

Diffusion Weighted and Diffusion Tensor Imaging in Pediatric Neuro-oncology

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Disclosure

- I have nothing to disclose
- No relevant financial relations interfering with my presentation
- No reference of any unlabeled or unapproved use of drugs



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Disclosure

- I have nothing to disclose
- Long term friend of René (really long term,...)



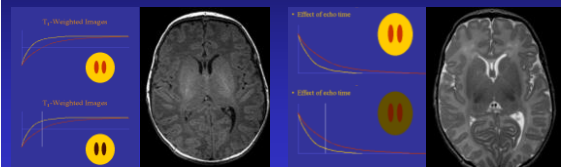
~ 1989-1990



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MR Image contrast

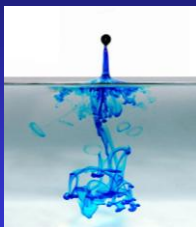
Anatomical MR imaging:
Differences in T1 or T2 relaxation times



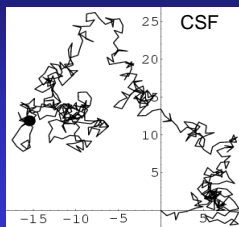
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How does DWI work?

Relies on Brownian motion
Diffusion/mobility of H₂O molecules in tissue



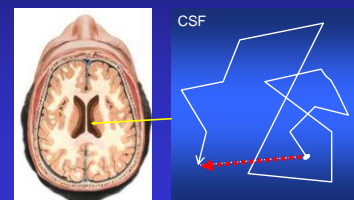
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How does DWI work?

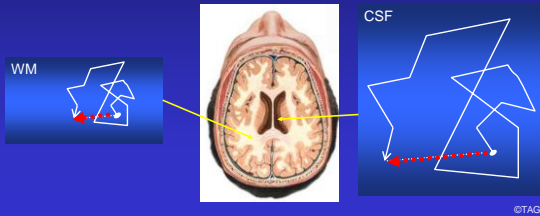
- Signal intensity related to the diffusion characteristics of water within the brain
- Image contrast related to differences in diffusion between tissues



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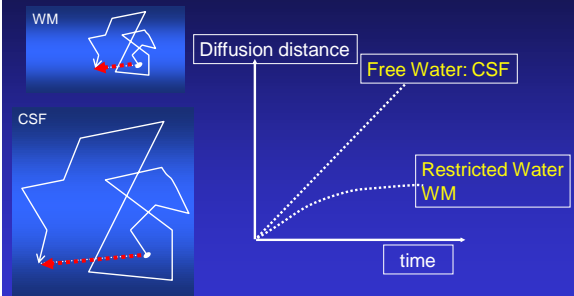
How does DWI work?

- Signal intensity related to the diffusion characteristics of water within the brain
- Image contrast related to differences in diffusion between tissues



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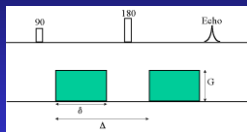
How does DWI work?



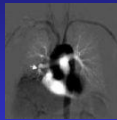
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How does DWI work?

- Differences in diffusion are visualized by using 2 diffusion gradients centered around the 180° refocussing pulse



Similar to PC-MRA

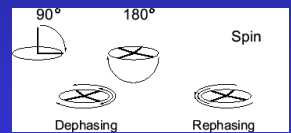
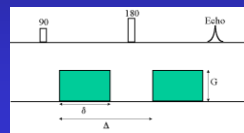


- Amplitude and duration of diffusion gradients determine degree of diffusion weighting (b-values 0, 1000 s/mm²)

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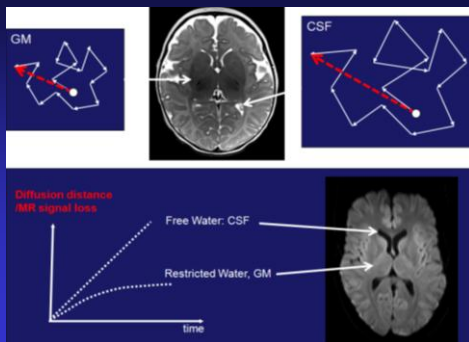
How does DWI work?

- Stationary spins keep (regain) their phase
- Moving spins dephase
- Fast moving spins (fast diffusion) dephase more (more signal loss) than slow moving spins (slow diffusion), less dephasing (less signal loss)



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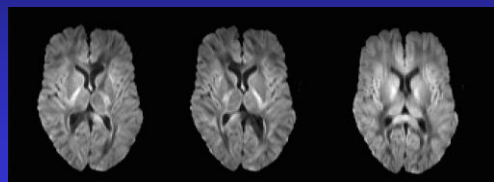
How does DWI work?



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How does DWI work?

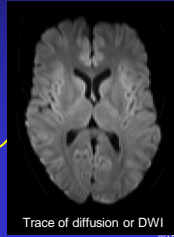
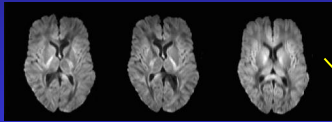
- DWI sequences "translate" diffusion in signal intensities
- Typically diffusion gradients are applied along multiple (at least 3) directions (Dxx, Dyy, Dzz)



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How does DWI work?

