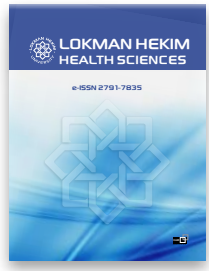
LOKMAN HEKIM HEALTH SCIENCES

DOI: 10.14744/lhhs.2026.03243
Lokman Hekim Health Sci 2026;6(4):739–748

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ORIGINAL ARTICLE

# Glymphatic System Research in Neurosurgery: A Bibliometric and Co-Word Network Analysis (2015–2026)

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## Abstract

**Introduction:** This study characterized the intellectual structure and emerging clinical themes at the intersection of glymphatic research and neurosurgery, with particular attention to the field's movement from a predominantly macroscopic cerebrospinal-fluid framework toward perivascular and parenchymal transport concepts.

**Methods:** Bibliographic metadata for 317 documents indexed in the Web of Science Core Collection from 2015 through the first quarter of 2026 were analyzed with the R-based bibliometrix package. Co-word analysis used Author Keywords after lower-case conversion, whitespace trimming, and exact-string deduplication; semantic, plural, spacing, and hyphen variants were not consolidated. Network centrality and community detection identified influential lexical nodes and thematic clusters. Results involving 2026 were interpreted descriptively because the year was incomplete.

**Results:** The dataset included 317 documents from 171 sources, 2,199 authors, and 10,694 cited references. Three thematic clusters were identified: acute neurosurgical insults and aquaporin-4-related clearance impairment; clinical translation and neuroimaging, including magnetic resonance imaging and diffusion tensor image analysis along the perivascular space (DTI-ALPS); and chronic hydrocephalus-neurodegeneration research linking idiopathic normal pressure hydrocephalus, dementia, and shunt-related management. Because 2026 was incomplete, no complete-period annual growth rate was reported.

**Discussion and Conclusion:** The network maps a research field increasingly integrating perivascular transport with established pressure-volume concepts. DTI-ALPS should be interpreted as a localized, structure-dependent diffusion biomarker rather than a direct measure of whole-brain glymphatic clearance. Proposed applications in surgical selection and outcome prediction require prospective clinical validation.

**Keywords:** Aquaporin 4; Bibliometrics; Diffusion tensor imaging; Glymphatic system; Hydrocephalus, normal pressure; Neurosurgery

Three concepts frame this analysis. The Monro-Kellie doctrine states that, within the rigid cranium, the combined volume of brain parenchyma, cerebrospinal fluid (CSF), and blood is essentially constant; expansion of one component must therefore be offset by reduction of another until compensatory reserve is exhausted and intracranial pressure rises.[1] The glymphatic system describes a perivascular fluid-transport framework in which CSF enters along periarterial spaces, exchanges with interstitial fluid, and drains through perivenous,

***Cite this article as:*** *Şahin ÖS. Glymphatic System Research in Neurosurgery: A Bibliometric and Co-Word Network Analysis (2015–2026). Lokman Hekim Health Sci 2026;6(4):739–748.*

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meningeal-lymphatic, and deep cervical-lymphatic pathways, thereby contributing to solute clearance.[2–4] Aquaporin-4 (AQP4) is a water channel concentrated at astrocytic end-feet that supports CSF-interstitial fluid exchange; altered AQP4 polarization has been associated with traumatic brain injury (TBI), subarachnoid hemorrhage, edema, and neurodegeneration.[3,5]

Clinical neurosurgery and neurocritical care traditionally conceptualize intracranial fluid kinetics and pressure-volume compliance through the Monro-Kellie doctrine.[1] In the classical bulk-flow model, CSF is produced by the choroid plexus, circulates through the ventricular system, and is absorbed through arachnoid granulations. Traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), and hydrocephalus are therefore commonly approached as disorders of pressure, obstruction, or macroscopic CSF circulation.[1] This framework remains clinically fundamental, but it does not by itself explain persistent parenchymal edema, delayed neuroinflammation, or progressive cognitive decline after intracranial pressure or ventricular size has been corrected.[6]

The glymphatic framework adds a parenchymal dimension to intracranial fluid transport. Experimental studies describe CSF entry along periarterial spaces, AQP4-facilitated exchange with interstitial fluid, and movement of solutes toward perivenous and lymphatic drainage pathways.[2,3] This pathway has been linked to the clearance of amyloid-beta, hyperphosphorylated tau, and other extracellular metabolites. The model is still evolving, and the relative contributions of diffusion, convection, vascular pulsatility, sleep, and white-matter microstructure remain under investigation.

In acute neurosurgical insults, secondary injury may extend beyond mass effect or vasospasm. TBI and SAH have been associated with loss of perivascular AQP4 polarization, obstruction of perivascular spaces by blood products, and impaired CSF-interstitial fluid exchange.[5,7] In idiopathic normal pressure hydrocephalus (iNPH), gait disturbance, urinary symptoms, and cognitive decline have also been studied in relation to altered perivascular transport.[8] Non-invasive imaging approaches, particularly the diffusion tensor image analysis along the perivascular space (DTI-ALPS) index and enlarged perivascular-space assessment, have consequently emerged as candidate markers of the local tissue environment.[9,10]

The Monro-Kellie and glymphatic frameworks address different levels of the same intracranial system. The former provides an established clinical model of compartmental volume and pressure, whereas the latter focuses on fluid exchange within and around the parenchyma. Current evidence does not justify replacing one model with the other. A more useful translational question is whether perivascular transport helps explain outcomes that are incompletely predicted by intracranial pressure, ventricular size, or conventional structural imaging. This distinction is important because conceptual novelty should not be mistaken for clinical validation.

Glymphatic concepts have expanded rapidly across neurology, neuroradiology, and neurosurgery since 2015. Descriptive reviews have summarized mechanisms and clinical applications, but the conceptual organization of the neurosurgical literature has not been quantitatively mapped. This study, therefore, used bibliometric and co-word network methods to characterize publication dynamics, influential sources and documents, and the thematic architecture of glymphatic research relevant to neurosurgical practice.

