Conclusions: Lumipulse G is a fully automated system that analyses the standard biomarkers of AD and correlates well with previously established methods. It also shows good inter-lab reproducibility. Method-specific reference values and decision limits previously established methods. It also shows good inter-lab reproducibility. Method-specific reference values and decision limits

Methods: We obtained de-identified EHR from one million Korean individuals (representativeness-validated)
from 2005 to 2012 (for 8 years) from Korean National Health Insurance Service database. EHR contained diagnoses (ICD-9/10), medications, laboratory values, annual health check-up database, and socio-demographics. [Event of interest] We used EHR from elders age above 65 years old: N=430,133. Our event of interest was the month of incidence of AD. We defined the incidence of AD based on diagnostic codes and prescription of anti-dementia (N=672). [Modeling] Total 100 sets of random bootstrap samples of controls with an equal number to AD cases were drawn repeatedly. [Validation] We trained and validated random forest, support vector machine, and logistic regression to predict incidence of AD in 1, 2, 3, and 4 subsequent years. Data was split into training (60%), validation (20%), and test set (20%). Results: In predicting future incidence of AD, random forest showed the best performance in 1 year prediction with accuracy of 0.76±0.03; in 2 year, 0.73±0.02; in 3 year, 0.67±0.03; in 4 year, 0.66±0.04. Average duration of EHR was 1936 days in AD and 2694 days in controls. Features selected in logistic regression included well-known AD risk factors (age, smoking, essential hypertension), as well as rela-

tive new, potential factors (waist, LDL and HDL-cholesterol, hemoglobin, urine glucose, amoxicillin. Conclusions: This is the first study reporting the promising utility of EHR in predicting future incidence of AD. The current prediction of future incidence of AD with maximum 76% accuracy (1 year) is surprising compared with other well-studied biomarkers. We expect that including EHR-based AD prediction will significantly improve individualized prediction of risk for AD. Towards EHR-based AD screening with practical utility, future research should test the generalizability of the model in independent data.

Table. Performance of classifiers trained on EHR

|       | Accuracy | Sensitivity | Specificity |
|-------|----------|-------------|-------------|
| 1 yr  | 0.759    | 0.758       | 0.760       |
|       | (0.753- | (0.750- | (0.750- |
| 2 yr  | 0.729    | 0.688       | 0.776       |
|       | (0.742- | (0.682- | (0.768- |
| 3 yr  | 0.667    | 0.616       | 0.725       |
|       | (0.661- | (0.608- | (0.716- |
| 4 yr  | 0.697    | 0.694       | 0.706       |
|       | (0.689- | (0.690- | (0.683- |

Performance metrics were from Random Forest which outperformed support vector machine and logistic regression.

Furthermore, CSF glucose is strongly associated with CSF total tau protein levels in AD patients. It is not known if CSF glucose is associated with regional tau deposition, however, and if such associations regionally vary depending on AD genetic risk factors, baseline diagnosis, or sex. Methods: Data from 142 aged adults was downloaded from the Alzheimer’s Disease Neuroimaging Initiative (ADNI). CSF glucose levels were derived from standard lab assays. Fully preprocessed F18-AV-1451 positron emission tomography scans where coregistered to the subject’s T1-weighted image in native space. Mean regional uptake in FreeSurfer defined regions was divided by mean uptake in the inferior cerebellum reference region to derive Standardized Uptake Value Ratios (SUVRs). Multiple linear regression regressed CSF glucose against regional AV-1451 SUVR in regions of interest. Due to the large number of cognitive normal subjects scanned (n=103), analyses were restricted to Braak stages 1/2 and 3/4. Interactions between CSF glucose and gender, family history of AD, and beta-amyloid (Aβ) status were also explored. Results: Higher CSF glucose was significantly associated with lower tau deposition in the caudal anterior cingulate gyrus (Braak 4). Moderation analyses showed that only Mild Cognitive Impairment (MCI) and AD participants drove this association. A gender x CSF glucose interaction showed that higher CSF glucose was related to lower hippocampal tau deposition (Braak 2) in women but not men. Finally, for subjects with AD parental history, higher CSF glucose was linked to less regional tau deposition in all Braak stage 3 and 4 regions, particularly the lingual gyrus, fusiform gyrus, and isthmus of cingulate gyrus. Conclusions: Taken together, these results suggest that higher CSF glucose levels may be protective against early tau deposition among women, as well as later tau deposition among subjects with cognitive impairment or a parental history of AD. Future work will examine similar associations with peripheral insulin resistance and moderation by regional amyloid deposition.

Mild Cognitive Impairment (MCI) and AD participants. Most existing efforts have focused on one dimension at a time (genetics, metabolomics, imaging...) without considering them simultaneously. Moreover, most models aim at classifying AD versus Cognitively Normal (CN) individuals but only few include MCI as well. We integrated clinical, metabolomics, imaging and genetic data of individuals from the Alzheimer Disease Neuroimaging Initiative Phase 1 dataset in order to build a model to classify AD, MCI and CN individuals as accurately as possible. Methods: Samples were divided into training (67 AD, 141 MCI, 78 CN) and validation datasets (34 AD, 70 MCI, 39 CN). After quality control, 4 clinical, 172 metabolomic, 12 imaging variables and 67 genetic variants were...