 55 min uptake

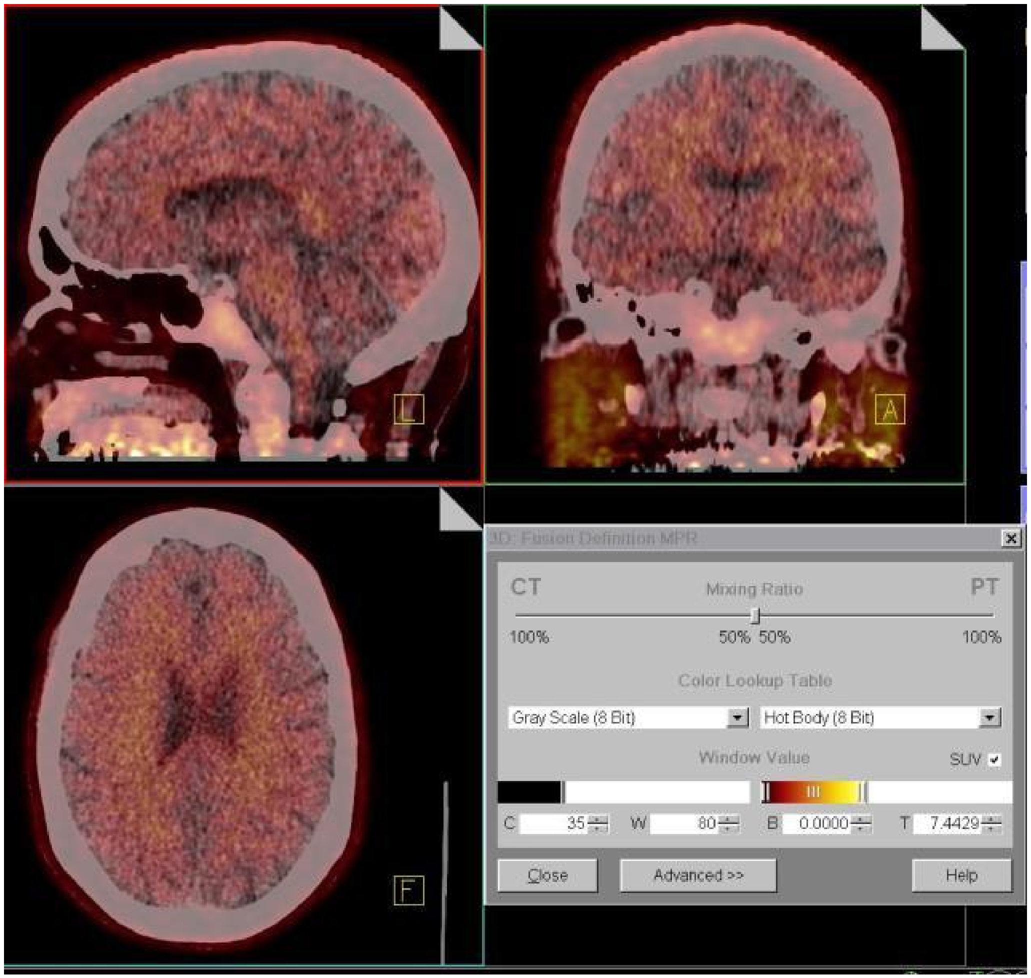


Amnestic MCI (aMCI)
- Male
- 78 years old
- 80 kg
- 52 min uptake

Early Alzheimer’s (eAD)
- Male
- 71 years old
- 84 kg
- 54 min uptake

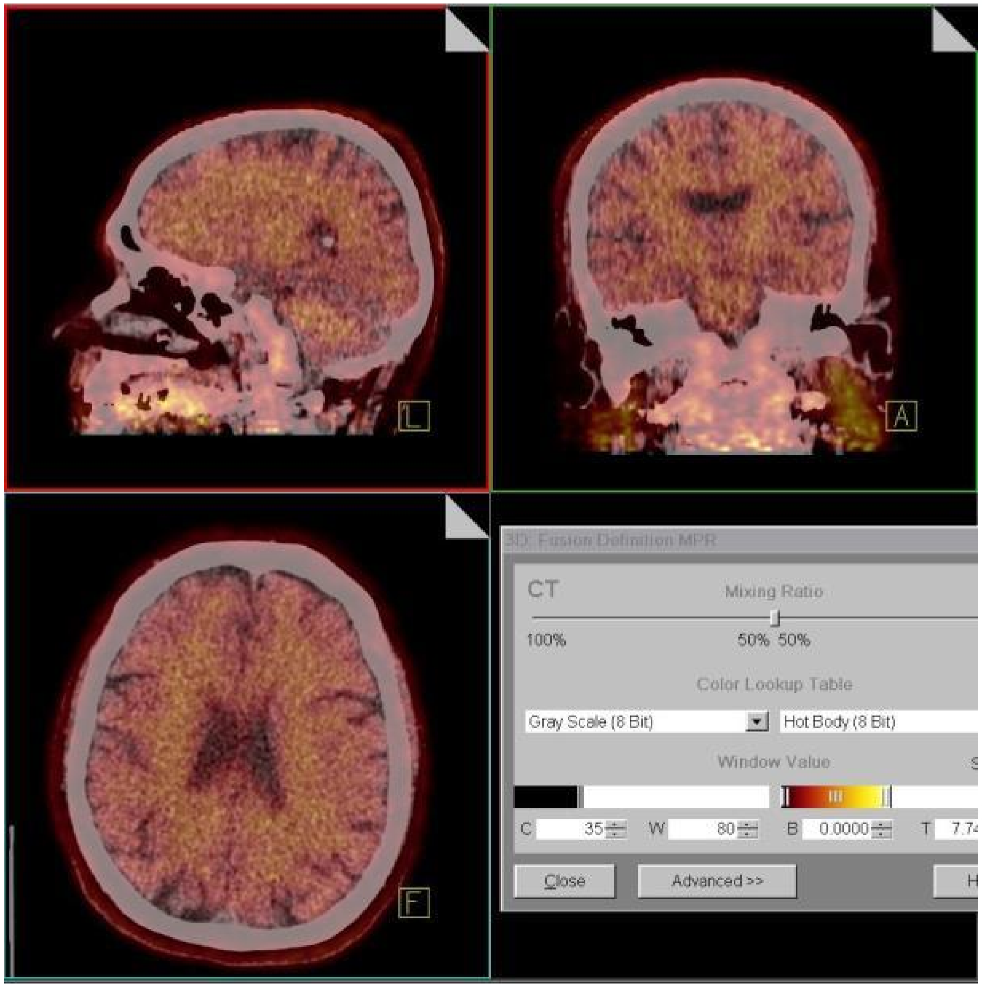
Assess for Subject Motion and CT-PET Misalignment

