Diffusion Imaging

102 THE ANATOMICAL RECORD (NEW ANAT.) 257:102–109, 1999

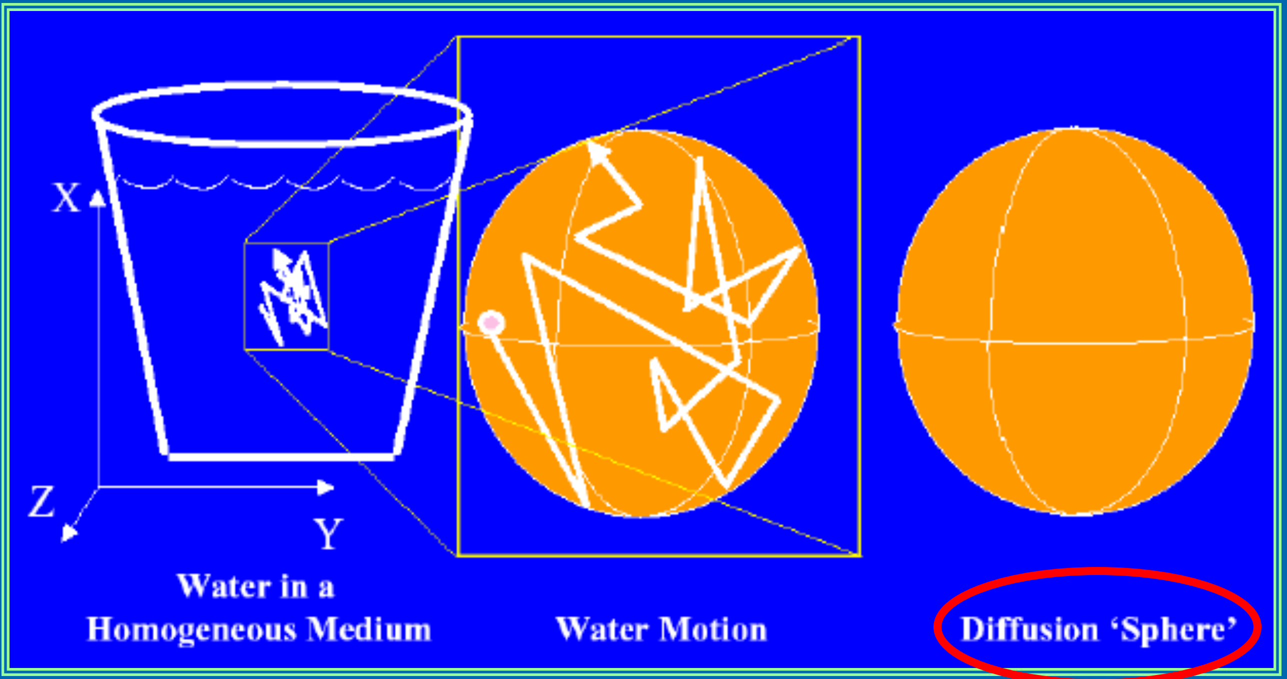
FEATURE ARTICLE

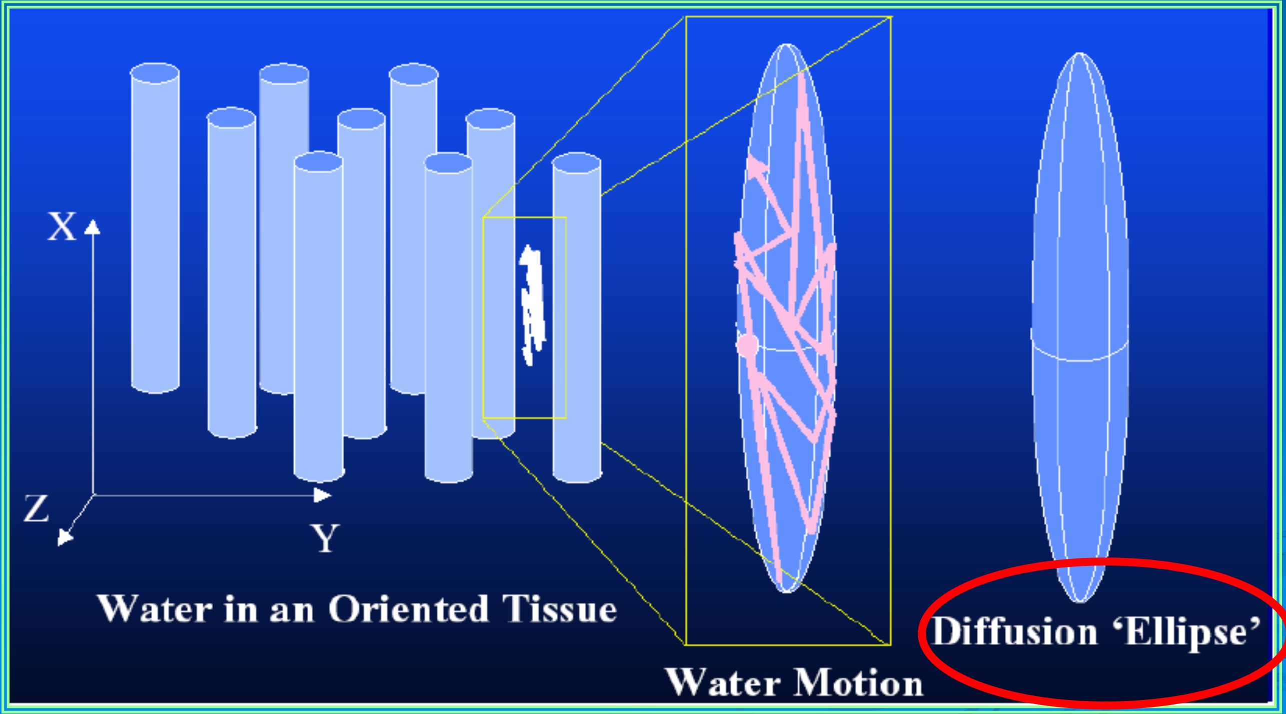
Diffusion Magnetic Resonance Imaging: Its Principle and Applications

SUSUMU MORI* AND PETER B. BARKER

Diffusion magnetic resonance imaging (MRI) is one of the most rapidly evolving techniques in the MRI field. This method exploits the random diffusional motion of water molecules, which has intriguing properties depending on the physiological and anatomical environment of the organisms studied. We explain the principles of this emerging technique and subsequently introduce some of its present applications to neuroimaging, namely detection of ischemic stroke and reconstruction of axonal bundles and myelin fibers. *Anat Rec (New Anat) 257:102–109, 1999.*

Water diffusion:
* Thermal energy
* Brownian motion





Water in a inhomogeneous medium

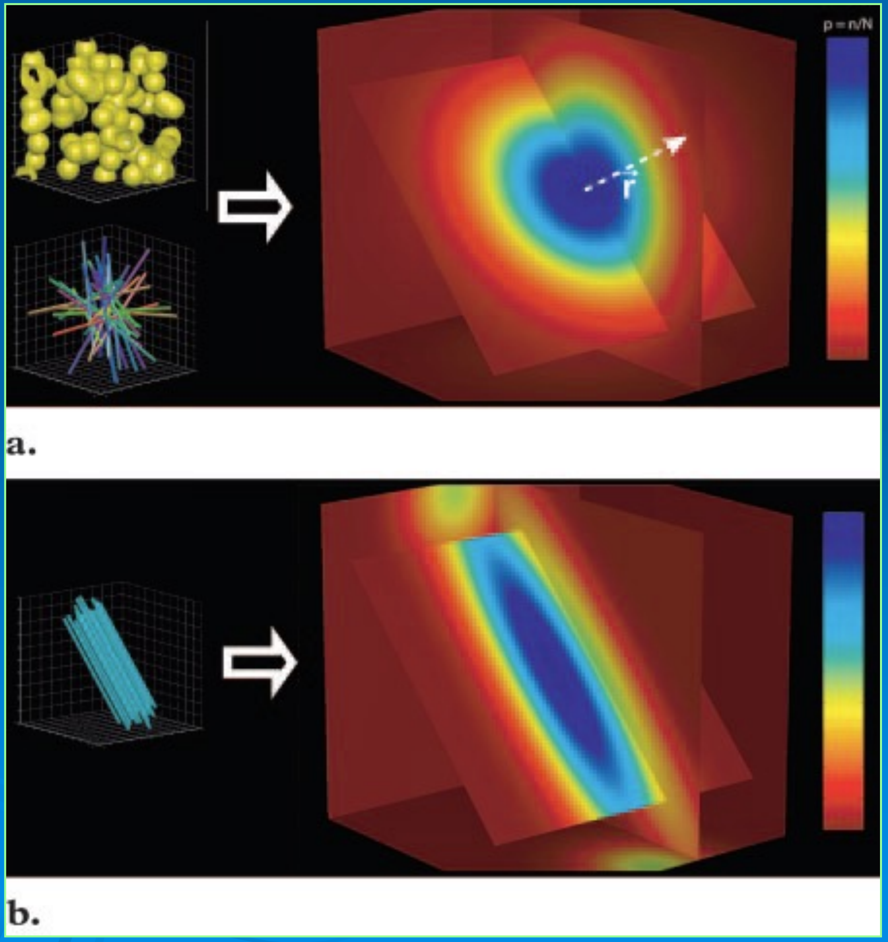
3D diffusion probability distributions

In a voxel that contains

a) spherical cells or randomly oriented tubular structures, such as axons

b) all the axons are aligned in the same direction

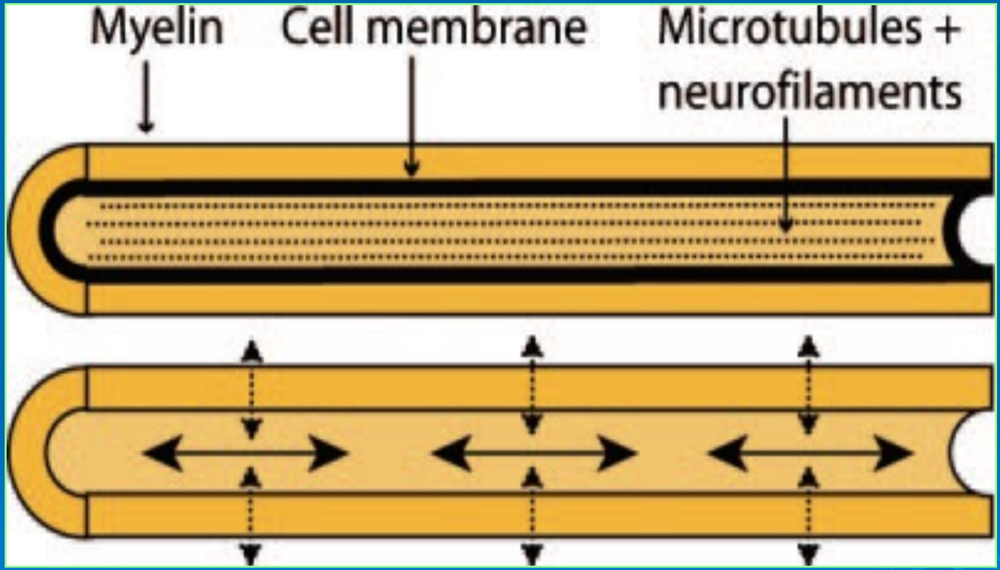
- ✓ The displacement distribution is cigar shaped and aligned with the axons.



Hagmann P. et al
RadioGraphics 2006; 26:S205–S223

Cellular elements and diffusion anisotropy

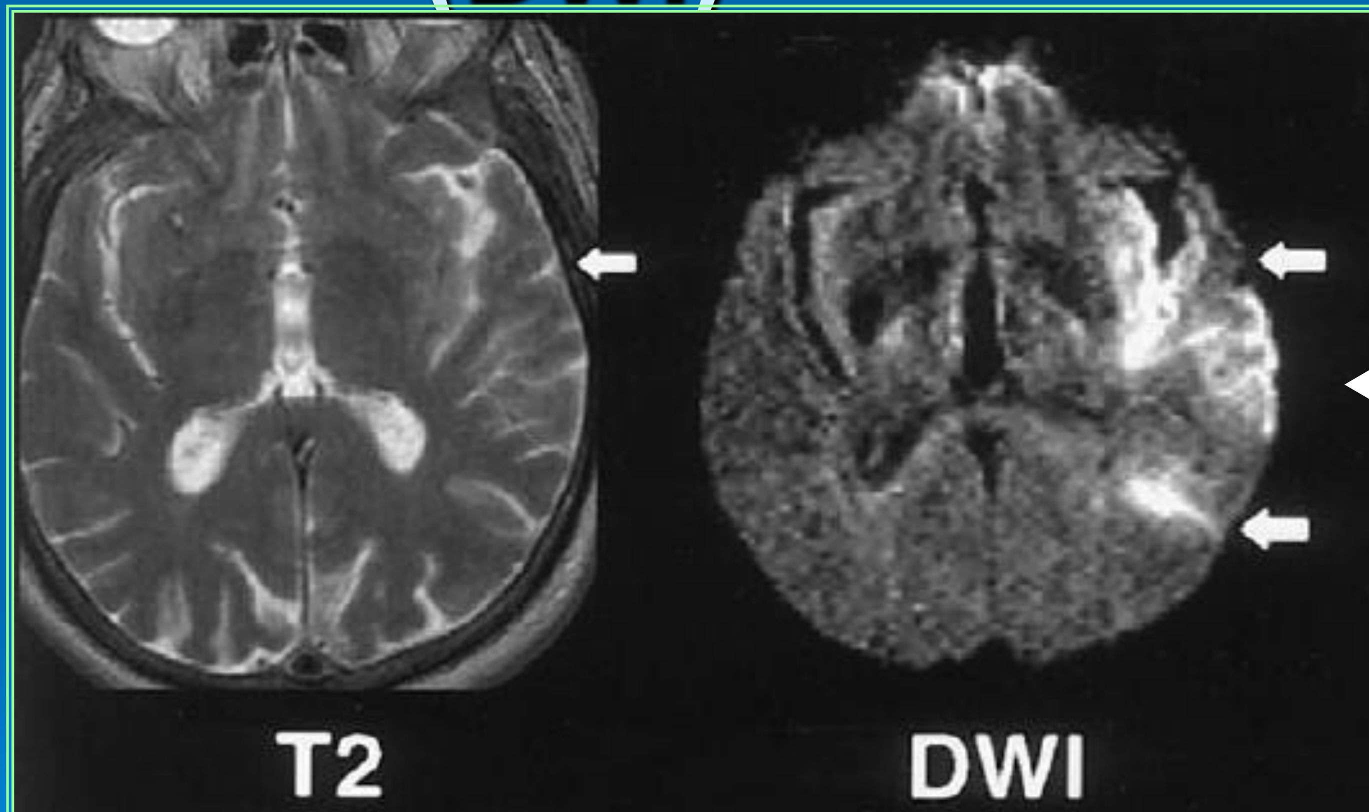
- **Neuronal tissue consists of tightly packed and coherently aligned axons**
  - **surrounded by glial cells**
  - **Often organized in bundles**
- **The movements of water molecules are hindered in a direction perpendicular to the axonal orientation**



Hagmann P. et al RadioGraphics 2006; 26:S205–S223

Diffusion weighted imaging (DWI)

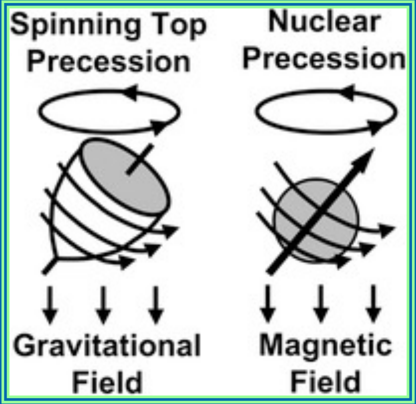
Ischemic stroke early diagnosis

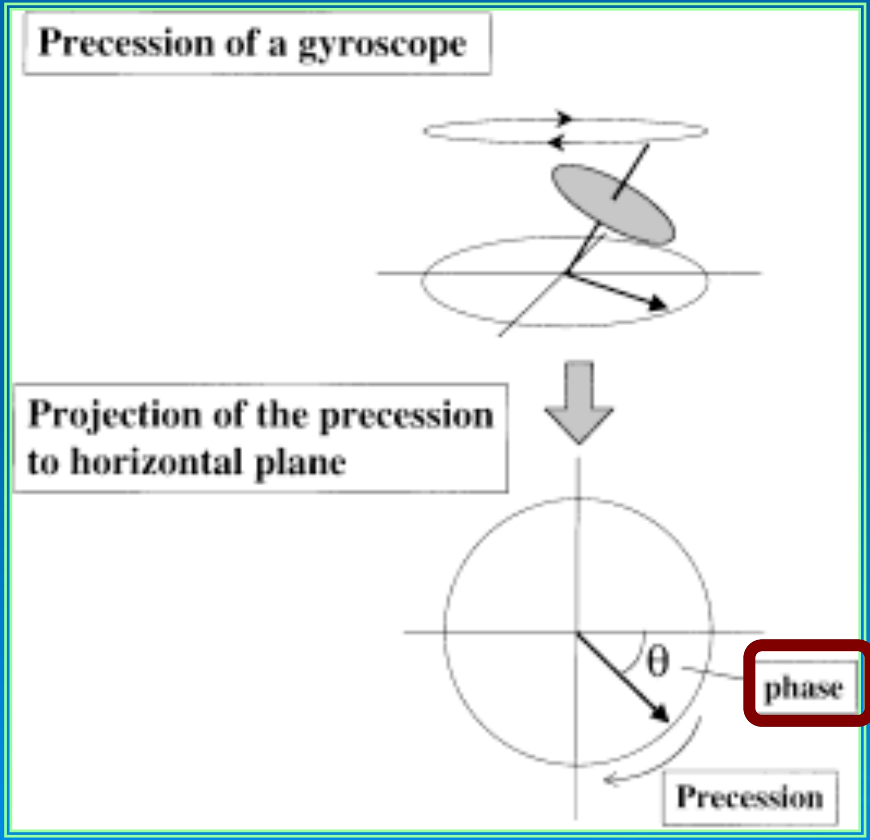


Diffusion weighting enables one to distinguish between rapid diffusion of protons (unrestricted diffusion) and slow diffusion of protons (restricted diffusion)

https://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-weighted-sequences

MRI physics

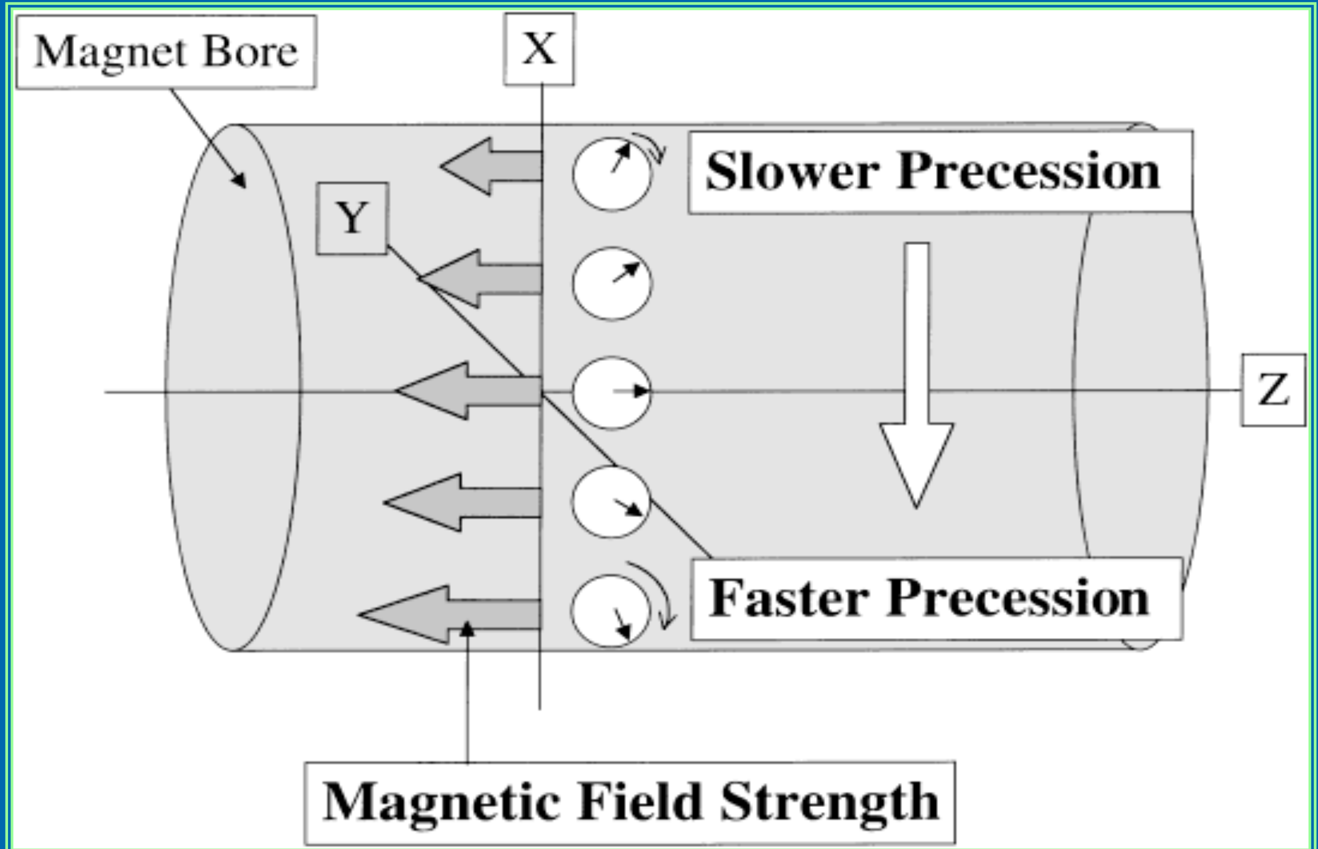




- In MRI, the signal behaves like a gyroscope that precesses at the resonance frequency
- If the position of the gyroscope is projected to the transversal plane such precession is presented as a rotating vector
  - The position of the vector is called phase.

