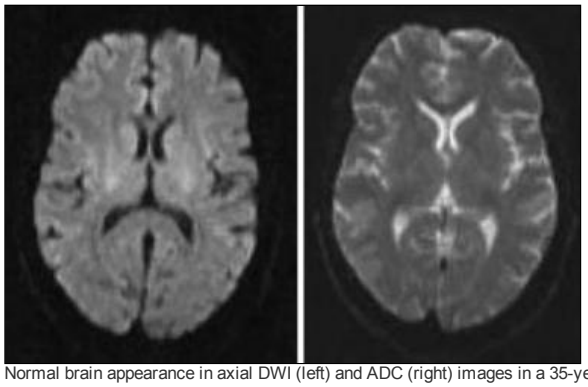
Diffusion Tensor Imaging

- Author: Avneesh Chhabra, MD; Chief Editor: James G Smirniotopoulos, MD more...

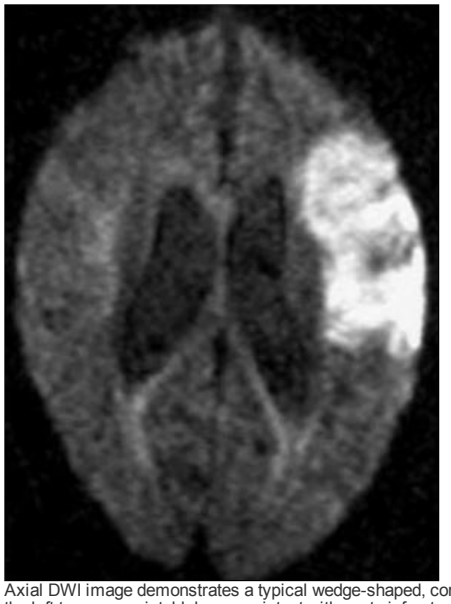
Updated: Apr 07, 2015

Background

Diffusion-weighted imaging (DWI) is a well-established magnetic resonance imaging (MRI) method for diagnosing cerebral ischemia. DWI is a routine protocol in most institutions that perform neuroimaging; normal states and abnormal conditions are easily interpreted through the use of DWI in conjunction with the use of apparent diffusion coefficient (ADC) imaging by correlating findings of hyperintensity on DWI images with findings of hypointensity on ADC images (see the images below).[1, 2]

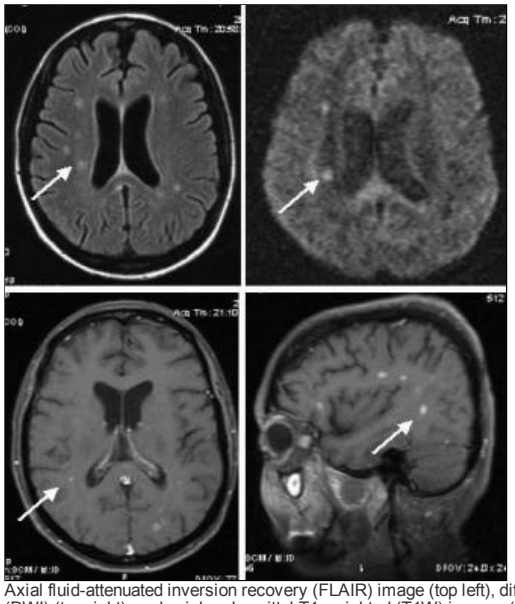


Normal brain appearance in axial DWI (left) and ADC (right) images in a 35-year-old man.

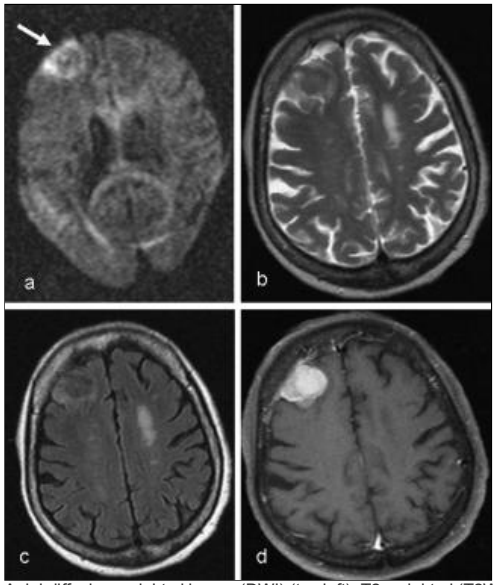


Axial DWI image demonstrates a typical wedge-shaped, cortical-based, hyperintense lesion in the left temporoparietal lobes consistent with acute infarct.

