Brain Mapping (fMRI and DTI) in Neurosurgical Planning and Guiding Neuronavigational Approach

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Outline

- fMRI and DTI Techniques and Methods
- Clinical Applications of brain mapping
- Clinical Challenges
- Future Developments

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- **fMRI and DTI Techniques and Methods**
- Clinical Applications of brain mapping
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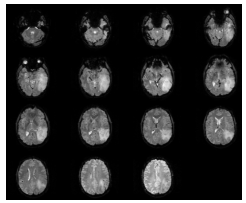
fMRI Techniques and Methods

- BOLD imaging

Blood **O**xygenation **L**evel **D**ependent

fMRI Sequence

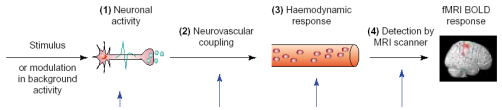
- Gradient-Echo Echo Planar Imaging (GE-EPI)
- Single-Shot
- T2*-weighted



Typical Parameters (1.5T)

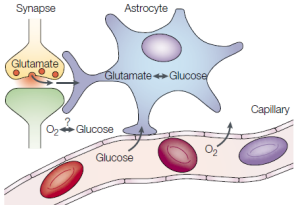
- 34 slices, 3 mm slice thickness
- TR=3000 ms, TE=50 ms, flip angle = 90 deg
- 64x64 matrix over a 240 mm FOV (3.75 mm in-plane resolution)
- Phase encoding AP
- 4 dummy scans

Stimulus to BOLD signal



Arthurs and Boniface *Trends in Neuroscience 2002*

Synaptic activity → BOLD



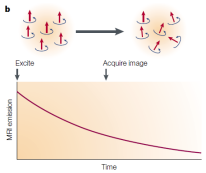
Proposed relationship between synaptic activity, neurotransmitter recycling and metabolic demand

Heeger and Ress. Nature Reviews Neuroscience 2002

Deoxyhaemoglobin

(Effect of deoxyhaemoglobin on the MRI signal)

- Deoxyhaemoglobin = paramagnetic
- ⇨ inhomogeneity into the nearby magnetic field
- ⇨ signal ↘



Heeger and Ress. Nature Reviews Neuroscience 2002

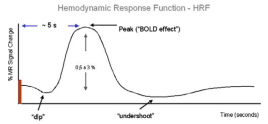
BOLD fMRI Response

- 3 phases:
  - metabolic demand ↗ oxygen consumption ↗ ⇨ deoxy-Hb concentration ↗ ⇨ signal ↘
  - after ~2 s, blood flow ↗↗ , vasodilation ↗↗ whereas oxygen consumption ↗ ⇨ deoxy-Hb concentration ↘ ⇨ signal ↗↗
  - after, some time for CBV to return to baseline ⇨ signal ↘ to below baseline

Heeger and Ress. Nature Reviews Neuroscience 2002

HRF

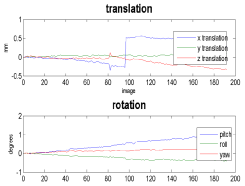
- Haemodynamic Response Function
  - Maximum delayed by 5-8 s
  - Dispersed by 3-4 sec
  - Spatial spread 2-3 mm



Amaro. Brain & Cognition 2006

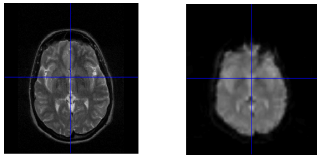
Pre-processing

- *Realign*: correct patient movements during the tests



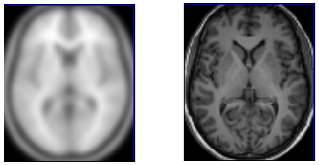
Pre-processing

- *Coregister*: Align fMRI images with a high-resolution image (e.g. 3D T1)



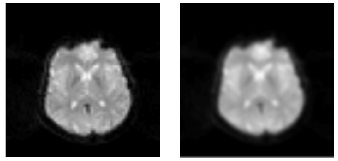
Pre-processing

- Normalize

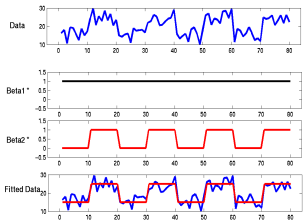


Pre-processing

- Smooth



Statistical analysis

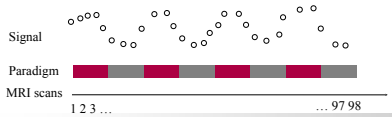


Threshold

- It's a statistical analysis
- 2 user-dependent parameters
  - p-value
  - Cluster-size
- Requires some expertise and knowledge of functional anatomy

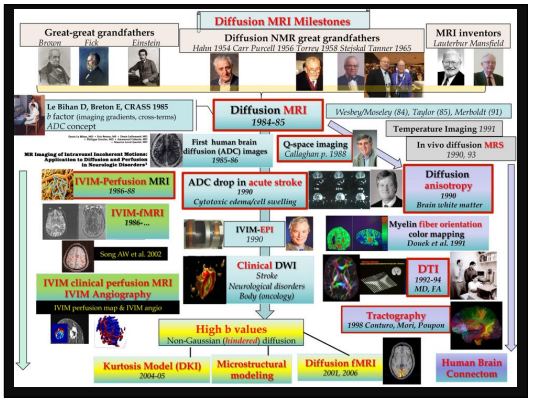
fMRI : Summary

- Sequential acquisition of EPI volumes
- Functional task versus rest
- BOLD effect: the activation induces a variation of the oxy- / deoxy-haemoglobine balance, which can be detected



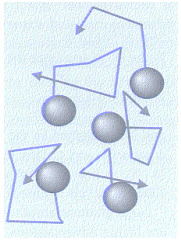
Diffusion Techniques and Methods

- Diffusion Weighted Imaging
- Diffusion Tensor Imaging
- Diffusion Kurtosis Imaging
- Intravoxel Incoherent Motion



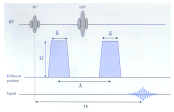
Diffusion

- Molecules undergo random translational motion
  - = Brownian Motion
  - = Diffusion
- Main molecule: H_2O
- The molecules probe the tissues at a microscopic scale



Diffusion Imaging (I)

- MRI can be made sensitive to these motions
- Pulsed gradient spin echo sequence
  - Spin Echo Sequence (90° - 180° pulses)
  - + diffusion gradients applied around the 180° pulse
  - The « b-factor » controls the diffusion weighting
  - The « b-factor » depends on G, δ, and Δ



Diffusion Imaging (II)

- Free diffusion
  - The spins acquire random phases
  - The phases cancel
  - Signal loss
- Hindered diffusion (cellular membranes, axonal architecture, myelin shield …)
  - Lower signal loss

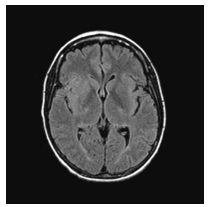
Diffusion Sequence (DWI)

- One acquisition without diffusion gradients (b = 0)
- 3 acquisitions with diffusion gradients (b = 1000) applied along 3 perpendicular directions (Slice, Frequency, Phase)
- Apparent Diffusion Coefficient (ADC)

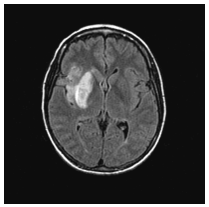
$$ADC = \frac{-1}{b} \ln\left(\frac{\text{image}(b=1000)}{\text{image}(b=0)}\right)$$

Diffusion (DWI): Clinical Application

Patient with suspicion for a stroke

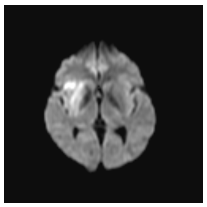


FLAIR Day 0

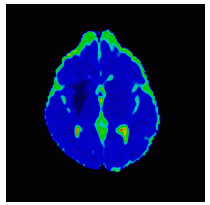


FLAIR Day 2

Diffusion (DWI): Clinical Application



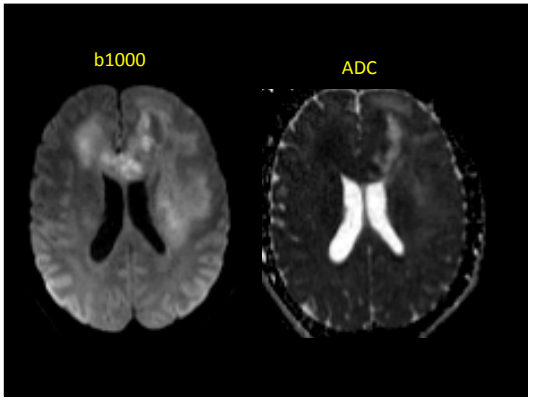
Diffusion Day 0

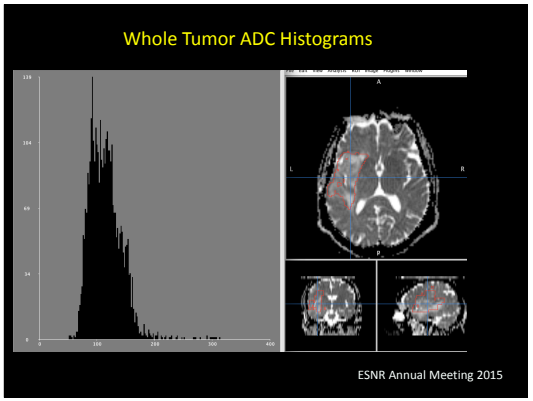


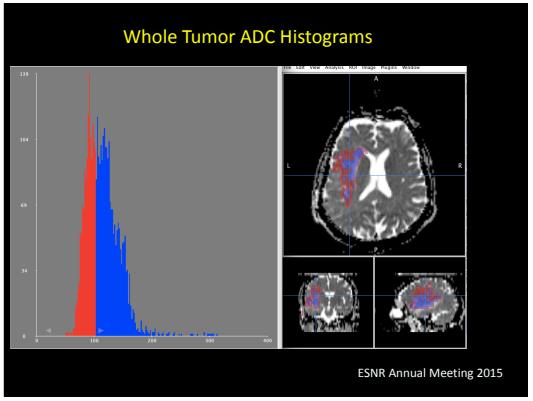
ADC Day 0

Tumor Cellularity - DWI

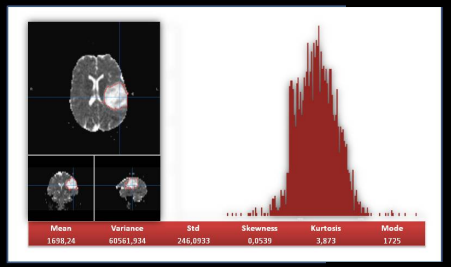
- ✓ Tissue cellularity or fluid with increased viscosity results in restricted diffusion pattern and presents with low ADC values
- ✓ Tissue necrosis, gliosis or free moving fluids results in elevated diffusion pattern and high ADC values
- ✓ High grade tumors are heterogeneous with areas of **hypercellularity** and areas of necrosis


b1000
ADC


Whole Tumor ADC Histograms
ESNR Annual Meeting 2015


Whole Tumor ADC Histograms
ESNR Annual Meeting 2015

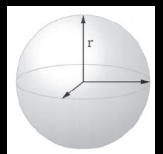
Whole Tumor ADC Histogram



ESNR Annual Meeting 2015

Anisotropy

- In water
  - No preferential diffusion direction
  - Isotropic diffusion
- In white matter tracts
  - Axonal architecture and myelin shield strenghten the diffusion along the fiber axis
  - Preferential diffusion direction
  - Anisotropic diffusion



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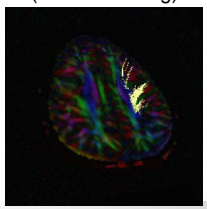
Diffusion Tensor Imaging

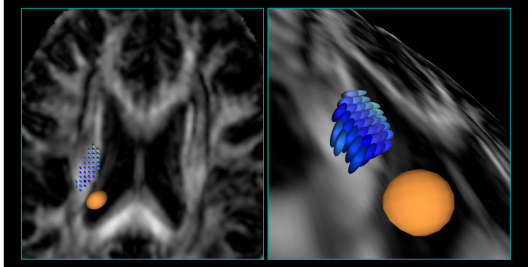
One can depict the white matter tracts
(+ fiber tracking)

