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The Basic physics of Diffusion-weighted Imaging (DWI) and Diffusion Tensor Imaging (DTI)

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Introduction

- **Magnetic resonance images may provide excellent contrast because of variations in:**
  - water proton density,
  - relaxation times (which reflect macromolecular content),
  - molecular Brownian motion (diffusion imaging),
  - flow,
  - the effects of contrast agents (CAs),
  - chemical composition (e.g., concentration of amides or lipids, or metabolites)
  - and even mechanical properties such as elastic constants and strain rates.

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Introduction

- **Magnetic resonance imaging connotes a class of images that can portray a range of types of information available using the same instrumentation.**

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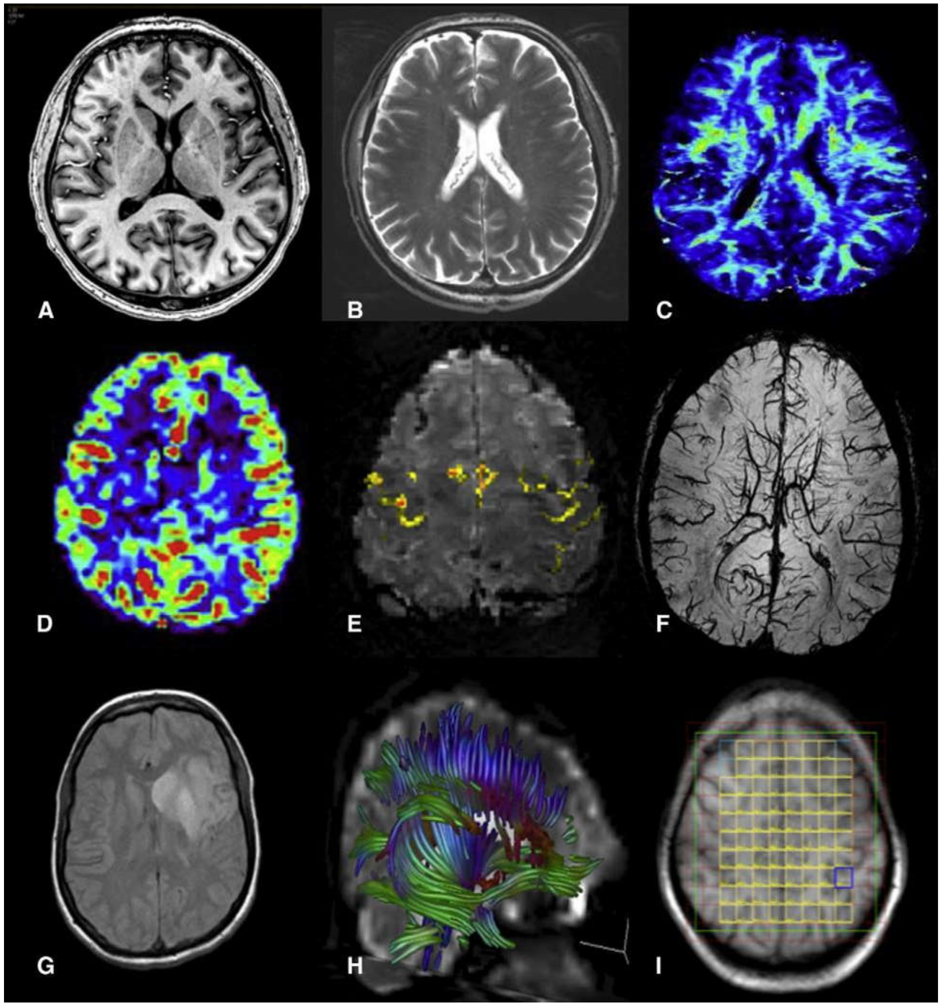

(A) T1 weighted, (B) T2 weighted, (C) a map of quantitative magnetization transfer pool ratio, (D) blood perfusion, (E) a blood oxygen level dependent (BOLD) map of activation, (F) a venogram, (G) diffusion weighted, (H) a diffusion tensor image (DTI) of white matter tracts and (I) multivoxel high-resolution MR spectra.

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MR Molecular Imaging

- **In-Direct approaches**
  - Diffusion Imaging
  - Dynamic Contrast-Enhanced MRI (Perfusion Imaging)
- **Direct approaches**
  - Magnetic Resonance Spectroscopy (MRS)
  - Use of Contrast Agents

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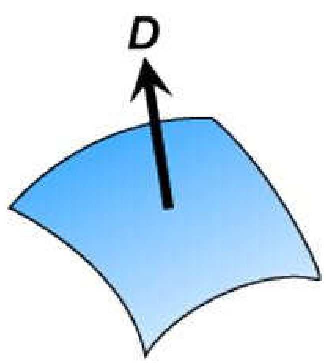
What is diffusion?

- Diffusion = Brownian motion
- Random movement of water and small molecules due to thermal collision
- Characterized by diffusion coefficient, D
- D reflects the flux of particles through a surface during a certain period of time, it therefore has units of area/time (e.g. mm^2/sec).



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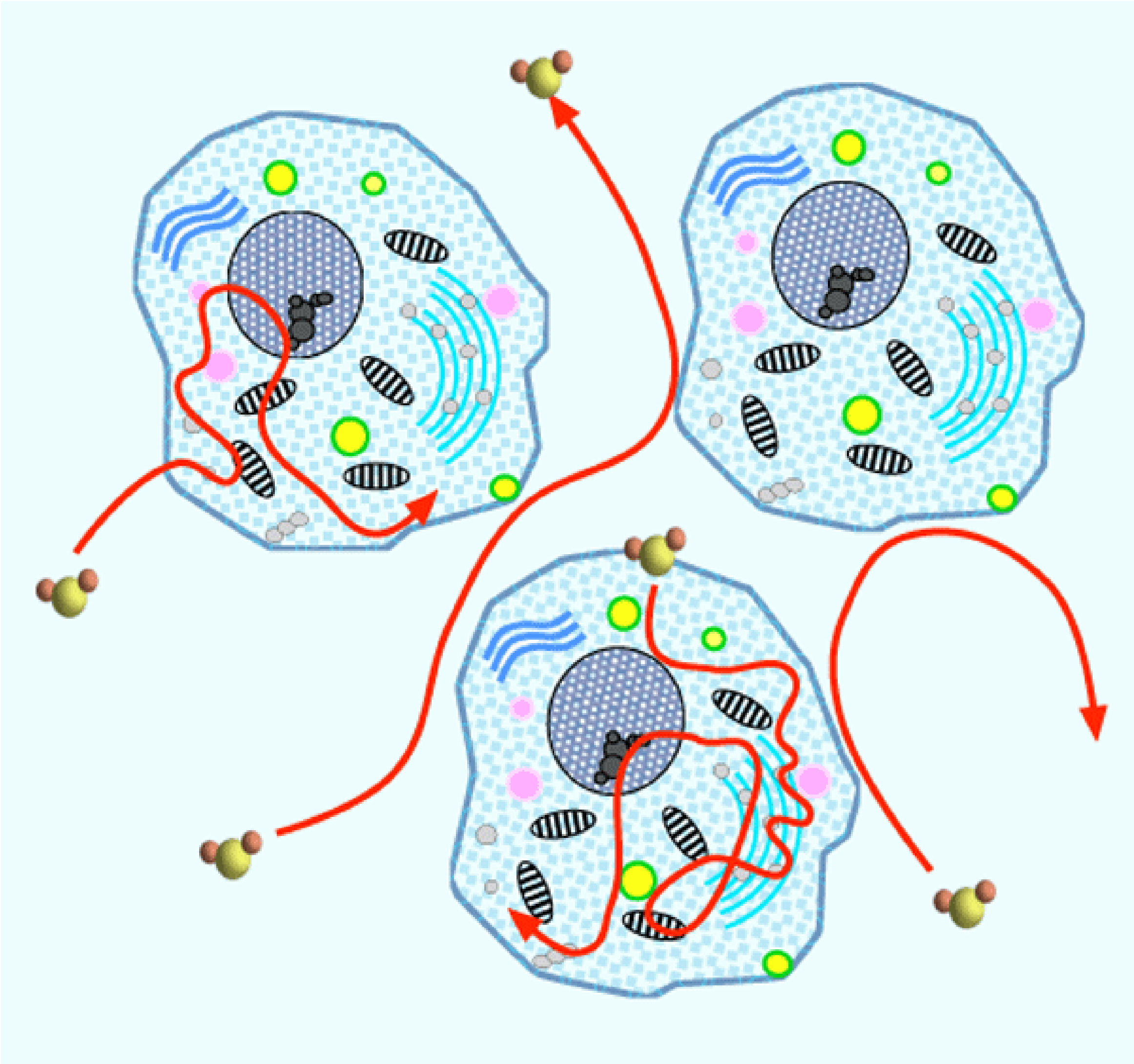
- Diffusion of water molecules is hindered in the intracellular compartment due to:

  - the presence of macromolecules
  - increased viscosity
  - multiple membranes



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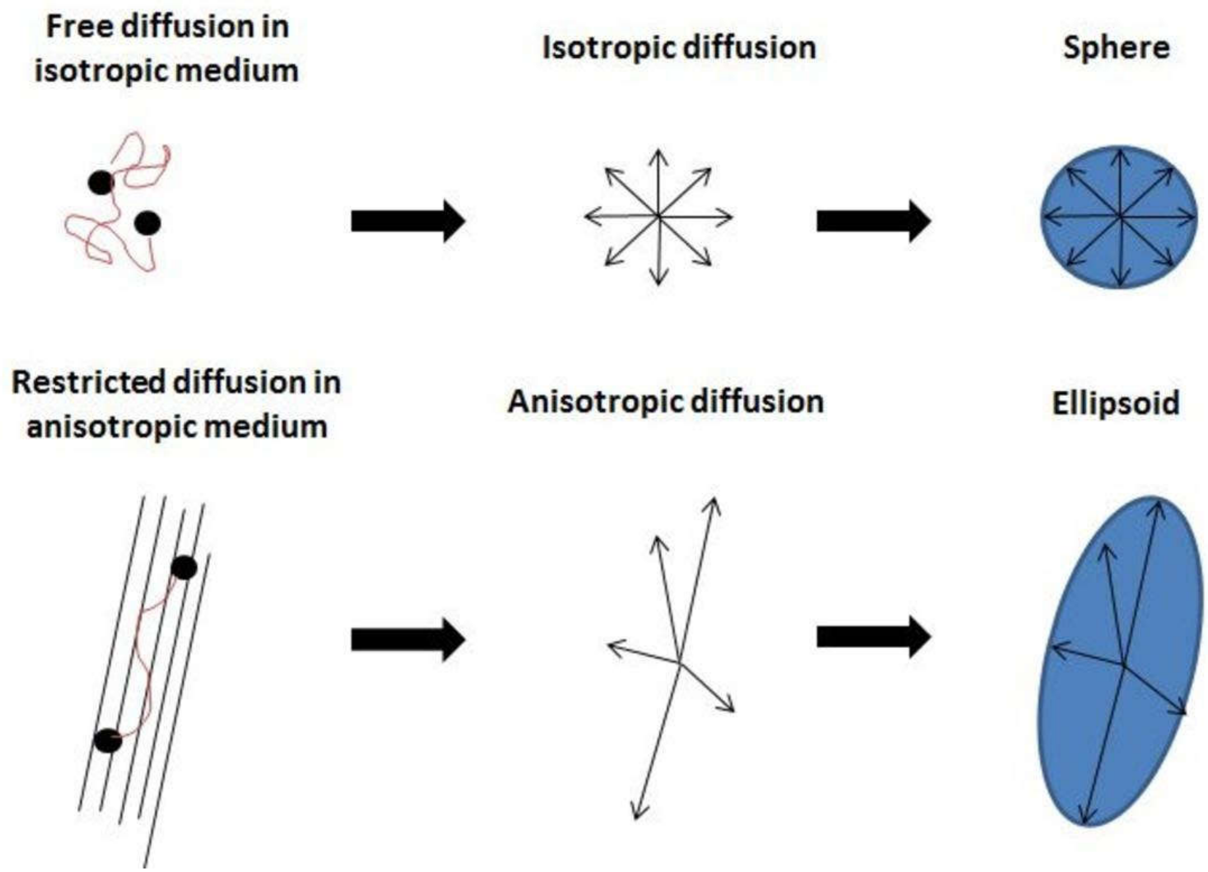
Isotropic vs Anisotropic Diffusion



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Isotropic vs Anisotropic Diffusion

- **Isotropic material**
  - Diffusion is same in every direction
  - Characterized by single diffusion coefficient (D)

- **Anisotropic material**
  - Diffusion varies with direction
  - Characterized by diffusion tensor, a 3×3 matrix

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Diffusion Tensor

$$\mathcal{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

$$\mathcal{D}_{isotropic} = \begin{bmatrix} D & 0 & 0 \\ 0 & D & 0 \\ 0 & 0 & D \end{bmatrix}$$

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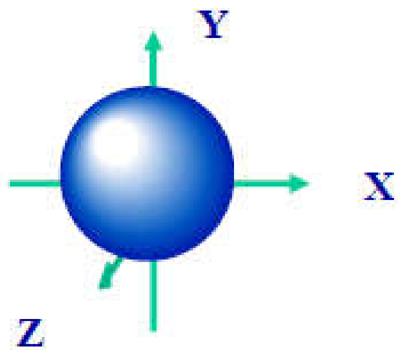
Isotropic vs Anisotropic Diffusion

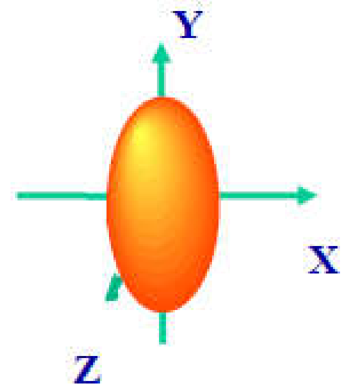
- Isotropic diffusion



$$D_{xx} = 1\ [mm^2/s]$$
$$D_{yy} = 1\ [mm^2/s]$$
$$D_{zz} = 1\ [mm^2/s]$$

$$D = D_{mean} = 1\ [mm^2/s]$$

- Anisotropic diffusion



$$D_{xx} = 0.6\ [mm^2/s]$$
$$D_{yy} = 1.8\ [mm^2/s]$$
$$D_{zz} = 0.6\ [mm^2/s]$$

$$D = D_{mean} = 1\ [mm^2/s]$$

???