DWI is also useful in the investigation of other brain disorders such as epilepsy, multiple sclerosis, brain abscesses, brain tumors, mild traumatic brain injury, and hypertensive encephalopathy (see the images below).[3, 4, 5, 6, 7, 8]

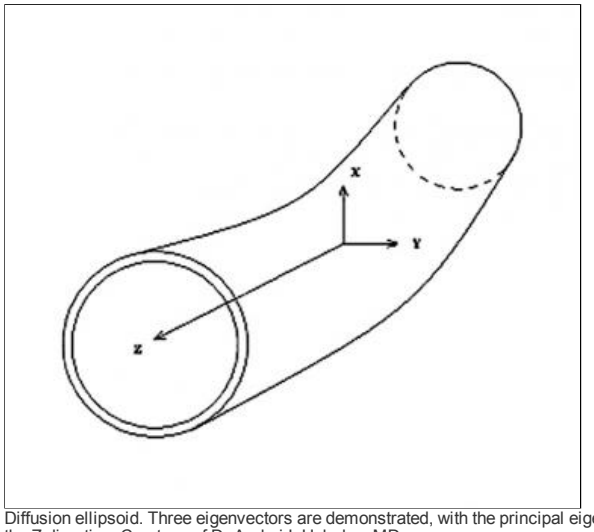


Axial fluid-attenuated inversion recovery (FLAIR) image (top left), diffusion-weighted image (DWI) (top right), and axial and sagittal T1-weighted (T1W) images (bottom) in a 40-year-old man with a history of intravenous drug abuse and fever demonstrate multiple enhancing focal brain lesions in the gray-white matter junction (arrow) compatible with septic emboli. The lesions are hyperintense on both FLAIR and DWI images.



Axial diffusion-weighted image (DWI) (top left), T2-weighted (T2W) image (top right), fluid-attenuated inversion recovery (FLAIR) image (bottom left), and contrast-enhanced T1W (bottom right) image demonstrate a right convexity meningioma, which appears hypointense on DWI image. The perilesional brain edema (arrow) is hyperintense on T2W and DWI sequences.

Diffusion, or brownian movement, denotes the random motion of molecules. All molecules exhibit such motion at temperatures greater than absolute zero. Diffusion is termed isotropic if the motion is equal in all directions. However, water diffuses asymmetrically in the white matter—that is, diffusion is restricted perpendicular to the long axis of the axons. By contrast, water diffuses faster along the *Z* axis (see the image below). This property is known as anisotropy; it may be used to define the direction of the axons in a particular voxel.[9]

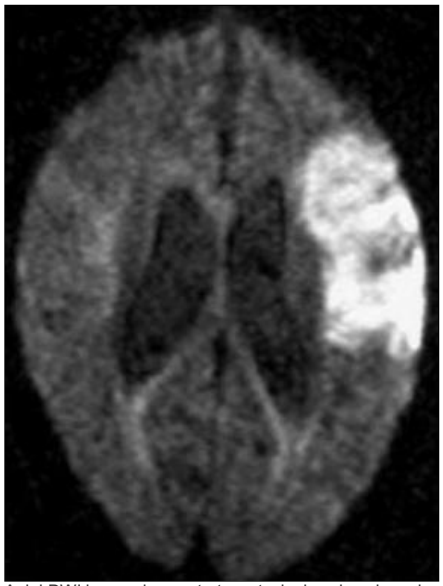


Diffusion ellipsoid. Three eigenvectors are demonstrated, with the principal eigenvector along the Z direction. Courtesy of Dr Andrei I. Holodny, MD.

Imaging and interpretation of water diffusion have improved with the development of diffusion tensor imaging (DTI). DTI allows direct in vivo examination of aspects of the tissue microstructure. DTI takes advantage of diffusion anisotropy to provide excellent details of the brain; for example, it enables mapping of the orientation of the white-matter tracts.

Tensor and Diffusion Ellipsoid

On DWIs commonly used to diagnose acute stroke (see the image below), diffusion is described by using the apparent diffusion coefficient (ADC). This is sufficient for pathologies in areas such as gray matter, where diffusion is usually isotropic.