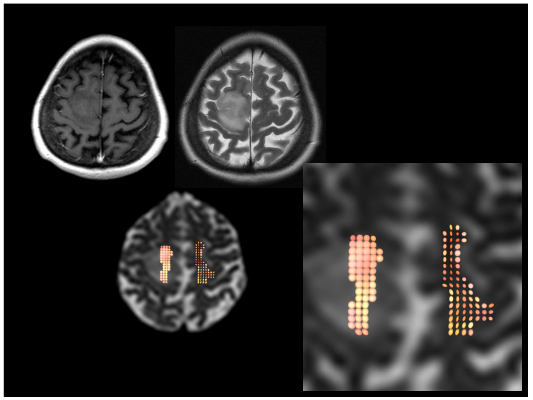


DTI sequence

- Similar to DWI sequence
- But diffusion gradients applied in at least 6 directions (3 orthogonal directions + 3 diagonal)
- For each pixel :
  - the diffusion tensor is estimated (3 × 3 matrix)
  - the tensor's main direction can be mathematically calculated
  - color-coding for main direction (red for RL, green for AP, blue for FH)
- The fibers along its whole lengths are tracked (fiber tracking)

DIFFUSION MODELS IN TISSUES

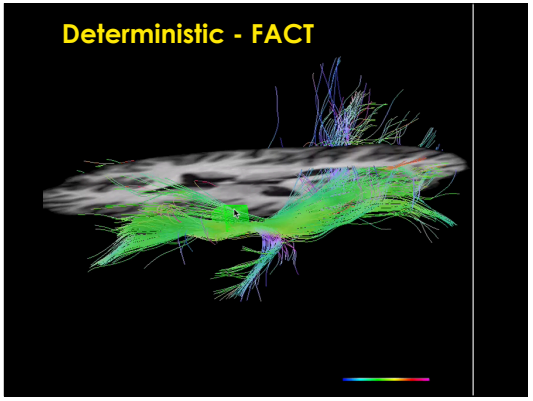


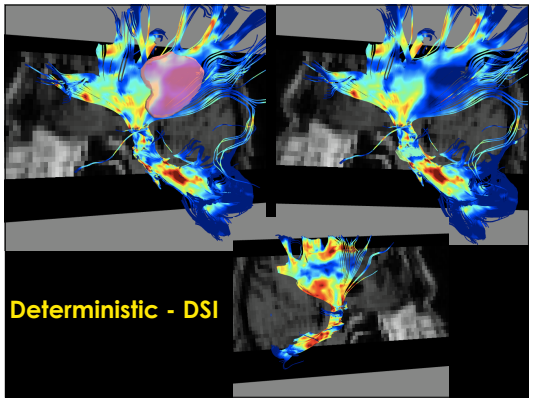


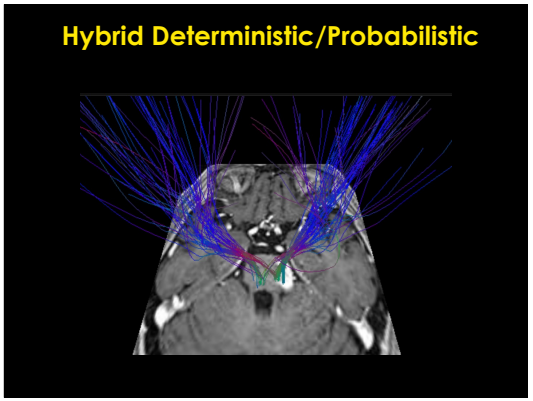
Acquisition and Post-Processing

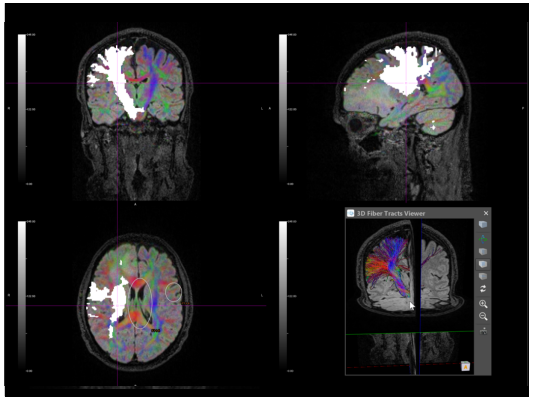
- Deterministic (FACT: Fiber Assignment by Continuous Tracking)
- Probabilistic (CSD: Constrained Spherical Deconvolution, FSL's TBSS: Tract-Based Spatial Statistics)
- Track Density Imaging (>256 directions)
- Q-ball (deterministic and probabilistic)
- NODDI: Neurite Orientation Dispersion Diffusion Imaging

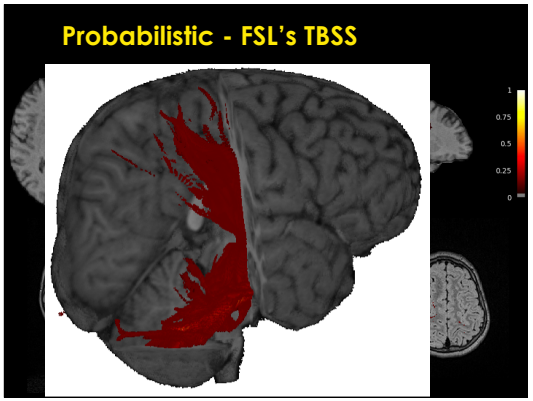
Deterministic - FACT

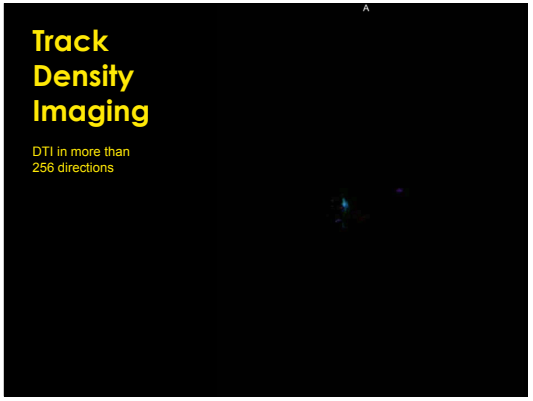


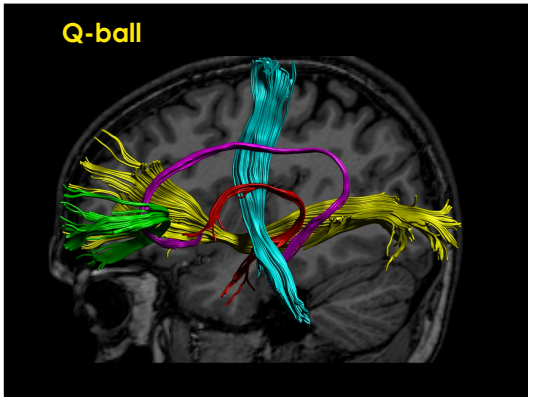

Deterministic - DSI

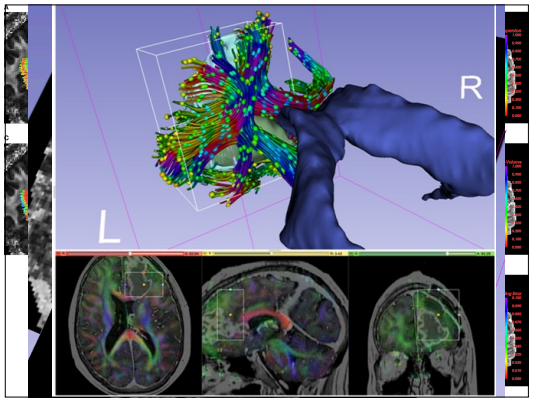

Hybrid Deterministic/Probabilistic


3D Fiber Tracts Viewer


Probabilistic - FSL's TBSS
1
0.75
0.5
0.25
0


Track
Density
Imaging
DTI in more than
256 directions


Q-ball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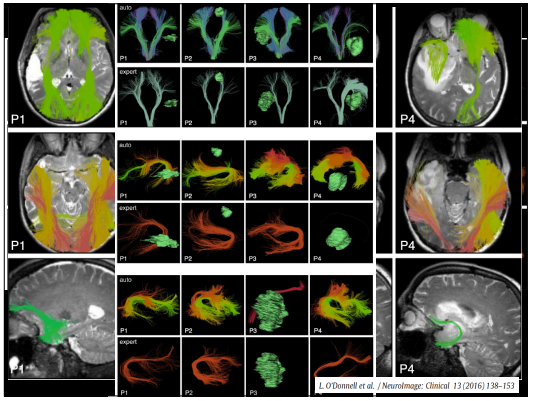
L


auto
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P1
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P4
L. O'Donnell et al. / NeuroImage: Clinical 13 (2016) 138–153

Fiberprint: a subject fingerprint based on sparse code pooling for white matter fiber analysis

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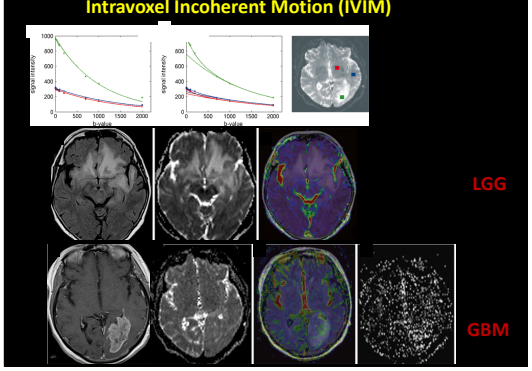
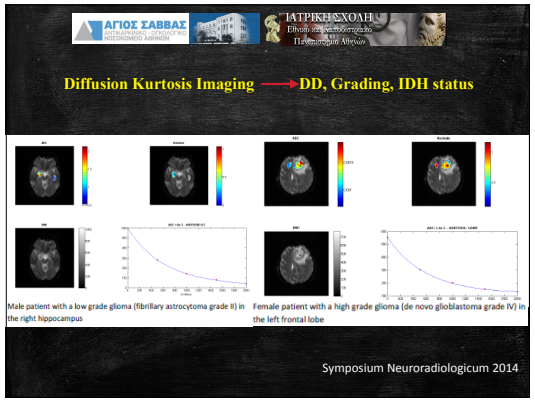
[b] *School of Computer Science & Center for Intelligent Machines, McGill University, 3480 University Street, Montreal, QC, Canada, H3A2A7*
[c] *Sorbonne Universités, UPMC Univ Paris 06, Inserm, CNRS, Institut du cerveau et la moelle (ICM) - Hôpital Pitié-Salpêtrière, Boulevard de l'hôpital, F-75013, Paris, France*
[d] *Inria Paris, Aramis project-team, 75013, Paris, France*
[e] *AP-HP, Departments of Neurology and Neuroradiology, Hôpital Pitié-Salpêtrière, 75013, Paris, France*

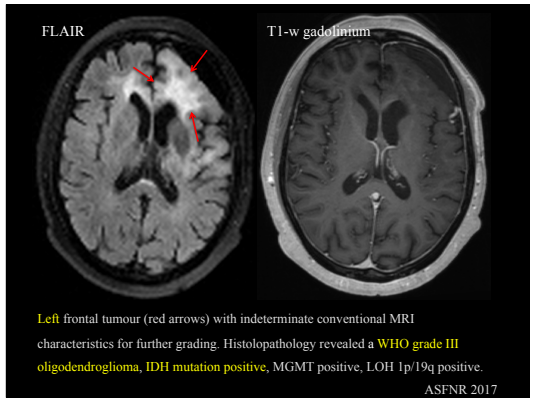
represent, a vely. Fiber trajectories sualization. ves), left

