ADNI DOD CSF: Analyses of Amyloid-β_{1-42}, Amyloid-β_{1-40}, total Tau and p-Tau$_{181}$ by the fully automated Elecsys immunoassays

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Summary

A total of 133 pristine aliquots prepared from CSF collected as part of the ADNI DOD project were analysed for four biomarkers: Amyloid-β(1-42) (Aβ_{1-42}), Amyloid-β(1-40) (Aβ_{1-40}), total tau (t-tau) and the tau phosphorylated at the threonine 181 position (p-tau$_{181}$), using Elecsys electro-chemi-luminescence immunoassays on a fully automated cobas e601 platform (Roche Diagnostics) and a single lot of reagents for each of the 4 measured analytes. The CSF aliquot samples from this project were processed alongside the ADNI/DIAN project CSF. Among the analysed samples were also 28 pooled quality control CSF samples: pool "56" for the purpose of tracking longitudinal performance of the Elecsys assay.

Method

CSF samples in this project were analysed using the Elecsys Aβ_{1-42}, Aβ_{1-40}, t-tau and p-tau$_{181}$ electrochemiluminescence (ECL) immunoassays on a fully automated cobas e601 analyzer (Roche Diagnostics). These immunoassays are currently under development and are for investigational use only. The Aβ_{1-42} assay has a measurement range of 200 to 1700 pg/mL, the Aβ_{1-40} assay: 11 to 43,000 pg/mL, the t-tau assay: 80 to 1300 pg/mL, and the p-tau$_{181}$ assay: 8 to 120 pg/mL. More details about these assays can be found in [1-3].

The analysis of samples in this project was set-up in two phases. In the first phase, the 133 ADNI-DOD samples were processed. In the second phase, the DIAN/ADNI samples were processed. A total of 1250 samples were processed within the entire project, including 28 internal CSF pool controls. The patient samples were processed in the amount of 80 per day, each day consisting of 2 batches of 40 patient samples each. The internal CSF pool control (Pool "56") was always processed as an additional sample (41st sample) at the end of each batch.

Results of the Pool "56" experiment are summarized in Figure 1.

Among the 133 ADNI-DOD samples (133 x 4 = 532 test results), a total of 28 results were missing: 21 Aβ_{1-42} results greater than 1700 pg/mL limit, 5 results with p-tau$_{181}$ below the 8 pg/mL limit, and 2 results of t-tau below the 80 pg/mL limit. In the 21 instances of missing values of Aβ_{1-42} biomarker, the results have been provided by Roche by extrapolation from the calibration curve above the 1700 pg/mL limit and are shown in a clearly marked column in the .CSV file "UPENNBIOMK_DOD_SCRNO_2017". The results that were below the lower

limit of the measurement ranges for t-tau and p-tau$_{181}$ were indicated as "<" the respective lower limits of the measurement ranges.

Please note:

The Elecsys β-Amyloid (1-42) CSF immunoassay in use is not a commercially available IVD assay. It is an assay that is currently under development and for investigational use only. The measuring range of the assay is 200 (lower technical limit) – 1700 pg/mL (upper technical limit). The performance of the assay beyond the upper technical limit has not been formally established. Therefore, use of values above the upper technical limit, which are provided based on an extrapolation of the calibration curve, is restricted to exploratory research purposes and is excluded for clinical decision making or for the derivation of medical decision points.

Dataset Information

This methods document applies to the following dataset available from the ADNI-DOD repository:

Dataset Name	Date Submitted
UPENNBIOMK_DOD_SCRNO_2017	12 December 2017

References

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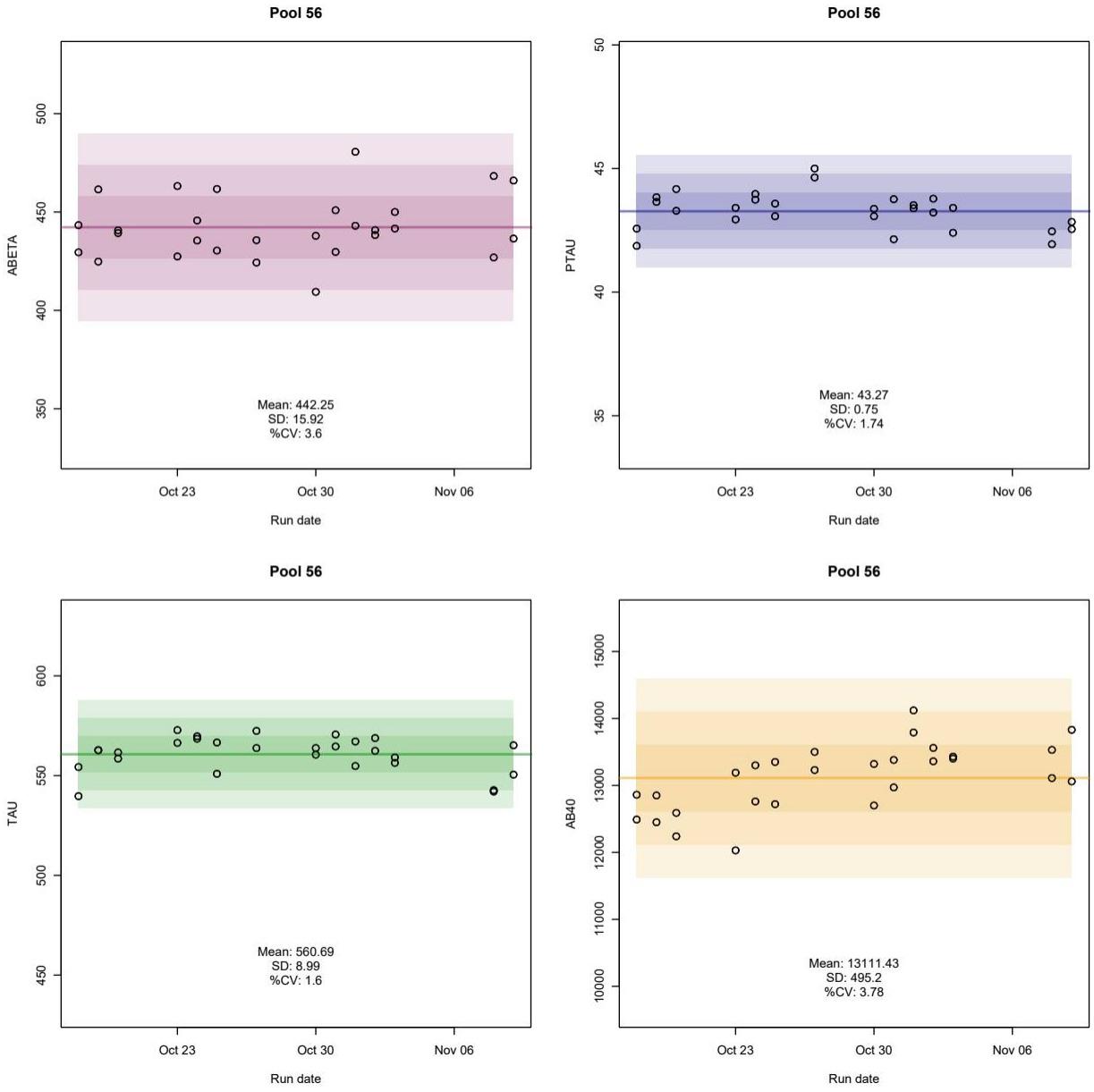

Figure 1: Longitudinal performance of the 28 repeats of CSF control Pool "56".