AI Systems for Accurate Staging and Monitoring of Alzheimer's Disease: The TRACE4AD™ Framework

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Objectives:

Alzheimer's disease (AD) is the most common neurodegenerative disorder worldwide, characterized by beta-amyloid and tau accumulation, leading to cognitive decline and dementia. Early detection and precise staging are crucial. This study evaluates the AI tool TRACE4AD™ for staging, profiling, diagnosis, and prediction of dementia progression, using neuropsychological data, neuroimaging, and biomarkers.

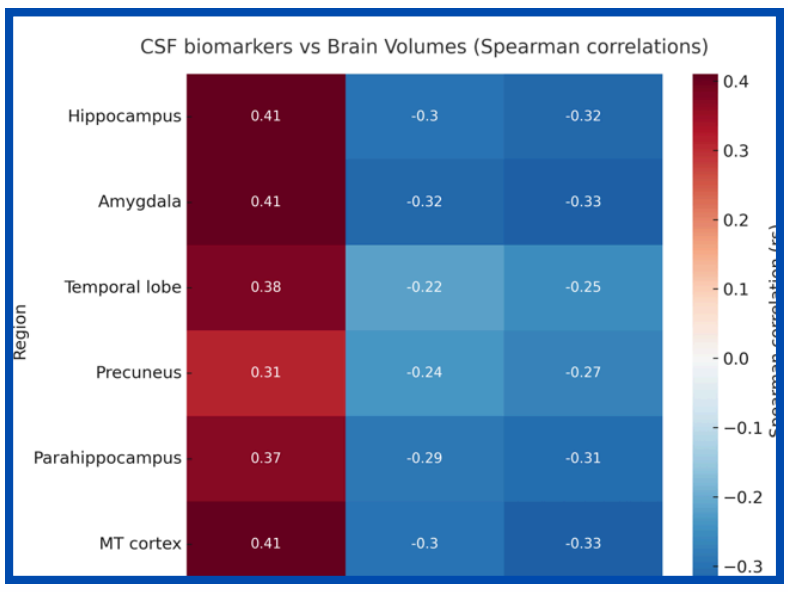
Methods:

797 participants underwent neuropsychological testing and MRI with MP-RAGE 3D T1-weighted scans. CSF biomarkers (Aβ42, t-tau, p-tau) were measured via lumbar puncture using Elecsys immunoassays. PET with [^{18}F]FDG was selectively applied. TRACE4AD™ classified dementia stage, subtype, and 24-month conversion risk, compared to clinical assessments, biomarkers, and follow-up data analyzed in R Studio.

Table 1. description of the sample

		Baseline			24-month follow up			
N. Subjects	Mean±SD	HS	MCI	AD	HS	ncMCI	cMCI	AD
795	73.54±7.52	300	361	134	288	188	116	113

Figure 2. spearman correlation Cerebralspinal Fluid vs brain volumes



Materials:

This observational multicenter study involved 797 participants from 63 ADNI centers in the US/Canada and three Italian centers (CDI Milano, IRCCS Policlinico San Donato, IRCCS Centro Neurolesi Bonino Pulejo). Participants were grouped as cognitively healthy (HS), subjective cognitive impairment (SCI), mild cognitive impairment (MCI), or Alzheimer's dementia (AD). Inclusion required adequate cognitive function, absence of comorbidities, and ability to complete neuropsychological tests, MRI, PET, and CSF analysis.

Results:

Of 797 participants, 426 completed neuropsychological testing and 485 had CSF biomarker analysis. TRACE4AD™ demonstrated high agreement with clinical staging (Cohen's kappa = 0.70–0.90). Notably, 42% of healthy individuals were reclassified as MCI, with 39% testing positive for Alzheimer's biomarkers. Diagnostic accuracy for AD and frontotemporal lobar degeneration (FTLD) was 89.3%. Conversion prediction within 24 months showed 85% accuracy, with 89% sensitivity and 82% specificity. Significant correlations were observed between brain volume loss, CSF biomarkers, and cognitive impairments.

Figure 1. ROC Curves: AI tool predicting conversion at 24-month

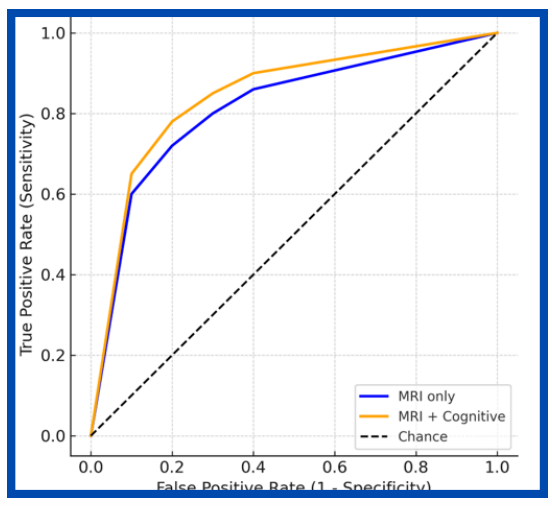


Table 2 Predictive model performance: accuracy, sensitivity, specificity

Condition	Sensitivity	Specificity	Accuracy	ROC-AUC
MRI only (N=705)	79% (95%CI 73-83%)	81% (95%CI 77-84%)	80% (95%CI 77-83%)	0.85 (95%CI 0.82-0.88)
MRI + Cognitive (N=341)	89% (95%CI 82-93%)	82% (95%CI 76-87%)	85% (95%CI 80-88%)	0.83 (95%CI 0.79-0.87)

Discussion

TRACE4AD™ proves to be a reliable decision support tool for AD management, with high accuracy in patient staging and profiling. It strongly correlates with biomarkers and longitudinal clinical data and aids early MCI detection. Comparable AI classifiers using SVM have shown similar effectiveness. TRACE4AD™ competes well with other AI tools like Icobrain and Quantib, providing explainability and robustness. However, variability in dementia subtype classification necessitates clinical oversight and biomarker confirmation.

Conclusions

TRACE4AD™ is an effective clinical tool for early identification, staging, and monitoring of Alzheimer's disease. Integrating MRI and neuropsychological data, it supports accurate assessment following European guidelines and Alzheimer Europe recommendations. Designed for clinicians specializing in cognitive disorders, it facilitates early diagnosis, prognosis, and personalized intervention for patients at risk of Alzheimer's.

Project funded by the Ministry of Economic Development (MISE) – Innovation Agreements (Ministerial Decree 31/12/2021): Project code: F/310019/01/X56

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