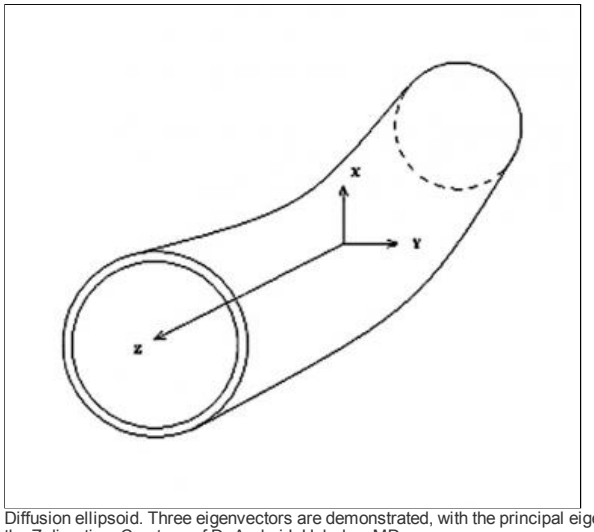
Axial DWI image demonstrates a typical wedge-shaped, cortical-based, hyperintense lesion in the left temporoparietal lobes consistent with acute infarct.

To measure the presence of anisotropy in the white matter requires a tensor *D*, which describes the mobility of molecules in a particular direction and correlation between these directions. The tensor is symmetric; at least 6 elements are required to characterize it.

The diffusion ellipsoid defines the magnitude and direction of the diffusion of water molecules in each voxel in the brain. The tensor may be diagonalized such that 3 elements, called eigenvalues, remain along the diagonal. Three eigenvalues — lambda 1, lambda 2, and lambda 3 — are derived.

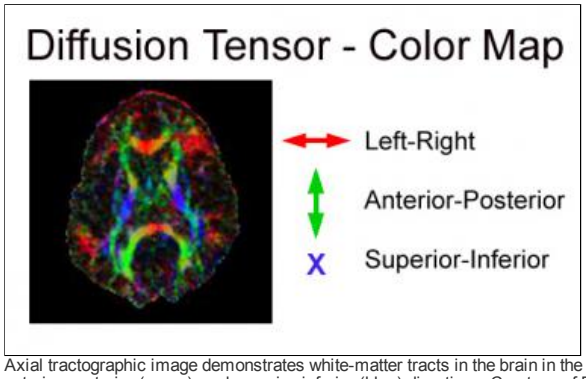
DTI allows clinicians to look at anisotropic diffusion in white-matter tracts, but it is limited in its ability to demonstrate spatial and directional anisotropy. Advanced methods such as color coding and tractography (fiber tracking) have been used to investigate directionality.

The eigenvector corresponding to the largest eigenvalue, termed the principal eigenvector, defines the main direction of diffusion of water molecules in that voxel (see the image below).

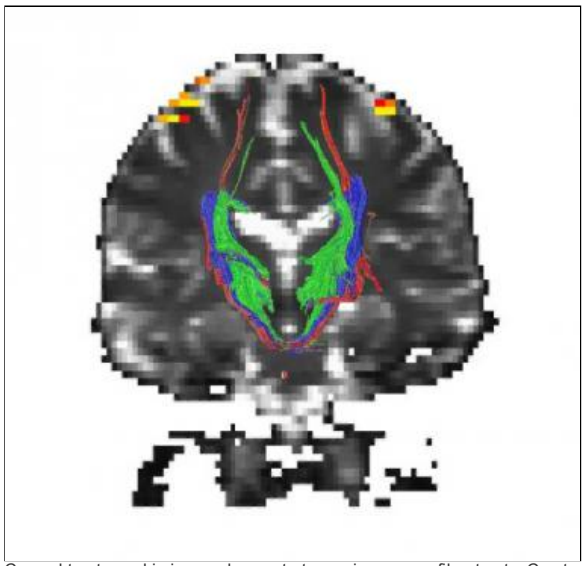


Diffusion ellipsoid. Three eigenvectors are demonstrated, with the principal eigenvector along the Z direction. Courtesy of Dr Andrei I. Holodny, MD.

Mapping the principal directional eigenvectors in each of the voxels forms the basis for tractography (see the images below); the assumption is that the principal eigenvector is aligned with the direction of the fiber bundle. On these images, the fibers are given different colors by their direction of diffusion: blue for superior and inferior; green for anterior and posterior; and red for left and right.



Axial tractographic image demonstrates white-matter tracts in the brain in the left-right (red), anterior-posterior (green), and superior-inferior (blue) directions. Courtesy of Dr Andrei I. Holodny, MD.



Coronal tractographic image demonstrates various nerve-fiber tracts. Courtesy of Dr Andrei I. Holodny, MD.

