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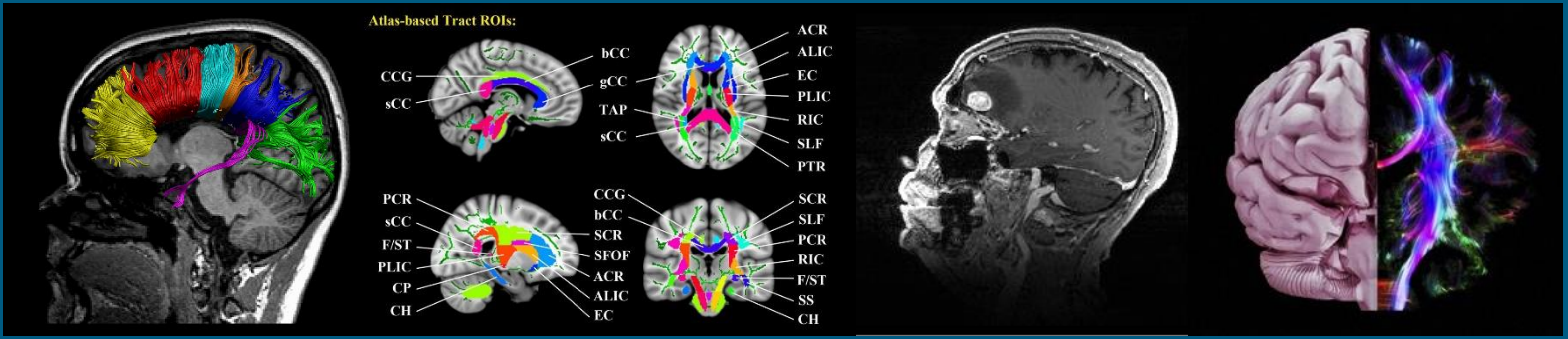
My experience in Juelich as a master student

Development and Applications of Novel Diffusion MRI Biomarkers in Neurology



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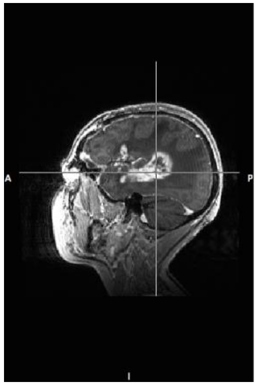
GGSWBS’14
July 2014

Julich
Internship: INM-4



Julich
Internship: INM-4

Autumn lectures
2015

Julich
Internship: INM-4

GGSWBS’16

Feb – Aug
2018

Julich
Master defense: INM-4

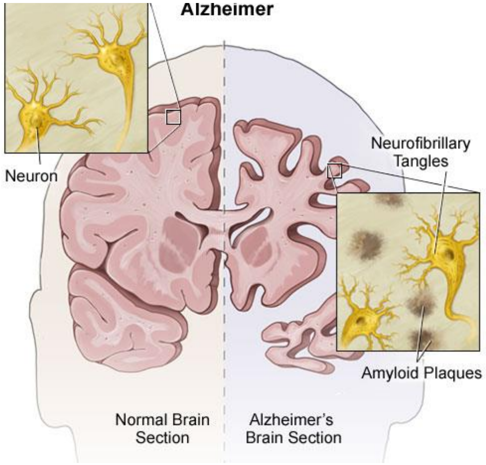
Outline

- Introduction (DTI, DKI)
- Applications: Gamma distribution function metrics as biomarker of maturation
- Multimodal Study of Brain Tumors

Introduction

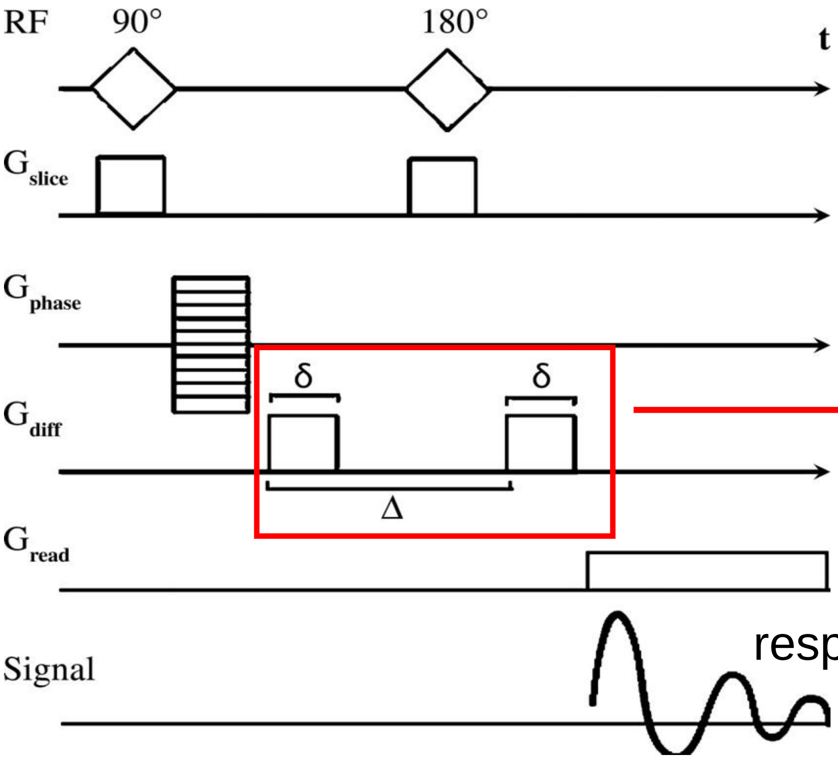
Diffusion MRI applications:

- neurodegenerative pathologies (Alzheimer’s and Parkinson’s diseases, etc.)
- stroke
- neurosurgical planning
- development and aging
- tumours



Introduction

Water Diffusion is random, microscopic movement due to thermal collisions



Diffusion MRI: pulsed field gradients

Diffusion weighting

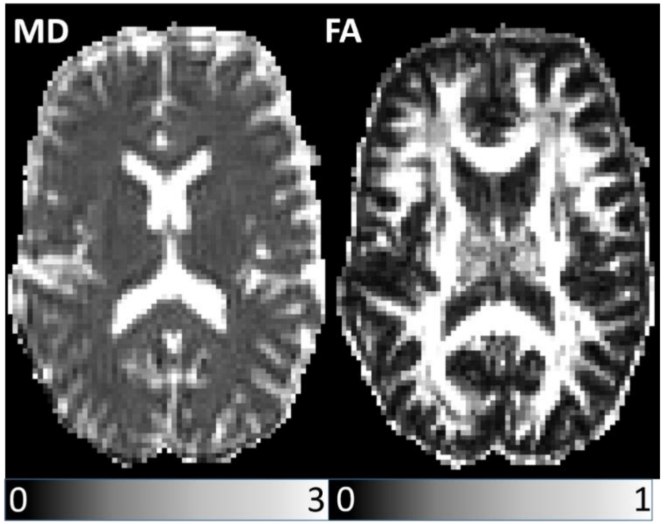
response signal

propagator

$$\psi_{diff} = \int P\left(z,t\right) e^{i\gamma G\delta z} dz$$

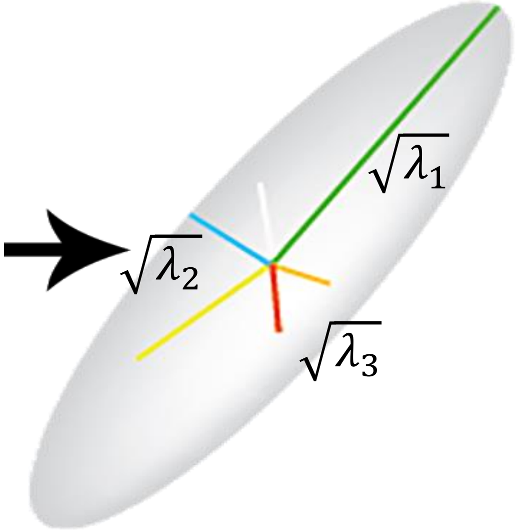
Introduction

Diffusion tensor imaging: accounts for diffusion anisotropy



Signal attenuation

$$S(\mathbf{b}) = S_0 e^{-\sum_{i,j} b_{ij} D_{ij}}$$



Tensor invariants:

Fractional Anisotropy

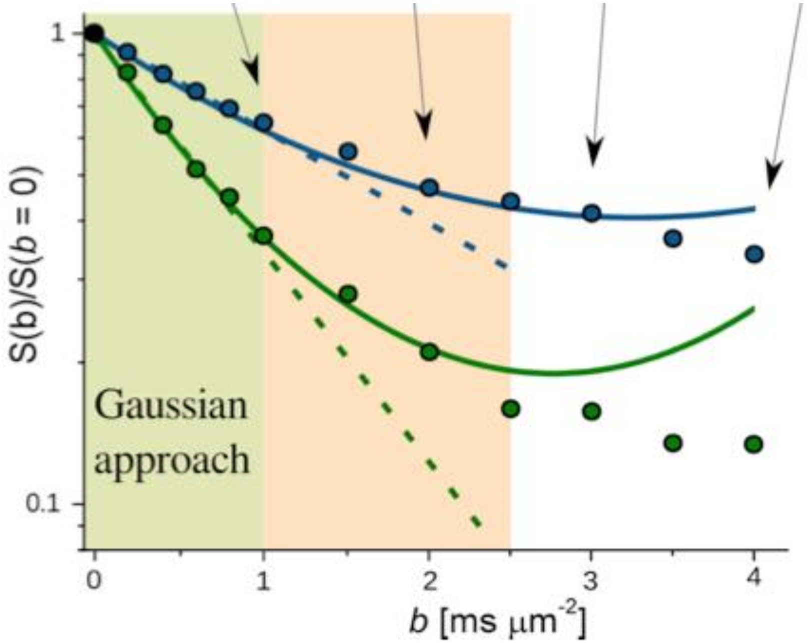
Mean Diffusivity

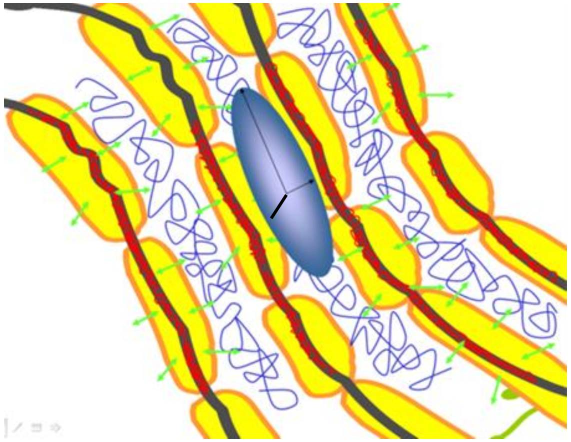
$$FA = \sqrt{\frac{3}{2}} \sqrt{\frac{(MD - \lambda_1)^2 + (MD - \lambda_2)^2 + (MD - \lambda_3)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