http://www.imaios.com/en/e-Courses/e-MRI/NMR/Precession-and-Larmor-frequency

Gradients and spin phase

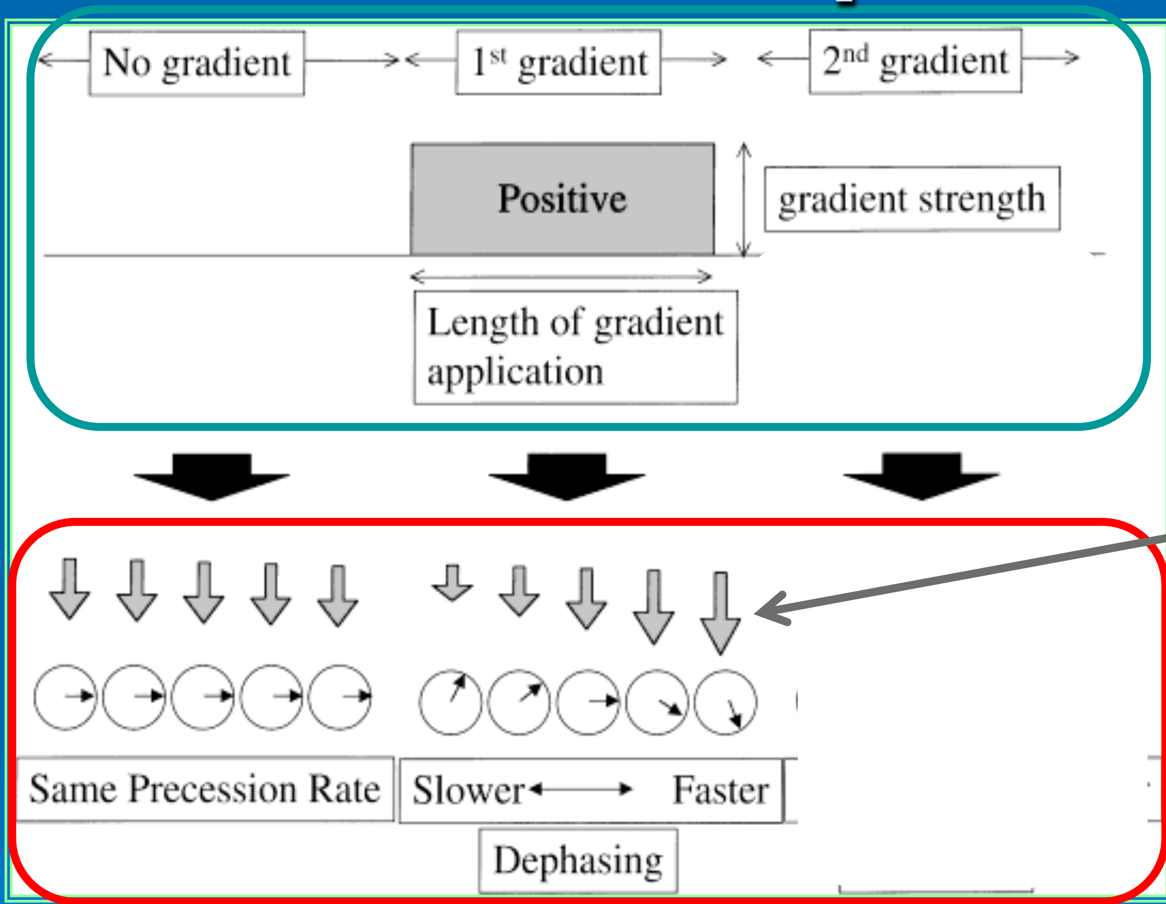


An example of an x-gradient

- Gradient units introduce linear magnetic field inhomogeneity
- Due to gradients, the Larmor frequency vary in the sample depending on the position of the protons

www.imaios.com/en/e-Courses/e-MRI/Signal-spatial-encoding/Magnetic-field-gradients
www.imaios.com/en/e-Courses/e-MRI/Signal-spatial-encoding/Phase-encoding

Gradients and phase

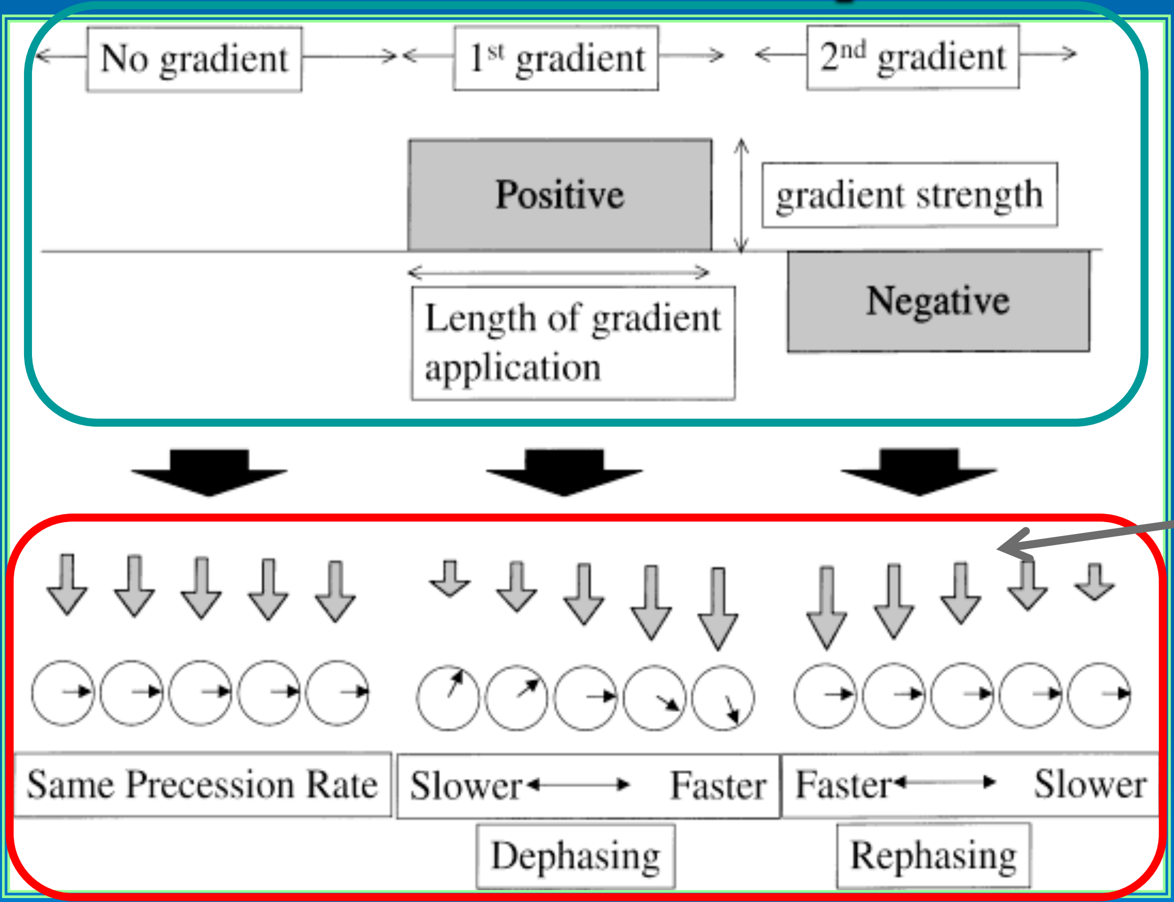


Gradient diagram (upper row) and signal phases (lower row) under application of a gradient.

The length of gray arrows indicates the strength of the magnetic field that is non-uniform during the application of the gradients.

- **After the 1st gradient application, signals lose their uniform phase because each proton starts to precess at different rates depending on its position in space**

Gradients and phase

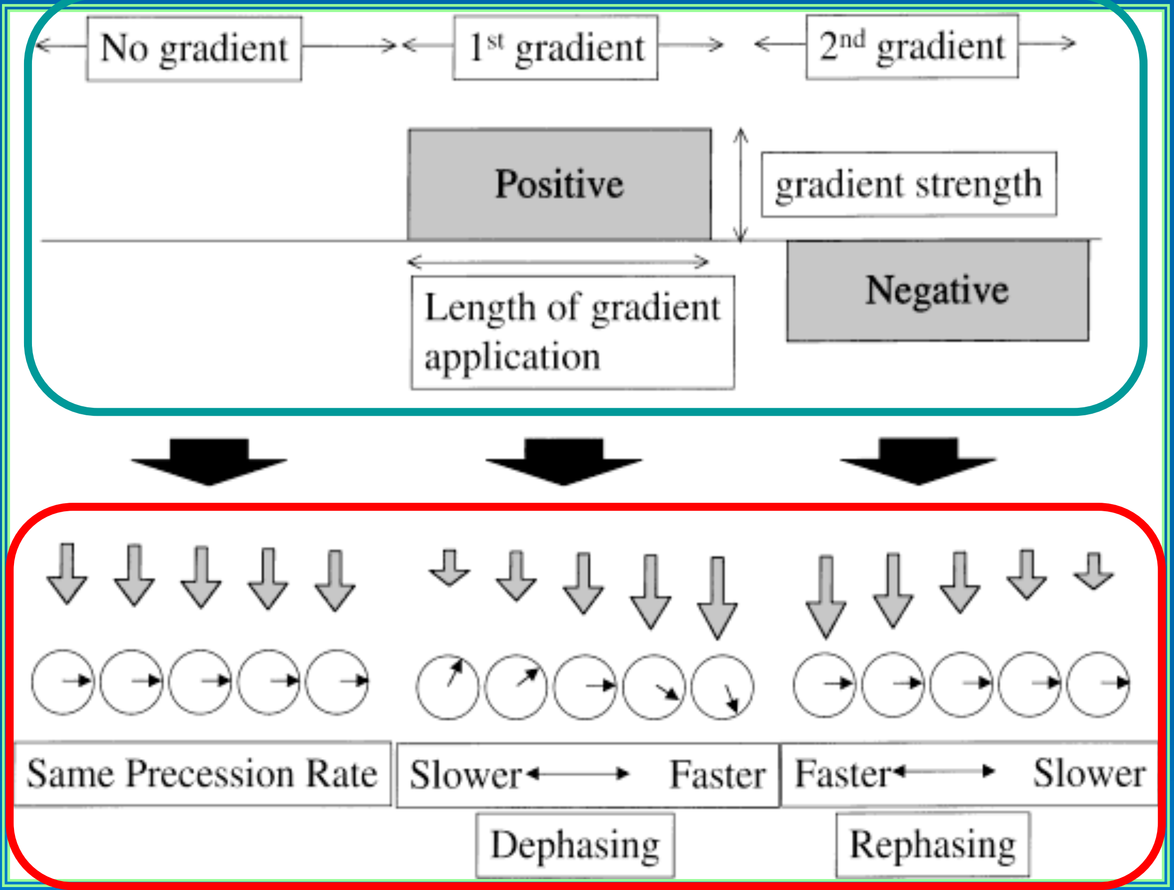


Gradient diagram (upper row) and signal phases (lower row) under application of a gradient

The length of gray arrows indicates the strength of the magnetic field that is non-uniform during the application of the gradients

- **After the 2nd gradient application of opposite magnitude, the system restores uniform phase**

Gradients and phase



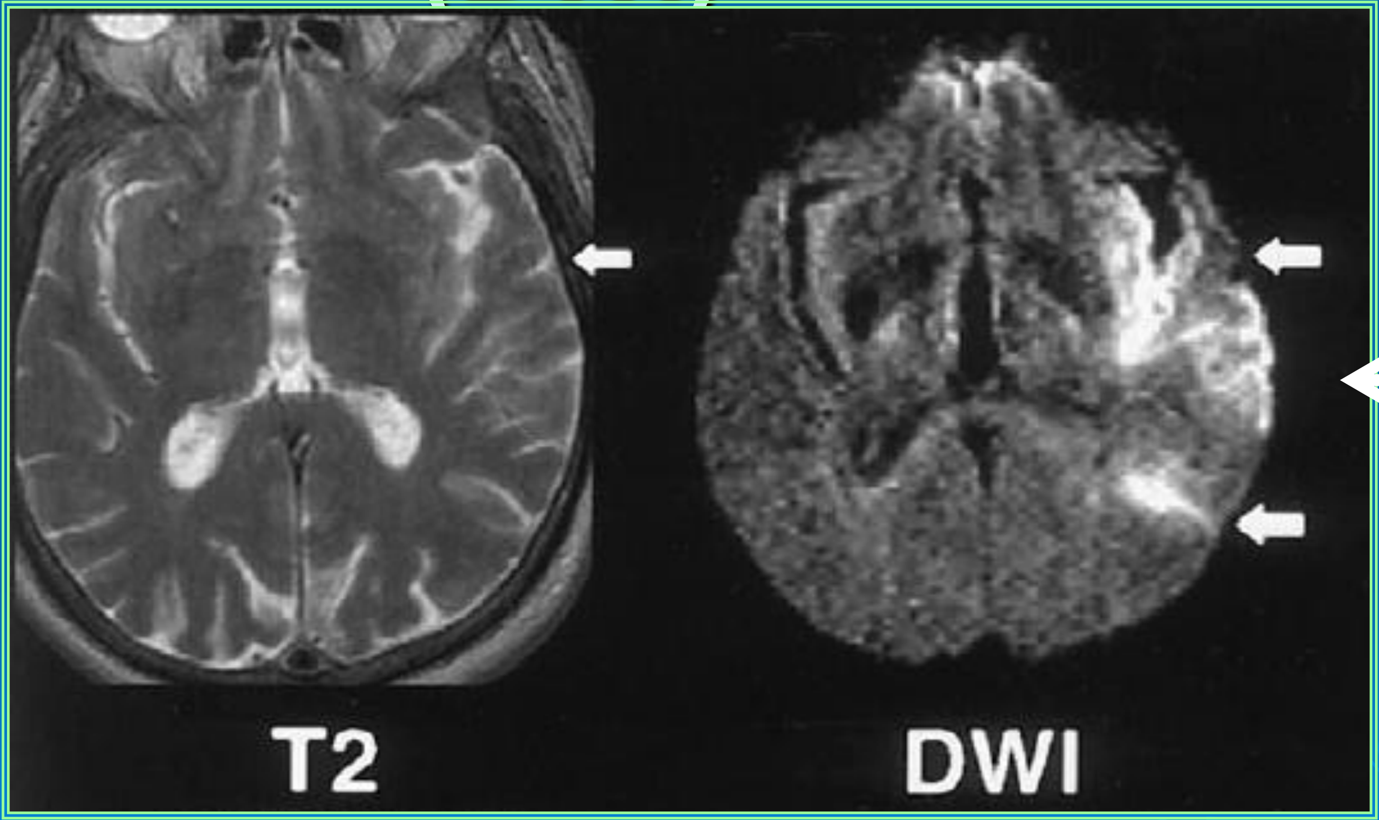
The rephasing is complete only when spins do not move by Brownian motion during the time in between the two applications of the gradient

Less complete the rephasing: More signal loss

- **After the 2nd gradient application of opposite magnitude, the system restores uniform phase.**

Diffusion weighted imaging (DWI)

Ischemic stroke early diagnosis



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https://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-weighted-sequences

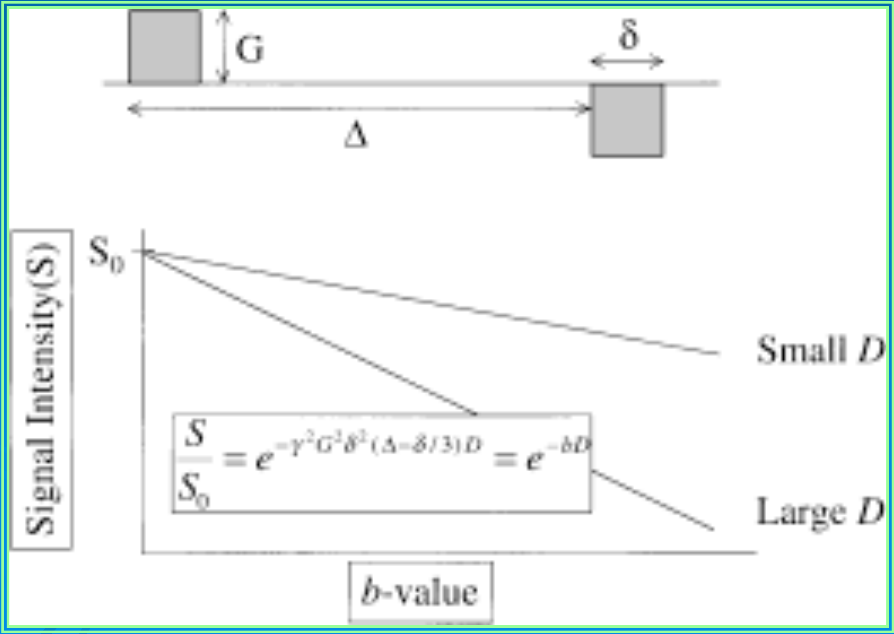
Diffusion gradients

The diffusional signal loss by the gradient application obeys the following equation

$$\frac{S}{S_0} = e^{-bD}$$

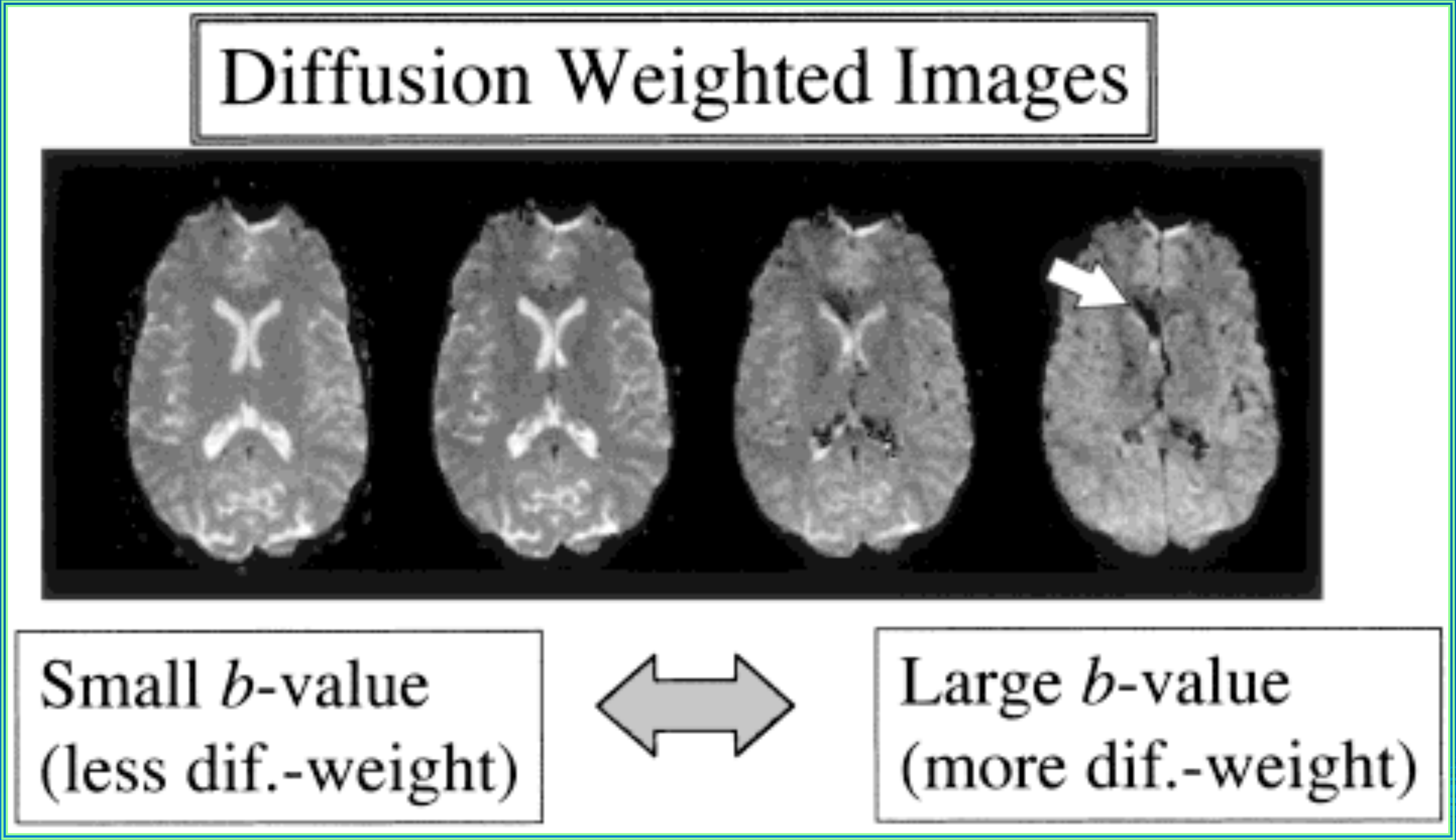
where S_0 is the signal intensity without the diffusion weighting (no gradient application) and S is the signal with the gradient application

- *D* is the diffusion constant
  - tissue dependent
- *b* depends on the gradients
  - Operator dependent



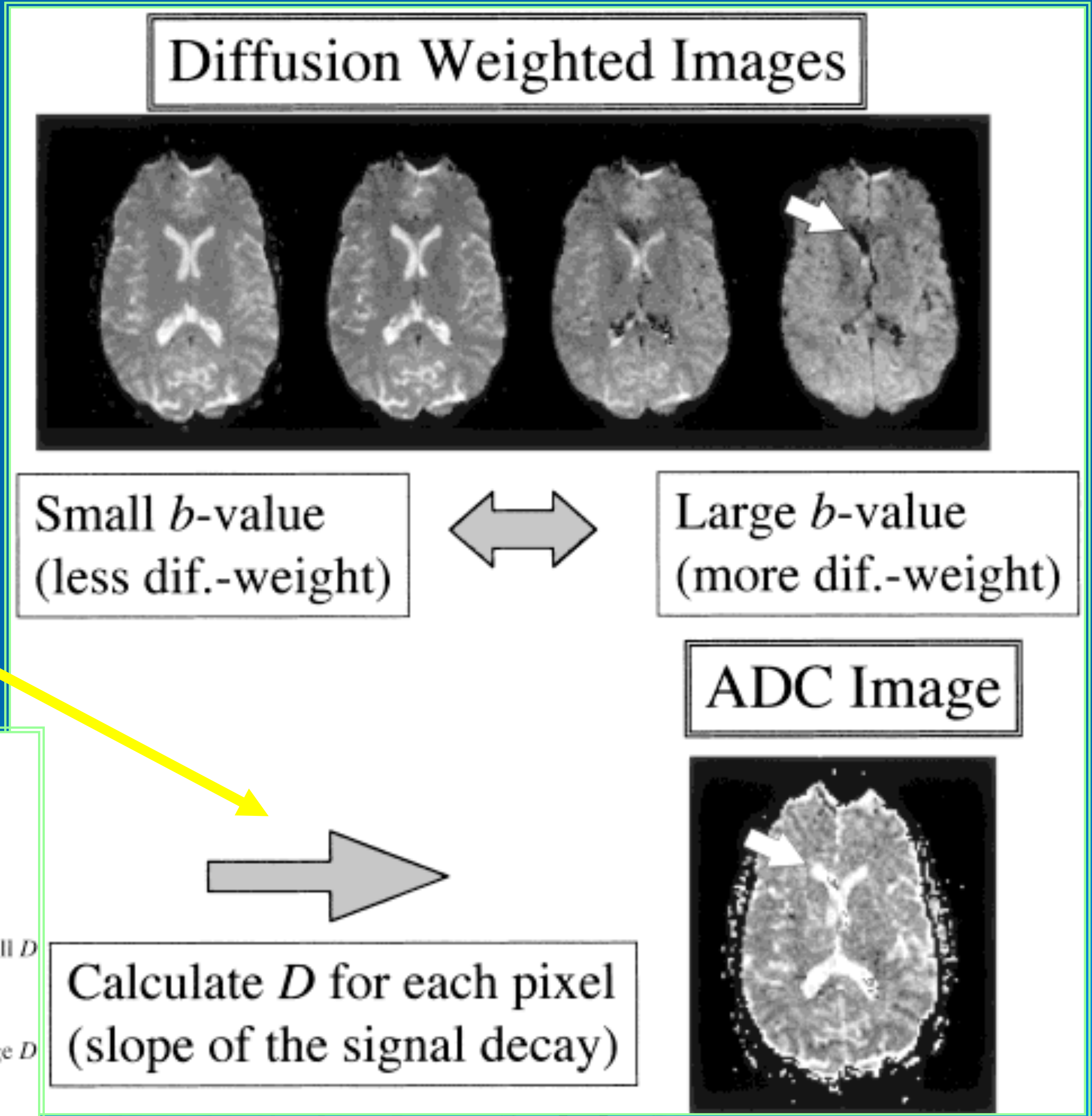
- Relationship between gradient application, signal loss, and diffusion constant (D)