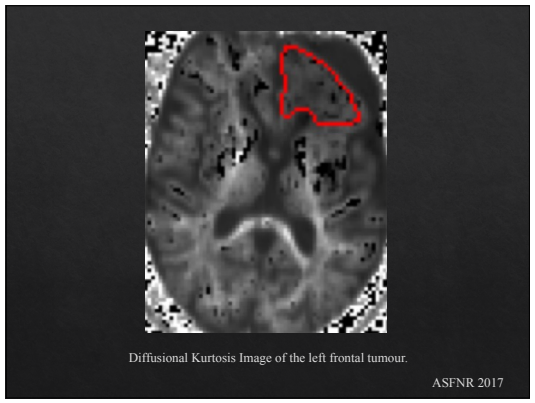
Figure 6: Subject fingerprint visualization. Color coded bundles from four subjects representing the magnitude of their corresponding RMS pooling function values. We use the same color code scheme as in Figure 5 (superior axial (top), left sagittal (middle), and anterior coronal (bottom) views respectively)

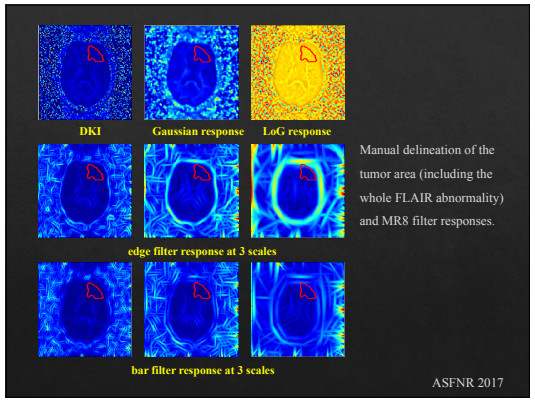
http://www.dtiatlas.org/



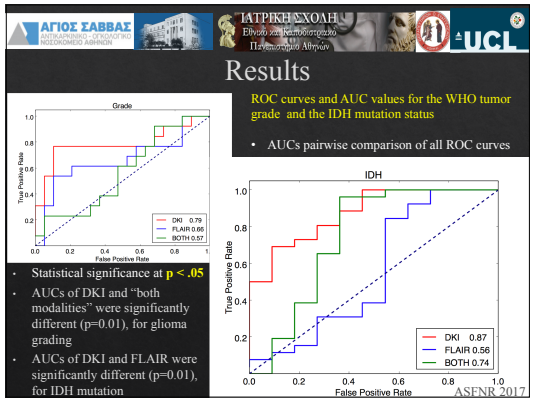

ΑΓΙΟΣ ΣΑΒΒΑΣ
ΙΑΤΡΙΚΗ ΣΧΟΛΗ
Diffusion Kurtosis Imaging ⟶ DD, Grading, IDH status
Male patient with a low grade glioma (fibrillary astrocytoma grade II) in the right hippocampus
Female patient with a high grade glioma (de novo glioblastoma grade IV) in the left frontal lobe
Symposium Neuroradiologicum 2014

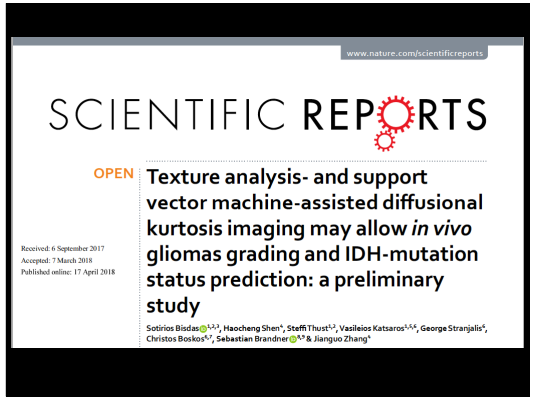

FLAIR
T1-w gadolinium
Left frontal tumour (red arrows) with indeterminate conventional MRI characteristics for further grading. Histolopathology revealed a WHO grade III oligodendroglioma, IDH mutation positive, MGMT positive, LOH 1p/19q positive.
ASFNR 2017


Diffusional Kurtosis Image of the left frontal tumour.
ASFNR 2017



Manual delineation of the tumor area (including the whole FLAIR abnormality) and MR8 filter responses.





Outline

- fMRI and DTI Techniques and Methods
- **Clinical Applications of brain mapping**
- Clinical Challenges
- Future Developments

Clinical Applications Outline

- **Our aim**: Help solve the neurosurgical problem and mainly preserve patient's neurological status
- Mapping of Motor Function
  - Neuroanatomy, Paradigm, Activation Map, Clinical Cases
- Mapping of Language Function
  - Neuroanatomy, Paradigm, Activation Map, Clinical Cases
- Mapping of Visual Function
  - Neuroanatomy, Paradigm, Activation Map, Clinical Cases
- fMRI and DTI in Clinical Practice
  - Some problems to overcome

Clinical Applications

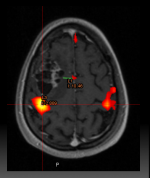
- **fMRI**
  - Presurgical Planning
    - Localization of Primary-Eloquent Cortex (Tumor, Epilepsy, Radiation, Implant)
    - Language Lateralization (Tumor, Epilepsy)
    - Memory lateralization **?** (Epilepsy)
- **DTI – FT**
  - Presurgical Planning
    - Tumor: Corticospinal Tract, Arcuate Fasciculus (SLF)
    - Epilepsy: Optic Radiation, especially Meyer's Loop
  - Understanding symptoms in every single patient

The Neurosurgical Problem

- **Surgery may induce brain damage**
  - Goal: Minimize (post-op) deficit
    - Damage to Eloquent Cortex (Motor, Sensory, Visual, Language) and Tracts to be avoided
  - Goal: Maximize Resection
- **Possible Solutions**
  - Clinical Information and morphological MRI
  - Presurgical fMRI and DTI
  - Neuro-Navigation
  - Awake Surgery
  - Intraoperative Imaging (US, CT, MRI)

Aims in presurgical fMRI and DTI

- **Feasibility of Treatment** (surgery, radiation) by estimating the risk for damage of the eloquent cortex and tracts
  - Localize eloquent cortex and tracts adjacent to the tumor
  - Estimate the Safety Margin
- **Planning the Surgical procedure**
  - What is the possible extent of the resection ?
  - What approach should be used ?
  - Selection of patients for intraoperative electric stimulation (***subtotal*** resection)
- **Neuronavigation**
  - Mis-registration due to per operative brain shift



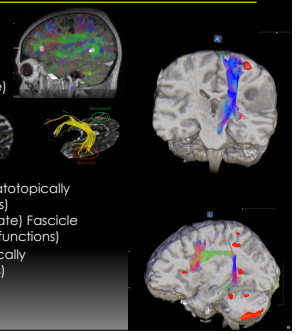
Finger Tapping in a young male patient with metastasis

Clinical fMRI: Available Evidence

- **There is no Controlled Study** showing modification of the surgical approach or improved outcome after pre-surgical fMRI
- Effect on therapeutic decision making (39 patients)*
  - Estimated Reduction in Operation Time 15-60 min
  - More aggressive surgery in 6 patients
  - Smaller Craniotomy in 2 patients
- **Risk for Postoperative deficit**
  - Yetkin 1997: Distance >2 cm: no risk for deficit, <1cm: 50% risk for deficit
  - Haberg 2004: Distance ≥1 cm reduces risk for postoperative deficit
  - Krishnan 2005: Distance<5 mm: risk for deficit

* Petrella et al, Radiology 2006

Targets for presurgical fMRI and DTI



- **Primary-eloquent cortex**
  - Motor (Sensory)
  - Language (Broca, Wernicke)
  - Hearing
  - Vision
  - Memory ?
- **Tracts**
  - Corticospinal Tract(s) (somatotopically predictable motor functions)
  - Superior Longitudinal (arcuate) Fascicle (less predictable language functions)
  - Optic Radiation (retinotopically predictable visual functions)

Demands

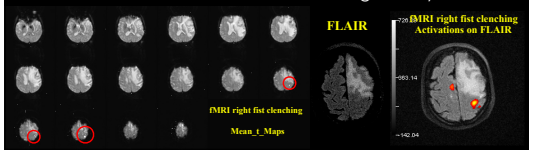
- Robust results in individual patient
- Paradigms/stimuli adapted for patients
- Limited acquisition time
- Validation with (difficult) gold standard models/methods

Clinical Protocol fMRI and DTI

Motor mapping - hand, foot, mouth	**4 min 30 sec (x3)**
Tactile (optional) - hand, foot	**4 min 30 sec (x2)**
Language - verb to noun, alliteration	**4 min 30 sec (x1)**
DTI	**5 min 30 sec**
3D T1 MPRAGE anatomical	**3 min 30 sec**
FLAIR	**4 min 30 sec**
Total Scantime	**~ 45 min**

Postprocessing

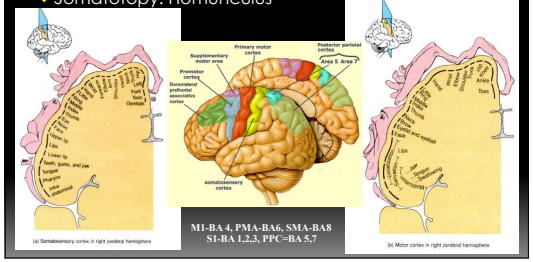
- **Tools**
  - Real time evaluation, advanced vendor tools, commercial or in-house developed software
- **Aim (s)**
  - Activation maps available for reading together with morphology
  - Transfer of data into the neuronavigation system



fMRI and DTI of Sensorimotor function

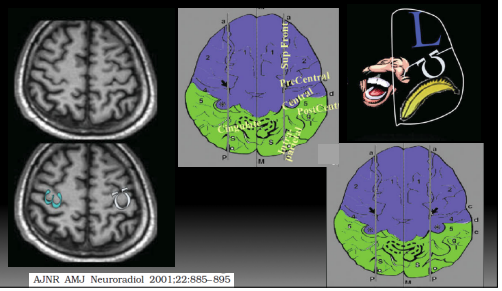
Motor mapping - Neuroanatomy

- Motor system: M1 executes voluntary movement
- Somatotopy: Homunculus



Motor mapping

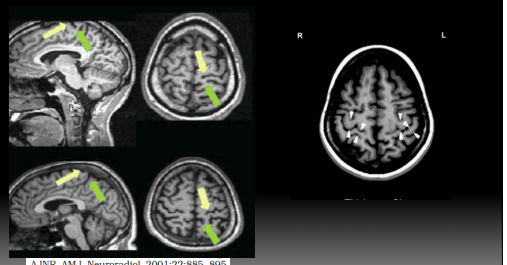
- Neuroanatomy in the axial plane: gyri and sulci
  - Handknob



AJNR AMJ Neuroradiol 2001;22:885–895

Motor mapping

- More Landmarks, cortex
  -Thickness sign (pre>post)



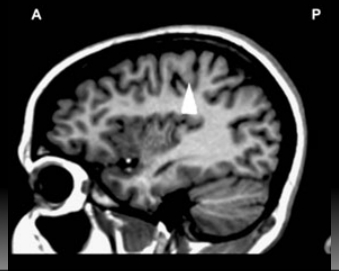
AJNR AMJ Neuroradiol 2001;22:885–895

Motor mapping

- More Landmarks, cortex
  - Bracket (or "moustache") sign (Cingulate)

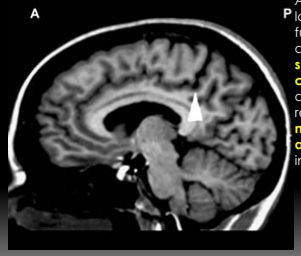
Motor mapping

- More Landmarks, cortex
  - Hook sign



Motor mapping

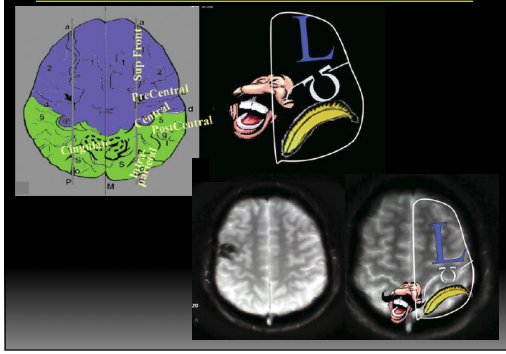
- More Landmarks, cortex
  - Pars Marginalis



