Predictive Prognosis Value of Baseline Volumetric MRI

Song Lai[1], and John Lackey[1]
[1]*Radiology, Thomas Jefferson University, Philadelphia, PA, United States*

Introduction: Atrophic changes have been proposed as biomarkers for differential diagnosis of Alzheimer's disease (AD) and amnestic mild cognitive impairment (MCI), and different atrophic rates have been observed in AD, MCI-to-AD converters (cMRI), stable MCI (sMCI), and normal healthy controls[1]. Measurement of atrophic changes, however, requires longitudinal MRI studies. The purpose of this study was to investigate the following questions: 1. Is it possible to use baseline volumetric MRI to predict MCI conversion to AD, i.e., to tell if a MCI patient is a cMCI or a sMCI? 2. What are the predictive values of APOE genotype, and clinical cognitive test scores?

Method: High resolution 3D T1-weighted MP-RAGE datasets at baseline and 24-month of 6 AD (4 female, 2 male, 75.1+/-1.7 yrs), 11 stable MCI (sMCI, 5 female, 6 male, 75.8 +/-1.7 yrs), 9 MCI converters (cMCI, 5 female, 4 male, 74.4 +/-1.9 yrs), 9 normal controls (5 female, 4 male, 75.3+/-1.7 yrs), and their APOE genotypes, as well as clinical cognitive test scores were obtained from the ADNI database. The 3D T1WI datasets were first analyzed using a robust automatic voxel-based morphometry (VBM) technique which combines a fully automated spatial normalization approach, dubbed HAMMER (Hierarchical Attribute Matching Mechanism for Elastic Registration) [2], in conjunction with a tissue mass preserving framework called RAVENS (Regional Analysis of Volumes Examined in Normalized Space) [3]. Four consecutive steps were carried out: removal of non-brain voxels, tissue segmentation, spatial normalization to a standardized template, and generation of a mass-preserving tissue density map (i.e. RAVENS map) for each tissue type (GM, WM, ventricles).

Measurements of volumes of individual brain structures: From the RAVENS maps of each individual subject's brain, the HAMMER technique generated measurement of the sizes of 93 brain structures. These 93 structures were labeled in the template brain. The tissue mass preserving deformation mechanism in RAVENS method allows for linearly translating the average density of each labeled structure in the RAVENS map into a measure of the size of that specific structure in the individual subject's brain. The RAVENS maps are the results of elastic registration of original brain regions to the standard template while preserving the original tissue volumes.

Group comparison to identify structures that are different between groups in comparison: Unpaired t-test was carried out to identify structures that are significantly different among groups in comparison.

Data-driven statistical analysis: In each group of subjects in comparison (i.e., normal, AD, sMCI, or cMRI), subjects were put into "model" or "test" group. Histograms of each brain structure of interest of the model data were generated, and a threshold of structural volume or atrophy rate was defined that gave the highest diagnostic accuracy for the model data. Then the volume or atrophy rate of the structure in each "test" subject was compared to the threshold to diagnose the subject. The diagnoses were compared with the known disease status of the test subjects to assess the diagnostic accuracy of using a specific structure for diagnosis purpose.

Results: Table 1 listed several structures that showed significant atrophy in the cMCI group. Most interestingly, 7 structures (right angular gyrus, left inferior occipital gyrus, left superior parietal lobule, left precentral gyrus, left superior occipital gyrus, and right middle temporal gyrus) showed distinctively different baseline volumes as compared with the stable MCI group, indicating that the baseline volumetric measurement of these structures may have predictive prognosis value for identifying MCI converters. Analysis of the diagnostic accuracy of these structures' baseline volumes, along with that of APOE genotype, and clinical cognitive test scores showed ~88% diagnostic accuracy (cMCI vs sMCI) using these structures' baseline volumes, while APOE genotype, and clinical cognitive test scores have much lower diagnostic accuracy for differentiating cMCI vs sMCI (<70%). MM Score, however, provides fairly high diagnostic accuracy for differentiating normal vs sMCI (88%), normal vs cMCI (77%), normal vs AD (90%), and sMCI vs AD (85%).

Discussion and Conclusions: This study has reinforced the value of MRI as a potential surrogate marker of AD and MCI. Importantly, this study provided evidence that it is possible to use baseline volumetric MRI to predict a MCI patient to be a converter or a stable MCI.