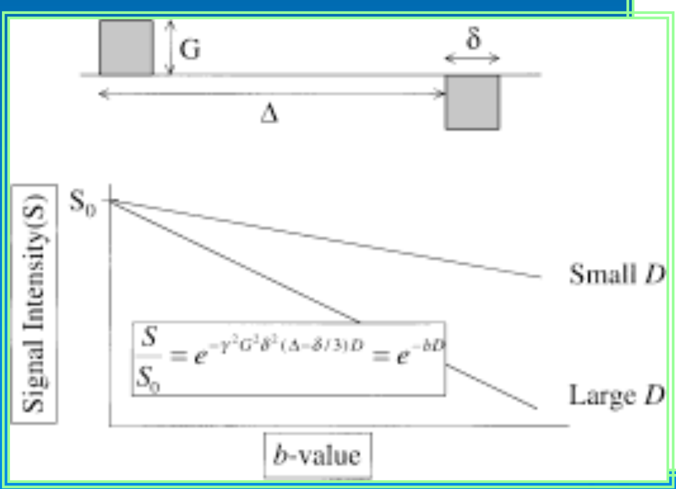
- When b value is plotted against the log of the signal decay, the slope represents the diffusion constant



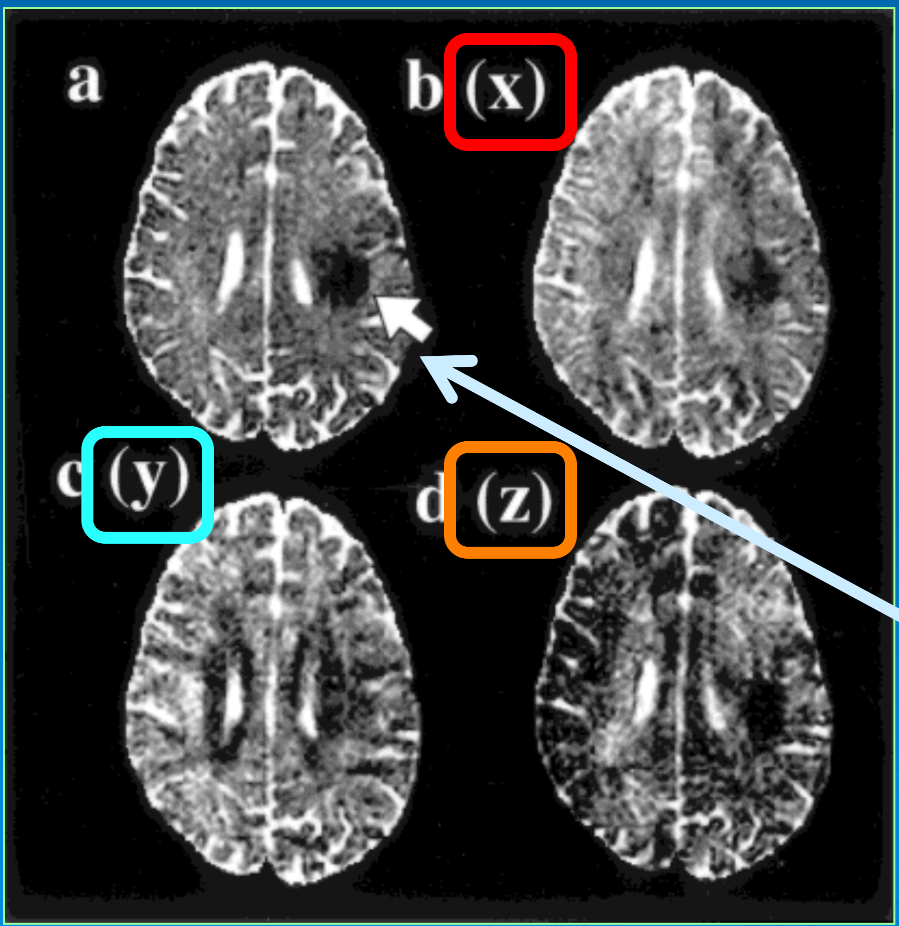
More diffusion weight less signal from CSF

- The **apparent diffusion constant (ADC) image** is calculated from <u>a series</u> of diffusion-weighted images with different b-values



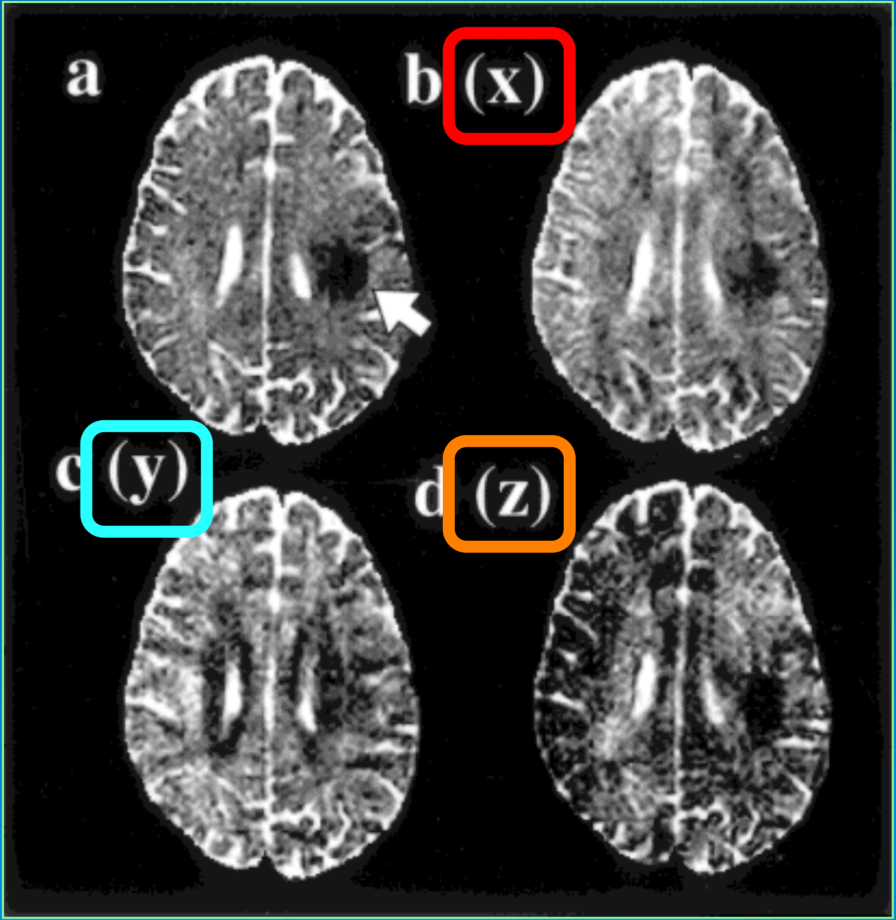


ADC maps and gradient directions



- **The contrast in the ADC map of brains varies depending on the direction of the diffusion gradients**
  - MRI can measure molecular diffusion along any axis by using 3 independent gradients that are orthogonal each other
  - The image shown in (a) is an image which is obtained by adding 3 ADC images recorded using x,y,z-gradients

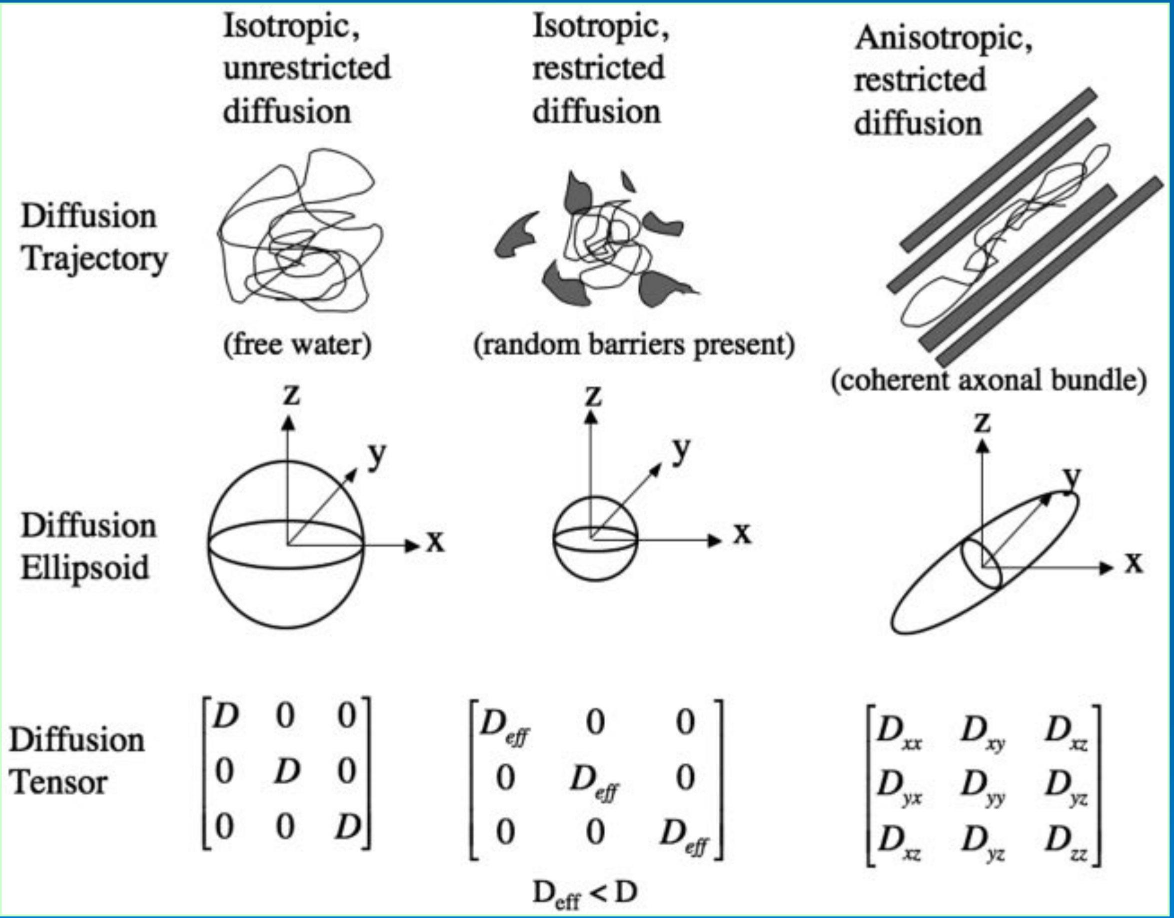
ADC maps and gradient directions



- ADC images of a human brain with stroke.
- The orientation dependent contrast is so great, that the location of ischemia, compared to artifactual signals, can no longer be easily differentiated

https://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-weighted-sequences

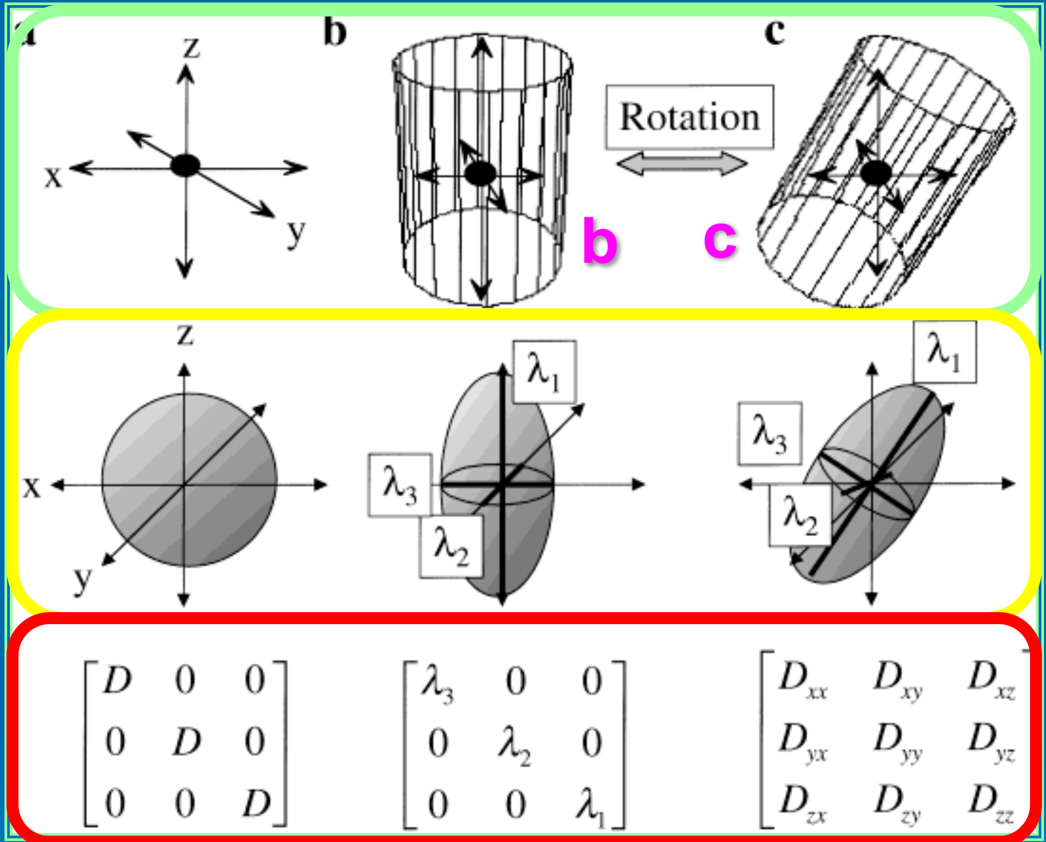
Anisotropic Diffusion



- The anisotropic diffusion can not be described by a single parameter
  - D is a scalar
  - The mathematical tool necessary is called *tensor*

Diffusion tensor

- Relationship between anisotropic diffusion, diffusion ellipsoids, and diffusion tensor
- In isotropic environment the diffusion ellipsoid is spherical
  - 1 diffusion constant, D
- In anisotropic environment water diffusion has directionality
  - e.g. cylindrical (b,c),
- The diffusion ellipsoid of water in a cylinder is elongated and has 3 principal axes, λ_1, λ_2, λ_3



AJNR Am J Neuroradiol 29:632–41 | Apr 2008 | www.ajnr.org

www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-tensor-anisotropy

Diffusion tensor

The diffusional signal loss by the gradient application obeys the following equation

$$\boxed{\frac{S}{S_0} = e^{-bD}}$$

In the presence of anisotropy, the tensor D fully describes molecular mobility along each direction and correlation between these directions

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

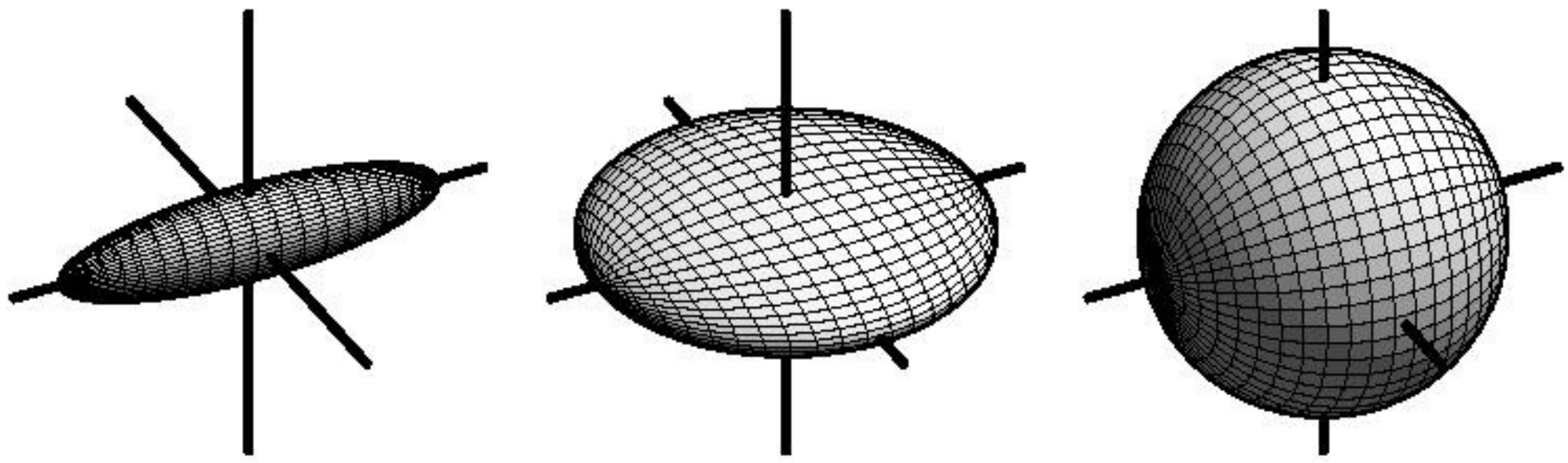
The diffusione tensor is symmetric:

$D_{ij} = D_{ji}$, with i, j = x, y, z

<u>9 elements but 6 independent values !</u>

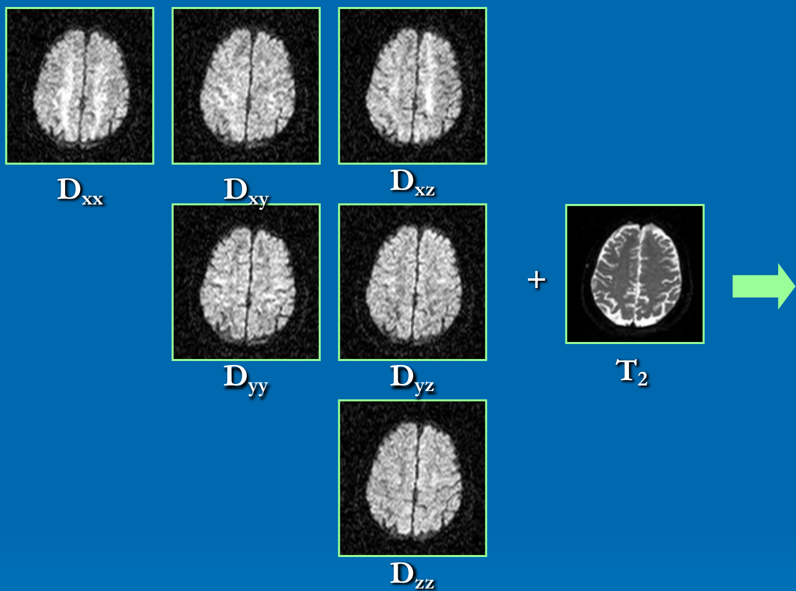
Graphical description

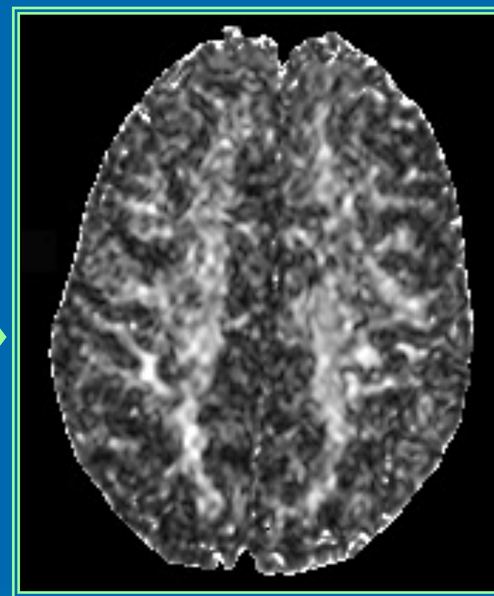
A good graphical description is given by a morphed sphere that reduces to an elipsoid with the <u>main axis parallel to the direction of the observed fibre</u>



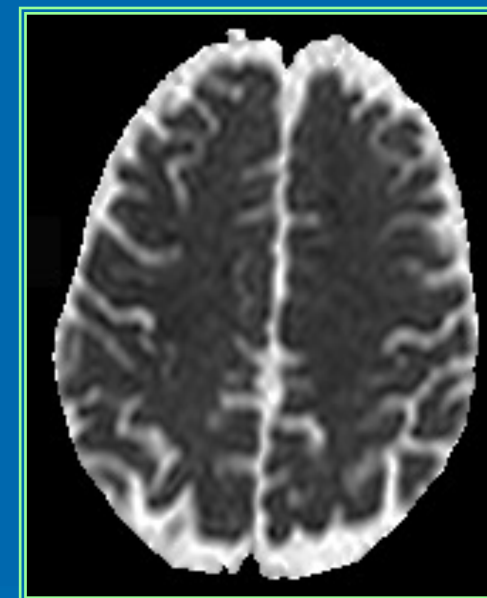
(a) Linear anisotropic diffusion (b) Planar anisotropic diffusion (c) Isotropic diffusion

DTI parameters





Fractional Anisotropy



Apparent Diffusion Coefficient

Fractional Anisotropy (FA):