HC



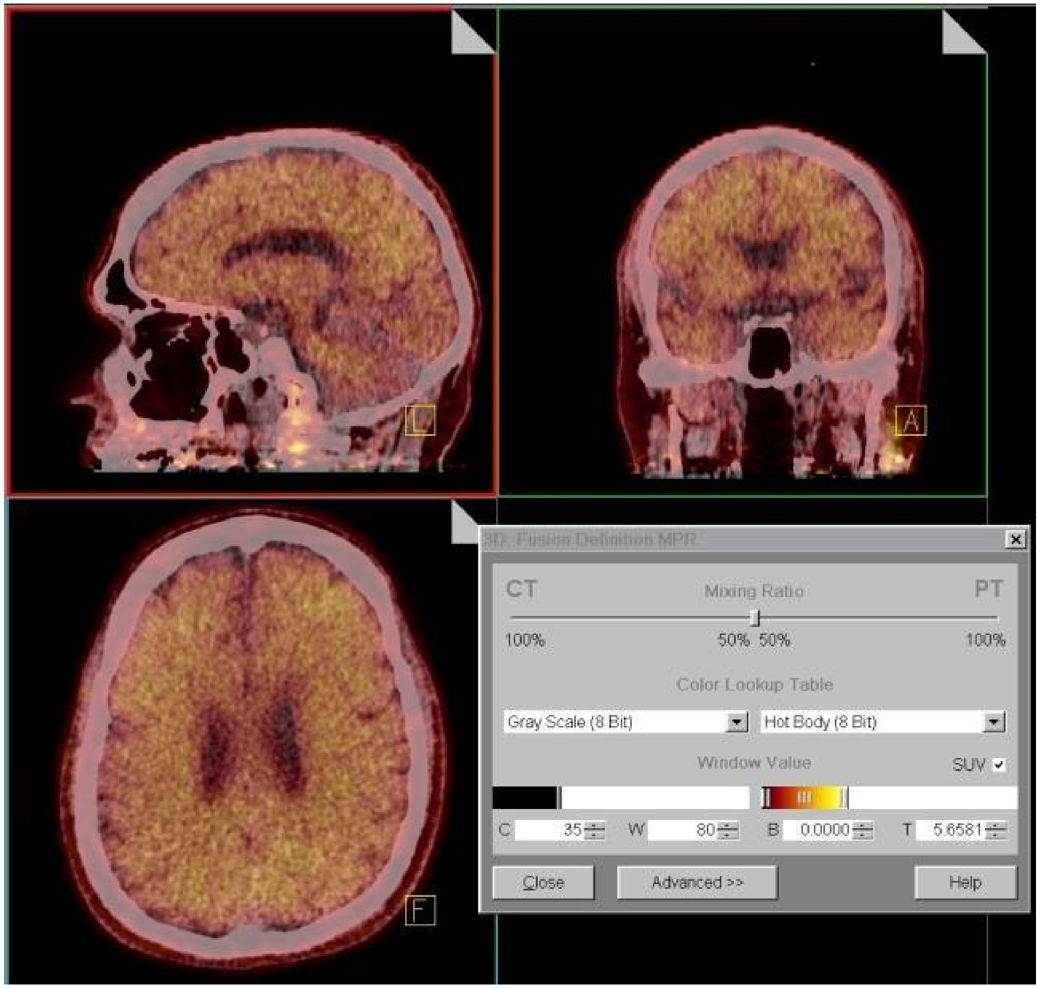
Assess for Subject Motion and CT-PET Misalignment

