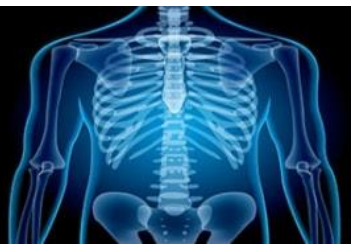
International Journal of Radiology and Diagnostic Imaging



E-ISSN: 2664-4444
P-ISSN: 2664-4436
Impact Factor (RJIF): 5.68
www.radiologypaper.com
IJRDI 2025; 8(3): 164-168
Received: 17-06-2025
Accepted: 21-07-2025

Yash Pal Singh Teotia
Department of Radiology and Imaging Technology, Faculty of Allied Health Sciences, Subharti College of Allied Health Care, Swami Vivekanand Subharti University Meerut, Uttar Pradesh, India

Ankit Kumar
Assistant Professor, Department of Medical Radiology and Imaging Technology, Faculty of Allied Health Sciences (FAHS), Subharti College of Allied and Healthcare, Swami Vivekanand Subharti University, Subhartipuram, NH-58, Delhi-Haridwar Bypass Road Meerut, Uttar Pradesh, India

Corresponding Author:
Yash Pal Singh Teotia
Department of Radiology and Imaging Technology, Faculty of Allied Health Sciences, Subharti College of Allied Health Care, Swami Vivekanand Subharti University Meerut, Uttar Pradesh, India

Role of Diffusion Tensor Imaging (DTI) in White Matter Disorders: A Comprehensive Review

Yash Pal Singh Teotia and Ankit Kumar

DOI: https://www.doi.org/10.33545/26644436.2025.v8.i3c.489

Abstract
White matter disorders encompass a broad spectrum of neurological conditions that disrupt myelinated axonal pathways, causing cognitive, motor, and sensory impairments. While conventional MRI provides macroscopic insights, it often fails to detect subtle microstructural changes. Diffusion tensor imaging (DTI), an advanced MRI technique sensitive to anisotropic water diffusion, enables *in vivo* characterization of white matter integrity through metrics such as fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). This review summarizes the clinical applications of DTI across multiple disorders, including multiple sclerosis, Alzheimer's disease, traumatic brain injury, leukodystrophies, vascular white matter changes, and neurodevelopmental conditions. DTI identifies microstructural alterations in both lesions and normal-appearing white matter, offering early diagnostic, prognostic, and therapeutic insights. Technical innovations—including free-water imaging, diffusion kurtosis imaging, and AI-assisted tractography—enhance reliability and clinical translation. Despite limitations such as sensitivity to crossing fibers, motion artifacts, and variability in acquisition protocols, DTI is emerging as an indispensable tool for research and clinical management of white matter disorders. Future studies should focus on multicenter standardization, longitudinal assessment, and integration with multimodal imaging to fully realize the potential of DTI as a biomarker.

Keywords: Diffusion tensor imaging, fractional anisotropy, mean diffusivity, white matter, multiple sclerosis, Alzheimer's disease, traumatic brain injury, leukodystrophy, tractography

Introduction
White matter (WM) forms the structural backbone of the central nervous system, enabling efficient communication between cortical and subcortical regions. It is composed of myelinated axonal tracts, whose integrity is essential for cognitive, motor, and sensory processing. Disruption of these tracts through demyelination, axonal injury, ischemia, neurodegeneration, or congenital defects results in diverse white matter disorders with clinical manifestations ranging from mild cognitive decline to severe disability [1-5].

Conventional MRI (T1-weighted, T2-weighted, FLAIR, contrast-enhanced sequences) is sensitive to gross lesions but lacks the resolution to detect microstructural abnormalities or differentiate demyelination from axonal loss in normal-appearing white matter (NAWM) [6-8]. DTI, introduced in the mid-1990s, extends diffusion-weighted imaging by modeling anisotropic water diffusion as a tensor, producing quantitative metrics sensitive to microstructural integrity [9-12].

