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Head-to-head comparison of the fully automated Elecsys pTau217 plasma assay and the Lumipulse pTau217 plasma assay

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Introduction

- Blood tests are a non-invasive and cost-effective method for detecting Alzheimer's disease pathology, including amyloid deposits.[1]
- Plasma phosphorylated tau 217 (pTau217) is a biomarker that has demonstrated high clinical utility in detecting amyloid pathology compared with other biomarkers.[2,3]
  - The Elecsys® Phospho-Tau 217 plasma prototype immunoassay (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) quantitatively determines plasma pTau217 levels to identify amyloid pathology and has received United States Food and Drug Administration Breakthrough Device Designation.[4]
  - The Lumipulse G pTau 217 plasma assay is a research use only assay from Fujirebio.[5]

Objective

- To perform a head-to-head method comparison study of the Elecsys and Lumipulse pTau217 assays.

Methods

- This head-to-head, blinded, method comparison study compared plasma pTau217 levels measured using the Elecsys and Lumipulse pTau217 assays in samples from a selected subset of patients from the amyloid screening population of the CREAD2 study (NCT03114657).[6]
- Amyloid status was determined by amyloid-positron emission tomography (PET) imaging with visual read or, if not available, by the cerebrospinal fluid (CSF) pTau181/β-amyloid(1–42) ratio, measured with the Elecsys Phospho-Tau (181P) CSF and Elecsys β-Amyloid(1–42) CSF immunoassays (Roche Diagnostics International Ltd, Rotkreuz, Switzerland).
- The receiver operating characteristic (ROC) area under the curve (AUC) with respect to amyloid status was calculated.
- A dual cutoff approach assessed the cutoffs at sensitivity and specificity of 90%. Positive percent agreement (PPA), negative percent agreement (NPA), positive predictive values (PPV) and negative predictive values (NPV), were calculated.
- The Pearson correlation coefficient between results from the two pTau217 assays was calculated.

Results

- This analysis included samples from 264 patients (80 [30.3%] were amyloid-negative and 184 [69.7%] were amyloid-positive; **Table 1**).

Table 1. Patient demographics and baseline characteristics by amyloid status.

	Amyloid-negative (n=80)	Amyloid-positive (n=184)	All (N=264)
Mean age (range), years	72.4 (50.0–85.0)	70.7 (53.0–85.0)	71.3 (50.0–85.0)
Female, n (%)	40 (50.0)	106 (57.6)	146 (55.3)
Race, n (%)			
White	69 (86.3)	166 (90.2)	235 (89.0)
Other*	11 (13.8)	18 (9.8)	29 (11.0)
Mean BMI (range), kg/m²	27.1 (20.0–36.8)	25.4 (15.8–42.4)	25.5 (15.8–42.4)
***APOE E4* alleles, n (%)**			
No copies	52 (65.0)	58 (31.5)	110 (41.7)
One copy	22 (27.5)	98 (53.3)	120 (45.5)
Two copies	6 (7.5)	28 (15.2)	34 (12.9)
Mean MMSE score (range)	25.1 (22.0–29.0)	24.5 (22.0–30.0)	24.7 (22.0–30.0)
PET status, n (%)			
Negative	61 (76.3)	0 (0.0)	61 (23.1)
Positive	0 (0.0)	147 (79.9)	147 (55.7)
Missing	19 (23.8)	37 (20.1)	56 (21.2)

*Other races included American Indian or Alaska Native, Asian, Black or African American, multiple races or unknown.
APOE E4, *Apolipoprotein E4*; BMI, body mass index; MMSE, Mini-Mental State Examination.

- For the Elecsys pTau217 assay, six (2.3%) measurements were below the corresponding limits of quantification compared with one (0.4%) measurement for the Lumipulse pTau217 assay, demonstrating sensitivity to measure pTau217 within the cohort of samples.
- For the Elecsys pTau217 assay, there were no measurements that exceeded the assay measuring range compared with two (0.8%) measurements for the Lumipulse pTau217 assay.

Results (cont.)

- Plasma pTau217 levels between the Elecsys and Lumipulse pTau217 assays were positively correlated (Pearson's r=0.883; ten outliers identified by Generalized Extreme Studentized Deviate were removed; **Figure 1**).
- The AUC by amyloid status for pTau217 was 0.907 (95% confidence interval [CI]: 0.858–0.957) with the Elecsys pTau217 assay and 0.862 (95% CI: 0.805–0.920) with Lumipulse (**Figure 2**).

Figure 1. Correlation of plasma pTau217 levels measured using Elecsys and Lumipulse pTau217 assays by amyloid status.

