

Non-inferiority of Ultra-Fast Wave-CAIPI MRI for Diagnostic Classification Combined with Plasma Biomarkers

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Ultra-fast MRI can support differential diagnosis in a memory clinic with similar discriminative performance to standard imaging.

INTRODUCTION

Background and Motivation:

- In dementia, access to MRI is limited and uneven across regions.
- For dementia diagnosis alone, only 32% of UK brain scans are MRI.¹
- In the US, < 18% of Medicare patients with cognitive symptoms receive MRI.²
- With disease-modifying therapies becoming more widely available, MRI demand is expected to rise, as their use requires multiple MRI scans for safety monitoring (e.g. ARIA surveillance).

The Opportunity:

- Ultra-fast sequences (e.g. Wave-CAIPI³ – acceleration factor x6) may improve access and throughput and are better tolerated by cognitively impaired patients during long scans.

METHODS

Cohort

- Patients referred to a memory clinic for routine investigation of cognitive difficulties (N = 99): normal (n=55), AD (n=26), FTLD (n=11), VCI (n=7).

Median age	60 (range 37-84)
Median MMSE	26.5 (range 8-30)

Imaging & fluid biomarkers

- Paired T1w and FLAIR — standard and ultra-fast (Wave-CAIPI) — acquired in the same session.
- Plasma: Simoa 4-plex (Aβ40, Aβ42, GFAP, NfL) + ALZpath pTau217.
- FreeSurfer, BaMoS, SPM (T1V)

Analysis

- Partial Least Squares Discriminant Analysis (PLS-DA), evaluated with paired cross-validation (10 repeats, 5 folds).
- Performance: balanced accuracy, macro-AUC.
- Feature stability: proportion of the 1,000 bootstrap resamples VIP > 1.

RESULTS

Performance of the two diagnostic pathways:

	Standard (SD)	Ultra-fast (SD)	Ultra-fast – Standard
Balanced accuracy	0.53 (0.02)	0.56 (0.05)	-0.02 [-0.02, 0.11]
Macro-AUC	0.92 (0.01)	0.91 (0.02)	-0.01 [-0.04, 0.01]

Feature rankings were highly correlated:
Spearman $\rho = 0.82$
Substantial feature overlap:
Jaccard similarity coefficient = 0.74

Biomarker	AD vs Normal	FTLD vs Normal	VCI vs Normal	AD vs FTLD	AD vs VCI	FTLD vs VCI
P-Tau217	++++			++++	++++	
Inferior Temporal*	++++	++++	+			+
GFAP	++++	+++	+++	++		
Inferior Parietal*	++++			++++	+	
Deep WMH (3)			++++	++++	++++	
Hippocampal occupancy score	++++	++++	+++			+
Deep WMH (2)			++++	++++	++++	
Frontal WMH			++++	++++	++++	
Insula*		++++	++			
Temporal pole left-right asymmetry*		++++	+++			++

Top features driving differential diagnosis (ultra-fast scan shown; standard scan concordant). *thickness

Feature stability across MRI protocols

Top 25 features

Feature	Standard (x2)	Ultra-fast (x6)
Inferior temporal	1.00	1.00
Plasma GFAP*	1.00	1.00
Plasma p-Tau217*	1.00	1.00
Hippocampal Occupancy Score	1.00	1.00
Inferior parietal	1.00	1.00
Supramarginal	1.00	0.99
Fusiform	0.99	1.00
Middle temporal	1.00	0.99
Plasma NfL	0.99	0.99
Lateral ventricles	0.97	0.98
Entorhinal	0.85	0.84
Banks STS	0.95	0.98
Caudal middle frontal	0.95	0.91
Superior temporal	0.96	0.95
Precuneus	0.96	0.91
Left-right mean thickness asymmetry	0.94	0.86
Insula	0.92	0.94
Isthmus Cingulate	0.74	0.92
Amygdala	0.81	0.91
Temporal pole mean thickness asymmetry	0.47	0.91
Lateral Occipital	0.85	0.85
Pars Opercularis	0.85	0.82
Pars Triangularis	0.85	0.48
Deep WMH (Layer 2)	0.68	0.94
Frontal WMH	0.65	0.54

Standard T1-weighted: 5 min 12 sec

Ultra-fast T1-weighted: 1 min 34 sec

Standard FLAIR: 5 min 32 sec

Ultra-Fast FLAIR: 1 min 59 sec

CONCLUSIONS

- Standard and Ultra-fast MRI showed similar multiclass balanced accuracy and macro-AUC.
- Feature profiles showed strong rank correlation between acquisitions, with substantial overlap in stable MRI and plasma predictors.
- Ultra-fast MRI preserved overall diagnostic information and feature pattern in this paired cohort.

REFERENCES & CONTACT

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