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DWI vs DTI

- DWI measures the net displacement of water

- DTI measures the degree and direction of diffusion

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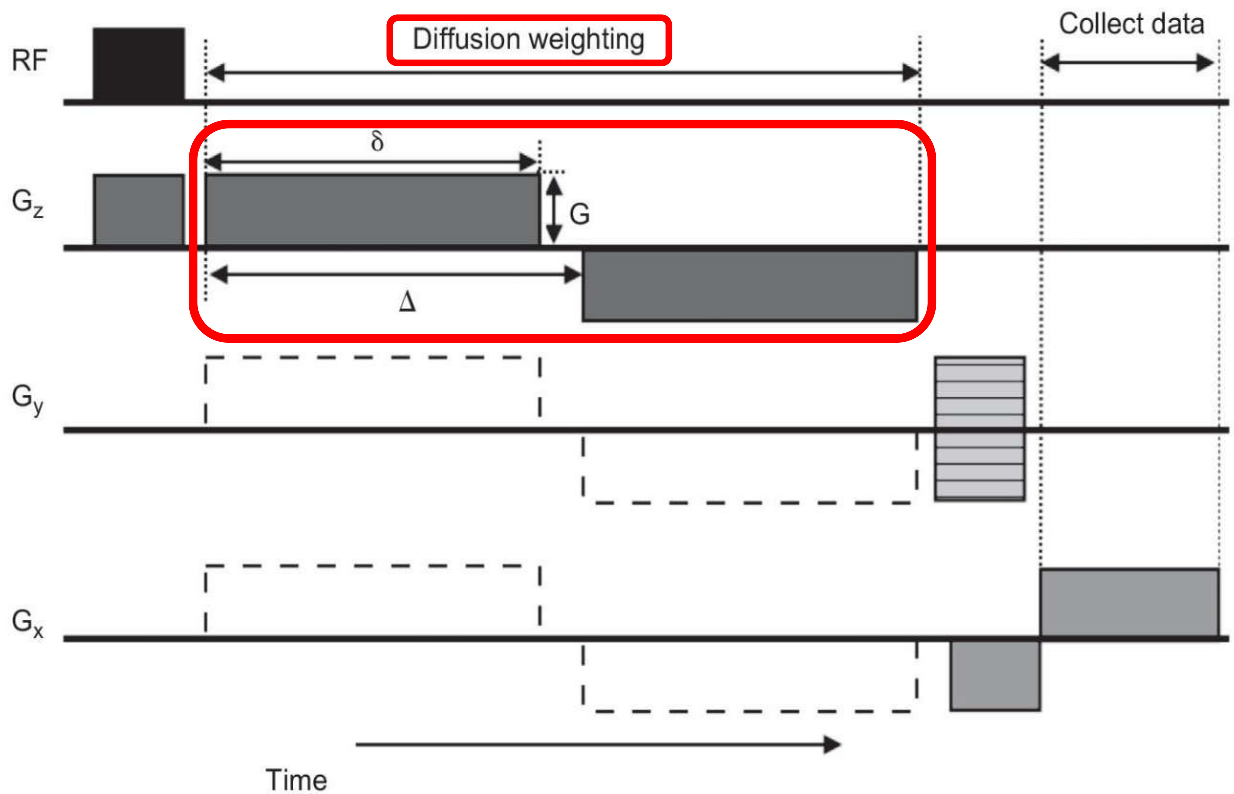
DWI or DW-MRI Mechanism

DWI pulse sequence



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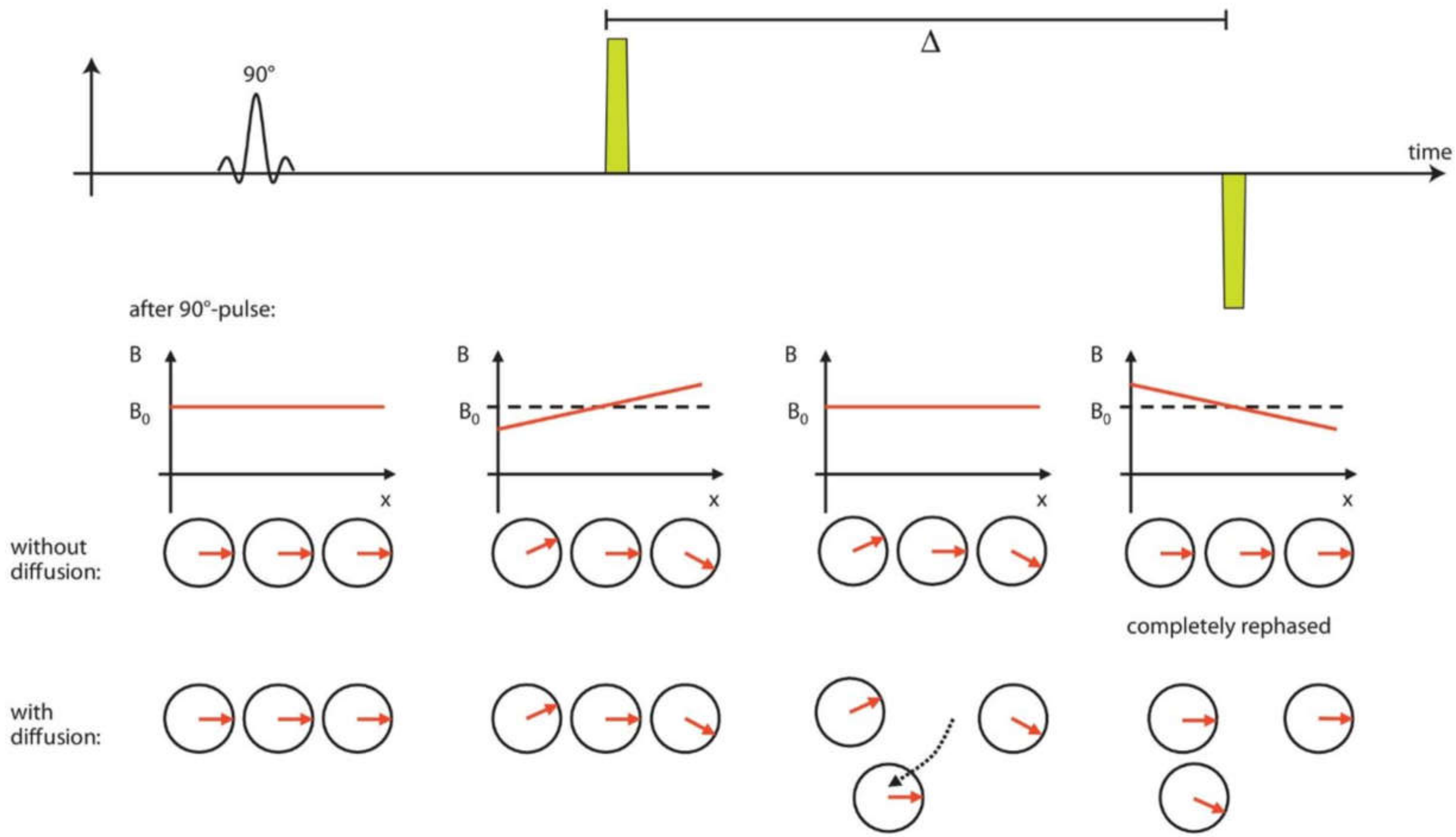
DWI or DW-MRI Mechanism



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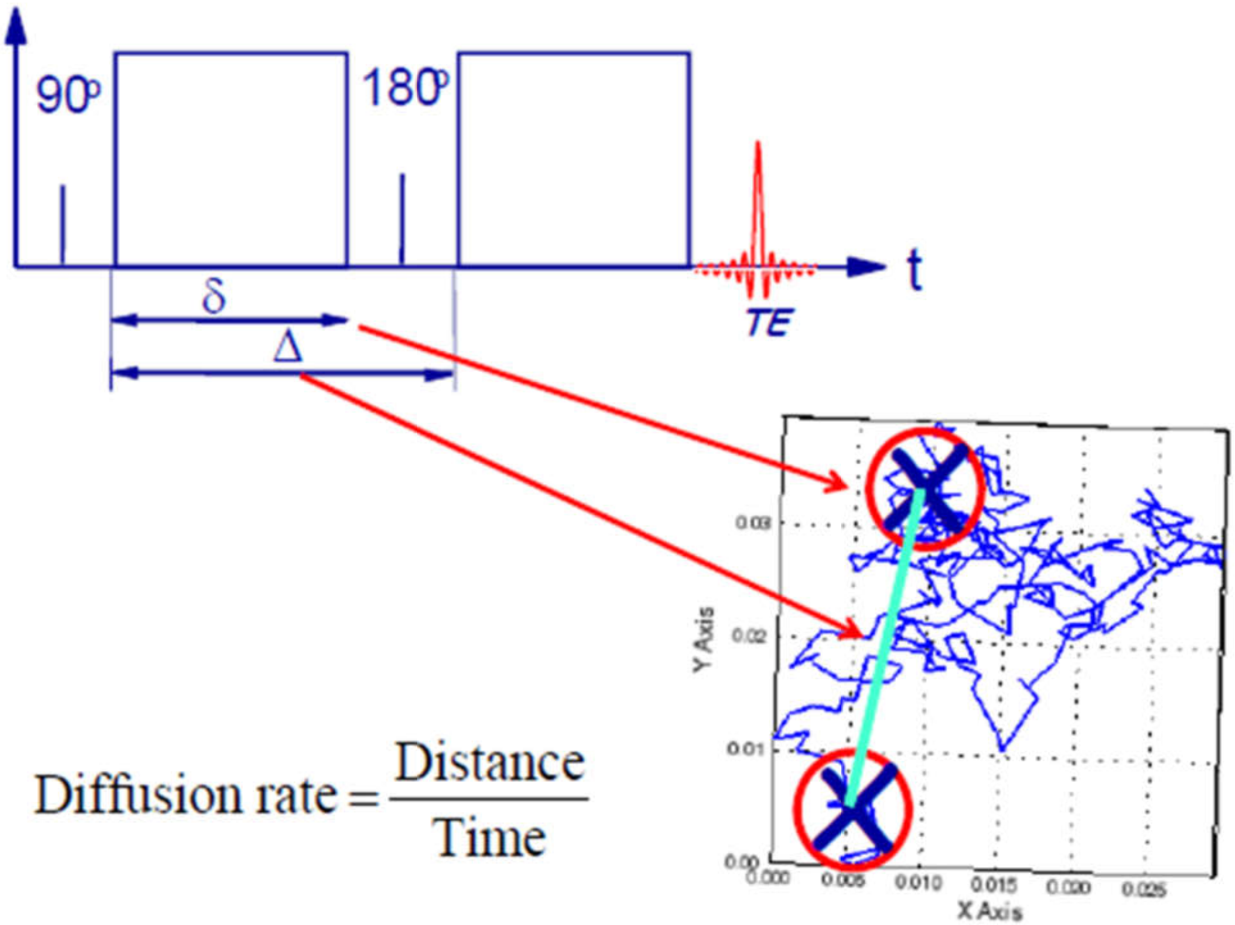

$$\text{Diffusion rate} = \frac{\text{Distance}}{\text{Time}}$$

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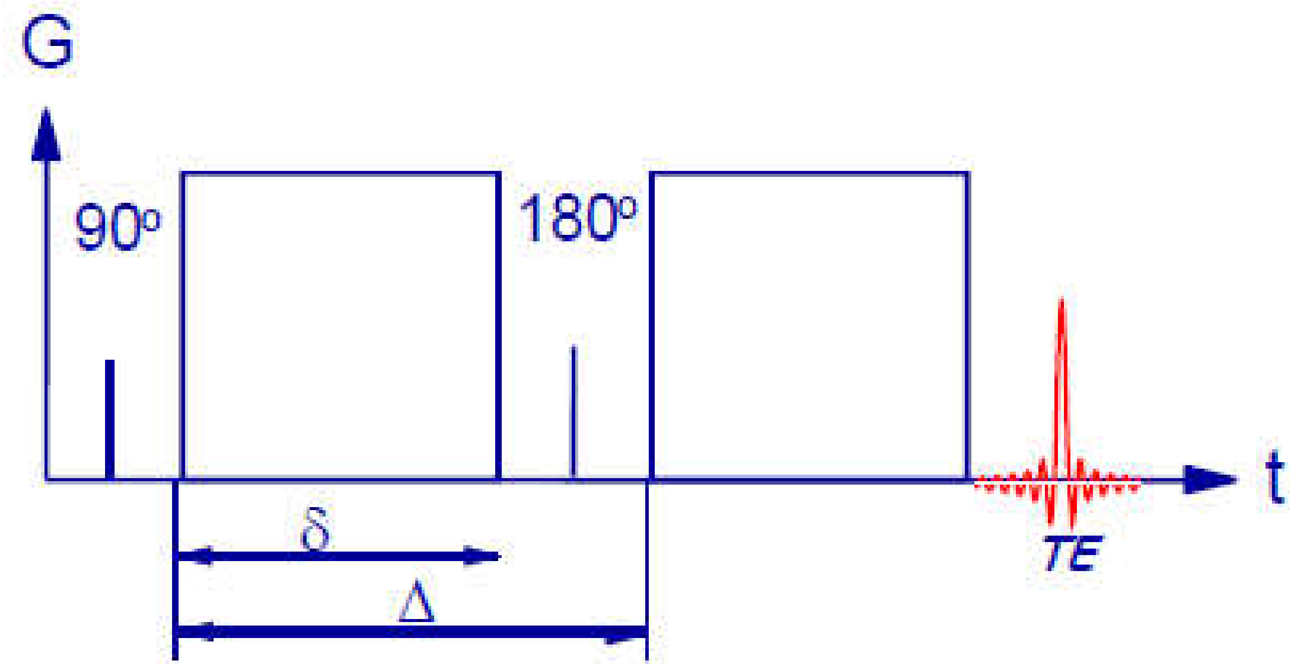
The Stejskal-Tanner Sequence for DWI



b-value (sensitivity) $\mathbf{b = \gamma^2 G^2 \delta^2 T_D\ [s/mm^2]}$

Diffusion time $\mathbf{T_D = \Delta - \delta/3}$

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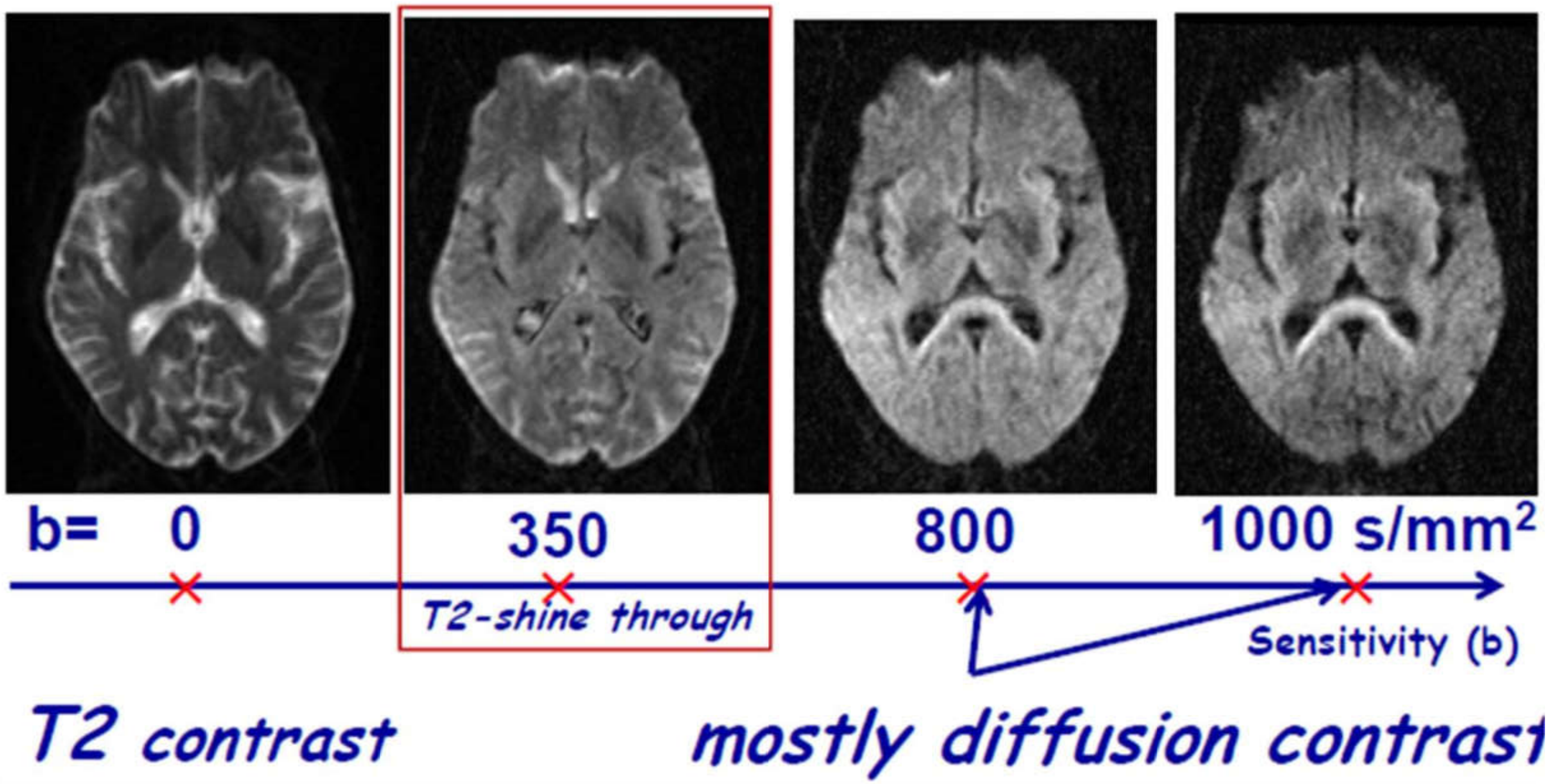
DWI Signal Equation