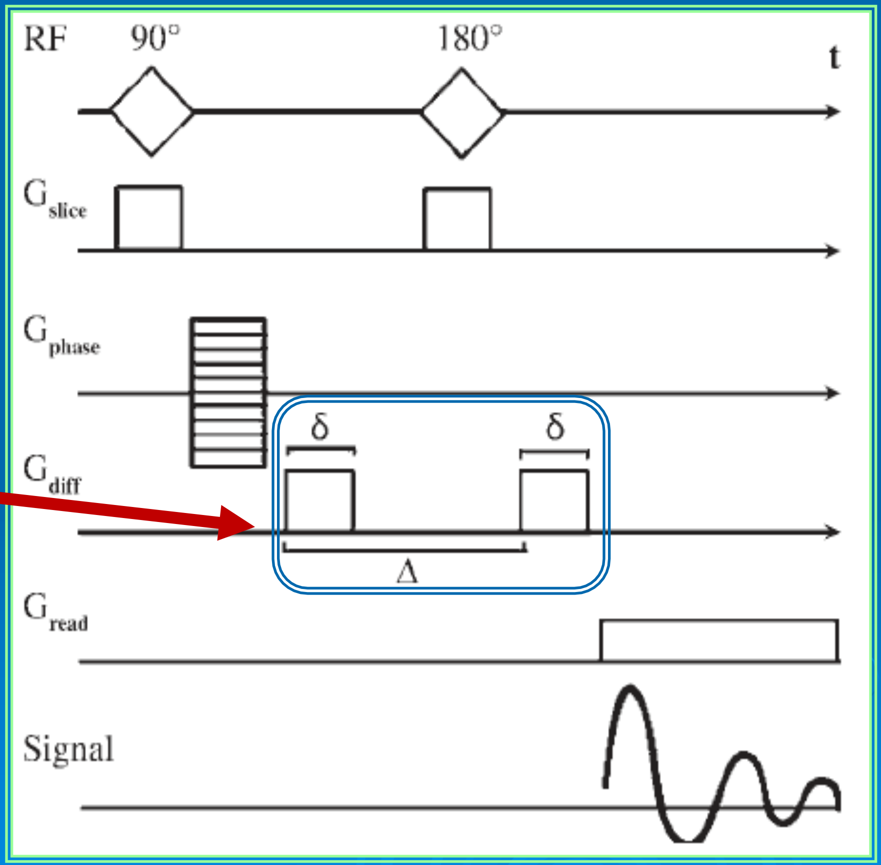
✓ between 0 e 1

- isotropic diffusion FA=0
- monodirectional diffusion FA=1

Diffusion weighted image acquisition

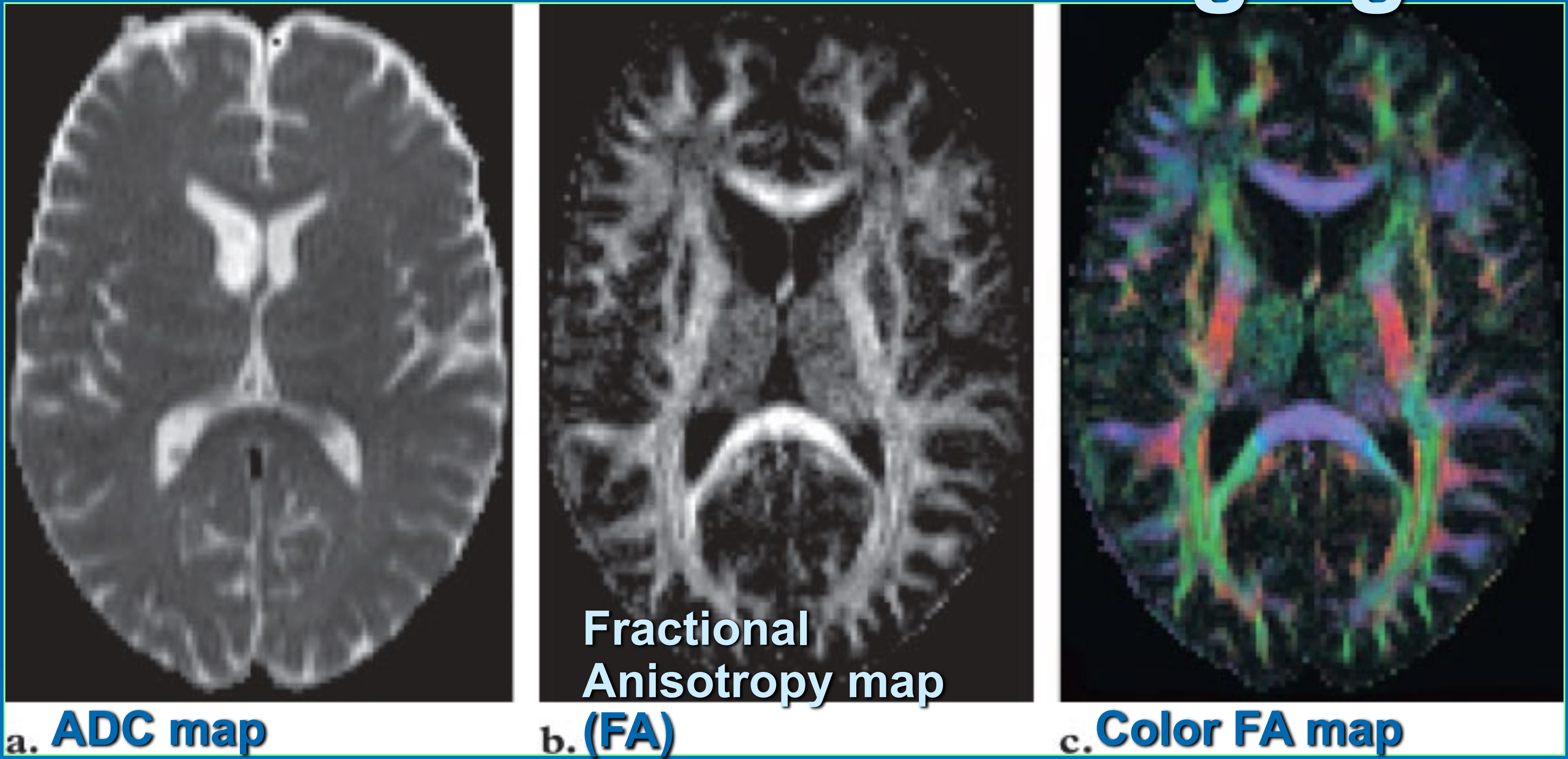
To calculate the diffusion tensor

- 6 diffusion weighted images
- a reference image
  - without diffusion gradient



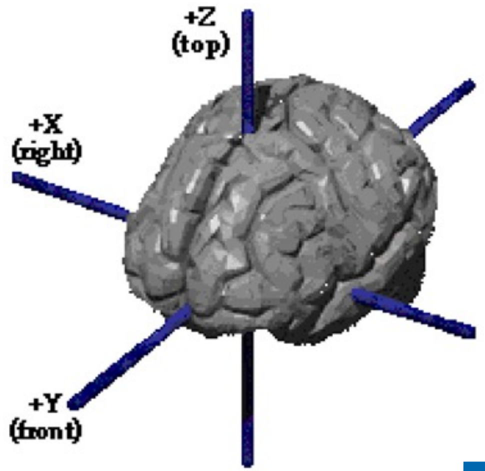
- In order to obtain better results a larger number of diffusion weighted images are acquired
  - 15, 32 gradient encoding directions or larger

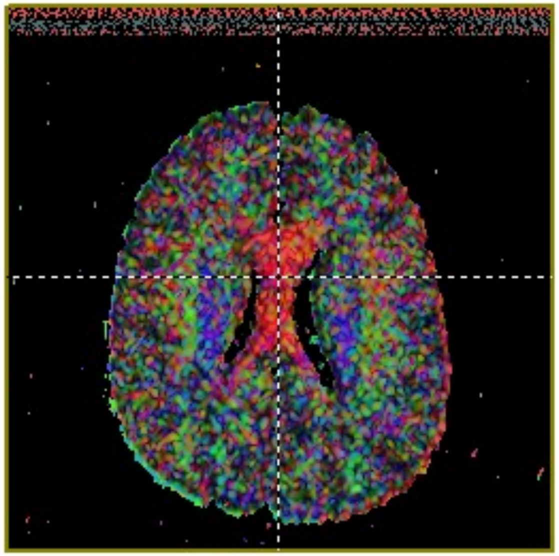
Diffusion Tensor Imaging



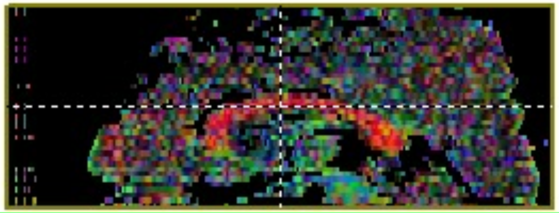
- ADC map: no information about direction
- FA map: information about the degree of anisotropy
- Color FA map: direction of the principal component
  - red, blue, and green representing diffusion along x, y, and z-axes, resp.

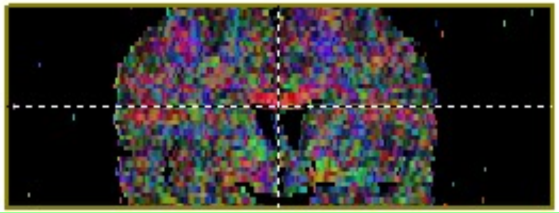
Color – coded results



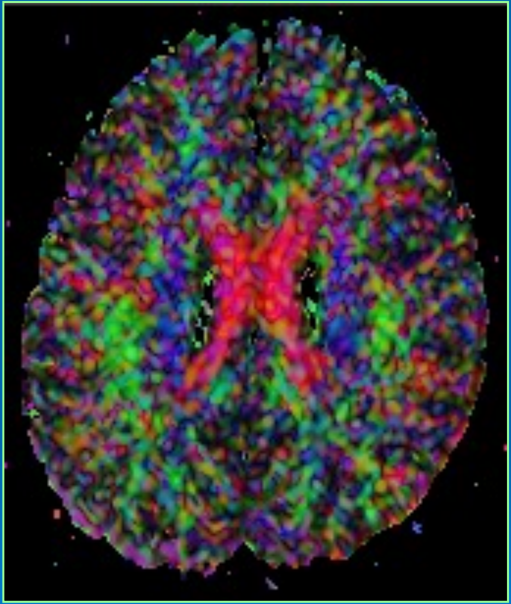


- Red: x
- Green: y
- Blue: z

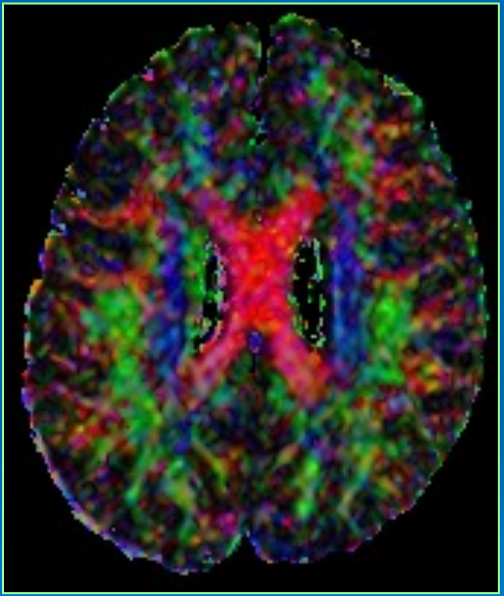




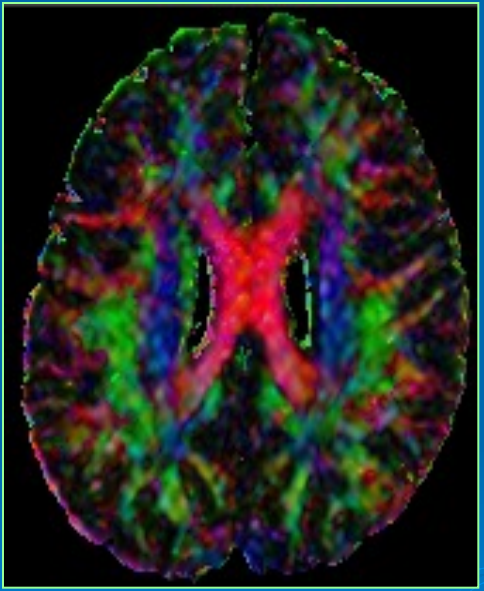
Quality vs. number of gradiets directions



6 directions



15 directions



32 directions

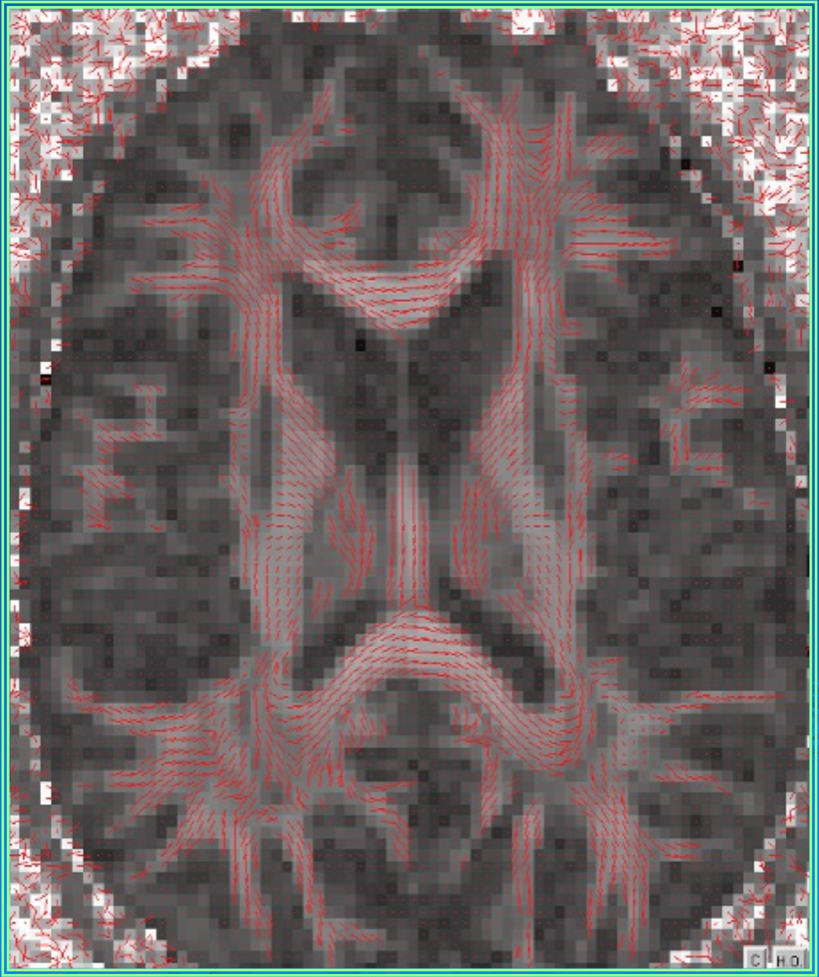
- Red: x
- Green: y
- Blue: z

Acquisition time is proportional to the acquisition time

Slides from Terry Peters

DTI-MRI summary

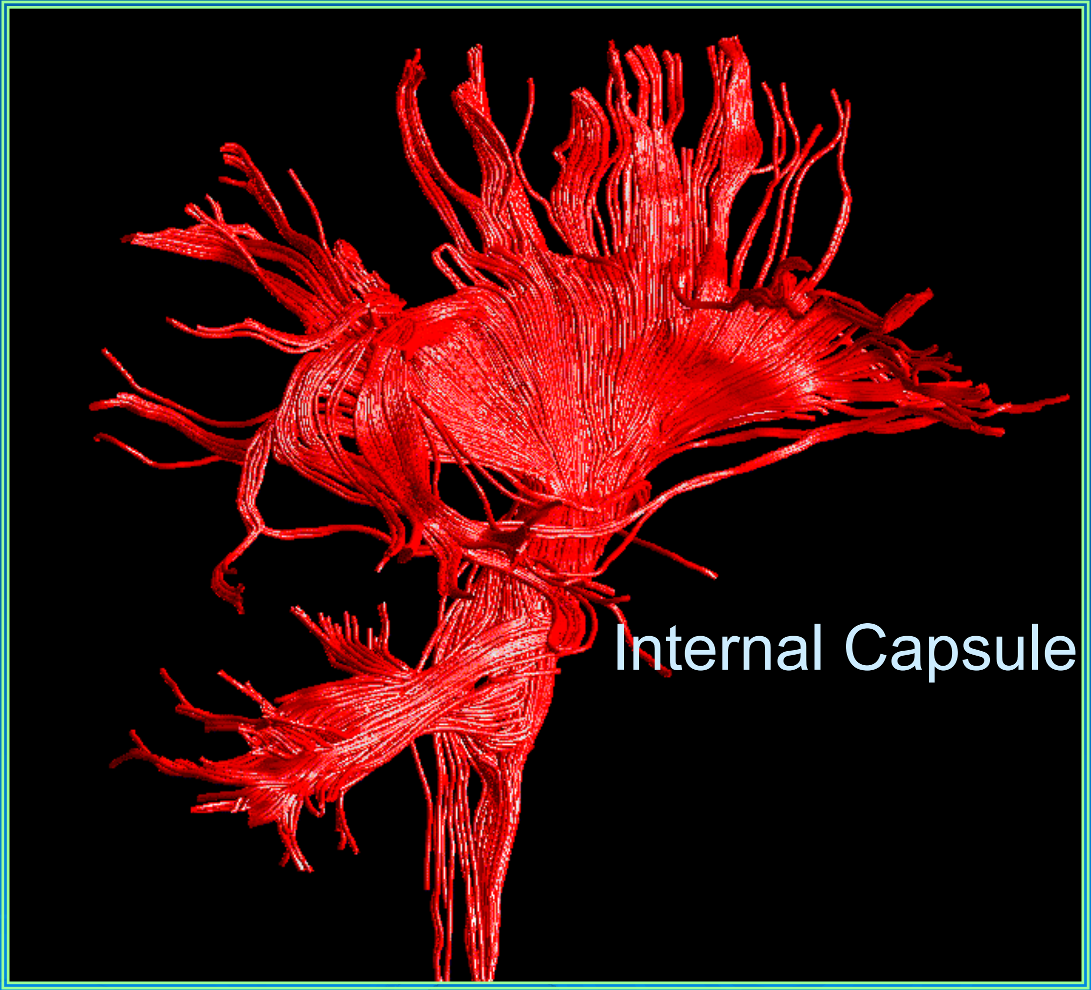
1. Image of diffuse fluid motion in brain
2. Construct "Tensor image"
   - extent of diffusion in each direction in each voxel in image
3. Diffusion along nerve sheaths defines nerve tracts
4. Create images of nerve connections/pathways



Slides from Terry Peters

Tractography

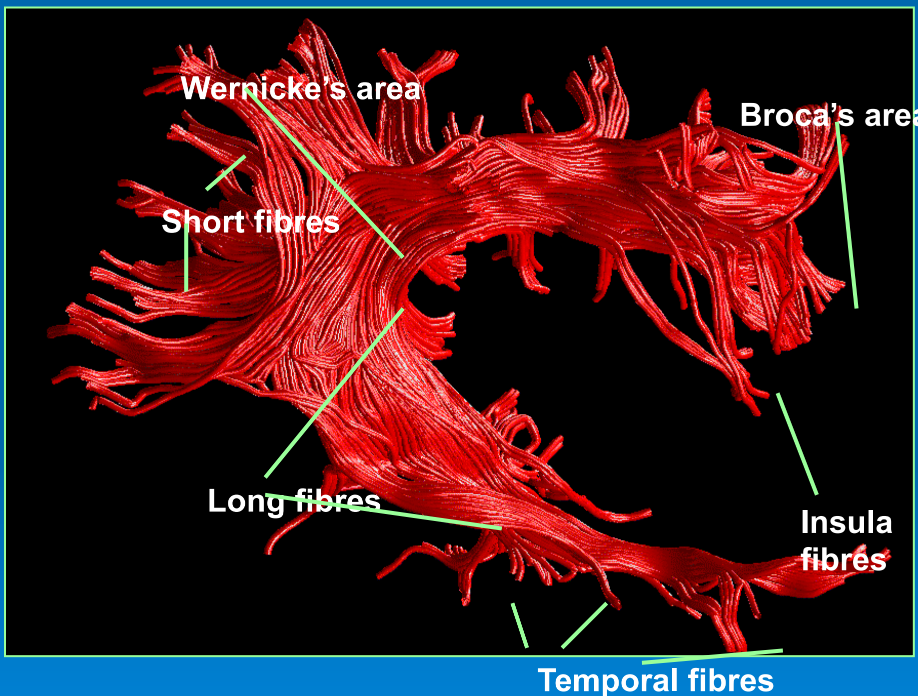
- Data analysed after scanning
- Identify "streamlines" of vectors
- Connect to form fibre tracts
- 14 min scan time



- Dr. D Jones, NIH

Slides from Terry Peters

Tractography

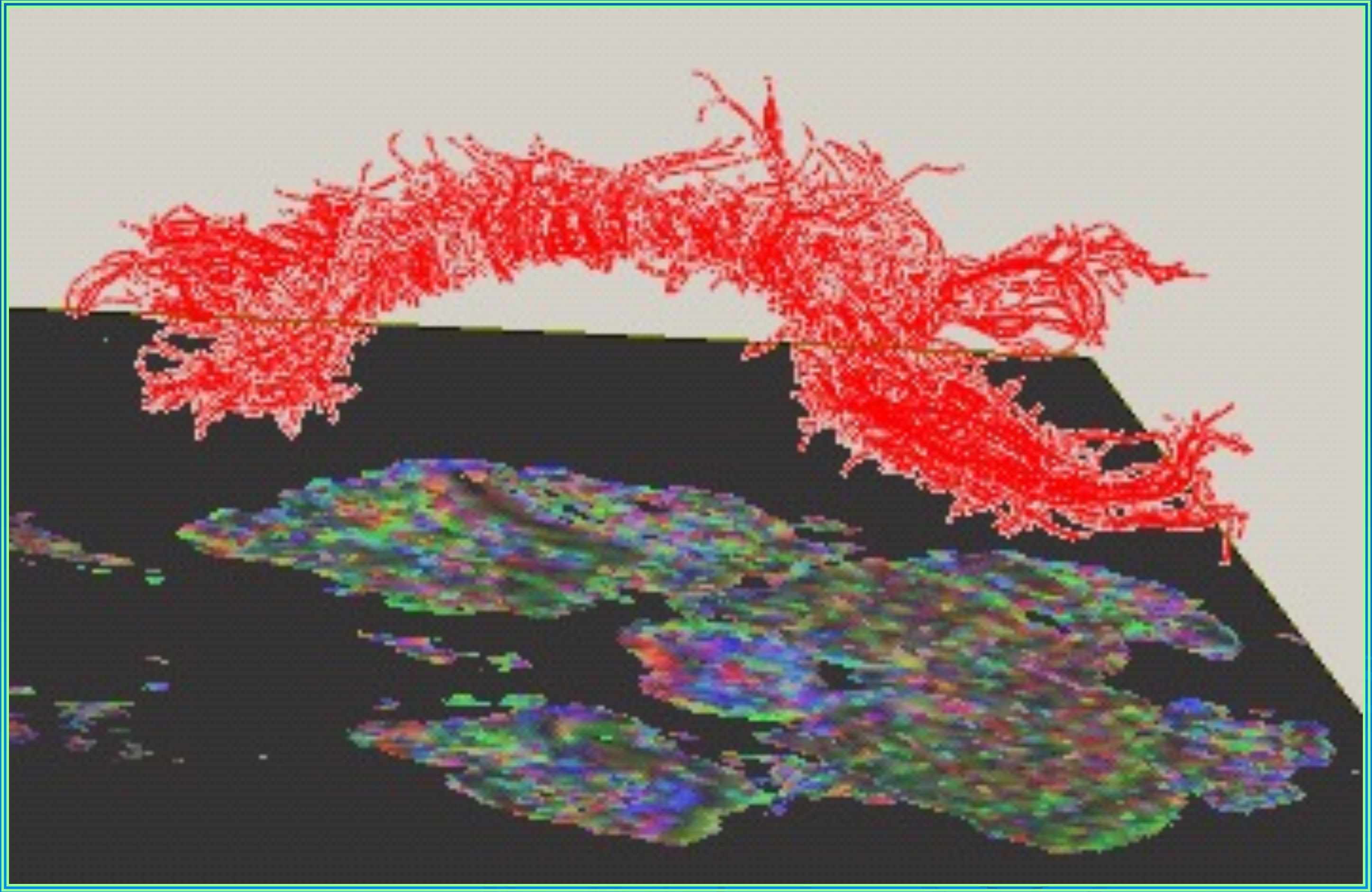


"just like Gray's Anatomy"!

