

Interstitial Fluid Volume (ISF Volume)

Definition: 'Interstitial Fluid Volume' refers to the total volume of fluid occupying the 'extracellular space' between cells within a tissue. In the central nervous system (CNS), it is the fluid that lies between neurons, glia, and capillaries—distinct from [cerebrospinal fluid](#) (CSF) and intracellular fluid.

Physiological Role:

- Serves as a medium for:
 1. **Nutrient transport**
 2. **Waste removal**
 3. **Ion exchange**
 4. **Intercellular signaling**
 - Provides mechanical support and maintains the extracellular matrix (ECM) environment.
 - Interfaces dynamically with [CSF](#) through the [glymphatic system](#) and perivascular pathways.
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Brain-Specific Characteristics:

- Estimated to occupy ~15–20% of total brain tissue volume under physiological conditions.
 - Closely regulated by:
 1. Capillary filtration through the [blood-brain barrier](#) (BBB)
 2. Aquaporin-4 channels on astrocytic endfeet
 3. Arterial pulsatility and sleep-wake cycles (via glymphatic function)
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Alterations in ISF Volume: ↑ ISF Volume:

- [Idiopathic normal pressure hydrocephalus](#) (iNPH)
- [Vasogenic edema](#)
- Aging-related extracellular matrix degradation

↓ ISF Volume:

- [Cytotoxic edema](#) (e.g., ischemic stroke)
 - Cellular swelling or inflammation
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Measurement Techniques:

- [Spectral diffusion analysis](#) ($\rightarrow F_{int}$)
 - [Diffusion MRI](#) (indirect estimation via ADC)
 - Tracer-based imaging in experimental models
 - Optical or microdialysis methods in animal studies
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Distinction from Related Terms:

- **Interstitial fluid volume fraction (F_{int}):**

Dimensionless ratio of ISF volume to total tissue volume.

- **CSF volume:** Located in ventricles and subarachnoid space; not part of ISF.
- **Extracellular volume:** Includes ISF + CSF + intravascular space (context-dependent).

— In a retrospective [cohort](#) Ishida *et al.* from the University hospitals—centres in [Tokyo](#), (e.g., Tokyo Metropolitan Geriatric Center) published in the *[Journal of Magnetic Resonance Imaging](#)* to compare [interstitial fluid volume fraction](#) (F_{int}) and [diffusivity](#) (D_{int}), derived via [spectral diffusion analysis](#), between [idiopathic normal pressure hydrocephalus](#) (iNPH) patients and healthy controls (HCs). In iNPH patients, spectral diffusion analysis revealed increased F_{int} and D_{int} in [periventricular hyperintensity](#) (PVH) regions of the [centrum semiovale](#) (CSO) and frontal [white matter](#) (FWM), while regions outside PVH did not differ from HCs ¹⁾.

Critical Review

* Strengths:

- Utilizes advanced spectral diffusion with non-negative least squares to separate [Interstitial Fluid Dynamics](#) an innovative approach.
- Well-defined region-based ROI analysis including CSO, FWM, [lenticular nucleus](#) (LN).
- Robust statistical treatment via Kruskal–Wallis with Dunn’s test; Spearman’s for correlations.

* Limitations & Concerns:

- **Retrospective design:** susceptible to [selection bias](#), especially with mismatched age demographics (mean HC age 47.5 vs iNPH 76.9 years).
- **Age confounders:** ISF measures increase with age; healthy ≥ 60 group is younger on average and unevenly represented, raising questions about matching.
- **Lack of clinical correlation:** imaging findings are intriguing but lack direct linkage to symptom severity or treatment outcome.
- **No intervention arm:** absence of longitudinal or shunt response data means limited clinical applicability.
- **Evidence level 3**, Technical efficacy stage 1: preliminary. Radiological [novelty](#), but early stage with limited validation.

Final Verdict

Score: 5.5 / 10 Spectral [diffusion](#) yields promising [imaging biomarkers](#) for PVH-affected regions in iNPH, but substantial [limitations](#) (age confounders, lack of clinical linkage, [retrospective](#) nature) undermine its current translational value.

Takeaway for Practicing Neurosurgeon

Spectral diffusion analysis identifies increased [interstitial fluid](#) volume and diffusivity in [periventricular hyperintensity](#) regions of elderly iNPH patients. However, due to age confounding and absence of correlation with clinical outcomes or shunt responsiveness, these metrics remain research curiosities rather than clinical tools. Prospective studies—ideally age-matched and linked to gait/cognitive improvement post-shunt—are needed before integrating into practice.

Bottom Line

Spectral diffusion draws attention to altered ISF dynamics in iNPH, yet further longitudinal, clinically-correlated validation is required before adoption.

1)

Ishida S, Yamada S, Oki T, Otani T, Hiratsuka S, Wada S, Mase M, Watanabe Y. Evaluation of [Interstitial Fluid Volume](#) and [Diffusivity](#) in Patients With [Idiopathic Normal Pressure Hydrocephalus](#) Using [Spectral Diffusion Analysis](#). J Magn Reson Imaging. 2025 Jul 4. doi: 10.1002/jmri.29834. Epub ahead of print. PMID: 40614019.

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