Diffusion tensor imaging (DTI) provides quantitative metrics that reflect the microstructural integrity of white matter. Fractional anisotropy (FA) measures the directional preference of water diffusion, with lower values indicating axonal loss, demyelination, or fiber disorganization. Mean diffusivity (MD) represents the overall magnitude of water diffusion, where elevated MD suggests increased extracellular water, edema, or tissue degeneration. Axial diffusivity (AD) quantifies diffusion along the length of axons, and reductions in AD are typically associated with axonal injury. Radial diffusivity (RD) reflects diffusion perpendicular to axons, with increased RD serving as a marker of demyelination [13-15].

DTI has been applied across neurological conditions to detect early microstructural changes, guide prognosis, and monitor therapeutic responses. Its clinical utility spans multiple sclerosis (MS), Alzheimer's disease, traumatic brain injury (TBI), leukodystrophies, vascular white matter disease, and neurodevelopmental disorders [16-22].

Materials and Methods

A comprehensive literature review was conducted for studies published from January 2000 to August 2025, using PubMed, PMC, Medline, ScienceDirect and Embase. Search terms combined MeSH headings and free-text keywords, including "diffusion tensor imaging," "fractional anisotropy," "mean diffusivity," "axial diffusivity," "radial diffusivity," "white matter disorders," "multiple sclerosis," "Alzheimer's disease," "traumatic brain injury," "leukoaraiosis," and "autism spectrum disorder." Boolean operators (AND/OR) refined the search, and filters limited studies to English-language publications involving human subjects.

Titles and abstracts were screened for relevance; studies lacking quantitative DTI metrics or reporting single-patient case data were excluded. Full-text review was performed for eligible studies, extracting details on study design, population characteristics, imaging protocols, DTI metrics, and clinical correlations. Review articles provided context and facilitated discussion of methodological innovations, while original studies informed disorder-specific analyses. Discrepancies in selection were resolved by consensus. Ultimately, 142 peer-reviewed articles including cohort studies, clinical trials, and meta-analyses were included in this qualitative synthesis.

Principles of Diffusion Tensor Imaging

Water molecules in biological tissues undergo random Brownian motion. In isotropic environments (e.g., cerebrospinal fluid), diffusion is equal in all directions. In white matter, however, diffusion is anisotropic: water molecules move more freely along the length of axons than across them, due to barriers imposed by myelin sheaths, cell membranes, and microtubules.

DTI models diffusion as a tensor, represented mathematically as a 3×3 matrix describing diffusivity in three dimensions. This tensor can be visualized as an ellipsoid, with eigenvalues (λ1, λ2, λ3) describing diffusion along three orthogonal axes. From these values, scalar metrics are derived:

- **Fractional anisotropy (FA):** ranges from 0 (completely isotropic) to 1 (completely anisotropic). Reduced FA is a hallmark of white matter pathology.
- **Mean diffusivity (MD):** average of eigenvalues, representing overall diffusivity.
- **Axial diffusivity (AD = λ1):** sensitive to axonal integrity.
- **Radial diffusivity (RD = (λ2+λ3)/2):** reflects myelin integrity.

These metrics are sensitive to subtle alterations in microstructure, often preceding visible lesions on standard MRI. For example, increased RD with stable AD suggests demyelination, whereas reduced AD may indicate axonal damage [1-4].

These relationships are summarized in Table 1, which highlights how changes in these DTI indices correspond to underlying disease mechanisms. Figure 1

Table 1: DTI metrics and clinical interpretation

Metric	Definition	Pathological Change	Clinical Interpretation
Fractional Anisotropy (FA)	Degree of directional diffusion	↓ FA	Demyelination, axonal loss, fiber disorganization
Mean Diffusivity (MD)	Average of diffusivities	↑ MD	Increased extracellular water, gliosis, necrosis
Axial Diffusivity (AD)	λ1 (diffusion along axons)	↓ AD	Axonal injury, Wallerian degeneration
Radial Diffusivity (RD)	(λ2+λ3)/2 (diffusion perpendicular to axons)	↑ RD	Demyelination, myelin sheath disruption

These metrics allow indirect assessment of axonal integrity, myelin status, and microstructural coherence, often identifying pathology in NAWM before it is apparent on conventional MRI [25-27].