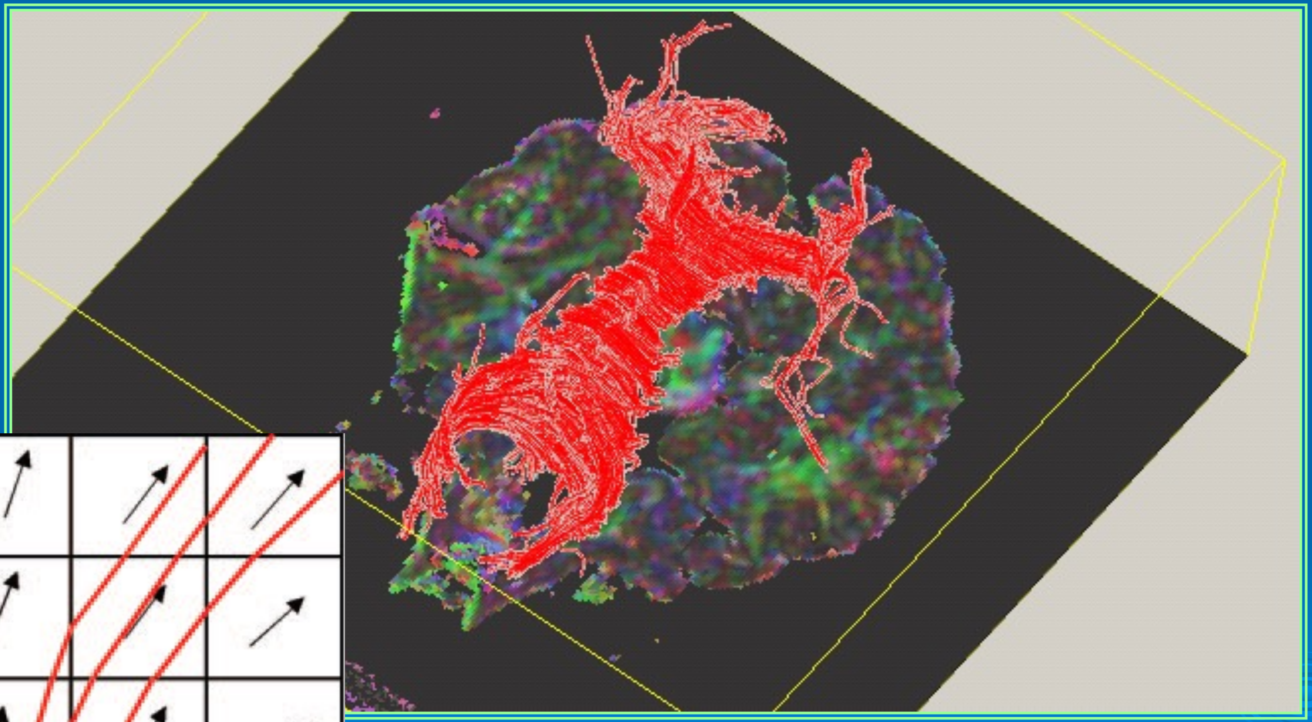
Superior Longitudinal Fasciculus

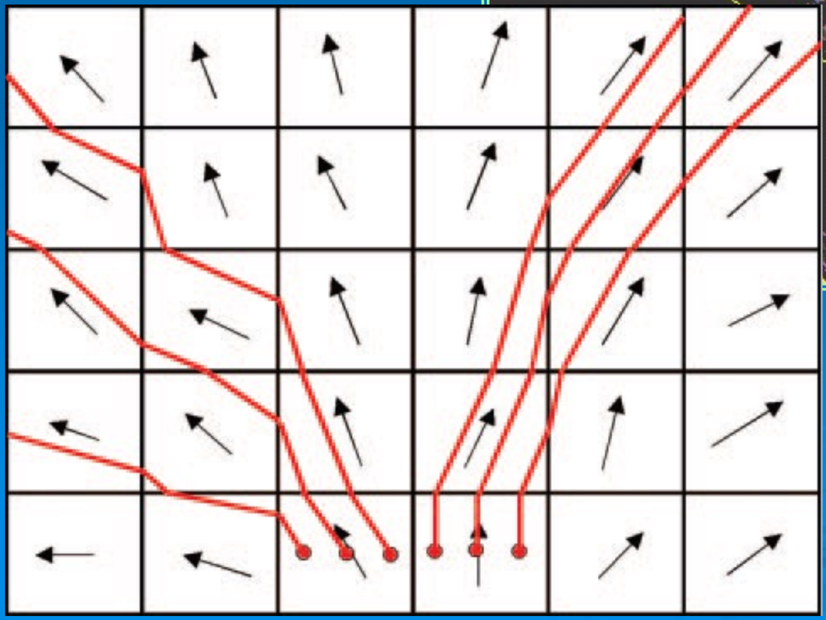
- Dr. D Jones, NIH USA

DTI: corpus callosum (1)



DTI: corpus callosum (2)





NMR IN BIOMEDICINE
NMR Biomed. 2002;15:468–480
Published online in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/nbm.781

Review Article

Fiber tracking: principles and strategies – a technical review

Susumu Mori* and Peter C. M. van Zijl

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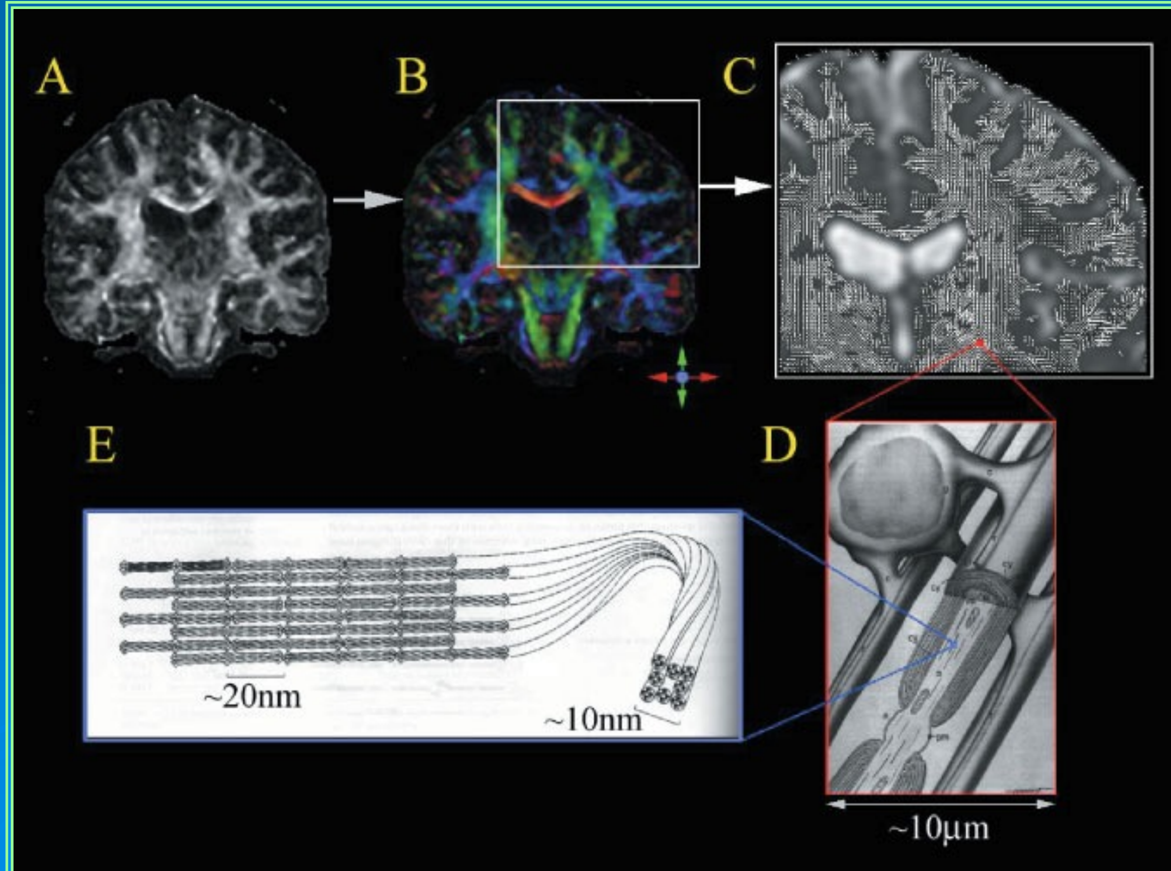
A. **Anisotropy map: white matter enhancement**
B. **Color map: white matter parcellated into various tracts**
C. **Each pixel contains bundles of axons and neuroglial cells**
   - $\sim 10\ mm^3$
D. **Cells dimensions**



Nerves geometry

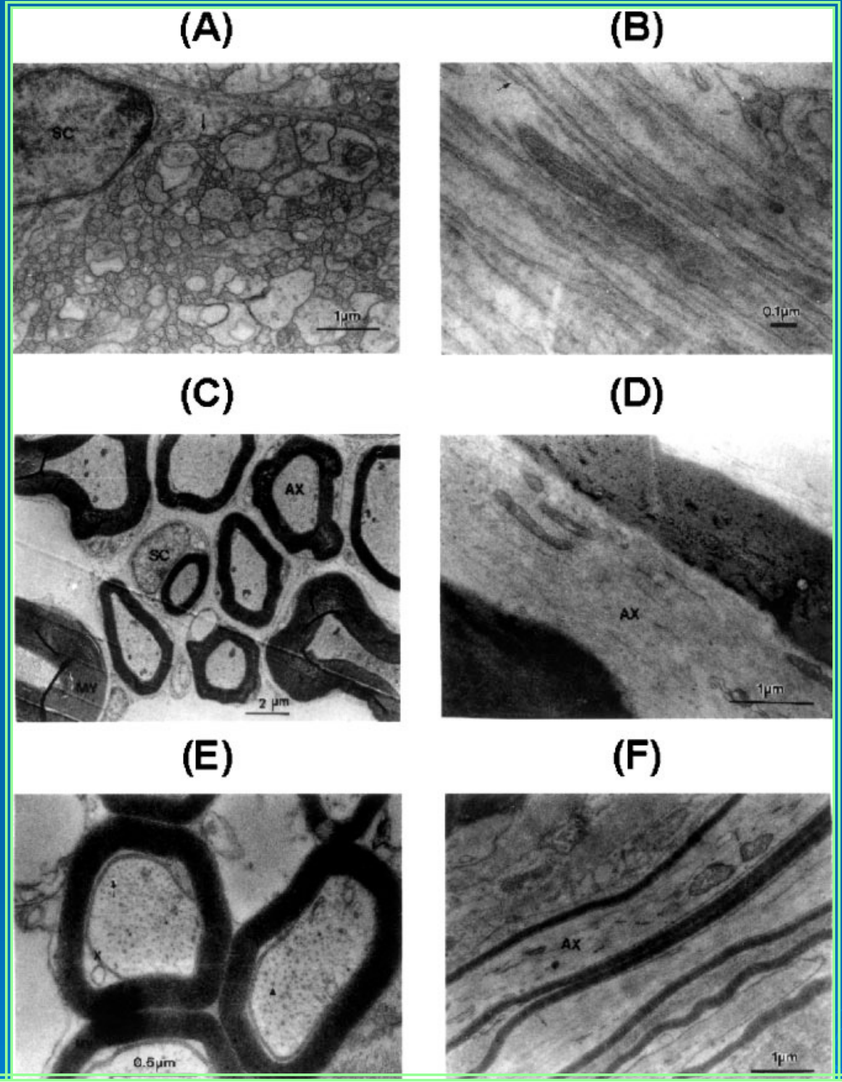
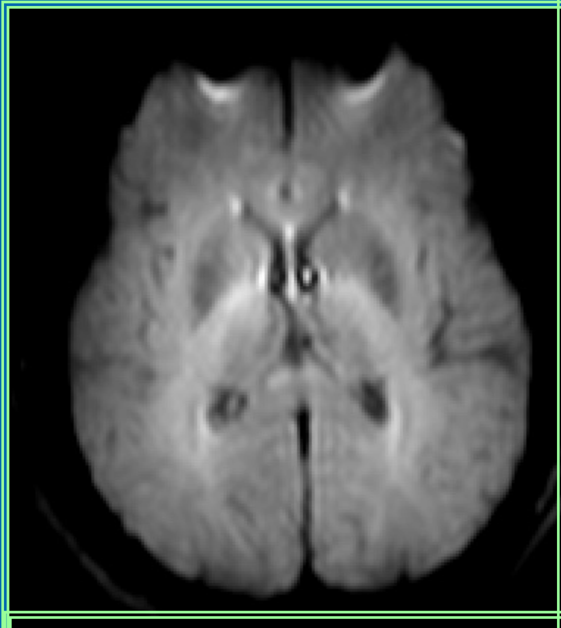
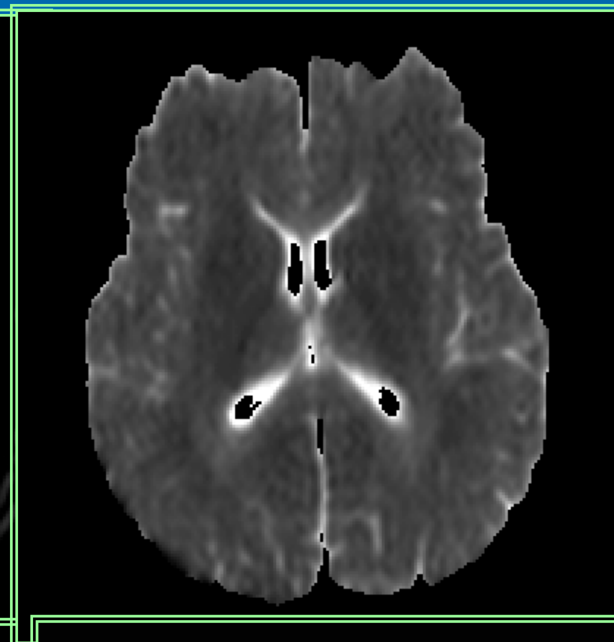


Figure 6. Electron micrographs of transverse (A, C, E) and longitudinal (B, D, F) sections from freshly excised non-myelinated olfactory (A, B), myelinated trigeminal (C, D), and myelinated optic (E, F) nerves of the garfish. *Olfactory nerve*: (A) The small (~0.25 µm diameter), circular, relatively homogeneous non-myelinated axons (arrow) are packed together tightly. Microtubules (seen as small dots within the axons) and a Schwann cell nucleus (SC) are visible. (B) Axonal membranes (arrow) run diagonally across the micrograph. *Trigeminal nerve*: (C) The axons (AX) have diameters ~3–6 µm and appear to have good circular shapes which is indicative of a structurally sound nerve.

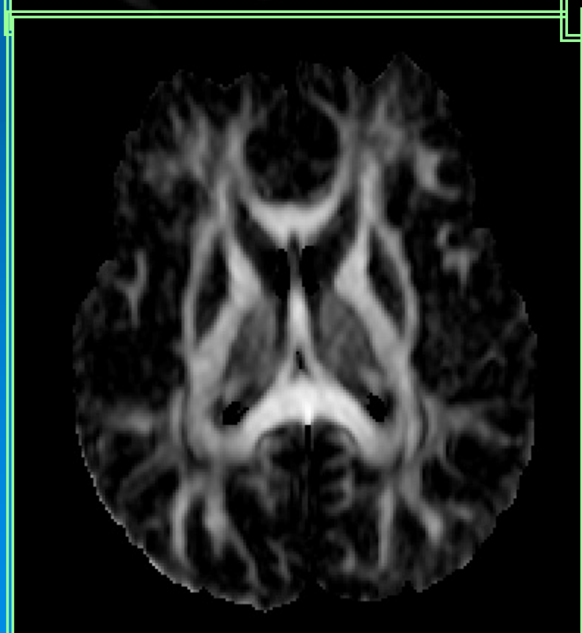
T2

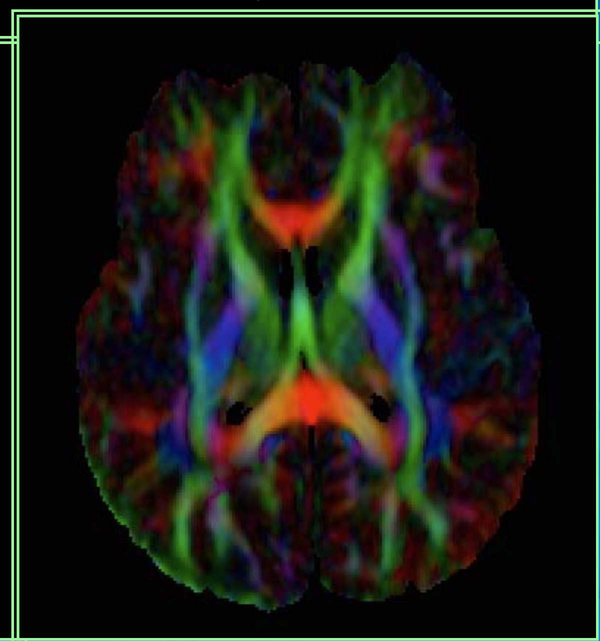




ADC
3 gradients
directions

DTI
FA





FA
Color
coded

Modeling diffusion

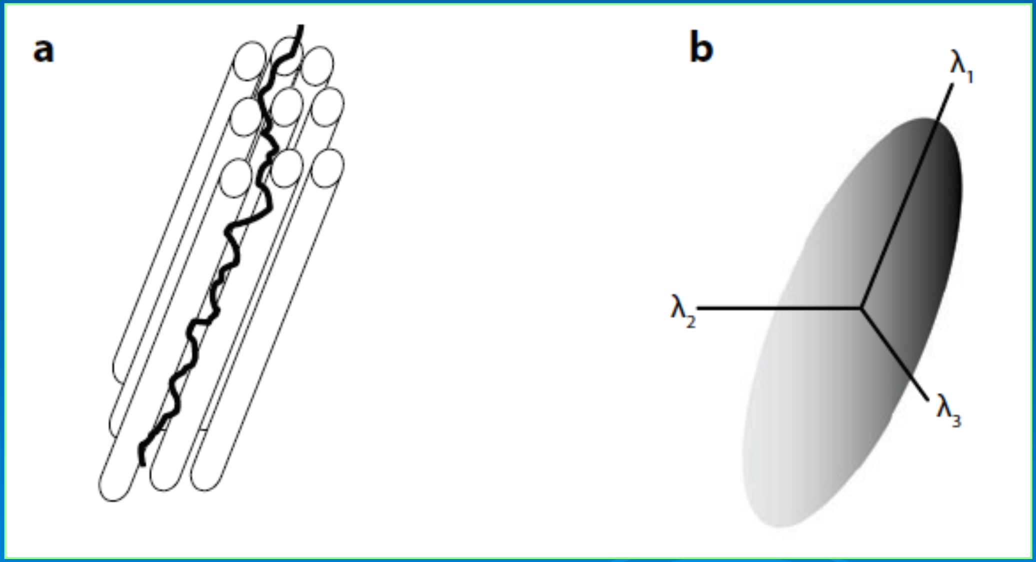

Using Diffusion Imaging to Study Human Connectional Anatomy

Heidi Johansen-Berg[1] and Matthew F.S. Rushworth[1,2]

a) **Schematic to illustrate diffusion of a water molecule (black line) within a fiber bundle.**

b) **The diffusion tensor model: Water diffusion <u>at each voxel</u> is modeled by a tensor**

- ✓ **characterized by its 3 principal eigenvectors and their associated eigenvalues (λ_1, λ_2, λ_3).**



Annu. Rev. Neurosci. 2009.32:75-94.

Modeling diffusion

Using Diffusion Imaging to Study Human Connectional Anatomy

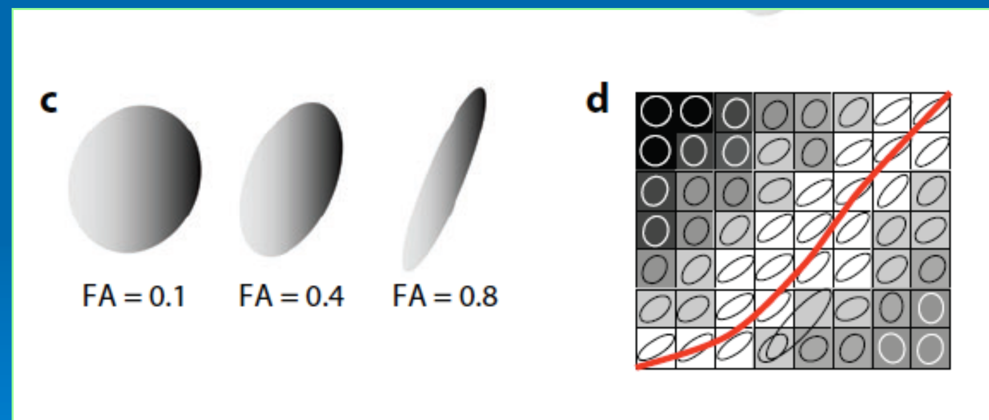
Heidi Johansen-Berg[1]
and Matthew F.S. Rushworth[1,2]

c) Fractional anisotropy (FA) is calculated from the tensor and ranges between 0 and 1

- reflects the shape of the tensor

d) Simple tractography proceeds by tracing a line through the tensor field, following the principal diffusion direction

- the grayscale reflects FA
  - from 0 (black) to 1 (white)]
- The corresponding tensors are illustrated by the ellipses shown at each voxel

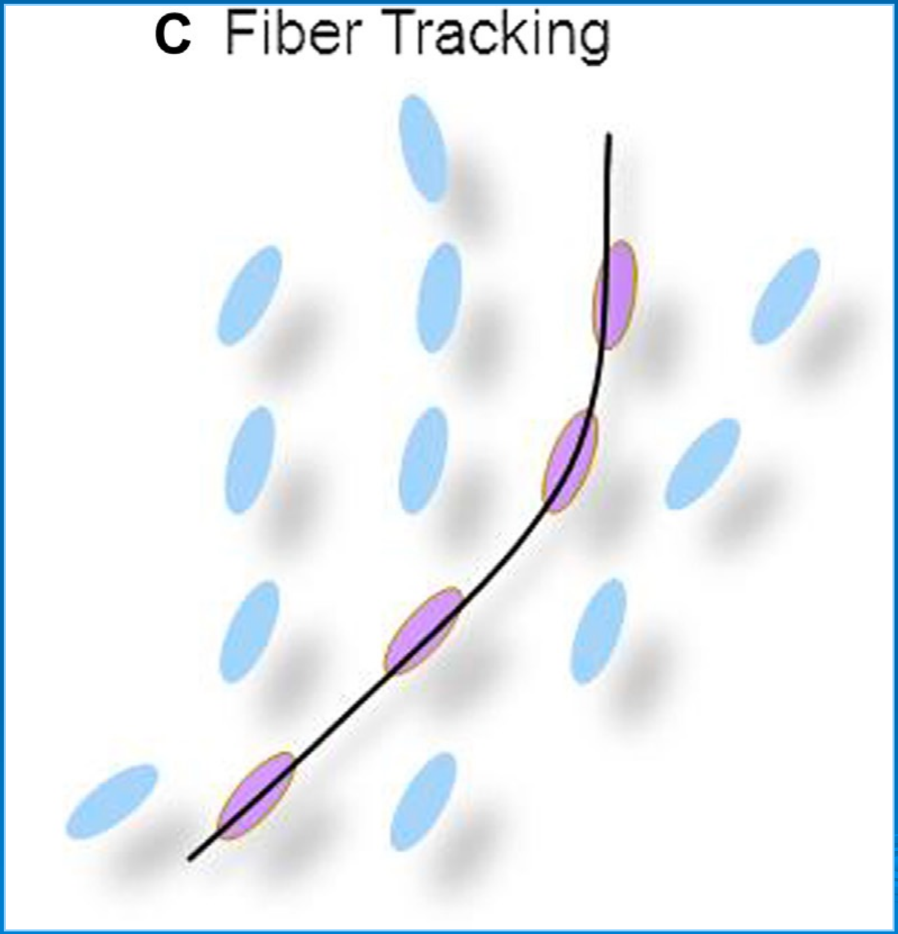


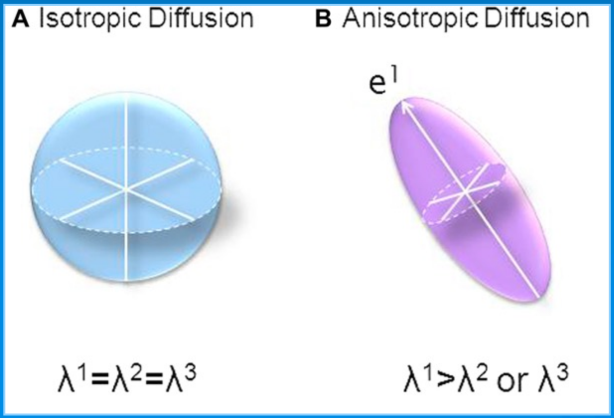
Annu. Rev. Neurosci. 2009.32:75-94.

