

Uncoupling of Perivascular Water and Ion Transport in Alzheimer's Disease: A Multimodal Tensor Imaging Study

P3-07



Hak Young Rhee¹, Geon-Ho Jahng², Key-Chung Park³

¹Department of Neurology, Kyung Hee University Hospital at Gangdong, Seoul, Republic of Korea

²Department of Radiology, Kyung Hee University Hospital at Gangdong, Seoul, Republic of Korea

³Department of Neurology, Kyung Hee University Hospital, Seoul, Republic of Korea

INTRODUCTION	METHODS	RESULTS	RESULTS	CONCLUSIONS
The Along the Perivascular Space (ALPS) framework is a validated neuroimaging metric that evaluates fluid transport dynamics along the perivascular spaces of medullary veins. This specific region is anatomically critical because the orthogonal arrangement of major white matter tracts minimizes structural interference, allowing for the precise isolation of pure glymphatic clearance signals. The glymphatic system plays a crucial role in AD pathogenesis. Currently, the DTI-ALPS index is the established non-invasive proxy for perivascular health, evaluating proton (water) diffusion along medullary veins Tissue viability critically depends on ionic conductivity—the mobility of essential electrolytes that maintain cellular homeostasis and the brain's electrical infrastructure. Does this distinct biophysical microenvironment follow the same pathological trajectory as water transport in AD?	Conductivity Tensor Imaging (CTI), derived from MREPT, maps high-frequency ion mobility. Yet, a conductivity-based ALPS (CTI-ALPS) has never been explored in neurological conditions. To introduce the novel CTI-ALPS index and evaluate whether this perivascular ion flow metric provides complementary diagnostic information to traditional DTI-ALPS across the AD continuum. This prospective study included 110 older adults (30 cognitively normal, 52 aMCI, and 28 mild-to-moderate AD) who were clinically diagnosed and evaluated using standardized neuropsychological tests. All participants underwent 3.0T MRI, including multi-shell diffusion MRI and multi-echo spin-echo MREPT. To quantify perivascular fluid dynamics, we calculated the DTI-ALPS index using a template-based ROI approach to extract directional diffusivities from the projection and association fibers.	To assess the perivascular ionic microenvironment, we developed the novel CTI-ALPS index. This was achieved by reconstructing high-frequency conductivity maps from MREPT phase data and applying the multi-compartment spherical mean technique (MC-SMT) to isolate the extra-neurite low-frequency conductivity tensor. By substituting the traditional diffusion tensor components with these directional conductivity metrics within the established ALPS framework, we successfully quantified the anisotropy of the electrical microenvironment, enabling a direct comparison between water transport and ion mobility. Group Comparisons DTI-ALPS (Fluid dynamics): significant progressive decrease as disease severity increased. Specifically, DTI-ALPS was significantly lower in the AD group compared to the CN group across multiple b-values (e.g., Left b=2000: P=0.041; Right b=2000: P=0.043).	CTI-ALPS (Ionic homeostasis): Remained relatively stable with no significant differences observed among the CN, aMCI, and AD groups (Left: P=0.317; Right: P=0.155). Correlation with Cognitive Decline DTI-ALPS: significant positive correlations with MMSE scores (e.g., Right b=2000: r=0.257, P=0.007), indicating that impaired perivascular fluid transport aligns closely with worsening cognitive function. CTI-ALPS: Exhibited weaker, non-significant correlations with MMSE scores (Left: P=0.057; Right: P=0.191). Methodological insensitivity: CTI-ALPS is derived through complex compartmental modeling (MC-SMT). Its dynamic range may be narrower than directional water diffusion, meaning subtle shifts in the ionic microenvironment might be obscured by reconstruction constraints or inter-individual variance.	Mathematical cancellation of ionic shifts: AD involves profound, opposing ionic alterations. While Na⁺/K⁺-ATPase failure drives a massive surge in extracellular Na⁺, there is a concurrent depletion of CSF K⁺, Cl⁻, Ca²⁺, and Mg²⁺. Because CTI measures aggregate conductivity, the conductive spike from Na⁺ is mathematically offset by the drop in other ions, resulting in a net-zero change. True preservation of tissue viability: It is highly plausible that while physical perivascular clearance (DTI) is impaired early, the surrounding cellular infrastructure actively compensates to maintain bulk extracellular ionic balance during the mild-to-moderate AD stages. The observed decoupling between impaired perivascular fluid dynamics and ostensibly preserved ionic homeostasis indicates that CTI-ALPS can serve as a complementary biophysical marker to assess residual tissue viability across the AD continuum.