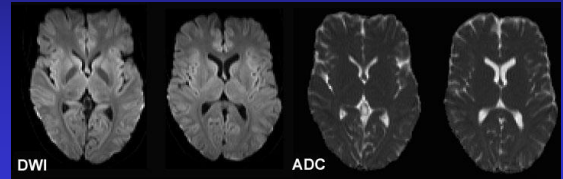
- DWI sequences "translate" diffusion in signal intensities
- Typically diffusion gradients are applied along multiple (at least 3) directions that are averaged



Trace of diffusion or DWI

How does DWI work?

- DWI sequences "translate" diffusion in signal intensities
- Apparent diffusion coefficient (ADC) is calculated (using different b-values: 0, 1000 s/mm²)



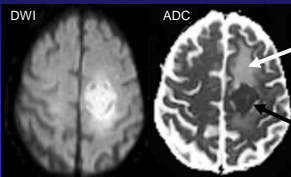
DWI

ADC

No T2 component

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DWI and ADC images



Increased diffusion (high ADC)

Restricted diffusion (low ADC)

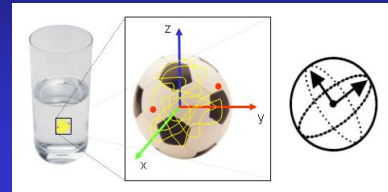
Malignant meningioma surrounded by white matter edema

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How does DWI work?

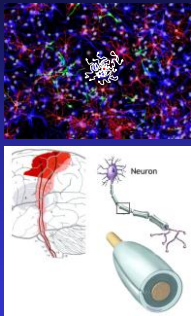
Sounds simple but diffusion weighted imaging is a bit more complicated

Diffusion is a 3D phenomena



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How does DWI work?

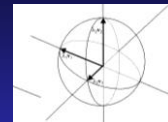
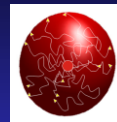


Isotropic diffusion

Anisotropic diffusion

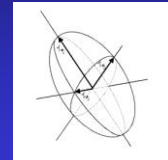
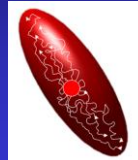
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How does DWI work?



Isotropic diffusion

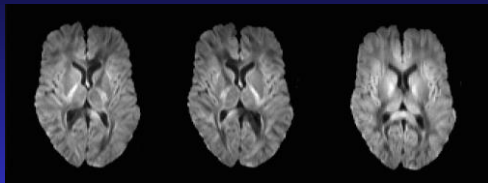
Eigenvalues
 $\lambda_1, \lambda_2, \lambda_3$



Anisotropic diffusion

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Anisotropic diffusion visualised

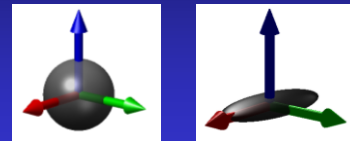


Diffusion gradients along different axis
Depending on relation 3D direction fiber course
and diffusion gradient,
~> various degrees of signal suppression

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How does DWI work?

How can we resolve the degree of
anisotropic diffusion for each voxel,
and

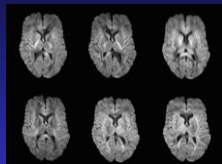


why do we want to know this ?

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Diffusion Tensor Imaging (DTI)

Dxx, Dxy, Dxz
Dyx, Dyy, Dyz
Dzy, Dzx, Dzz



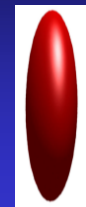
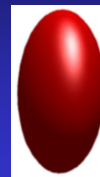
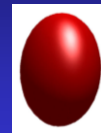
$D_{xy} = -D_{yx}$, $D_{xz} = -D_{zx}$, $D_{yz} = -D_{zy}$
6 Diffusion directions

3D Shape, Magnitude and Direction of diffusion

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How does DTI work?

- We can calculate degree of anisotropy (FA)
- FA=0: 100% isotropic diffusion
- FA= 1: 100% anisotropic diffusion



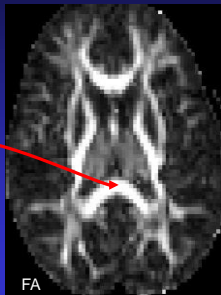
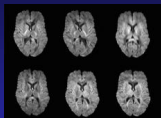
FA 0 (spheric)

(ellipsoid) 1

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How does DTI work?

Anisotropic diffusion (FA) mapped for each voxel



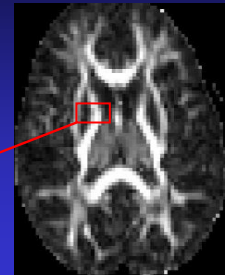
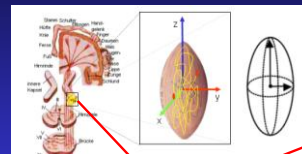
FA-map:
Signal intensity
related to
magnitude of
anisotropic diffusion

↑

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How does DTI work?

Topographic distribution of anisotropic diffusion



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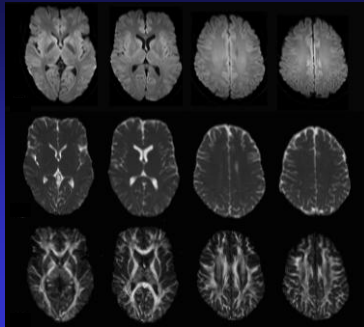
How does DTI work?

DTI gives

DWI

ADC

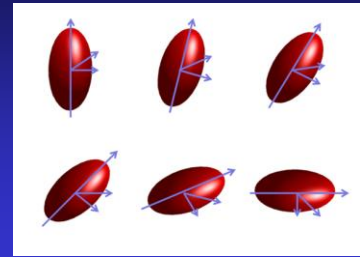
FA



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How does DTI work?

