IC-P-002 IMPACT OF MORPHOLOGICALLY DISTINCT AMYLOID ß (Aß) DEPOSITS ON 18F-FLORBETABEN (FBB) PET SCANS

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Background: Morphologically distinct Aß deposits, such as diffuse or neuritic Aß plaques (DIFF, NEUR), and vascular Aß (VASC) may be present in Alzheimer's disease (AD). FBB has been validated as a biomarker of NEUR. It was the aim of this project to investigate the impact of the different forms of Aß deposits on FBB PET scans. **Methods:** Brain tissue was collected from 87 end-of-life patients (64 AD patients) who underwent a FBB PET scan before death. Aß immunohistochemistry (IHC) was used for assessment of VASC. Aß IHC and Bielschowsky silver stain were used for assessment of NEUR and DIFF in frontal, occipital, anterior cingulate and posterior cingulate cortices. Cortical SUVRs were obtained in all ROIs using cerebellar grey matter as reference region. A linear regression model was fitted for each ROI as: $SUVR=a_0+a_n\times n+a_d\times d+a_v\times v$, where a_0, a_n, a_d, a_v are constants, and n=NEUR, d=DIFF and v=VASC. n, d, and v were assigned two values: 0=Ab absent; 1=Ab present. **Results:** In ROIs with high frequency of Aß (frontal, posterior cingulate), both DIFF (a=0.32 and 0.42) and NEUR (a=0.27 and 0.21) contributed significantly to the SUVR. In regions with low frequency of Aß (occipital, anterior cingulate), only DIFF contributed significantly to the SUVR (a=0.24 and 0.55). Presence of VASC contributed significantly to the SUVR only in the occipital region (a=0.13). **Conclusions:** There was a significant impact of DIFF and VASC on FBB SUVR in brain regions characterized by low Ab load. These results underline the importance of measuring the topographic distribution of Ab aggregates and suggest the potential utility of FBB in detecting both DIFF and VASC Aß deposits.

Table
Coefficient values from the fitted models to each regional SUVR for each type of amyloid deposition (p values)

Region	$a_{diffuse}$	$a_{neuritic}$	$a_{vascular}$
Frontal	0.32 (0.001)*	0.27 (0.002)*	0.09 (0.22)
Posterior cingulate	0.42 ($<10^{-4}$)*	0.21 (0.01)*	-0.03 (0.77)
Occipital	0.24 (0.0001)*	0.10 (0.07)	0.13 (0.01)*
Anterior cingulate	0.55 ($<10^{-4}$)*	0.09 (0.37)	-0.02 (0.85)

* Statistically significant ($p<0.05$). Coefficient values>0 indicate contribution to SUVR

IC-P-003 AUGMENTING AMYLOID PET INTERPRETATIONS WITH QUANTITATIVE INFORMATION IMPROVES CONSISTENCY OF CEREBRAL AMYLOID DETECTION