MRI Technique

Brain MRI should be performed with a 1.5- or 3-T MRI machine. High gradient strength in the range of 20-60 mT/m with a slew rate of 120 T/m/s is ideal. Typical parameters for a single-shot spin-echo echo-planar imaging (EPI) sequence are a repetition time (TR) of 6000 ms, an echo time (TE) of 100 ms, and a field of view of 24 cm to obtain 3- to 5-mm axial or coronal sections with a 5-mm intersection gap. The acquisition matrix is 96 × 96 with a reconstruction matrix of 128 × 128. The images are obtained by using 4 linearly increasing *b* values in 6-7 noncolinear

directions (b_{max} = 703-1000 s/mm^2). In addition, a T2-weighted (T2W) image is obtained without diffusion weighting (b = 0 s/mm^2).

Image Interpretation

A prudent approach to image interpretation is to use an image workstation different from the one used to acquire the images. Motion artifacts and image distortion may be corrected by using a coregistration program and filtration.[10]

Diffusion tensor measurements result in a rich data set. Diffusion anisotropy may be measured by applying simple or complicated mathematical formulas. However, an easy and common way to summarize diffusion measurements on diffusion tension images (DTIs) is to calculate parameters for overall diffusivity and for the degree of anisotropy.[11]

Imaging findings include the apparent diffusion coefficient (ADC), which is a measure of the magnitude of molecular motion divided by overall diffusivity; fractional anisotropy (FA), which is the measure of the portion of the diffusion tensor that results from anisotropy (ie, a measure of the directionality of the molecular motion of water); relative anisotropy (RA), or the ratio between anisotropic and isotropic portions of the diffusion tensor; and the volume ratio (VR), which expresses the relationship between the diffusion ellipsoid volume and that of a sphere, the radius of which is the averaged diffusivity.[12]

Maps of both FA and RA may be presented as gray-scale images. Maps of mean diffusivity and FA may be generated by using Pierpaoli and Basser's method on a pixel-by-pixel basis. Regions of interest (ROI) are placed on both maps to calculate diffusivity and FA.

FA is sensitive to low values of diffusion anisotropy; VR is sensitive to high values of diffusion anisotropy; and RA is linearly scaled for different levels of anisotropy. Both FA and RA vary from 0 (isotropic) to 1 (anisotropic). The values of measurements in pediatric brains markedly differ from those in adult brains; values vary with increasing age. Mean diffusivity is approximately 0.7 X 10^{-3} in adults and 2 X 10^{-3} in neonates. Because anisotropy is greater in ordered structures, such as myelinated axons, DTIs provide useful information regarding the myelination of white matter.

In one study, to measure developmental changes and sex and hemispheric differences of neural fibers in white matter, 52 healthy persons ranging in age from 2 months to 52 years underwent DTI to measure FA, ADC, axial diffusivity (AD), and radial diffusivity (RD). The tracts of interest (TOI) followed were the corpus callosum (CC), cingulum hippocampus (CGH), inferior longitudinal fasciculus (ILF), and superior longitudinal fasciculus (SLF). The investigators found that for all TOIs, FA increased with age, whereas ADC, AD, and RD values decreased with age. In infants, growth rates of both FA and RD were larger than those of AD. According to the authors, developmental patterns differ by TOIs and myelination, along with the development of white matter, which can be mainly expressed as an increase in FA and a decrease in RD.[13]

In many pathologic conditions, FA and ADC vary because of altered diffusivity and disorganization of the white-matter fibers, leading to decreased anisotropy. These measurements may become abnormal even before the lesion is morphologically apparent on conventional MRIs and may therefore help in early detection and in defining the extent of these lesions.[14]

FA and ADC may vary independently. This may be explained by the fact that damaged or malformed brain has glia and neurons, respectively. Therefore, they have enough cell density to prevent effects on ADC; however, because of the disorganization, FA is reduced.

Artifact

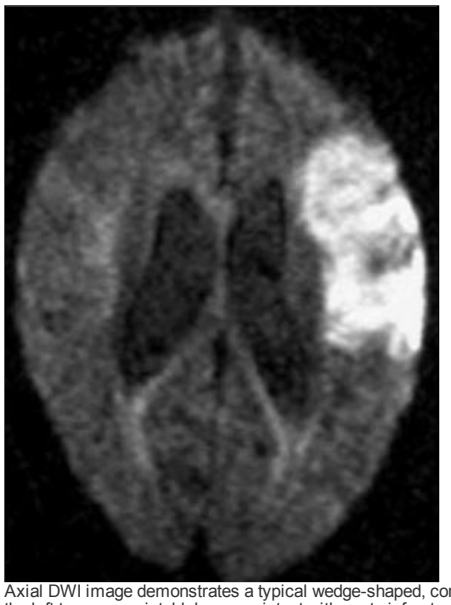
The main artifacts in DTI data are associated with acquiring DWI data from which the diffusion tensor is estimated or measured. Artifacts include misregistration of data, which is a result of eddy currents; ghosting, which results from motion artifacts; and signal, which results from susceptibility variations. These artifacts may be minimized by using motion-corrected multishot EPI techniques such as periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER) and sensitivity-encoding EPI (SENSE-EPI).[15, 16, 17]