$$S = S_0 \cdot e^{-TE/T2} \cdot e^{-b \cdot D}$$



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T2-effects in DWI (T2 shine-through)

$$S = S_0 \cdot e^{-TE/T2} \cdot e^{-b \cdot D}$$

- DW images are both T2- and Diffusion-weighted
- Long T2 lesions can increase DWI signal mimicking restricted diffusion
- Clarified by reviewing ADC images (Apparent Diffusion Constant images)

$$ADC = \frac{-\ln(\frac{S}{S_0})}{b} \quad [mm^2/s]$$

$$S = S_0 \, e^{-b \cdot ADC}$$

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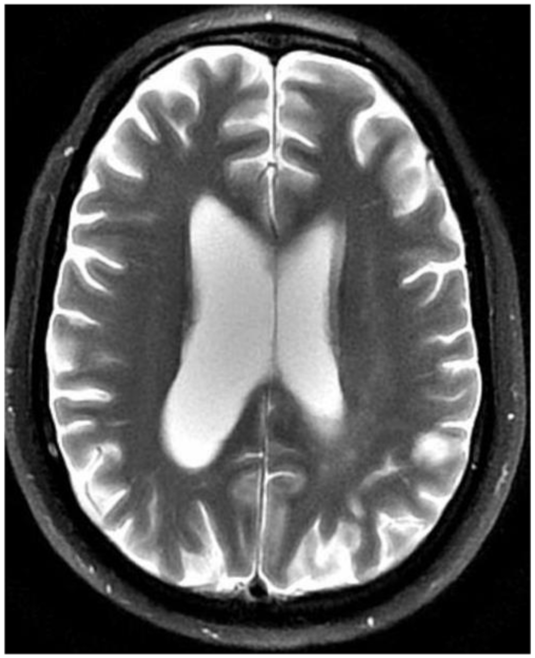
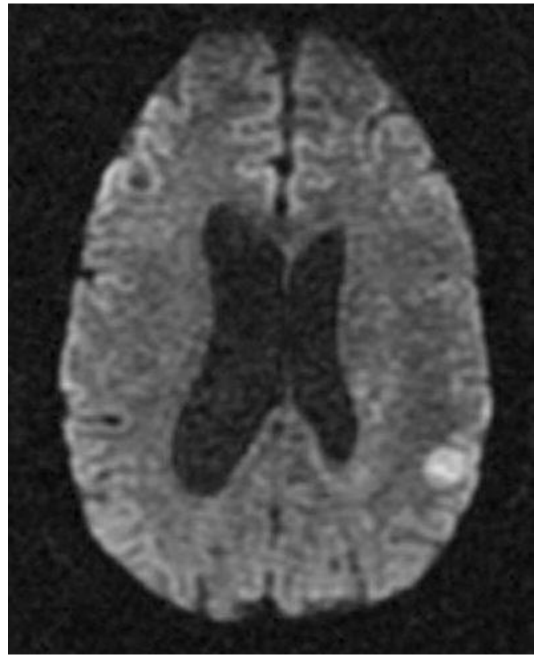


T2-weighted SE image



Trace DW image

ADC Map

Rounded left parietal lesion (a glioma) shows moderate brightness on Trace DW image. This is not due to restricted diffusion, however, as the lesion is also bright on the ADC map (implying increased diffusivity). The T2-weighted SE image confirms the brightness on the Trace image is a T2 "shine-through" effect.

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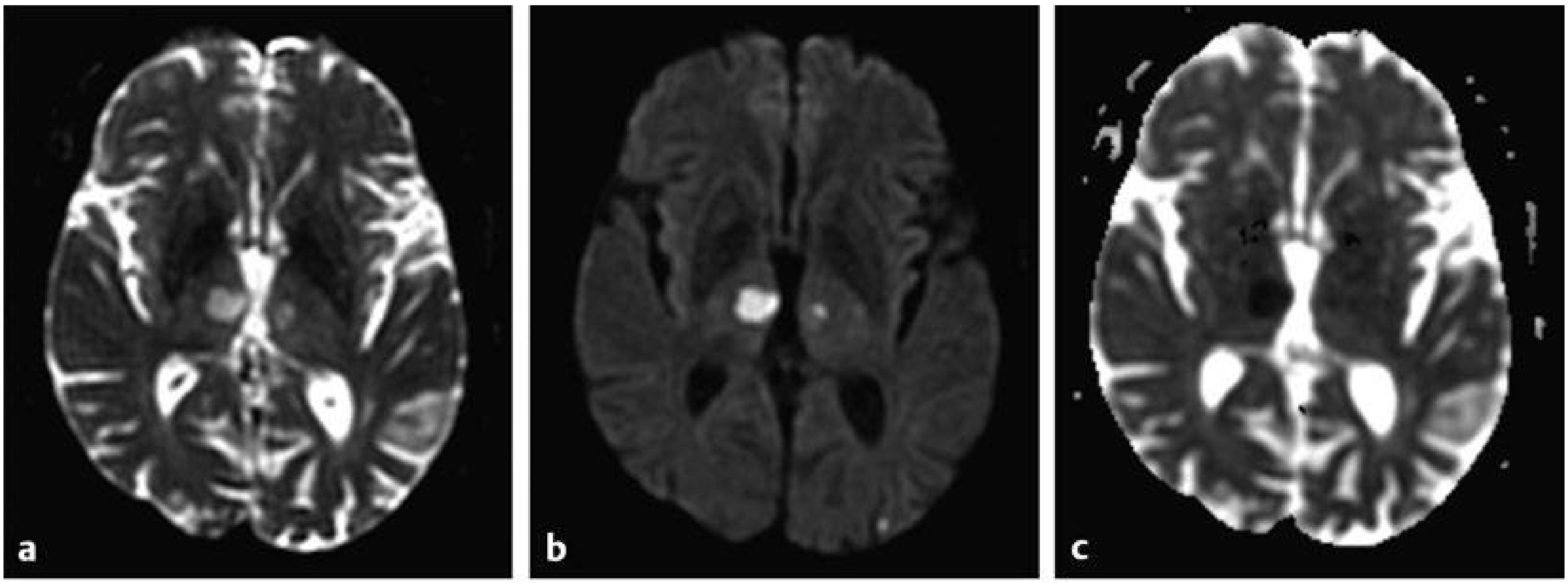
DWI vs ADC-map



b = 0 (T2-W)   **b = 1000 (DWI)**   **b = 1000 (ADC)**

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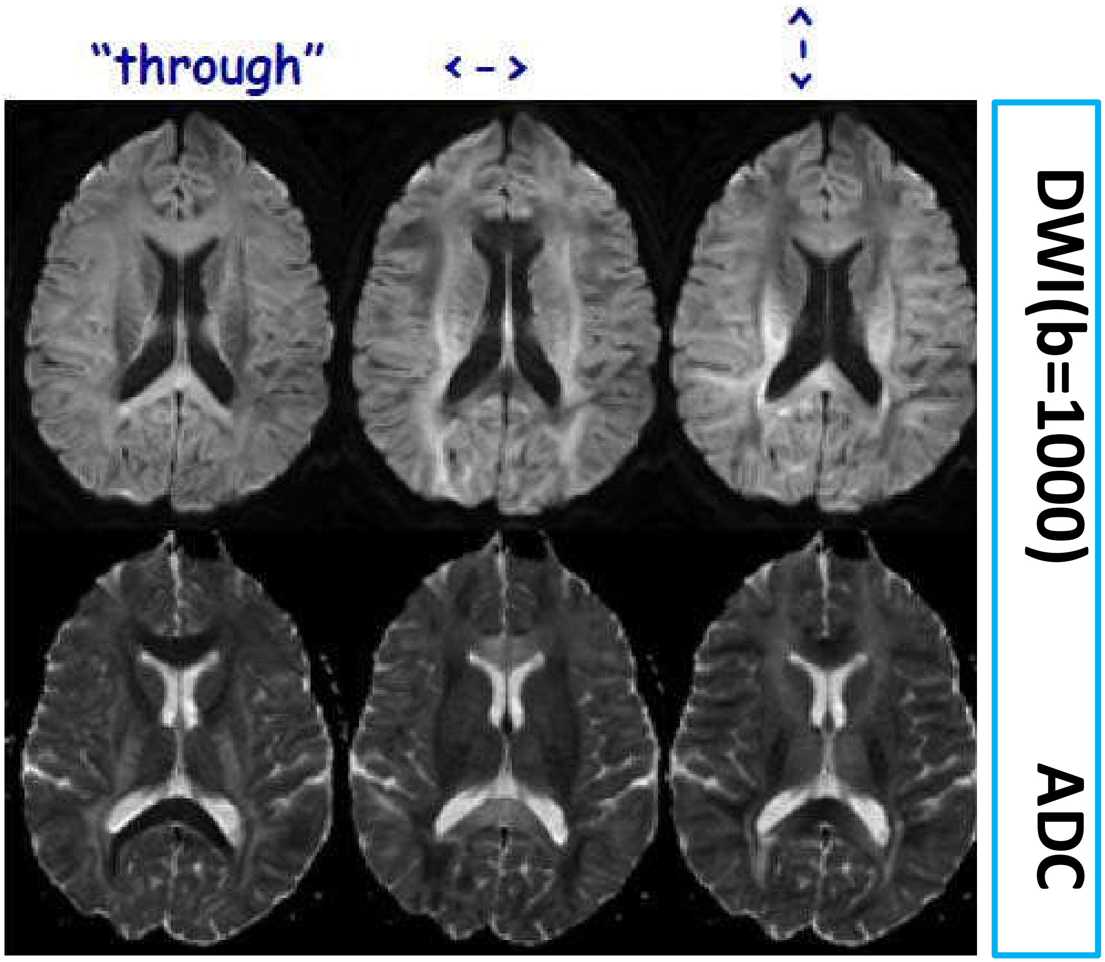
Directional Dependent Diffusion



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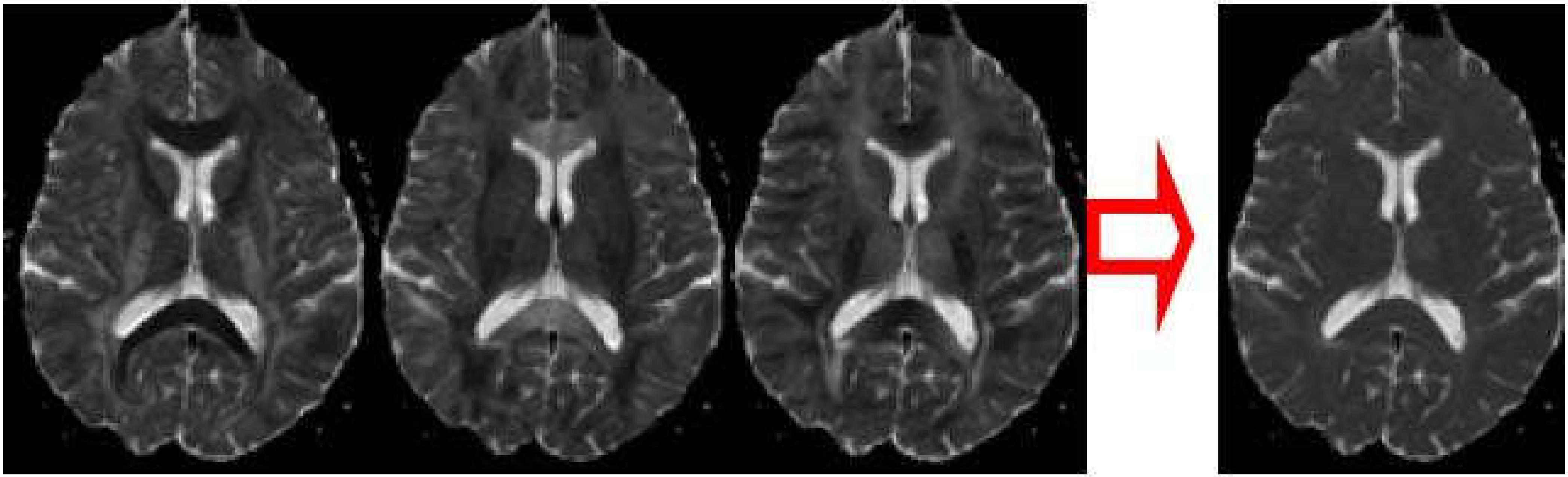
Slice Read Phase "Trace"



$$\frac{ADC_{zz} + ADC_{yy} + ADC_{xx}}{3} \Rightarrow ADC_{mean}$$

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Selection of Optimal b-value

- **The "optimal" choice of *b*-value is not clearly defined and depends upon:**
  - Field strength
  - Number of signals averaged
  - Anatomical features
  - Predicted pathology

- The brains of neonates and young infants have much higher water content than adults with T2- and ADC-values 25-40% longer.
  - In these patients the *b*-value is often made shorter, in the range of 600-700 s/mm^2.