$$MD \equiv \frac{\lambda_1 + \lambda_2 + \lambda_3}{3} = \bar{\lambda}$$

Introduction

Non- gaussian Diffusion Kurtosis Imaging (DKI)





Water diffusion is <u>anisotropic</u> and <u>restricted</u>

$$\ln \frac{S(b)}{S_0} = -bD_K + \frac{1}{6}(bD_K)^2 K + \vartheta(b^3)$$

Monoexponential

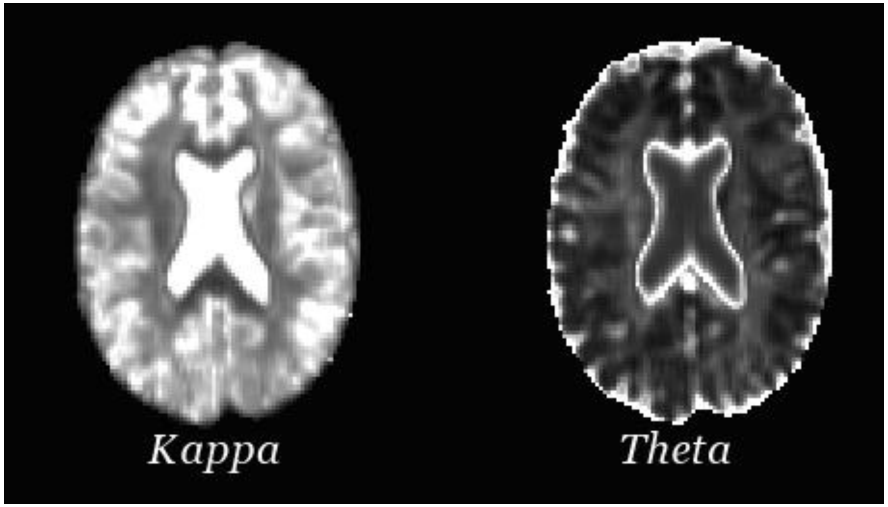
Non-exponential

Mean kurtosis:

$$MK \equiv \frac{1}{5} \mathrm{Tr}(\mathbf{K}) = \langle \mathbf{K} \rangle$$

Non- Gaussian method:
Gamma Distribution Function Imaging

F. Grinberg et al., PLOS ONE, 2014



$$S(b) = \int P(D)\exp(-bD)\,dD$$

$$P_G(D,\kappa,\theta) = D^{\kappa-1}\frac{\exp(-D/\theta)}{\Gamma(\kappa)\theta^{\kappa}}$$

Free parameters

Kappa: $\kappa = \langle D\rangle^{\wedge}2/\sigma_G^2$

Theta: $\theta = \sigma_G^2/\langle D\rangle$

Application of Gamma Distribution function to children and adults

In particular we are interested Following questions…

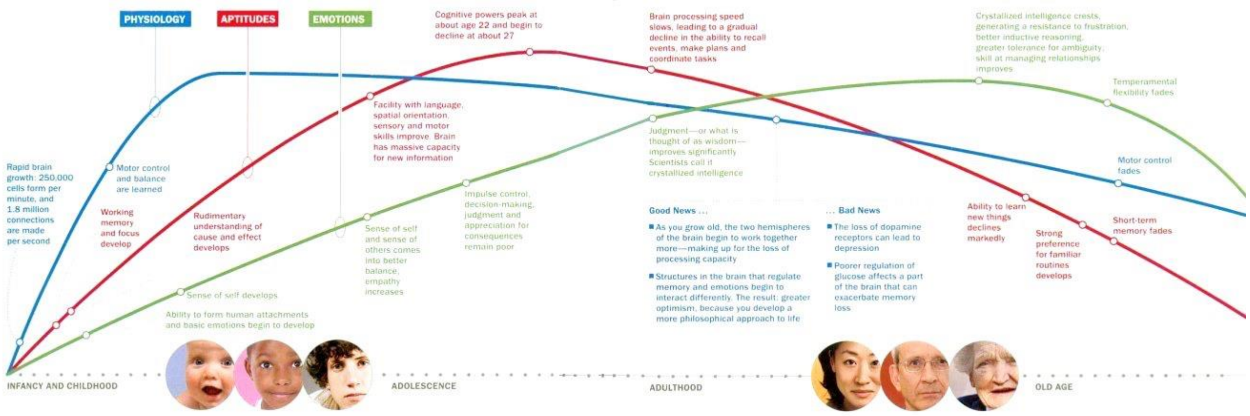
1. Are the GDF parameters efficient in tracking the differences between children and adults?