## Materials and Methods

### Data Source and Search Strategy

Bibliographic metadata were retrieved from the Web of Science (WoS) Core Collection (Clarivate Analytics, Philadelphia, PA, USA) during the first quarter of 2026. The analysis covered publications from 2015 through the retrieval period in 2026. The search was treated as a partial-year snapshot, and all analyses involving 2026 were interpreted descriptively. The Topic field was searched using the following Boolean expression:

TS= (["glymphatic system" OR "glymphatic pathway" OR "perivascular space*"] AND ["neurosurg*" OR "subarachnoid hemorrhage" OR "intracranial hemorrhage" OR "traumatic brain injury" OR "hydrocephalus" OR "increased intracranial pressure"]).

### Inclusion and Exclusion Criteria

Records published from 2015 through the first quarter of 2026 were screened for relevance to the intersection of glymphatic pathways and neurosurgical disease. Eligible records included full-length research articles, review articles, early-access records, and other scholarly documents with complete bibliographic metadata and cited-reference information. Letters, editorials, meeting abstracts without complete reference mapping, records labeled as retracted, and incomplete records were excluded. WoS document labels may overlap (for example, an article may also be designated Early Access); therefore, document-type categories were not treated as mutually exclusive, and exact subtype totals are not reported. No language restriction was applied. The 2026 publication count and the

**Table 1.** Baseline bibliometric characteristics of glymphatic system and neurosurgery literature (2015–2026)

| Category | Indicator | Value |
|---|---|---|
| Temporal scale | Analyzed timespan | 2015 through first quarter of 2026 |
| Source dynamics | Total sources | 171 |
| Source dynamics | Total documents | 317 |
| Document age | Mean document age | 3.68 years |
| Citation impact | Mean citations per document | 31.00 |
| Citation impact | Total cited references | 10,694 |
| Conceptual metadata | Keywords Plus | 759 |
| Conceptual metadata | Author Keywords | 770 |
| Collaboration | Total authors | 2,199 |
| Collaboration | Single-authored documents | 5 |
| Collaboration | Mean co-authors per document | 8.55 |
| Collaboration | International co-authorship rate | 26.18% |

Metadata were extracted from the Web of Science Core Collection and analyzed using bibliometrix/biblioshiny. The 2026 observation period was incomplete; therefore, no complete-period annual growth rate is reported.

2024–2026 thematic interval were interpreted descriptively because the final year was incomplete.

### Data Analysis and Visualization

Full records and cited references were exported from WoS in plain-text format. Bibliometric processing and visualization were performed with the R-based bibliometrix package (version 4.0) through the biblioshiny interface within RKWard (version 0.7.5). Descriptive analyses included source distribution according to Bradford's Law, author productivity according to Lotka's Law, global citations, fractionalized authorship, and international collaboration. Annual publication output was inspected descriptively, but a single annual scientific growth rate was not retained in the revised report because the 2026 observation period was incomplete.

Conceptual-structure analysis was based exclusively on Author Keywords (DE). Keywords Plus (ID) were not entered into the co-word matrix; their count is reported descriptively in Table 1. In the original analysis, Author Keywords were converted to lower case, leading and trailing spaces were removed, and exact duplicate strings were standardized. No semantic synonym merging, singular-plural consolidation, spacing harmonization, or hyphen-variant consolidation was applied. Consequently, source variants such as "normal-pressure hydrocephalus" and "normal pressure hydrocephalus" remain separate lexical nodes. A post hoc merge was not undertaken during revision because it would alter the reported network topology without a prespecified thesaurus. The complete Author Keyword preprocessing rules, retained lexical variants, and representative examples are provided in Appendix 1.

A co-occurrence matrix was constructed from the minimally standardized Author Keywords. Betweenness centrality, closeness centrality, and PageRank were calculated to characterize node position, and the Walktrap algorithm was used for community detection. The thematic map categorized clusters by centrality and density. The thematic-evolution analysis compared 2015–2023 with 2024 through the first quarter of 2026; the latter interval is descriptive because it includes an incomplete year.

Betweenness centrality was used to identify keywords that connect otherwise distinct parts of the network, closeness centrality described the relative distance of a node from other nodes, and PageRank estimated prestige according to the importance of connected terms. These metrics were interpreted as properties of the literature network, not as measures of biological importance. Analyses were descriptive; no patient-level data, hypothesis tests, or clinical-effect estimates were generated.

## Results

### Macro-Level Bibliometric Profile

The search yielded 317 documents published across 171 sources, with 10,694 cited references. The dataset included 2,199 authors, a mean of 8.55 authors/document, and an international co-authorship rate of 26.18%. The mean document age was 3.68 years and the mean citation count was 31.00/document. Because the retrieval included only the first quarter of 2026, a complete-period annual scientific growth rate was not reported. Baseline characteristics are presented in Table 1.

**Table 2.** Top 10 globally cited landmark documents

| Rank | Seminal study | DOI | Total citations | Normalized citation score |
|---|---|---|---|---|
| 1 | Jessen, 2015, Neurochem Res | 10.1007/s11064-015-1581-6 | 1,552 | 7.34 |
| 2 | Ringstad, 2017, Brain | 10.1093/brain/awx191 | 566 | 4.28 |
| 3 | Plog, 2015, J Neurosci | 10.1523/JNEUROSCI.3742-14.2015 | 421 | 1.99 |
| 4 | Dichgans, 2017, Circ Res | 10.1161/CIRCRESAHA.116.308426 | 410 | 3.10 |
| 5 | Ringstad, 2018, JCI Insight | 10.1172/jci.insight.121537 | 400 | 6.34 |
| 6 | Lee, 2015, J Neurosci | 10.1523/JNEUROSCI.1625-15.2015 | 329 | 1.55 |
| 7 | Simon, 2016, BBA-Mol Basis Dis | 10.1016/j.bbadis.2015.10.014 | 261 | 3.69 |
| 8 | Mortensen, 2019, J Neurosci | 10.1523/JNEUROSCI.1974-18.2019 | 209 | 3.55 |
| 9 | Schain, 2017, J Neurosci | 10.1523/JNEUROSCI.3390-16.2017 | 195 | 1.47 |
| 10 | Eide, 2019, J Cereb Blood Flow Metab | 10.1177/0271678X18760974 | 185 | 3.14 |

Citation metrics were derived from Web of Science. Normalized citation score is interpreted relative to publication year and disciplinary cohort.

