>1.5). Normalised regional MR volumes were compared between the high- and low-risk sub-sets. **Results:** Among ADNI participants, 39% were classified as high-risk. Fourteen of 83 regions across the brain were significantly smaller in the high-risk group *(P* <0.05, uncorrected), including the hippocampus, temporo-parietal regions, insula, orbito-frontal regions and lateral occipital regions. Among AIBL participants, 29% were classified as high-risk. Twenty-six of 83 regions across the brain were significantly smaller in the high-risk group *(P* <0.05, uncorrected), including the hippocampus, temporo-parietal regions, amygdala, orbito-frontal regions and medial occipital regions. Nine regions in AIBL, and one region in ADNI, remained significant after correction for multiple comparisons *(P* <0.05). **Conclusions:** This study shows volumetric differences - at baseline - in cognitively normal individuals differing in amyloid-based risk status for the development of Alzheimer's disease. The consistency of regional differences observed in two independent groups suggests that volumetric MRI can reveal structural brain changes that precede the onset of clinical symptoms.It may therefore be useful in identifying early signs of neurodegeneration in healthy elderly individuals, potentially providing a useful early screening tool, or outcome measure for clinical trials.

P2-225 CAN THE PERFORMANCE OF THE FSL/SIENA WHOLE BRAIN ATROPHY MEASURE BE IMPROVED AT 3T AND 1.5T ON ADNI BACK-TO-BACK MPRAGES BY USING A NON-DEFAULT SETTINGS?

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Background: To test a previous report of improved performance of the FSL/Siena whole brain atrophy algorithm by using non default settings at both 3T and 1.5T. **Methods:** As part of the Alzheimer's Disease Neuroimaging Initiative (ADNI) study, high quality MPRAGE (a T1 weighted 3D MRI sequence) from 200 subjects visit pairs is available to compare the reproducibility of brain atrophies over 12 to 18 month intervals at both 3T and 1.5T. This is because in ADNI all subjects received back-to-back (BTB) MPRAGEs with the second MRPAGE acquisition starting within seconds of the completion of the first. Also as part of ADNI, 131 subjects received BTB scans at multiple time points and two field strengths of 3T and 1.5T. For this study FSL/Siena was applied to the 200 subject visit pairs for 88 different combinations of options and the two field strengths requiring a total of 9 core years of calculations. For each combination of options and field strengths Siena's BTB reproducibility was quantified as the median of the absolute value of the difference between the BTB percentage brain volume change (PBVC) yielded by Siena. **Results:** For Siena option combinations -B (bias field correction and neck cleanup turned on) and f = 0.1 to 0.3 (which selects the fractional intensity threshold) provided the smallest reproducibility of 0.26 to 0.27 for 1.5T. However, bootstrapping provided a 95% confidence interval on the reproducibility up to 0.29. Options that often yielded poor reproducibilities included the -S option (eye and optic nerve cleanup turned on) and f > = 0.5. The range of the 3T results made an optimal option combination less clear. For the 69 subjects with two visit pairs each, no significant correlation was found between the BTB differences of the 0 to 12 month and 6 to 18 month visit pairs bearing out their treatment in this analysis as independent measures. **Conclusions:** For the ADNI MPRAGEs at 1.5T the -B option with f = 0.3 will likely yield the best BTB PBVC reproducibility for Siena - supporting the previous report and differing from the Siena default value of f = 0.5. For 3T the optimum choice is less clear.