Clinical Applications

Specific qualitative features established for conventional MRI may be used to distinguish normal from abnormal brain development. The changes in apparent diffusion coefficient (ADC) occur predominantly in the first 6 months of life and are believed to be related to decreasing total water content, myelination, and organization of the white-matter tracts. All of these processes decrease diffusivity. Because diffusion tension imaging (DTI) technique allows improved objectivity and sensitivity in the detection of subtle developmental changes, it may prove to be more useful than the relatively subjective evaluation used with conventional MRI sequences.[18]

Stroke

Diffusion-weighted imaging (DWI) and DTI have been extensively used to detect acute ischemic brain injury (see the image below).



Axial DWI image demonstrates a typical wedge-shaped, cortical-based, hyperintense lesion in the left temporoparietal lobes consistent with acute infarct.

In the acute phase of ischemia, ADC is reduced and fractional anisotropy (FA) values are increased. In the chronic phase of ischemia, ADC is higher than normal. In contrast to the elevation of the ADC in chronic stroke, diffusion anisotropy remains significantly lower in the infarcted area than in the similar contralateral region of the brain, even 2-6 months after an ischemic stroke. By combining ADC and anisotropy data, the severity of strokes may be assessed and acute ischemic changes may be distinguished from chronic ischemic changes; that difference may affect treatment. Also, ADC values increase if purely vasogenic edema is present—for example, in the reversible posterior leukoencephalopathy syndrome or in high-pressure hydrocephalus.[19, 20]

Epilepsy

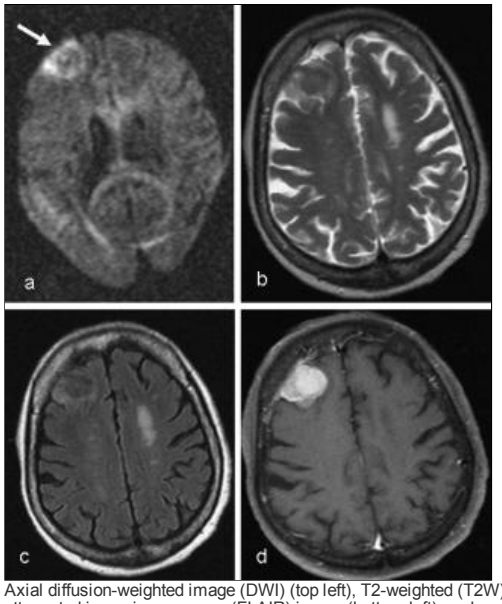
A common cause of epilepsy is mesial temporal sclerosis or hippocampal sclerosis in patients with chronic epilepsy. Findings seen on DTIs include increased diffusivity and decreased anisotropy caused by the loss of structural organization and expansion of the extracellular fluid space. Changes in DTI may also extend to areas of the brain that appear morphologically normal on conventional MRIs. In this way, the DTI may define the true extent of pathology and improve preoperative planning.

Refractory extratemporal neocortical epilepsy may be caused by malformations in cortical development (MCD); these malformations may not be apparent on conventional MRI. However, differences in ADC in the affected region, as compared with the contralateral normal brain, may be seen; this helps in presurgical planning. However, DTI may erroneously depict regions of presumed seizure onset by showing subtle structural abnormalities caused by head injury or ischemia.

Brain tumors

DTI has demonstrated a potential in distinguishing gliomas and solitary metastasis in the brain parenchyma. Significantly higher mean diffusivity and lower FA, as compared with levels in normal-appearing white matter, have been demonstrated in the peritumoral regions of both gliomas and metastases.

Peritumoral mean diffusivity of metastases and meningioma (see the image below) is significantly higher than that of gliomas, whereas the FA values are similar, confirming the infiltrative nature of gliomas. Tractography combined with functional MRI may potentially help in preoperative planning of brain tumors by mapping areas of active infiltration.[21]



Axial diffusion-weighted image (DWI) (top left), T2-weighted (T2W) image (top right), fluid-attenuated inversion recovery (FLAIR) image (bottom left), and contrast-enhanced T1W (bottom right) image demonstrate a right convexity meningioma, which appears hypointense on DWI image. The perilesional brain edema (arrow) is hyperintense on T2W and DWI sequences.