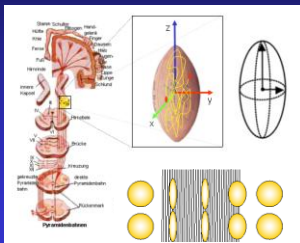
Diffusion is a 3D process: Magnitude + **Direction**



Depending on the location of the voxel (microstructure) different ellipsoid orientation ©TAGM

How does DTI work?

DTI allows to determine orientation of the diffusion tensor for each voxel

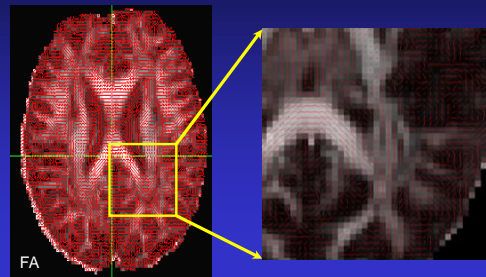


Coronal

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How does DTI work?

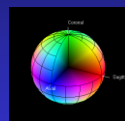
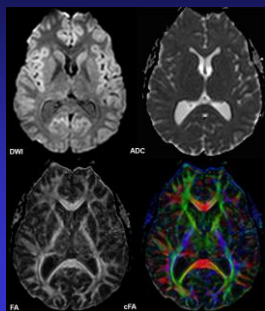
DTI: Direction may be superimposed on FA magnitude map



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How does DTI work?

Directionality can be color coded



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How does DTI work?

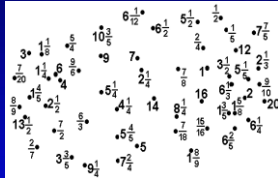
Finally, magnitude and directionality information can be postprocessed to study fiber tracts



Tractography

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It is all about connecting the dots



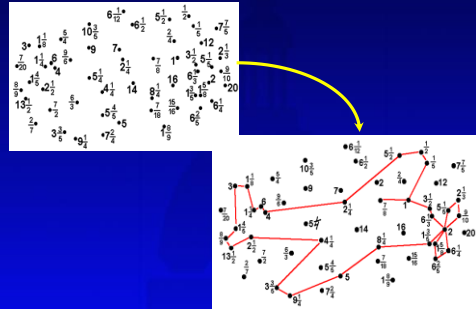
"Connect the dots puzzle"

because believing
the dots will connect
down the road
will give you the confidence
to follow your heart,
even when it finds you off
the well worn path

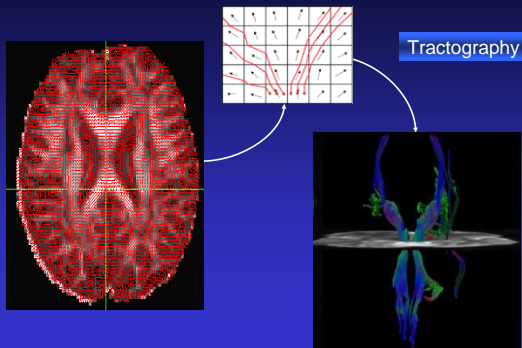
- STEVE JOBS



It is all about connecting the dots



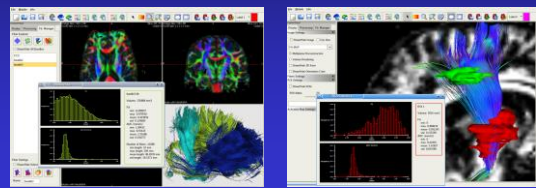
DTI ~> Tractography



©TAGM

DTI ~> Tractography

- Multiple post-processing programs
- Different approaches
 - deterministic
 - probabilistic

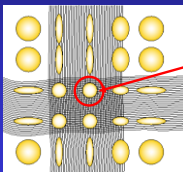
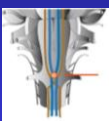


INRIA Sophia Antipolis Research project ASCLEPIOS Cedex France

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How does DTI work?

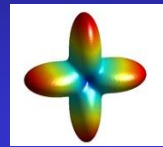
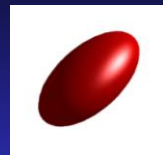
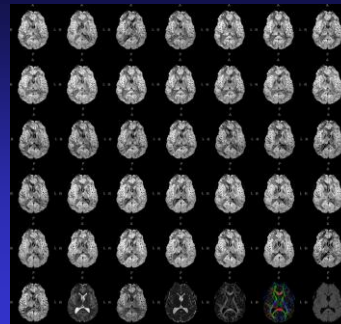
- One final issue,.....
- There is one more complicating issue,....
- What about crossing fibers in a voxel,.....



Voxel may appear
isotropic due to
averaging within a
voxel

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Multi-tensor DTI



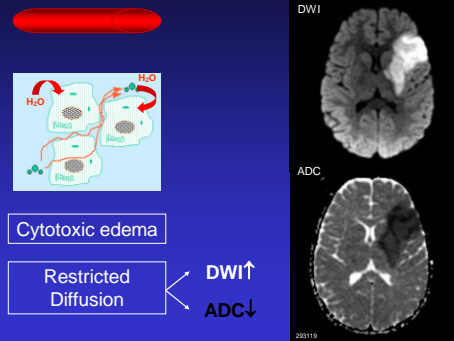
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Why is DWI/DTI so exciting?