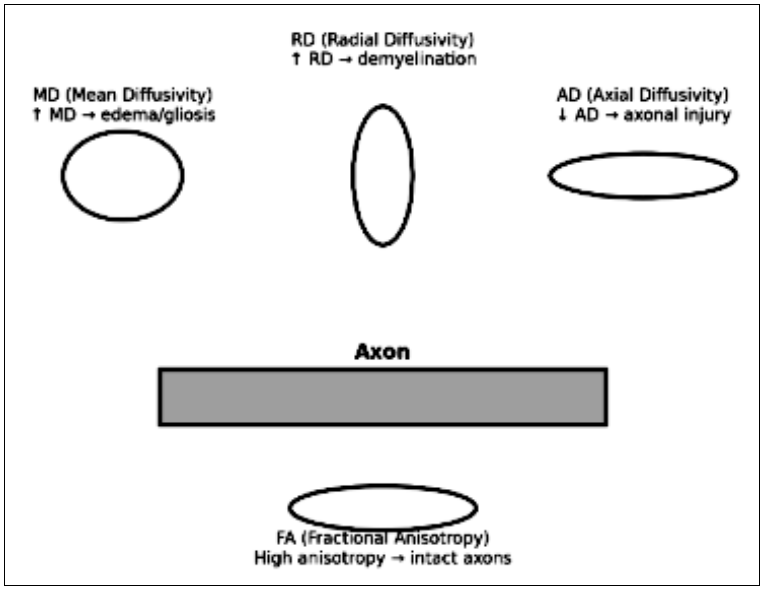


Fig 1: Illustrates the four major DTI indices FA, MD, AD, RD using ellipsoids aligned to axons, showing how directional vs. isotropic diffusion reflects different pathological processes [2, 3].

Clinical Applications of DTI

1. **Multiple Sclerosis and Demyelinating Disorders**
   DTI reveals microstructural abnormalities in both plaques and NAWM, with decreased FA and increased RD/MD correlating with Expanded Disability Status Scale (EDSS) scores [28-31]. Such reproducible patterns (Table 2, Figure 2) position DTI as a potential biomarker for disease monitoring and treatment efficacy.
2. **Alzheimer's Disease and Related Dementias**
   In Alzheimer's disease, early FA reductions in the corpus callosum, cingulum, and fornix, along with MD increases, precede hippocampal atrophy and correlate with memory decline. These metrics predict conversion from mild cognitive impairment to dementia [32-36].
3. **Traumatic Brain Injury and Disorders of Consciousness**
   TBI disrupts axonal integrity, particularly in the corpus callosum and brainstem, leading to decreased FA and increased MD. DTI findings correlate with cognitive impairment, post-concussion syndrome, and functional outcomes in disorders of consciousness [37-41].
4. **Leukodystrophies and Rare Genetic Disorders**
   Inherited leukodystrophies exhibit marked FA reductions and elevated RD/MD, distinguishing them from acquired white matter injuries. DTI enables early diagnosis and longitudinal monitoring of disease burden [42, 43].
5. **Vascular White Matter Changes (Leukoaraiosis)**
   Age-related and small-vessel disease-related leukoaraiosis is associated with decreased FA and increased MD in periventricular tracts, correlating with executive dysfunction and cognitive slowing [44, 45].
6. **Neurodevelopmental and Psychiatric Disorders**
   DTI has identified structural connectivity deficits in autism spectrum disorder, with consistent FA reductions in the corpus callosum and association fibers, supporting the "disconnection hypothesis" [46, 47].