Only five documents were single-authored, indicating that the field is predominantly collaborative. The combination of a relatively young mean document age and a high mean citation count suggests rapid uptake of foundational work, although citation accumulation is uneven and favors early mechanistic and imaging studies. The international co-authorship rate of 26.18% also indicates that most documents were produced within national or institutional networks rather than large cross-border consortia.

## Bradford's Law and Productive Sources

Bradford's Law identified a core zone of 10 journals containing 85 documents (26.81% of the dataset). Frontiers in Neurology (n=13), Fluids and Barriers of the central nervous system (n=12), and Neurology (n=11) were the most productive sources. Journal of Neurotrauma (n=10) and World Neurosurgery (n=7) demonstrate the presence of glymphatic research within clinically oriented neurosurgical literature. The complete distribution of the 10 most productive sources is presented in Appendix 2.

The core zone spans neurology, neurotrauma, vascular neurology, neuroscience, and neurosurgery rather than a single specialty. This dispersion is consistent with the interdisciplinary character of glymphatic research and may also explain why clinically relevant evidence is distributed across journals with different methodological traditions and readerships.

## Productive Authors and Fractionalized Contributions

Eide PK (13 documents) and Ringstad G (12 documents) had the highest publication counts, followed by Li J and Nedergaard M (8 documents each). Fractionalized publication scores were 4.15 for Eide PK and 3.15 for Ringstad G, indicating substantial individual contribution within their publication networks. In contrast, Li J had a fractionalized score of 0.91 despite eight documents, reflecting participation in larger collaborative teams. Detailed productivity and fractionalized authorship indicators for the 10 most productive authors are presented in Appendix 3.

## Global Citation Structure

Jessen et al.[11] was the most globally cited document, with 1,552 citations and an annual average of 129.30. Clinical magnetic resonance imaging (MRI) studies by Ringstad et al.[12] in Brain and JCI Insight[13] received 566 and 400 citations, respectively; the latter had the highest normalized citation score (6.34). Other highly cited documents included experimental work on post-traumatic transport impairment by Plog et al.[14] and vascular cognitive impairment by Dichgans and Leys.[15] The top-10 cited documents are listed in Table 2.

The citation structure was dominated by a small group of foundational mechanistic reviews and human tracer-imaging studies. This pattern indicates that the intellectual backbone of the field continues to depend on early descriptions of the pathway and on a limited number of translational MRI cohorts. Citation rank should nevertheless be interpreted cautiously because older publications have had more time to accumulate citations and may receive attention for controversy as well as confirmation.

## Co-Word Network and Thematic Structure

The Author Keyword co-occurrence network is separated into three thematic communities (Fig. 1). Betweenness