Multiple sclerosis

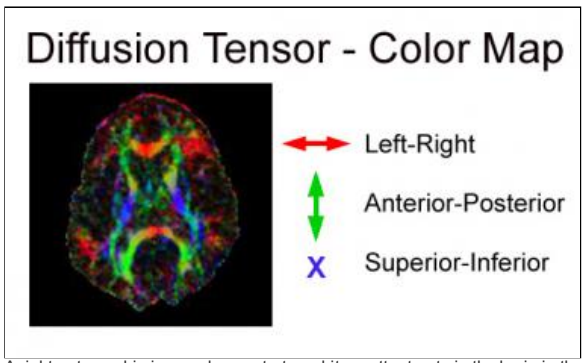
Various studies have demonstrated potential advantages of DTI in the diagnosis and follow-up of MS lesions. In MS, FA values are more sensitive than ADC values with regard to white-matter abnormalities. The lesions with destructive pathology or acuity generally have increased diffusivity and decreased FA values. On conventional T2-weighted and fluid-attenuated inversion recovery (FLAIR) images, normal-appearing white matter adjacent to the MS lesions may also demonstrate abnormality; thus, the actual extent of the lesions becomes apparent. In some cases, the gray matter around the white-matter lesions is abnormal; this indicates that disease may not be isolated to the white matter.[22]

Demyelinating versus dysmyelinating disorders

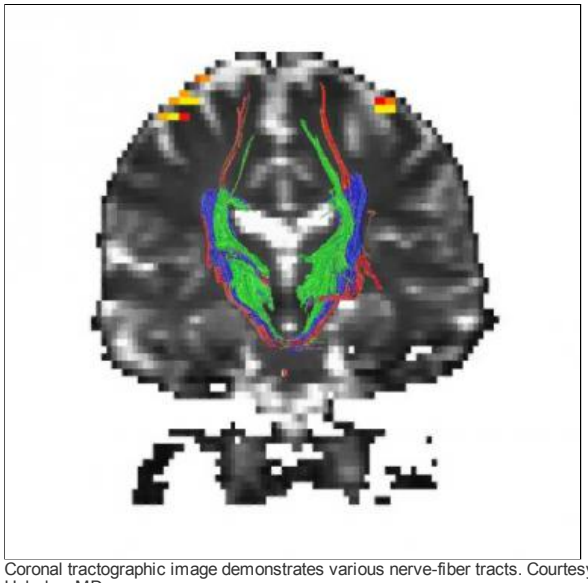
Diffusional anisotropy is present in dysmyelinating disorders such as Pelizaeus-Merzbacher disease; by contrast, it may be lost in demyelinating disease such as Krabbe disease or Alexander disease.[23] Also, in contrast to relatively high signal intensity of the lesions of Krabbe disease on DWI, the lesions in Alexander disease have signal intensity. Therefore, DWI is clinically useful in differentiating dysmyelination from demyelination, as both have lesions of high intensity in the white matter, as shown on T2-weighted images.

Tractography

Tractography potentially solves a problem for a neurosurgeon in terms of minimizing functional damage and determining the extent of diffuse infiltration of pathologic tissue to minimize residual tumor volume. In this way, tractography facilitates preoperative planning. Tractographic images (see the images below) may help to clarify whether a tumor is compressing, abutting, or infiltrating the contiguous white-matter tracts. However, no consensus has been reached about an appropriate criterion standard for assessing the accuracy of DTI, and this technique is primarily investigational at present.[24]



Axial tractographic image demonstrates white-matter tracts in the brain in the left-right (red), anterior-posterior (green), and superior-inferior (blue) directions. Courtesy of Dr Andrei I. Holodny, MD.



Coronal tractographic image demonstrates various nerve-fiber tracts. Courtesy of Dr Andrei I. Holodny, MD.

Conclusion

Diffusion in structured tissue, such as white matter, is anisotropic. Diffusion tension imaging (DTI) can be used to measure anisotropy per voxel and provides the directional information relevant for magnetic resonance tractography or fiber tracking in vivo. The recent development of DTI allows for direct examination of the brain microstructure, and DTI has become a useful tool for investigation of brain disorders such as stroke, epilepsy, MS, brain tumors, and demyelinating and dysmyelinating disorders. However, further improvements in the technique and in postprocessing analysis are needed to increase the widespread utility of DTI in both research and clinical applications.