Modeling diffusion

Fiber tracking is initiated at a pixel or region of interest (ROI) and tracking is propagated along adjacent ellipsoids that meet certain thresholds for FA and trajectory curvature

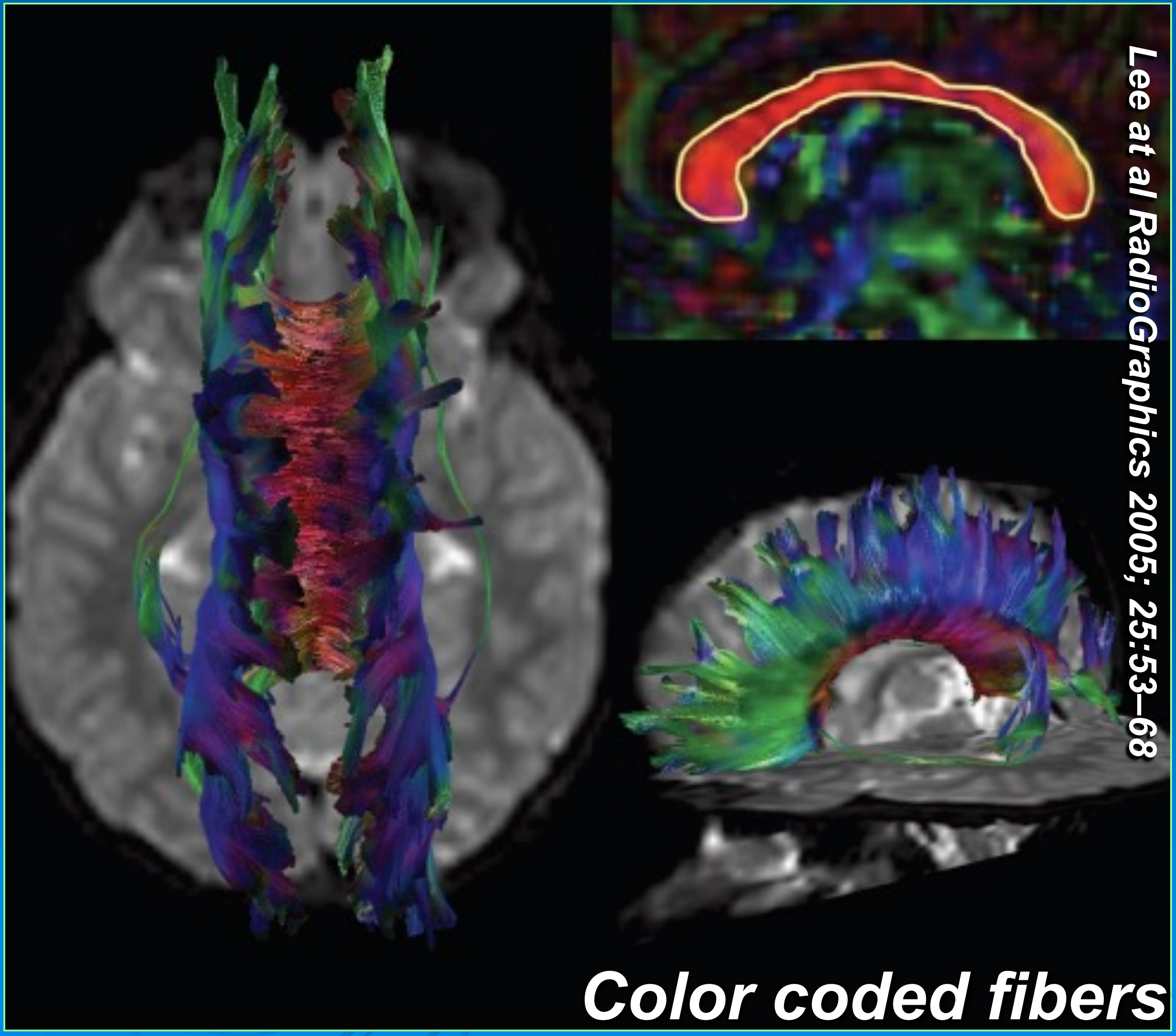
Lerner et al World Neurosurg. (2014) 82, 1/2:96-109





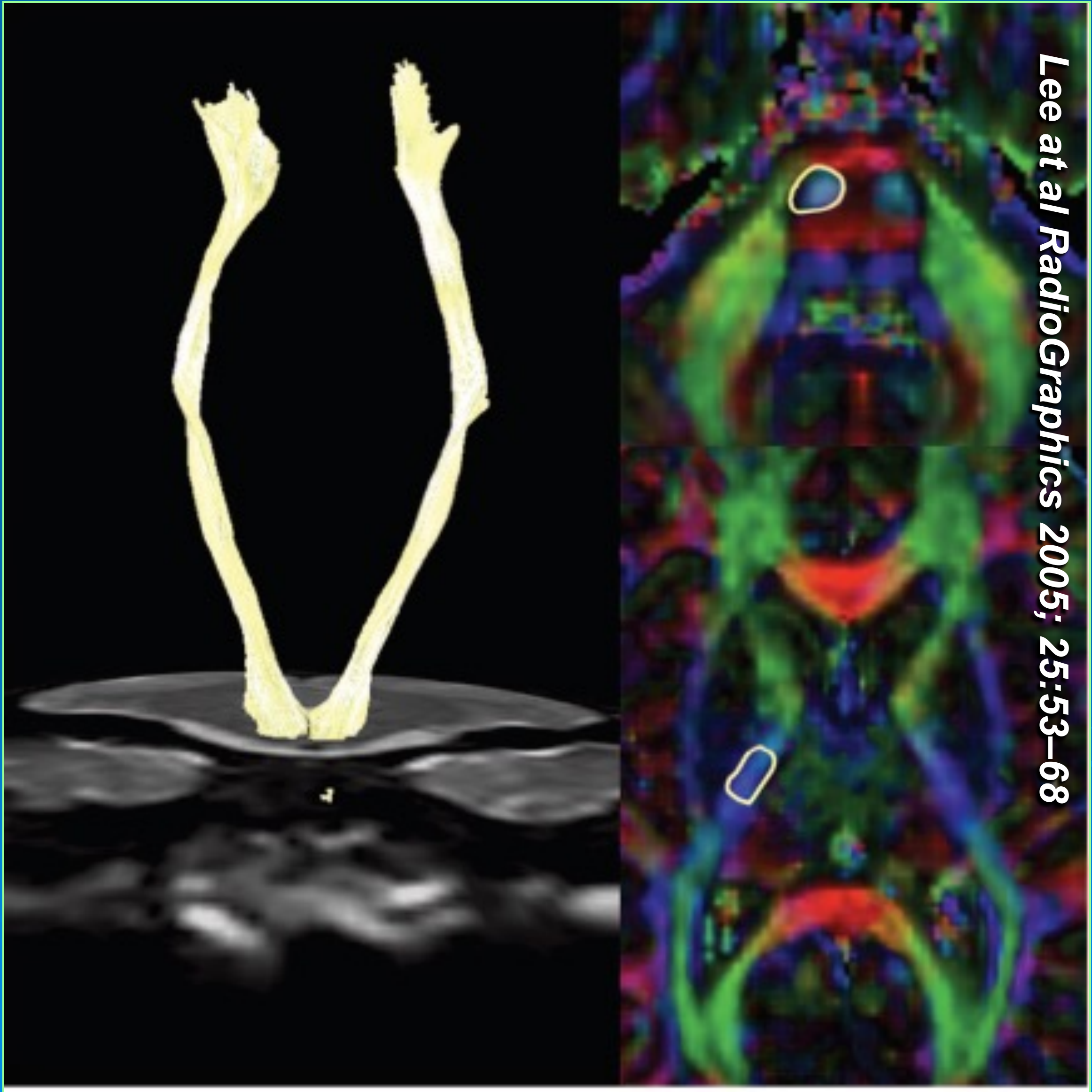
FT of the corpus callosum

- **FT images of the corpus callosum (left and bottom right) are <u>generated from a single ROI</u> at the precise anatomic locations on the sagittal color map (top right).**

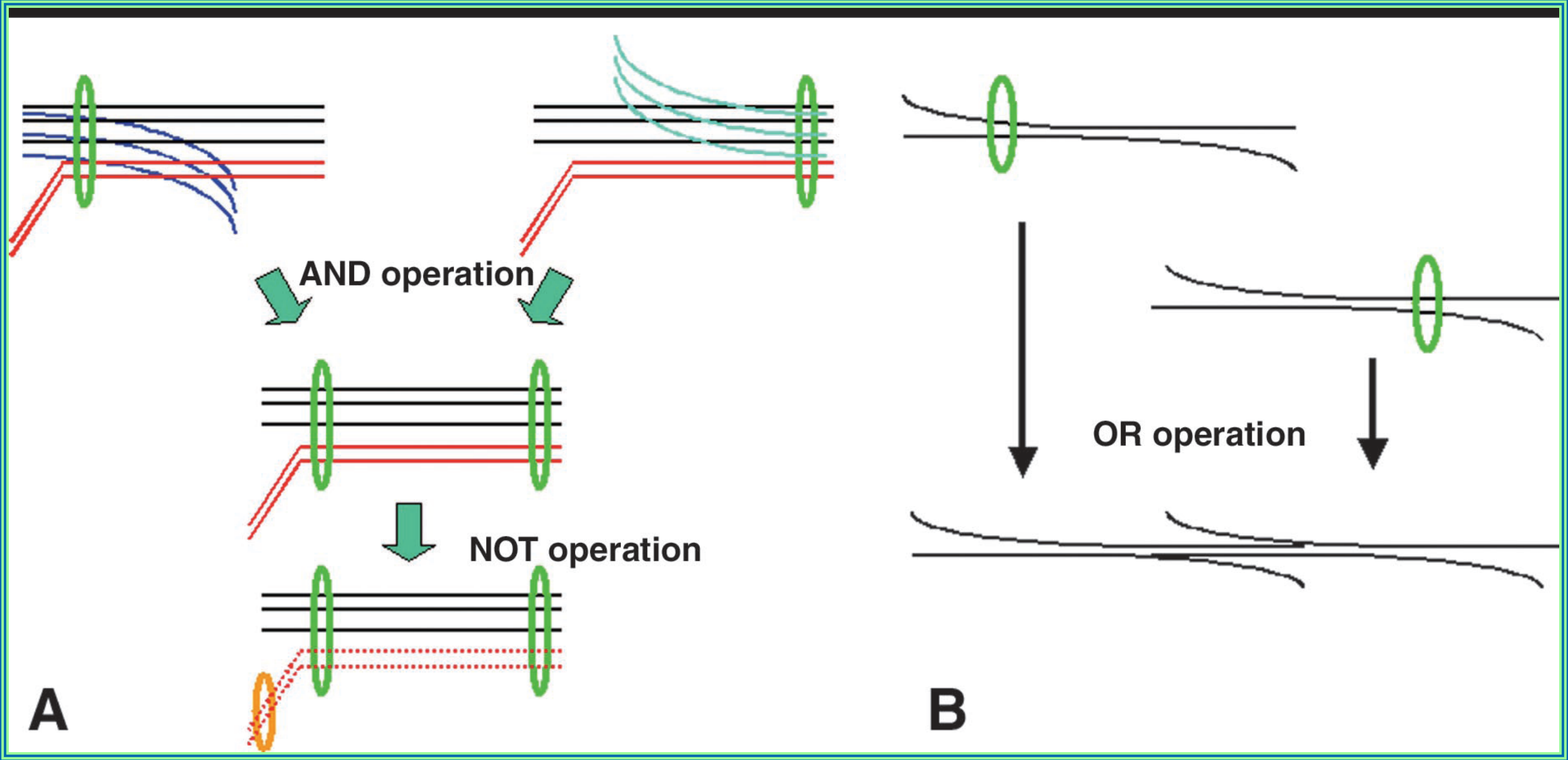


FT of the CST

- FT image of the corticospinal tract generated from the fibers connecting two ROIs in the longitudinal pontine fibers and the posterior limb of the internal capsule



Lee at al RadioGraphics 2005; 25:53–68



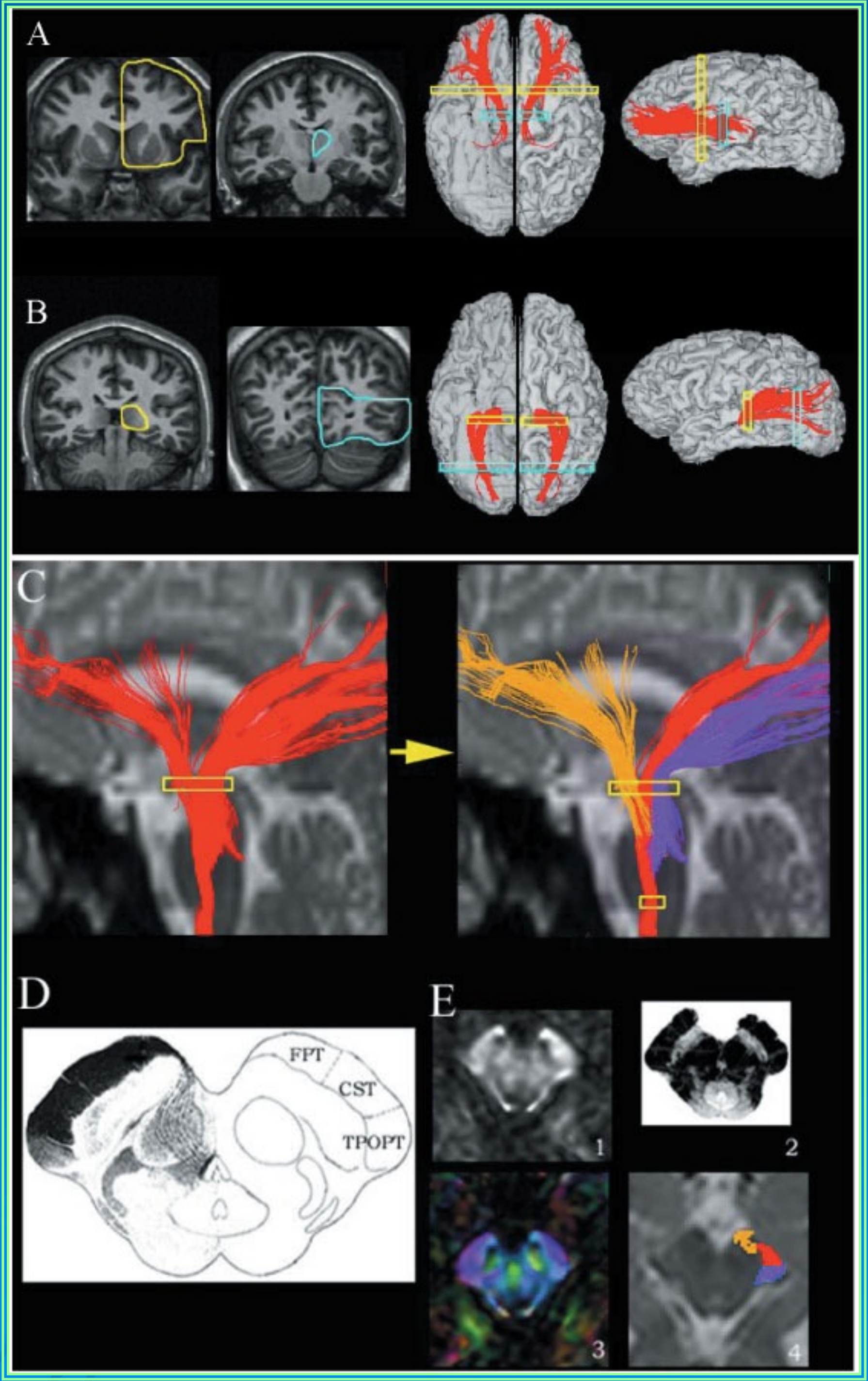
Three operations used FT: AND, NOT, OR

A. **Two ROIs (green) are placed on anatomic landmarks. When the AND operation is used, tracts that penetrate both ROIs are selected. NOT operation is used to remove specific tracts that penetrate one or multiple ROIs (orange). In this example, red tracts are removed.**

B. **OR operation.**

Multi-ROI tracking approach

Figure 4. Example of using the multi-ROI approach to reconstruct white matter tracts of interest. Coronal images show the locations of two reference ROIs for each tract. The reconstruction results for the anterior (A) and posterior (B) thalamic radiation are presented in the axial and sagital view. Images in (C)–(E) show examples of the parcellation of homogeneous-looking white matter based on 3D tract trajectories. Results of tract reconstruction that penetrate the cerebral peduncle are shown in (C). Tracts excluded by the second ROI at the lower pons level are shown by green and blue. Yellow boxes indicate the locations of ROIs. The postulated parcellation of the cerebral peduncle based on anatomical studies is shown in (D). Images in (E) shows anisotropy map (E-1), histological preparation (E-2), color-coded map (E-3), and T_2-weighted image with the location of reconstructed results superimposed (E-4). The figures were reproduced from Mori *et al.*[52] (A,B), Stieltjes *et al.*[42] (C,E) and Carpenter[49] (D) with permission



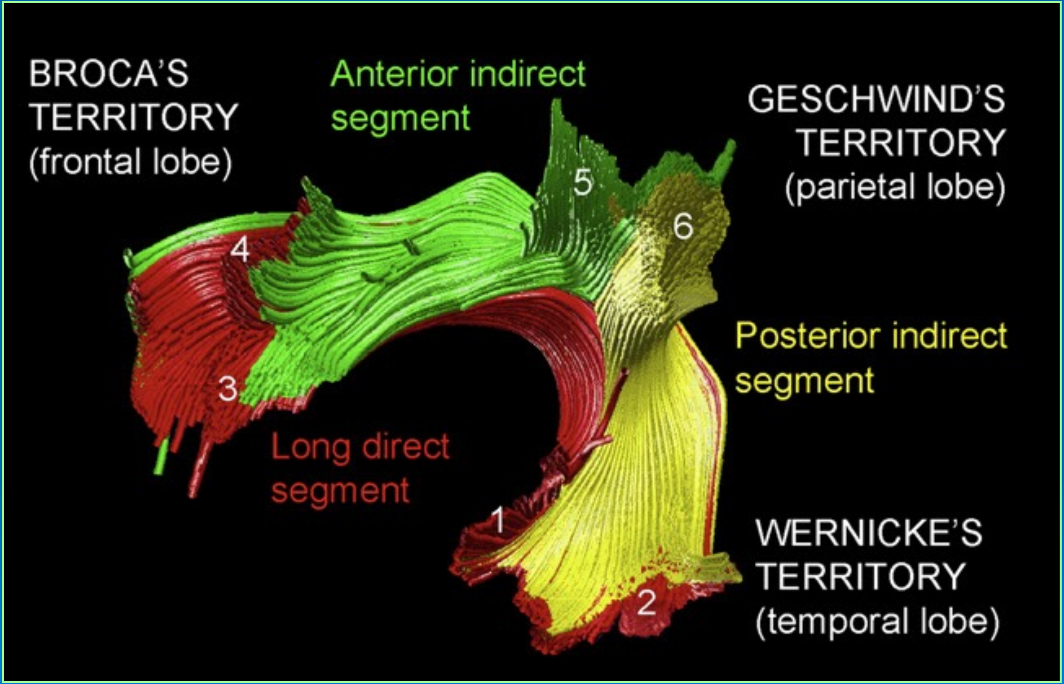
Additional material

- https://www.youtube.com/watch?v=J_aamnpRJE8

Studying connections in the living human brain with diffusion MRI

Derek K. Jones*

c o r t e x 4 4 (2 0 0 8) 9 3 6 – 9 5 2



The arcuate fasciculus and the disconnection theme in language and aphasia: History and current state

c o r t e x 4 4 (2 0 0 8) 9 5 3 – 9 6 1

Marco Catani[a,*] and Marsel Mesulam[b]

A diffusion tensor imaging tractography atlas for virtual in vivo dissections

CORTEX 44 (2008) 1105–1132

Marco Catani[a,b,] and Michel Thiebaut de Schotten[a,b,c]*

Abstract

- Diffusion tensor imaging (DTI) tractography allows perform virtual dissections of white matter pathways in the living human brain. [..]
- Here […] we provide a template to guide the delineation of ROIs for the reconstruction of the association, projection and commissural pathways of the living human brain. The template can be used for single case studies and case–control comparisons.
- An atlas of the 3D reconstructions of the single tracts is also provided as anatomical reference in the Montreal Neurological Institute (MNI) space.

Corpus callosum

- Anatomy. The corpus callosum is the largest bundle of the human brain […]
- Identification on the color maps:
  - **The red fibers of the body of the corpus callosum are ventral to the cingulum and medial to the lateral ventricles (MNI 35 to 29).**
  - **The body of the corpus callosum separates into the genu, anteriorly (MNI 27 to 1), and the splenium, posteriorly (MNI 27 to 11).**
    - **The tapetum is not visible on the color map.**
- Delineation of the ROIs on the FA maps:
  - **A single ROI (CC) is defined around the body, the genu and the spleniumof the corpus callosum (MNI 35 to 5). The shape of the regions follows the anatomy of the different parts of the corpus callosum, butterfly-shaped for the body, horseshoe-shaped for genu and splenium.**

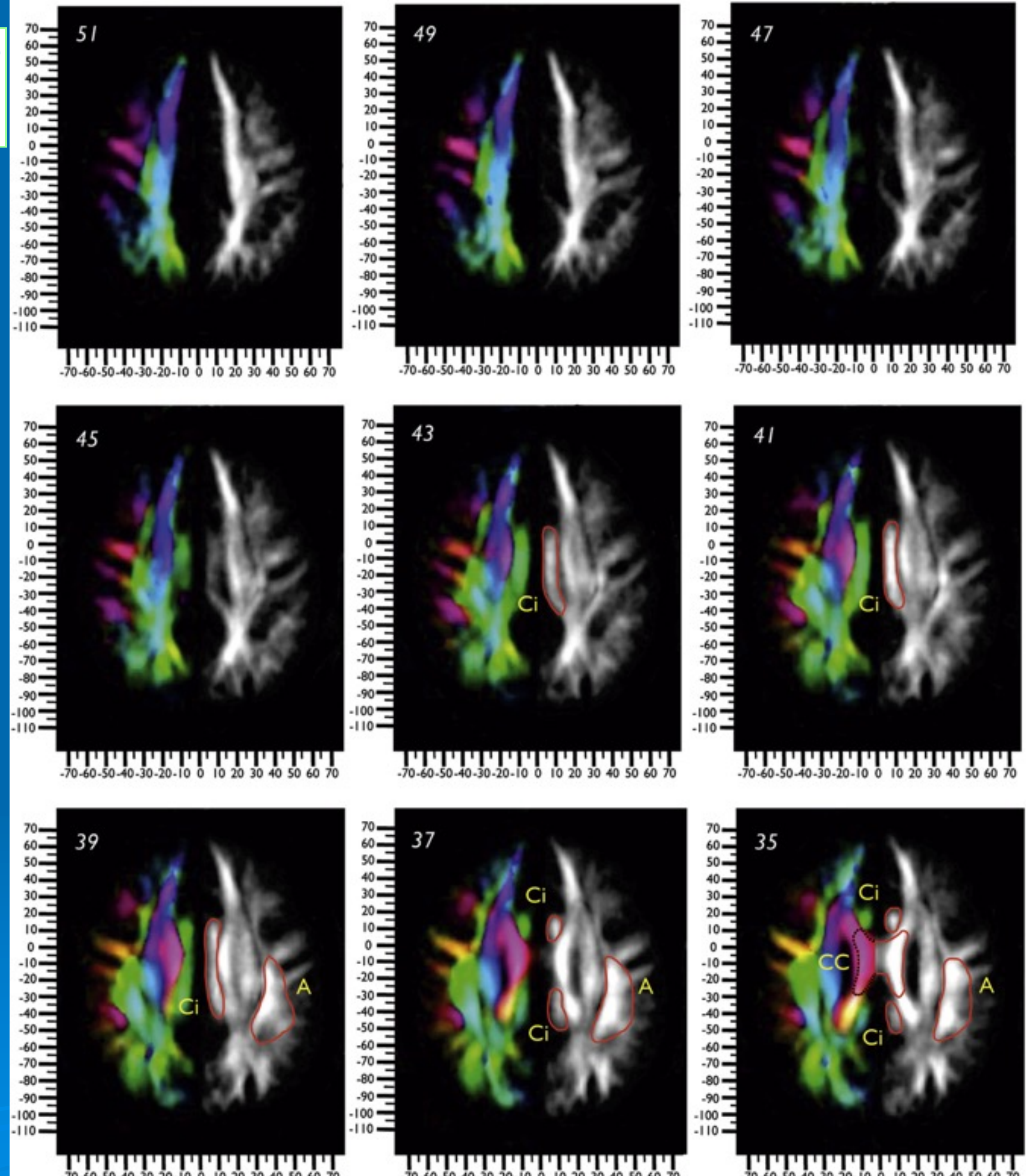
A diffusion tensor imaging tractography atlas for virtual in vivo dissections

