Quantifying $T_{1\rho}$ in Alzheimer's Disease

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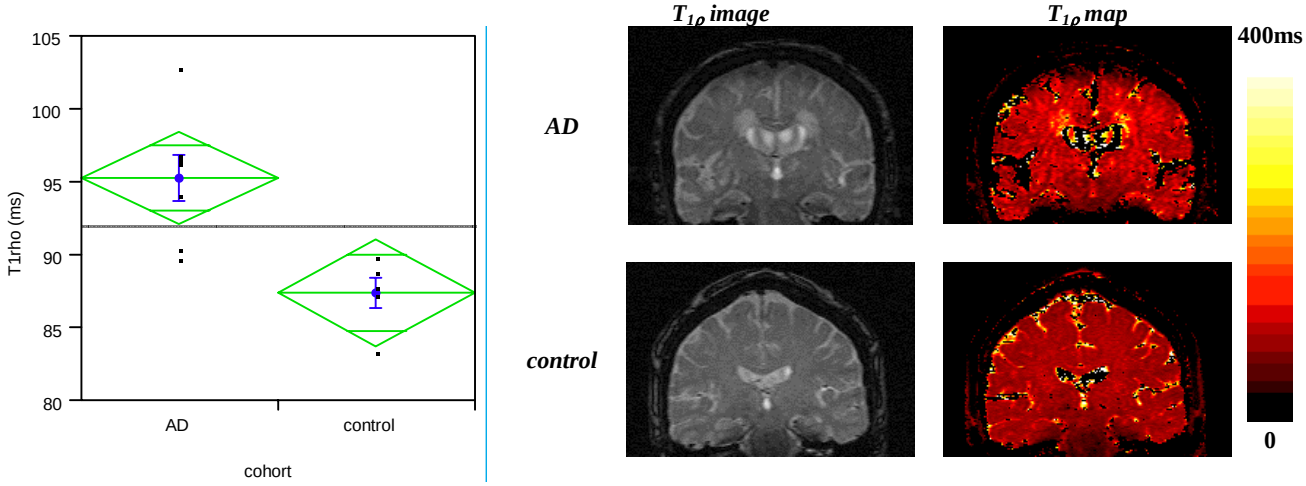
Introduction

Conventional MRI techniques have proven inadequate in observing the actual senile plaques (SP) and neurofibrillary tangles (NFT) underlying the pathology of Alzheimer's Disease (AD) in humans *in vivo*. An alternate contrast mechanism to conventional T_1 and T_2-weighted images is $T_{1\rho}$, or "T-1-rho", the spin-lattice relaxation time constant in the rotating frame, which determines the decay of the transverse magnetization in the presence of a "spin-lock" radio-frequency field. In previous studies, differences in T_2 relaxation times could not discern between patient and control populations (1). Whereas quantifying T_2* with MRI can be prone to errors from susceptibility-induced signal losses if not performed carefully and the T_2-weighted MR signal is degraded by diffusion, $T_{1\rho}$-weighted MR images are not affected by any such losses and $T_{1\rho}$ typically has a greater dynamic range than T_2* or T_2 in biological tissues. Consequently, $T_{1\rho}$ contrast has been successfully applied in delineating tumors (2), gliomas (3) and other cancerous tissue. $T_{1\rho}$-weighted MRI has shown some promise in generating tissue contrast based on variations in protein content. Others have shown that $T_{1\rho}$ MRI can map the distribution of glycosaminoglycans in cartilage (4). The purpose of our study was to determine whether there are any changes in $T_{1\rho}$ relaxation times in patients with AD compared to age-matched controls.

Materials and Methods

The Institutional Review Board of the University of Pennsylvania approved all experiments. MR imaging was performed on 7 patients (mean age: 77±7) with AD and 5 controls (mean age: 73±7) on a Siemens Sonata 1.5 Tesla clinical scanner with the vendor-supplied head coil. The AD patients were diagnosed as such by a neurologist (C.C.) based on their psychiatric history and standard cognitive testing. An oblique coronal $T_{1\rho}$-weighted image of a slice perpendicular to the AC/PC plane was obtained. This slice was chosen to include the head of the hippocampus. $T_{1\rho}$ pre-encoded Turbo Spin-Echo (TSE) pulse sequence (5) with TE/TR= 12/2000ms, TSL (duration of spin-lock pulse)= 20, 40, 60 and 80ms, slice thickness=2mm, FOV=22cm, Matrix= 256 x 128, echo train length=4 for a total imaging time of 6 minutes for four images. Each image pixel's signal intensity was fitted as a function of TSL by a linear least-squares algorithm to generate $T_{1\rho}$ maps. A single user manually selected a region of interest in each map in the parenchyma in the right medial temporal lobe and recorded average $T_{1\rho}$ values. Statistical analysis was performed with the JMP software package. A student's t-test was performed to determine any significant difference between the values obtained in patients and controls.

Results and Discussion



The graph on the left above shows $T_{1\rho}$ values from all subjects in both cohorts. The average $T_{1\rho}$ for the AD group was 95.3±1.4ms (mean ± std. error) and for controls was 87.5±1.7ms and the difference was statistically significant ($p<0.005$). Typical $T_{1\rho}$ MR images (grayscale images) and corresponding $T_{1\rho}$ maps (color images) are shown on the middle and right columns, respectively. The $T_{1\rho}$ maps represent values from 0 (black) to values > 400ms (white) as indicated in the color bar. Furthermore, pixels that did not converge during the fitting routine, such as background pixels and CSF-containing ventricle and sulcal pixels (with very long $T_{1\rho}$~1s) were set to black for improved visualization of parenchyma in the $T_{1\rho}$ maps. This is the first demonstration of imaging AD pathology in humans using $T_{1\rho}$ imaging. Our results indicate that clinically-confirmed AD results in the prolongation of $T_{1\rho}$ relaxation time in brain tissue. Future applications of this technique would include attempts to categorize the patient population into incipient AD (Mild Cognitive Impairment) or advanced AD on the basis of $T_{1\rho}$ times.

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References:

1. Campeau, N.G., *et al. Radiology* **205**: 197-201, 1997.
2. Markkola, A.T., *et al. Magn Reson Imaging* **16**: 377-383, 1998.
3. Aronen, H.J., *et al. Magn Reson Imaging* **17**: 1001-1010, 1999.
4. Shapiro, E.M., *et al. Magn Reson Med* **47**: 284-291, 2002.
5. Borthakur, A., *et al. J Magn Reson Imaging* **19**: 403-409, 2004.