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BIOMARKERS

POSTER PRESENTATION

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Quantitative analysis of 6,150 real-world amyloid Positron Emission Tomography (PET) scans from the Imaging Dementia–Evidence for Amyloid Scanning (IDEAS) study

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Abstract

Background: Amyloid-PET had been widely used and validated in research settings, using highly selected samples, harmonized acquisition protocols, co-registration with MRI, and central interpretation by highly experienced experts. In contrast, in clinical settings, more heterogeneous acquisition, reconstruction, and interpretation may compromise the accuracy of the imaging. We quantitatively analyzed real-world amyloid-PET scans to assess their validity.

Method: IDEAS acquired 18,295 amyloid PET scans at 343 PET facilities in patients with MCI or dementia using ^{18}F-florbetapir, ^{18}F-florbetaben, or ^{18}F-flutemetamol. Scans were visually interpreted at each site as either negative or positive for cortical tracer retention. Scans from consenting patients were archived. As of December 1, 2021, amyloid-PET scans from 6,263 unique participants were available for analysis. Exclusion for lack of valid images or clinical data and failure of quality checks resulted in 6,150 (98.2%) valid scans. We analyzed the scans using a recently validated PET-only processing pipeline designed to process heterogeneous amyloid-PET scans (Iaccarino et al, 2022) and quantified cortical uptake in Centiloid (CL) units. A previously established neuropathology-based threshold of 24.4 CL was used to define amyloid-PET positivity independent of visual reads.

Result: Mean CL was higher in dementia (mean±SD = 53±51) than in MCI (40±48) (mean difference: 13; 95%CI: 10-15). Mean CL of visually negative scans (3±27) was very close to 0, as expected for patients without amyloid accumulation, and significantly lower than visually positive scans (72±41) (mean difference: 69; 95%CI: 67-70) (table 1). High concordance was found between local visual reads and CL-based positivity (86.5%, Cohen's κ=0.72, figure 1). CL exhibited a bimodal distribution, with most scans clearly positive or negative, and a minority of visual-quantitative discordant scans surrounding the positivity threshold (figure 2). CL negatively correlated with MMSE (r=-0.19, p<.001, figure 3). CL further correlated with the level of confidence

in the diagnosis of Alzheimer's Disease (AD), as was indicated by clinicians before the performance of PET (r=0.13, p<.001, figure 4).

Conclusion: A large heterogeneous dataset of real-world amyloid-PET scans analyzed quantitatively, shows high concordance with visual reads, and expected relationships with clinical and neuropsychological measures of AD.

	All	MCI	Dementia	Effect size
n (% of all)	6,150	3,858 (63%)	2,292 (37%)	
Age - mean (SD)	75.7 (6.3)	75.1 (6.0)	76.6 (6.6)	**0.24*** **
Male (%)	3016 (49%)	1911 (50%)	1105 (48%)	0.01
MMSE - mean (SD)	24.7 (4.8)	26.7 (2.9)	21.3 (5.4)	**1.35*** **
Centiloids - mean (SD)	44.6 (49.2)	39.9 (47.7)	52.5 (50.7)	**0.26*** **
FBP/FBB/FLUTE	3,996/1,774/380	2,448/1,162/248	1,548/612/132	0.04
Visually positive (%)[#]	3,739 (60.8%)	2,132 (55.3%)	1,607 (70.1%)	**0.15*** **
Quantitatively positive (%)[&]	3,649 (59.3%)	2,095 (54.3%)	1,554 (67.8%)	**0.19*** **

Table 1: Patient and scan characteristics.
FBP=Florbetapir; FBB=Florbetaben; FLUTE=Flutemetamol
*** = p<0.001 Bonferroni-corrected for multiple comparisons. Effect size is Cohen's d for continuous and Cramer's V for discrete variables.
[#] For 2 patients with MCI and 1 with dementia, results of visual reads were not available.
[&] Centiloids > 24.4

	Visual -	Visual +	Total
Quantitative - (<24.4 CL)	2,039	460	2,499
Quantitative + (>24.4 CL)	369	3,279	3,648
Total	2,408	3,739	6,147