aMCI

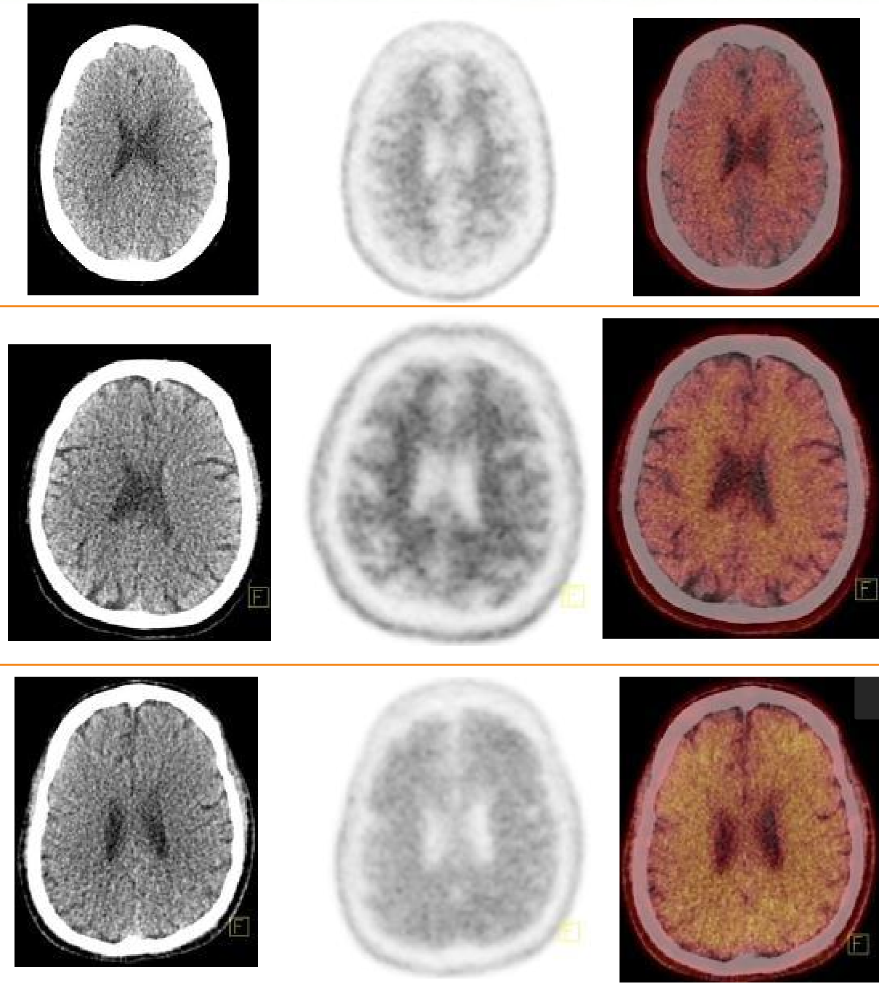


Assess for Subject Motion and CT-PET Misalignment

eAD



Static PET/CT Images

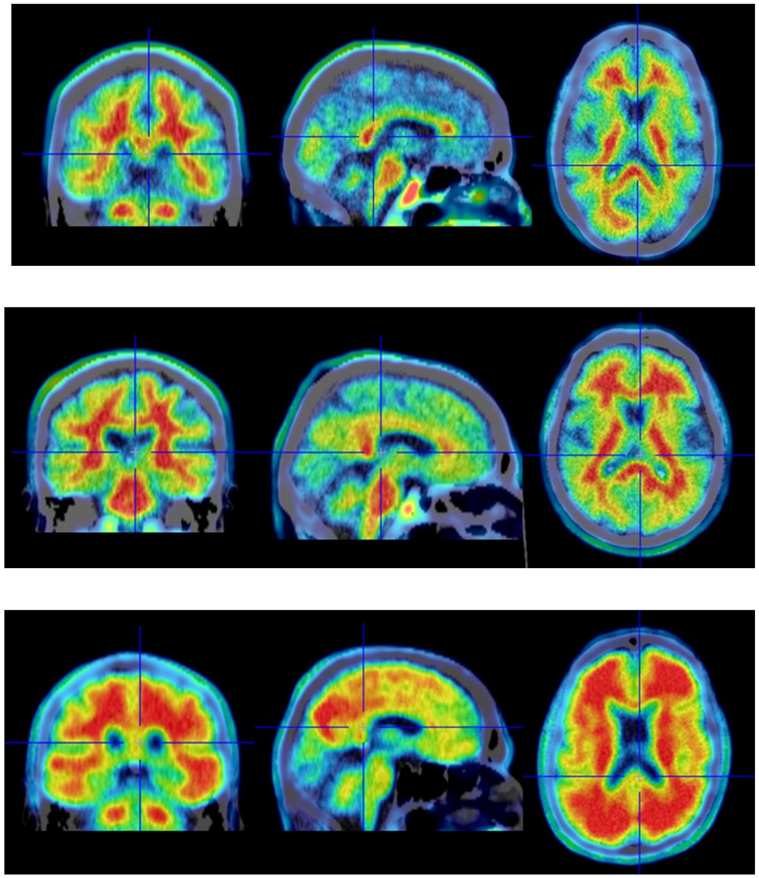


HC

aMCI

eAD

Test scans - ADMdx

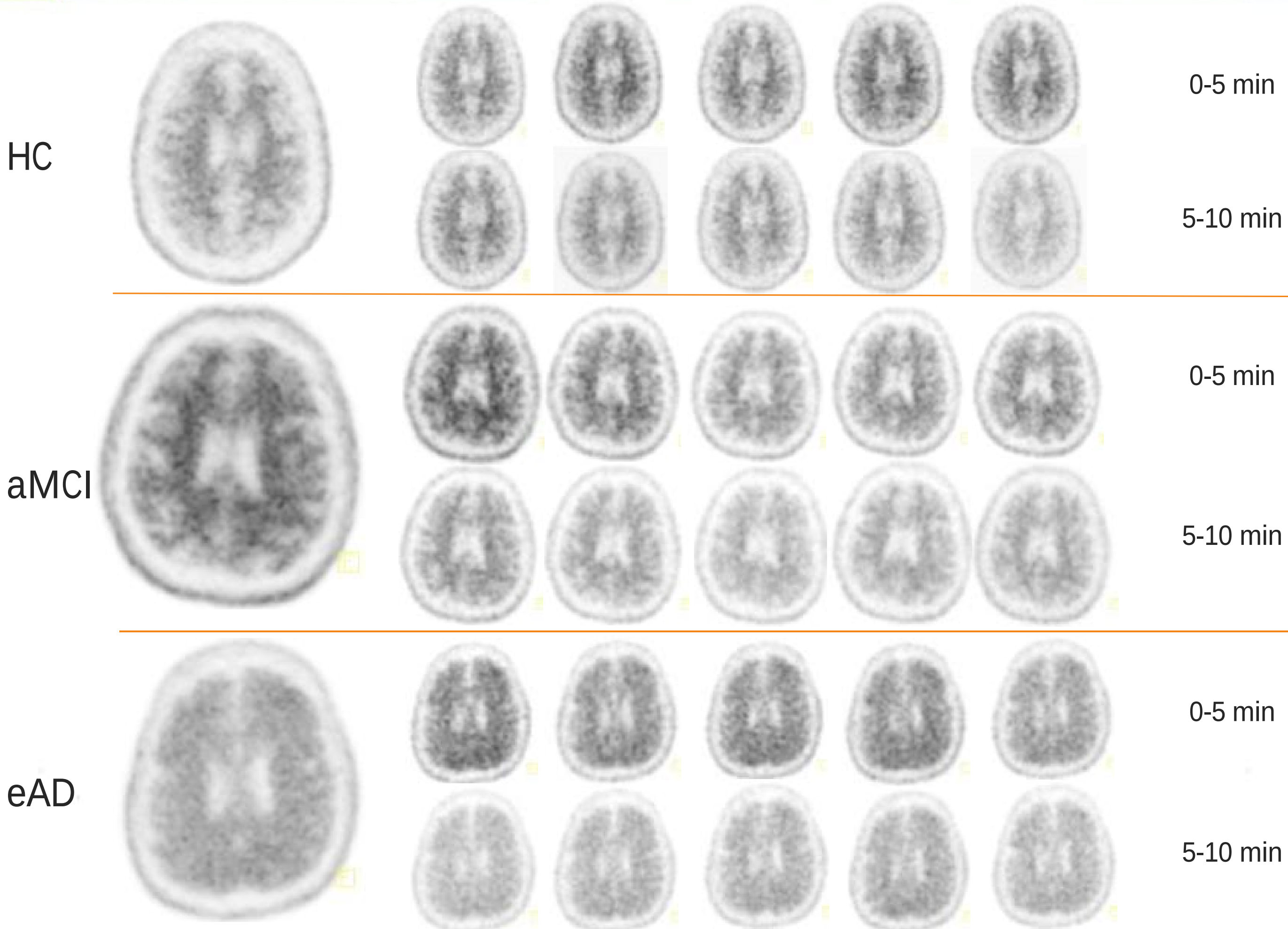