- Differentiates restricted vs. increased diffusion
- Restricted diffusion
 - High cellularity (small extracellular space)
 - Acute ischemic tissue injury (critical perfusion or vascular complication)
- Increased diffusion
 - Large cells with large cytoplasm
 - Widened extracellular space (vasogenic edema)
 - Reactive/inflammatory
 - Metastatic disease

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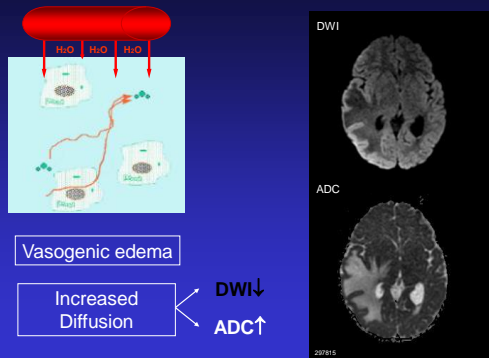
Cytotoxic edema in ischemia



Acute MCA Ischemia, ICA Dissection

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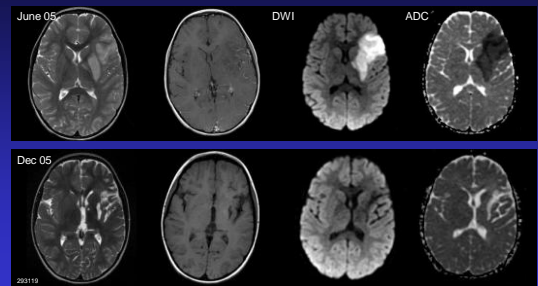
Vasogenic edema (reactive)



TSC

©TAGM

Cytotoxic edema: usually irreversible

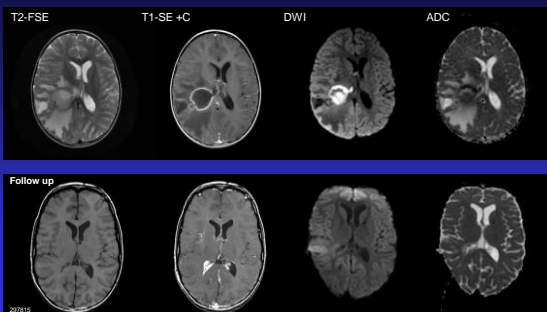


Acute MCA Ischemia

Prognostic information

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Vasogenic edema: usually reversible



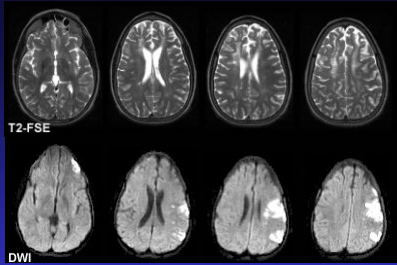
TSC

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Why is DTI so exciting?

- **Early** identification of tissue at risk for ischemic injury (in combination with PWI)
 - Vessel encasement, compression
 - Vessel infiltration, stenosis, tumor thrombus
 - Steal phenomena
- Early identification of postoperative vascular complication (may initiate treatment to salvage tissue)

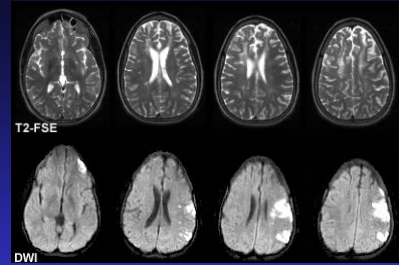
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What is the most likely diagnosis?

1. Acute stroke
2. Chronic stroke
3. Acute on chronic stroke

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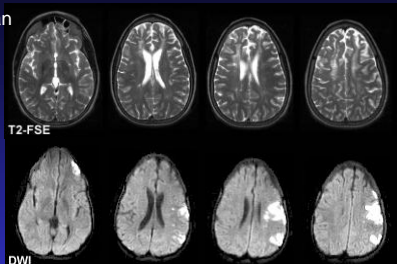


What is the most likely diagnosis?

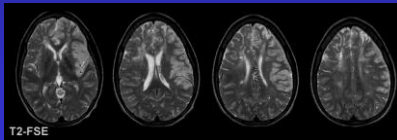
3. Acute on chronic stroke (SSD)

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Initial scan

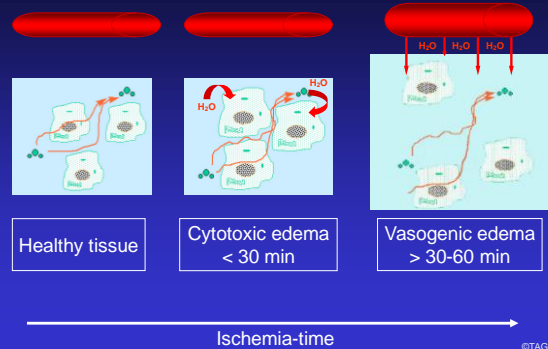


+ 24h



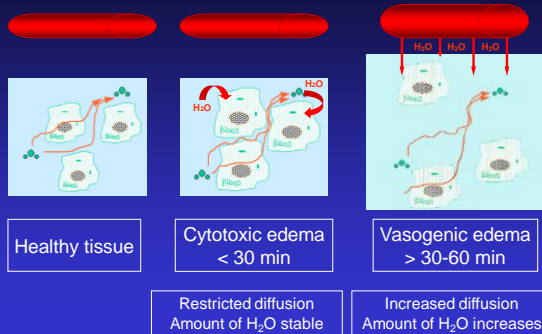
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Why is DWI earlier positive ?