2. Can we extend our knowledge about more subtle microstructural development of specific fibres based on GDF?

Diffusion kurtosis metrics as biomarkers of microstructural development: A comparative study of a group of children and a group of adults

F. Grinberg et al., Neuroimage, 2017

Brain Development and Ageing – Lifelong Changes



Rapid brain growth: 250,000 cells form per minute, and 1.8 million connections are made per second

Motor control and balance are learned

Working memory and focus develop

Rudimentary understanding of cause and effect develops

Sense of self develops

Ability to form human attachments and basic emotions begin to develop

Cognitive powers peak at about age 22 and begin to decline at about 27

Facility with language, spatial orientation, sensory and motor skills improve. Brain has massive capacity for new information

Sense of self and sense of others comes into better balance, empathy increases

Impulse control, decision-making, judgment and appreciation for consequences remain poor

Brain processing speed slows, leading to a gradual decline in the ability to recall events, make plans and coordinate tasks

Judgment—or what is thought of as wisdom—improves significantly. Scientists call it crystallized intelligence

Good News …

- As you grow old, the two hemispheres of the brain begin to work together more—making up for the loss of processing capacity
- Structures in the brain that regulate memory and emotions begin to interact differently. The result: greater optimism, because you develop a more philosophical approach to life

… Bad News

- The loss of dopamine receptors can lead to depression
- Poorer regulation of glucose affects a part of the brain that can exacerbate memory loss

Crystallized intelligence crests, generating a resistance to frustration, better inductive reasoning, greater tolerance for ambiguity, skill at managing relationships improves

Temperamental flexibility fades

Motor control fades

Ability to learn new things declines markedly

Strong preference for familiar routines develops

Short-term memory fades

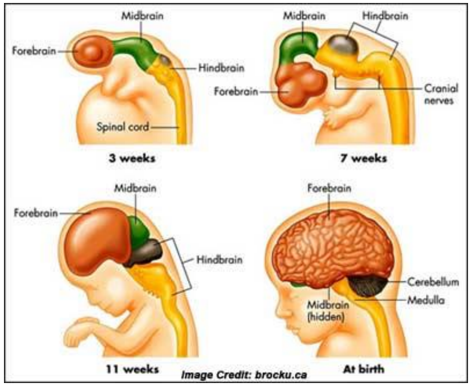
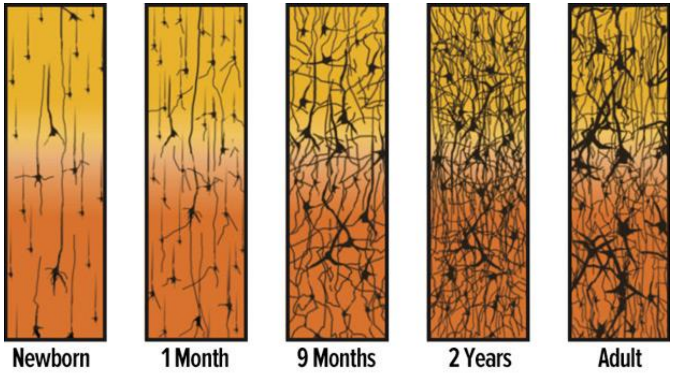
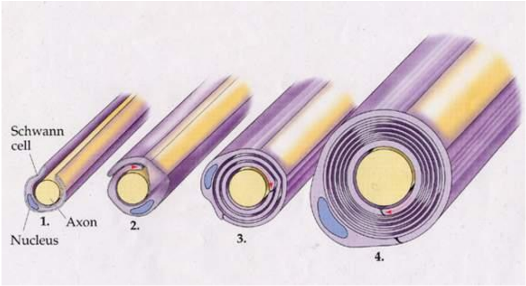


Image Credit: brocku.ca





Human brain undergoes life-long changes in many aspects: anatomic, physiological, mental, and also microstructural. Typical trajectories of the changes are often U-shaped or inverted-U-shaped.