HC

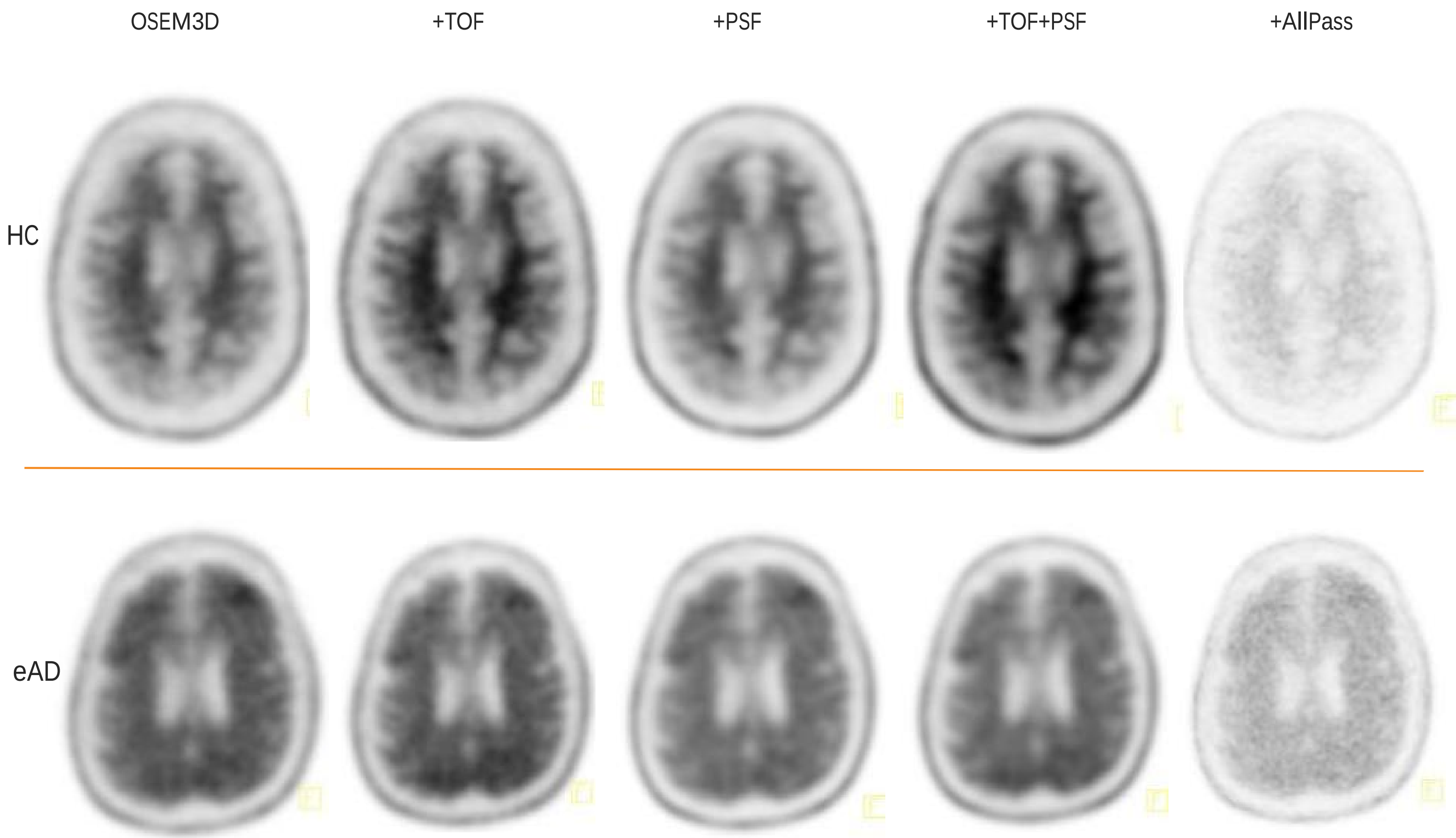
aMCI

eAD

Dynamic PET Images – 1 minute frames



Effect of Reconstruction Algorithm

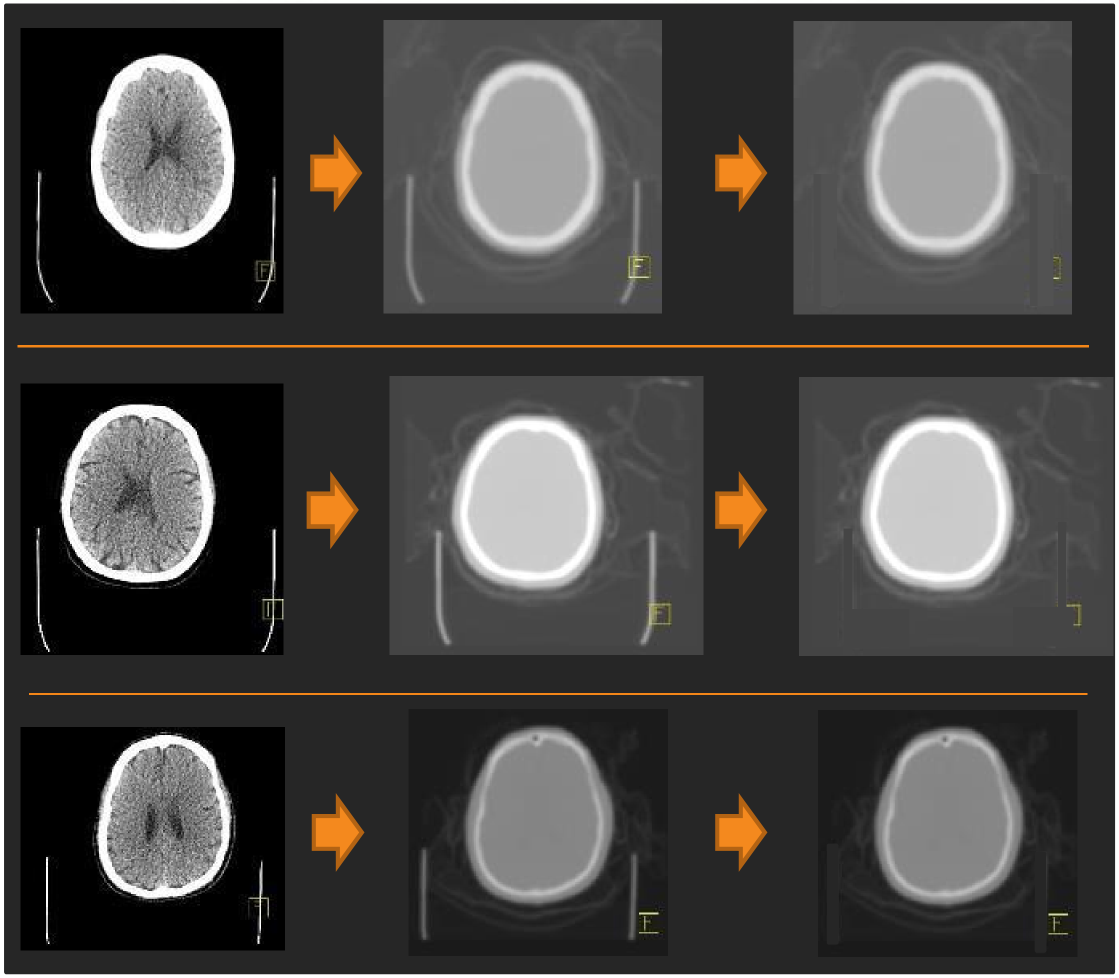


Remove Head Holder From mu-Map

HC

aMCI