- **A useful rule of thumb is to pick the *b*-value so that ($b \times$ ADC) ≈ 1.**

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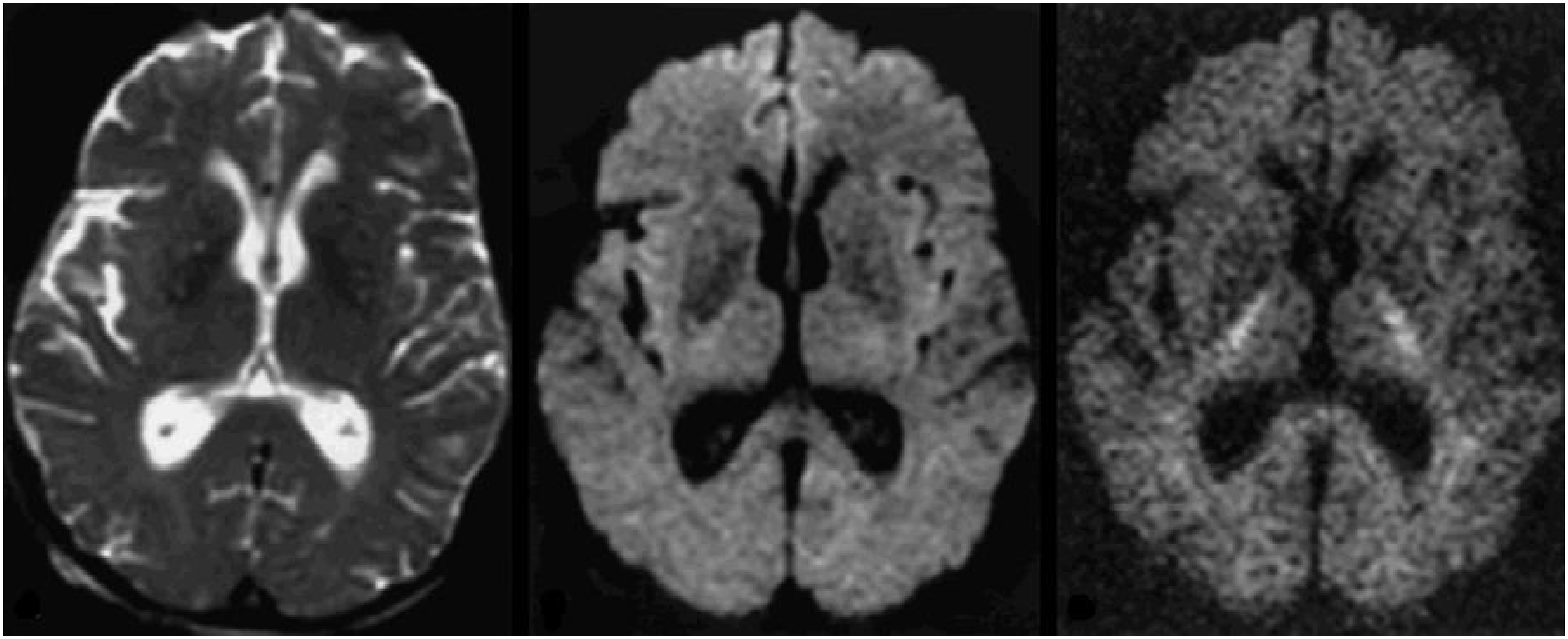

Brain DWI images using 3 different *b*-values (0, 1000, and 3000 s/mm²)

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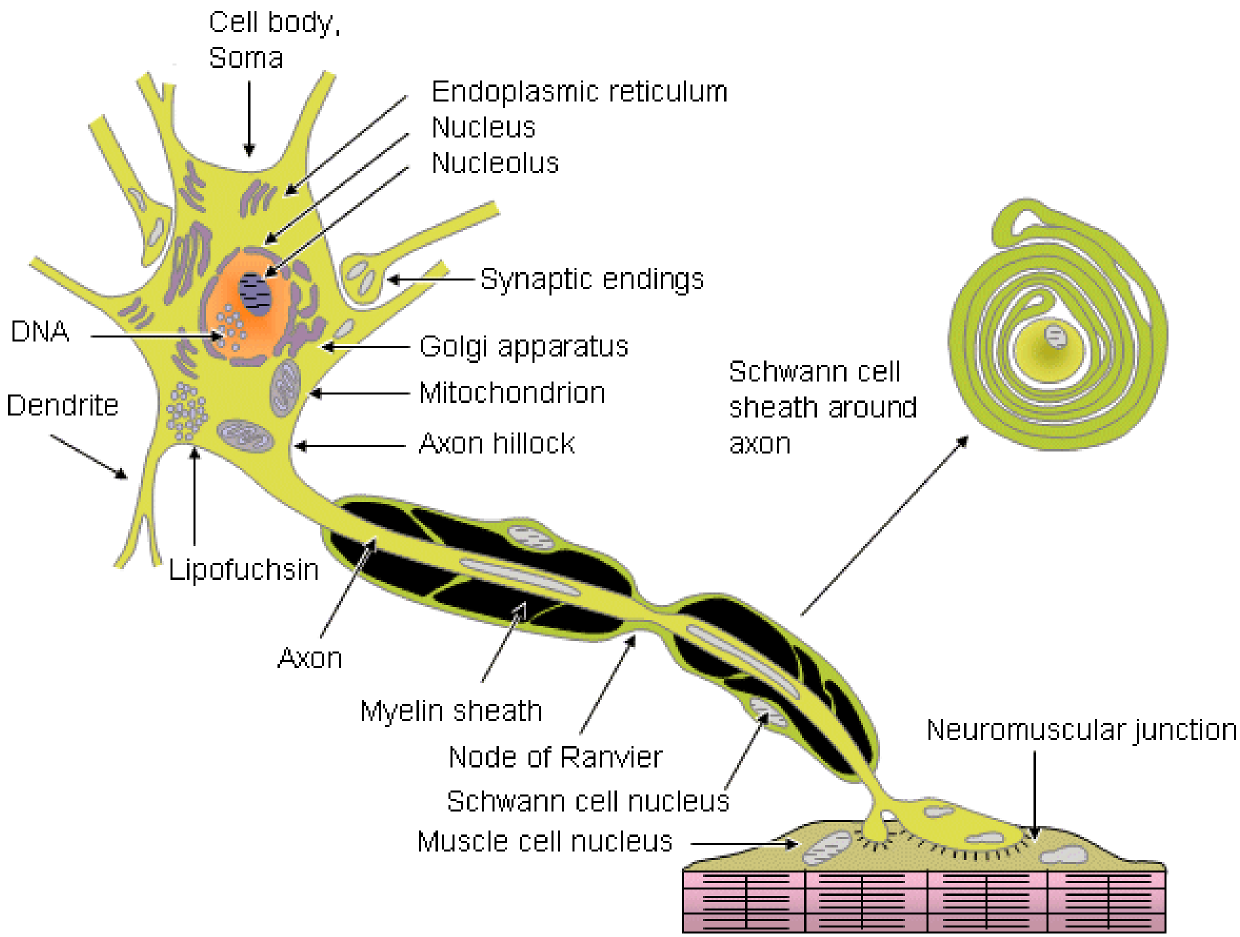
Diffusion Tensor Imaging (DTI)



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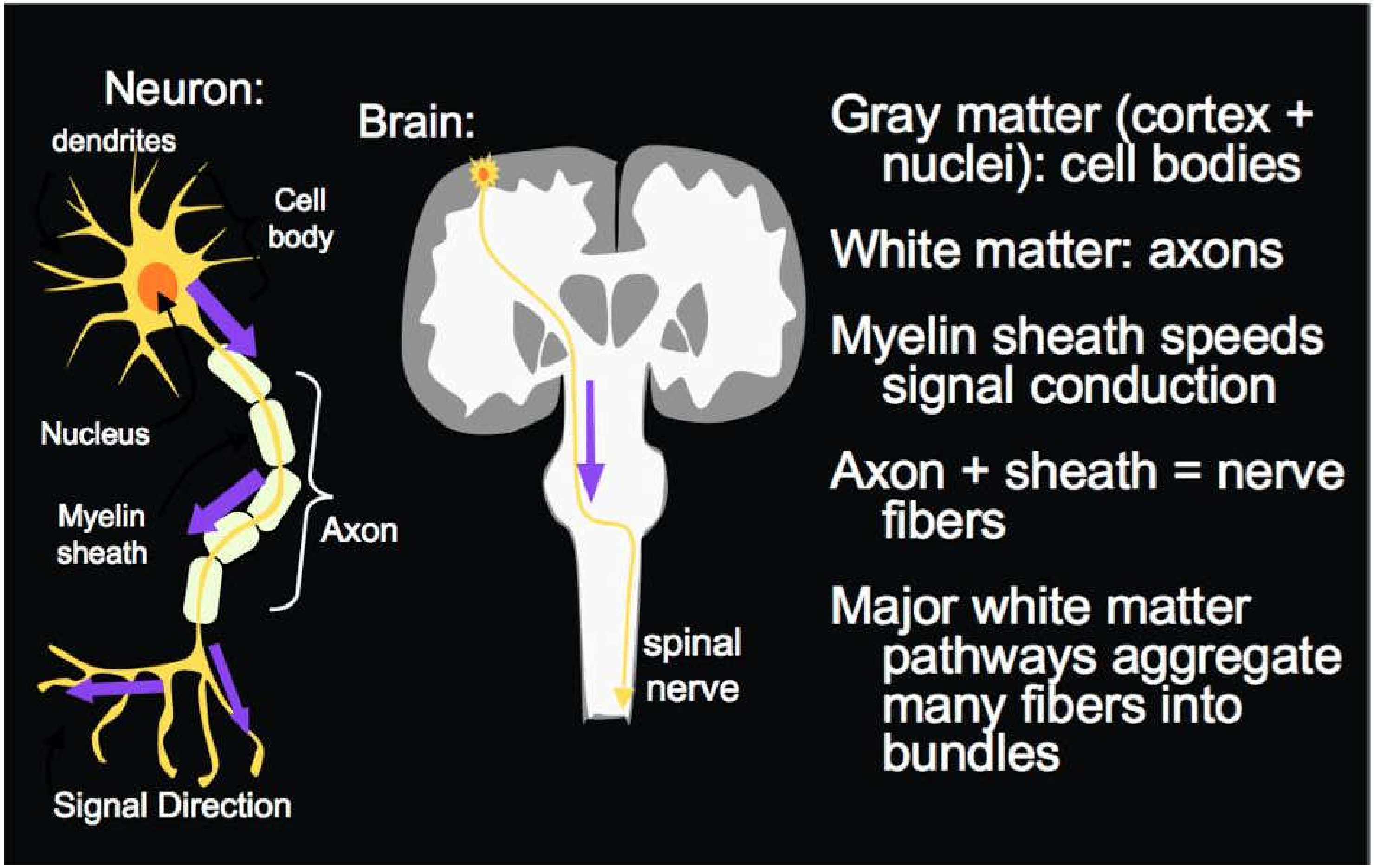

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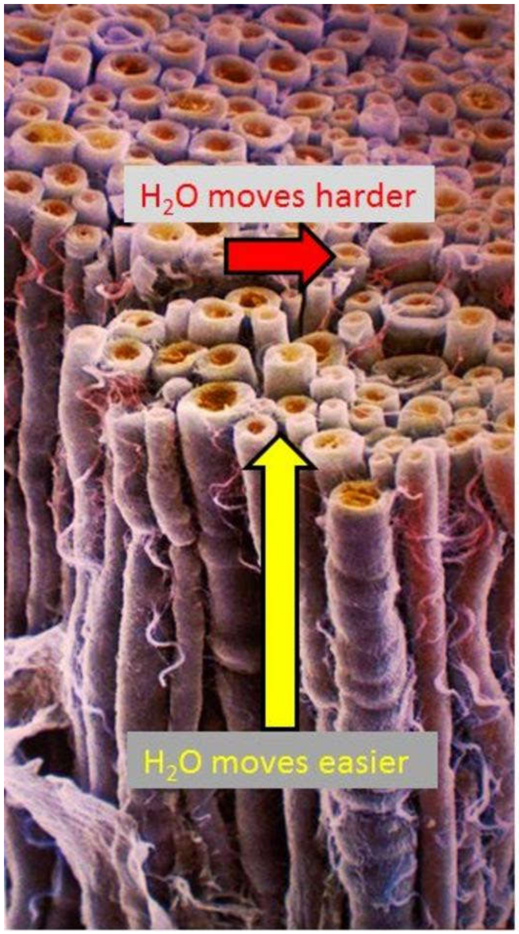

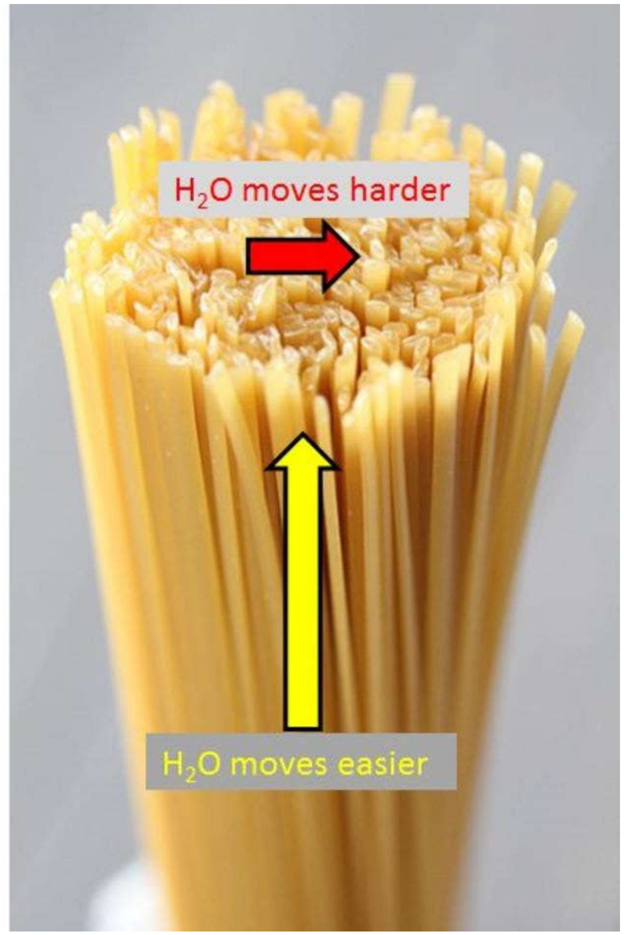

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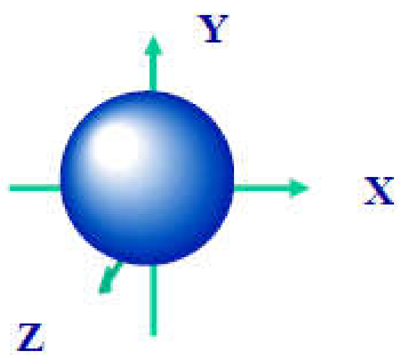
Isotropic vs Anisotropic Diffusion

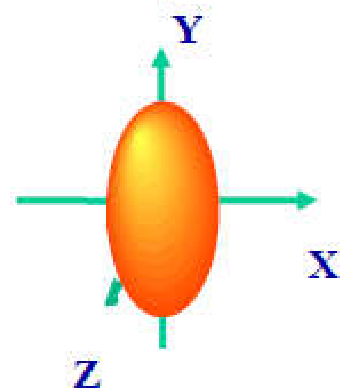
- Isotropic diffusion



$$ADC_{xx} = 1\ [mm^2/s]$$
$$ADC_{yy} = 1\ [mm^2/s]$$
$$ADC_{zz} = 1\ [mm^2/s]$$

$$\mathbf{ADC_{mean} = 1\ [mm^2/s]}$$

- Anisotropic diffusion



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$$ADC_{zz} = 0.6\ [mm^2/s]$$

$$\mathbf{ADC_{mean} = 1\ [mm^2/s]}$$

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- DTI measures the degree and direction of diffusion

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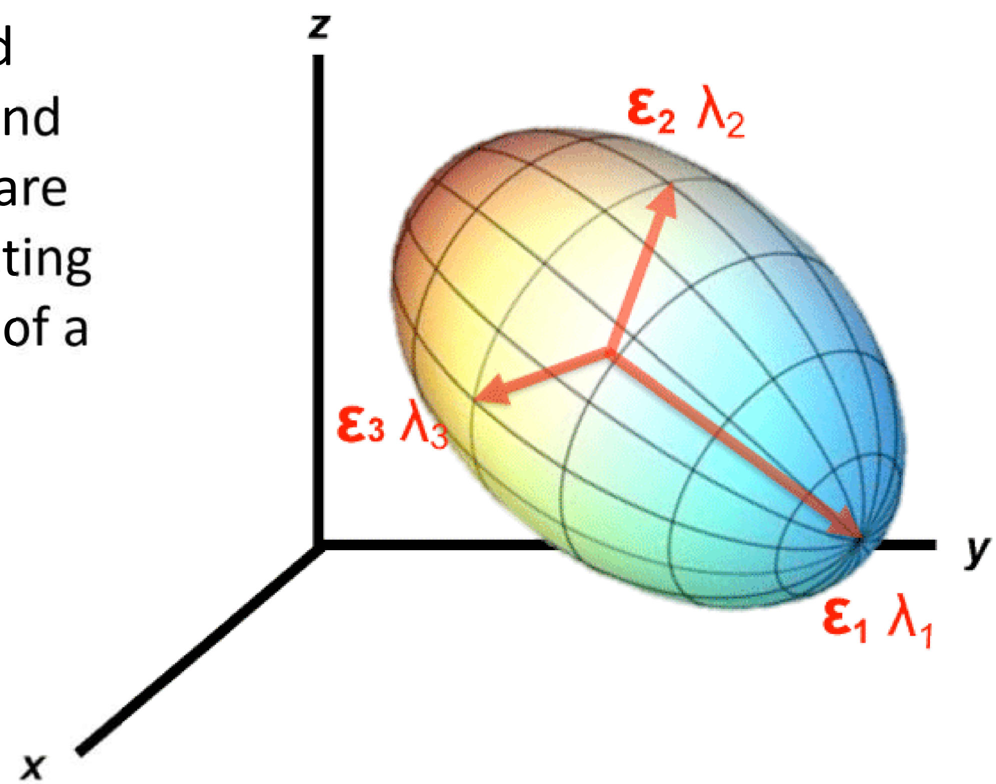
Diffusion Tensor Imaging (DTI)

- DTI comprises a group of techniques where calculated *eigenvalues* (λ_1, λ_2, and λ_3) and *eigenvectors* (ε_1, ε_2, and ε_3) are used to create images reflecting various diffusion properties of a tissue.