References: [1] Risacher SL, et al., Neurobiology of Aging, 2010, 1401-18. Petersen, R.C., 2003. [2] D. Shen, et al., IEEE Trans Med Imaging, 2002. 21(11): 1421-39. [3] Davatzikos, et al., Neuroimage, 2001. 14(6): 1361-9.

Table 1. Baseline Volumes (in mm3) and Annual Atrophy Rate of A Few Selected Structures And Their Comparisons Between Different Patient Groups.

		Normal	sMCI	cMCI	AD	cMCI / Normal	cMCI / sMCI	cMCI / AD
structure		**mean±sd**	**mean±sd**	**mean±sd**	**mean±sd**	**p**	**p**	**p**
lateral ventricle left	volume	22181±10100	26458±15407	26154±13819	29552±12589	0.4962	0.9638	0.6373
	atrophy	0.0350±0.0852	**0.0325±0.0314**	**0.1536±0.0773**	**0.1077±0.0489**	**0.0070**	**0.0002**	0.2215
lateral ventricle right	volume	21291±9990	23149±14611	23232±10207	27608±11718	0.6888	0.9887	0.4563
	atrophy	0.0278±0.0793	**0.0274±0.0296**	**0.1550±0.0654**	**0.1097±0.0604**	**0.0019**	**0.0000**	0.1990
lateral front-orbital gyrus right	volume	10358±1422	9172±1473	9742±2064	8923±1360	0.4717	0.4806	0.4098
	atrophy	-0.0116±0.0536	-0.0182±0.0304	**-0.0893±0.0653**	**-0.0436±0.0305**	**0.0139**	**0.0047**	0.1360
angular gyrus right	volume	8832±1403	7982±1166	9907±1557	7858±1280	0.1433	**0.0054**	**0.0193**
	atrophy	-0.0021±0.0670	-0.0120±0.0970	**-0.0805±0.0640**	0.0290±0.0769	**0.0218**	0.0860	**0.0102**
inferior occipital gyrus left	volume	3706±1430	2836±1375	4057±923	2643±829	0.5447	**0.0357**	**0.0099**
	atrophy	-0.0359±0.0738	0.0416±0.1588	**-0.0959±0.0995**	-0.0490±0.0553	0.1656	**0.0369**	0.3159
superior parietal lobule left	volume	12257±1750	11865±2029	14721±2135	11447±1610	**0.0165**	**0.0067**	**0.0071**
	atrophy	**-0.0375±0.0403**	-0.0385±0.0581	**-0.0506±0.0537**	-0.0068±0.0637	0.5650	0.6368	0.1736
precentral gyrus left	volume	9786±972	10670±2281	13842±1846	10796±2163	**0.0000**	**0.0035**	**0.0118**
	atrophy	-0.0033±0.0605	-0.0176±0.0571	**-0.0624±0.0680**	-0.0009±0.0526	0.0690	0.1263	0.0846
lateral front-orbital gyrus left	volume	10076±1900	8905±1769	9058±2309	8416±1092	0.3226	0.8684	0.5397
	atrophy	-0.0099±0.0752	-0.0157±0.0427	**-0.0953±0.1089**	**-0.0535±0.0317**	0.0707	**0.0385**	0.3814
superior occipital gyrus left	volume	3826±809	3928±844	5644±985	3620±315	**0.0006**	**0.0005**	**0.0003**
	atrophy	-0.0181±0.0778	0.0090±0.0623	**-0.0969±0.0730**	-0.0054±0.0347	**0.0415**	**0.0026**	**0.0140**
middle temporal gyrus right	volume	19104±2073	16950±2504	21043±3375	16910±2474	0.1614	**0.0060**	**0.0236**
	atrophy	**-0.0294±0.0340**	**-0.0297±0.0352**	**-0.0615±0.0456**	-0.0553±0.0566	0.1098	0.0952	0.8182
superior temporal gyrus right	volume	11396±1305	10700±1822	13136±2310	10552±856	0.0667	**0.0167**	**0.0222**
	atrophy	-0.0118±0.0240	0.0044±0.0430	**-0.0635±0.0321**	-0.0499±0.0504	**0.0013**	**0.0010**	0.5304

Note: The selected structures showed significant atrophy in the MCI converter group. Statistically significant measures ($p<0.05$) are denoted in bold.