Introduction:
Hippocampal atrophy is the most established and validated imaging biomarker in Alzheimer’s disease (AD). Because manual hippocampal segmentation of large datasets is prohibitively effortful and time consuming, it is beneficial to acquire the use of automated methods. The objective of this study is to directly compare the performance of our automated and manual hippocampal segmentation approaches.

Methods:
We applied AdaBoost - our automated hippocampal segmentation algorithm - to the baseline 1.5T T1-weighted MRI imaging data of 136 mild cognitive impairment (MCI) participants in the ADCS Donepezil/Vitamin E trial. This dataset was previously manually segmented. We used reliability and Pearson’s correlation statistics to directly compare the hippocampal volumes extracted with each method. Next, we applied the radial distance method to 3D surfaces reconstructed from each segmentation set (Figure 1). We investigated the statistical power to detect 3D significant differences between MCI subjects who converted to AD (MCIc, N=87) and those who remained stable (MCInc, N=49) during the 3-year trial. For 3D multiple comparisons correction, we applied permutation statistics with a threshold of p<0.01.

Results:
The agreement between the methods was excellent – Cronbach’s Alpha was 0.89 for the right and 0.83 for the left hippocampus. Correlation analyses revealed significant concordance between the automated and manually derived volumes – right r=0.81, left r=0.72. Significant baseline differences between MCIc and MCInc were detected with both methods (manual method: right \( p_{\text{corrected}}=0.09 \), left \( p_{\text{corrected}}=0.004 \); automated method: right \( p_{\text{corrected}}=0.017 \), left \( p_{\text{corrected}}=0.019 \). Both methods detected AD-like baseline regional differences showing greater subicular and CA1 involvement in MCIc relative to MCInc (Figure 2), but these differences were more pronounced in the automated vs. the manually segmented hippocampal dataset (Figure 3).

Conclusions:
AdaBoost can reliably segment the hippocampus as demonstrated by reliability and correlation statistics. Our work also suggests that AdaBoost segmentations provide superior statistical power relative to manual segmentations for detecting disease-associated hippocampal changes in medium to large datasets. AdaBoost may prove to be immensely useful for hippocampal analyses of clinical trial datasets especially in the preclinical (i.e., latent) disease stages.

Acknowledgments:
This study was generously supported by the Alzheimer’s Association UCLA Chapter, the Easton Consortium for Alzheimer’s Disease, and the NIH National Institute of Neurological Disorders and Stroke (AG034920).