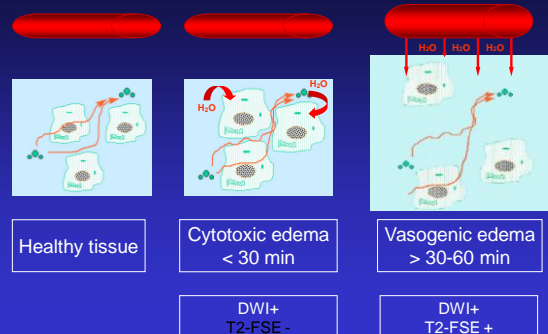
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Why is DWI earlier positive ?



©TAGM

Why is DWI earlier positive ?



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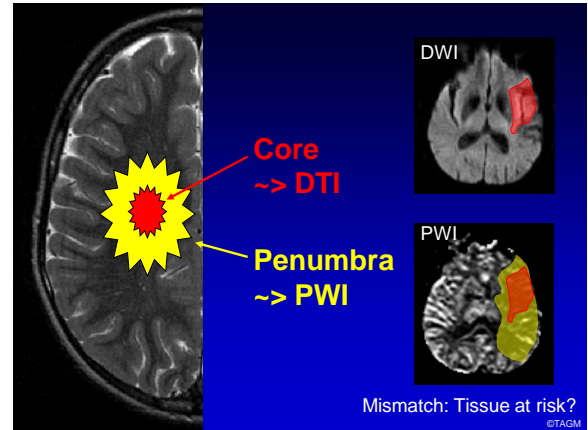
Why is early diagnosis important ?

- Because “time = brain”

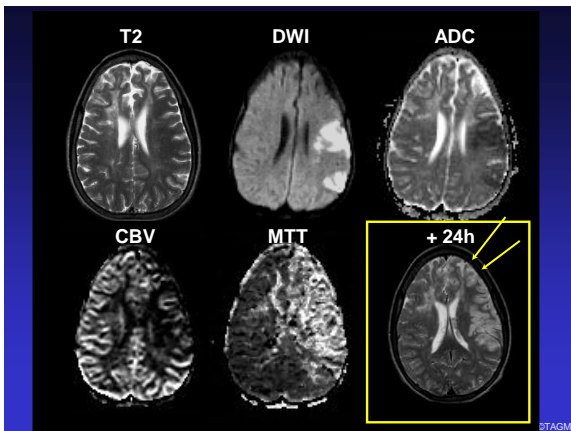


- The earlier the diagnosis, the earlier therapeutic procedures can be started
- Neuroprotective agents, hypothermia, hyperventilation, recanalization, antibiotics, steroids,.....

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©TAGM

Why is DTI so exciting?

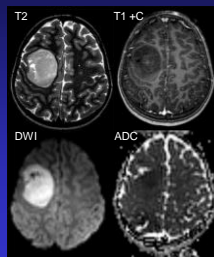
- DTI allows to characterize lesions
 - Kind of lesion (Tumor, abscess, hematoma,...)
 - Infiltrative, displacing, disrupting WM tracts

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How does DTI work?

What kind of lesion?

1. Hematoma
2. Solid tumor
3. Abscess
4. Cyst
5. I do not know

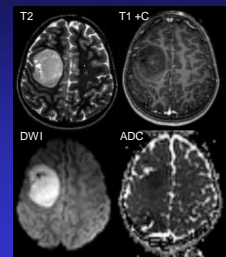


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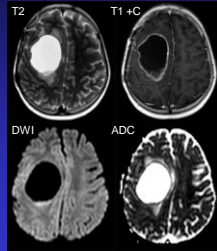


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How does DTI work?

What kind of lesion?

1. Hematoma
2. Necrotic tumor
3. Abscess
4. Cyst
5. I do not know

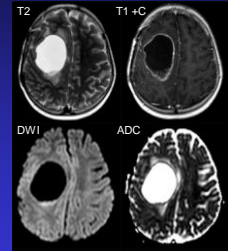


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How does DTI work?

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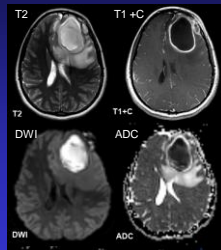


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How does DTI work?

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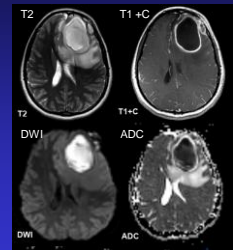


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How does DTI work?

What kind of lesion?

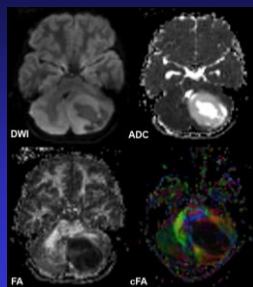
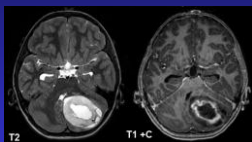
1. Hematoma
2. Necrotic tumor
3. Abscess
4. Cyst
5. I do not know



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DTI allows to characterize lesions

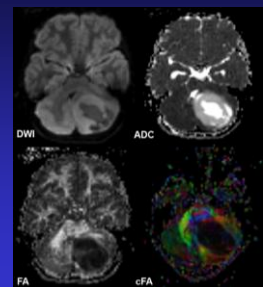
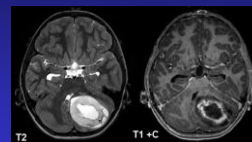
Where to biopsy?



