T_{1RHO} MRI AS A CLINICAL BIOMARKER OF ALZHEIMER'S DISEASE

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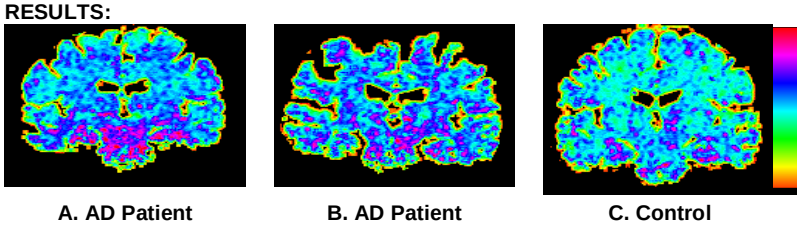
OBJECTIVE: To demonstrate $T_{1\rho}$ as a biomarker for AD in diagnosed patients and examine its usage as an early predictor of AD biochemical changes before the onset of the disease in at risk populations.

BACKGROUND: Alzheimer's Disease (AD) is the most commonly diagnosed form of dementia in the elderly population (1). Current diagnosis occurs after the onset of symptoms such as memory loss and confusion, and the definitive diagnosis occurs post-mortem and is characterized by neuronal cell death, neurofibrillary tangles (NFT), senile plaques (SP) of amyloid-β protein, and gray matter atrophy. Earlier diagnosis of AD pathology or AD pre-disposition would open the path to treatments before the onset of the disease. Visualization of AD using MRI is currently being investigated, but NFT and SP formations are much smaller than the resolution of clinical MRI, and other methods such as morphological measurements of brain volume changes are difficult to reproduce and occur after the onset of symptoms. $T_{1\rho}$ relaxation times are sensitive to plaque deposition in a mouse model of AD (2). Biochemical changes in the early stages of AD will change the $T_{1\rho}$ relaxation before cellular death and the onset of symptoms.

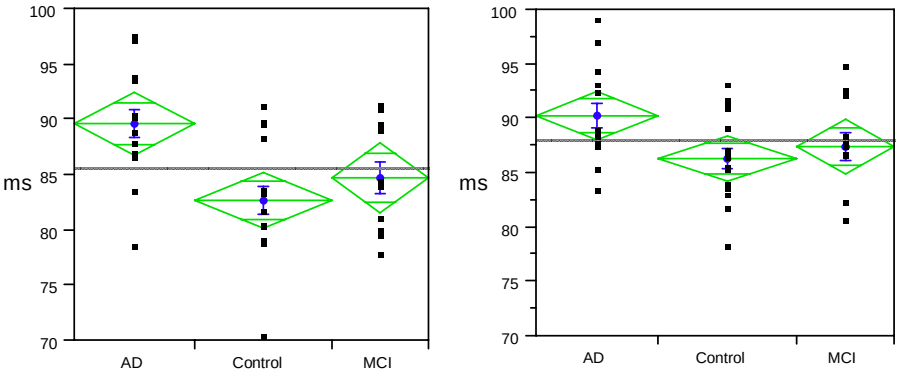
METHODS: A large scale study of biomarkers for AD patients, Mildly Cognitively Impaired patients (MCI), and age-matched control patients is currently being conducted through the Center of Excellence for Research on Neurodegenerative Diseases (CERND). For all patients enrolled in the study, MRI brain data is being collected on clinical 1.5 Tesla scanners and the patients are followed for two years. Currently, 14 AD patients, 11 MCI patients, and 16 controls have been scanned. The relevant sections of the protocol are a high resolution MP-RAGE for automated region of interest (ROI) analysis and an inversion-recovery prepped 2-D TSE-based $T_{1\rho}$. The $T_{1\rho}$ parameters are: TE/TR = 12/2000ms, FOV=24cm, slice thickness=2mm, matrix=256x128, turbo factor=5, TI = 860ms for fluid suppression. Four images are obtained with TSL=20,40,60,80ms for a total acquisition of 6 min. Plane prescription is defined to be perpendicular to the AC/PC plane and must include the head of the hippocampus. The four MRI contrasts were exponentially fit on a pixel-by-pixel basis to create a color-coded map of the $T_{1\rho}$ value at each location. Automated segmentation of brain was performed with the MP-RAGE data and provided masks for both gray and white matter of left and right temporal lobes (TL). Masks were selectively applied to automatically report average$T_{1\rho}$ values in both regions.

RESULTS:



A. AD Patient **B. AD Patient** **C. Control**

Figure 1: Color-coded maps of $T_{1\rho}$ values of AD patients (A & B). Increased $T_{1\rho}$ values are seen in the temporal lobe (TL) and brain stem regions as well as increased sulcal space compared to an age-matched control (C). A goal of the current study is to compare $T_{1\rho}$ values with brain atrophy rates in the same patients.



A. White Matter TL **B. Grey Matter TL**

Figure 2: Average (±std. error) of $T_{1\rho}$ in the AD, control, and MCI cohorts in white matter (A) and gray matter (B) of the MTL. A 5% increase in $T_{1\rho}$ was present in AD over control in the gray matter ($p<0.05$), while an 8% increase in $T_{1\rho}$ ($p<0.01$) was observed in white matter. The MCI cohort's average $T_{1\rho}$ values were between the AD and control cohorts. While increased $T_{1\rho}$ in gray matter could indicate AD-related pathology, white matter hyper-intensities have been previously reported in T_2-weighted MRI of AD patients (3).

CONCLUSIONS: A statistically significant increase in both the gray and white matter of the temporal lobes is seen in AD patients over age-matched controls. MCI patients show a bi-modal distribution with one group having increased $T_{1\rho}$ values in both ROIs while the other group shows no significant increase. One control patient showed significantly increased $T_{1\rho}$ in both gray and white matter. This study will follow these patients for the next 3 years with the further goal of correlating these early $T_{1\rho}$ increases with cognitively normal and MCI patients who develop AD.

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