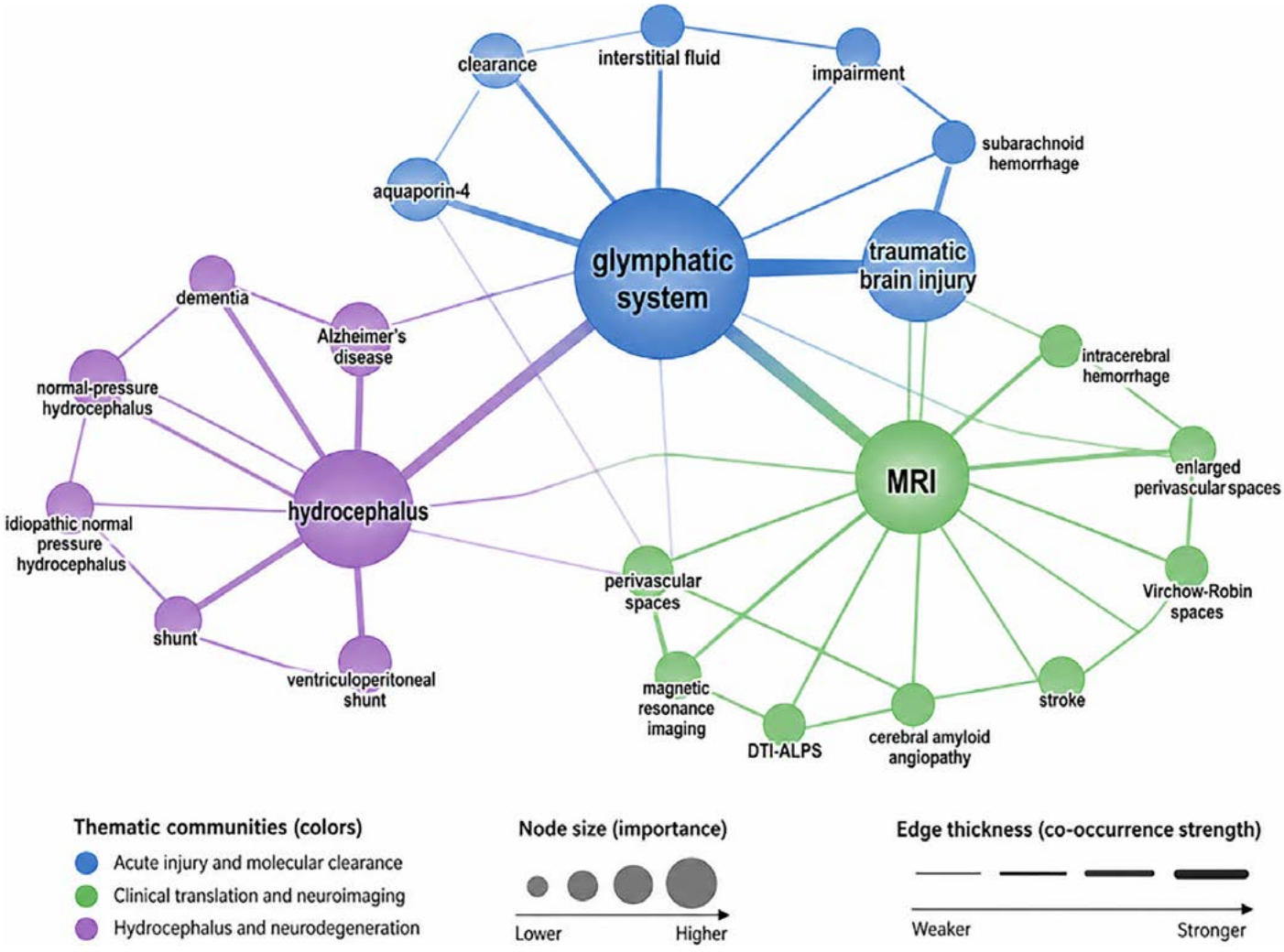


**Figure 1.** Author-keyword co-occurrence network of glymphatic research relevant to neurosurgery from 2015 through the first quarter of 2026. Node size represents PageRank, edge thickness indicates co-occurrence strength, and node colors denote communities identified using the Walktrap algorithm. The network comprises three principal thematic communities: acute injury and molecular clearance; clinical translation, neuroimaging, and perivascular spaces; and chronic hydrocephalus and neurodegeneration. Only lower-case conversion, whitespace trimming, and exact-string deduplication were applied. Consequently, semantically related spelling, spacing, singular–plural, and hyphenation variants remain represented as separate lexical nodes.

centrality, closeness centrality, and PageRank values for the principal nodes are presented in Table 3. Node distance represents relative conceptual proximity, whereas edges indicate keyword co-occurrence. Because only exact-string standardization was applied, centrality values represent the displayed lexical nodes rather than fully harmonized clinical concepts.

The central position of the glymphatic system node shows that it connects acute injury, imaging, and chronic disease vocabularies. MRI also acts as an important bridge, whereas the chronic hydrocephalus and dementia nodes form a more clinically focused community. The strategic map complements these node-level measures by distinguishing highly developed themes from broadly connected foundational themes.

### *Cluster 1: Acute Injury and Molecular Clearance*

The "glymphatic system" node had the highest betweenness centrality (255.13) and PageRank (0.0935), functioning as the principal bridge in the network. Acute neurosurgical conditions were represented by "traumatic brain injury" (betweenness 44.09; PageRank 0.0390) and "subarachnoid hemorrhage" (betweenness 9.57). Molecular and transport-related nodes included "aquaporin-4," "interstitial fluid," "clearance," and "impairment," linking acute injury with perivascular transport research.[16,17]

### *Cluster 2: Clinical Translation and Neuroimaging*

The second cluster was anchored by "MRI" (betweenness 71.84; PageRank 0.0418) and "perivascular spaces"

**Table 3.** Co-word thematic clusters and representative centrality structure

| Cluster | Representative high-centrality terms | Dominant research axis | Interpretation |
|---|---|---|---|
| Cluster 1 | Glymphatic system; traumatic brain injury; impairment; interstitial fluid; clearance; cerebrospinal fluid; subarachnoid hemorrhage; aquaporin-4 | Acute injury, neurotrauma, AQP4, and molecular clearance | Research linking acute neurosurgical insults with perivascular transport, astrocytic dysfunction, and clearance impairment. |
| Cluster 2 | MRI; perivascular spaces; magnetic resonance imaging; cerebral amyloid angiopathy; stroke; Virchow-Robin spaces; enlarged perivascular spaces; intracerebral hemorrhage | Clinical translation and advanced neuroimaging | Imaging-based translation, including DTI-ALPS and enlarged perivascular spaces as indirect markers of local tissue and small-vessel properties. |
| Cluster 3 | Alzheimer's disease; brain; dementia; normal pressure hydrocephalus; idiopathic normal pressure hydrocephalus; shunt | Chronic hydrocephalus, neurodegeneration, and cognitive decline | Conceptual overlap between chronic clearance-related hypotheses, CSF dynamic disorders, neurodegeneration, and shunt-related research. |

Centrality metrics indicate bibliometric network position, not biological importance or clinical causality. Key reported node values include glymphatic system (betweenness 255.13; PageRank 0.0935), MRI (betweenness 71.84; PageRank 0.0418), traumatic brain injury (betweenness 44.09; PageRank 0.0390), perivascular spaces (betweenness 24.73), and subarachnoid hemorrhage (betweenness 9.57). CSF: Cerebrospinal fluid; DTI-ALPS: Diffusion tensor image analysis along the perivascular space; MRI: Magnetic resonance imaging.

(betweenness 24.73). Additional nodes included "magnetic resonance imaging," "cerebral amyloid angiopathy," "stroke," "Virchow-Robin spaces," "enlarged perivascular spaces," and "intracerebral hemorrhage." DTI-ALPS appeared within this translational imaging axis, reflecting the effort to derive non-invasive markers of perivascular and interstitial fluid-related tissue properties.[9,10,18–20]

### *Cluster 3: Chronic Neurodegeneration and Hydrocephalus*

The third cluster connected "Alzheimer's disease," "dementia," "normal-pressure hydrocephalus," "normal pressure hydrocephalus," and "idiopathic normal pressure hydrocephalus" with treatment-related terms such as "shunt" and "ventriculoperitoneal shunt".[12,21] The strategic thematic map positioned acute injury terms within the motor-theme quadrant, MRI and perivascular-space terms near the niche-motor boundary, and the glymphatic-system and CSF cluster within the basic-theme quadrant (Fig. 2).

## Discussion

### Acute Neurosurgical Insults

The network demonstrates that acute neurotrauma, hemorrhage, AQP4, and clearance concepts form a closely connected research domain. This bibliometric association does not itself establish a biological mechanism; rather, it identifies the concepts that recur together in the literature. Experimental studies provide the mechanistic basis for interpreting these links. TBI has been associated with loss of perivascular AQP4 polarization and impaired transport of injury-related biomarkers.[14,22] Such changes may reduce CSF-interstitial fluid exchange and contribute to retention of cellular debris, extracellular hemoglobin, and inflammatory mediators.