Contributor Information and Disclosures

Author
Avneesh Chhabra, MD Staff Radiologist, Department of Radiology, Drexel University College of Medicine

Avneesh Chhabra, MD is a member of the following medical societies: American Medical Association, American Roentgen Ray Society, Radiological Society of North America

Disclosure: Nothing to disclose.

Coauthor(s)
Robert A Koenigsberg, MSc, DO, FAOCR Professor, Director of Neuroradiology, Program Director, Diagnostic Radiology and Neuroradiology Training Programs, Department of Radiology, Hahnemann University Hospital, Drexel University College of Medicine

Robert A Koenigsberg, MSc, DO, FAOCR is a member of the following medical societies: American Osteopathic Association, American Society of Neuroradiology, Radiological Society of North America, Society of NeuroInterventional Surgery

Disclosure: Nothing to disclose.

Kiran Batra, MD, DNB Neuroradiology Fellow, Radiology Resident, Drexel University College of Medicine

Kiran Batra, MD, DNB is a member of the following medical societies: American Roentgen Ray Society, Radiological Society of North America, Pennsylvania Radiological Society

Disclosure: Nothing to disclose.

Specialty Editor Board
Bernard D Coombs, MB, ChB, PhD Consulting Staff, Department of Specialist Rehabilitation Services, Hutt Valley District Health Board, New Zealand

Disclosure: Nothing to disclose.

C Douglas Phillips, MD, FACR Director of Head and Neck Imaging, Division of Neuroradiology, New York-Presbyterian Hospital; Professor of Radiology, Weill Cornell Medical College

C Douglas Phillips, MD, FACR is a member of the following medical societies: American College of Radiology, American Medical Association, American Society of Head and Neck Radiology, American Society of Neuroradiology, Association of University Radiologists, Radiological Society of North America

Disclosure: Nothing to disclose.

Chief Editor
James G Smirniotopoulos, MD Professor of Radiology, Neurology, and Biomedical Informatics, Program Director, Diagnostic Imaging Program, Center for Neuroscience and Regenerative Medicine (CNRM), Uniformed Services University of the Health Sciences

James G Smirniotopoulos, MD is a member of the following medical societies: American College of Radiology, American Roentgen Ray Society, American Society of Head and Neck Radiology, American Society of Neuroradiology, Association of University Radiologists, Radiological Society of North America, American Society of Pediatric Neuroradiology

Disclosure: Nothing to disclose.

Additional Contributors
David S Levey, MD Orthopedic and Neurospinal MRI, Forensic Diagnostic Radiologist; President, David S Levey, MD, PA, San Antonio, Texas

David S Levey, MD is a member of the following medical societies: International Society of Forensic Radiology and Imaging, Forensic Expert Witness Association, Technical Advisory Service for Attorneys, Bexar County Medical Society, Texas Medical Association

Disclosure: Nothing to disclose.