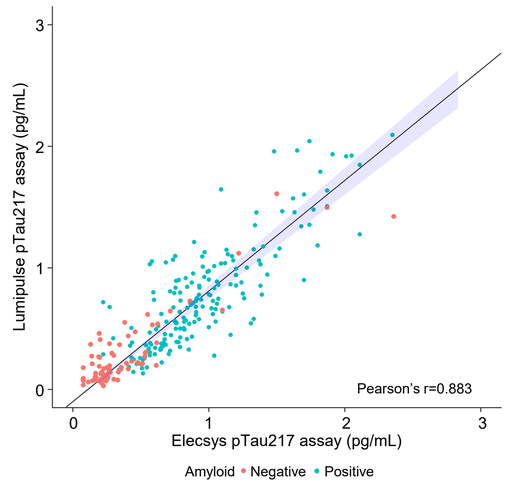
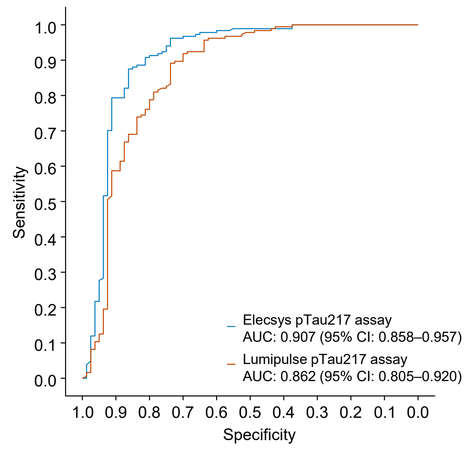


Figure 2. ROC curves with AUC for pTau217 with respect to amyloid status* measured using the Elecsys and Lumipulse pTau217 assays.

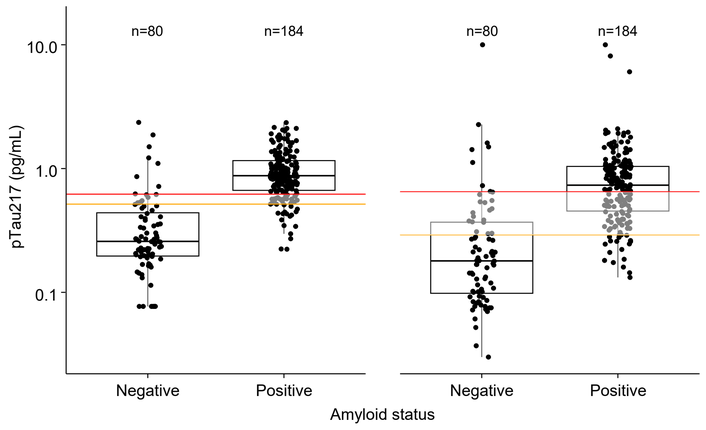


*Sensitivity/specificity were calculated with respect to amyloid status, determined by amyloid-PET visual read, if available, or otherwise using the Elecsys CSF pTau181/β-amyloid(1–42) ratio.

- Both the Elecsys and Lumipulse pTau217 assays demonstrated good discrimination of amyloid-negative and amyloid-positive samples with the 90% sensitivity and 90% specificity cutoffs (**Figure 3**).
  - For the Elecsys pTau217 assay, 10.2% of samples were in the intermediate zone between the two cutoffs compared with 28.0% with the Lumipulse pTau217 assay.

Figure 3. Dual cutoff approach of 90% sensitivity (orange line) and 90% specificity (red line) for the (A) Elecsys pTau217 assay and (B) Lumipulse pTau217 assay*.

(A) Elecsys pTau217 assay **(B) Lumipulse pTau217 assay**



Cutoff, %	PPA	NPA	PPV	NPV
(A) Elecsys pTau217 assay levels				
90% sensitivity	90.2	81.3	91.7	78.3
90% specificity	79.3	90.0	94.8	65.5
(B) Lumipulse pTau217 assay levels				
90% sensitivity	90.2	70.0	87.4	75.7
90% specificity	58.7	90.0	93.1	48.6

*Each box represents the interquartile range (25th–75th percentile) with the horizontal bold line showing the median value and whiskers representing the upper and lower boundaries for the extreme limits. The orange line represents the 90% sensitivity cutoff, and the red line represents the 90% specificity cutoff.

Conclusions

- The Elecsys pTau217 assay detects amyloid pathology with high accuracy and is highly correlated with the Lumipulse pTau217 assay.
- The fully automated Elecsys and Lumipulse pTau217 assays have clinical potential for detecting amyloid pathology. However, the assays need to be fully validated and approved by regulatory bodies before clinical use.

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