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Background: Establishing reliable methods for interpreting the presence or absence of elevated cerebral amyloid plaque on PET scans is increasingly important for radiologists with the greater availability of molecular PET imaging in clinical practice. We examined the value of adding quantitative amyloid PET information to the interpretation of amyloid-PET scans. **Methods:** A total of 60 nondemented (CDR 0) adults over age 65 (mean age 73.6 years) were evaluated with amyloid-PET imaging using florbetapir as part of screening for a Alzheimer's disease prevention study at the University of Kansas Alzheimer's Disease Center. Images were first interpreted visually (Visual Read) as either 'elevated' or 'not elevated' using FDA-approved methods by two different raters. Images were then re-evaluated after the reader considered quantitative analyses (VisualQuant Read) using MIMneuro software to compare the image to a standard atlas. We examined the frequency of interpretation changes after quantitative information was considered and whether this information improved the inter-rater agreement of interpretations. We also examined how the Visual Reads and VisualQuant Reads compare to a purely quantitative read where a scan was determined to be elevated based on an SUVR>1.1 in six regions of interest (anterior cingulate, inferior medial frontal, lateral temporal, posterior cingulate, precuneus, and superior parietal). Simple percent agreement and Cohen's kappa were used to measure agreement. **Results:** 60 scans were interpreted by two blinded raters. The initial Visual Read was changed after the introduction of quantitative information in 6.7% (n=4) of scans for Rater 1 and 11.7% (n=7) for Rater 2. Initial Visual Reads were changed from non-elevated to elevated in 9 of the 11 (81.8%) scans that were changed. Agreement of reads across raters was 90% (54 of 60; Kappa=0.75) for Visual Reads and increased to 95% (n=57, Kappa=0.89) for the VisualQuant Reads. Quantitative only assessments (SUVR >1.1) were concordant with VisualReads (86.7% for Rater 2 and 90.0% for Rater 1) but concordance was higher with the VisualQuant Reads (95.0% - 96.7%). **Conclusions:** Augmenting the radiological interpretation of amyloid PET scans with quantitative information appears to improve the consistency in interpretations for the early detection of the presence of cerebral amyloid accumulation.

IC-P-004 THE ASSOCIATION BETWEEN AMYLOID BURDEN AND LANGUAGE OUTCOMES IN THE WISCONSIN REGISTRY FOR ALZHEIMER'S PREVENTION (WRAP)

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Background: The early diagnosis of Alzheimer's Disease (AD) depends upon clinical manifestations of difficulties with learning and memory which negatively impact activities of daily living (Dubois et al., 2007). Beta-amyloid (1-42) (Aβ42) accumulation, may be a first major stage of presymptomatic AD (Sperling et al., 2011). Language deficits, based on retrospective analysis and prospective cohort studies, may also be present years or decades before diagnosis (Snowdon et al, 1996; Garrard et al 2005; Forbes-McKay

Table 1
Regions of Interest and Language Outcomes from WRAP

	Boston Naming Test		Phonemic Fluency		Semantic Fluency		Syntactic Complexity - Discourse		Semantic Units - Discourse		Speech Fluency (Mazes)	
Region of Interest[†]	*F-statistic*	*P-value*	*F-statistic*	*P-value*	*F-statistic*	*P-value*	*F-statistic*	*P-value*	*F-statistic*	*P-value*	*F-statistic*	*P-value*
Inferior Frontal Gyrus	0.03	0.86	1.07	0.30	0.03	0.86	4.56	0.04*	0.34	0.56	0.59	0.45
Superior Temporal Gyrus	0.00	0.98	0.02	0.90	0.14	0.71	1.10	0.30	0.13	0.72	0.94	0.34
Anterior Cingulate	0.11	0.75	2.05	0.15	0.06	0.81	4.99	0.03*	0.00	0.95	0.20	0.66
bal 8 Regions of Interest	0.04	0.84	0.76	0.38	0.12	0.73	2.71	0.11	0.08	0.79	0.25	0.66
Superior Medial Gyrus	0.00	0.99	0.02	0.90	0.01	0.95	0.13	0.73	0.13	0.72	0.08	0.78
itoFrontal Medial Cortex	0.03	0.86	0.67	0.41	0.01	0.91	4.51	0.04*	0.34	0.56	0.13	0.72

