Sensitivity of Brain Volumetry: A FreeSurfer-Based Segmentation Study of Brain Data Acquired with the ADNI Protocol vs. GE BRAVO

Zhaoying Han[1], Julian Maclaren[1], Alexander Brost[1], Sjoerd B Vos[1,2], Christoph Seeger[1,3], Nancy Fischbein[1], and Roland Bammer[1]

[1]*Center for Quantitative Neuroimaging, Department of Radiology, Stanford University, Palo Alto, CA, United States,* [2]*Image Sciences Institute, University Medical Center Utrecht, Utrecht, Netherlands,* [3]*Pattern Recognition Lab, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany*

Target audience: Researchers working on brain volumetric measurements as biomarkers for neurodegenerative diseases.

Introduction: Quantitative measurement of brain structures is potentially a powerful approach for early detection and monitoring of neurodegenerative diseases, such as Alzheimer's disease (AD) [1-3]. Translating this approach into clinical practice will involve comparing a patient's brain volume to those in a particular patient population, or to normal subjects (e.g. [4]). There are now a number of freely available online databases containing T1W brain volumes of normal subjects, such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) project database. The key question is whether it is valid to compare a patient's volumetric measurements with the normative ranges obtained from an existing database. The aim of this study was to choose the well-defined standard protocol from the ADNI project and compare it to the standard GE BRAVO sequence used in clinical routine at our institution and assess comparability of volumetric measurements.

Methods: T1W MRI volumes from 18 healthy subjects (29.1±3.7 years old, 9 male and 9 female) were acquired with a GE 3T MR750 scanner using an 8-channel head coil. For each subject, the acquisition included 8 scans interleaved between two protocols: (a) a 3D IR-SPGR protocol specified by ADNI and (b) the standard 3D GE BRAVO sequence used in clinical routine at our institution. Most protocol parameters were identical: TI 400ms; TR 7.3ms (ADNI), 8.1ms (BRAVO); TE 3.0ms (ADNI), 3.1ms (BRAVO); flip angle 11°; matrix size 256x256; in-plane FOV 27x27cm; 192 sagittal slices; slice thickness 1.2mm; accelerated factor 1.75 with ASSET (ADNI) and ARC [~GRAPPA] (BRAVO); and acquisition time 5:37 (ADNI); 5:17 (BRAVO). In total 144 volumes were acquired and subsequently processed with FreeSurfer v5.1.0 [5] to segment the lateral ventricles and subcortical structures (Table 1), which are of most interest for clinical use. Statistical analyses of structure volumes within each protocol and across protocols were conducted using one-way and two-way ANOVA respectively.

Structures	*P value (left)*	*P value (right)*	*Perf_diff*
Lateral ventricle	**<0.0001***	**<0.0001***	**-3.12%**
Thalamus	0.244	0.391	**0.32%**
Caudate	0.065	**0.016***	**-1.32%**
Putamen	**0.0003***	0.059	**-2.26%**
Pallidum	0.389	0.719	**0.38%**
Hippocampus	**<0.0001***	**<0.0001***	**5.80%**
Amygdala	**<0.0001***	0.921	**-3.89%**

Table 1: ANOVA analysis between ADNI and BRAVO (* means p < 0.05).

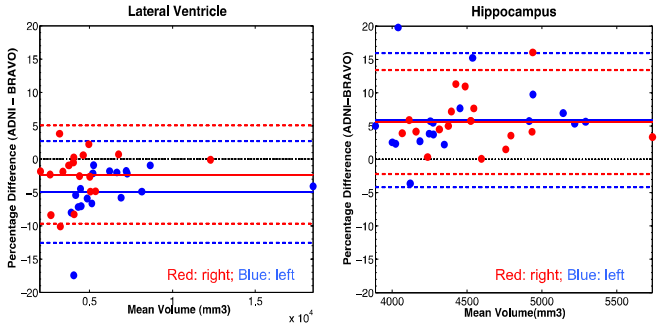

Fig. 1: Bland-Altman plots showing mean volume difference in percentage vs. mean volume for the lateral ventricles (left) and the hippocampus (right) between ADNI and BRAVO.

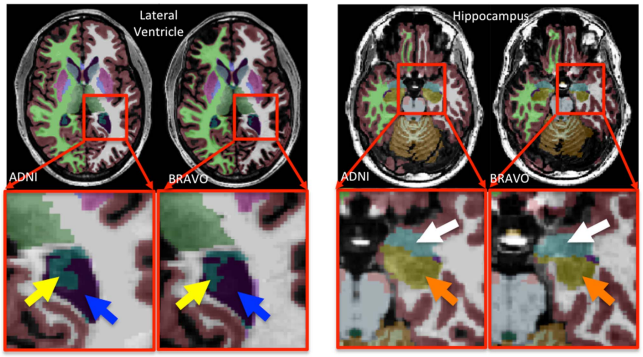

Fig. 2: FreeSurfer segmentation output for two subjects to show visual differences in volumes between ADNI and BRAVO.

Results: One-way ANOVA analyses within each protocol show no statistically significant differences (p>0.05) among four scans for all the subcortical structures and the ventricles. Two-way ANOVA analysis between the two protocols shows statistically significant volume differences for the lateral ventricles and the hippocampus volumes in both hemispheres, summarized in Table 1. For each structure, the mean volumes of both hemispheres across subjects and scans for ADNI ($\bar{A}$) and BRAVO ($\bar{B}$) were compared in terms of percentage difference defined as: $Perc\_diff = (\bar{A} - \bar{B}) / \frac{(\bar{A}+\bar{B})}{2} * 100$, shown in Table 1. Bland-Altman plots in Fig.1 show the mean volume difference vs. the percentage differences between ADNI and BRAVO protocols for the lateral ventricles (left) and the hippocampus (right), where each dot denotes a subject. The upper and bottom (dashed) lines are limits of agreement specified as mean ± 1.96 std. Fig. 2 shows two examples of visual differences in FreeSurfer output between the two protocols. The left lateral ventricle (blue arrows) of the ADNI protocol is smaller than that of the BRAVO protocol, probably due to the differences in classifying the choroid-plexus (yellow arrows). The left hippocampus segmented area (orange arrows) is larger in the ADNI scan than in the BRAVO, which may be related to the smaller left amygdala (white arrows) in ADNI (p<0.0001 in Table 1) caused by boundary differences between the amygdala and the hippocampus.

Discussion & Conclusion: This study shows that the ADNI protocols and the standard GE BRAVO protocol - although tightly matched in terms of scan parameters - have statistically significant differences in estimated volumes of the lateral ventricles and the hippocampus with FreeSurfer segmentations. Since these structures are popular biomarkers for AD and other neurodegenerative diseases, caution needs to be exercised in comparing a patient's volumetric information to a normative database using different protocols in clinical practice.

References: [1] Jack C.R.Jr. et al., Alzheimers Dement. 2011. 7:474-485. [2] McEvoy L.K. et al., Expert Rev Neurother. 2010; 10(11): 1675-1688. [3] Schuff, N. et al., Brain 2009; 132:1067-1077. [4] Brewer J.B. Behavioural Neurology 2009; 21:21-28. [5] Dale, et al. Neuroimage 9:179-194. **Acknowledgements:** NIH (2R01 EB00271108-A1, 5R01 EB008706, 5R01 EB01165402-02), the Center of Advanced MR Technology at Stanford (P41 EB015891), Lucas Foundation, Oak Foundation.