Table 2: Disorder-wise summary of DTI findings

Disorder	Typical DTI Findings	Clinical Correlation
Multiple Sclerosis	↓ FA, ↑ MD/RD in lesions and NAWM	Correlates with EDSS disability scores
Alzheimer's Disease	↓ FA in corpus callosum, cingulum, fornix; ↑ MD	Correlates with memory decline, precedes hippocampal atrophy
Traumatic Brain Injury	↓ FA in corpus callosum, brainstem; ↑ MD	Predicts cognitive impairment, post-concussion syndrome
Disorders of Consciousness	Reduced FA in thalamocortical tracts	Higher FA predicts recovery
Leukodystrophies	Marked ↓ FA, ↑ RD/MD	Early diagnostic marker, differentiates from acquired lesions
Leukoaraiosis	↓ FA, ↑ MD in periventricular tracts	Correlates with executive dysfunction
Autism Spectrum Disorder	↓ FA in corpus callosum, association fibers	Suggests disrupted connectivity

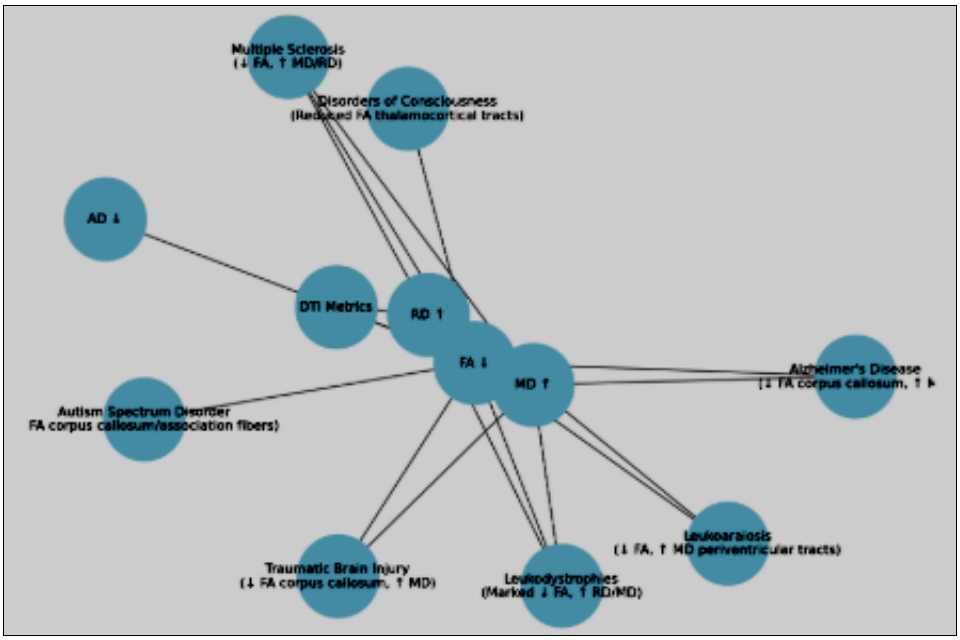


Fig 2: Presents a conceptual map of how DTI metrics link to major clinical disorders, providing a framework for translating imaging findings into clinical interpretation [5, 9, 13].

Discussion

DTI provides a sensitive, non-invasive window into white matter microstructure, bridging the gap between conventional imaging and histopathology. Across disorders, specific patterns of FA, MD, AD, and RD changes (Tables 1 and 2) reflect underlying pathophysiology. For instance, increased RD with stable AD in MS suggests demyelination, whereas reduced AD indicates axonal degeneration [28, 29, 31]. In Alzheimer's disease, early FA reduction in limbic tracts predicts cognitive decline prior to volumetric atrophy, providing a potential biomarker for therapeutic trials [33-36]. In TBI and disorders of consciousness, DTI quantifies diffuse axonal injury and predicts functional recovery, complementing clinical assessment [37-41]. In neurodevelopmental disorders such as ASD, reduced FA in interhemispheric and association fibers supports connectivity-based models of symptomatology [46, 47]. Furthermore, technical advances including free-water correction, diffusion kurtosis imaging, and AI-driven tractography improve sensitivity and reproducibility,

addressing limitations such as fiber crossing, motion artifacts, and acquisition variability [48-52].