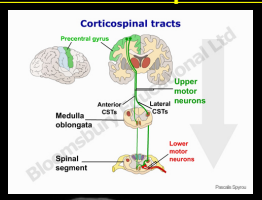
Anatomically identifiable landmarks for specific functions could be described **solely for the central region**, and even there reliability reaches a **maximum of approximately 95%** in healthy volunteers. *

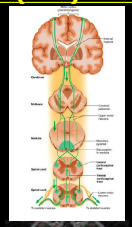
* Slippich C, *Clinical functional MRI 2007*

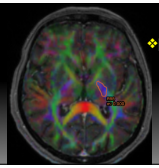
Motor mapping - Summary

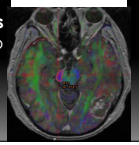


Corticospinal Tract (CST)





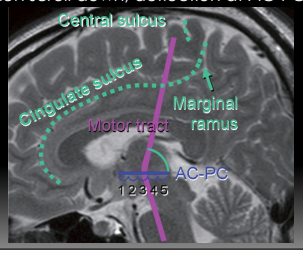




- **Few Landmarks**
  - Posterior limb of Internal Capsule
  - Cerebral Peduncle

A quick way to identify the CST

- "Poor man's tractography"
  - Identify the precentral gyrus
  - Point out with the mouse
  - Then scroll down, deflection at AC-PC line



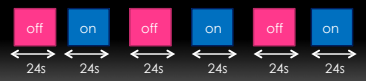
Yamada et al, *JMRI 2007*

Patient Selection for Motor Mapping

- Neuroanatomy can not be appreciated from morphology
  - Distortion of the Rolandic area
  - Only hand area has landmarks
- Morphology indicates involvement of the CST
- Clinical status and imaging findings disagree
- Recurrent tumors, second operation, plasticity ?

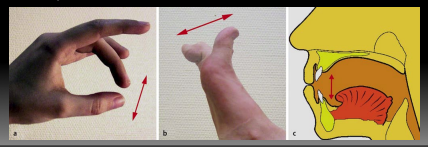
Motor Stimulation, Paradigms

- At least two conditions are required
- Generally block design
- Motor experiments
  - movement / rest (finger, foot, tongue, lip)
  - movement 1 / movement 2 (complex vs simple or one body part vs another)



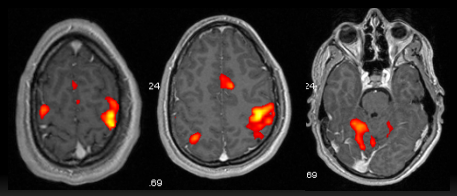
Motor Stimulation, Paradigms

- Paradigms must be adapted to the patient clinical status
  - Hand: Finger tapping, fist clenching (> 3 Hz)
  - Toe flexion/extension(> 1 Hz, avoid foot movement)
  - Tongue up/down movement, mouth closed
  - Alternatives: contralateral limb, passive movement, sensory stimulation



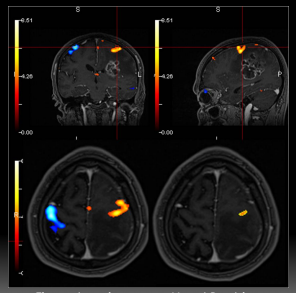
Activation Map from Finger-tapping

- Non selective activation of the motor system
- Indication of task performance



Motor vs Sensory Mapping

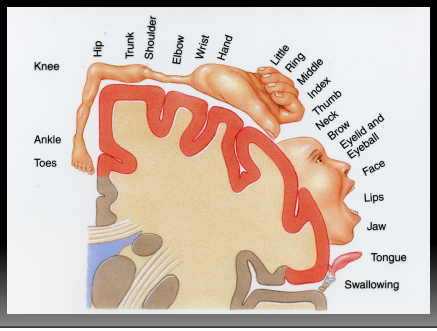
- Tightly wired activation in the sensory cortex



Finger tapping Hand Brushing

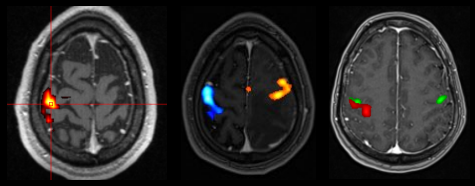
Somatotopy in M1

- Motor Homunculus



Contrast and Activation Map

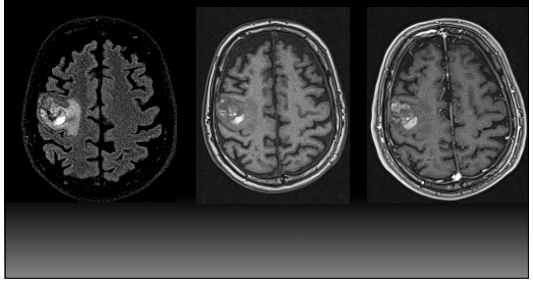
- Activation Map is Contrast dependent



Finger tapping vs Rest Right vs Left Hand Motion Hand vs Tongue

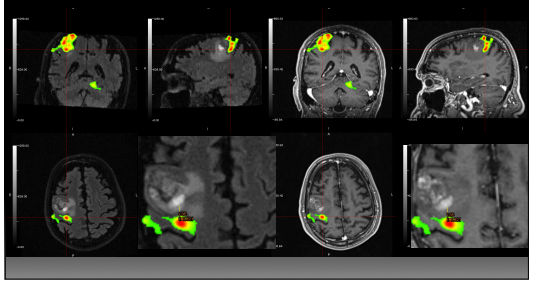
Preoperative fMRI: Clinical Case 1

- Frontal tumor in close proximity of M1 (HMA)



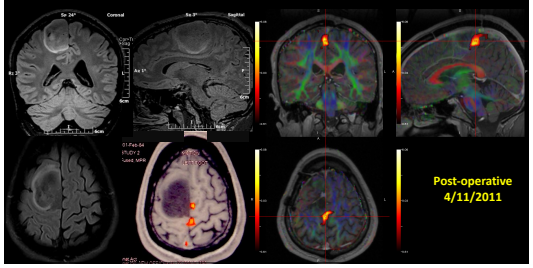
Preoperative fMRI: Clinical Case 1

- Frontal tumor in close proximity of M1 (HMA)
- fMRI risk for deficit, total resection possible



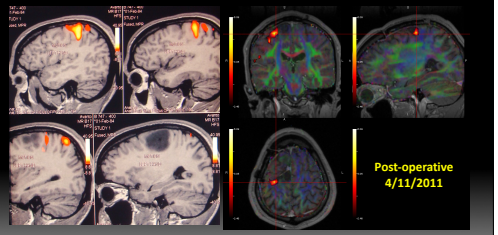
Pre- and post-operative fMRI: Clinical Case 2

- Fronto-parietal low grade glioma: male 26 yrs
- Primary function in closest proximity: motor foot representation (< 1cm)

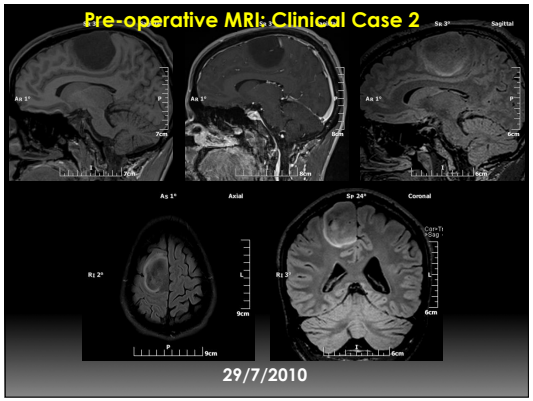


Pre- and post-operative fMRI: Clinical Case 2

- Frontoparietal low grade glioma: male 26 yrs
- Primary function in close proximity: motor hand representation (> 1cm)

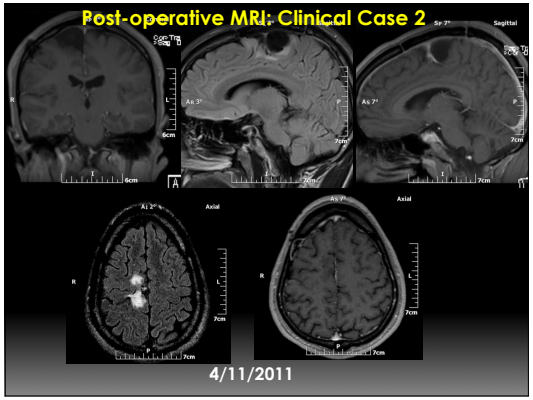


Pre-operative MRI: Clinical Case 2



29/7/2010

Post-operative MRI: Clinical Case 2



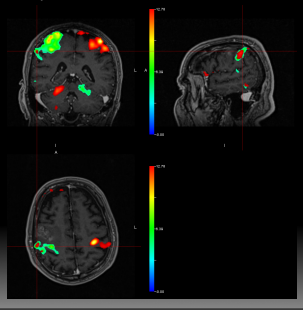
4/11/2011

Additional Findings

- Plasticity
  - Primary motor co-activation
  - Increased activation of secondary motor cortex
- Alteration of BOLD-Response

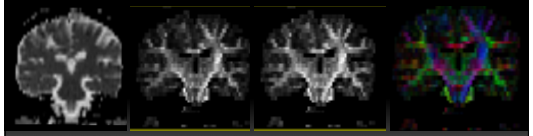
Additional Findings

- Primary motor co-activation



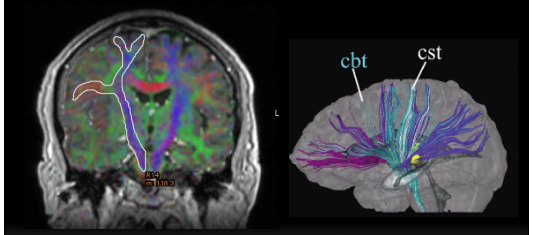
DTI of the Corticospinal Tract (CST)

- Parameter maps: ADC, RA, FA, color coded FA (CC-FA)
- In clinical practice FA and CC-FA maps are used



ADC RA FA CC-FA

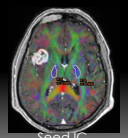
CST on the CC-FA map

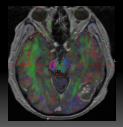


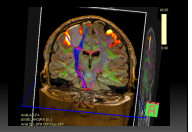
Wakana et al, Radiology 2004

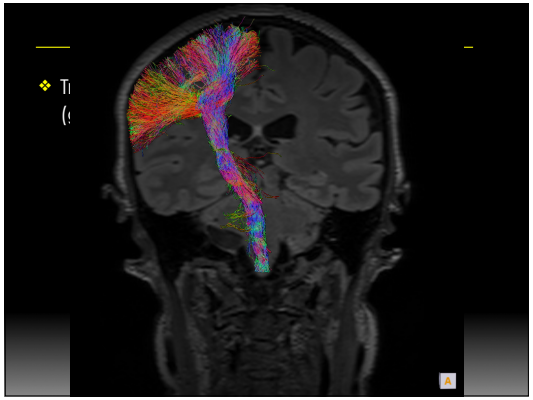
Fiber Tractography (FT) of the CST: Methods

- **Deterministic**
  - One (1) ROI in the PLIC
  - Two (2) ROIs, cerebral peduncle/motor cortex, PLIC/motor cortex
  - Seed ROIs from fMRI activation (especially when anatomy is distorted)
- Probabilistic, HARDI, . . .