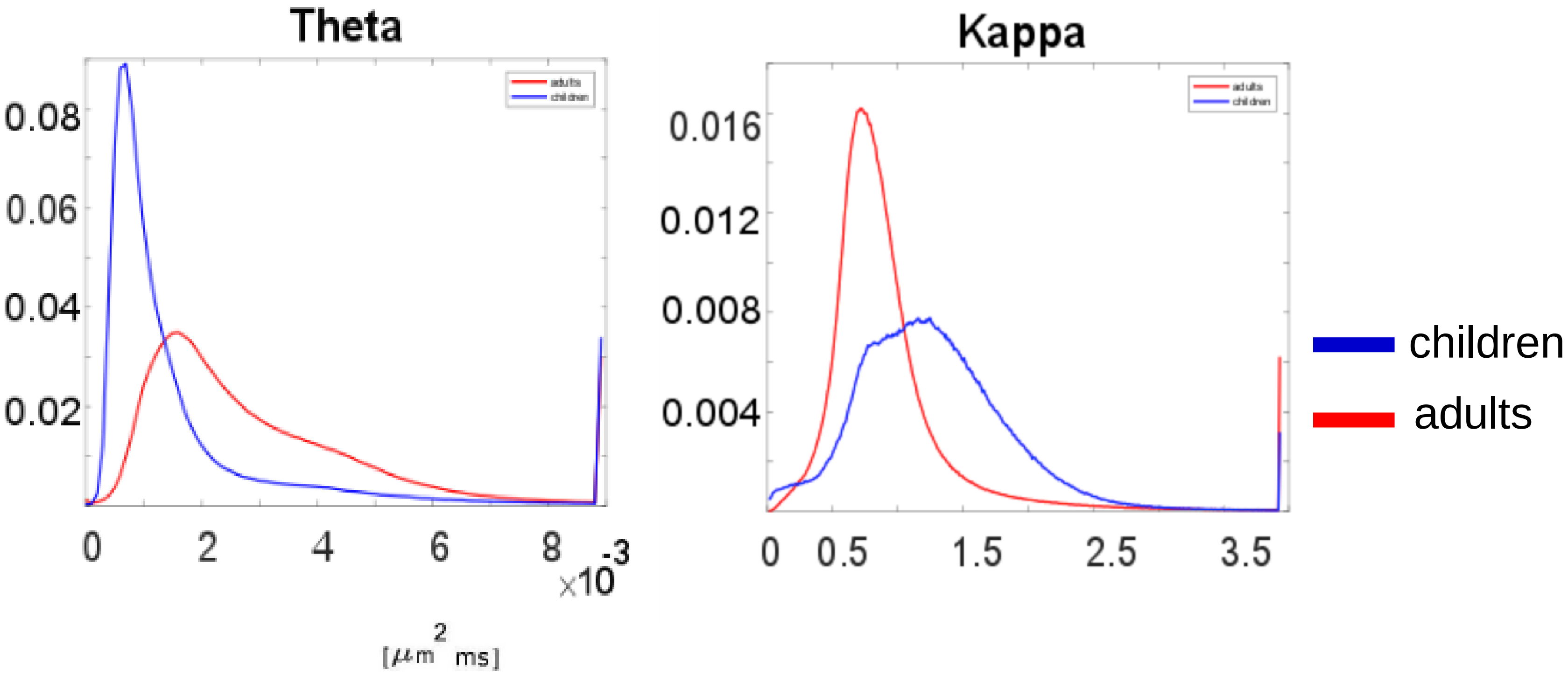
Two groups for comparison children and adults

Children
n=20
(9-12) years

Adults
n=21
(38-64) years

whole-body 3T Siemens MAGNETOM Tim-Trio scanner

Averaged histograms



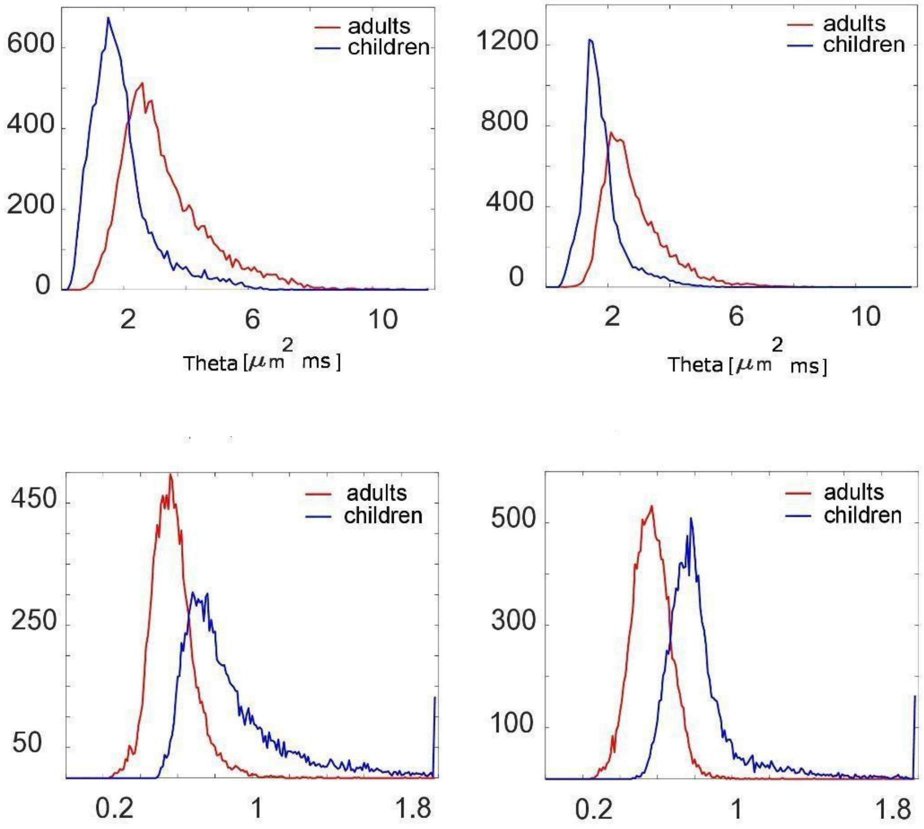
Whole brain averaged histograms show large shifts between the group of children and the group of adults

