



Title: ***Combining Amyloid Imaging and Measurement of Regional Cerebral Glucose Metabolism to Evaluate Dementia State and Progression***

Authors: Dawn C. Matthews¹, Lisa Mosconi², Randolph D. Andrews¹, Terry F. Brown¹, Karl Rickert¹, Wai H. Tsui², Yi Li², Rachel Mistur², Mony J. de Leon² and the Alzheimer's Disease Neuroimaging Initiative*

Affiliations: ¹Abiant, Inc., ²New York University Center for Brain Health

Amyloid imaging with [¹¹C-PIB] PET and similar tracers has shown great promise in increasing the specificity of Alzheimer's Disease (AD) diagnosis and in measuring therapeutic impact on amyloid accumulation. Despite marked differences in PIB retention between cognitively normal (NL) individuals and AD patients, high tracer uptake (reflecting higher amyloid burden) is measured in ~25% NL, while uptake within normal range (low burden) is found in ~10% AD patients. Moreover, a continuum of low to high burden is found in MCI patients. Amyloid levels have been found to plateau in later disease stages while clinical symptoms continue to progress (Klunk, 2006). Measurement of regional glucose metabolism (rCMRglc) using FDG PET provides complementary information that can be used to evaluate disease status and progression. Amyloid levels were measured in the longitudinal [11C]-PIB scans of 50 ADNI subjects (36 M, 14 F) who were followed 24 +/- 12 months. This included 11 NL who remained NL, 3 NL who declined to MCI, 21 non-converting MCI, 6 MCI who declined to AD, and 6 AD. PIB uptake was measured in 32 pre-selected regions of interest (ROI) and normalized to cerebellum (Price, 2005). rCMRglc was measured in FDG PET scans of the same subjects within the same ROI. Our main analyses focused on the posterior cingulate cortex, medial frontal and prefrontal gyri, parietal and temporal lobes, thalamus, and hippocampus. ROI measurements were made using an automated method that has been demonstrated to achieve accurate, rapid sampling, and to optimize sensitivity and specificity without compromise from spatial normalization, smoothing, adjacent region spillover, atrophy, and white matter noise, for both FDG and PIB-PET (Mosconi, 2005; Li, 2008). We observed a negative correlation between hippocampal (HIP) rCMRglc at baseline and subsequent amyloid load. In subjects who showed clinical progression (converting to MCI or AD, or with declining cognitive scores), rCMRglc levels in HIP and other AD regions declined, while amyloid load increased in most but not all subjects. The combination of information obtained from amyloid imaging with rCMRglc information on neuronal function, particularly in the HIP, can provide enhanced insight to the onset and progression of dementias.

* Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (www.loni.ucla.edu/ADNI). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. ADNI investigators include (complete listing available at www.loni.ucla.edu/ADNICollaboration/ADNI_Manuscript_Citations.pdf).