Marco Catani[a,b,] and Michel Thiebaut de Schotten[a,b,c]*

A diffusion tensor imaging tractography atlas for virtual in vivo dissections

Marco Catani[a,b,] and Michel Thiebaut de Schotten[a,b,c]*

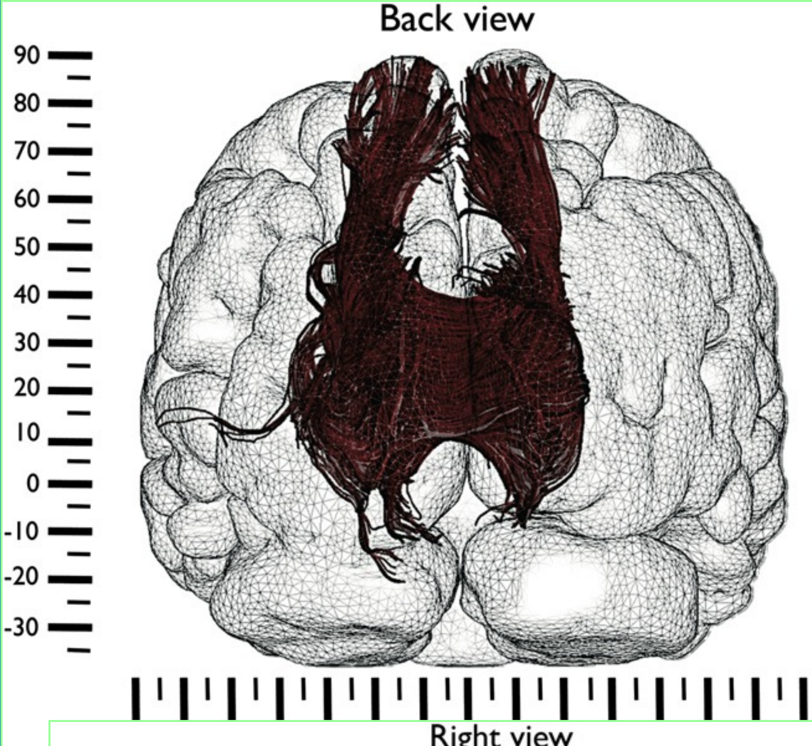
- **<u>Diffusion tensor image template of an average data set and delineation of ROIs</u>**
- **The FA maps on the right provide information about the general anatomy**
  - **the major association, commissural and projection white matter tracts**
- **The color maps on the left provide additional information on the local orientation of the tracts**
  - **red color indicates a laterolateral direction green color an anterior–posterior direction, and blue color a dorsal–ventral direction.**
  - **Other colors indicate intermediate directions.**

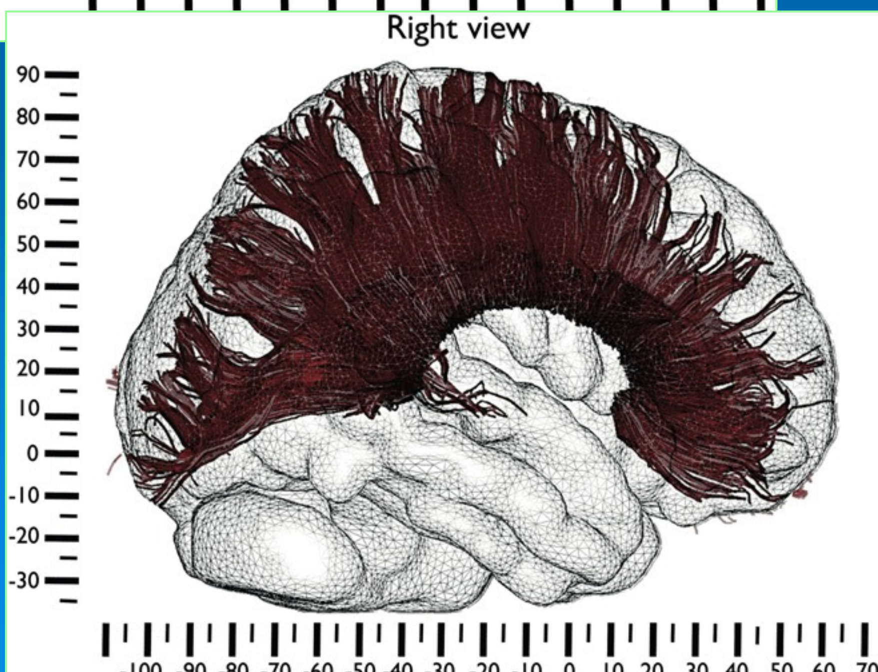


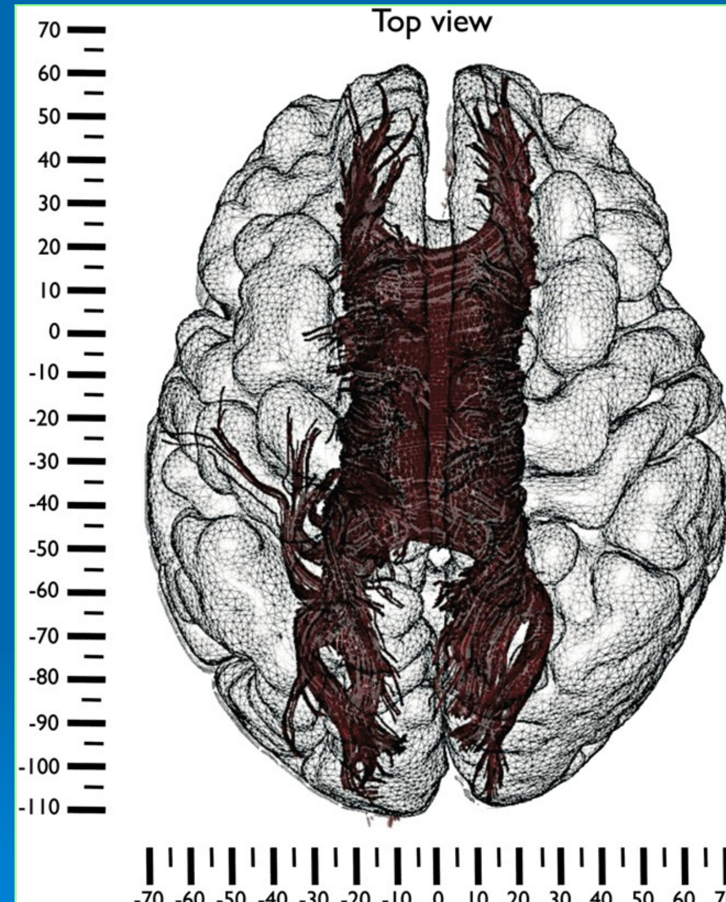
ROIs legend

A	Arcuate	Fx	Fornix body	SCP	Superior cerebellar peduncle
AC	Anterior Commissure	Fl	Fimbriae of fornix left	MCP	Middle cerebellar peduncle
CC	Corpus Callosum	T	Temporal	ICP	Inferior cerebellar peduncle
Ci	Cingulum	O	Occipital	DCN	Deep cerebellar nuclei
CP	Cerebral peduncle	IC	Internal capsule		
E	External/Estreme capsule				

Corpus callosum







A diffusion tensor imaging tractography atlas for virtual in vivo dissections

Marco Catani[a,b,*] *and Michel Thiebaut de Schotten*[a,b,c]

Material and methods (1)

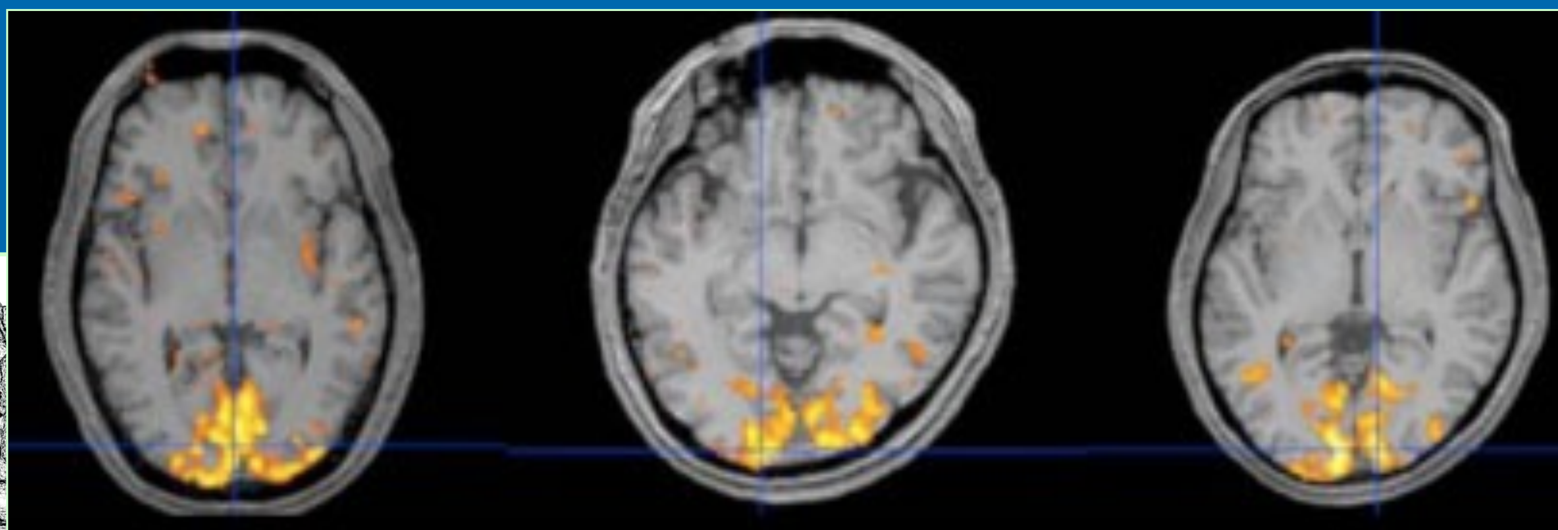
- 12 right-handed male subjects
  - 34.3 ± 5.7 years old
- MRI data were acquired using echo-planar imaging at 1.5 T [..] with a standard head coil for signal reception
- T1-weighted anatomical images were acquired [..]
- DTI axial slices acquisition parameters: repetition time 19 s; [..] voxel size $1.88 \times 1.88 \times 2$ mm^3, 200 independent directions, <u>b-value 3000 s/mm^2</u>

A diffusion tensor imaging tractography atlas for virtual in vivo dissections

Marco Catani[a,b,] and Michel Thiebaut de Schotten[a,b,c]*

Material and methods (2)

- […] The 12 data sets were spatially normalized and averaged […]. Briefly, the method includes the following steps:
  1. registration of individual T1 images with the diffusion tensor data sets;
  2. normalization of the registered T1 using both linear and non-linear parameters;
  3. normalization of the diffusion tensor data sets using the deformation parameters derived from (ii);



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Marco Catani[a,b,] and Michel Thiebaut de Schotten[a,b,c]*

AFFINE REGISTRATION

An affine transform can include rotation, scaling, shearing and translation

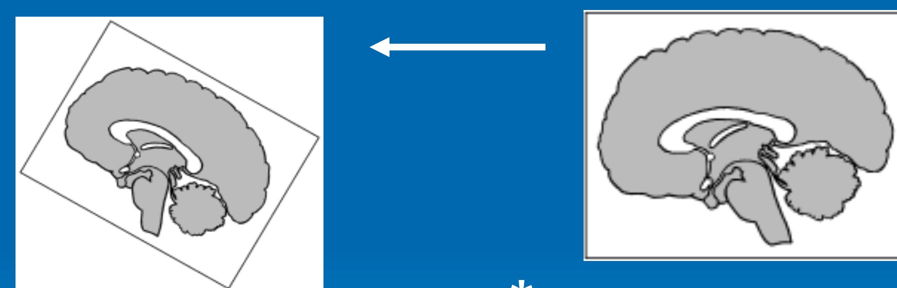
Rigid registration includes only rotation and translation

Translation

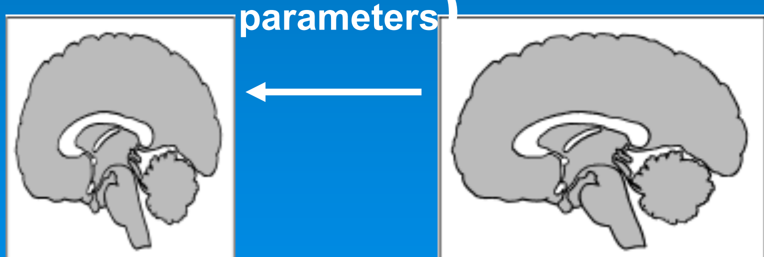
(3 parameters)

Rotation

(3 parameters)

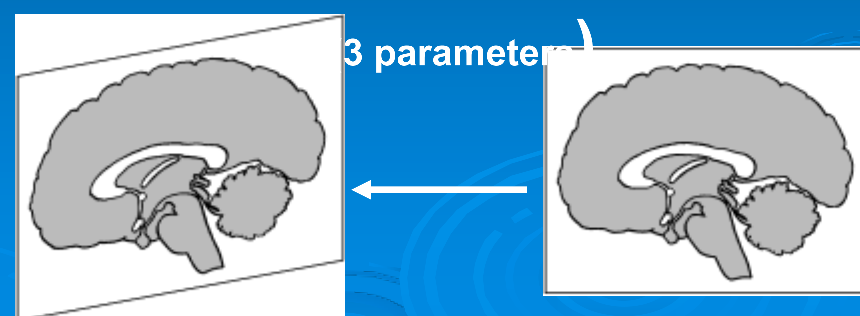


scaling (3 parameters)



Shearing *

(3 parameters)



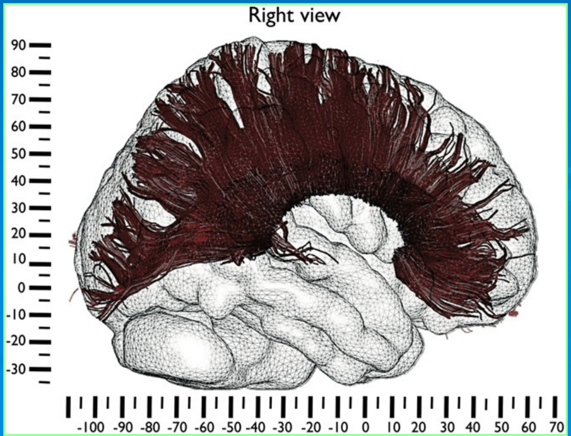
* **Shearing slides one edge of an image along the X or Y axis, creating a parallelogram**

Material and methods (3)

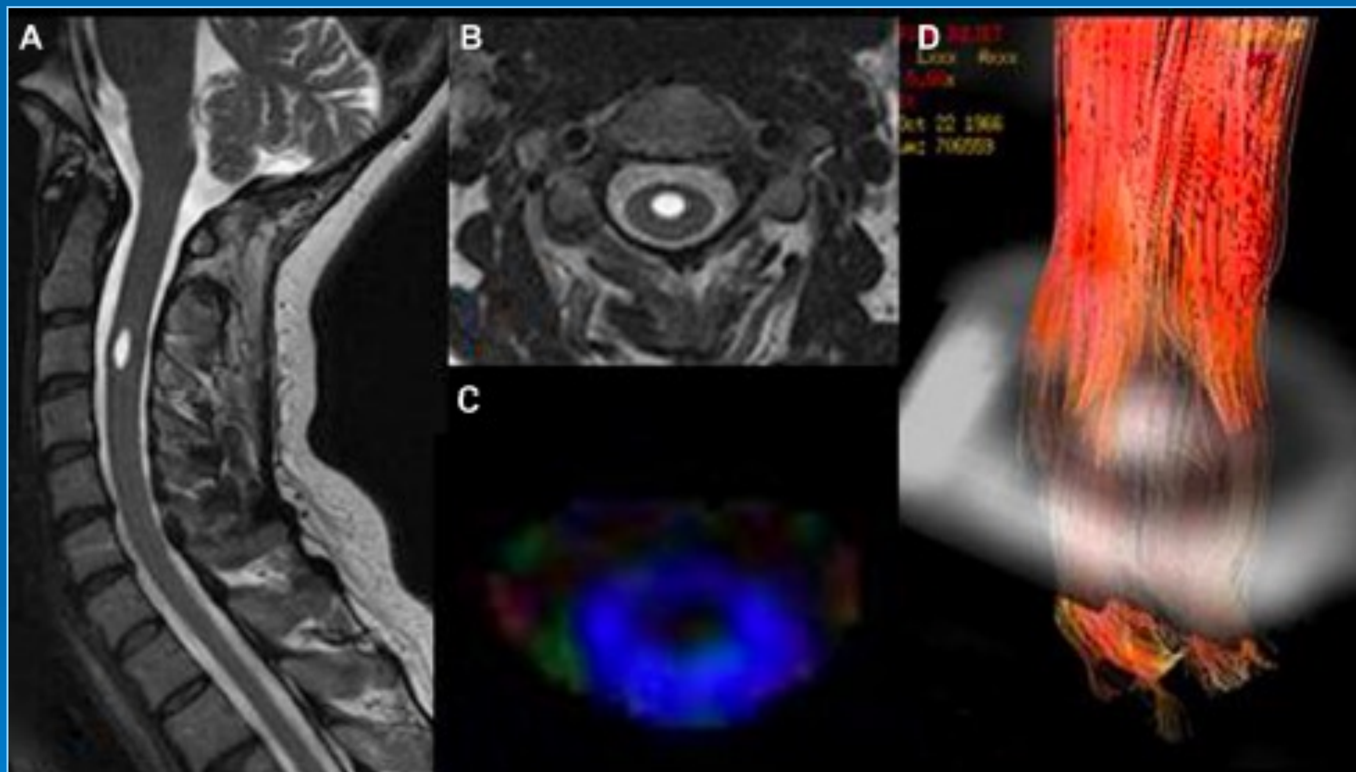
- […] The 12 data sets were spatially normalized and averaged […].
- For the normalization we used statistical parametric mapping software (SPM5, www.fil.ion.ucl.ac.uk/) [..]
  - Images were spatially normalized to the standard T1 template provided in SPM5.
- The 3D tractography reconstructions of each tract were registered in the MNI space and visualized within a glass brain using BRAINVISA 3.0.2.

A diffusion tensor imaging tractography atlas for virtual in vivo dissections

Marco Catani[a,b,] and Michel Thiebaut de Schotten[a,b,c]*



Applications of DTI to spinal cord

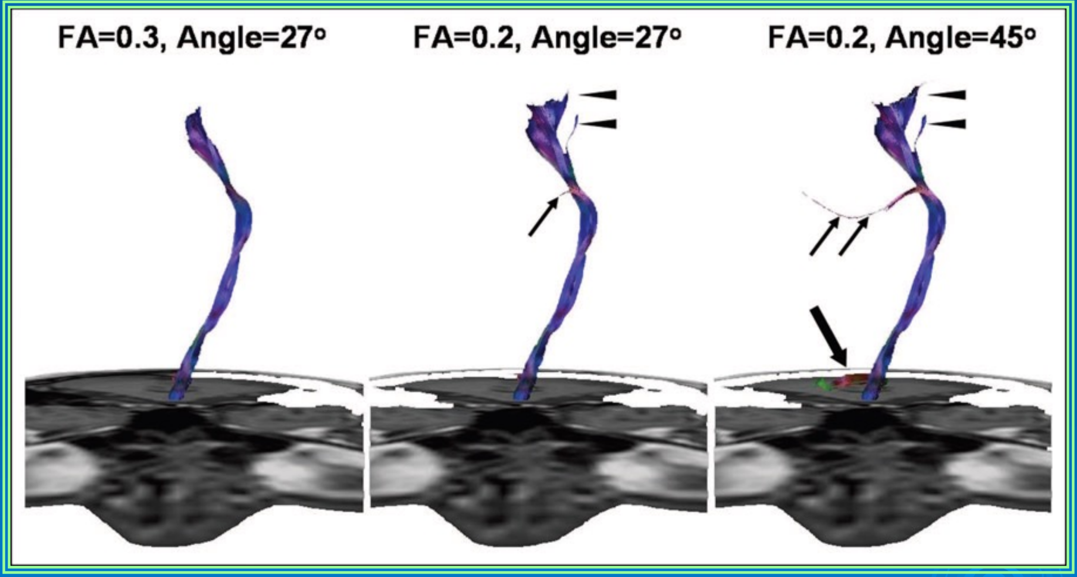


(A) and (B) T2-weighted images demonstrate a focal syrinx in the central spinal cord
(C) FA map demonstrates no fiber tracts running through the lesion
(D) Tractography shows displacement of the fiber tracts around the syrinx.