References

1. Souillard-Scemama R, Tisserand M, Calvet D, Jumadilova D, Lion S, Turc G, et al. An update on brain imaging in transient ischemic attack. *J Neuroradiol*. 2015 Feb. 42(1):3-11. [Medline].
2. Hakimelahi R, Vachha BA, Copen WA, Papini GD, He J, Higazi MM, et al. Time and diffusion lesion size in major anterior circulation ischemic strokes. *Stroke*. 2014 Oct. 45(10):2936-41. [Medline].
3. Bammer R. Basic principles of diffusion-weighted imaging. *Eur J Radiol*. 2003 Mar. 45(3):169-84. [Medline].
4. Le Bihan D, Mangin JF, Poupon C, et al. Diffusion tensor imaging: concepts and applications. *J Magn Reson Imaging*. 2001 Apr. 13(4):534-46. [Medline].
5. Mori S, van Zijl PC. Fiber tracking: principles and strategies - a technical review. *NMR Biomed*. 2002 Nov-Dec. 15(7-8):468-80. [Medline].
6. Sundgren PC, Dong Q, Gómez-Hassan D, Mukherji SK, Maly P, Welsh R. Diffusion tensor imaging of the brain: review of clinical applications. *Neuroradiology*. 2004 May. 46(5):339-50. [Medline].
7. Shenton ME, Hamoda HM, Schneiderman JS, Bouix S, Pasternak O, Rathi Y, et al. A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. *Brain Imaging Behav*. 2012 Jun. 6(2):137-92. [Medline].
8. Cavaliere C, Aiello M, Di Perri C, Fernandez-Espejo D, Owen AM, Soddu A. Diffusion tensor imaging and white matter abnormalities in patients with disorders of consciousness. *Front Hum Neurosci*. 2014. 8:1028. [Medline]. [Full Text].
9. Moseley ME, Cohen Y, Kucharczyk J, Mintorovitch J, Asgari HS, Wendland MF. Diffusion-weighted MR imaging of anisotropic water diffusion in cat central nervous system. *Radiology*. 1990 Aug. 176(2):439-45. [Medline].
10. Miller JH, McKinstry RC, Philip JV, et al. Diffusion-tensor MR imaging of normal brain maturation: a guide to structural development and myelination. *AJR Am J Roentgenol*. 2003 Mar. 180(3):851-9. [Medline].
11. Pierpaoli C, Basser PJ. Toward a quantitative assessment of diffusion anisotropy. *Magn Reson Med*. 1996 Dec. 36(6):893-906. [Medline].
12. Mandl RC, Schnack HG, Zwiers MP, van der Schaaf A, Kahn RS, Hulshoff Pol HE. Functional diffusion tensor imaging: measuring task-related fractional anisotropy changes in the human brain along white matter tracts. *PLoS ONE*. 2008. 3(11):e3631. [Medline].
13. Uda S, Matsui M, Tanaka C, Uematsu A, Miura K, Kawana I, et al. Normal Development of Human Brain White Matter from Infancy to Early Adulthood: A Diffusion Tensor Imaging Study. *Dev Neurosci*. 2015 Mar 17. [Medline].
14. Zou K, Huang X, Li T, Gong Q, Li Z, Ou-yang L, et al. Alterations of white matter integrity in adults with major depressive disorder: a magnetic resonance imaging study. *J Psychiatry Neurosci*. 2008 Nov. 33(6):525-30. [Medline].
15. Wu M, Chang LC, Walker L, Lemaitre H, Barnett AS, Marenco S, et al. Comparison of EPI distortion correction methods in diffusion tensor MRI using a novel framework. *Med Image Comput Comput Assist Interv Int Conf Med Image Comput Comput Assist Interv*. 2008. 11:321-9. [Medline].
16. Bammer R, Auer M, Keeling SL, et al. Diffusion tensor imaging using single-shot SENSE-EPI. *Magn Reson Med*. 2002 Jul. 48(1):128-36. [Medline].
17. Pipe JG, Farthing VG, Forbes KP. Multishot diffusion-weighted FSE using PROPELLER MRI. *Magn Reson Med*. 2002 Jan. 47(1):42-52. [Medline].
18. Bammer R, Augustin M, Strasser-Fuchs S, et al. Magnetic resonance diffusion tensor imaging for characterizing diffuse and focal white matter abnormalities in multiple sclerosis. *Magn Reson Med*. 2000 Oct. 44(4):583-91. [Medline].
19. Yang Q, Tress BM, Barber PA, et al. Serial study of apparent diffusion coefficient and anisotropy in patients with acute stroke. *Stroke*. 1999 Nov. 30(11):2382-90. [Medline].
20. Sundgren PC, Edvardsson B, Holtas S. Serial investigation of perfusion disturbances and vasogenic oedema in hypertensive encephalopathy by diffusion and perfusion weighted imaging. *Neuroradiology*. 2002 Apr. 44(4):299-304. [Medline].

21. Lu S, Ahn D, Johnson G, Law M, Zagzag D, Grossman RI. Diffusion-tensor MR imaging of intracranial neoplasia and associated peritumoral edema: introduction of the tumor infiltration index. *Radiology*. 2004 Jul. 232(1):221-8. [Medline].

22. Commowick O, Fillard P, Clatz O, Warfield SK. Detection of DTI white matter abnormalities in multiple sclerosis patients. *Med Image Comput Comput Assist Interv Int Conf Med Image Comput Comput Assist Interv*. 2008. 11:975-82. [Medline].

23. Ono J, Harada K, Mano T, et al. Differentiation of dys- and demyelination using diffusional anisotropy. *Pediatr Neurol*. 1997 Jan. 16(1):63-6. [Medline].

24. Bammer R, Acar B, Moseley ME. In vivo MR tractography using diffusion imaging. *Eur J Radiol*. 2003 Mar. 45(3):223-34. [Medline].

25. Wang VY, Lam HI, Ennis DB, Young AA, Nash MP. Passive ventricular mechanics modelling using MRI of structure and function. *Med Image Comput Comput Assist Interv Int Conf Med Image Comput Comput Assist Interv*. 2008. 11:814-21. [Medline].