Seed IC

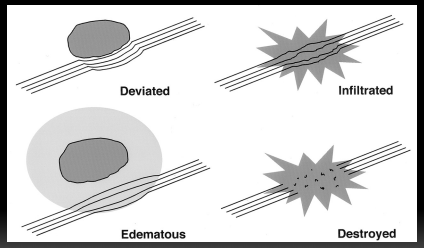

Seed CP, target PMA


Seed IC, target PMA



Assessment of WM integrity

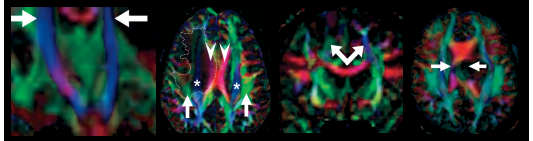
- Visual assessment is commonly used in clinical practice
- Types of involvement



Field et al, *JMRI 2004*

Assessment of WM integrity

- Types of involvement (visual assessment)
  "dislocation", "infiltration", "destruction"



normal FA
Displacement

↓ FA, normal orientation
Vasogenic edema

↓ FA, disorientation
Tumour infiltration

Isotropy
Tract disruption

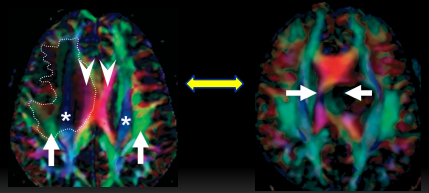
Field et al, *JMRI 2004*

Assessment of WM integrity

- The caveat in clinical DTI

Low FA to near isotropy → false-negative DTI

The tract is present however can not be identified with DTI

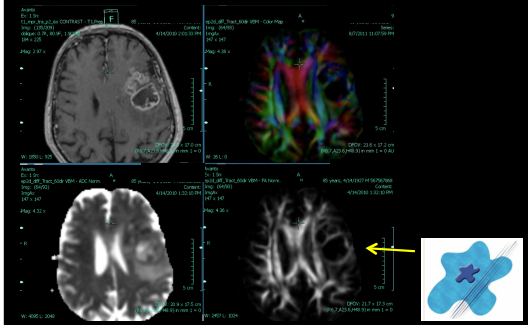


↓ FA, normal orientation
Vasogenic edema

Isotropy
Tract disruption

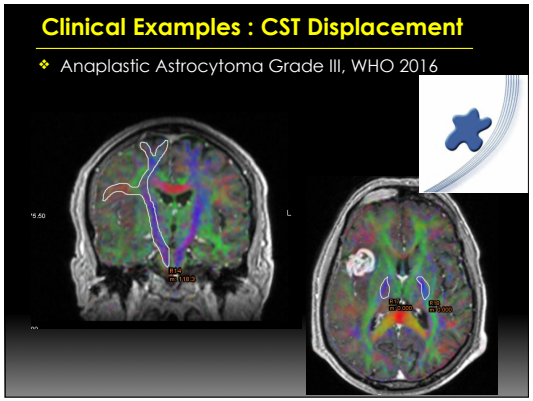
Field et al, *JMRI 2004*

Assessment of White Matter Integrity - Edema

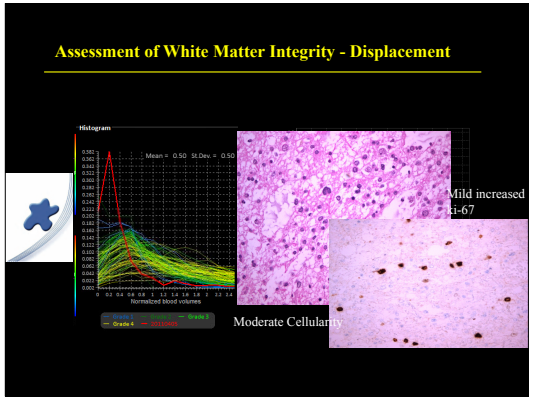


Clinical Examples : CST Displacement

- Anaplastic Astrocytoma Grade III, WHO 2016

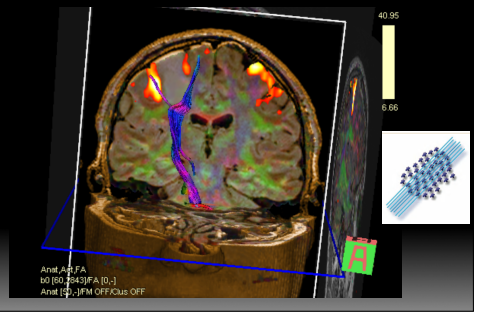


Assessment of White Matter Integrity - Displacement



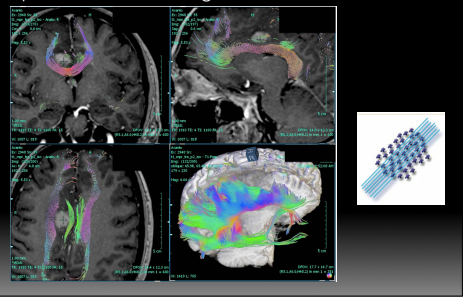
Clinical Example: CST Infiltration

- Anaplastic Oligodendroglioma of the SM region



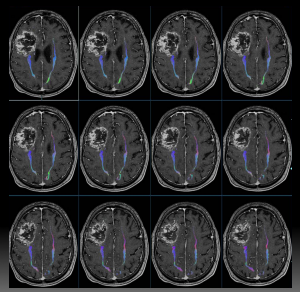
Clinical Example

- Infiltration of the Corpus Callosum and displacement of the cingulum

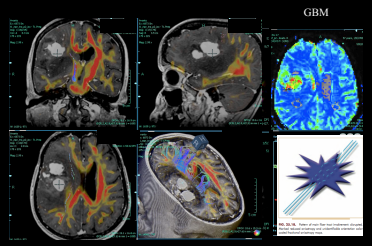


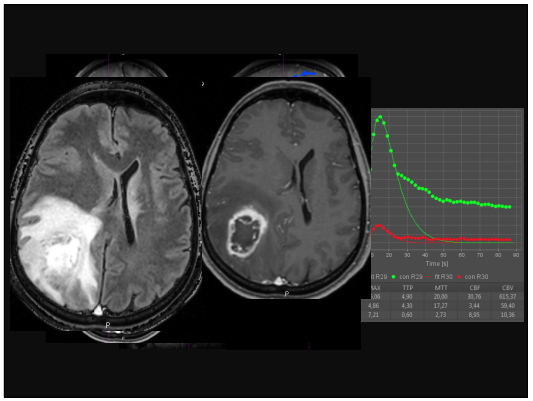
Clinical Example : CST Disruption

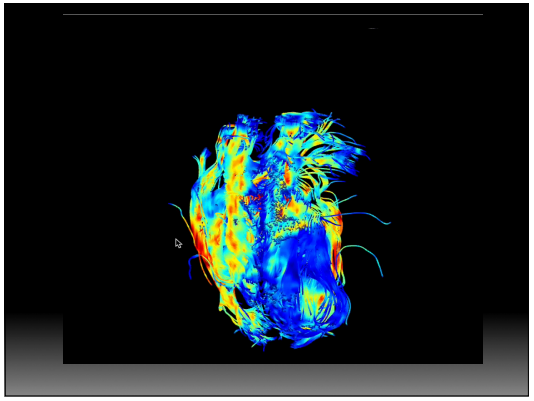
- Glioblastoma Multiforme



Assessment of White Matter Integrity - Disruption







Assessment of WM integrity

- Be aware of possible false negative DTI-FT
  - Reduced anisotropy is common around tumors
- Rules of Thumb
  - In low grade gliomas false negative DTI-FT does not rule out persisting fiber tracts
  - In high grade gliomas DTI-FT may be indicative of the degree of WM involvement
- Good Correspondence (92-95%) is reported between DTI reconstructed tracks and positive functional subcortical DESs site for the CST * #
- Use your common sense

* Coenen VA et al ,*Surg Neurol. 2003*
Bello L et al, *Neuroimage. 2008*

fMRI and DTI of Language

Language Network

Classical Language Model

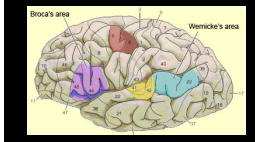
- Expressive area
- Receptive area – Arcuate fascicle
- Geschwind's area
- Prec. / Insular motor area
- Visual & auditory input, motor output

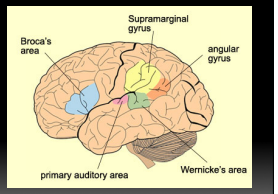
Cognitive Language Model

- Distributed Network
  - Frontal: IFG, MFG
  - Temporal: STG, MTG, FFG, PT
  - Parietal: SMG, AG, IPL
- Both hemispheres, commonly left dominance
- High inter-individual variability, no anatomical landmarks !
- Handedness, age, multilingual, task dependent

Language Network

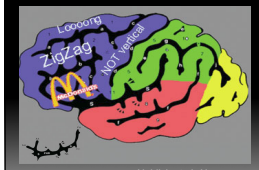
- Areas involved in Language Processing

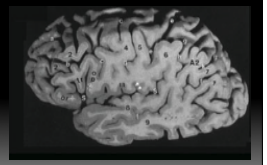




Language Primary Cortex

- Landmarks in the sagittal plane
  - Inferior and Middle Frontal Gyrus (IFG, MFG)
  - Supramarginal and Angular Gyrus (SMG + AG = IPL)
  - Superior and Middle Temporal Gyrus (STG, MTG)
  - Planum Temporale (PT) and fusiform gyrus (FFG)

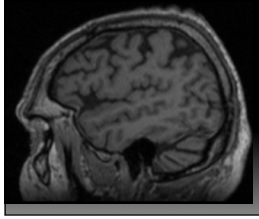


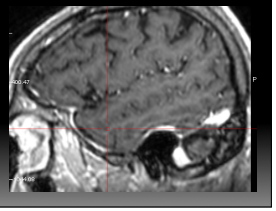


Naidich et al. *Neurosurgery 1995* - Sunaert, *JMRI 2006*

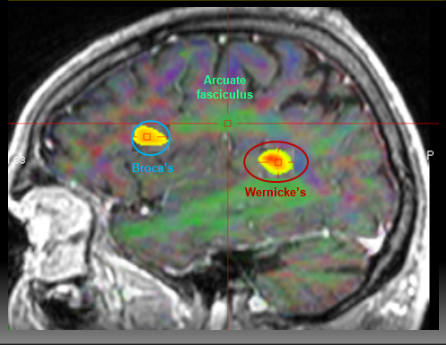
Language Primary Cortex

- Anatomical Landmarks: Sagittal plane
  - "M" sign for IFG
  - Sylvian fissure for SMG, AG
  - Temporal Sulci for STG, MTG

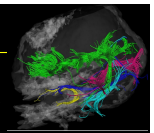




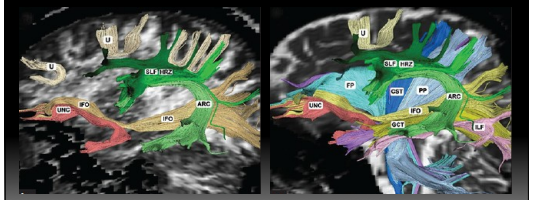
Language



Language Tracts

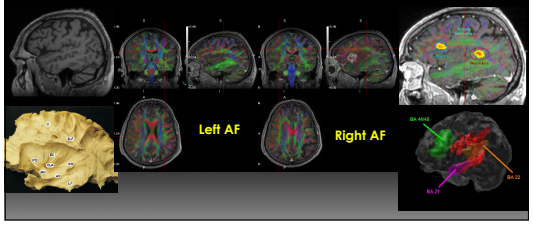


- WM tracts involved in Language
  - Arcuate fasciculus, AF (dorsal pathway), part of SLF
  - Uncinate fasciculus, inferior fronto-occipital (IFO) and inferior longitudinal fasciculus (ILF) (ventral pathway)



Language, Arcuate fasciculus (AF)

- **Landmarks**
  - No specific for AF; IFG, STG, Sylvian Fissure
  - Perisylvian boomerang shaped, connects frontal and temporal areas
  - Discernible in CC-FA maps