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DTI allows to characterize lesions

Where to biopsy?
~> Solid rim of the tumor



Differentiation between solid and cystic/necrotic components

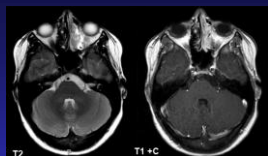
Guides tumor biopsy

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DTI allows to characterize lesions

What kind of lesion?

1. Hematoma
2. Tumor
3. Abscess
4. Cyst
5. I do not know



Do you see the lesion?

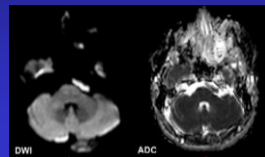
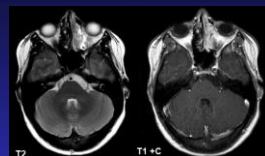
Wait for additional information from DWI/DTI

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DTI allows to characterize lesions

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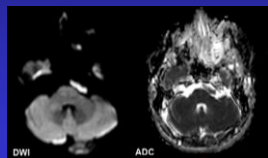
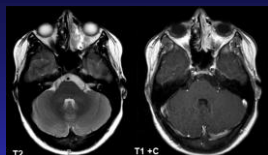


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DTI allows to characterize lesions

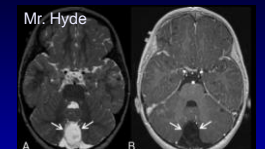
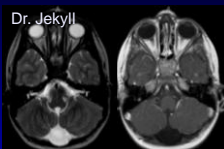
What kind of lesion?

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DTI allows to characterize lesions



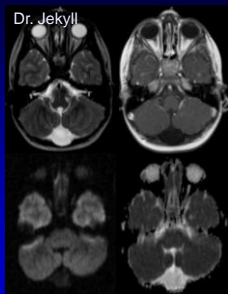
Which patient has a truly "benign" lesion?

1. Dr. Jekyll
2. Mr. Hyde
3. Dr. Jekyll and Mr. Hyde
4. None of them

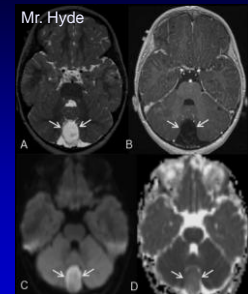


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DTI allows to characterize lesions



Dr. Jekyll: Arachnoid cyst

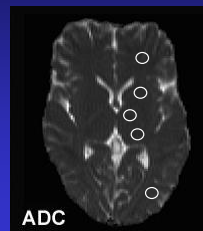


Mr. Hyde: Epidermoid

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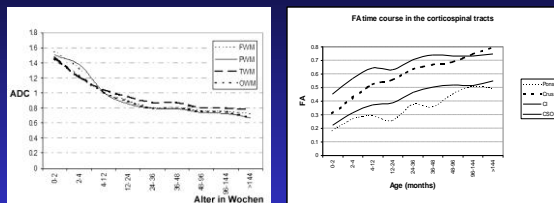
Why is DTI so exciting?

- DTI gives quantitative information



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DTI gives quantitative information



ADC-Values ↓

FA-Values ↑

Schneider JF et al, Neurology 2004

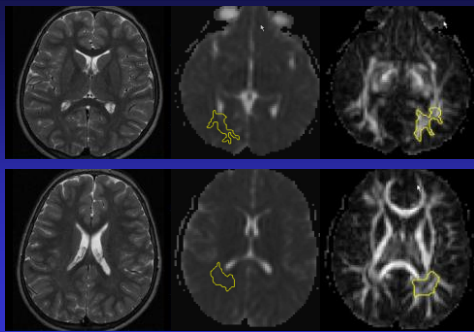
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Quantitative analysis of WM pathologies

- White matter diseases
- Treatment related demyelination
 - Radiation therapy
 - Chemotherapy
- White matter infiltration?
- Response to tumor treatment?
- Tumor histology?
- Tumor grading?

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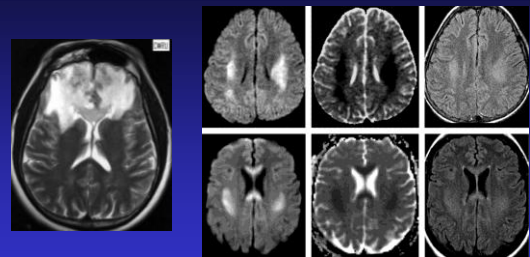
DTI as biomarker of tissue injury



Schneider et al, AJNR May 2003

©TAGM

Treatment related WM injury



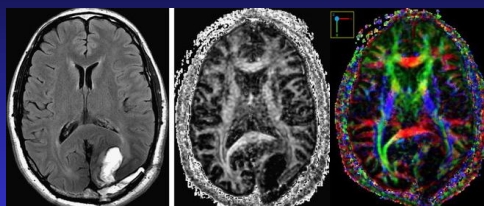
Radiation therapy

Intrathecal MTX therapy

DTI may show injury/recovery before apparent on T1/T2 MRI

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Tumor infiltration of white matter tract

