# What is so Hard about Diffusion Tensor Theory? The Fast and Easy "Tract" to Learning Diffusion Tensor Imaging and Tractography

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# Objectives



- Describe the physical principle and mathematics of diffusion tensor imaging (DTI)
- Describe the utilization of DTI data
- Explain the principle of tractography
- Review the normal anatomy of the major fiber tracts of the brain in correlation with tractography
- Illustrate the applications of DTI to characterize encephalopathies including stroke, neoplasm and demyelinating pathologies.



## Diffusion Weighted Imaging (DWI)

- Molecules move in Brownian motion, or molecular diffusion, which is the concept that any molecule in a fluid will be randomly displaced due to agitation by thermal energy
- Diffusion of water molecules can occur via the following mechanisms:
  - Random diffusion due to concentration differences (Fick's law of diffusion)
  - Response to factors such as temperature or ion-ion interaction and a combination of other factors
- Diffusion Weighted Imaging (DWI) is based on the motion of water molecules and involves two magnetic field gradient pulses added to a conventional spin echo pulse, diminishing the signal of moving water molecules and increasing the signal of stationary or "restricted" water molecules
- The two gradient pulses must be equal in magnitude and timing before and after the 180° pulse of the spin echo pulse sequence
- The first pulse dephases the magnetization of moving and static spins. The second pulse rephases static spins but not moving spins, eliciting a strong signal from stationary water molecules.



Areas of unrestricted diffusion within the CSF spaces of the ventricles and sulci demonstrate relatively decreased signal intensity (hypointensity). Areas of restricted diffusion demonstrate relatively increased signal intensity (hyperintensity).





## **DWI Physics**

• The diffusion weighted signal equation is

 $S=S\downarrow0~e\uparrow-bADC$ 

 $S_0$  = signal intensity at b = 0

ADC = Apparent diffusion coefficient

- b-value identifies the measurement's sensitivity to diffusion and determines the strength and duration of the diffusion gradients.
- Higher b-values give stronger signal attenuation for free water molecules
- b-values (measured in s/mm<sup>2</sup>) measure the degree of diffusion weighting applied, indicating the strength and duration of the diffusion gradients

 $b=\gamma 12 \ G12 \ \delta 12 \ (\Delta - \delta/3)$ 

 $\gamma$  = gyromagnetic ratio

- G = gradient strength
- $\delta$  = duration of gradient

 $\Delta$  = time between pulsed gradients

#### ADC

 ADC is the apparent diffusion coefficient and reflects the presence of restrictions, such as viscosity, spatial barriers, and spin-spin interactions in biological tissues



Basic diffusion weighted spin echo sequence diagram



# Diffusion Tensor Imaging (DTI)

- Diffusion Tensor Imaging compiles data from numerous DWI acquisitions, each with a different orientation of the diffusion sensitizing gradient pulses, to generate voxels representative of the rate of diffusion and preferred direction of diffusion at various points in space
  - The minimum number of directions to form an image is 6 (anteriorly, posteriorly, superiorly, inferiorly, right, left), however in practice normally 12, 16 or 32+ are done
- Diffusion is anisotropic in the white matter fiber tracts
  - Diffusion anisotropy is determined by the orientation of the fiber tracts
  - The principle direction of diffusion within an axon is influenced by microstructures and macrostructures
    - Microstructures: intra-axonal organization, density of fiber, cell packing and degree of myelination
    - Macrostructures: Variability in the orientation of the white fiber tracts

### Isotropic vs Anisotropic

ISOTROPIC = same in every direction.

- Brownian motion of unrestricted water molecules is random and isotropic, moving in every direction.
  - For instance, water molecules within cerebrospinal fluid and gray matter of the brain demonstrate isotropic motion.
- The degree of isotropic motion can be represented as a numerical magnitude of diffusivity independent of direction, known as the diffusion coefficient, which is defined by the proportionality of the root mean square displacement of water molecule movement and the square root of the time of the motion.
- Therefore, DWI is a visual representation of scalar data utilizing pixels.
- An isotropic environment is analogous to a sphere.