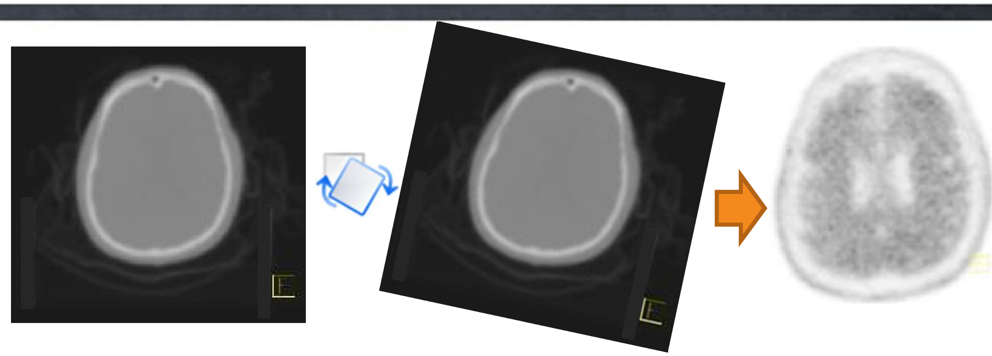
eAD



Simulate Patient Motion and CT-PET Misalignment

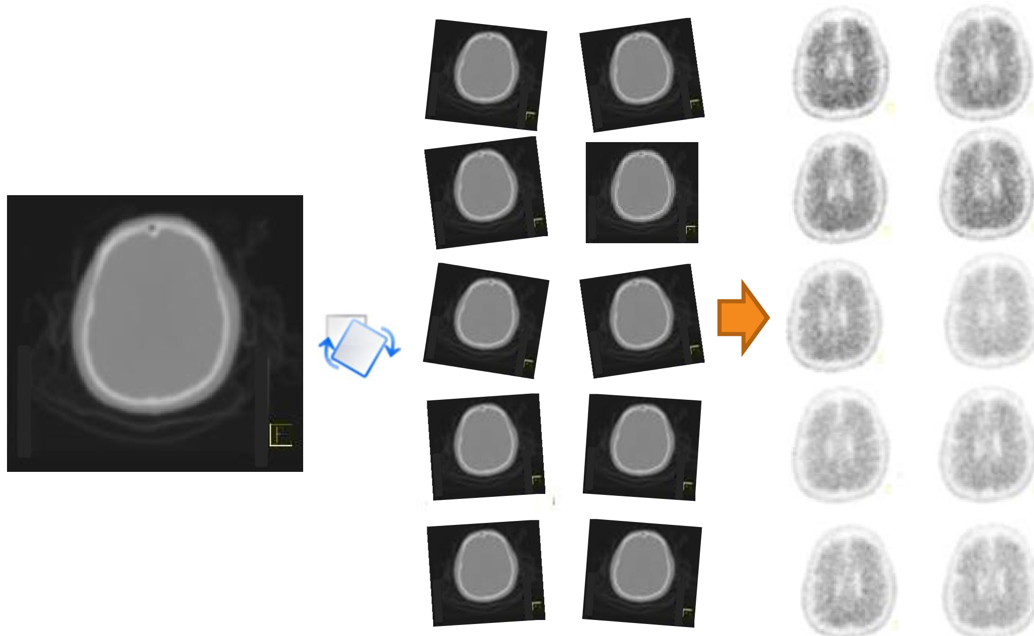
Misalign mu-Map

- Recon static PET
- Simulates movement between CT and PET



Misalign mu-Maps

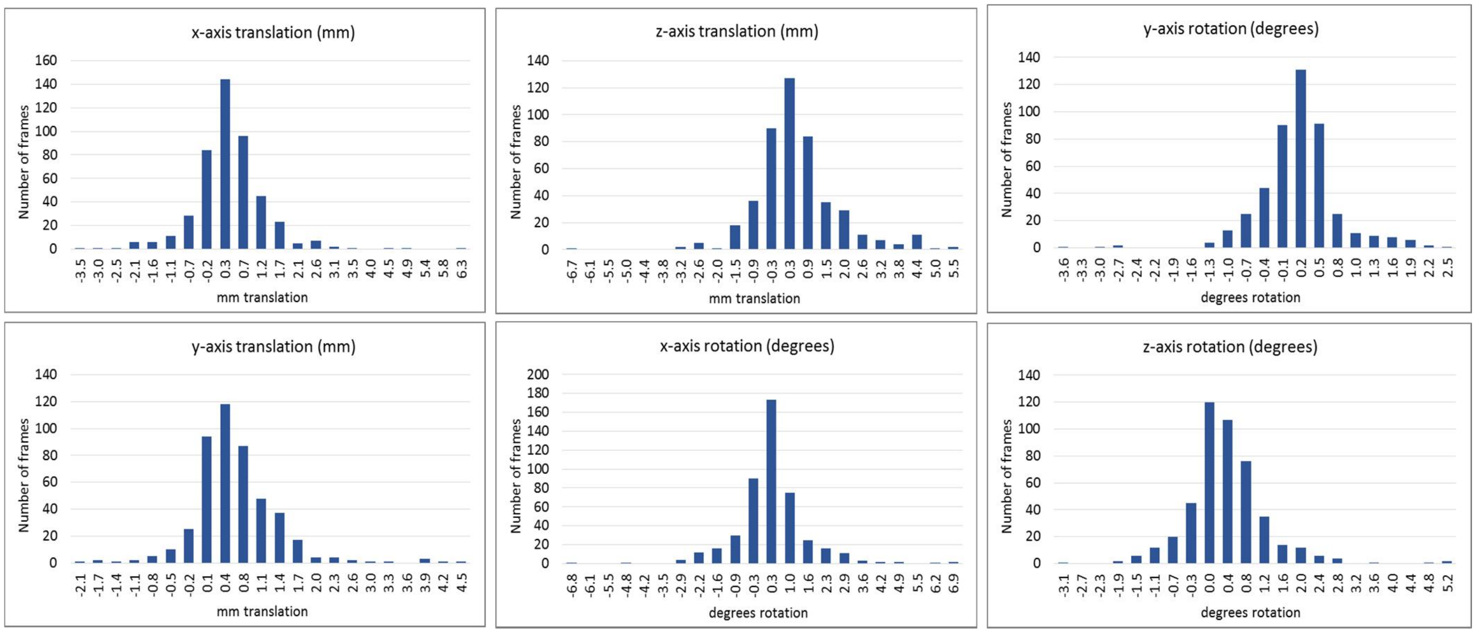
- Recon dyn PETs
- Simulates movement during PET and between CT and PET



Subject motion – example from late MCI to mild AD scans

SPM corrections needed to re-align images, using a neurological or right-handed coordinate system

