COMPARATIVE ASSESSMENT OF SUVR METHODS AND REFERENCE REGIONS IN AMYLOID PET STUDIES

Gregory Klein, Mehrul Samatul, David Sloan, David Scott, Joyce Suh
BioClinica, Newark, CA, USA - email: Gregory.klein@bioclinica.com

INTRODUCTION
• We compare results of standard uptake value ratio (SUVR) analyses of Alzheimer’s Disease Neuroimaging Initiative (ADNI) florbetapir PET scans using a native space compared to SPM template methods and a variety of possible SUVR reference regions.
• The objective is to find a method with highest longitudinal effect size to allow a sufficiently powered clinical trial efficacy measure using the smallest number of subjects.

METHODS

Population
• Quantitative analysis of longitudinal florbetapir data from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) study were completed for 391 subjects clinically diagnosed as:
  - 152 Normal
  - 60 Late Mild Cognitive Impairment (LMCI)
  - 140 Early Mild Cognitive Impairment (EMCI)
  - 5 Late Moderate Cognitive Impairment (MCI)

Numerous reference regions were evaluated:
- cerebellar grey (CG)
- precuneus
- frontal, temporal and cingulate regions
- subcortical white matter (WM)
- cerebral white matter (WM
cereb)
- cerebellar white matter (WMcereb)
- whole cerebellum (WC)
- whole brain (WB)
- eroded subcortical white matter (WMeroded)
- AAL grey
- AAL white

Three different quantification methods each with specific reference regions were evaluated for computation of the SUVR:
- Freesurfer (FS) SUVR Method
  - four cortical regions were obtained by Freesurfer on the T1-MRI data in native patient space compared to SPM template methods and a variety of possible SUVR reference regions.
- AAL Grey-Masked SPM Method (AAL)
  - PET data were normalized to Talairach space using SPM.
  - Activity from white matter regions are excluded by masking the PET with a grey matter mask obtained by an SPM segmentation of the subject’s cerebral cortex.
  - A global SUVR was obtained as the average of 5 bilateral cortical areas defined on the AAL ROI atlas.

Across longitudinal analyses,  and across all patient groups, the Freesurfer method was generally superior across all patient groups. Looking into effect size of individual regions, the Freesurfer native space approach showed largest differences between AD and normals in regions traditionally showing high Aβ load, including the precuneus, frontal, temporal, and cingulate regions. The putamen was also seen to have a high effect size in the Freesurfer analysis.

DISCUSSION / CONCLUSIONS
• Results indicate that while effect size in a cross-sectional analysis does not vary greatly across different SUVR methods or reference regions, there is a large difference seen in the longitudinal analysis. This is an important consideration in the selection of methods for use as an efficacy endpoint in clinical trials.
• A region reference including white matter consistently performs better in both the cross-sectional and longitudinal analyses. Possible reasons for this compared to pons, brainstem or cerebellar regions include increased noise of the lateral reference regions due to their position at the outer extremes of the axial PET scanner field of view, methodological difficulties in correct segmentation of these regions compared to white matter, or possibly increased biological variability in these regions compared to white matter.

REFERENCES
1. Knoebe et al. ADNI PET Preprocessing 2009 http://adni.loni.usc.edu/methods/pet-analysis/pre-processing/

ACKNOWLEDGMENTS
The authors thank Susan Landau and Bill Jagust for extremely helpful discussions about this analysis.