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Diffusion Tensor Imaging (DTI)

- "Regular" diffusion-weighted (DW) imaging produces images based on only the sum or average of the eigenvalues.

- The sum of the eigenvalues ($\lambda_1+\lambda_2+\lambda_3$) is called the trace, while their average (= trace/3) is called the mean diffusivity (MD) or apparent diffusion coefficient (ADC).

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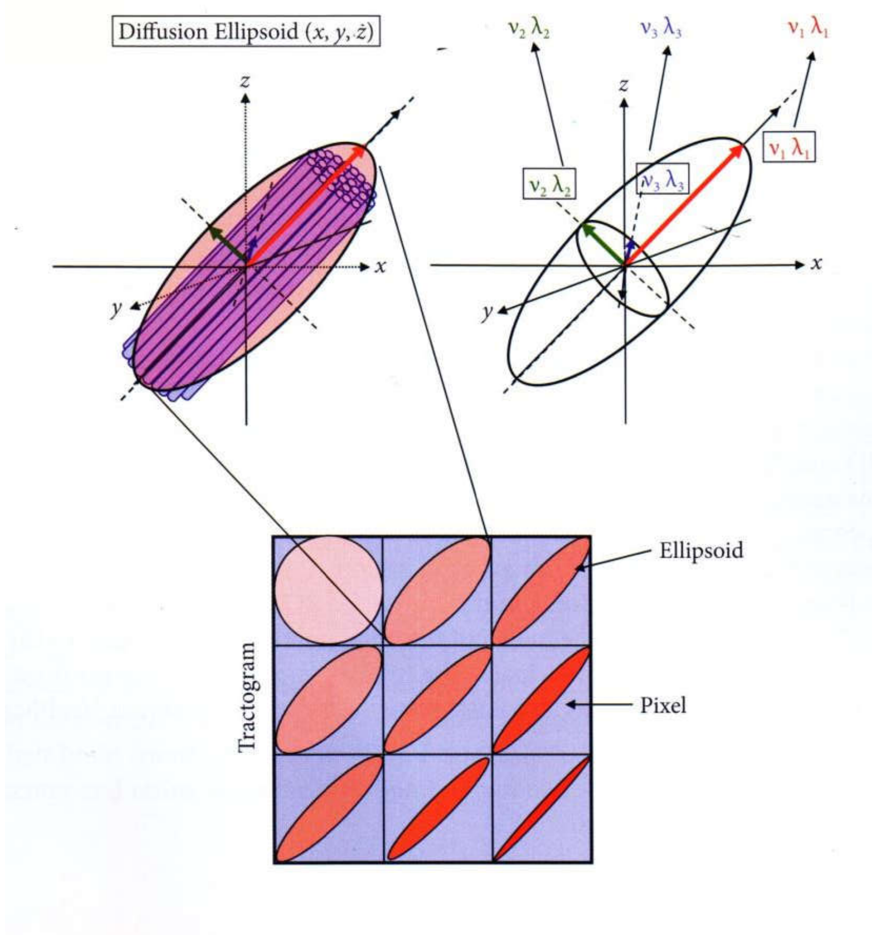

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Diffusivity Measures

- **Trace**

- Reflects the overall water content.
- Is a commonly used clinical measure, which gives an indication of the overall diffusivity in a given voxel.
- Is completely rotationally independent, and therefore unlike with ADC, changes in Tr(*D*) can be attributed solely to changes in tissue structure.

- An important metric in the assessment and diagnosis of stroke.

$$\mathrm{Tr(D)} = \lambda_1 + \lambda_2 + \lambda_3 = D_{xx} + D_{yy} + D_{zz}$$

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Diffusivity Measures

Mean Diffusivity (MD or D)

- Characterizes the overall mean squared displacement of molecules (average ellipsoid size).
- Is simply a scaled version of the trace Tr(*D*).
- Is a measure of the overall diffusivity in a particular voxel regardless of direction.
- Can be used to delineate the area affected by stroke.

$$D = \frac{Tr(D)}{3} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3} = \frac{D_{xx} + D_{yy} + D_{zz}}{3}$$

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Diffusivity Measures

Axial Diffusivity (AD)

- Axial (or longitudinal or parallel) diffusivity, $\lambda_{||}$
- Is simply the diffusivity along the principal axis of the diffusion ellipsoid and is given by λ_1

Radial Diffusivity (RD)

- Radial (or transverse or perpendicular) diffusivity, $\lambda_{\perp}$
- Is a measure used to express the diffusivity perpendicular to the principal direction of diffusion

$$\lambda_{\perp} = \frac{\lambda_2 + \lambda_3}{2}$$

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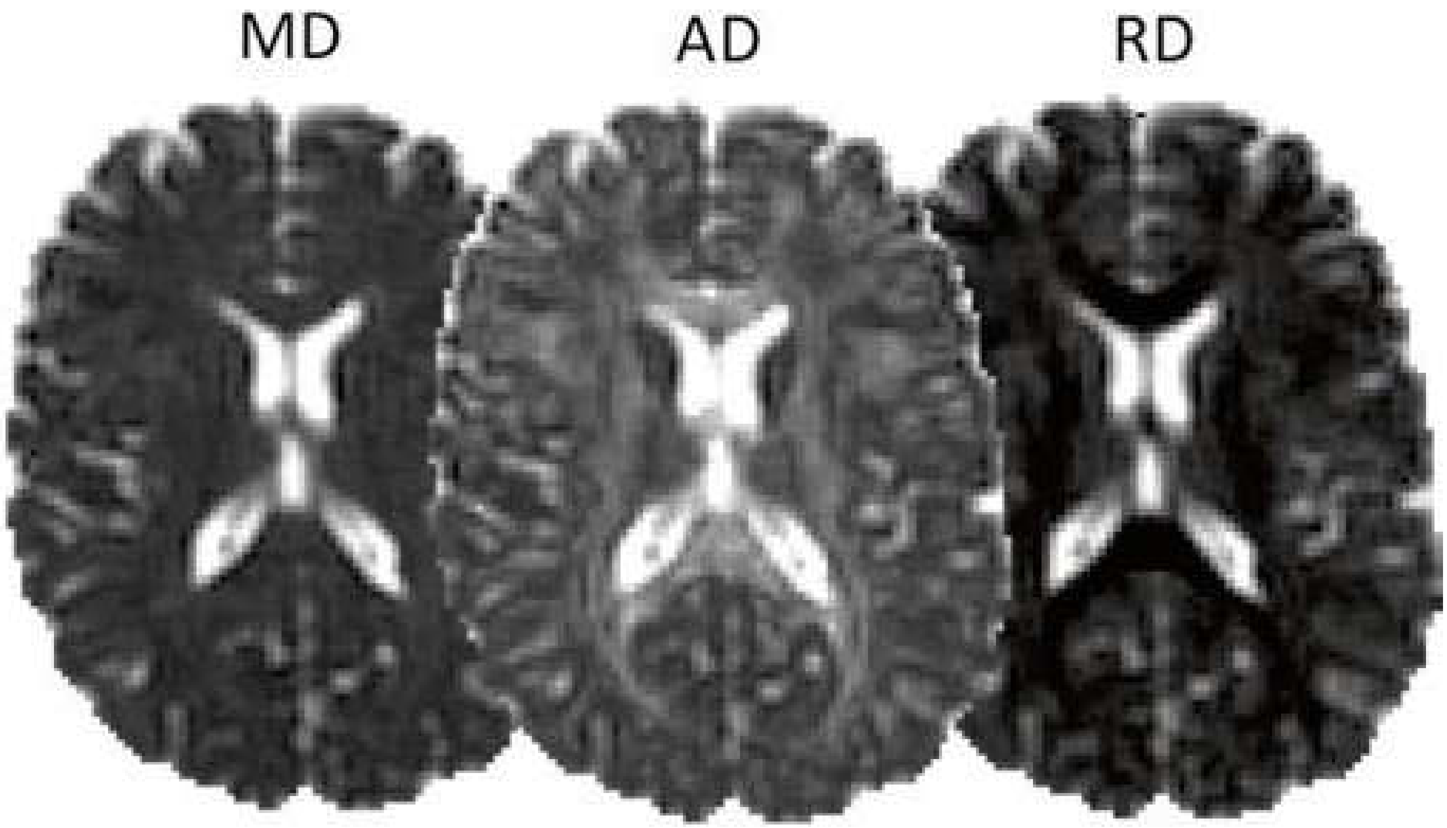

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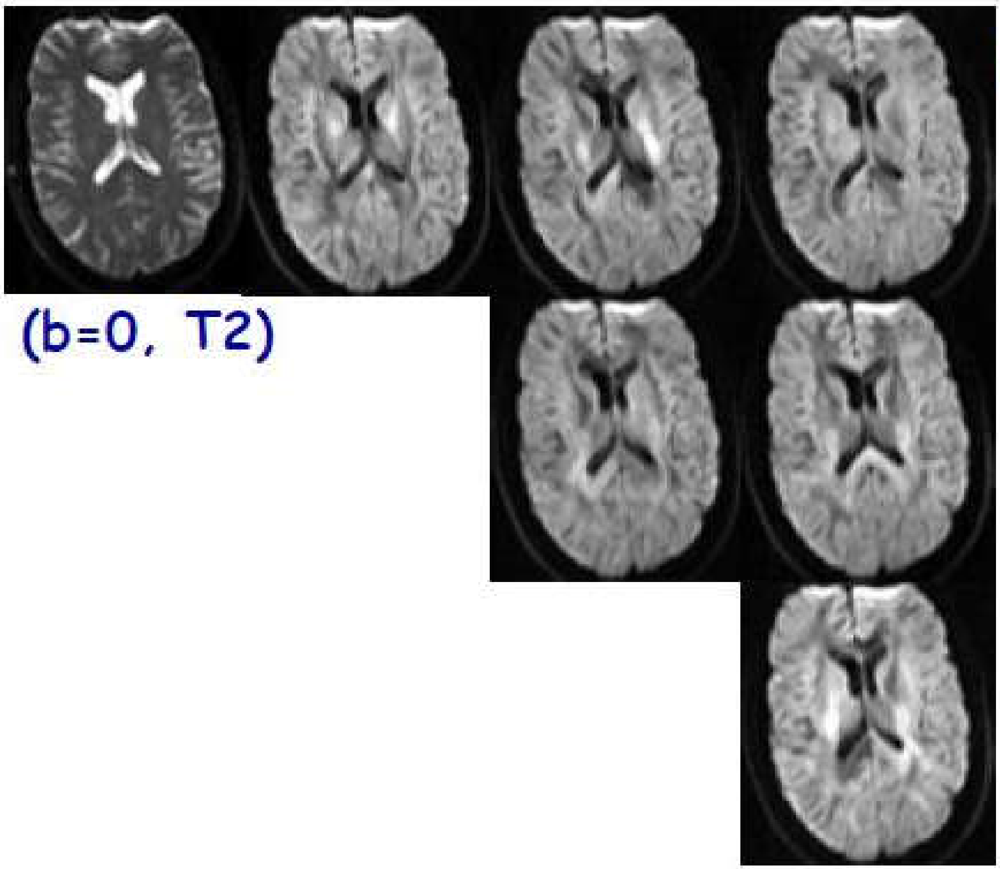
The Measurements



$(DW_{xx}, DW_{xy}, DW_{xz}, DW_{yy}, DW_{yz}, DW_{zz})$

(b=0, T2)

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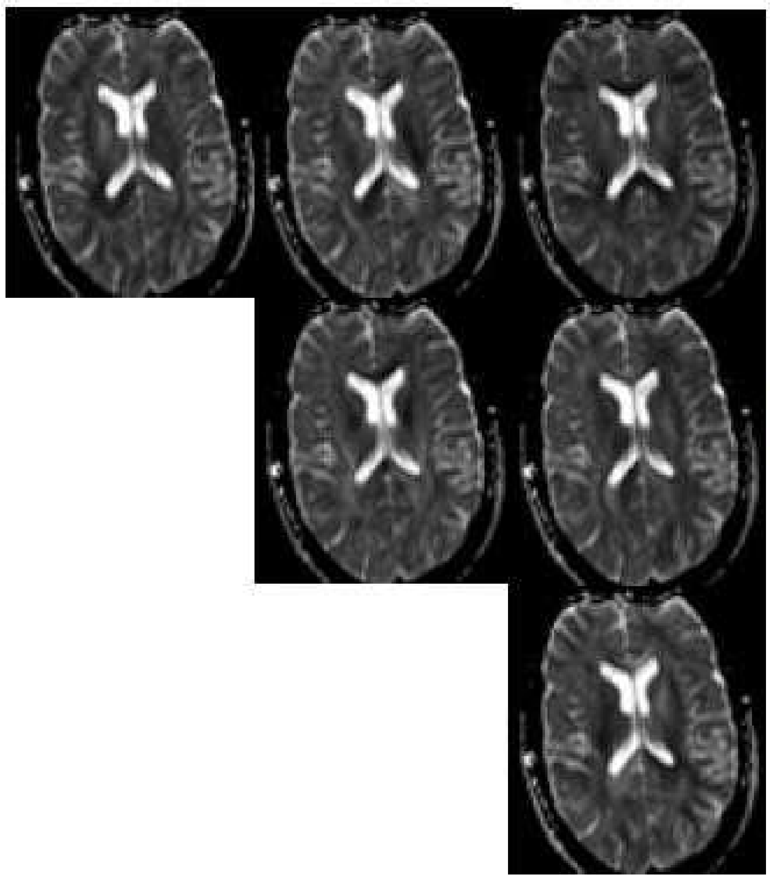
Calculations (I)



