

Arterial Spin-labeling MRI at the Cortical-CSF Interface: A Novel Imaging Biomarker in Alzheimer Disease

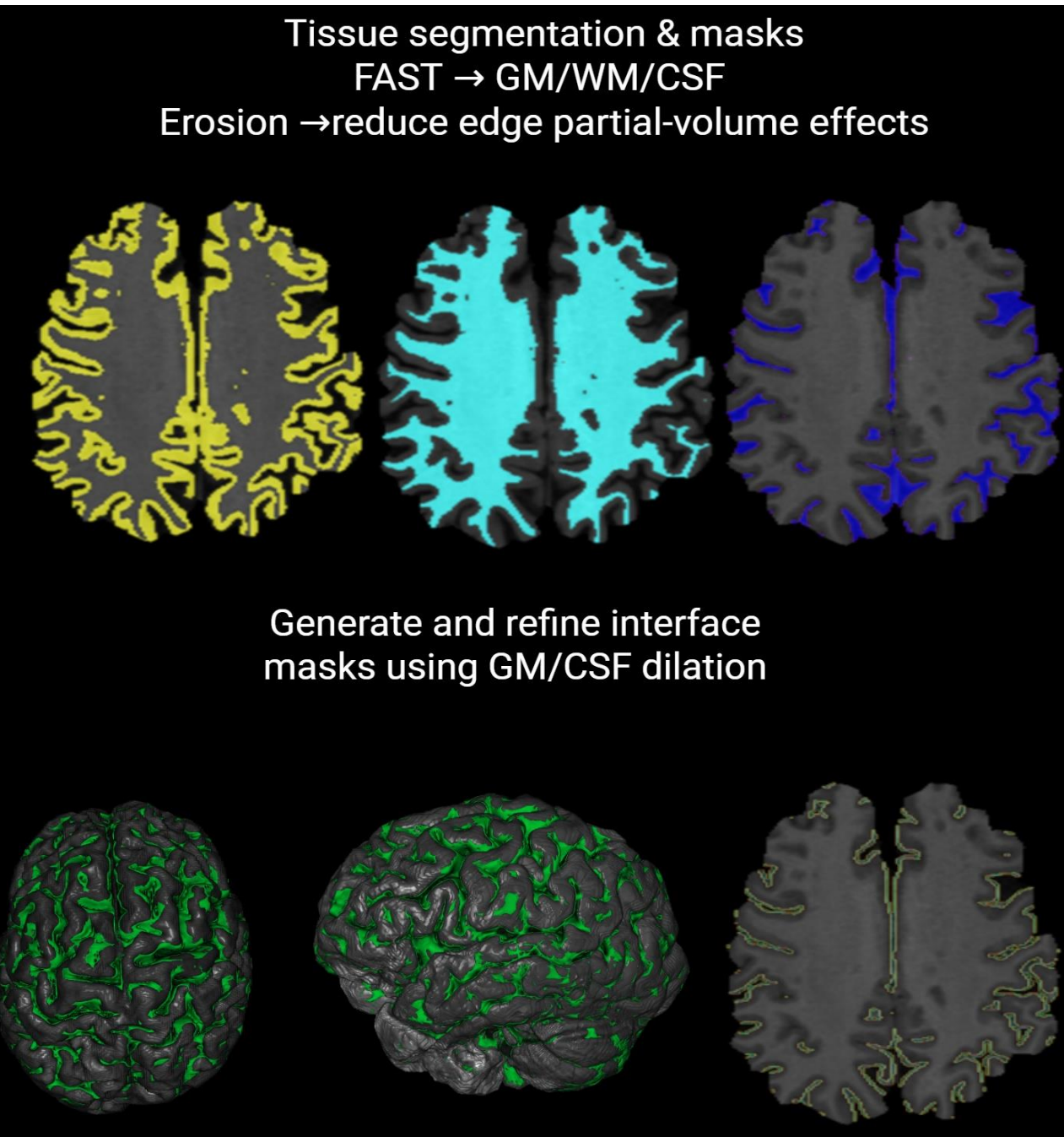
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ASL-derived cortical-CSF interface (IF) perfusion is significantly reduced in Alzheimer disease and provides complementary information beyond conventional cerebral perfusion measurements.

- Impaired cerebrospinal fluid (CSF) dynamics and clearance pathways are increasingly recognized as contributors to Alzheimer disease (AD).
- Arterial spin-labeling (ASL) MRI can detect perfusion signal adjacent to CSF spaces, providing a noninvasive measure of CSF-adjacent water transport physiology.

Objective: To determine whether IF-perfusion differs between patients with AD and cognitively normal controls and evaluate its potential as an imaging biomarker.