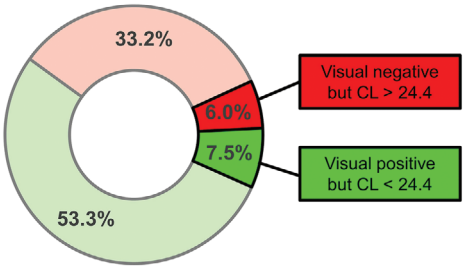

Figure 1: Concordance of local visual reads with centiloid quantification (24.4 positivity threshold).
Concordance = 86.5%; Cohen's κ = 0.72 (0.70 - 0.74); CL = centiloids.

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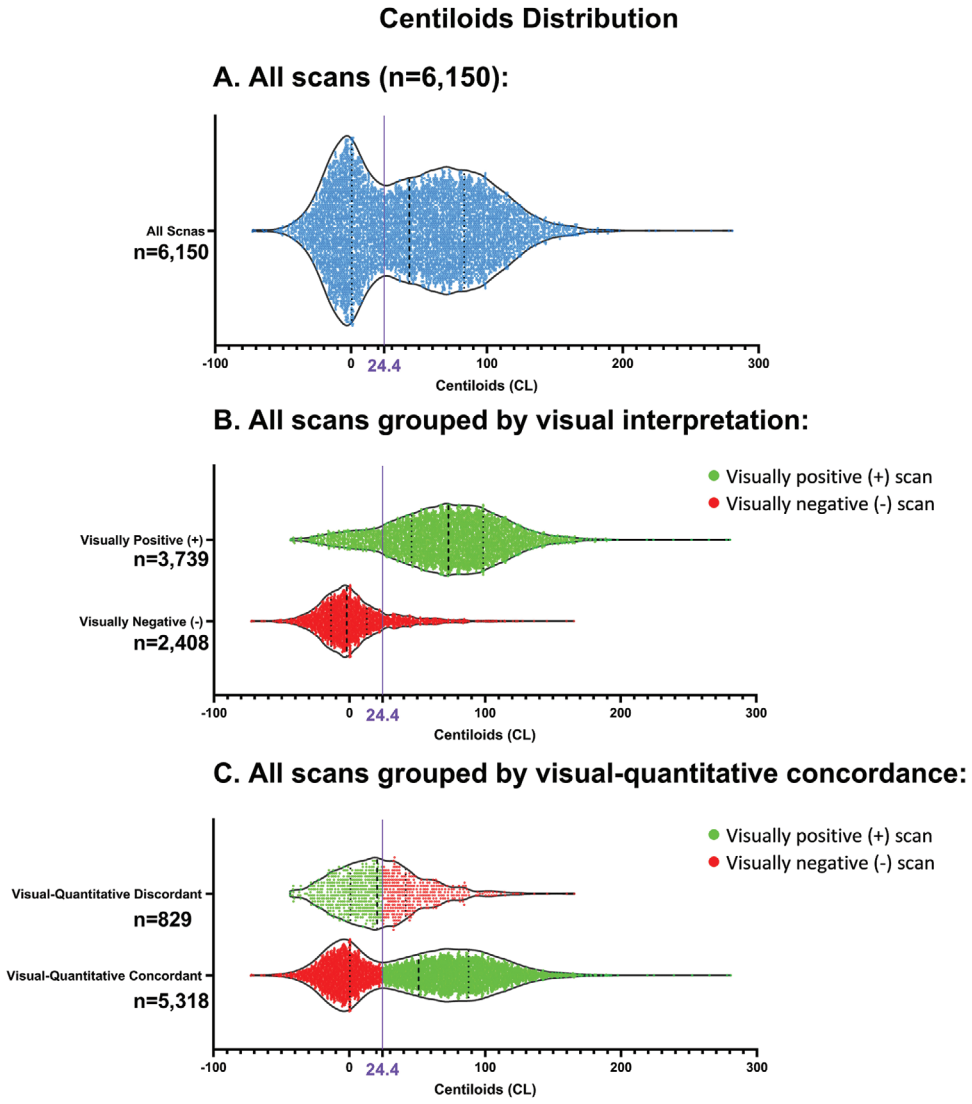

Figure 2: Violin plots displaying Centiloids (CL) distribution (n = 6,150). CL exhibited a bimodal distribution, with most scans clearly positive or negative, and a minority of visual-quantitative discordant scans surrounding the CL-based positivity threshold. Mean CL of visually negative scans (3; SD = 27; Panel B) was very close to 0, as expected for patients without amyloid accumulation.