$(ADC_{xx}, ADC_{xy}, ADC_{xz},$
$ADC_{yy}, ADC_{yz},$
$ADC_{yy})$

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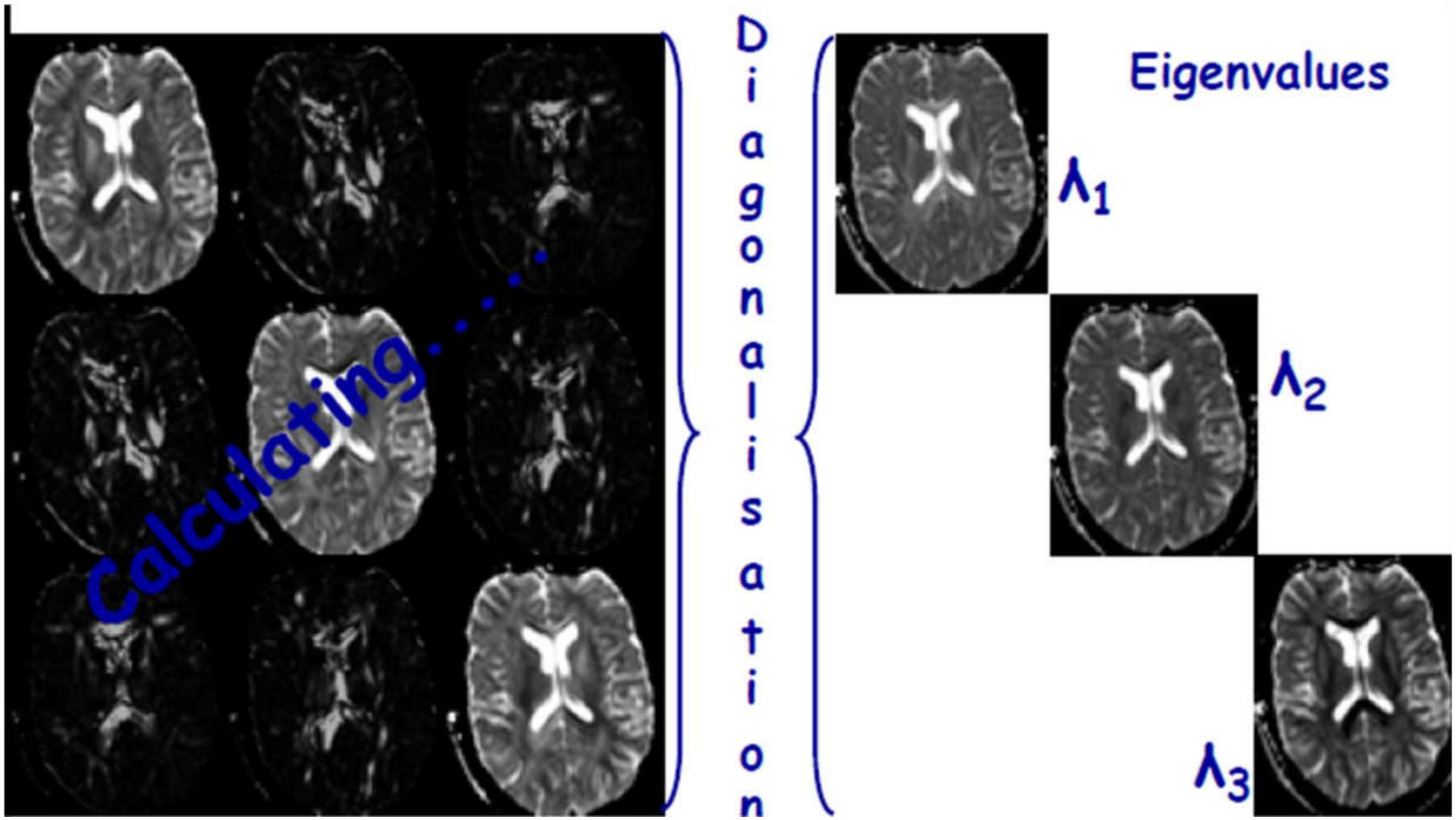
Calculations (II): the Diffusion Tensor



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Diffusion Tensor Imaging (DTI)

- **Three diffusion tensor imaging techniques in common use are**
  - the fractional anisotropy map (FA-map)
  - the principal diffusion direction map
  - fiber-tracking maps (Tractography)

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Fractional Anisotropy Map (FA-map)

- Fractional anisotropy (FA) is an index for the amount of diffusion asymmetry within a voxel, defined in terms of its eigenvalues:

$$FA = \sqrt{\frac{(\lambda_1-\lambda_2)^2+(\lambda_2-\lambda_3)^2+(\lambda_1-\lambda_3)^2}{2({\lambda_1}^2+{\lambda_2}^2+{\lambda_3}^2)}}$$

- The value of FA varies between 0 and 1.
- For perfect isotropic diffusion, $\lambda_1 = \lambda_2 = \lambda_3$, the diffusion ellipsoid is a sphere, and FA = 0.
- With progressive diffusion anisotropy, the eigenvalues become more unequal, the ellipsoid becomes more elongated, and the FA → 1.

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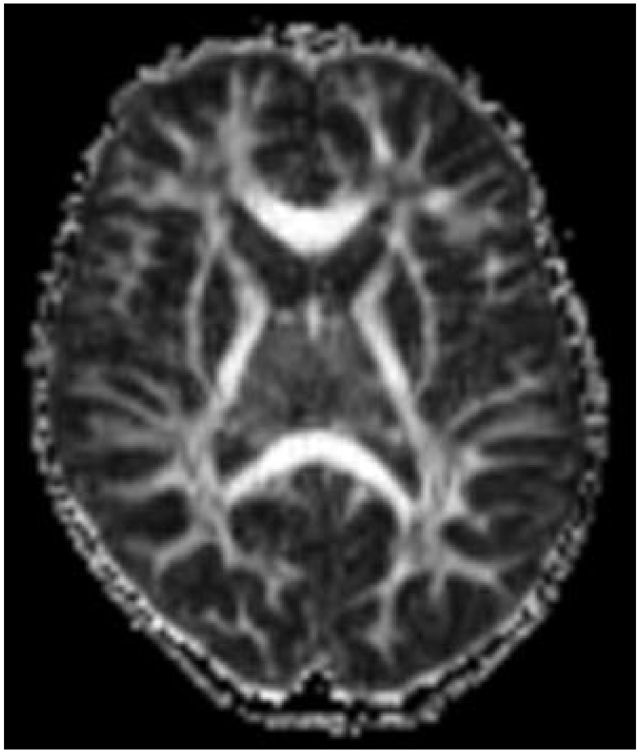
Fractional Anisotropy Map (FA-map)

- The FA-map is a gray-scale display of FA values across the image. Brighter areas are more anisotropic than darker areas.



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Principal Diffusion Direction Map

- This is a map that assigns colors to voxels based on a combination of anisotropy and direction.
- It is also called the colored fractional anisotropy map, fiber direction map or diffusion texture map.
- The color assignment is arbitrary, but the typical convention is to:
  - the orientation of the principal eigenvector (ε_1) control hue
  - fractional anisotropy (FA) control brightness

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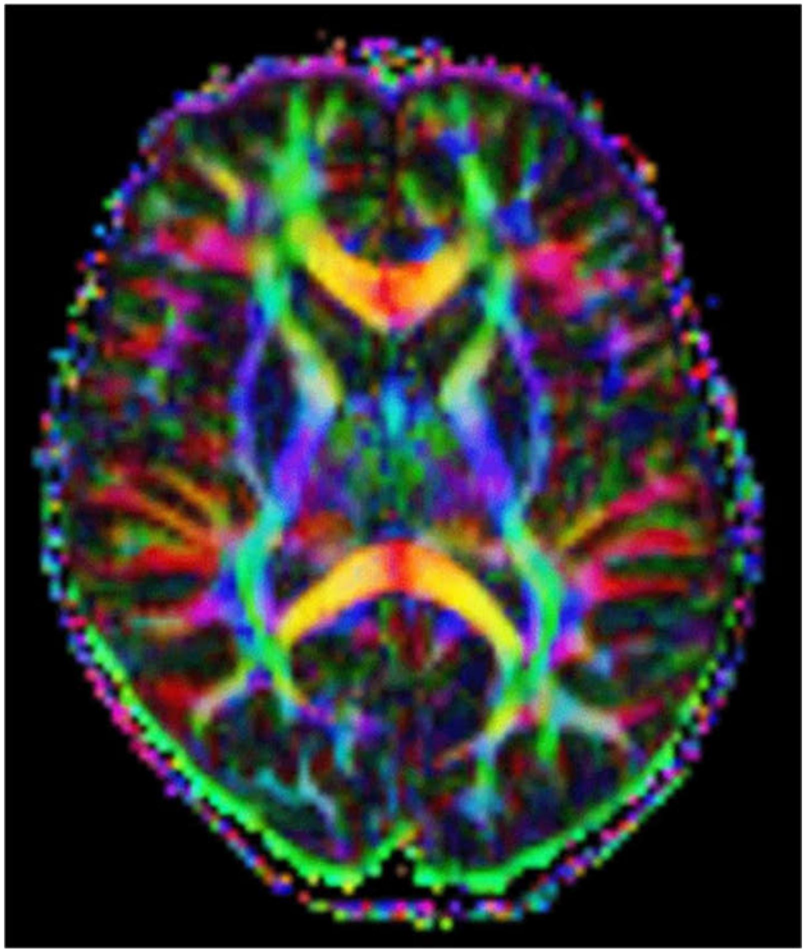
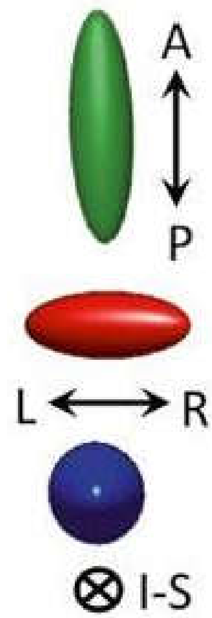
Principal Diffusion Direction Map





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Fiber-Tracking Maps (Tractography)

- Axonal tracts are commonly mapped using a deterministic method known as FACT (fiber assignment by continuous tracking).
- In this method the user selects "seed voxels" in a certain area of the brain and automated software computes fiber trajectories in and out of that area.
- This is accomplished by following the primary eigenvector (ε_1) in each voxel until it encounters a neighboring voxel, at which time the trajectory is changed to point in the direction of the new eigenvector.

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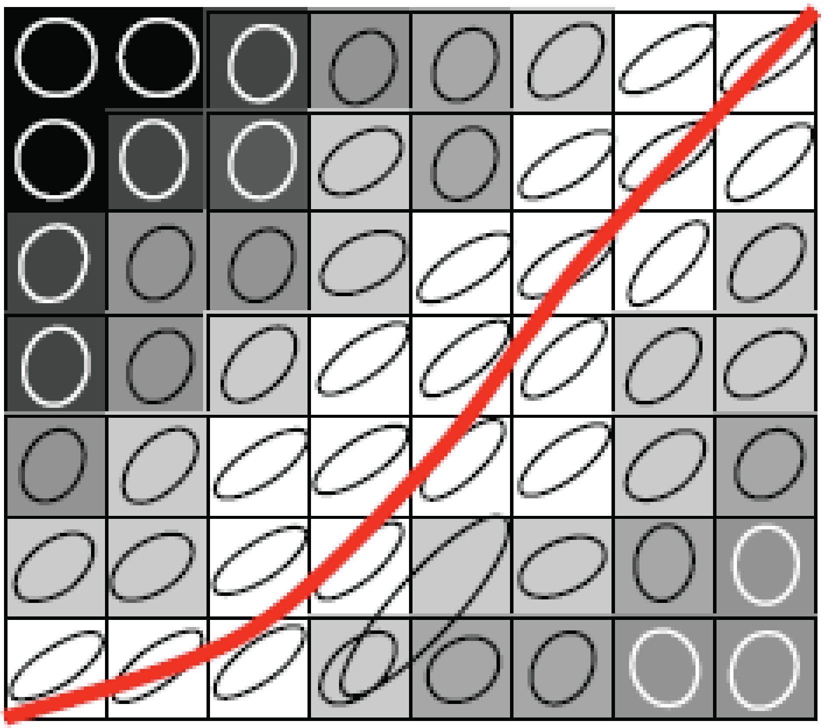
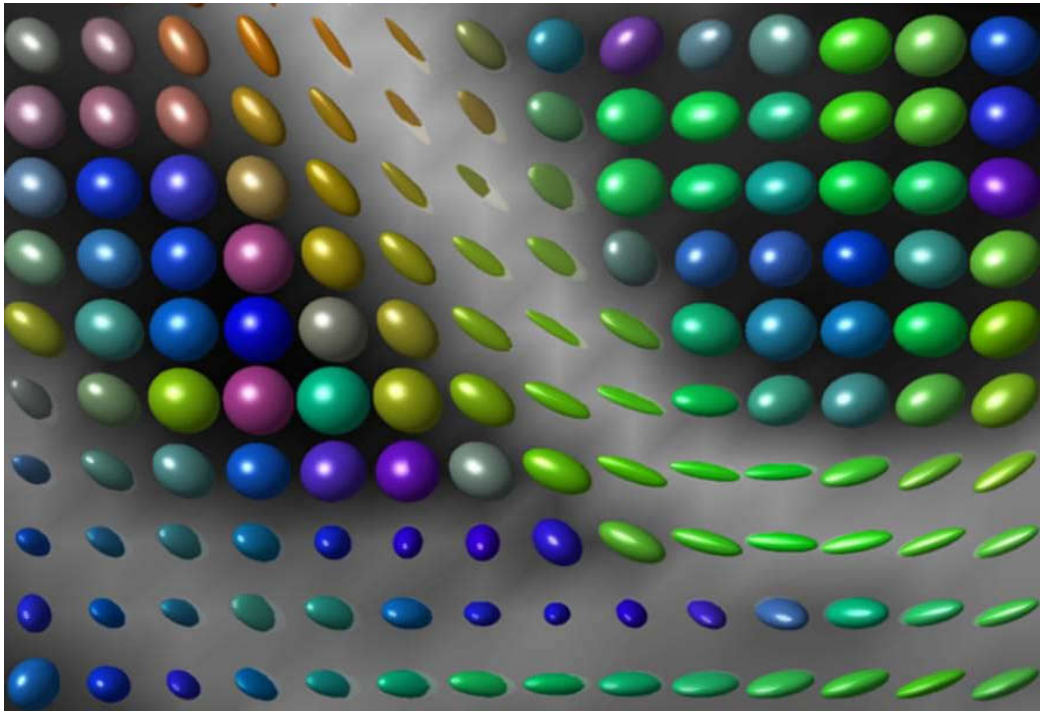
Tractography

- ✓ Voxels are connected based upon similarities in the maximum diffusion direction.





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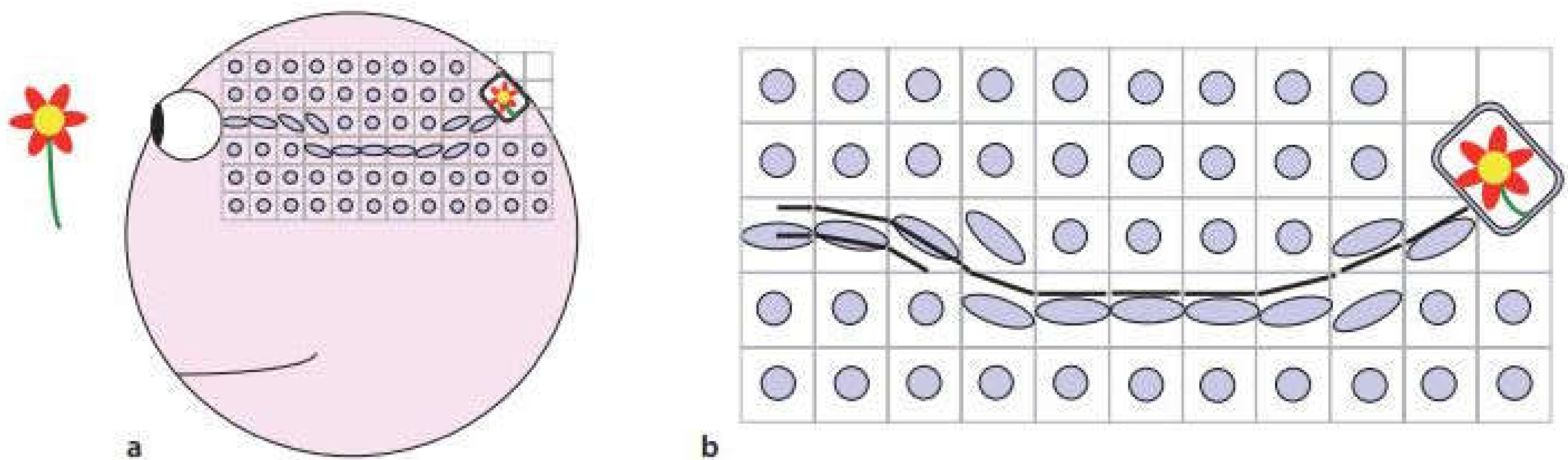