ANISOTROPIC = NOT the same in every direction.

- Water molecule motion within an axon is directionally limited as the water molecules are more free to diffuse along the length of the axon.
- The degree of anisotropic motion at any given point space can be represented as a vector, accounting for both rate and principle direction of diffusion, and may be represented visually utilizing tensors (voxels).
- An anisotropic environment is analogous to an ellipsoid.





# **DWI** Physics

- The direction of maximum diffusivity coincides with fiber tract orientation and is contained within a 3 x 3 matrix of Apparent Diffusion Coefficient (ADC) tensor
  - Diffusion anisotropy in 3 dimensions can be characterized by a 3x3 second rank tensor, a mathematical matrix containing 9 elements
- A diffusion tensor is graphically depicted as an ellipsoid
  - Diameter of the ellipsoid in any direction estimates the diffusivity in that direction
  - An ellipsoid can be characterized by SIX (6) parameters at a minimum. Three parameters to specify the shape and three parameters to specify the directions of the ellipsoid
    - Eigenvectors (v) direction of the ellipsoid (orientation)
    - Eigenvalues ( $\lambda$ ) shape of the ellipsoid (diffusivities)

### *ADC=*[**■***ADC↓xx* &*ADC↓xy* &*ADC↓xz* @*ADC↓yx* & *ADC↓yy* &*ADC↓yz* @*ADC↓zx* &*ADC↓zy* &*ADC↓zz* ]

- The diffusion data is acquired to make the ADC tensor diagonally symmetric
  - $ADC_{xy} = ADC_{yx}$
  - $ADC_{xz} = ADC_{zx}$
  - $ADC_{yz} = ADC_{zy}$
- Different diffusivities can occur along various directions, but diagonal symmetry allows full characterization of the ellipsoid tensor along six independent axes







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# **DTI Physics**

What should I do with this matrix of diffusion measurements? It is rather complicated to work with a matrix of 9 elements. How do I produce something meaningful from the measurements?

- The ADC tensor can be simplified through coordinate transformation
- The coordinate transformation selects a local region of interest (voxel) and re-expresses the diffusivity relative to the local region
- The transformation is achieved through DIAGONALIZATION of the matrix tensor utilizing linear algebra
  - Diagonalization results in a set of three eigenvectors and eigenvalues reflecting the diffusivities within a voxel of a particular local region

**TRANSFORMATION** changes frame of reference from the scanner to the local region of interest

#### THIS IS A MATTER OF CHANGING PERSPECTIVES

If I make some of the elements of the matrix zero, I can simplify the diffusion tensor matrix. This reduces the complexity of subsequent calculations!

- $\lambda = v \uparrow -1 [ADC] v$  DIAGONALIZATION
  - v = eigenvector matrix
  - $v^1$  = inverted eigenvector matrix

complex 9 non-zero element matrix with 6 distinct elements (6 dimensional)

 $ADC = [\blacksquare ADC \downarrow xx \& ADC \downarrow xy \& ADC \downarrow x$ 

 $\lambda = [\blacksquare \lambda \downarrow 1 \& 0 \& 0 @ 0 \&$ 





Resultant diffusion tensor after diagonalization, a simple matrix with 3 nonzero diagonal elements (3 dimensional)

# **DTI Physics**

### What should I do with the eigenvalues of diffusion coefficients now? How should I represent the extent of anisotropy?

- First, I gather the diffusion ellipsoid with the three eigenvalues and eigenvectors for each voxel representing the imaged object
  - Eigenvectors (v): v<sub>1</sub>, v<sub>2</sub>, v<sub>3</sub>
    - Three principle axes of the ellipsoid (directions)
  - Eigenvalues ( $\lambda$ ):  $\lambda_1$ ,  $\lambda_2$ ,  $\lambda_3$ 
    - Magnitudes of the diffusion ellipsoid





## **DTI Physics**

- I realize that it is impractical to display the diffusion ellipsoid for each pixel of the screen because of limited visual capability of the human eyes
- I then calculate invariant metrics (VR, MD, RA, and FA) and use them to make SCALAR MAPS which demonstrate MAGNITUDES of anisotropy or diffusion independent of the principle direction of diffusion