Language Tracts

- WM tracts involved in Language
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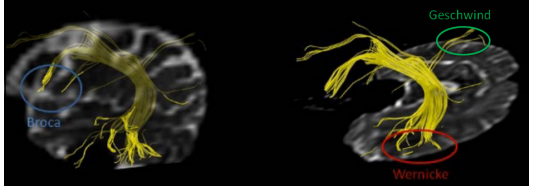
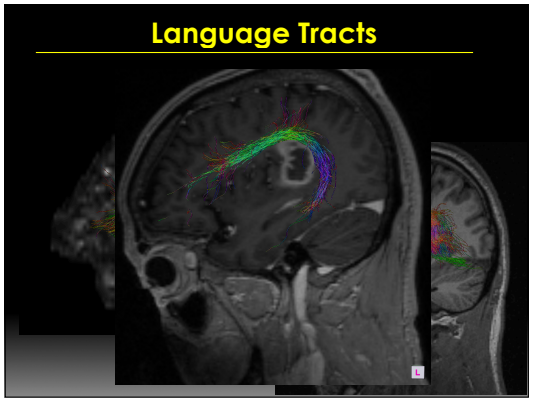
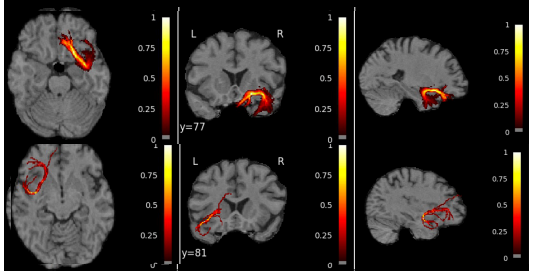


Language Tracts



Language, ILF, IFOF, Uncinate

- **Landmarks**
  - No specific
  - Discemible in CC-FA maps

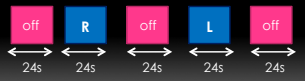


Selection of Candidates for Language Mapping

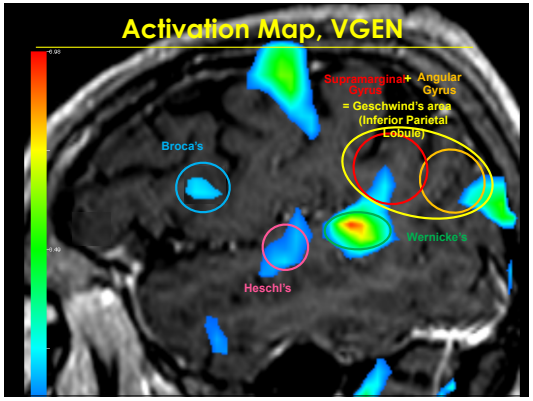
- Independent from anatomical landmarks !
- Absolute:
  - Impairment of Language Function from left and right hemispheric tumors
  - Left fronto-parietal, temporo-parietal tumors without impaired language
- Relative:
  - Left-handers and multi-linguals
  - Second operation (recurrent tumors), reorganization ?

Language Paradigms

- Simplest: condition vs rest
  - Word generation from a letter (WGEN)
  - Verb generation from a Noun (VGEN)
  - reading a text, listening to text; all versus rest
- High level and low level condition
  - Semantic decision/tone decision
  - Sense words/no sense words

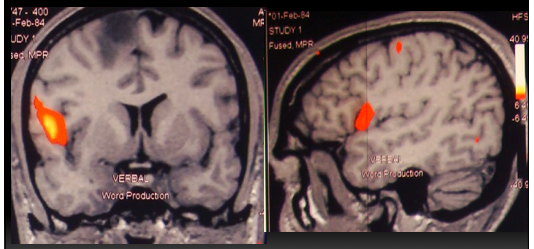


Activation Map, VGEN

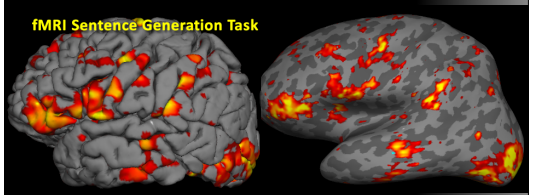


Activation Map, WGEN

- Broca's area right, Left Handed male patient 26 y

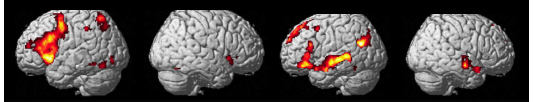


Activation Map



Activation Map, Language Stimulation

- Activation is dependent on the paradigm, due to differences in linguistic control
- Multiple tasks may be used, however results may be conflicting



Niskanen et al, *Neuroradiology 2012*

Activation Map, Language Stimulation

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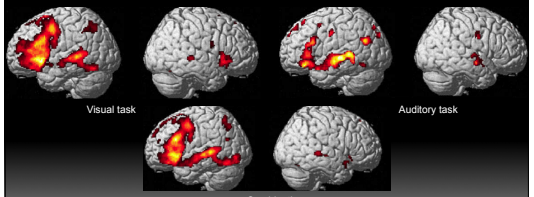
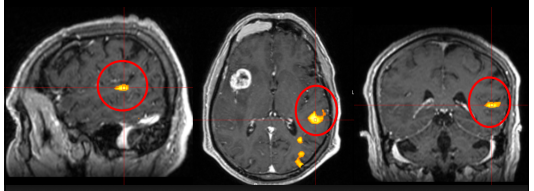


Niskanen et al, *Neuroradiology 2012*

Wernicke's area

- Speech arrest due to temporal electrical stimulation mapping occurs in focal areas of 1 cm^2

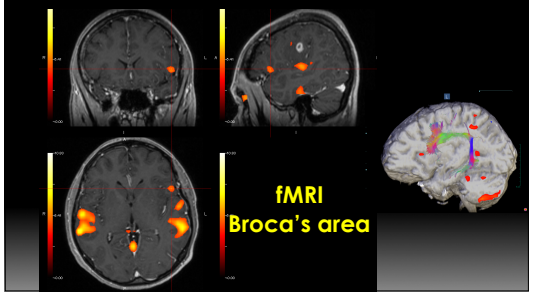


Paradigm: Verb to Noun generation

Ojemann et al, *Neurosurgery 1989*

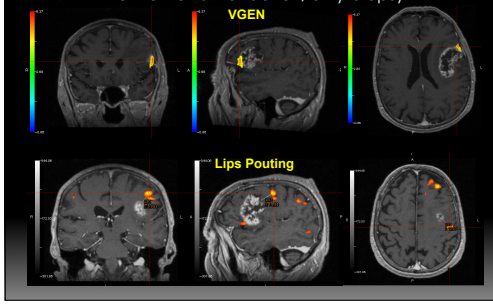
Language Stimulation: Clinical Case 1

- Dysphasic Patient with Frontal tumor > 1cm Broca's area
- fMRI no risk for deficit, total resection possible



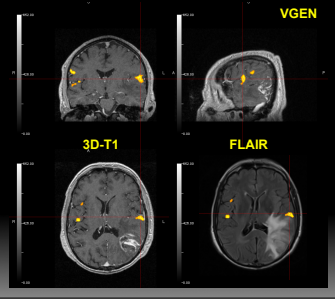
Language Stimulation: Clinical Case 2

- Frontal tumor in closest proximity of Broca's
- fMRI extreme risk for deficit, only biopsy

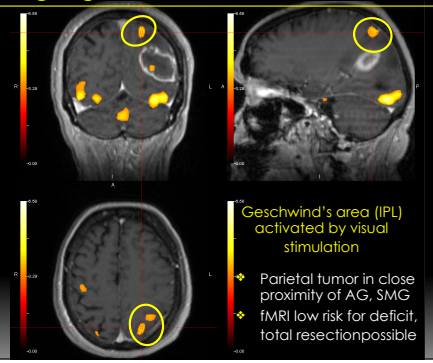


Language Stimulation: Clinical Case 3

- Frontal tumor in closest proximity of Planum Temporale
- fMRI extreme risk for deficit, only biopsy



Language Stimulation: Clinical Case 4

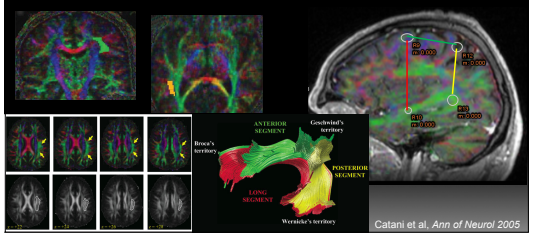


Geschwind's area (IPL) activated by visual stimulation

- Parietal tumor in close proximity of AG, SMG
- fMRI low risk for deficit, total resectionpossible

DTI – FT of the Arcuate Fasciculus

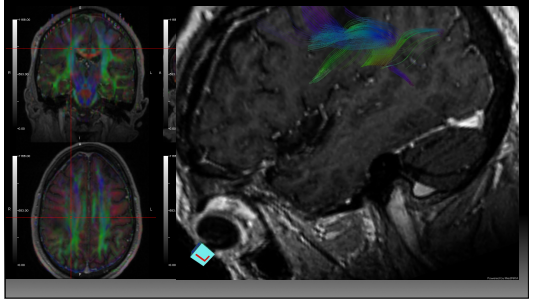
- Tractography of the AF using the 2 ROIs seeding:
  - ***anterior segment***: Latero-prefrontal Cortex → Inferior Parietal Lobule
  - direct **(long) segment**: Latero-prefrontal Cortex → Temporal Lobe
  - ***posterior segment***: Inferior Parietal Lobule → Temporal Lobe



Catani et al, *Ann of Neurol 2005*

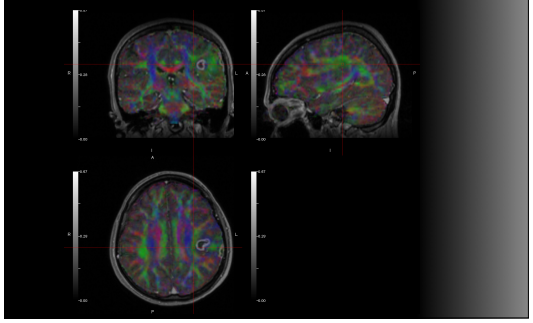
Clinical Example 1, Displacement

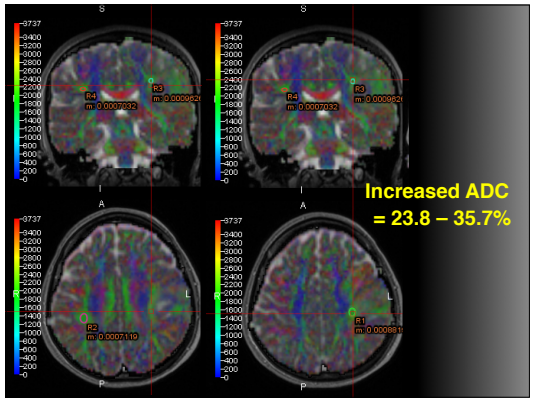
- Fibrillary Astrocytoma Grade II, with displacement of the right AF medially and caudally