Regional analysis in white matter

Sagittal Stratum | Retrolenticular part internal capsule

Theta

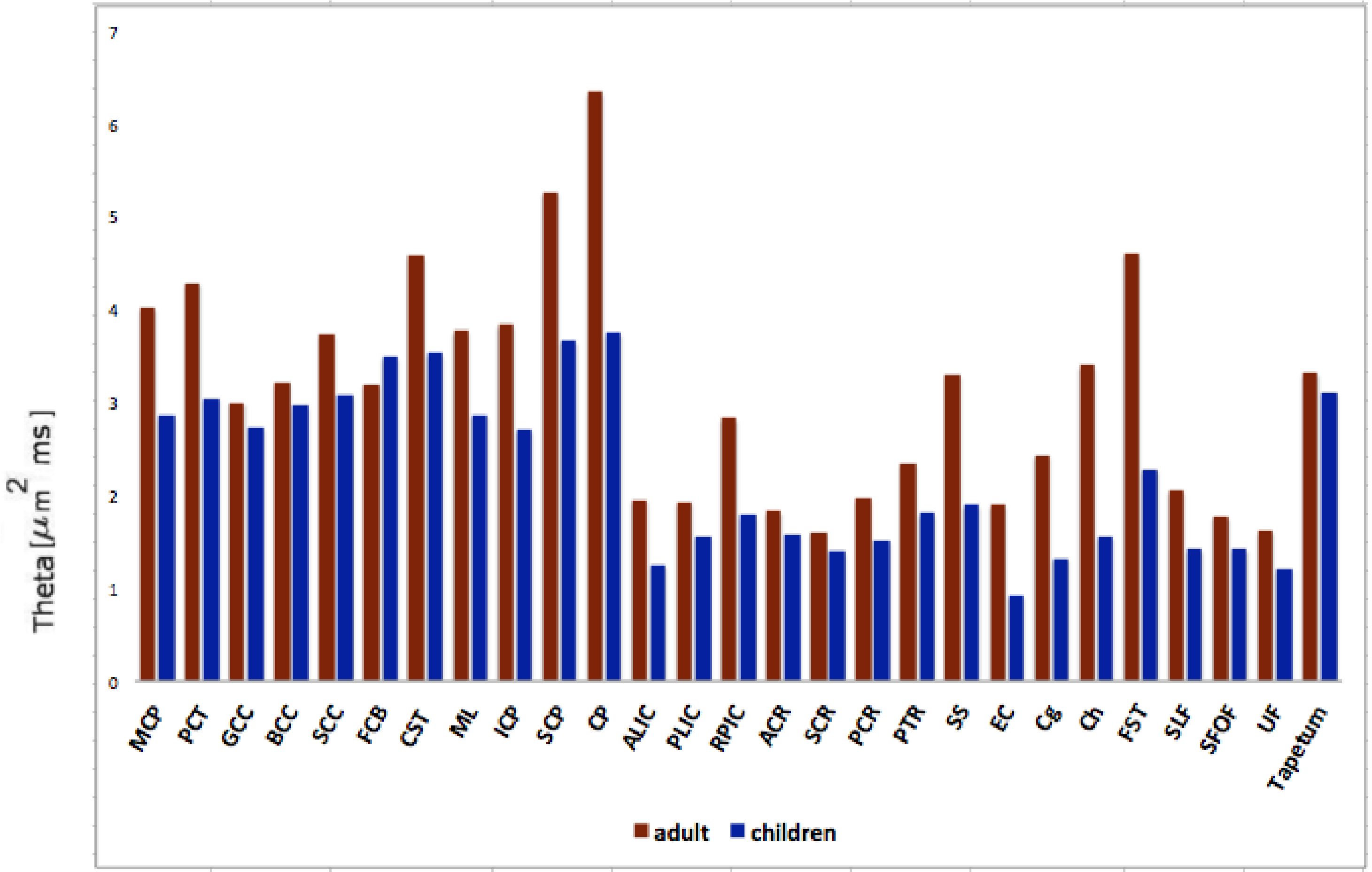
Kappa



Regional analysis shows large shifts for various fibers