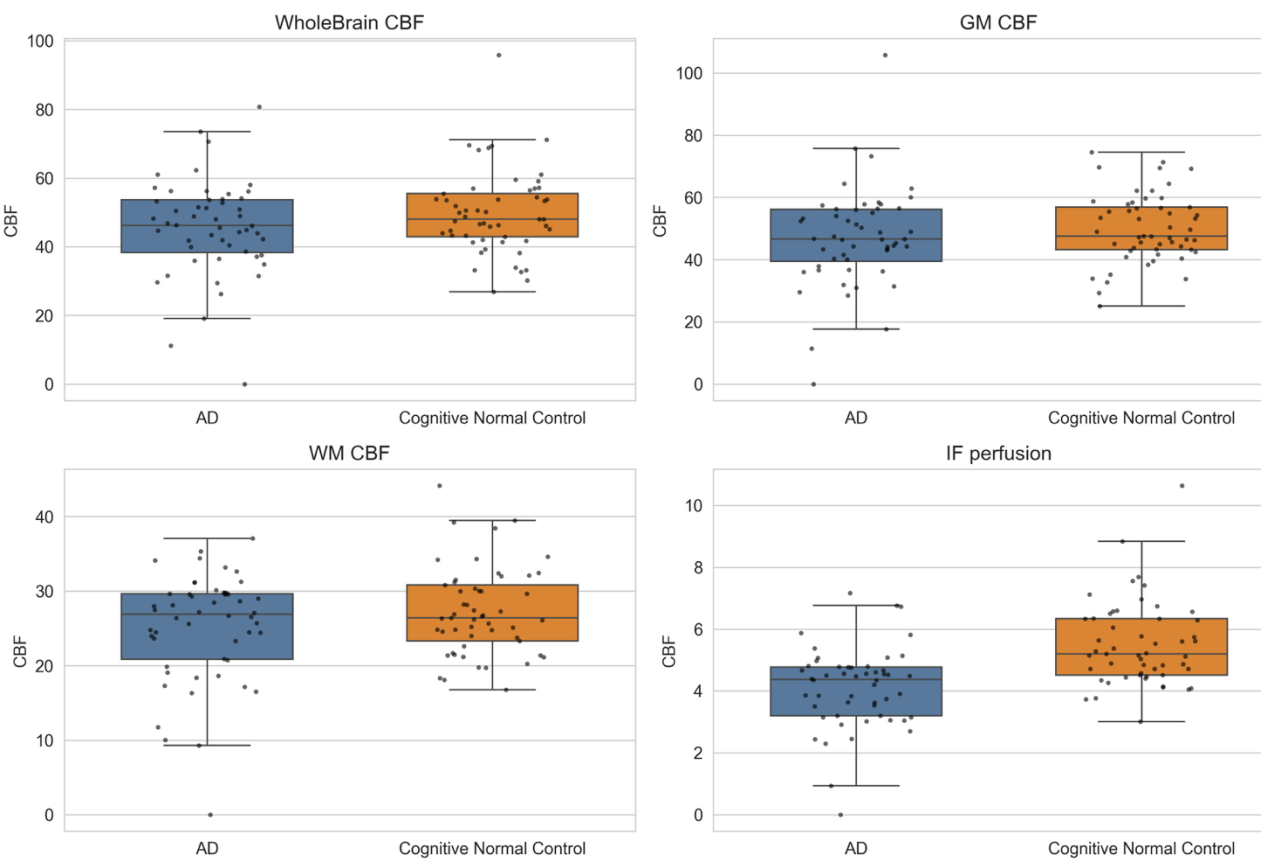


- Retrospective study (Clinical diagnosed AD +age-matched cognitive normal control)
- MRI protocol included multi-delay pseudo-continuous ASL and 3D T1-weighted imaging.

Post-processing pipeline:

- Brain extraction and tissue segmentation
- Partial-volume correction
- Cortical-CSF interface (IF) mask generation
- Registration to CBF space
- Macrovascular signal exclusion
- Global CBF and 12 regional CBF measurements were extracted.
- Group comparisons used Wilcoxon rank-sum tests
- Multivariable regression adjusted for age, sex, scanner vendor, and acquisition site.
- Predictive modeling used LASSO logistic regression with nested repeated cross-validation and SHAP interpretation.

- **104 participants:** 51 AD, 53 control
- Global CBF did not differ between groups.
- Interface masks demonstrated >99% CSF purity with minimal tissue contamination.
- **IF-perfusion was significantly lower in AD** (4.3 vs. 5.2 mL/100 g/min; $p<0.001$).



- IF-perfusion remained independently associated with AD after multivariable adjustment ($\beta = -1.88$, $p = 0.025$).
- ROC analysis for IF-perfusion: **AUC = 0.78**, sensitivity = 71%, specificity = 66%). In the IF-only model, lower IF-perfusion was significantly associated with AD (OR = 0.39, 95% CI: 0.25-0.60, $p < 0.001$).

- IF-perfusion calculated from routinely obtained ASL is significantly reduced in AD in comparison to cognitively normal patients.
- IF-perfusion may represent a promising imaging marker of altered CSF-adjacent water transport physiology.

1. Petitcherc L, et al. *NMR Biomed.* 2023.
2. Petitcherc L, et al. *NeuroImage.* 2021.
3. Jack CR Jr, et al. *Alzheimers Dement.* 2024.
4. Mahammedi A, et al. *AJNR.* 2025.
5. Huang SY, et al. *Alzheimers Dement.* 2024.

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Representative 3D visualization of the cortical-CSF interface (IF) perfusion (mL/100 g/min) overlaid on T1-weighted anatomy in AD and cognitively normal participants.
Surface renderings demonstrate the IF-perfusion mask overlaid on the corresponding T1-weighted brain. The top row (panel A and B) shows an example participant with Alzheimer disease (AD) cohort, and the bottom row (panel C and D) shows an example cognitively normal control. Views are presented from posterior-coronal and sagittal perspectives to illustrate the spatial distribution of the IF along the cortical-CSF interface, with reduced values seen in patient with AD.