[†] Regions reported here are a sum of left and right hemispheres

and Venneri, 2005; Ahmed et al 2013). Given these findings, we investigated whether rates of amyloid burden would be associated with language outcomes from both standardized tests and non-standardized connected speech samples in a healthy, at-risk cohort. **Methods:** Participants were recruited from the Wisconsin Registry for Alzheimer's Prevention (WRAP), a longitudinal cohort (n>1500) enriched for positive family history of AD. The present analyses included 188 WRAP subjects (mean age=61; 68% female; 38% *APOE*-4+) who had undergone [C-11]Pittsburgh compound B ([C-11]PiB) positron emission tomography (PET) scan, a Fluorodeoxyglucose ([F-18] FDG PET) scan and a 3.0 Tesla magnetic resonance imaging (MRI) scan. Neuropsychological language measures from their most concurrent WRAP visit were used; a subset of 48 individuals had transcribed speech samples from a picture description task and were used for the discourse analysis measures. **Results:** We constructed a series of linear models using separate regions of interest (ROI) as predictors, including one global measure, an average of 8 ROIs. Adjusting for the covariates of age, sex and baseline literacy, we found significant associations between areas of the frontal cortex (Inferior Frontal Gyrus-Right (p = .04) and Left (p=.05), Anterior Cingulate- Right (p=.05) and Left (p=.04), and Orbitofrontal Cortex Right (p=.03) and Left (p=.05) and the syntactic complexity measure from the connected speech samples. No other language outcomes were significantly associated with the hypothesized ROIs. **Conclusions:** We found an association between amyloid burden in areas of the frontal cortex and a spontaneous speech measure of syntactic complexity. This preliminary analysis suggests that discourse analysis may be a sensitive and informative measure of early cognitive change, particularly when paired with other biomarkers of AD pathology such as amyloid burden.

IC-P-005 **THE INCREMENTAL DIAGNOSTIC VALUE OF 18F-FLORBETAPIR IMAGING IN NATURALISTIC PATIENTS WITH COGNITIVE IMPAIRMENT: THE INDIA-FBP STUDY**

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Background: The 18F-Florbetapir PET amyloid tracer, recently approved by FDA and EMA, has a relatively long radioactive half-life (110-min), making amyloid imaging logistically feasible. However, the added diagnostic value is unclear. We aim to evaluate the incremental diagnostic value of 18F-Florbetapir amyloid PET on top of routine assessment for diagnosis of cognitive impairment. **Methods:** The study, completed in December 2014, includes 26 Healthy elderly Controls (HC) and 228 patients with a diagnostic probability of Alzheimer Disease (AD) between 15% and 85% accessing 20 Italian memory clinics. Patients complete their diagnostic work-up according to usual local practice. Physicians formulate a clinical diagnosis and rate their diagnostic confidence (0-100%). Patients and HC then undergo amyloid PET with 18F-Florbetapir; diagnoses and diagnostic confidence are revised. Diagnostic confidence increase was evaluated by Wilcoxon Signed Rank Test. **Results:** To date, data from 140 patients were processed. Of these, before PET scan, 95 patients were diagnosed with AD (Table 1); 27 with FrontoTemporal Disease (FTD; Table 2); 3 with Lewy Body Disease (LBD; Table 3); 10 with Vascular Dementia (VD), Parkinson's Disease Dementia (PDD), and Cortical Basal Degeneration (CBD); and 5 with other pathologies. Thirty AD (31.6%) tested negative to amyloid-imaging. Positive scans occurred in 11 FTD (40.7%), in 2 LBD (66.7%), in 7 VD-PDD-CBD (70%), and in 4 HC (15.4%). 75% of positive HC were men aged over 69 (Figure 1). The diagnosis after amyloid-imaging was changed in: 86.7% of AD with negative scan; 90.9% of FTD, 50% of LBD and 100% of VD with positive scan. The diagnostic confidence increased significantly after amyloid-PET for both patients with confirmed diagnosis of AD (11.8% increase V=49, $p<.05$; Figure 2) and those with confirmed diagnosis of non-AD (13.6% increase; V=0, $p<.05$; Figure 3). 243 PET scans were evaluated by two nuclear medicine physicians, who disagreed on 32 cases (rate of

Table 1
Diagnosis after PET in 95 patients with a clinical diagnosis of AD before PET.

	Amy PET	
Diagnosis after PET	Aβ+	Aβ-
Same (AD)	63 (96.9%)	4 (13.3%)
FTD	1 (1.5%)	5 (16.7%)
VD	-	13 (43.3%)
LBD	1 (1.5%)	-
SNAP	-	3 (10%)
Other	-	5 (16.7%)
Total	65 (100%)	30 (100%)