Average across all frames, referenced to frame 1 of each scan

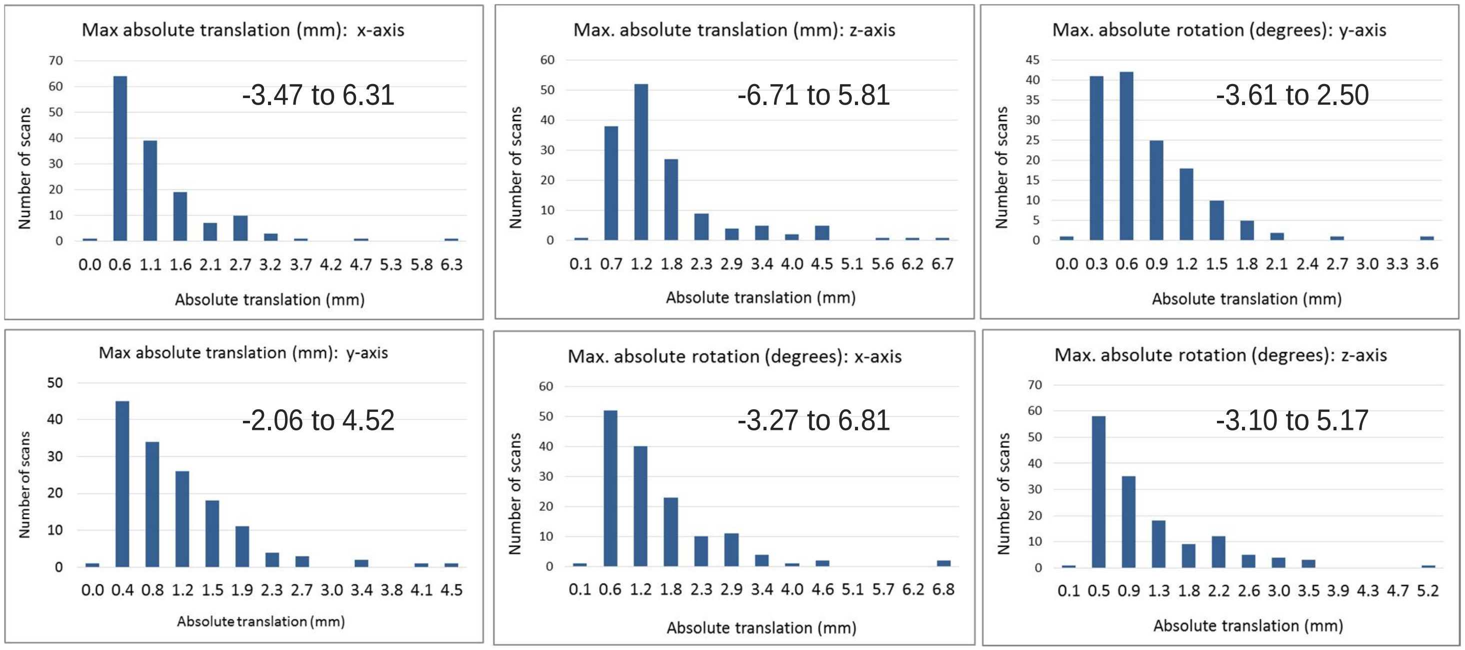


- However, depending upon the site and disease severity, subject motion can be as great as 1 to 2 cm and/or many degrees. Study motion typically spans a greater range with greater disease severity (e.g. moderate AD, FTD).

Subject motion – example from 140 late MCI to mild AD scans

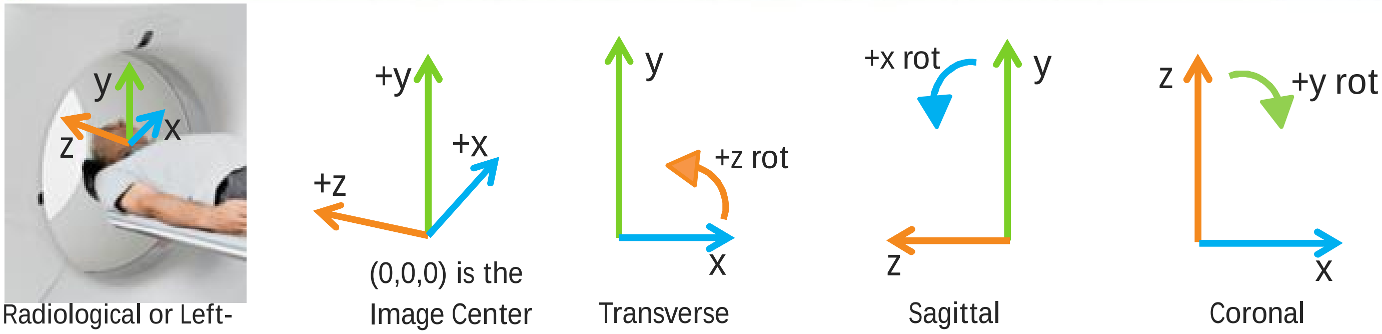
SPM corrections needed to re-align images, using a neurological or right-handed coordinate system

Maximum absolute translation or rotation per scan



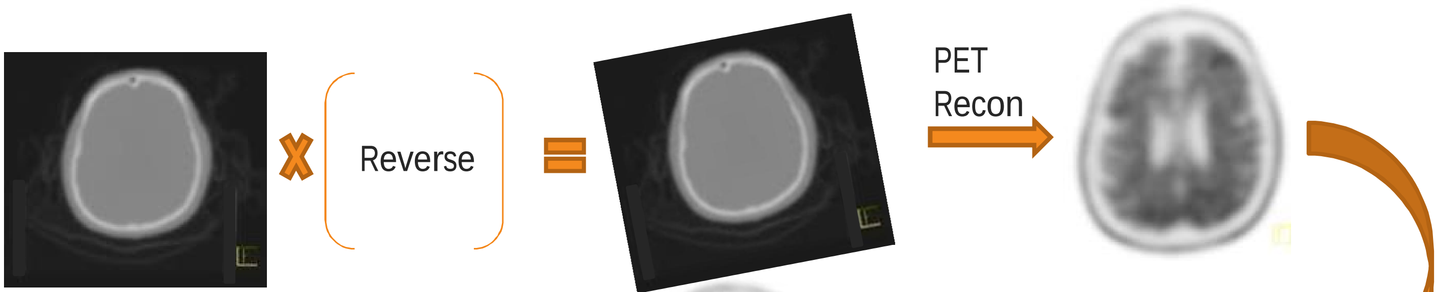
Depending upon the site and disease severity, subject motion can be as great as 1 to 2 cm and/or many degrees. Study motion typically spans a greater range with greater disease severity (e.g. moderate AD, FTD).

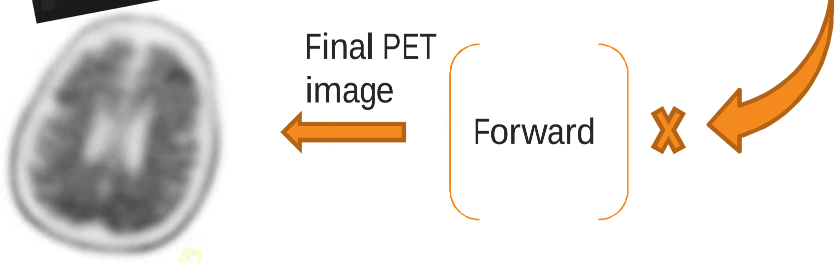
Frame of Reference and Technical Details for Project