#### **Volume Ratio**

 $VR = \lambda \downarrow 1 \ \lambda \downarrow 2 \ \lambda \downarrow 3 \ /(\lambda \ ) \uparrow 3$ 

#### **Mean Diffusivity**

 $MD = \lambda \downarrow 1 + \lambda \downarrow 2 + \lambda \downarrow 3 /3$ 

#### **Relative Anisotropy**

 $RA = \sqrt{(\lambda \downarrow 1 - \lambda) + (\lambda \downarrow 2 - \lambda) \uparrow 2} + (\lambda \downarrow 3 - \lambda) \uparrow 3 / \sqrt{3} \lambda$ 

#### **Fractional Anisotropy**

 $FA = \sqrt{3}/2 \quad \sqrt{(\lambda \downarrow 1 - \lambda) + (\lambda \downarrow 2)} \\ -\lambda ) \uparrow 2 + (\lambda \downarrow 3 - \lambda) \uparrow 3 \quad /\sqrt{\lambda \downarrow 1} \quad \uparrow 2 + \lambda \downarrow 2 \quad \uparrow 2 + \lambda \downarrow 3 \quad \uparrow 2$ 

with the trace 
$$\lambda = \lambda \sqrt{1} + \lambda \sqrt{2} + \lambda \sqrt{3}$$

FA reflects the anisotropic fraction of the magnitude of the diffusion tensor. FA varies between 0 (isotropic diffusion) and 1 (infinite anisotropy)



Axial gray scale FA map of the brain at the level of the caudate nuclei. The degree of brightness indicates the degree of anisotropy on a gray scale FA map.



Alternatively, a color scale can be used to represent the degree of anisotropy. Coronal reconstructed color scale FA map of the brain at the level of the caudate nuclei (red = higher anisotropy, blue = lower anisotropy)



## DTI to Tractography

- Tractography uses the directional information of DTI to generate a 3 dimensional map of the white matter tracts within the brain
- How can I use the information from the eigenvalues and eigenvectors to show the direction of the fiber tracts?
  - The eigenvector with the largest value, usually denoted as v<sub>1</sub>, is assumed to represent the principle direction of diffusion and thus the dominant local fiber orientation. Decomposing v<sub>1</sub>, into three components (x, y, z) results in 3 images and difficult interpretation. Instead, a directional encoded color (DEC) map can be generated, representing each orthogonal direction of v<sub>1</sub>





 $\lambda_1 v_1$ 



 $\lambda_2 v_2$ 

 $\lambda_3 v_3$ 

## Tractography

Tractography uses various mathematical algorithms to bidirectionally track the course of white matter fiber tracts passing through a selected region of interest. The most commonly used tracking algorithm follows the principle directions of diffusion (the principle eigenvectors) of adjacent voxels (tensors) so long as the fractional anisotropy is above a set threshold and the principle direction of diffusion is within a given range (cone of probability)



### Start!

The white squares are 2-D representations of voxels within a given plane.

The red arrows represent the principle eigenvector, the primary direction of diffusion for each tensor.

The green spheres represent isotropic tensors which by definition have no principle eigenvector and are below the threshold of fractional anisotropy. They terminate the tracking algorithm.



The yellow ellipsoids represent tensors with fractional anisotropy below threshold and primary direction of diffusion beyond the acceptable range of angular variance. They also terminate the tracking algorithm.



The blue ellipsoids represent tensors with fractional anisotropy and direction within the given thresholds described above.



The translucent disc represents a region of interest, the starting point at which the algorithm begins tracking the principle direction of diffusion from voxel to voxel.



Note that tractography based on DTI data has limited angular resolution and difficulty accurately representing crossing fiber tracts.