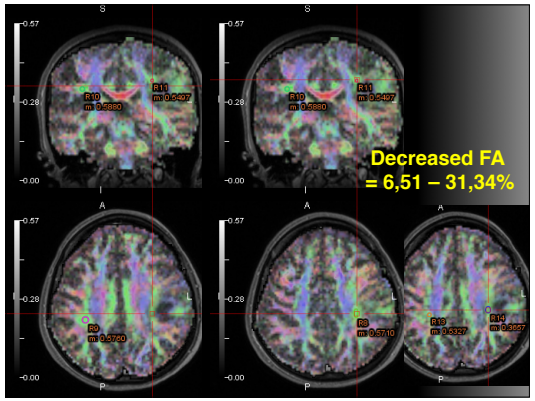


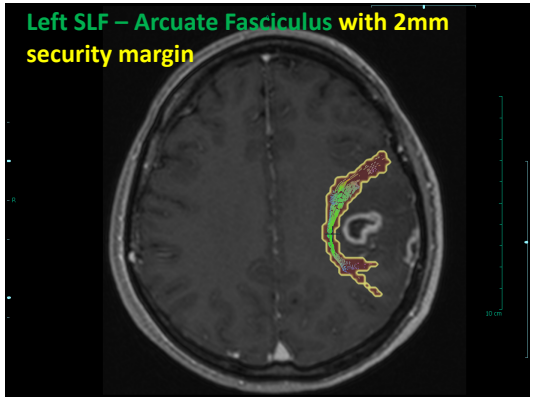
Clinical Example 2, Infiltration

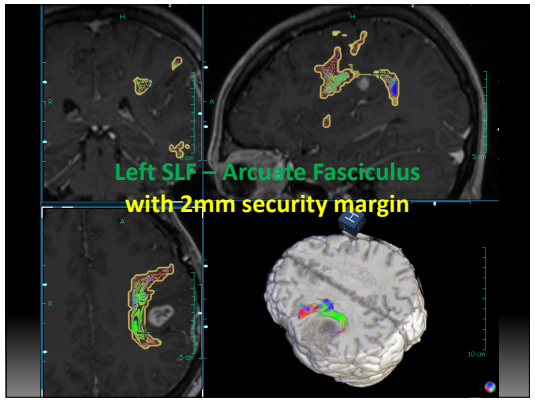
- Dysphasic Patient with multifocal GBM




Increased ADC
= 23.8 – 35.7%


Decreased FA
= 6,51 – 31,34%


Left SLF – Arcuate Fasciculus with 2mm
security margin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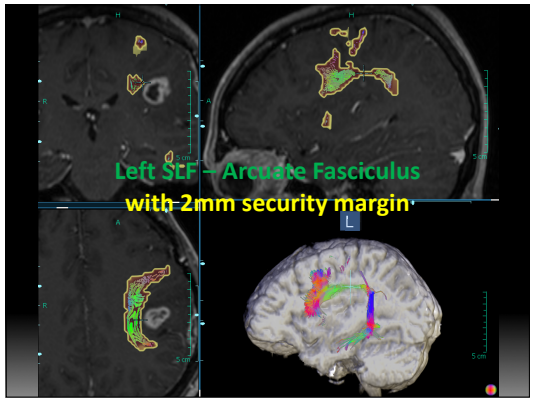
with 2mm security margin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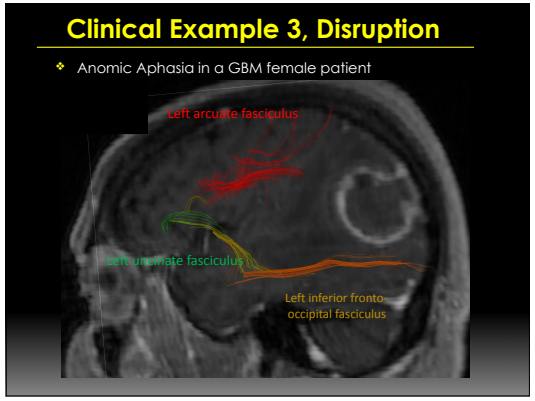
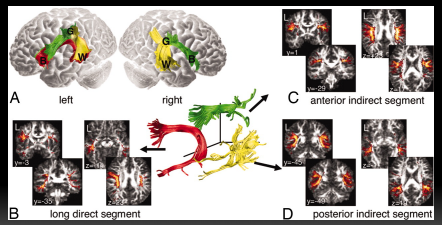

Clinical Example 3, Disruption
Anomic Aphasia in a GBM female patient
Left arcuate fasciculus
Left uncinate fasciculus
Left inferior fronto-occipital fasciculus

Arcuate Fasciculus

- Caveat: Variants
  - Asymmetry or absence of the AF
  - Variations due to gender and age



Left–right hemispheric differences in perisylvian language pathways.

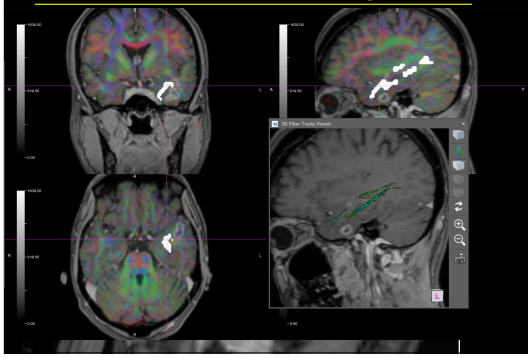
Catani M et al. PNAS 2007;104:17163-17168

Validation of AF tractography

- Positive stimulation sites and fiber tracts correspond "well" (81%) *
- False negatives occur especially when the tract is invaded by the tumor
- Language disorders are specific for each tract
- There is no absolute representation of language and speech in the brain ! ! !

* Leclercq et al , Neurosurgery 2011

ILF, IFOF, Uncinate tractography

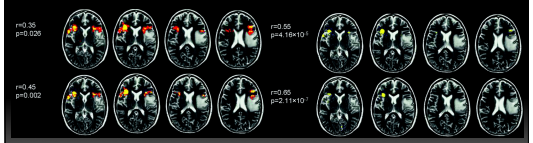


Language Lateralization

- A central question in Epilepsy Surgery
- fMRI may be helpful to determine laterality
  - Visual Assessment

Laterality Index: LI = (L-R) / (L+R)
Right Dominance -1<LI<0
Left Dominance 0<LI<1

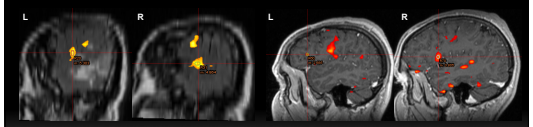
- Caveats: Paradigm, threshold, ROI . . .



Ruff I et al. AJNR 2008

Language Lateralization

- Language dominance is typical (L) or atypical
- Atypical language dominance is far more common in epilepsy patients (27% compared with 8% of controls*)
- Falsely categorized language dominance may be particularly high in extra-temporal epilepsy#

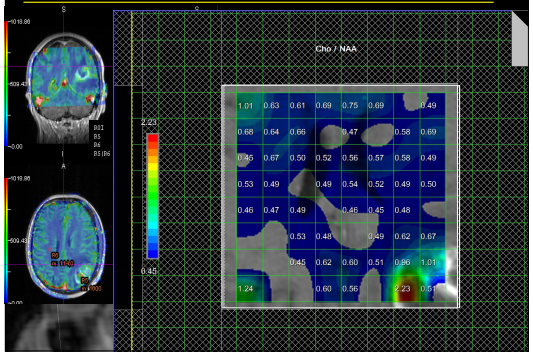


Typical LI = 0,06>0

Atypical LI = - 0,17<0

* Briellmann et al, Epilepsia 2008
\# Woermann et al, Neurology 2003

Language Lateralization - Bilingual



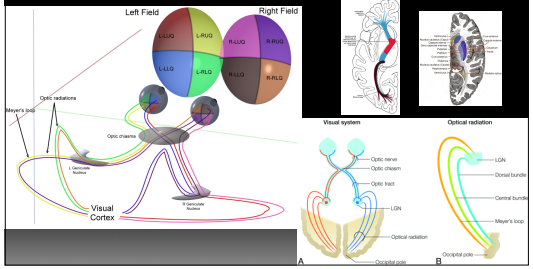
Who needs a Wada test ? *

- fMRI may possibly replace Wada tests in the majority of patients with clearly lateralized language *
- Indications for Wada test
  - (1) inability to perform the fMRI task
  - (2) validation of atypical or inconclusive language activation
  - (3) region selective testing of cognitive functions
  - (4) evaluation of propagation of ongoing interictal bilateral epileptiform EEG activity
  - (5) assessment of motor localization

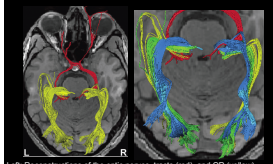
* Wagner et al , JNNP 2012

DTI – FT in Epilepsy

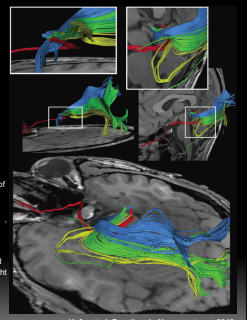
- Meyer's loop
  - Anterior temporal lobe resection causes damage to Meyer's loop resulting in quadrantanopia ("pie in the sky") in 68-100% of patients



Tractography of Meyer's loop



Left: Reconstructions of the optic nerves, tracts (red), and OR (yellow).
Right: Dissection of the OR into the Meyer loop (yellow), the central bundle (green), and the dorsal bundle (blue). The use of 1.8-mm isotropic voxels reduces the voxel size of a more conventional 2.5-mm acquisition by a factor of 2.7. Nevertheless, this resolution is still not good enough to avoid "kissing" effects between the optic nerve and neighboring eye muscles.

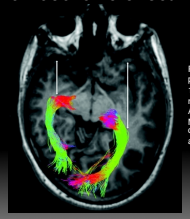


Reconstructions of the optic nerve and tract (red), the Meyer loop (yellow), the central bundle (green), and the dorsal bundle (blue) in different planes. White boxes show magnifications of the area around the LGN. Upper left: Fiber bundles of the right hemisphere. Upper right and bottom: Fiber bundles of the left hemisphere.

Hofer et al, Frontiers in Neuroanatomy 2010

Tractography of Meyer's loop

- **Methods:**
  - Probabilistic tractography has the best condition
  - Caveat false positive from surrounding tracts
  - Large inter-individual differences *

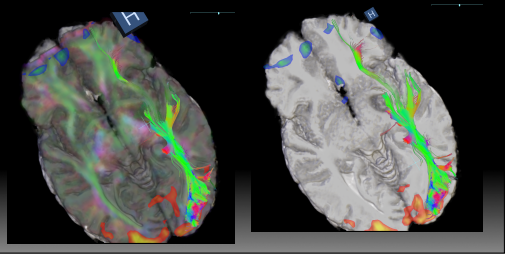


Reconstructed OR by using the probabilistic method of CSD in a 17-year-old male adolescent with a small right cerebral hemisphere. Arrows indicate the distances from the Meyer's loop to the anterior TPs. Note the differences in position between the right and left OR *

* Mandelstam et al , AJNR 2012

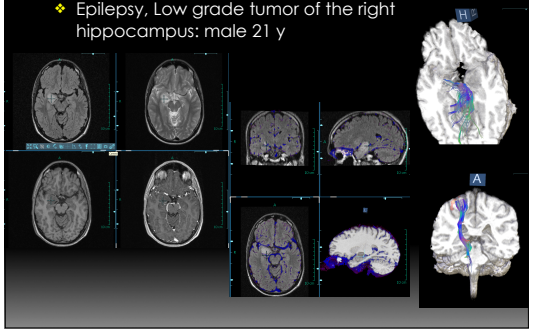
DTI of Meyer's Loop: Clinical Case

- Epilepsy, Low grade tumor of the right hippocampus: male 21 y



Preoperative MRI: Clinical Case

- Epilepsy, Low grade tumor of the right hippocampus: male 21 y



Outline

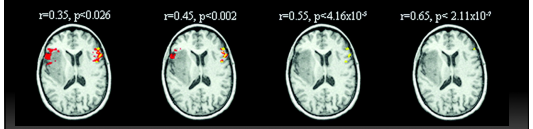
- fMRI and DTI Techniques and Methods
- Clinical Applications of brain mapping
- **Use in the clinical practice and clinical challenges**
- Future Developments

Role of the Neuroradiologist

- Study design and setup
  - knowledge of normal anatomy, selection of paradigm (task), patient information
- Data acquisition (MR scanning)
- Post-processing with data analysis
- Interpretation of results
- Interpretation and reporting of results

Clinical fMRI: Pitfalls

- **Sources of error**
  - Tumor to lesion distance depends on the threshold
  - Activation is unspecific (necessary vs dispensable)
  - False negative fMRI occurs – absence of activation
  - Task- and therefore patient- dependent



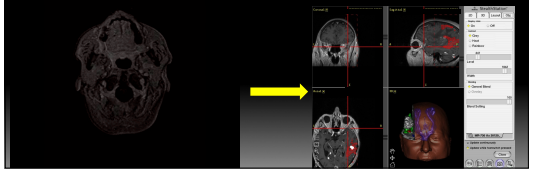
Ruff I et al. AJNR Am J Neuroradiol 2008;29:528-535