Radiological or Left-Handed Coordinate System

Technical Details of transformations and reconstructions

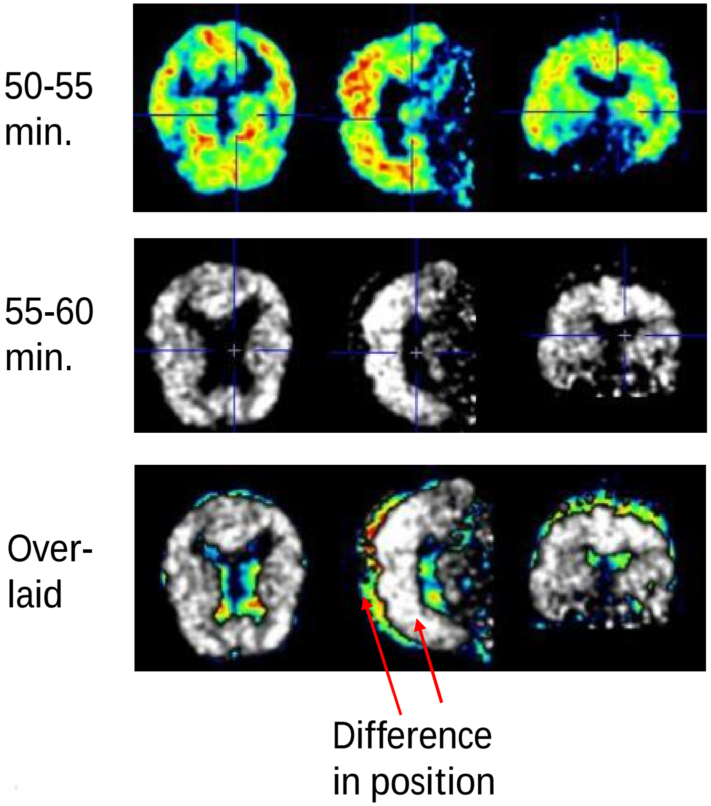




Order of Forward Transformations

1. translations
2. z-axis rotation
3. y-axis rotation
4. x-axis rotation

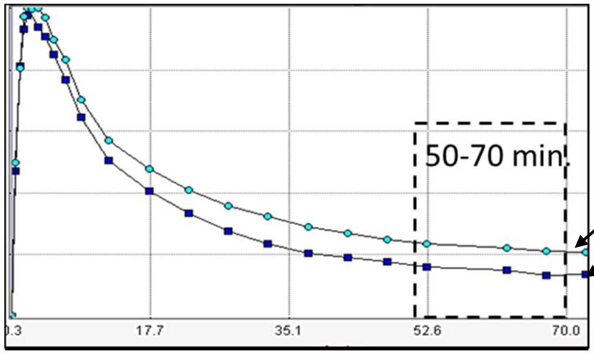
Severe subject motion example (ADNI 1)



Motion during scan causes artifact due to:

- Sampling of blended/ incorrect tissue regions
- Attenuation over- or under-correction due to misalignment with Tx scan
- Motion correction does not remove the embedded artifact, especially with severe movement

Subject Motion: Impact on SUVR

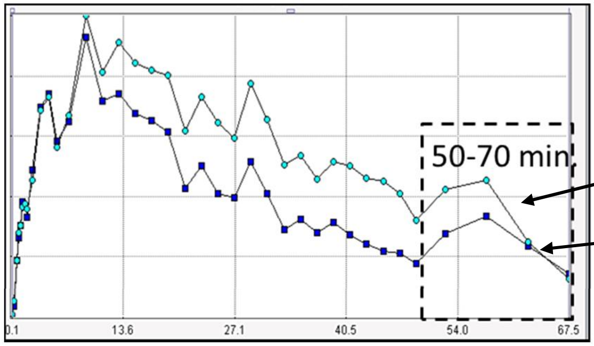


Scan of subject with minimal movement

Target Region

Reference region

SUVR relatively constant throughout 50-70 minute time window



Scan of subject with severe motion

Target Region

Reference region

SUVR at 50-55 minutes = 1.5; SUVR at 60-65 minutes = 1.0, a 50% difference

In cases of severe motion, motion correction does not remove embedded artifact

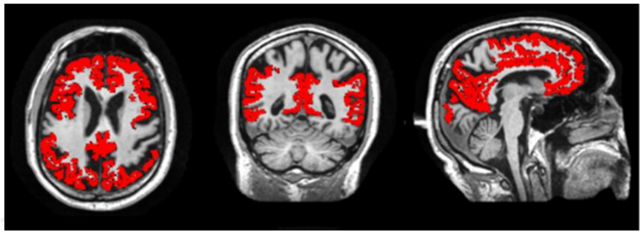
Misalignment Parameters – simulate patient movement

	X trans (mm)	Y trans (mm)	Z trans (mm)	X rot (deg)	Y rot (deg)	Z rot (deg)
Baseline	0	0	0	0	0	0
Set 1	5	0	0	0	0	0
Set 2	0	5	0	0	0	0
Set 3	0	0	5	0	0	0
Set 4	0	0	0	5	0	0
Set 5	0	0	0	0	5	0
Set 6	0	0	0	0	0	5
Set 7	5	5	5	0	0	0
Set 8	0	0	0	5	5	5
Set 9	5	5	5	5	5	5
…						

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

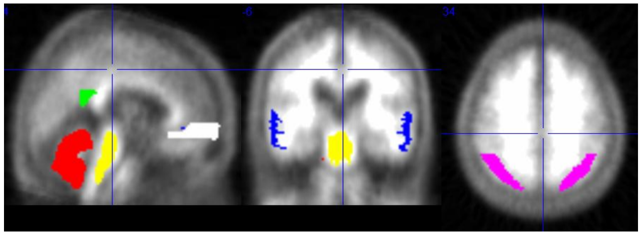


Image Analysis

- For the Baseline and multiple Sets of images → SUVRs calculated
  - Will use ADMdx's PET Amyloid Analysis Package

- Δ SUVR measures will be calculated
  - $\Delta SUVR = \left(\frac{SUVRset_n - SUVRbase}{SUVRbase}\right)$ x 100%

QIBA Mission

QIBA seeks to improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients, and time.