**INTRODUCTION**

Diffusion-Weighted (DWI) and Diffusion-Tensor Imaging (DTI) assess microstructural brain tissue changes by measuring Apparent Diffusion Coefficient (ADC) and Fractional Anisotropy (FA) of water molecules. As Alzheimer’s disease (AD) progresses, neuronal degeneration and cerebral atrophy may manifest as an increase in ADC values owing to increased diffusivity of water molecules, and a decrease in FA values reflecting a loss in fiber tract integrity. This work reports results of whole-brain histogram analysis applied to those data on Normal Controls (NC), MCI and AD subjects from the ROSAS study, a monocentric observational study that was carried out in Toulouse, France.

**METHODS**

Population

The ROSAS study is a monocentric observational study which ran in Toulouse, France, and was designed to identify and evaluate the clinical usefulness of AD biomarkers by collecting samples from Normal Controls (NC), Mild Cognitive Impairment (MCI) and AD subjects, following them for up to 4 years.

408 subjects aged 65 years or older were enrolled, including 110 Normal Controls (NC), no memory complaints, MMSE≥26 and CDR=0, 100 Mild Cognition Impaired (MCI, MMSE≥24 and CDR=0.5, memory impairment based on RAVLT and who did not meet DSM IV criteria for dementia) and 198 AD (12>MMSE<26 and CDR>0.5 and meeting DSM IV criteria for dementia) 14 MCI, 36 MCI and 49 AD, respectively. Among MCI subjects, conversion to dementia during the course of the study was defined as an increase in CDR to >0.5.

MRI Data

- **DWI protocol** used an echo-planar imaging in the axial plane on 31 slices of 4 mm with no inter-slice gap. The acquisition matrix was 112x89 (reconstructed at 256x256) over a FOV of 230x230 mm. 15 directions were acquired, using 2 b values (0 and 1000 s/mm²).
- **DTI protocol** used an echo-planar imaging in the axial plane on 50 slices of 2.2 mm with no inter-slice gap. The acquisition matrix was 100x100 (reconstructed at 256x256) over a FOV of 234x234 mm. 15 directions were acquired, using 2 values (0 and 2000 s/mm²).
- Scans were collected up to 3 times between Baseline and Month-48, at one site using a Philips Achieva 3T scanner, for consenting subjects. n=129, including 44 NC, 36 MCI and 49 AD. 14 MCI converted to AD during the study (MCI-c) while the others did not convert (MCI-nc).

Image processing

- DWI ADC maps were used as generated on the scanner. DTI ADC and FA maps were centrally computed from the native DTI directional images.
- All maps were quality controlled to discard scans exhibiting major artifacts (motion, ghosting, strong distortion, etc.).

**RESULTS**

Baseline correlations (see Fig. 1)

- Comparing ADC results between DWI and DTI data at Baseline, mean and SD were highly correlated, while correlation on height was moderate, and weak on peak.
- No strong correlation was found between FA and ADC parameters at Baseline.

Global and pairwise differences between groups in the rate of changes across scans were tested using a parametric approach (Wilcoxon test) without adjustment for the covariates, as a robustness analysis. The pairwise differences were assessed based on the parametric model.

- All maps were processed with no cutoff to keep the effect of cerebral atrophy.

- Nonbrain voxels were automatically masked out using histogram-based thresholding and morphological operations performed on b₀ images.

**CONCLUSIONS**

- **DWI-ADC standard deviation showed good ability to differentiate NC from other groups at Baseline.** Mean and height were only able to differentiate NC from AD. Peak was not sensitive enough. DWI-ADC and DTI-FA showed limited value with such whole brain histogram approach.

- **DWI-ADC standard deviation also performed well longitudinally, in particular in distinguishing NC from MCI-converters from converters, which could be used to monitor treatment efficiency in a disease-modifying therapy.**

- While cross-sectional results may suffer from extending assessments into a multi-center setting, longitudinal results may be more robust to that respect.

**Abbreviations**

- ADC: Apparent Diffusion Coefficient.
- FA: Fractional Anisotropy.
- DWI: Diffusion Weighted Imaging.
- DTI: Diffusion Tensor Imaging.
- MCI: Mild Cognitive Impairment.
- NC: Normal Controls.
- AD: Alzheimer’s disease.