Clinical DTI: Pitfalls

- **Sources of error**
  - False negative DTI-FT
  - Motion artefacts, distortion
  - Lack of gold standard
  - Operator dependent
- **Prior Clinical Knowledge of tract integrity may increase sensitivity**

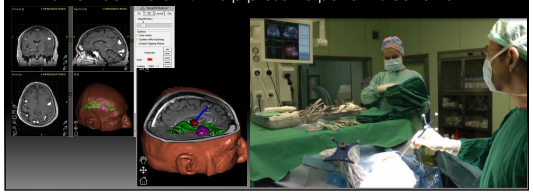
Interpretation and Report

- **fMRI**
  - Quality assessment and diagnostic accuracy of activation maps
    - Patient performance/co-operation
    - Selection of Paradigm-Task
    - Presence of artifacts (motion, susceptibility)
    - Adequate threshold
  - Description of essential activation for each fMRI paradigm
  - Distance between lesion and closest functional area

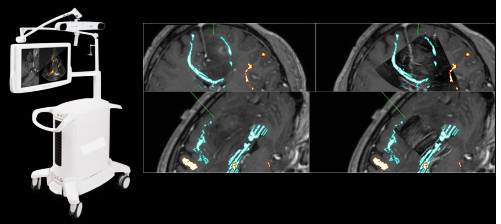


Interpretation and Report

- **DTI – Fiber Tractography**
  - Quality assessment
  - Description of tracts adjacent to tumor, type of involvement
  - Tractography results for single tracts
- **Discuss the results with the neurosurgeon**
  - Remember the aim: "Help preserve patient's condition"

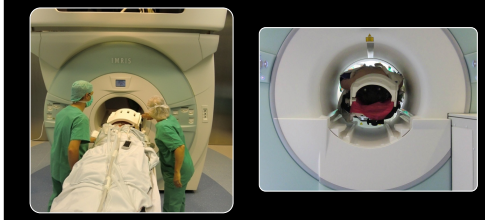


Intraoperative US (iUS) in Interactive Image-Guided Neurosurgery



Symposium Neuroradiologicum 2014

Intra-operative MRI (iMRI) preparation



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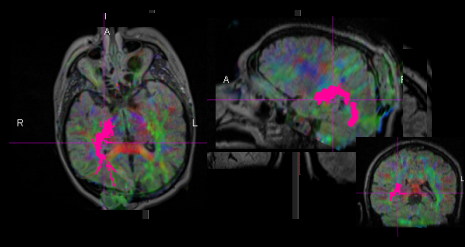
Intra-operative MRI (iMRI): DTI-FT



Symposium Neuroradiologicum 2014

Outline

- fMRI and DTI Techniques and Methods
- Clinical Applications of brain mapping
- Clinical challenges
- **Future Developments**

Future (?) Developments

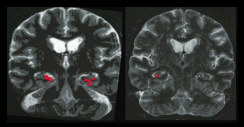
- Higher field >3T fMRI and DTI **?** ↑↑↑ artefacts
- Localization of seizure foci / EEG triggered fMRI
- Mild cognitive impairment/***Dementia***-early diagnosis
- Psychiatric Diseases
- Drug Action
- Stroke rehabilitation/***Coma patients***
- Cerebral Paresis
- Multiple sclerosis

The day after tomorrow

- Criminology: Lie detection
- Economy/Politics: Decision making process – **Neuromarketing** (product or other choice)

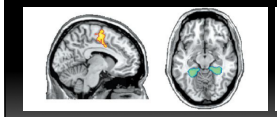
? ? ? Ethical ? ? ?

Developments

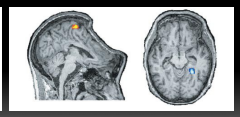


Normal Volunteer

Alzheimer's patient



Normal Volunteer

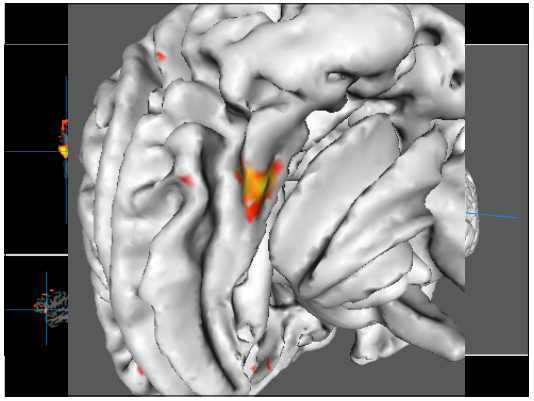


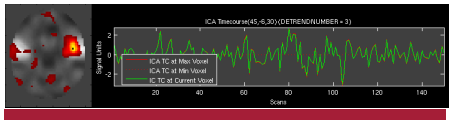
Coma patient

Resting-State fMRI

Resting-State fMRI

- fMRI technique
- The patient is not stimulated with a paradigm
- Less demanding than task-based fMRI
- Study the functional connectivity of the brain





Resting-State fMRI in Preoperative, Postoperative and *even* in an Intraoperative MR-Setting

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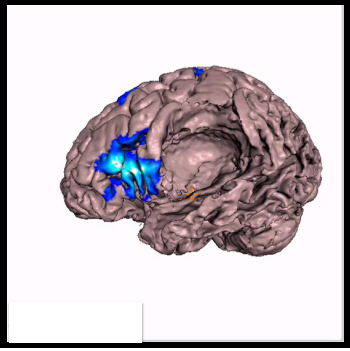
Intra-operative MRI (iMRI): RS-fMRI



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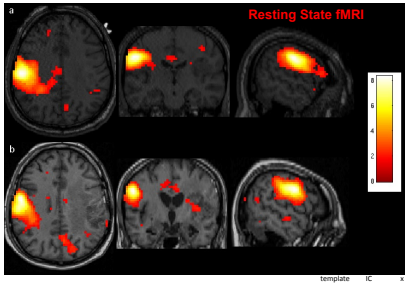


a Pre-therapy 13/3/2013

b post-therapy 26/8/2013

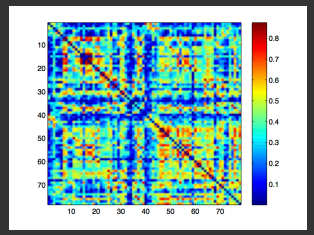
Sensorimotor RSN
Template 7

	template	IC	x	y	z	z-score
MOT	7	28	-57	-19	34	8,6
DMN	53	11	-6	-55	34	6,3
VIS	46	17	0	-91	4	6,98

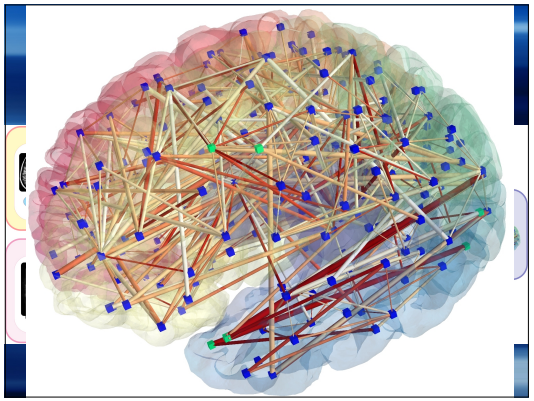
after

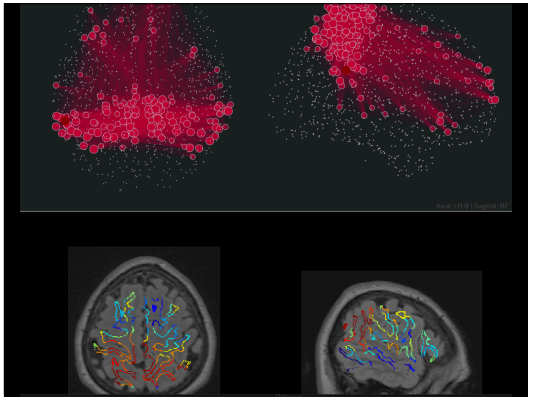
	template	IC	x	y	z	z-score
MOT	7	28	-54	-7	31	8,33
DMN	53	11	-3	-55	34	8,26
VIS	46	17	0	-85	4	8,89

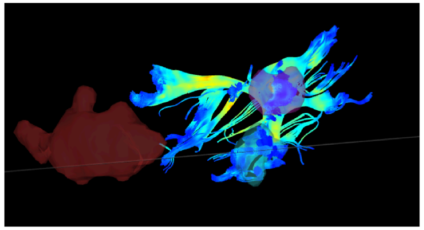
Resting State fMRI



Connectivity Matrix







Red: Broca Area

Green: Wernicke Area

Deterministic Tractography using as seed areas those that have been identified on the resting state fMRI experiment of the current patient.

Conclusions

- **fMRI and DTI may add valuable information to the pre-operative work-up of brain tumor patients**
  - However, there is no class 1 or even class 2 evidence regarding their impact on survival
- **Each has its limits and sources of error**
  - These must be taken into account when grading the diagnostic accuracy and interpreting results
- **The Future may bring**
  - Standardized and improved imaging methods
  - Lesion studies, comparison with gold standard
  - Reference material and guidelines for interpretation
  - New applications

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Review

The role of Advanced MRI in the Diagnostic and Therapeutic Approach of Brain Tumors

Katsaros VK, Papanikolaou N

Pages 34-52

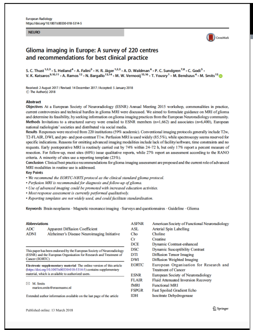
Katsaros VK, et al. MOJ 2013:1;34-52.

MMOF

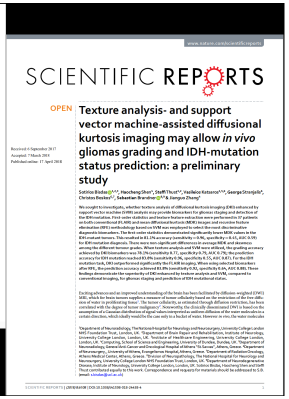
EPOS™ Electronic Presentation Online System — ESR European Society of Radiology

Protocol combining advanced and functional MRI with neuropsychological evaluation for patient-tailored therapy decision and treatment of brain masses

Poster No.: C-1980
Congress: ECR 2014
Type: Scientific Exhibit
Authors: V. K. Katsaros[1], S. Bisdas[2], A. Katsarou[1], E. Liouta[1], N. Papanikolaou[3], G. Stranjalis[1]; [1]Athens/GR, [2]Tübingen/DE, [3]Iraklion, Crete/GR
Keywords: CNS, Neuroradiology brain, Oncology, MR-Diffusion/Perfusion, MR-Functional imaging, MR-Spectroscopy, Physiological studies, Surgery, Decision analysis, Multidisciplinary cancer care, Image registration, Neoplasia
DOI: 10.1594/ecr2014/C-1980



Glioma imaging in Europe: A survey of 220 centres and recommendations for best clinical practice



SCIENTIFIC REPORTS

OPEN

Texture analysis- and support vector machine-assisted diffusional kurtosis imaging may allow *in vivo* gliomas grading and IDH-mutation status prediction: a preliminary study

Welcome

The 3rd edition of Advanced MRI In Neuro-Oncology (AMRINO) is here again!

This 2-day Neuroradiology Course/Workshop (July, 20th-21st 2018) in London, led by experienced Clinical Neuroradiologists and MRI Clinical Scientists, embraces the role of MRI in Neuro-Oncology.

The material will be exclusively centered on advanced MRI application techniques in Neuro-Oncology, the teaching sessions will be accompanied by interactive discussions with case material, and the hands-on workshops will familiarize the users with the advanced MRI post-processing.

http://amrino.org/

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- Ass. Prof. Sotirios Bisdas, MD, PhD, Department of Neuroradiology, UCL, UK
- Dr. Laurent Hermoye, PhD, Brussels, Belgium
- Evangelia Liouta, M.Sc, Neuropsychologist, Department of Neurosurgery, University of Athens, Greece


Thank you
for your attention