### **Brain Anatomy and Connectivity**

- The 3 descriptive neuroanatomical classifications:
  - Surface Anatomy (Image A)
    - Describes the appearance and topographic organization of gyral convolutions and the interposed sulci.
  - Sectional Anatomy (Image B)
    - Describes the spatial organization of superficial (e.g. cortex), subcortical and deep (e.g. basal ganglia) structures conventionally within orthogonal planes.
  - Connectional Anatomy (Image C)
    - Describes the course from start to finish of connecting pathways.



Right–sided central sulcus and perirolandic primary motor and sensory gyri denoted by asterisk (\*). Corticospinal tract denoted by arrows.



### **Connectional Neuroanatomy**

- The fiber tracts have been classified into 3 groups based on the general course of the fiber tracts:
  - Association fibers interconnect cortical areas in each hemisphere. These fibers include cingulum, superior and inferior occipitofrontal fasciculi, uncinate fasciculus, superior longitudinal fasciculus, and inferior longitudinal fasciculus.
  - Projection fibers interconnect cortical areas with deep nuclei, brain stem, cerebellum, and spinal cord. There are both efferent and afferent fibers. Projection fibers include the corticospinal, corticobulbar, and corticopontinetracts, as well as the optic radiations
  - *Commissural fibers* interconnect similar cortical areas between opposite hemispheres. Fibers of the corpus callosum and anterior commissure



### **Association Fibers**

- Cingulum
  - The cingulum begins in the parolfactory area of the cortex below the rostrum of the corpus callosum, then courses within the cingulate gyrus, and, arching around the entire corpus callosum, extends forward into the parahippocampal gyrus and uncus.
- Superior Occipitofrontal Fasciculus
  - The superior occipitofrontal fasciculus lies beneath the cingulum. It connects occipital and frontal lobes, extending posteriorly along the dorsal border of the caudate nucleus
  - Portions of the superior occipitofrontal fasciculus parallel the superior longitudinal fasciculus but they are separated from the superior longitudinal fasciculus by the corona radiata and internal capsule
- Inferior Occipitofrontal Fasciculus
  - The inferior occipitofrontal fasciculus connects the occipital and frontal lobes but is far inferior compared with the superior occipitofrontal fasciculus.
  - It extends below the insula. Posteriorly, the inferior occipitofrontal fasciculus joins the inferior longitudinal fasciculus, the descending portion of the superior longitudinal fasciculus, and portions of the optic radiation tract to form most of the sagittal stratum, a large and complex bundle that connects the occipital lobe to the rest of the brain
- Superior Longitudinal Fasciculus
  - This tract sweeps along the superior margin of the insula in a great arc, gathering and shedding fibers along the way to connect frontal lobe cortex to parietal, temporal, and occipital lobe cortices. The superior longitudinal fasciculus is the largest association bundle
- Inferior Longitudinal Fasciculus
  - This fiber tract connects temporal and occipital lobe cortices. This tract traverses the length of the temporal lobe
  - It joins with the inferior occipitofrontal fasciculus, the inferior aspect of the superior longitudinal fasciculus, and the optic radiations to form much of the sagittal stratum



### **Projection Fibers**

- Corticospinal, Corticopontine, and Corticobulbar Tracts
  - The corticospinal, corticobulbar and corticopontine tracts are major efferent projection fibers that connect motor cortex to the brain stem and spinal cord.
  - Corticospinal fibers converge into the corona radiate and continue through the **posterior limb** of the internal capsule to the cerebral peduncle on their way to the lateral funiculus.
  - Corticobulbar fibers converge into the corona radiata and continue through the genu of the internal capsule to the cerebral
    peduncle where they lie medial and dorsal to the corticospinal fibers. Corticobulbar fibers predominantly terminate at the cranial
    motor nuclei
  - Corticopontine fibers converge into the corona radiata and travel along side the corticospinal fibers. The tract is named according
    the origination: frontopontine, parietopontine, temporopontine or occipitopontine tract. These fibers terminate at the cranial nuclei
    in the pons
- Corona Radiata
  - A white matter sheet that continues ventrally as the internal capsule and dorsally as the centrum semiovale. It contains both descending and ascending axons that carry nearly all of the neural signals from and to the cerebral cortex. The corona radiata is associated with the corticospinal tract, the corticopontine tract, and the corticobulbar tract
- Internal Capsule
  - A large and compact fiber bundle that serves as a major conduit of fibers to and from the cerebral cortex and is readily identified on directional DTI color maps.
  - The anterior limb lies between the head of the caudate and the rostral aspect of the lentiform nucleus. The anterior limb passes projection fibers to and from the thalamus (thalamocortical projections) as well as frontopontine tracts, all of which are primarily anteroposteriorly oriented
  - The posterior limb lies between the thalamus the posterior aspect of the lentiform nucleus. The fibers are the superior-inferiorly oriented fibers of the corticospinal, corticobulbar, and corticopontine tracts
- Optic radiation
  - The optic radiation connects the lateral geniculate nucleus to occipital (primary visual) cortex. The more inferior fibers of the optic radiation sweep around the posterior horns of the lateral ventricles and terminate in the calcarine cortex; the more superior fibers take a straighter, more direct path.