A: All scans; B: All scans grouped into visually positive (top) and negative (bottom); C: All scans grouped into visually-quantitatively discordant (top) and concordant (bottom). In panels B and C, data points of visually positive (+) scans are in green and negative (-) in red. The purple lines indicate the 24.4 CL-based positivity threshold. Black dashed lines indicate medians and quartiles. Three scans for which visual interpretations were not available are displayed in panel A only.

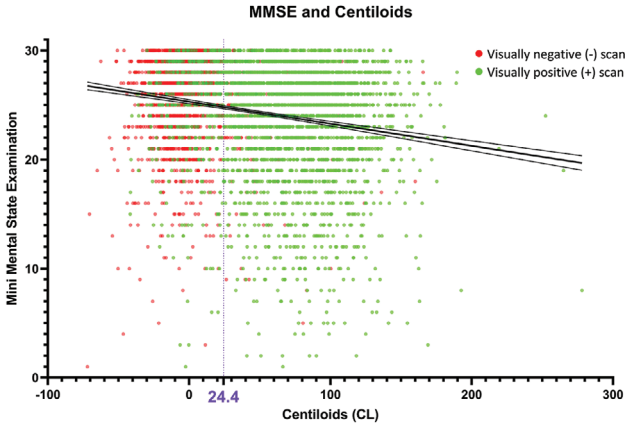

Figure 3: Mini Mental State Examination correlated with Centiloids ($r = -0.19$, $p < 0.001$, $n = 4,817$). Red and green data points indicate visually negative (-) and positive (+) scans, respectively. Curve of best fit and 95% confidence interval are shown in black. Vertical purple line indicates the 24.4 centiloids positivity threshold. For 1 patient visual read was not available (gray dot).

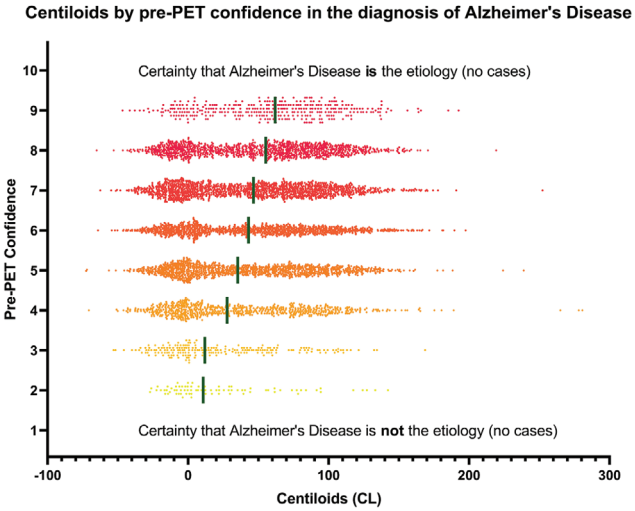

Figure 4: Centiloids (CL) correlated with pre-PET confidence in the diagnosis of Alzheimer's Disease (AD) ($r = 0.13$, $p < .001$, $n = 6,150$). Green lines indicate median CL. Clinicians indicated their level of confidence in the diagnosis of Alzheimer's Disease before the performance of PET, based on clinical presentation. Confidence was expressed on a 1-10 Likert scale, with 1 indicating that AD is certainly not the etiology, and 10 that it certainly is. Because inclusion criteria required that etiology would be uncertain and that AD would be a consideration, no patients received confidence levels of 1 or 10.