

【Overview presentation】

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## High diagnostic performance of the random-access HISCL pTau-217, Aβ42 and Aβ40 plasma assays in detecting amyloid pathology across clinical stages

<p>Authors</p>	<p>Inge M.W. Verberk<sup>1</sup>, Thomas Claessen<sup>1, 2</sup>, Daniel Antwi-Berko<sup>1</sup>, Hans Heijst<sup>1</sup>, Azzam Aladdin<sup>1</sup>, Yuko Sasaki Mori<sup>3</sup>, Roman Boeer<sup>4</sup>, Argonde C. van Harten<sup>1, 2</sup>, Charlotte E. Teunissen<sup>1</sup></p> <p><sup>1</sup> Neurochemistry Laboratory, Laboratory Medicine, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Neuroscience  <sup>2</sup> Alzheimer Center Amsterdam, Neurology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Neuroscience  <sup>3</sup> Sysmex R&amp;D Center Europe GmbH  <sup>4</sup> Sysmex Europe SE</p>
<p>Overview presentation</p>	<p><b>Objectives</b></p> <p>Alzheimer's disease (AD) blood biomarkers detecting cerebral amyloid-beta (Aβ) pathology are being implemented in clinical and trial settings. Plasma assays on high-performing automated random-access platforms are considered particularly relevant for implementation. Sysmex developed phosphorylated (p)Tau-217, Aβ42 and Aβ40 assays on their random-access HISCL™-5000/HISCL™-800 platform, which we sought to validate for their potential to detect Aβ pathology.</p> <p><b>Methods</b></p> <p>We selected plasma samples across clinical stages from the Amsterdam Dementia Cohort: subjective cognitive decline (SCD; 50 Aβ-, 50 Aβ+), mild cognitive impairment (MCI; 50 Aβ-, 50 Aβ+) and AD-dementia (50 Aβ+). Groups were age/sex-matched (average±SD age 66±5.6y, 40%F). Samples were measured on the HISCL™-5000 in duplicates for pTau-217, Aβ42 and Aβ40, and on the Lumipulse as benchmark. Mann-Whitney U and ROC-AUC analyses were conducted.</p>

	<p><b>Results</b></p> <p>Average coefficient of variation for the three HISCL assays was &lt;3.5% in duplicate measurements. HISCL pTau-217 levels were increased in the A<math>\beta</math>+ compared to the A<math>\beta</math>- groups, with a stepwise increase in levels from SCD A<math>\beta</math>+ to MCI A<math>\beta</math>+ to AD-dementia (all: <math>p^{\text{FDR}} &lt; 0.01</math>). HISCL plasma A<math>\beta</math>42/40 levels were decreased in the A<math>\beta</math>+ compared to the A<math>\beta</math>- groups (<math>p^{\text{FDR}} &lt; 0.001</math>), with no difference between the A<math>\beta</math>+ groups. HISCL pTau-217 and A<math>\beta</math>42/40 discriminated A<math>\beta</math>+ from A<math>\beta</math>- with ROC-AUC=0.93 (95%CI: 0.90–0.96), and ROC-AUC=0.80 (95%CI: 0.74–0.86) respectively. Results in the intermediate ranges bounded by 90%-specificity and 90%-sensitivity thresholds were 12.1% for pTau-217 and 39% for A<math>\beta</math>42/40. ROC-AUCs for HISCL pTau-217 and HISCL A<math>\beta</math>42/40 were slightly larger than ROC-AUCs for Lumipulse measurements (both: DeLong's <math>p=0.02</math>).</p> <p><b>Conclusions</b></p> <p>HISCL™-5000/HISCL™-800 plasma pTau-217 and A<math>\beta</math>42/A<math>\beta</math>40 were validated as robust and accurate biomarkers to detect A<math>\beta</math> pathology across the clinical AD continuum. These random-access assays could aid in streamlining clinical decision-making.</p>
Session	Theme A: $\beta$ -Amyloid Diseases / A04.h. Imaging, Biomarkers, Diagnostics: CSF- and blood-based biomarkers (SHIFT 02-431)