A related pattern has been described after SAH. Blood and degradation products may enter or obstruct cortical perivascular spaces, limiting CSF movement through the parenchyma.[23] Inflammation and altered ependymal or perivascular transport have also been implicated in acquired hydrocephalus.[24,25] These observations broaden the pathophysiological discussion beyond macroscopic CSF obstruction, but they do not displace the Monro-Kellie doctrine or established pressure-management principles. The clinical value of glymphatic-directed monitoring or treatment remains investigational.

For neurosurgical research, the main implication is that pressure control and parenchymal transport may represent complementary targets rather than competing explanations. Experimental models suggest that the timing of AQP4 depolarization, sleep-wake state, vascular pulsatility, anesthesia, and blood-product clearance can modify transport after injury. These factors are rarely measured together in clinical cohorts. Future neurotrauma and SAH studies should therefore align imaging time points with intracranial pressure, edema, perfusion, neurological outcome, and treatment exposure before proposing glymphatic-specific interventions.

### Neuroimaging and DTI-ALPS

The prominence of MRI-related nodes reflects the field's transition from experimental tracer studies toward clinically applicable imaging. Intrathecal contrast-enhanced MRI has demonstrated delayed tracer clearance in iNPH, but its invasive nature limits routine application.[12,21] DTI-ALPS

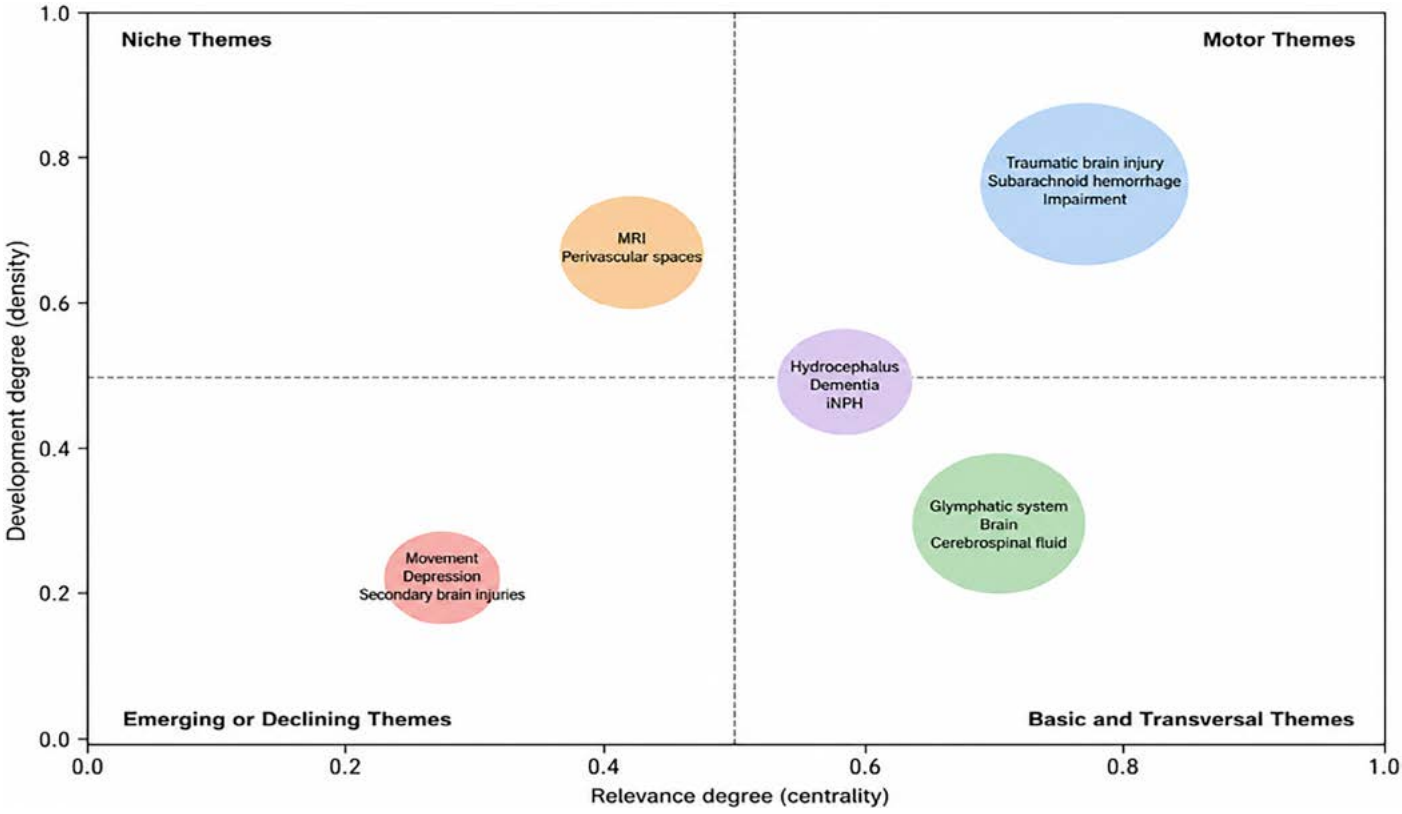


**Figure 2.** Strategic thematic map of glymphatic research relevant to neurosurgery from 2015 through the first quarter of 2026. Author-keyword clusters are positioned according to centrality, representing thematic relevance, and density, representing thematic development. Traumatic brain injury, subarachnoid hemorrhage, and impairment constitute a motor theme. Magnetic resonance imaging and perivascular-space research form a relatively developed but less central niche theme. Glymphatic-system, brain, and cerebrospinal-fluid terms constitute a basic and transversal theme, whereas movement, depression, and secondary brain-injury terms appear as emerging or declining themes. The hydrocephalus, dementia, and idiopathic normal pressure hydrocephalus cluster occupies an intermediate position near the centrality–density boundary, reflecting its transitional role between established clinical relevance and thematic development.

was developed as a non-invasive diffusion-based approach and is calculated as a dimensionless ratio of directional diffusivity components in projection- and association-fiber regions at the level of the lateral ventricular body.[9,18]

DTI-ALPSindex=mean(Dxx,proj,Dxx,assoc)/mean(Dyy,proj, Dzz,assoc)

DTI-ALPS does not directly measure fluid flow or whole-brain glymphatic clearance. It reflects localized directional Brownian motion and is influenced by white-matter architecture, fiber orientation, crossing fibers, extracellular geometry, age, acquisition protocol, and the relative behavior of numerator and denominator diffusivity terms.[9,26,27] It is therefore more appropriately interpreted as a structure-dependent, spatially fixed-point diffusion biomarker of the local tissue environment. A lower index should be reported as a lower DTI-ALPS value rather than automatically labeled as glymphatic failure.