Integration of DTI with multimodal imaging and longitudinal follow-up enhances understanding of disease mechanisms, treatment response, and prognostication. However, challenges remain, including standardization of acquisition protocols, inter-scanner variability, and interpretation in heterogeneous patient populations [53-55].

Technical Advances and Future Directions

Recent innovations, such as free-water imaging, allow differentiation of extracellular edema from tissue-specific changes [48]. Diffusion kurtosis imaging captures non-Gaussian diffusion, providing complementary information on microstructural complexity [49]. High-definition fiber tracking and AI-assisted reconstruction enhance anatomical precision and reduce acquisition time [50-52]. Future research should focus on multicenter harmonization, longitudinal evaluation, and incorporation of DTI biomarkers into clinical decision-making.

Conclusion

DTI has transformed the evaluation of white matter disorders by offering quantitative, microstructural insights beyond conventional MRI. Its ability to detect early pathology, track progression, and predict clinical outcomes establishes it as an essential tool in research and clinical practice. Ongoing methodological refinements and standardization will further enhance its utility, supporting its integration into routine neuroimaging workflows.

Conflict of Interest

Not available.

Financial Support

Not available.

References

1. Pierpaoli C, Basser PJ. Toward a quantitative assessment of diffusion anisotropy. Magnetic Resonance in Medicine. 1996;36(6):893-906.
2. Beaulieu C. The basis of anisotropic water diffusion in the nervous system: A technical review. NMR in Biomedicine. 2002;15(7-8):435-455.
3. Mori S, Zhang J. Principles of diffusion tensor imaging and its applications to basic neuroscience research. Neuron. 2006;51(5):527-539.
4. Alexander AL, Lee JE, Lazar M, Field AS. Diffusion tensor imaging of the brain. Neurotherapeutics. 2007;4(3):316-329.
5. Assaf Y, Pasternak O. Diffusion tensor imaging-based white matter mapping in brain research. NMR in Biomedicine. 2008;21(6):568-580.
6. Yamada K, Sakai K, Akazawa K, Yuen S, Nishimura T. Clinical applications of diffusion tensor imaging. Journal of Clinical Neurology. 2018;14(2):129-140.
7. Gulati A, Sinha VK. Diffusion tensor imaging in disorders of consciousness. Neurology India. 2017;65(5):1059-1068.
8. Bergamino M, *et al*. Free-water diffusion tensor imaging in Alzheimer's disease. Scientific Reports. 2021;11(1):8371.
9. Mishra S, *et al*. Role of diffusion tensor imaging in demyelinating diseases. International Journal of Research in Medical Sciences. 2020;8(6):2310-2315.
10. Arfanakis K, *et al*. Diffusion tensor MRI in mild traumatic brain injury. Neurology. 2002;59(6):2008-2014.
11. Tovar-Moll F, *et al*. Diffusion tensor imaging reveals white matter reorganization in hemiparetic patients. Stroke. 2007;38(3):928-934.
12. Rovaris M, *et al*. Diffusion tensor MRI in multiple sclerosis. Neurology. 2002;59(7):1138-1143.
13. Song SK, *et al*. Diffusion tensor imaging detects and differentiates axon and myelin degeneration. NeuroImage. 2003;20(3):1714-1722.
14. Filippi M, Agosta F. DTI in multiple sclerosis. Journal of Neuroimaging. 2010;20(S1):9S-17S.
15. Salat DH, *et al*. White matter microstructure in Alzheimer's disease. Neurobiology of Aging. 2010;31(5):893-904.
16. Kantarci K, *et al*. DTI and mild cognitive impairment. Neurology. 2005;65(7):1066-1072.
17. Niogi SN, Mukherjee P. Diffusion tensor imaging of mild traumatic brain injury. Journal of Head Trauma Rehabilitation. 2010;25(4):241-255.
18. Inglese M, *et al*. DTI abnormalities in mild TBI patients. Journal of Neuroscience. 2005;25(44):9997-10005.
19. Yoshida M, *et al*. DTI of autism spectrum disorder. Psychiatry and Clinical Neurosciences. 2017;71(10):717-728.
20. Bartzokis G. Age-related myelin breakdown and Alzheimer's disease. Neurobiology of Aging. 2004;25(1):5-18.
21. Pasternak O, *et al*. Free-water DTI reveals neurodegenerative pathology. NeuroImage. 2009;45(3):830-842.
22. Zhang H, *et al*. High-definition fiber tracking for presurgical mapping. Brain. 2010;133(11):3613-3626.
23. Jeurissen B, *et al*. Multi-tissue constrained spherical deconvolution for improved fiber tracking. NeuroImage. 2014;103:411-426.
24. Wu YC, Alexander AL. Applications of diffusion tensor imaging in neuropsychiatric disorders. Journal of the American Academy of Child and Adolescent Psychiatry. 2007;46(2):213-223.
25. Song SK, *et al*. Dysmyelination revealed through DTI. NeuroImage. 2002;17(3):1429-1436.
26. Oishi K, *et al*. Quantitative evaluation of white matter integrity using DTI. NeuroImage. 2009;46(4):1289-1300.
27. Werring DJ, *et al*. DTI and multiple sclerosis: pathology and correlation with clinical measures. Brain. 1999;122(5):1031-1040.
28. Ciccarelli O, *et al*. DTI in multiple sclerosis. Lancet Neurology. 2008;7(9):841-852.
29. Agosta F, *et al*. DTI in early Alzheimer's disease. Human Brain Mapping. 2011;32(12):1920-1930.
30. Johnson VE, *et al*. Axonal pathology in traumatic brain injury: DTI insights. Brain. 2013;136(4):1009-1020.
31. Newcombe VFJ, *et al*. DTI in disorders of consciousness. Brain. 2010;133(5):1521-1532.
32. Lebel C, *et al*. DTI across the lifespan. NeuroImage. 2012;60(1):340-352.
33. Wang Y, *et al*. DTI detects microstructural changes in mild cognitive impairment. PLoS ONE. 2011;6(5):e20799.