P2-226 CROSS-SECTIONAL CEREBRAL VOLUMETRIC DIFFERENCES AND ASSOCIATIONS WITH ESTIMATED TIME TO AGE-AT-ONSET IN FAMILIAL ALZHEIMER'S DISEASE: FINDINGS FROM THE DIAN STUDY

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Background: A key challenge for Alzheimer's disease (AD) research is to identify the most reliable markers of early disease progression. Autosomal dominant AD provides a unique opportunity to study the earliest changes. We assessed cross-sectional volumes of whole brain, ventricles, and hippocampi within the Dominantly Inherited Alzheimer Network (DIAN) cohort. **Methods:** 158 participants were included: 55 of whom were non-carriers (NC); 59 were asymptomatic carriers (aMut+) with Clinical Dementia Rating (CDR) of 0; and 44 were symptomatic carriers (sMut+) with CDR>0. All participants underwent volumetric T1-weighted MRI. Automated segmentation techniques were used to delineate the whole brain, ventricles, and hippocampi. All volumes were adjusted for total intracranial volume and age. Ventricular and hippocampal volumes were additionally adjusted for sex. The relationships with time to expected age-at-onset, estimated from affected parent's age-at-onset, were also examined. **Results:** Statistically significant *(P* <0.001) differences were observed in brain, ventricles and hippocampi between the sMut+ and both NC and aMut+. There were no significant differences between the aMut+ and the NC, although a trend was observed for whole-brain volumes. The Figure shows average corrected volumes in each group. In addition, the aMut+ showed significant *(P* <0.05) correlations between time to expected age-at-onset and whole-brain and ventricular volumes. For the sMut+, similar significant correlations *(P* <0.05) were observed between the predicted age-at-onset and whole-brain and hippocampal volumes. **Conclusions:** Participants with dementia already had significantly greater atrophy: smaller brain and hippocampal volumes and larger ventricles. Unaffected carriers did not show significant differences compared to non-carriers: this overlap may be due to the wide normal range in regional brain volumes, and the inclusion of carriers who are many years before expected age-at-onset. Notably there was a significant association between estimated age-at-onset and brain volume in

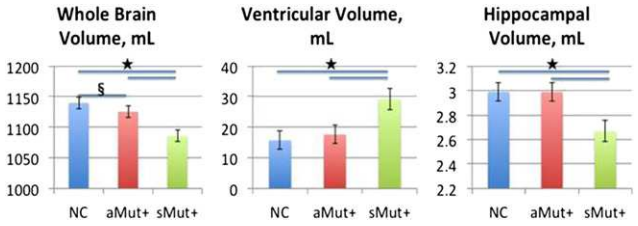

Figure 1. Average volumes (error bars represent 95% confidence intervals) for the structures of interest. All volumes have been adjusted for covariates of Total Intracranial Volume and Age. The Ventricles and Hippocampi have additionally been adjusted for gender. *indicates $P<0.001$. - § indicates ($P=0.075$) between aMut+ brain volume vs. NC brain volume.

asymptomatic carriers suggesting atrophy increases (possibly non-linearly) prior to symptoms. Longitudinal measurements of atrophy may be a more sensitive biomarker than cross-sectional measures: the ongoing follow-up of DIAN subjects will allow this to be assessed.

P2-227 CROSS-VENDOR IMPLEMENTATION AND TEST-RETEST ANALYSIS OF ADNI2 FUNCTIONAL MRI (FMRI) AND DIFFUSION TENSOR IMAGING (DTI) SEQUENCES FOR MULTICENTER CLINICAL TRIALS IN ALZHEIMER'S DISEASE

