

Longitudinal Multimodal Magnetic Resonance Imaging Analysis of Lecanemab Treatment in Mild Cognitive Impairment: A Pilot Study

Structural, perfusion, and microstructural changes during 12 months of treatment

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Background / Objective

Lecanemab targets soluble amyloid-β protofibrils and reduces amyloid burden in patients with mild cognitive impairment. Its effects on brain volume, cerebral blood flow, and DTI-derived microstructural integrity remain unclear.

Objective: evaluate 12-month changes in brain volume, CBF, FA, MD, cognition, and CSF biomarkers.

Participants / Timeline

n	8	MMSE-J	25.0 ± 2.1
Sex	F/M = 6/2		
Age	71.6 ± 7.0	MoCA-J	19.3 ± 1.3
ApoE	3/3: 5 3/4: 1 4/4: 2	Aβ42/40	0.044 ± 0.008
		p-tau181	91.6 ± 45.0

Biomarker-supported MCI cohort receiving lecanemab every 2 weeks.

Baseline
MRI / cognition / CSF

6 months (6m)
MRI / cognition / CSF

9 months (9m)
MRI / cognition

12 months (12m)
MRI / cognition / CSF

MRI methods

Scanner	3T Siemens Lumina, 32-channel coil
T1w	3D-MPRAGE; 1 × 1 × 2 mm³
pCASL	PLD 2,000 ms; 1.8 × 1.8 × 5 mm³
DTI	30 directions; b = 1,500 s/mm²

- Volume:** FreeSurfer longitudinal processing.
- CBF:** FSL BASIL / oxford_asl.
- DTI:** topup, eddy, dtifit.
- Regions:** whole brain, hippocampus, PCC, precuneus, cingulum (CG), and cingulum (hippocampus).
- Statistics:** Wilcoxon signed-rank tests; uncorrected p-values.

Key findings

Cognition

Neuropsychological scores remained stable, with no significant deterioration.

CSF

Aβ42, Aβ42/40 ratio, and p-tau181 improved at 6 and 12 months.

Volume / CBF

Brain volume declined, while CBF remained stable.

DTI

Whole-brain FA decreased and MD increased; regional FA was relatively preserved.

Regional FA/MD summary — primary analysis

Region	6m	FA 9m	12m	6m	MD 9m	12m
Whole brain	↓	↓	↓	↑	↑	↑
Left hippocampus	—	—	—	↑	↗	↑
Right hippocampus	—	—	↘	↑	↑	↑
Left PCC	—	—	—	↑	—	—
Right PCC	—	—	—	—	—	—
Left precuneus	—	—	—	↑	↑	↗
Right precuneus	—	—	↓	↗	—	—
Cingulum (CG)	—	—	—	—	—	↑
Cingulum (hipp.)	—	—	—	—	—	—

↑ increase ↓ decrease ↗↘ trend — n.s.

Interpretation

CBF remained stable in whole-brain and regional analyses despite volume decline.

Regional MD increased in the hippocampus, left precuneus, and cingulum (CG), whereas FA was relatively preserved.

Inference: longitudinal treatment-period observations, not definitive causality.

Sensitivity analysis

High-MD voxels were excluded within each ROI using a CSF-derived threshold: **0.9 × 95th percentile of MD within a CSF mask**.

Pattern unchanged: only left hippocampal MD at 9 months changed from trend to significant increase.

Regional FA/MD summary — sensitivity analysis

Region	6m	FA 9m	12m	6m	MD 9m	12m
Whole brain	↓	↓	↓	↑	↑	↑
Left hippocampus	—	—	—	↑	↗→↑	↑
Right hippocampus	—	—	↘	↑	↑	↑
Left PCC	—	—	—	↑	—	—
Right PCC	—	—	—	—	—	—
Left precuneus	—	—	—	↑	↑	↗
Right precuneus	—	—	↓	↗	—	—
Cingulum (CG)	—	—	—	—	—	↑
Cingulum (hipp.)	—	—	—	—	—	—

Conclusion

- Cerebral blood flow:** stable
- Brain volume:** declined
- DTI:** mixed microstructural changes
- Partial-volume sensitivity analysis:** main results remained robust
- Implication:** multimodal MRI may help monitor treatment-period brain changes

Limitations

- Small sample size.
- No control group.
- Uncorrected p-values.

Publication note: Based on Takahashi et al., Frontiers in Aging Neuroscience 2025;17:1651596. AAIC update includes partial-volume sensitivity analysis.