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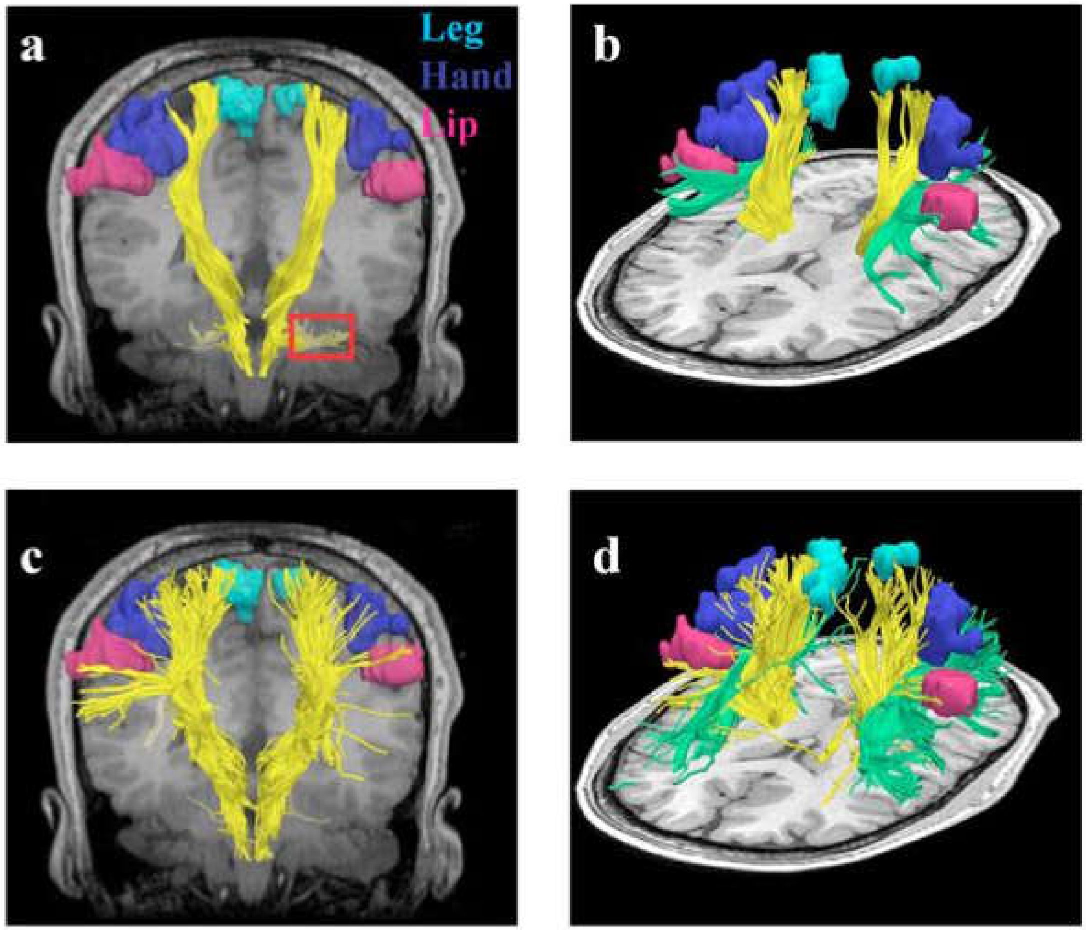

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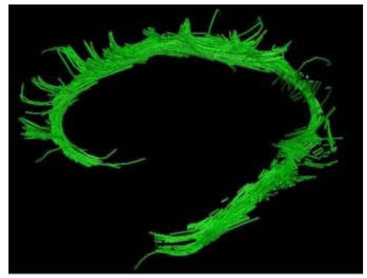
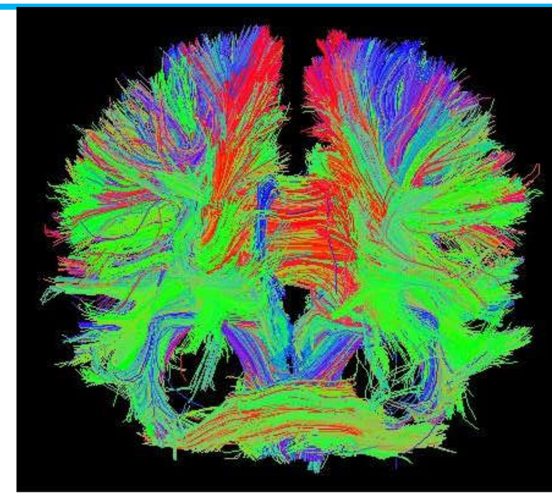
Tractography

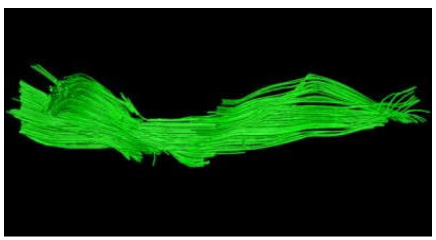
CORPUS CALLOSUM



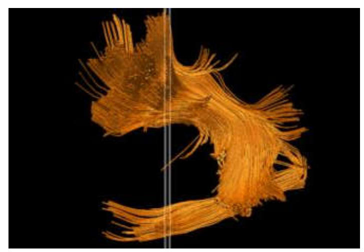
CINGULATE



WHOLE BRAIN

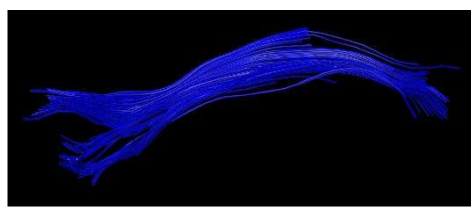


IFOF



ARCUATE

UNCINATE



ILF

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DWI and DTI Applications

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Restricted Diffusion

- Restricted Diffusion = Bright DWI = Low ADC

- **Most important:**
  - Infarction
  - Abscess
  - Lymphoma
  - Intra-myelinic edema

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Intracranial diseases with restricted diffusion (bright on DW images)

Category	Examples
Vascular	**Infarction (venous or arterial), diffuse hypoxic injury, posterior reversible encephalopathy (PRES)**
Neoplastic	**Lymphoma**, **epidermoid**, **xanthogranuloma** of choroid plexus, medulloblastoma, malignant glioma, malignant meningioma, primitive neuroectodermal tumor (PNET), atypical teratoid-rhabdoid tumor, metastases
Infectious	**Abscess**, **empyema,** meningoencephalitis (herpes), Creutzfelt-Jakob disease
Traumatic	**Hematoma**, **diffuse axonal injury (DAI)**, **Wallerian degeneration**, **status epilepticus**, contusion
Toxic/Metabolic	**Carbon monoxide (CO)**, **drugs** (heroin, vigabatrin, carbamazepine, methotrexate)**, hypoglycemia**, hyperglycemia, Wernicke's, congenital biochemical disorders (phenylketonuria, glutaric aciduria, urea cycle defects, maple syrup urine disease, Canavan's, many others)
Demyelinating	**Acute disseminated encephalomyelitis (ADEM),** osmotic demyelination, multiple sclerosis, delayed post-anoxic encephalopathy, Marchiava-Bignami

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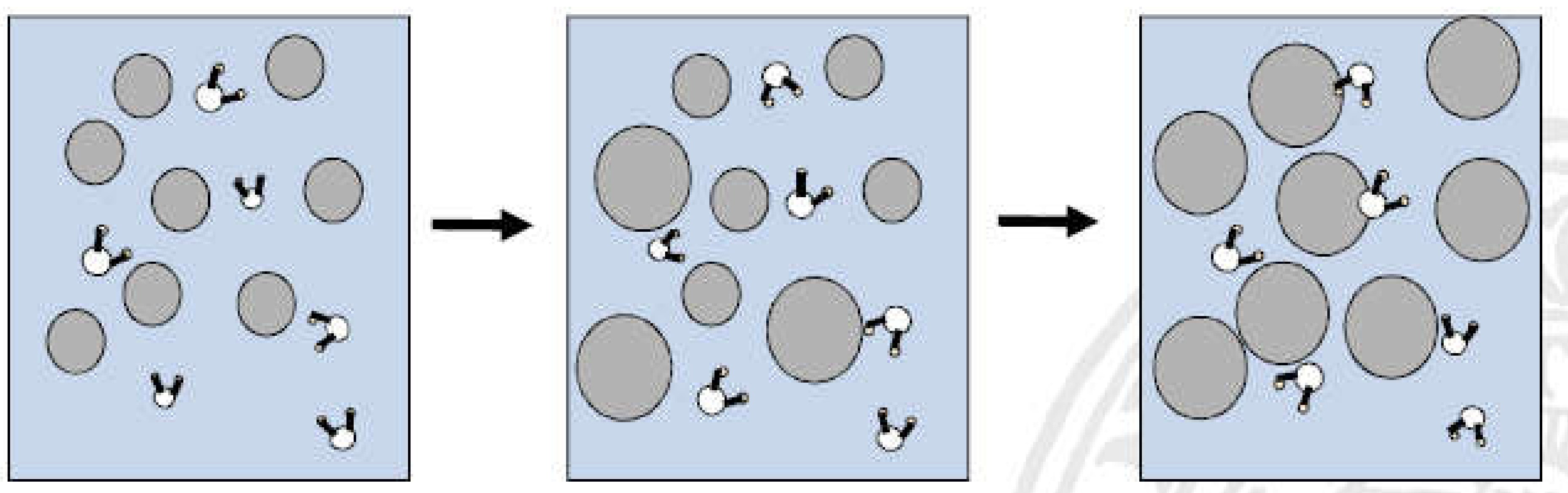
Clinical Cases (Diffusion)

Diffusion in Stroke: Early phase



Progressive cytotoxic edema → diffusion decrease

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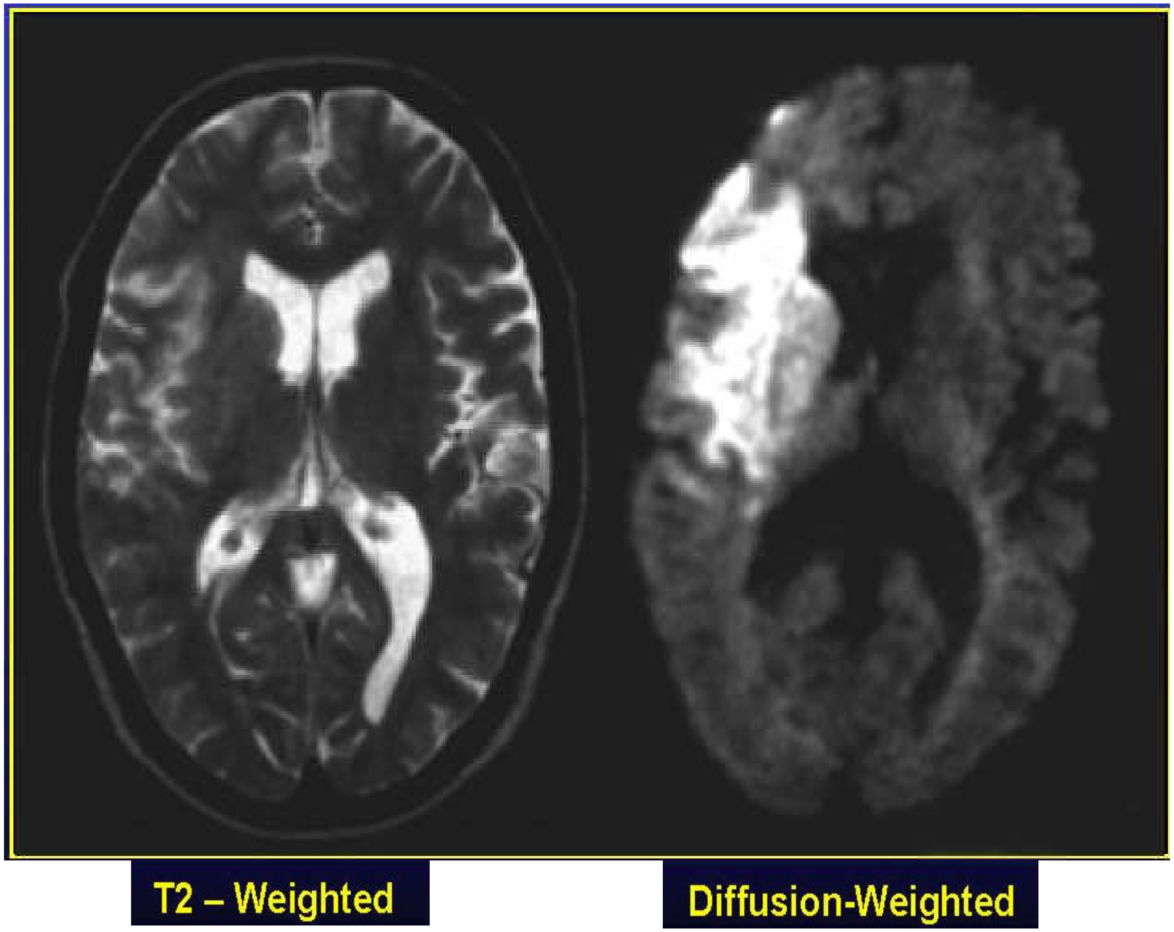
Acute Ischemia



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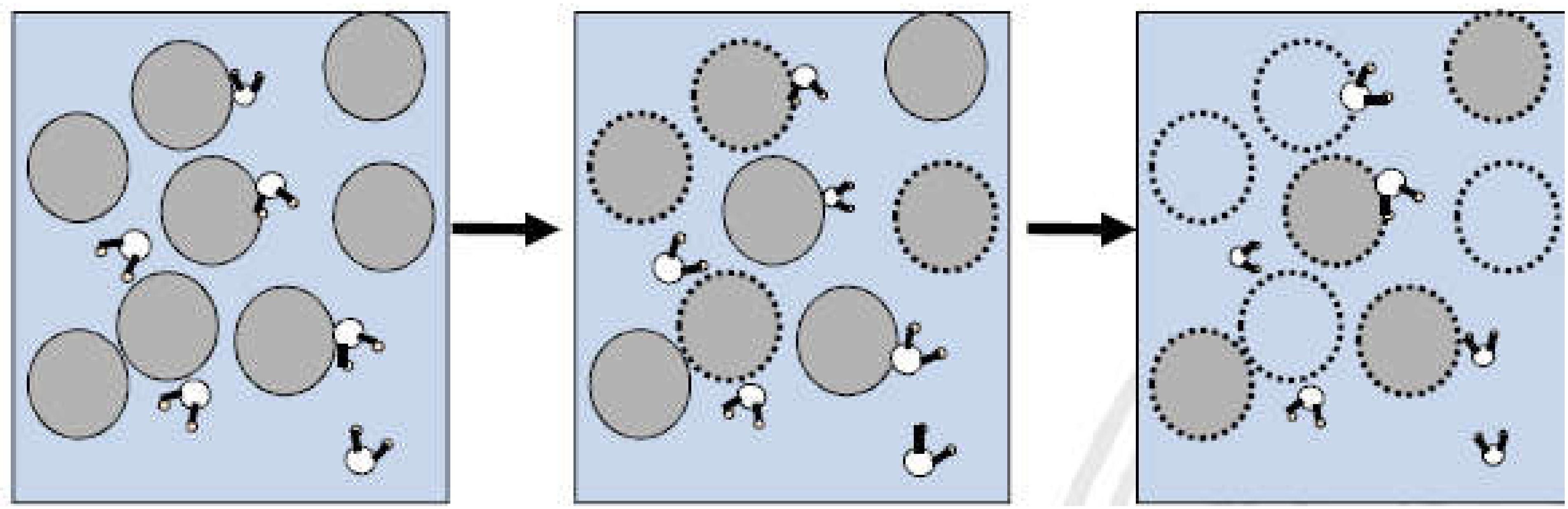
Clinical Cases (Diffusion)