Longitudinal studies have reported changes in DTI-ALPS after tap testing or shunt surgery in iNPH.[10,19] These observations are clinically promising, but they remain associations and do not prove that shunting restores glymphatic flow. Multimodal imaging, standardized acquisition, prespecified clinical outcomes, and prospective validation are required before DTI-ALPS can contribute to surgical indication or outcome prediction. Enlarged perivascular spaces likewise represent a morphological marker associated with small-vessel disease and cerebral amyloid angiopathy, but their meaning is heterogeneous and should not be reduced to a single clearance mechanism.[20]

The ratio structure of DTI-ALPS creates an additional interpretive challenge: an identical index may arise from different combinations of numerator and denominator diffusivity. Between-study comparisons can also be affected by scanner platform, acquisition plane, diffusion directions, echo time, head position, region-of-interest placement, and white-matter lesions. These sources of variation support reporting the constituent diffusivity values and technical protocol alongside the summary index. In multicenter

research, harmonization and test-retest assessment should precede the use of pooled thresholds.

DTI-ALPS may still be valuable when used as one component of a multimodal framework. Convergent assessment could include structural perivascular-space burden, free-water imaging, phase-contrast CSF measures, intrathecal tracer MRI in selected research settings, sleep and vascular variables, and longitudinal clinical outcomes. The key question is not whether a single index represents the entire glymphatic system, but whether a reproducible imaging panel provides incremental information beyond established clinical and radiological predictors.

## Hydrocephalus and Neurodegeneration

The chronic cluster links iNPH, Alzheimer's disease, dementia, and shunt-related management. This pattern reflects an active literature examining whether impaired perivascular transport contributes to overlapping cognitive and gait phenotypes. Tracer MRI studies have demonstrated delayed clearance in iNPH,[12,21] while mechanistic reviews describe possible convergence between hydrocephalus-related hydrodynamic disturbance and neurodegenerative protein accumulation.[25,28,29]

It has been hypothesized that CSF diversion may improve the pressure environment supporting perivascular exchange, and post-operative increases in DTI-ALPS have been reported.[10] However, the present co-word analysis cannot determine whether such imaging changes represent restored glymphatic transport, altered white-matter diffusivity, or both. DTI-ALPS and related measures may eventually complement clinical assessment, tap testing, and established imaging markers, but they should not currently be used as stand-alone criteria for shunt selection or for differentiating iNPH from primary neurodegeneration.

The overlap between iNPH and neurodegenerative disease is clinically important because both may present with cognitive impairment, gait dysfunction, ventriculomegaly, and white-matter change. A biomarker that merely correlates with disease severity may not distinguish reversible hydrodynamic dysfunction from irreversible neurodegeneration. Studies evaluating neurofluid markers should therefore include appropriate disease controls, standardized tap-test or infusion-test protocols, post-operative follow-up, and outcomes that separate gait, cognition, continence, and quality of life.

## Clinical and Research Implications

The network identifies three priorities for the next phase of the field. First, mechanistic studies should connect molecular and perivascular observations to clinically measurable endpoints rather than relying on pathway terminology alone. Second, neuroimaging studies should prioritize reproducibility, transparent preprocessing, and external validation. Third, neurosurgical cohorts should test whether neurofluid markers improve decisions beyond established variables such as symptoms, ventricular morphology, intracranial pressure, CSF drainage response, age, comorbidity, and conventional MRI findings.

For clinical practice, the present results support awareness rather than immediate protocol change. Glymphatic concepts may offer plausible explanations for delayed injury, cognitive decline, and variable response to CSF diversion, but the evidence base is not yet sufficient to define treatment thresholds. The most defensible near-term application is the design of prospective studies in which imaging and biological markers are collected alongside standard neurosurgical assessments. This approach can determine incremental predictive value and reduce the risk of adopting a mechanistically attractive but insufficiently validated biomarker.

For bibliometric research, future analyses should integrate multiple databases, publish a prespecified thesaurus and complete preprocessing log, distinguish Author Keywords from database-generated terms, and conduct sensitivity analyses comparing unmerged and harmonized networks. Dynamic analyses should use complete calendar years or explicitly model partial-year data. These steps would improve reproducibility and clarify whether apparent thematic shifts reflect genuine scientific development or changes in indexing and terminology.

## Limitations and Future Directions

Several limitations require emphasis. First, this study used a single bibliographic database. This improves metadata consistency but may omit relevant records indexed elsewhere. Second, the co-word analysis was based on Author Keywords, which depend on authors' terminology and may underrepresent concepts that appear only in titles or abstracts. Keywords Plus were reported descriptively but were not included in the network. Third, only lower-case conversion, whitespace trimming, and exact-string deduplication were applied; semantic synonyms, plural forms, spacing variants, and hyphen variants were not merged. This preserves the original source vocabulary but fragments concept weight across related lexical nodes and may affect centrality estimates. Fourth, citation indicators favor older publications and do not fully capture the influence of recent studies.

Fifth, the 2026 records covered only the first quarter; therefore, the 2024–2026 thematic-evolution interval is descriptive, and no complete-period annual growth rate is reported. Finally, co-word networks quantify lexical association and the organization of a literature; they do not establish biological causality, diagnostic accuracy, treatment mechanisms, or clinical effectiveness. Mechanistic interpretations in this discussion are derived from cited experimental and clinical studies, not from network centrality itself.

Future research should use prospectively registered, multicenter imaging protocols; harmonized DTI acquisition and region-of-interest placement; multimodal measures of CSF and interstitial-fluid dynamics; and clinically meaningful endpoints. Such studies are necessary to determine whether DTI-ALPS, perivascular-space burden, or other neurofluid markers add value beyond established neurosurgical assessment.