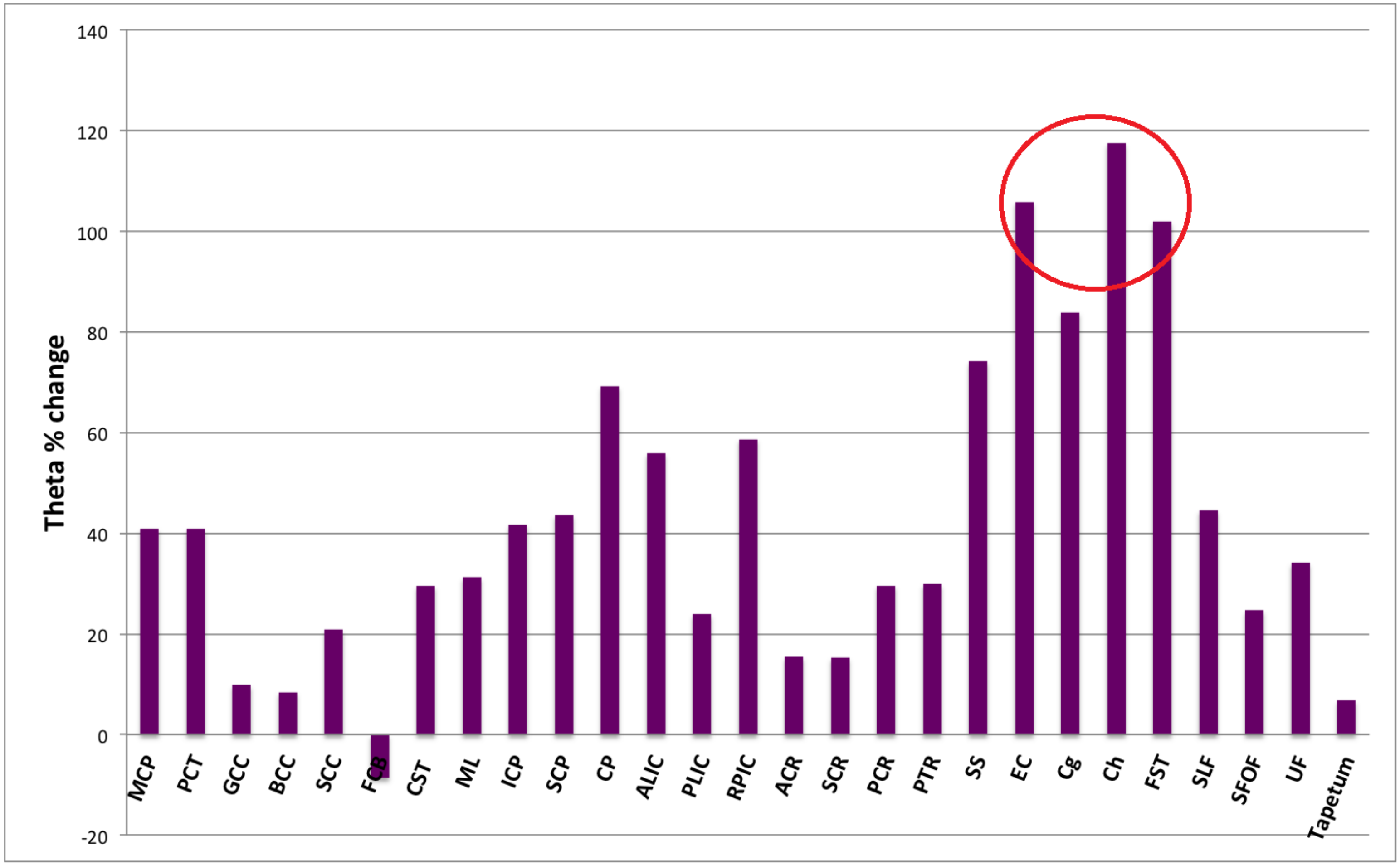
Regional Analysis

Differences between the mean values of theta in various region



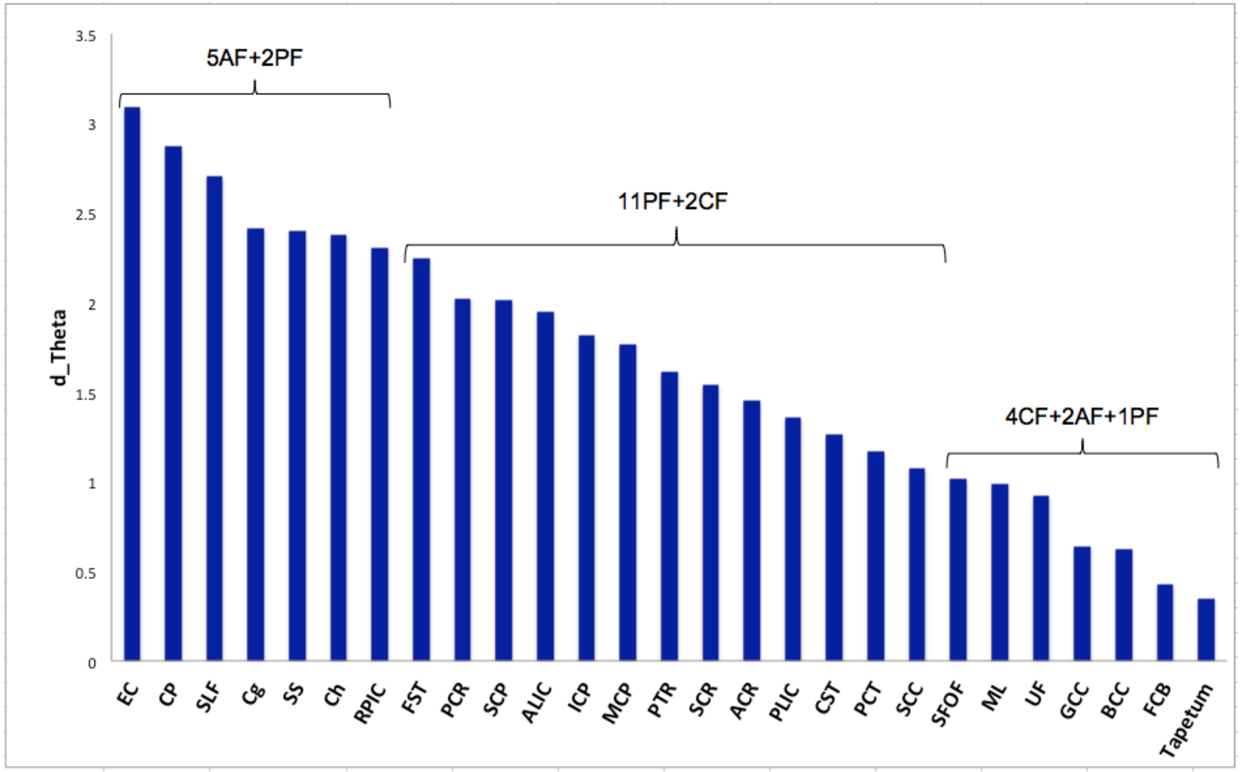
Theta values are larger in adults than children in all fibres