Diffusion in Stroke: Late phase



Progressive cell membrane Lyses + vasogenic edema → diffusion increase

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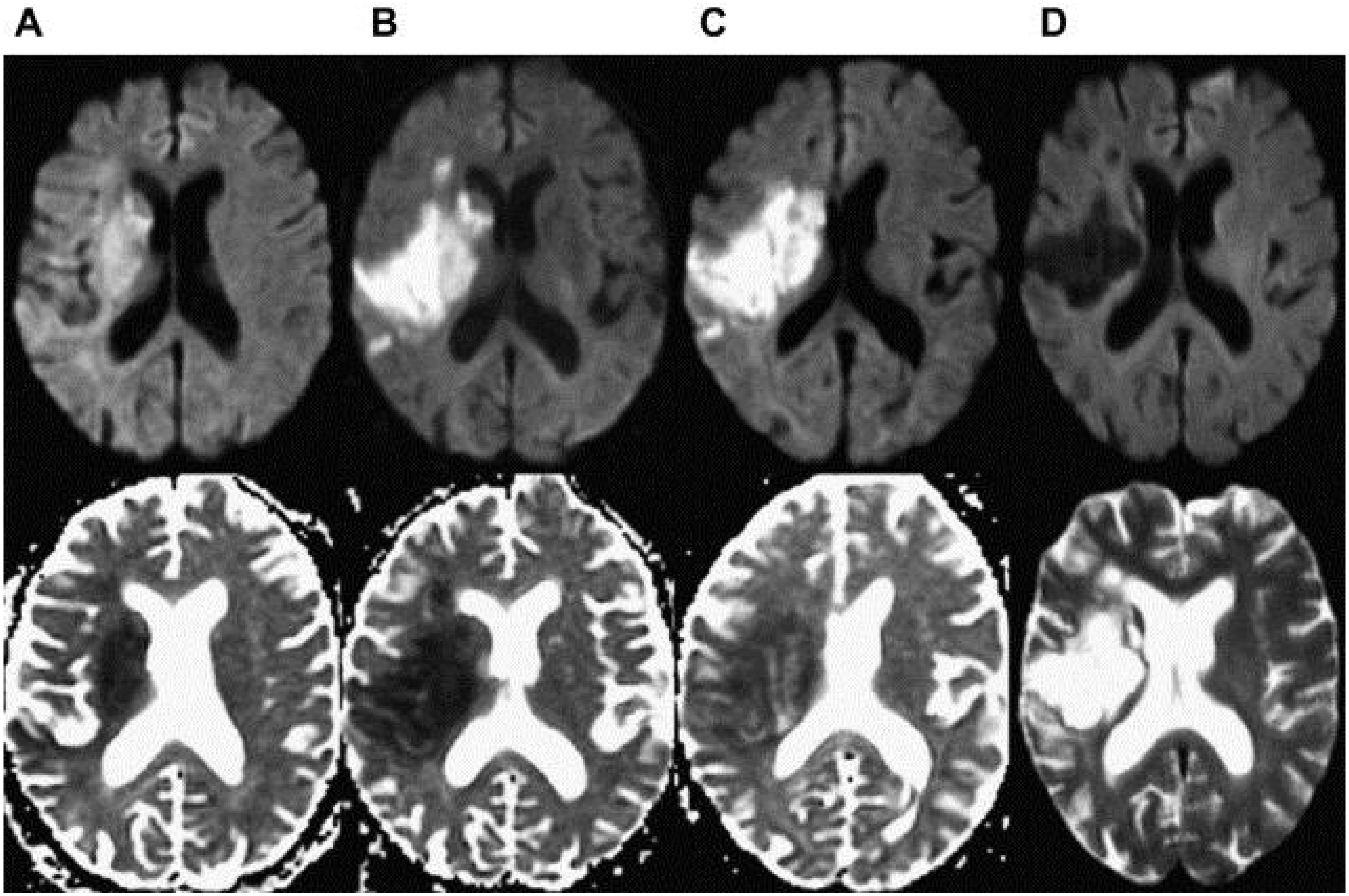

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Table 5.1 Time course of thromboembolic infarction of the middle cerebral artery

	< 6 hours	3 days	7 days	30 days
T2	Isointense	Bright	Bright	Bright
DW imaging	Bright	Very bright	Bright	Isointense
ADC	Dark	Very dark	Dark	Bright

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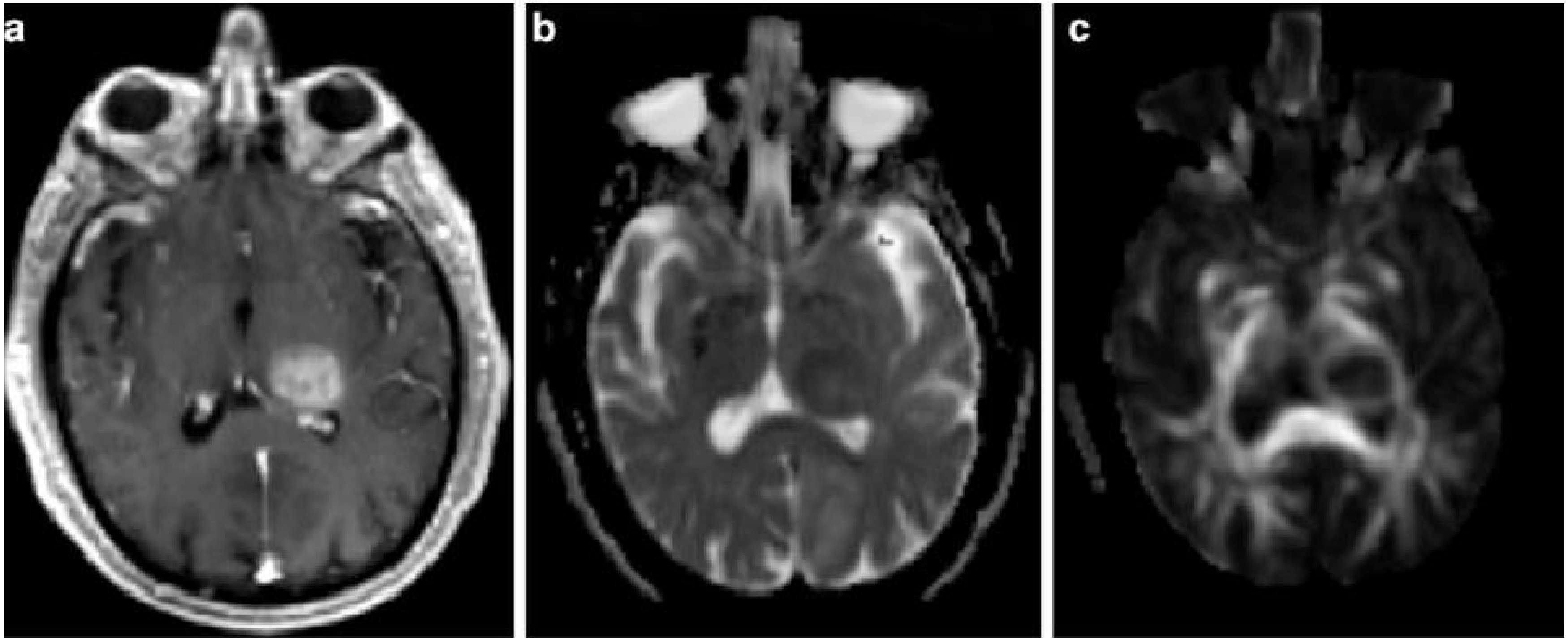
Clinical Cases (Diffusion)

Glioblastoma in left thalamus



(a) CE T1-weighted image, (b) ADC map shows restricted diffusion, (C) FA

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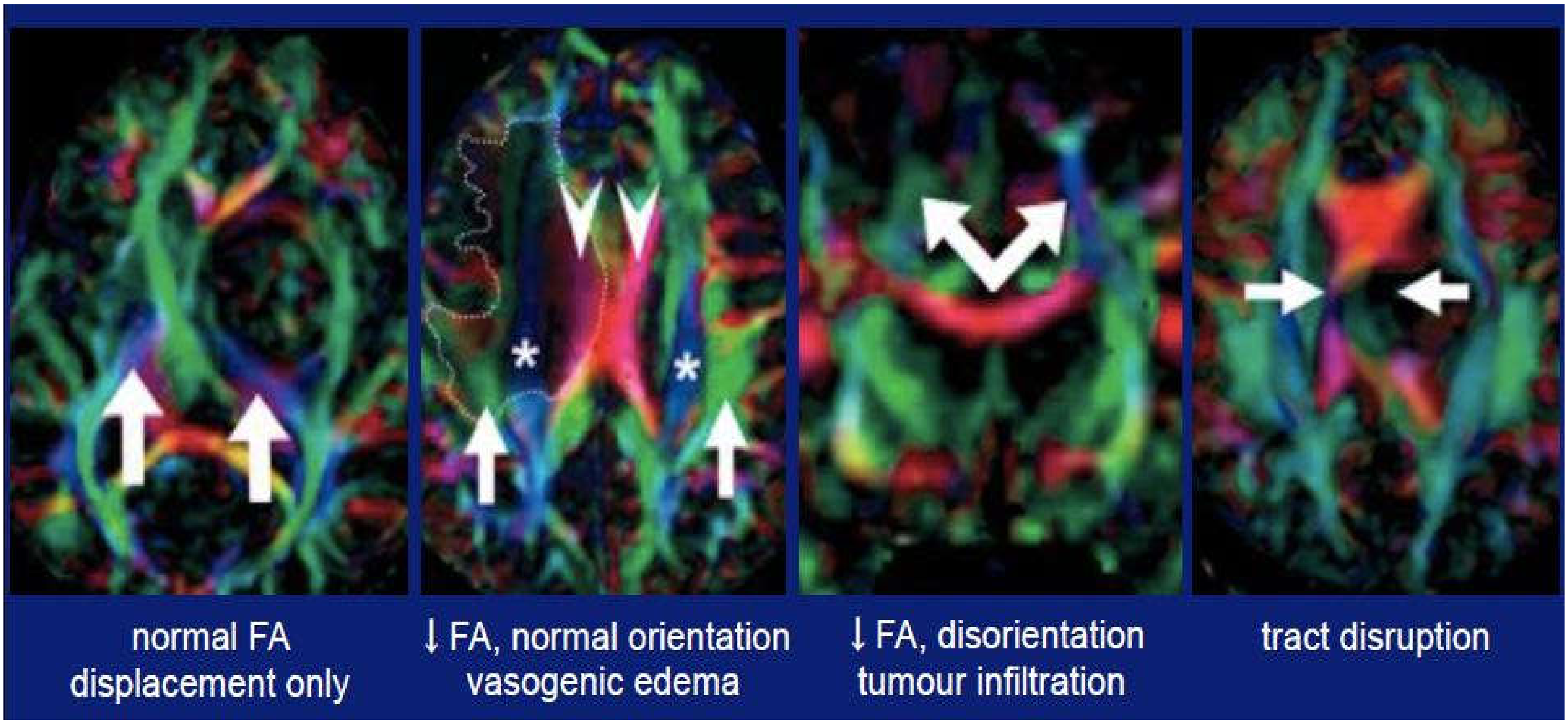
Tract Integrity



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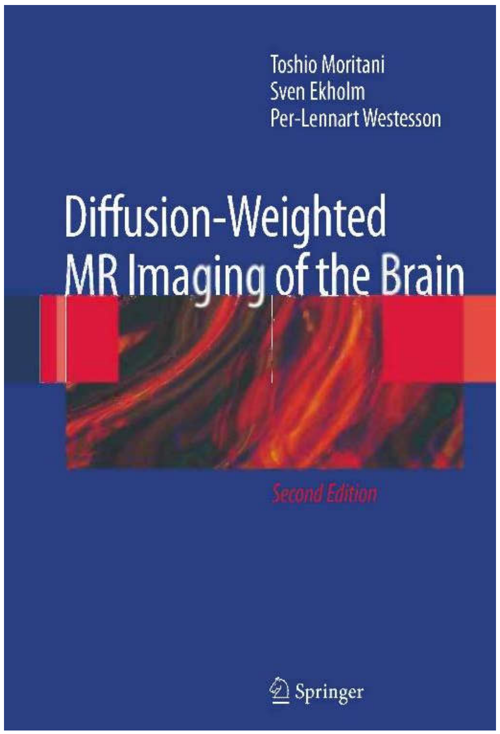
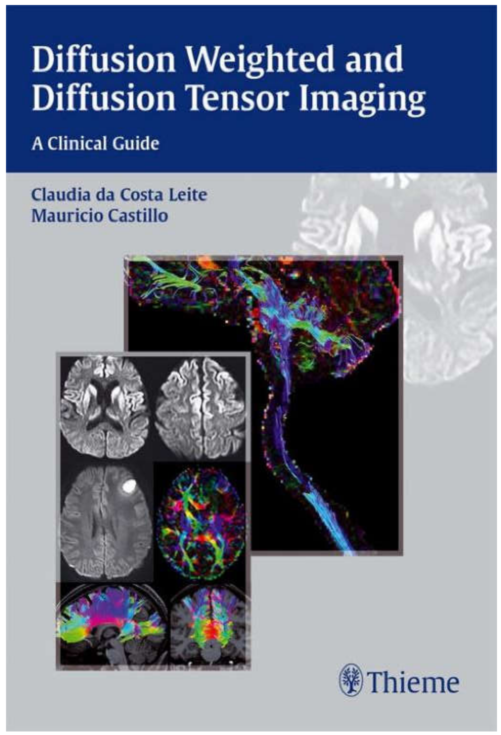
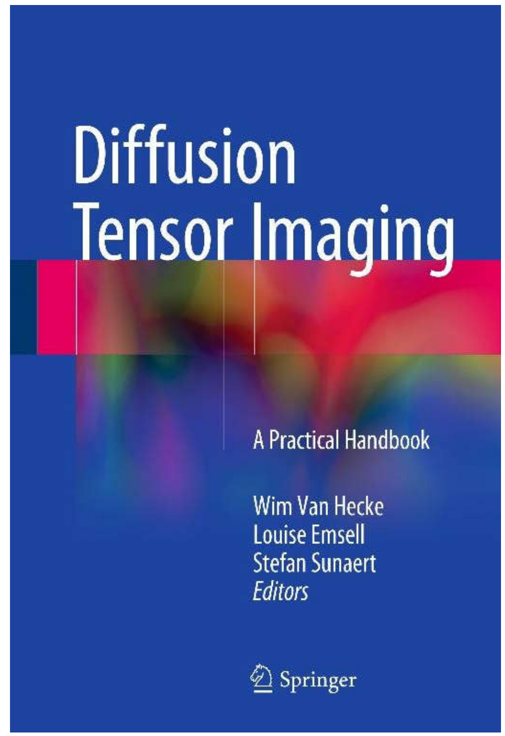
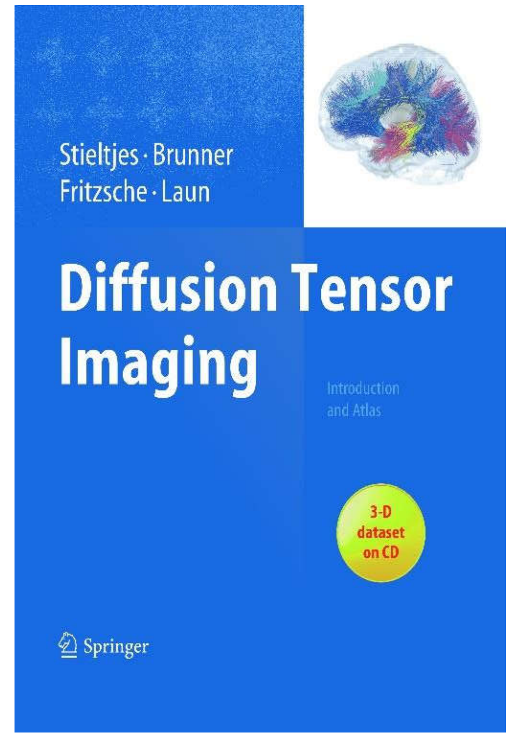
Suggested References









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