## Conclusion

This bibliometric and co-word analysis maps the intellectual structure of glymphatic research relevant to neurosurgery. The literature is organized around acute injury and AQP4-related transport, clinical translation through MRI-based measures, and chronic hydrocephalus-neurodegeneration research. The findings document a growing research emphasis on perivascular and parenchymal transport that complements, rather than replaces, the Monro-Kellie pressure-volume framework.

DTI-ALPS should be interpreted as a localized, structure-dependent diffusion biomarker, not as a direct measure of whole-brain glymphatic clearance. Its proposed roles in shunt selection, differential diagnosis, and outcome prediction remain hypotheses requiring prospective validation. The network is therefore best understood as a map of research priorities and conceptual relationships, not as evidence of causal mechanisms or established clinical protocols.

**Ethics Committee Approval:** This bibliometric study used published bibliographic metadata and did not involve human participants, animals, or identifiable private information; ethics committee approval was not required. This bibliometric and science-mapping study was based exclusively on published bibliographic metadata retrieved from the Web of Science Core Collection. It did not involve human participants, animals, clinical interventions, biological materials, identifiable personal data, patient records, or sensitive private information. Therefore, ethics committee approval and informed consent were not required.

**Informed Consent:** Not applicable. This study is a bibliometric analysis based on publicly available secondary data and did not involve human participants.

**Conflict of Interest:** The author declares no conflicts of interest related to this work.

**Financial Disclosure:** This study received no specific grant from public, commercial, or non-profit funding agencies.

**Use of AI for Writing Assistance:** Generative artificial intelligence was used solely for language refinement, grammatical editing, and formatting support. It was not used to generate, analyze, or interpret the bibliometric data or to make scientific decisions. The author critically reviewed and verified all scientific content and assumes full responsibility for the accuracy, integrity, and final version of the manuscript.

**Data Availability:** The complete search strategy and analytical procedures are reported in the manuscript. The bibliographic dataset may be shared by the corresponding author subject to Clarivate licensing conditions. The bibliographic metadata analyzed in this study were retrieved from the Web of Science Core Collection. Derived bibliometric outputs and analytical matrices are available from the corresponding author upon reasonable request, subject to Clarivate licensing conditions.

**Peer-review:** Double blind peer-reviewed.

## References

1. Wilson MH. Monro-Kellie 2.0: The dynamic vascular and venous pathophysiological components of intracranial pressure. J Cereb Blood Flow Metab 2016;36(8):1338-50. [CrossRef]
2. Plog BA, Nedergaard M. The glymphatic system in central nervous system health and disease: Past, present, and future. Annu Rev Pathol 2018;13:379-94. [CrossRef]
3. Iliff JJ, Wang M, Liao Y, Plog BA, Peng W, Gundersen GA, et al. A paravascular pathway facilitates CSF flow through the brain parenchyma and the clearance of interstitial solutes, including amyloid-beta. Sci Transl Med 2012;4(147):147ra111. [CrossRef]
4. Da Mesquita S, Fu Z, Kipnis J. The meningeal lymphatic system: A new player in neurophysiology. Neuron. 2018;100(2):375-88. [CrossRef]
5. Yang Z, Li P, Wei J. Perceiving traumatic brain injury from the glymphatic system. Mol Psychiatry 2025;30(11):5546-62. [CrossRef]
6. Treffy RW, Eraky AM, Hussain O, Hedayat HS. Glymphatics for the neurosurgeon. Neurosurg Pract 2023;4(3):e00051. [CrossRef]
7. Gaberel T, Gakuba C, Goulay R, Martinez De Lizarrondo S, Hanouz JL, et al. Impaired glymphatic perfusion after strokes revealed by contrast-enhanced MRI: a new target for fibrinolysis? Stroke 2014;45(10):3092-6. [CrossRef]
8. Eide PK, Lashkarivand A, Hagen-Kersten ÅA, Gjertsen Ø, Nedregaard B, Sletteberg R, et al. Intrathecal contrast-enhanced magnetic resonance imaging of cerebrospinal fluid dynamics and glymphatic enhancement in idiopathic normal pressure hydrocephalus. Front Neurol 2022;13:857328. [CrossRef]