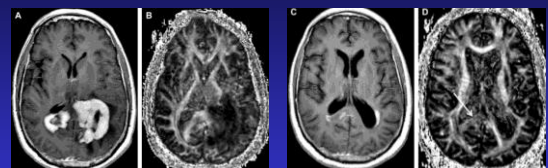


GBM: Planning prior to radiation therapy after surgical debulking
DTI shows infiltration of lateral splenium of corpus callosum, loss of FA

Gupta A, et al, Neuroimaging Clin N Am 2010; 20: 379-400

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Monitoring of treatment response



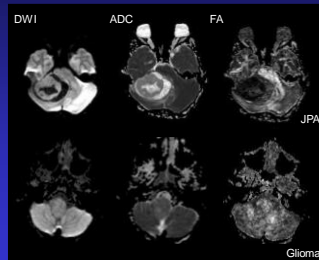
Lymphoma: Post chemo-radiotherapy recovery of anisotropic diffusion in left splenium; gliosis in right splenium of the corpus callosum

Gupta A, et al, Neuroimaging Clin N Am 2010; 20: 379-400

©TAGM

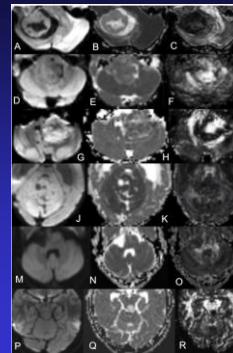
Tumor histology/grading?

Holy grail, Tumor histology?



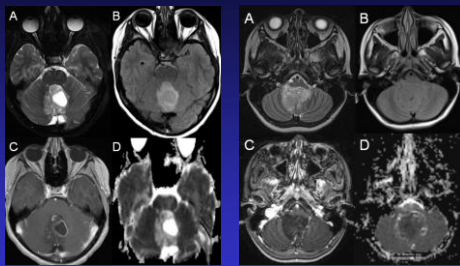
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Prediction of tumor grade?



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Prediction of tumor grade?



Contradicting results,....

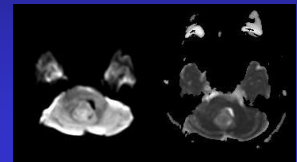
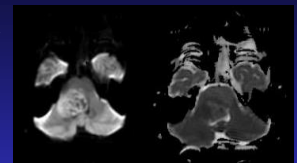
Correlation between Apparent Diffusion Coefficient and Histology of Pediatric Cerebellar Tumors: Does it Matter?

Andrea Piovetti^{1,2}, Aaron Mendel¹, Kenneth J. Cohen¹, Michael A. Gidycz¹, Marina Schmitt¹, Eugen Beldar¹, Thany A. G. M. Huysman¹

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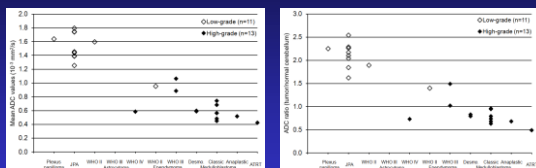
Restricted versus increased diffusion

- Restricted diffusion (low ADC) high cellularity
 - Medulloblastoma
 - GBM
 - High grade glioma
- Increased diffusion (high ADC) "fluid rich" tumor cells
 - JPA
 - Ependymoma



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Prediction of tumor grade?



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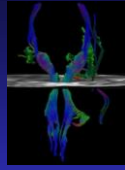
Tumor histology/grading?

- Holy grail, not yet!!!
- Maybe for differentiating:
 - High vs. low-grade gliomas
 - Low ADC in highly cellular/highly malignant lesions
 - Low FA in higher grade gliomas
 - Metastasis versus malignant gliomas
 - Peritumoral edema versus tumor infiltration
 - DTI helpful (restricted diffusion due to tumor infiltration versus reactive vasogenic edema)

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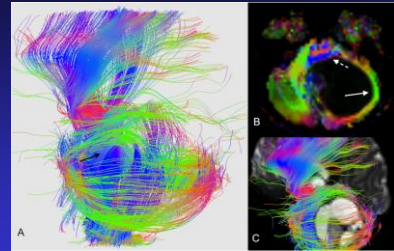
Why is DTI so exciting?

- Tractography studies WM tracts
 - Deviation
 - Deformation
 - Infiltration
 - Interruption
- Identify patterns/highways of tumor extension
- Planning of surgery (+fMRI, gray matter info)
- Follow up after treatment (surgery, chemotherapy, radiation therapy)



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Cortico-spinal tract displacement

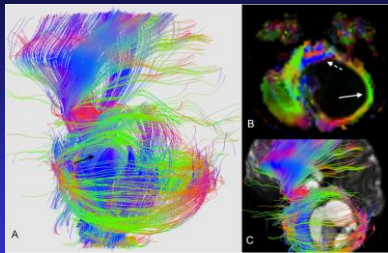


High versus low grade?