### **Commissural Fibers**

### Corpus Callosum

- The largest white matter fiber bundle
- The corpus callosum consists of fibers connecting corresponding areas of cortex between the hemispheres.
- Fibers traversing the callosal body are transversely oriented, whereas the fibers traversing the genu and splenium arch anteriorly and posteriorly to reach the anterior and posterior poles of the hemispheres.

### • Anterior Commissure

• The anterior commissure crosses through the lamina terminalis. Its anterior fibers connect the olfactory bulbs and nuclei. The posterior fibers connect middle and inferior temporal gyri









Directional encoded color (DEC)







#### Directional encoded color (DEC)







Directional encoded color (DEC)







Directional encoded color (DEC)

# Terminology for DTI imaging and tractography



- Deviation
  - Any portion of tract course is altered by bulk mass effect while maintaining tract coherence, with "coherence" implying that multiple adjacent fiber trajectories follow parallel pathways or they diverge/converge in an ordered fashion.
- Infiltration
  - Any portion of a tract shows significantly reduced anisotropy while retaining sufficiently ordered structure to allow its identification on directional color maps and to allow fiber tracking to proceed.
- Interruption
  - Any portion of a tract is visibly discontinuous on anisotropyweighted DEC maps, and/or fiber tracking is discontinuous. Note also that a tract may be interrupted either partially or completely
- Splaying
  - A tract separated by a lesion into distinct bundles deviated in different directions.



## **Clinical Applications**

### Stroke

- DWI is used to detect ischemic changes in the setting of acute stroke.
- DTI demonstrates increased fractional anisotropy in regions of reversible ischemia in the setting of acute stroke and can also help characterize the chronicity of ischemia.
- Tractography can demonstrate Wallerian degeneration, in some cases more precisely than conventional MR techniques.
- Tractography can be used to monitor post treatment white matter tract reorganization.

### Neoplasm

- DTI and tractography can demonstrate the involvement of white matter tracts by tumor, whether infiltrated, disrupted or displaced.
- DTI can better delineate the actual extent of certain tumors such as gliomas that may be underestimated with conventional MR.
- Increases in diffusivity surrounding tumors may help differentiate between peritumoral infiltration from peritumoral edema, for instance, vasogenic edema surrounding metastases.
- Tractography in conjunction with functional MRI (fMRI) is useful in determining the involvement and/or spatial relationship of tumor with respect to the white matter tracts and eloquent areas of the brain.
- DTI and tractography with or without fMRI can aid in preoperative planning and help predict postsurgical outcomes and potential morbidity, allowing for more informed decisions in patient management.