9. Taoka T, Ito R, Nakamichi R, Nakane T, Kawai H, Naganawa S. Diffusion tensor image analysis along the perivascular space (DTI-ALPS): Revisiting the meaning and significance of the method. Magn Reson Med Sci 2024;23(3):268-90. [CrossRef]
10. Yang Y, Yan M, Liu X, Li S, Lin G. Alterations of glymphatic system before and after shunt surgery in patients with idiopathic normal pressure hydrocephalus: a longitudinal study. Eur J Neurol 2025;32(5):e70200. [CrossRef]
11. Jessen NA, Munk ASF, Lundgaard I, Nedergaard M. The glymphatic system: A beginner's guide. Neurochem Res 2015;40(12):2583-99. [CrossRef]
12. Ringstad G, Vatnehol SAS, Eide PK. Glymphatic MRI in idiopathic normal pressure hydrocephalus. Brain 2017;140(10):2691-705. [CrossRef]
13. Ringstad G, Valnes LM, Dale AM, Pripp AH, Vatnehol SS, Emblem KE, et al. Brain-wide glymphatic enhancement and clearance in humans assessed with MRI. JCI Insight 2018;3(13):e121537. [CrossRef]
14. Plog BA, Dashnaw ML, Hitomi E, Peng W, Liao Y, Lou N, et al. Biomarkers of traumatic injury are transported from brain to blood via the glymphatic system. J Neurosci 2015;35(2):518-26. [CrossRef]
15. Dichgans M, Leys D. Vascular Cognitive Impairment. Circ Res 2017;120(3):573-91. [CrossRef]
16. Hou C, Liu Q, Zhang H, Wang W, Wang B, Cui X, et al. Nimodipine attenuates early brain injury by protecting the glymphatic system after subarachnoid hemorrhage in mice. Neurochem Res 2022;47(3):701-12. [CrossRef]
17. Braun M, Sevao M, Keil SA, Gino E, Wang MX, Lee J, et al. Macroscopic changes in aquaporin-4 underlie blast traumatic brain injury-related impairment in glymphatic function. Brain 2024;147(6):2214-29. [CrossRef]
18. Taoka T, Masutani Y, Kawai H, Nakane T, Matsuoka K, Yasuno F, et al. Evaluation of glymphatic system activity with the diffusion MR technique: Diffusion tensor image analysis along the perivascular space (DTI-ALPS) in Alzheimer's disease cases. Jpn J Radiol 2017;35(4):172-8. [CrossRef]
19. Hasegawa S, Yoshimaru D, Hayashi N, Shibukawa S, Takagi M, Murai H. Analyzing the relationship between specific brain structural changes and the diffusion tensor image analysis along the perivascular space index in idiopathic normal pressure hydrocephalus. J Neurol 2024;272(1):56. [CrossRef]
20. Wardlaw JM, Benveniste H, Nedergaard M, Zlokovic BV, Mestre H, Lee H, et al. Perivascular spaces in the brain: Anatomy, physiology and pathology. Nat Rev Neurol 2020;16(3):137-53. [CrossRef]
21. Eide PK, Ringstad G. Delayed clearance of cerebrospinal fluid tracer from entorhinal cortex in idiopathic normal pressure hydrocephalus: A glymphatic magnetic resonance imaging study. J Cereb Blood Flow Metab 2019;39(7):1355-68. [CrossRef]
22. Iliff JJ, Chen MJ, Plog BA, Zeppenfeld DM, Soltero M, Yang L, et al. Impairment of glymphatic pathway function promotes tau pathology after traumatic brain injury. J Neurosci 2014;34(49):16180-93. [CrossRef]
23. Goulay R, Flament J, Gauberti M, Naveau M, Pasquet N, Gakuba C, et al. Subarachnoid hemorrhage severely impairs brain parenchymal cerebrospinal fluid circulation in nonhuman primate. Stroke 2017;48(8):2301-05. [CrossRef]
24. Karimy JK, Reeves BC, Damisah E, Duy PQ, Antwi P, David W, et al. Inflammation in acquired hydrocephalus: Pathogenic mechanisms and therapeutic targets. Nat Rev Neurol 2020;16(5):285296. [CrossRef]
25. Reeves BC, Karimy JK, Kundishora AJ, Mestre H, Cerci HM, Matouk C, et al. Glymphatic system impairment in alzheimer's disease and idiopathic normal pressure hydrocephalus. Trends Mol Med 2020;26(3):285-95. [CrossRef]
26. Ringstad G. Glymphatic imaging: A critical look at the DTI-ALPS index. Neuroradiology 2024;66(2):157-60. [CrossRef]
27. Haller S, Moy L, Anzai Y. Evaluation of diffusion tensor imaging analysis along the perivascular space as a marker of the glymphatic system. Radiology. 2024;310(1):e232899. [CrossRef]
28. Eide PK. Adult hydrocephalus and the glymphatic system. Neurosurg Clin N Am 2025;36(2):127-40. [CrossRef]
29. Nedergaard M, Goldman SA. Glymphatic failure as a final common pathway to dementia. Science 2020;370(6512):50-6. [CrossRef]

**Appendix 1.** Author keyword preprocessing rules, standardization procedures, retained lexical variants, and representative examples

| Processing domain | Rule | Implementation/implication |
|---|---|---|
| **Source field** | Author keywords (DE) only | Keywords plus (ID) were excluded from the co-word matrix. |
| Case normalization | Converted to lower case | Applied before network construction. |
| Whitespace | Leading and trailing spaces removed | Internal spacing variants were not harmonized. |
| Exact duplicates | Exact duplicate strings standardized | Only identical post-normalization strings were consolidated. |
| Semantic synonyms | Not merged | A prespecified semantic thesaurus was not used. |
| Singular/plural variants | Not merged | Variants remained separate lexical nodes. |
| Hyphen variants | Not merged | Example: normal-pressure hydrocephalus vs normal pressure hydrocephalus. |
| Post hoc harmonization | Not undertaken | Avoided alteration of reported topology after analysis. |
| Interpretation | Lexical-node level | Centrality values represent displayed terms, not fully harmonized clinical concepts. |

**Appendix 2.** The 10 most productive sources in glymphatic research relevant to neurosurgery, including publication counts and Bradford core-zone classification

| Rank | Source journal | Article count | Cumulative count | Bradford zone |
|---|---|---|---|---|
| 1 | Frontiers in Neurology | 13 | 13 | Zone 1 |
| 2 | Fluids and barriers of the CNS | 12 | 25 | Zone 1 |
| 3 | Neurology | 11 | 36 | Zone 1 |
| 4 | Journal of Neurotrauma | 10 | 46 | Zone 1 |
| 5 | Experimental Neurology | 7 | 53 | Zone 1 |
| 6 | Scientific Reports | 7 | 60 | Zone 1 |
| 7 | Stroke | 7 | 67 | Zone 1 |
| 8 | World Neurosurgery | 7 | 74 | Zone 1 |
| 9 | Frontiers in Neuroscience | 6 | 80 | Zone 1 |
| 10 | Brain Communications | 5 | 85 | Zone 1 |

The top 10 sources accounted for 85 records (26.81% of the dataset). CNS: Central nervous system

**Appendix 3.** The 10 most productive authors, including total publications and fractionalized authorship scores

| Rank | Author | Total articles | Fractionalized articles |
|---|---|---|---|
| 1 | Eide | 13 | 4.15 |
| 2 | Ringstad | 12 | 3.15 |
| 3 | Li | 8 | 0.91 |
| 4 | Nedergaard | 8 | 1.54 |
| 5 | Jiang | 6 | 0.46 |
| 6 | Werring | 6 | 0.6 |
| 7 | Xia | 6 | 0.79 |
| 8 | Zhang | 6 | 0.54 |
| 9 | Dong | 5 | 0.37 |
| 10 | Greenberg | 5 | 0.43 |

Fractionalized article counts account for the number of co-authors per document.

**Appendices note:** The supplementary tables contain descriptive bibliometric outputs and preprocessing documentation. They do not introduce additional patient-level data, inferential analyses, or clinical-effect estimates beyond those reported in the main manuscript.