Poretti A, Moolenaar A, Hulstman TA, JMRI 2012; 35: 32-47

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Cortico-spinal tract displacement

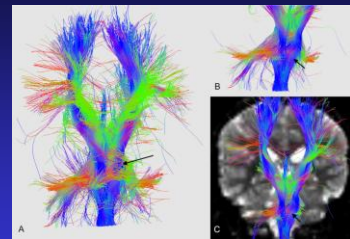


Pilocytic astrocytoma:
Displacing fibers, non-infiltrative

Poretti A, Moolenaar A, Hulstman TA, JMRI 2012; 35: 32-47

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Cortico-spinal tract displacement

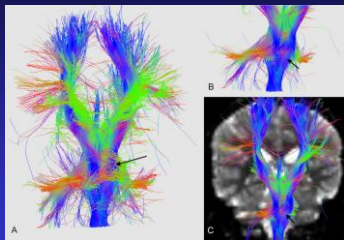


High grade versus low grade?

Poretti A, Moolenaar A, Hulstman TA, JMRI 2012; 35: 32-47

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Cortico-spinal tract displacement

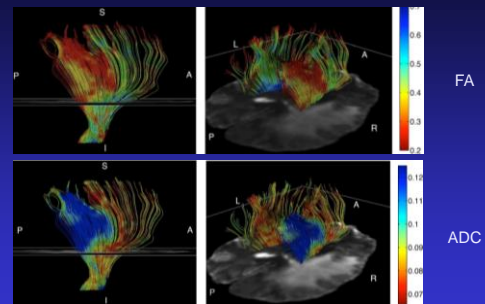


Diffuse intrinsic brainstem glioma:
Paucity of transverse pontine fibers,
infiltration of corticospinal/lemniscal tracts

Poretti A, Moolenaar A, Hulstman TA, JMRI 2012; 35: 32-47

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Tumor infiltration of white matter tract

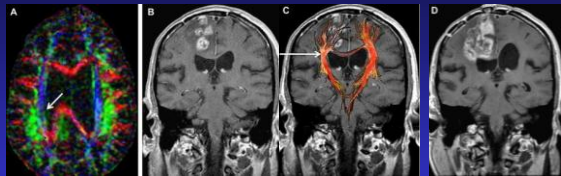


Loss of FA and increased ADC along infiltrated segments of CST

Cardenas et al, Neuroimage 2010; 50: 27-39

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Pathways of tumor infiltration

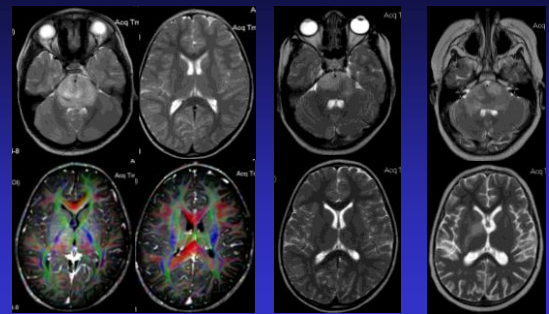


GBM: Highway of tumor extension (right corticospinal tract)

Gupta A, et al. Neuroimag Clin N Am 2010; 20: 379-400

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Pathways of tumor infiltration



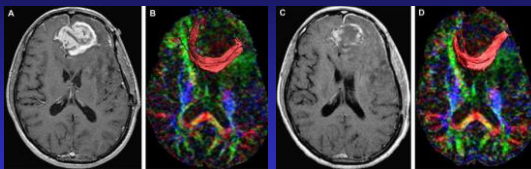
July 11th, 2012

November 5th, 2012

April 15th, 2013

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Recovery of tract displacement

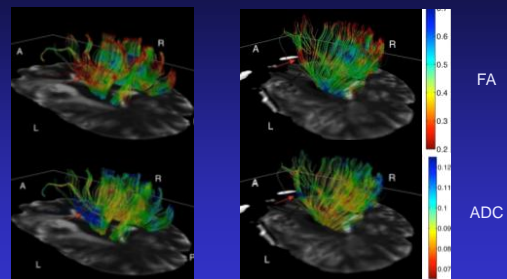


GBM: Improving splaying and displacement of genu of the corpus callosum after surgery

Gupta A, et al. Neuroimag Clin N Am 2010; 20: 379-400

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Monitoring of treatment response

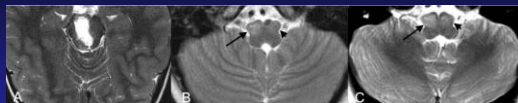


Malignant glioma: Pre and post surgery

Cardenas et al. Neuroimage 2010; 50: 27-39

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Analysis of functional systems



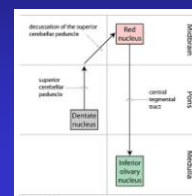
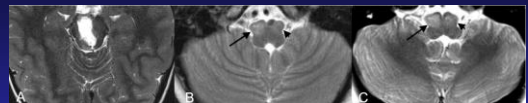
What are the findings

What is the diagnosis?

Which functional circuit is involved?

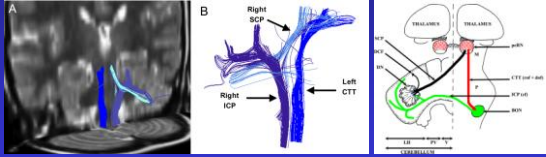
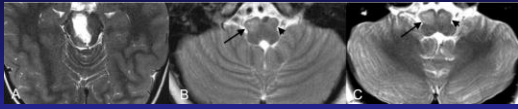
©TAGM

Analysis of functional systems



©TAGM

Analysis of functional systems



Moeddel A, Poretti A, Huisman TA. AJNR 2012

Summary

Multimodality imaging

- Anatomical imaging: T1, T2, T2*, T1-GD,...
- Functional imaging: DTI, PWI, ¹H-MRS, ...



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