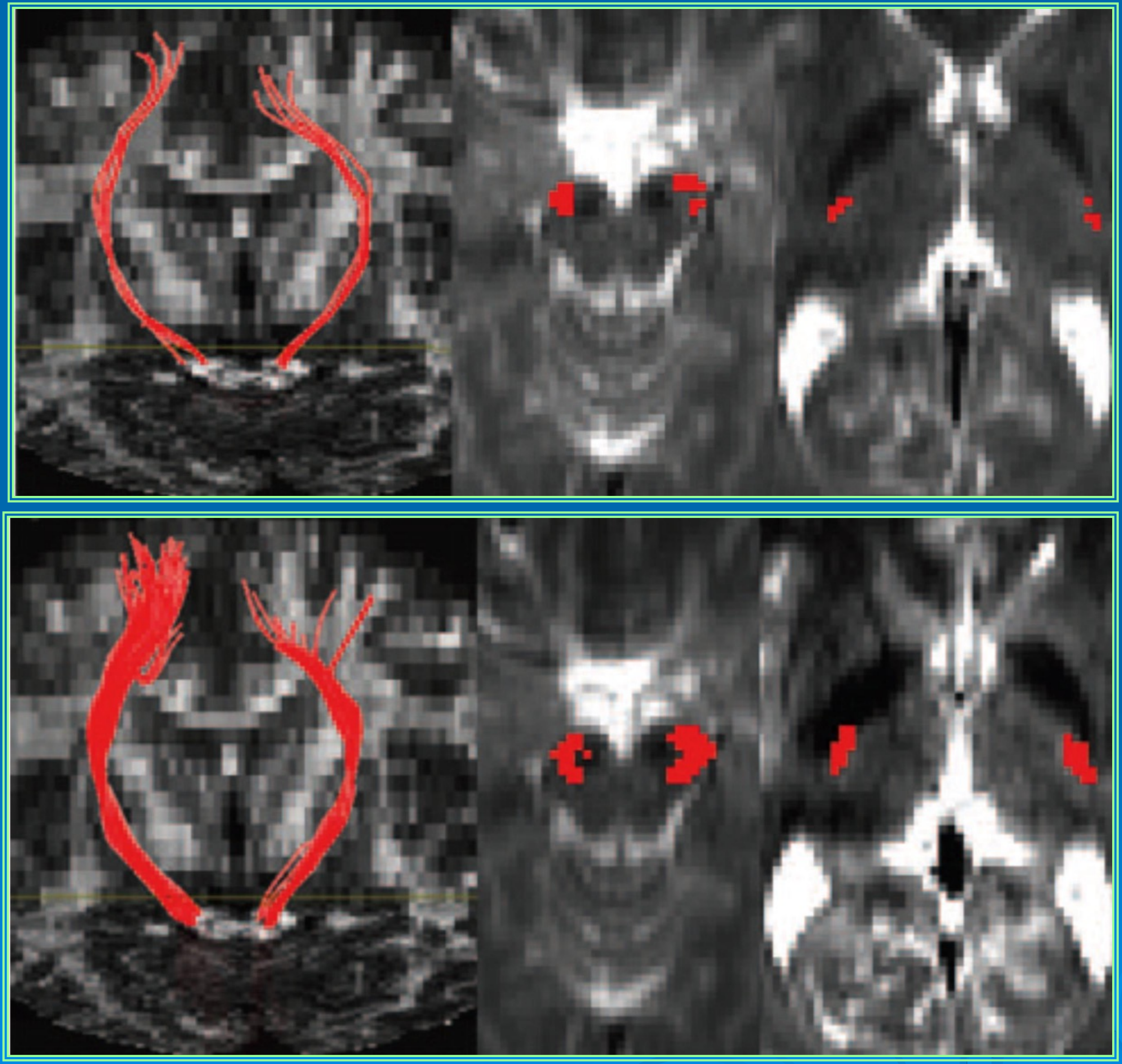
Lerner et al World Neurosurg. (2014) 82, 1/2:96-109

Tracking parameters

- **Effects of different threshold values for termination of fiber tracking.**
  - **lowering the FA threshold and increasing the trajectory angle generates more fibers and contralateral connections than increasing the FA threshold and lowering the trajectory angle.**



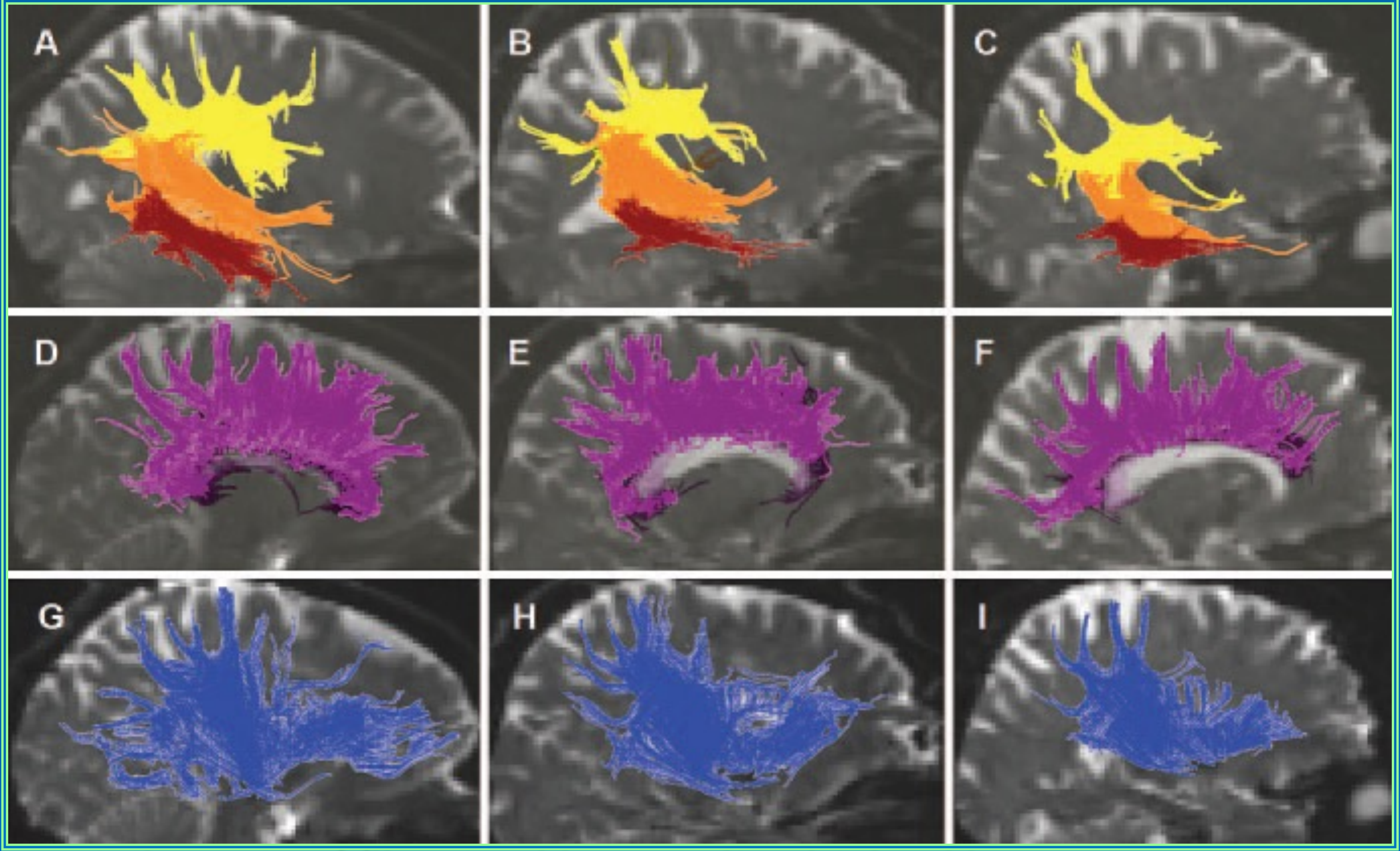
Lee at al RadioGraphics 2005; 25:53–68



1.5 T
vs
3 T

Okada et al Radiology: Volume 238: Number 2—February 2006

Ageing

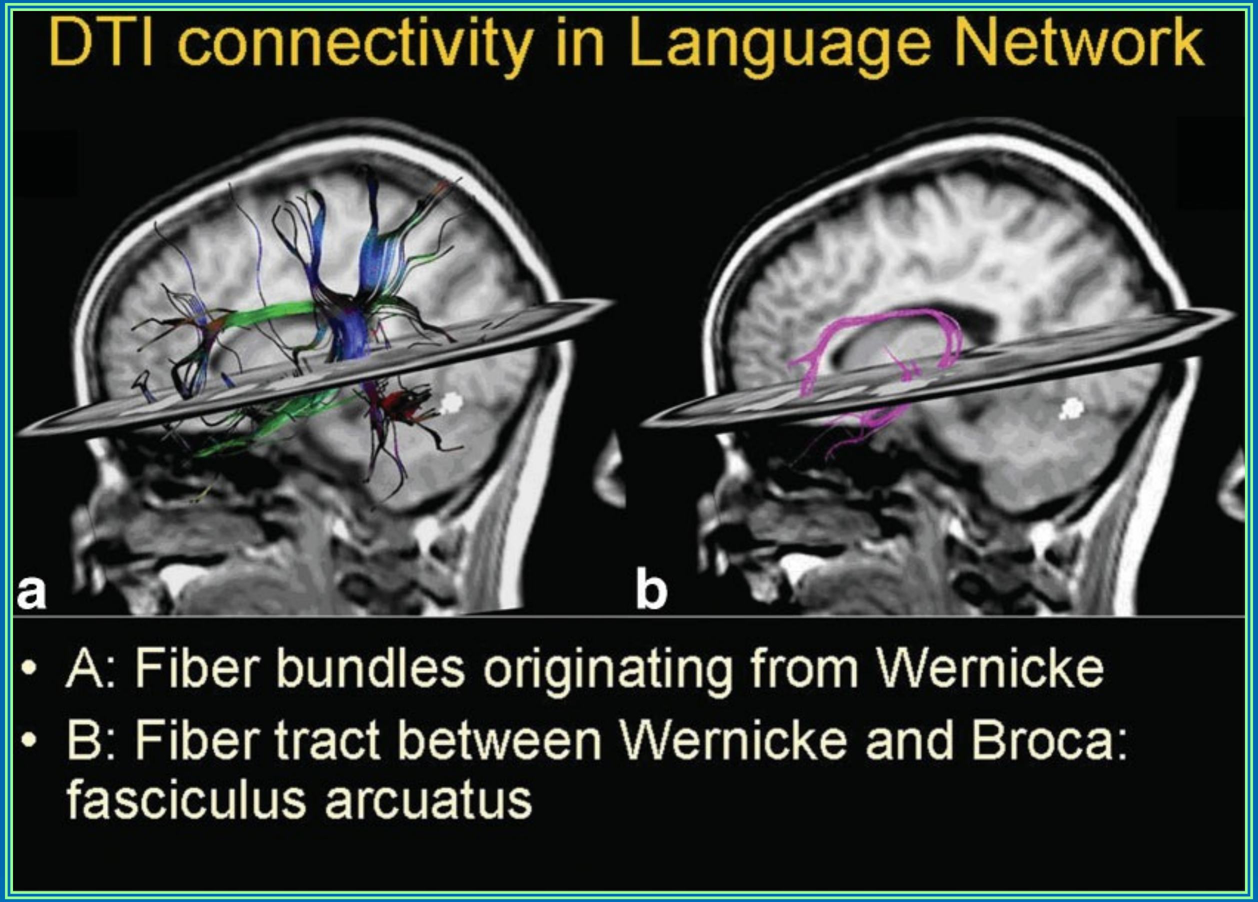


Representative sets of fiber-tracking results obtained in:

- ✓ A, D, G, a 25-year-old man
- ✓ B, E, H, a 55-year-old man
- ✓ C, F, I, an 81-year-old woman
- ✓ A–C, Association fibers are divided into superior longitudinal (yellow), inferior fronto-occipital (orange), and inferior longitudinal (red) fasciculi.
- ✓ D–F, Callosal fibers (purple)
- ✓ G–I, projection fibers (blue)

Stadlbauer et al. Age-related Central Nervous System Degradation
Radiology (2008) 247:179

fMRI & DTI



a: Fiber bundles originating from a ROI corresponding to the activation site of Wernicke’s area

- interconnected with the temporal pole, cerebellum, parietal lobe, perirolandic region, and frontal areas

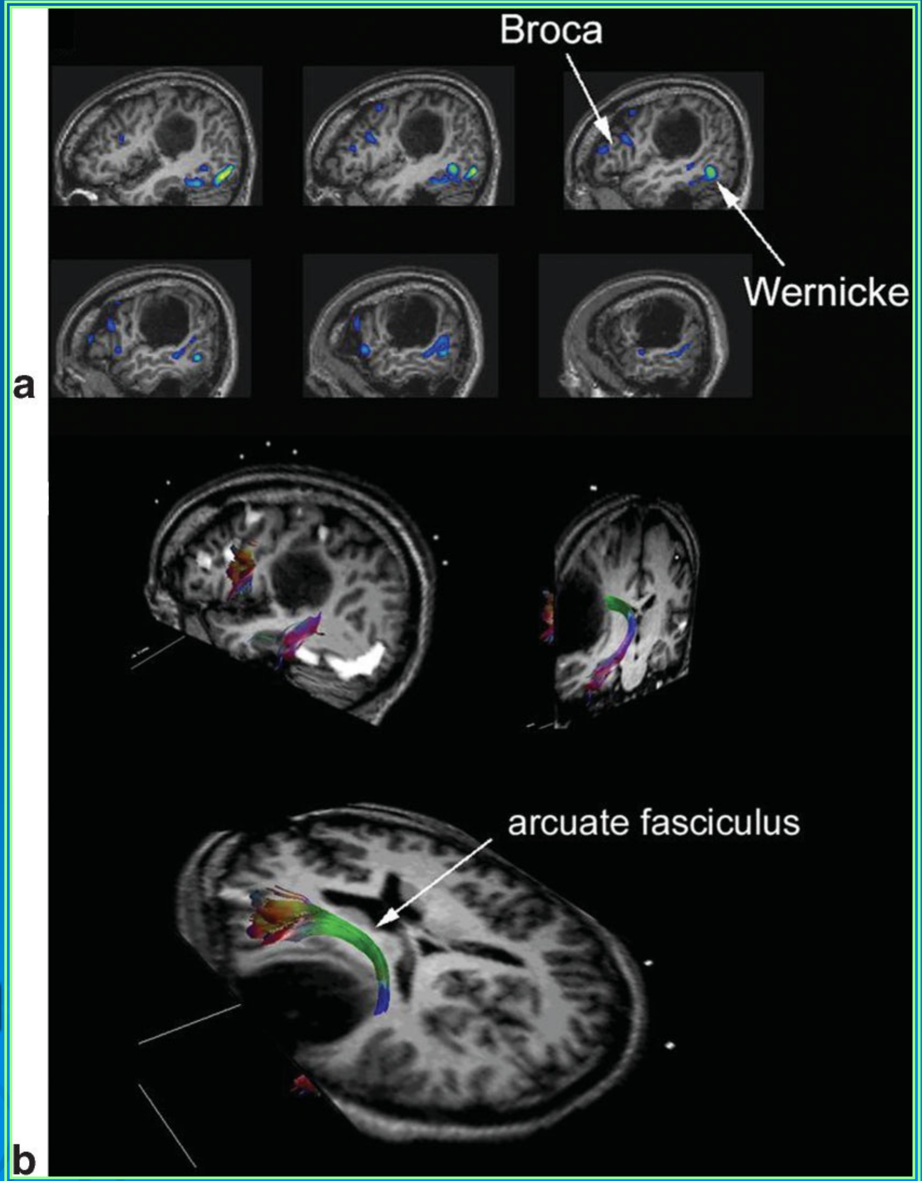
b: DTI fiber tracking between Wernicke’s and Broca’s regions.

MR imaging revealed a low-grade tumoral mass in the left supramarginal and angular gyri

fMRI & DTI

a) fMRI during a verbal fluency task depicts a left lateralized language, with Wernicke's area in the middle temporal gyrus and Broca in the inferior frontal gyrus. <u>Both eloquent areas are some distance of the lesion.</u>

b) Fiber-tracking depicting the arcuate bundle between Wernicke and Broca. The bundle seems to be displaced medially by the mass effect of the lesion and <u>its middle part is adjacent to the tumor border.</u>

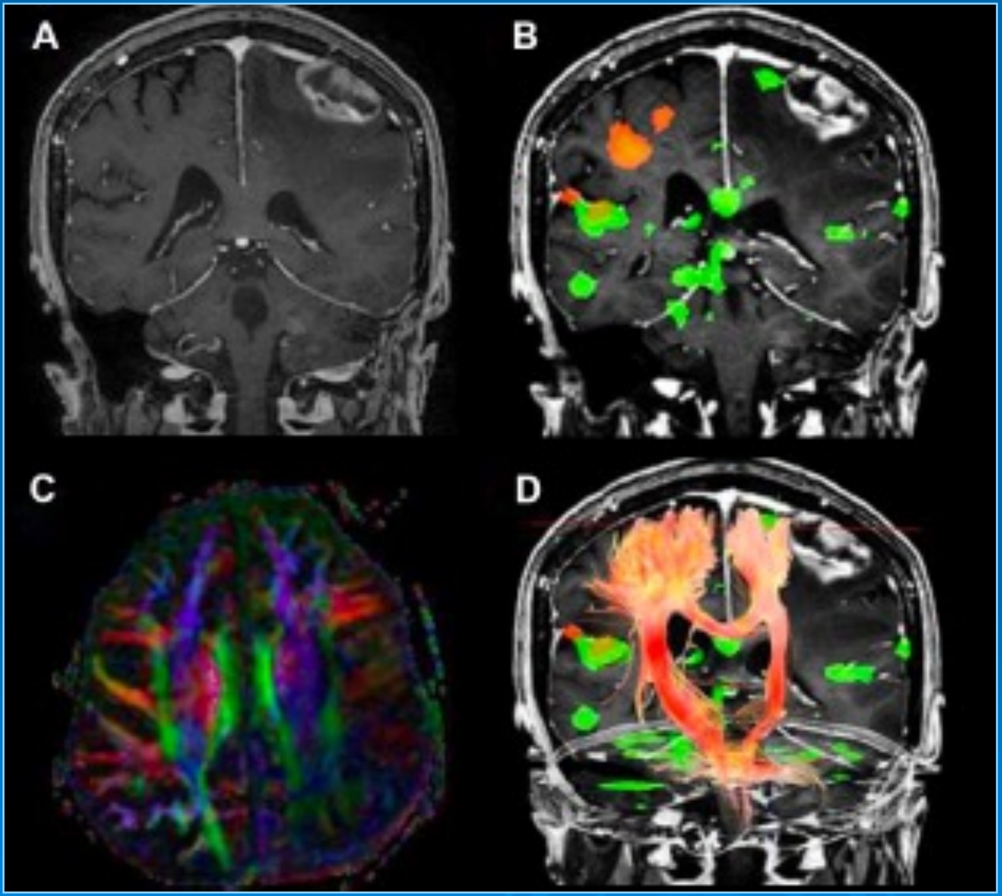


Clinical applications

Fusion of fMRI and tractography for surgical planning

(A) Gadolinium-enhanced image shows a melanoma metastasis with surrounding vasogenic edema

(B) fMRI shows the metastasis results in medial displacement of the motor activation area on the left
- **shown in green**



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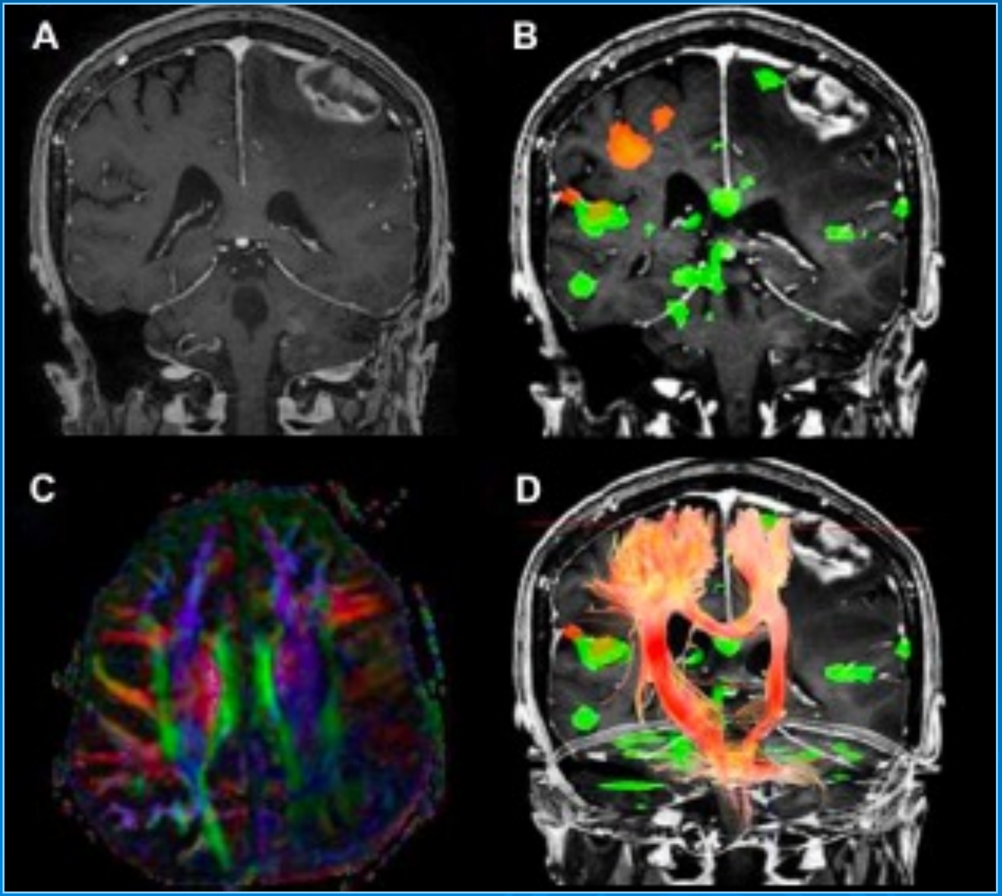
Clinical applications

Fusion of fMRI and tractography for surgical planning

C. FA map reveals less-robust anisotropy in the posterior left centrum semiovale and parietal subcortical white matter in the region of the tumor likely related to both displacement of fibers by the tumor and loss of anisotropy caused by vasogenic edema.



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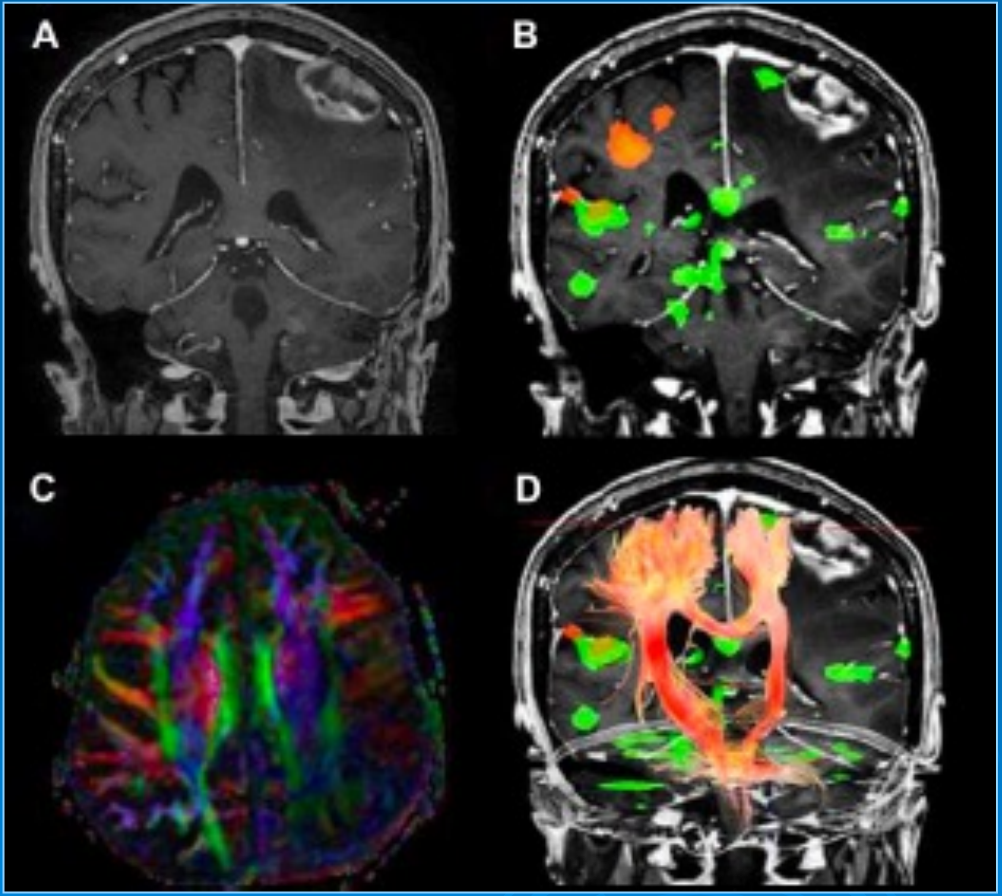
Clinical applications

Fusion of fMRI and tractography for surgical planning

D. **Tractography demonstrates displacement of the fiber tracts medially surrounding the area of motor activation.**



Lerner et al World Neurosurg. (2014) 82, 1/2:96-109