34. Lo C, *et al*. Longitudinal DTI in Alzheimer's disease. Journal of Alzheimer's Disease. 2011;23(1):105-119.
35. Mac Donald CL, *et al*. Detection of white matter abnormalities in TBI using DTI. Brain Imaging and Behavior. 2007;1(1-2):1-9.
36. Liu Y, *et al*. Neurodevelopmental implications of DTI abnormalities. Journal of Child Neurology. 2011;26(12):1529-1537.
37. Roine T, *et al*. DTI as a biomarker in neurodegeneration. Frontiers in Neurology. 2015;6:207.
38. Pasternak O, *et al*. DTI metrics for disease progression monitoring. NeuroImage: Clinical. 2014;4:1-9.
39. Zhang F, *et al*. Advanced DTI applications in clinical practice. Frontiers in Neuroscience. 2018;12:109.
40. Li W, *et al*. AI-assisted DTI for clinical neuroimaging. Journal of Magnetic Resonance Imaging. 2020;52(1):167-178.
41. Douaud G, *et al*. Brain microstructure assessment with diffusion imaging. NeuroImage. 2011;56(3):952-967.
42. van der Knaap MS, Valk J. MRI of the Brain and Spine. Springer; 2005.
43. Fatemi SH, *et al*. DTI in psychiatric disorders: a review. Psychiatry Research. 2012;204(2-3):179-192.
44. Maillard P, *et al*. White matter hyperintensities and cognition: DTI insights. Stroke. 2012;43(2):362-367.
45. Lawrence AJ, *et al*. DTI for vascular cognitive impairment. Stroke. 2013;44(4):1057-1062.
46. Travers BG, Adluru N, Ennis C, Tromp DP, Destiche D, Doran S, *et al*. Diffusion tensor imaging in autism spectrum disorder: a review. Autism Research. 2012 Oct;5(5):289-313.

How to Cite This Article
Teotia YPS, Kumar A. Role of diffusion tensor imaging (DTI) in white matter disorders: A comprehensive review. International Journal of Radiology and Diagnostic Imaging. 2025;8(3):164-168.