

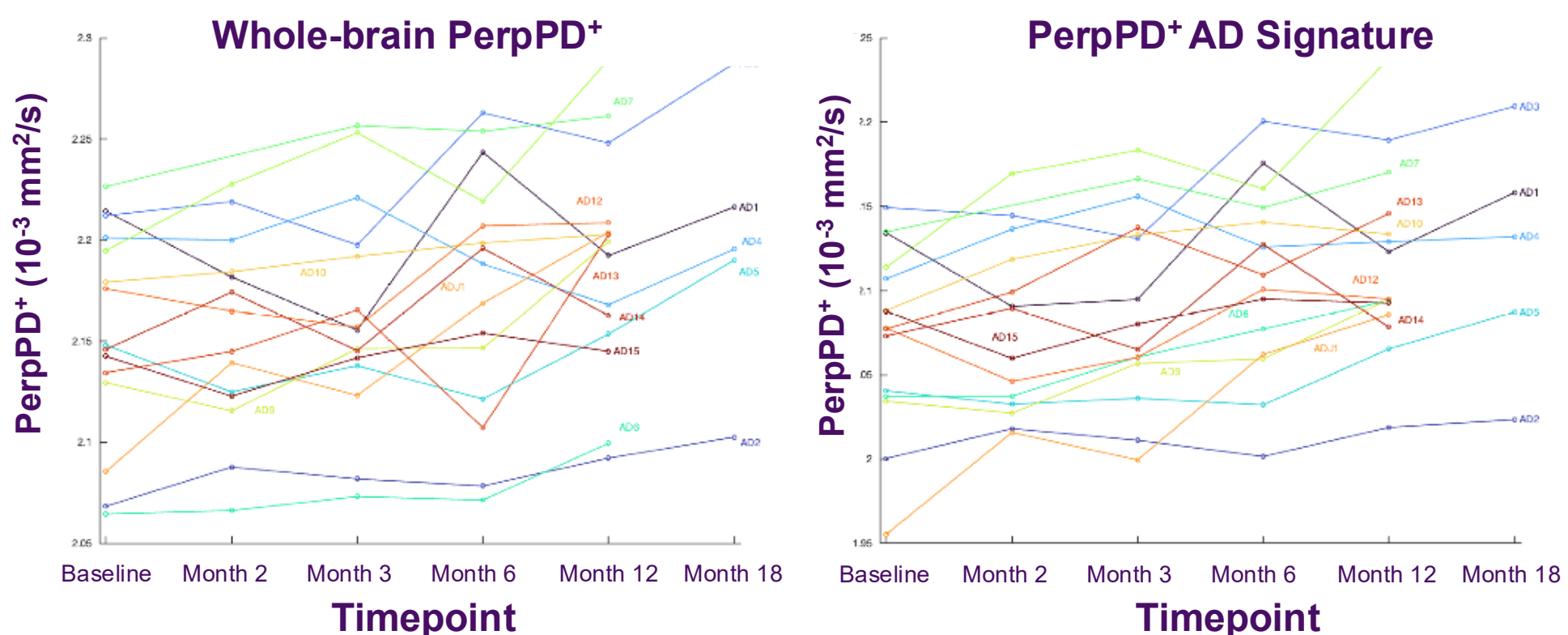
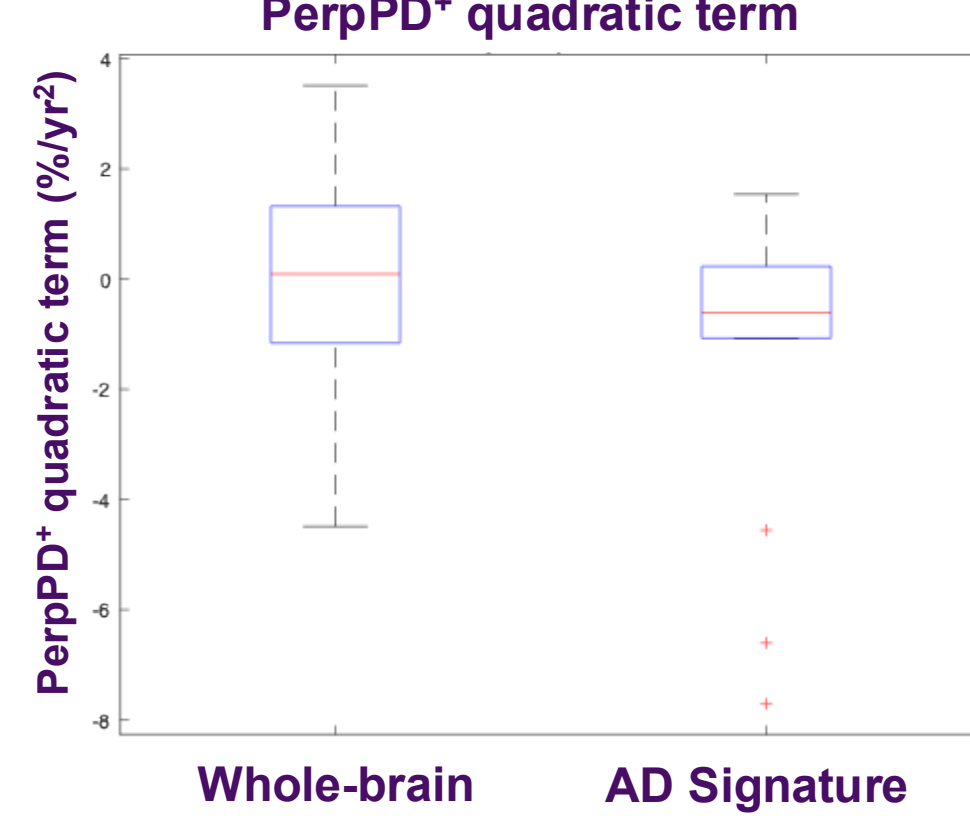
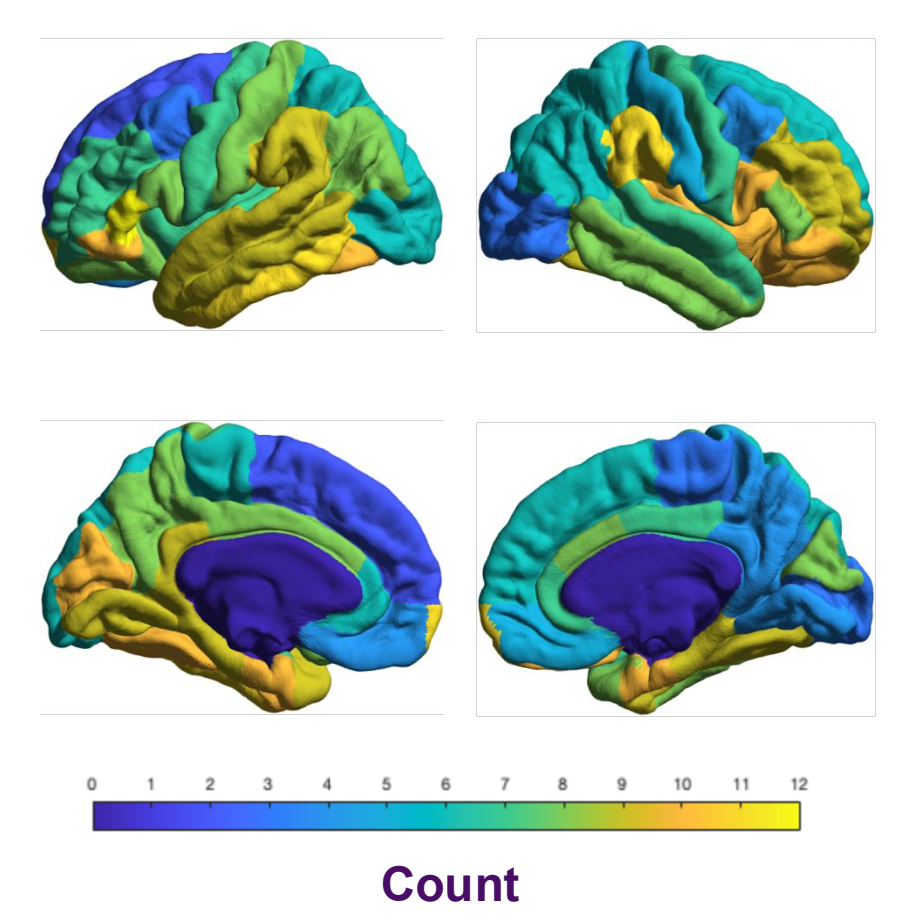
Apparent Deceleration of Microstructural Neurodegeneration in a Real-World Study of AD Patients Treated with Lecanemab

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Preliminary analysis of a diffusion MRI measure of cortical microstructure in real-world longitudinal data from Lecanemab-treated AD patients shows a tendency for apparent within-subject deceleration, consistent with a treatment benefit slowing neurodegeneration

INTRODUCTION		RESULTS		REFERENCES
The amyloid-beta immunotherapy Lecanemab was associated with a 27% slowing of CDR-SB progression (van Dyck et al., 2023), but exhibited accelerated brain volume loss (Alves et al., 2023). It has been noted (Belder et al., 2024) that the hippocampi were relatively spared despite being strongly associated with atrophy in untreated AD, and it might be hypothesised that ‘pseudo-atrophy’ would be spatially distributed, with treatment-related benefit more localised in AD-specific regions. We explore this hypothesis using a diffusion-MRI-derived measure of cortical microstructural integrity or disarray.		