### **Clinical Applications**

### Demyelinating Disease (i.e. Multiple Sclerosis)

- Fractional anisotropy is more sensitive than mean diffusivity for detection of demyelinating lesions such as those of Multiple Sclerosis (MS).
- Abnormal diffusion in the corpus callosum may be the earliest imaging finding of MS, leading to early detection.
- DTI demonstrates findings that help characterize different types of MS, such as Relapsing-Remitting, Secondary-Progressive , and Primary-Progressive.
- Normal DTI does not exclude patients with early relapsing-remitting MS as they can demonstrate normal diffusivity.
- Mean diffusivity is higher in secondary-progressive MS than relapsing-remitting MS.
- While primary-progressive MS can demonstrate relatively few lesions on conventional MR sequences considering the severity of clinical symptoms, widespread albeit small diffusion and anisotropy abnormalities of the normal appearing white matter have been reported.
- Tractography has demonstrated that MS lesions can interrupt white matter fibers similarly to tumors.
- DTI and tractography may potentially differentiate between lesions which involve only myelin destruction or axonal injury and quantify the degree of axonal loss and/or demyelination.
- The correlation between the degree of corticospinal fiber tract loss and a supratentorial MS lesion load may permit quantification of axonal transection and Wallerian degeneration from MS lesions.



# **Clinical Cases**



DWI





ADC

ADC

DWI and ADC images showed acute stroke of the left occipital lobe in 2013

### **CASE 1: OLD STROKE**

- 54 year old male with history of • HTN, coronary disease.
- Symptoms acute onset of visual • disturbance and right-sided weakness





T2W

DWI, ADC and T2w images show old stroke of the left occipital lobe in 2014

DWI









**CASE 1: OLD STROKE** 

Directional encoded color (DEC) images in 2014 show loss of anisotropy of the encephalomalacia in the left occipital lobe (white arrow). There is diminished inferior fronto-occipital/inferior longitudinal fasciculus (red arrow)

Tractography in 2014 shows the left occipital encephalomalacia (white arrow) and displacement/ diminution of the fiber tracts in the left occipital lobe (green arrow)







FLAIR T1 with contrast MR images obtained in 2012 showed well-defined extra-axial mass involving the planium sphenoidale compatible with meningioma (white arrow)

### CASE 2: PLANUM SPHENOIDALE MENINGIOMA

- 66 year old with history of HTN, diabetes mellitus, and ischemic stroke.
- Patient has known history of stable meningioma involving planum sphenoidale





MR images obtained in 2014 showed welldefined extra-axial mass involving the planium sphenoidale compatible with meningioma (white arrow)



FLAIR

T1 with contrast



### **CASE 2: PLANUM SPHENOIDALE MENINGIOMA**

FA map shows the mass without internal anisotropy (yellow arrow)







Tractography shows deviation of the right uncinated fasciculus/ inferior fronto-occipital fasciculus (red arrow). Normal contralateral tract on the left (blue arrow)

Directional encoded color (DEC) map shows splaying of the uncinated fasciculus/inferior fronto-occipital fasciculus by the mass (white arrow). The normal inferior longitudinal fasciculus/inferior fronto-occipital fasciculus (red arrow)





T1 post contrast shows ring enhancing mass in the left fronto-parietal lobe (white arrow)

### **CASE 3: GLIOBLASTOMA MULTIFORME**

- 59 year old with HTN and gout.
- Symptoms 2 days of word finding difficulty



FLAIR: Mass with vasogenic edema (white arrow)



Marked elevation of Choline peak (red arrow)



Large lipid peak (red arrow)

MR Spectroscopy shows elevated choline and lipid peaks indicating high grade tumor



### **CASE 3: GLIOBLASTOMA MULTIFORME**



FA map shows the mass creates an area void of normal anisotropy (white arrow)





DEC map shows the mass (white arrow) results in an area void of normal anisotropy. Displacement and partial destruction of the left superior longitudinal fasciculus (red arrow)





T1 with contrast

Well-defined ring enhancing lesion in the right periventricular white matter (yellow arrow). The lesion is hyperintense on DWI and FLAIR

**FLAIR** 



- 24 year old male with hypertension and complex partial seizures, blindness, and left extremity weakness.
- Multiple lesions are identified on brain MRI
- Brain biopsy demonstrated histopathological features of a demyelinating process, most likely multiple sclerosis (MS)



DWI



Additional ring enhancing lesion in the left temporal lobe (white arrow)



### **CASE 4: MULTIPLE SCLEROSIS**







FA map shows reduced anisotropy on the right (blue arrow) due to the presence of the lesion