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Background: Strong evidence of neurobiological effects in clinical trials could facilitate the development of new treatments for Alzheimer's disease. It is expected that cohorts of ~100 prodromal subjects per arm are required to obtain significant results with both vMRI and more recently developed methods such as Diffusion Tensor Imaging (DTI) and resting state functional Magnetic Resonance Imaging (rs-fMRI). For time-efficient trial execution, multi-center studies are required to provide rapid enrollment and making the collection of robust data across different scanner types is essential. The second phase of the Alzheimer's Disease Neuroimaging Initiative (ADNI-2) has established standardized 3T sequence parameters for DTI on GE systems and rs-fMRI on Philips systems respectively. Our objective was to implement both DTI and rs-fMRI on Philips, Siemens, and GE scanners and to evaluate their consistency prior to their use in a multi-center clinical trial. **Methods:** The ADNI-2 parameters for each sequence were implemented as closely as practicable across vendors. Four young healthy volunteers were imaged across 5 scanners in 2 countries as described in Table 1. Each session comprised two DTI and two rs-fMRI acquisitions. Images were assessed for the presence of gross artifacts and preprocessed using BrainVISA/Connectomist-2.0 for DTI, Statistical Parametric Mapping (SPM8) and CORSICA for rs-fMRI. The DTI data were assessed quantitatively by mean FA measurements on manually-delineated ROIs in the splenium and genu of the corpus callosum, and rs-fMRI data by mean correlation between sets of predefined nodes in the Default Mode (DMN; (0,47,-3), (0,-56,32), (-49,-66,36), (52,-59,33)) and Sensorimotor (SMN; (-51,-11,43), (47,-9,41)) networks. **Results:** For DTI, scan-rescan variability values for the genu and splenium FA values were -7% to 7% and -5% to 7% respectively (Figure (a)). For rs-fMRI, scan-rescan variability was -11% to 14% for the SMN. The DMN measure was more variable (-9% to 70%; Figure (b)) but consistent with values calculated from other test-retest rs-fMRI data sets. DTI measures were more consistent across scanner vendors. **Conclusions:** The reproducibility and consistency of both sequences was within the range of previously published test-retest values. However, results were less stable across scanner type, which may be an important covariate for statistical analysis, especially for rsfMRI.

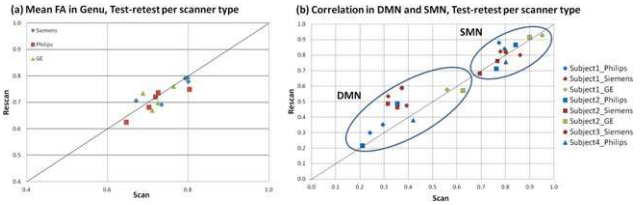

Table 1

	Siemens		Philips		GE
	Trio Tim VB15	Verio VB17	Achieva 3.2	Achieva 2.6	Signa HDx
Volunteer 1 sessions	2 sessions	-	2 sessions	-	2
Volunteer 2 sessions	2 sessions	-	2 sessions	-	2
Volunteer 3	-	1 session	-	-	
Volunteer 4	-	-	-	1 session	-

P2-228 CHARACTERIZING BRAIN AMYLOID CHANGES USING PIB-PET: PROGRESSION, CLINICAL CORRELATES, PIB STATUS AND OPTIMIZED SAMPLING

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Background: Positron emission tomography (PET) imaging of amyloid beta (Aβ) is increasingly used as a diagnostic tool and as an endpoint for clinical trials in Alzheimer's disease (AD). The use Aβ-PET endpoints requires an understanding of amyloid progression rates within the target population, and the impact of sampling methods. The goal of this longitudinal study was to characterize 11 C-Pittsburgh compound B (PiB)-PET changes in a multi-center setting within clinical subpopulations, using accurate sampling techniques and a comparison of optimized reference regions. **Methods:** Twenty clinically normal (NL), 45 MCI and 18 AD subjects with serial PiB scans (range 2-4) from the Alzheimer's disease Neuroimaging Initiative (ADNI) database were examined. U sing an automated region-of-interest technique tailored for PiB analysis, global cortical PiB standardized uptake value ratios (SUVR) were calculated using 50-70 min summed PiB images and the following reference regions: whole cerebellum (WCer), cerebellar gray matter, crus gray matter, pons, and centrum ovale. A mixed model for repeated measures was used to compare PiB progression over 36 months across clinical outcome groups and as a function of baseline PiB levels (PiB+ vs PiB-). **Results:** At baseline and at 36 months, PiB retention showed a correlation with clinical status such as: AD>MCI>NL. Among these, stable NL (n = 17) and MCI (n = 29) had lower PiB retention than MCI decliners to AD (n = 15) and AD (n = 18; $P<0.05$). The rate of PiB