Fig.1 - Longitudinal trajectories of n=15 cases treated with Lecanemab, for microstructural PerpPD⁺ over whole-brain and AD Signature meta-region  Fig.2 - Box-plot of longitudinal quadratic terms (percentages of baseline values)  Fig.3 - Regional count of subjects with negative quadratic term for PerpPD⁺ 		1- van Dyck CH et al., Lecanemab in Early Alzheimer's Disease. N Engl J Med. 2023 Jan 5;388(1):9-21. . 2- Alves F et al., Accelerated Brain Volume Loss Caused by Anti-β-Amyloid Drugs: A Systematic Review and Meta-analysis. Neurology. 2023 May 16;100(20):e2114-e2124. 3- Belder CRS, et al., Brain volume change following anti-amyloid β immunotherapy for Alzheimer's disease: amyloid-removal-related pseudo-atrophy. Lancet Neurol. 2024 Oct;23(10):1025-1034. 4- Torso M, et al., In Vivo Detection of Changes Related to Cortical Columnar Organization and Neuroinflammation Across the AD Continuum. J Prev Alzheimers Dis. 2022;9(4):769-779. 5- Torso M, et al., Predicting progression from MCI to dementia using cortical disarray measurement from diffusion MRI. Alzheimers Dement. 2025 May;21(5):e70310.
METHODS		CONCLUSIONS		CONTACT
This real-world study (jRCT1031240123) recruited patients seeking disease-modifying therapy at NHO Niigata National Hospital between January 2024 and November 2025. 15 patients (13 with baseline CDR=0.5, 2 with CDR=1) had more than three time-points at the time of analysis (one with four, nine with five, and 5 with six: baseline, 2m, 3m, 6m, 12m and 18m). All participants underwent MRI including 32-direction diffusion tensor imaging and 3D T1-weighted imaging. A cortical microstructural measure, PerpPD⁺, was calculated (Torso et al., 2022), across Desikan-Killiany regions, an AD Signature meta-region (Torso et al., 2025), and over the whole-brain. Simple quadratic regression models were fitted within-subject, and the quadratic term (positive for acceleration and negative for deceleration) was extracted for cross-subject analysis.		This preliminary analysis of a microstructural measure of cortical neurodegeneration shows a tendency for apparent deceleration in regions commonly affected by neurodegeneration, potentially consistent with a hypothesised spatial separation of pseudo-atrophy and treatment-related slowing of neurodegeneration.		  ged@oxbraindx.com ged.ridgway@oxfordbraindiagnostics.com 