Tractogrpahy shows destruction of fiber tract (red arrow) by the lesion in the right periventricular parenchyma



Demyelinating lesion (white arrow) with destruction of the fiber tract of the right corona radiate. Note the normal corona radiate on the left (yellow arrow)



# Limitations of Diffusion Tensor Imaging

- Diffusion tensor imaging characterizes the principal eigenvector but lacks the angular resolution to characterize crossing fiber tracts well
  - Imaging methods have been developed to overcome this limitation, such as diffusion spectrum imaging (DSI) and Q-ball imaging, but they take longer to acquire.
- Current DTI tractography algorithms can only estimate an approximation of the true course of the fiber tracts by interpolating the most probable course between adjacent voxels utilizing the directions of maximum diffusivity (maximum diffusion coherence).
- Current quantitative limitations of DTI tractography preclude accurate and precise measurement of the number of fibers within a given region of interest or tract.
- The lower fractional anisotropy within edematous brain parenchyma can prematurely interrupt the DTI tractography tracking algorithm, interrupting the fiber tract and overestimating the true margin of a pathological process, such as a tumor.
  - Lowering the threshold of fractional anisotropy can result in increased noise and erroneous tract elongation.
- User defined tract prolongation thresholds can limit reproducibility.



### Conclusion

- DTI is a relatively new advanced magnetic resonance imaging technique that makes possible exquisite characterization of the white matter tracts of the brain as well as a broad spectrum of neuropathological processes.
- DTI and tractography are currently not broadly utilized, and there are technical limitations to overcome.
- DTI is becoming more readily available, and its many adjunctive clinical imaging applications provide the radiologist and clinician with more precise insight into various neuropathophysiologic processes which may help better guide patient management.



### **THANK YOU!**

### References

#### ARTICLES

- Hagmann P, Jonasson L, Maeder P, Thiran JP, Wedeen VJ, Meuli R. Understanding diffusion MR imaging techniques: from scalar diffusion-weighted imaging to diffusion tensor imaging and beyond. *Radiographics*. 2006 Oct;26 Suppl 1:S205-23.
- Nucifora PG, Verma R, Lee SK, Melhem ER. Diffusion-tensor MR imaging and tractography: exploring brain microstructure and connectivity. *Radiology*. 2007 Nov;245(2):367-84.
- Melhem ER, Mori S, Mukundan G, Kraut MA, Pomper MG, van Zijl PC. Diffusion tensor MR imaging of the brain and white matter tractography. AJR Am J Roentgenol. 2002 Jan;178(1):3-16.
- Huston JM, Field AS. Clinical applications of diffusion tensor imaging. Magn Reson Imaging Clin N Am. 2013 May;21(2):279-98.
- Stephen M. Hesseltine, MD; Yulin Ge, MD; Meng Law, MD, FRACR. Applications of diffusion tensor imaging and fiber tractography. Applied Radiology. 2007 May; Vol 36 Number 5. Retrieved from <u>www.appliedradiology.com</u>
- Jellison BJ, Field AS, Medow J, Lazar M, Salamat MS, Alexander AL. Diffusion tensor imaging of cerebral white matter: a pictorial review of physics, fibertract anatomy, and tumor imaging patterns. AJNR Am J Neuroradiol. 2004 Mar;25(3):356-69

#### BOOKS

- Schmahmann JD, Pandya DN. *Fiber Pathways of the Brain*. 2006. New York, NY: Oxford University Press.
- Catani M, Thiebaut de Schotten. Atlas of Human Brain Connections. 2012. New York, NY: Oxford University Press.
- Stieltjes B, Brunner RM, Fritzsche KH, and Frederik BL. *Diffusion Tensor Imaging and Atlas*. 2013. Berlin, Germany: Springer.
- Arfken G, Webers H, Harris F. Mathematical Methods for Physicists, Seventh Edition: A Comprehensive Guide. 2012. Academic Press; 7th edition
- J. A. Schouten. Tensor Analysis for Physicists, Second Edition. 2011. Dover Publications; 2nd Edition

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