Implementing robust amyloid PET quantification in multi-center studies: AMYPAD approach to address data acquisition, processing, interpretation and data sharing challenges

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Abstract: Introduction: Amyloid-positron emission tomography (PET) is pivotal to Alzheimer's management, with the Centiloid standardizing measurements across tracers. AMYPAD trials (Diagnostic and Patient Management Study [DPMS] and Prognostic and Natural History Study [PNHS]) aimed to validate robust quantification in clinical settings. We report our comprehensive approach to amyloid-PET implementation, comprising scan acquisition, harmonization, data storing, and data sharing strategies. Methods: Data from 28 scanners were harmonized using Hoffman phantoms. Three quantification workflows were compared: AmyPype (PET-only), IXICO-LEAP, and the standard Centiloid pipeline (magnetic resonance imaging [MRI]-based). Distributions of Centiloids were assessed using Gaussian Mixture Modeling. Results: Binary quantification showed excellent concordance between pipelines (≥ 96%) and compared to visual reads (>90%). DPMS Centiloids had a bimodal distribution while the PNHS showed a more skewed distribution toward higher Centiloids modeled with three Gaussians (1st Gaussian mean + 2SD = 12 CL, emerging pathology). Discussion: The harmonization framework, providing strong cross-method correlations in AMYPAD, has been adopted by EARL as the Brain PET/CT accreditation standard and provides a practical approach for other multi-center cohorts to implement similar strategies.

22 December 2025 - Alzheimer's & Dementia: Translational Research & Clinical Interventions.

https://doi.org/10.1002/trc2.70190