Group differences in percentage for Theta parameter



Fibre ranking based on Cohen’s d of Theta

Protracted maturation



1st quartile:
All 4 CFs+2 AFs+1 PFs

2 middle quartile
between:1st and 4th quartiles
All 1 PFs+2CFs

4th quartiles:
All 5 AFs+ 2 PFs

Cohen’s d (effect size):

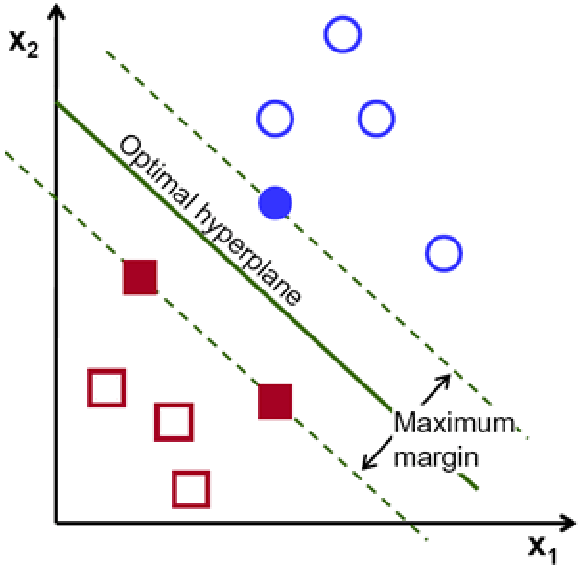
$$d = \frac{M_1 - M_2}{SD_{pooled}}$$

≈ 0.2 - ‘small’
≈ 0.5 - ‘medium’
≈ 0.8 - ‘large’
> 1.2 – ‘very large’

7 association fibres
14 Projection fibres
6 Commissural Fibres

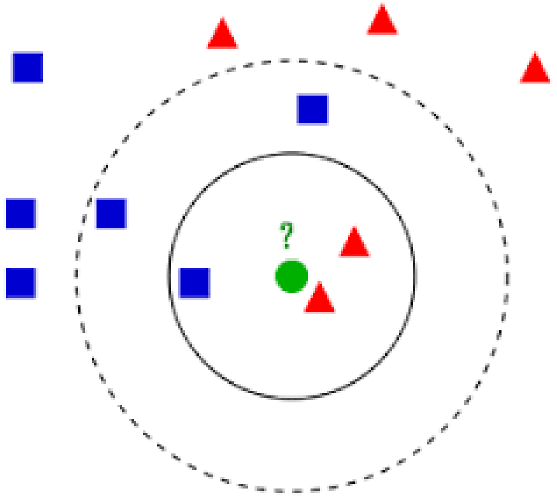
Classifiers: Support Vector Machine and k Nearest Neighbour algorithm

SVM



SVM algorithm is based on finding the hyper plane that gives the largest minimum distance to the training examples

kNN

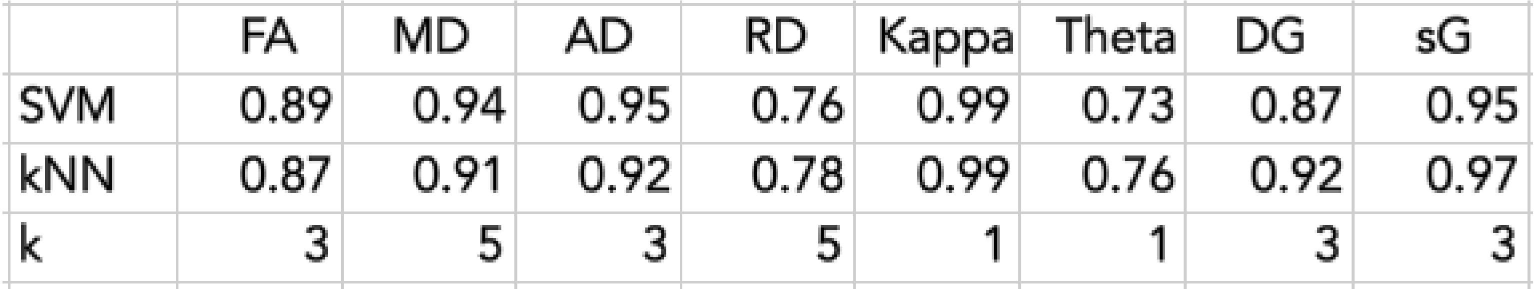


An object is classified by a majority vote of its neighbors, with the object being assigned to the class most common among its k nearest neighbors

Normalization of feature vector: $X'_i = \frac{X_i \quad X_{min}}{X_{max} \quad X_{min}}$

Classification based on DTI and GDF metrics of different regions

Accuracies of classification (Alpha=0.01)



	FA	MD	AD	RD	Kappa	Theta	DG	sG
SVM	0.89	0.94	0.95	0.76	0.99	0.73	0.87	0.95
kNN	0.87	0.91	0.92	0.78	0.99	0.76	0.92	0.97
k	3	5	3	5	1	1	3	3

DTI

GDF

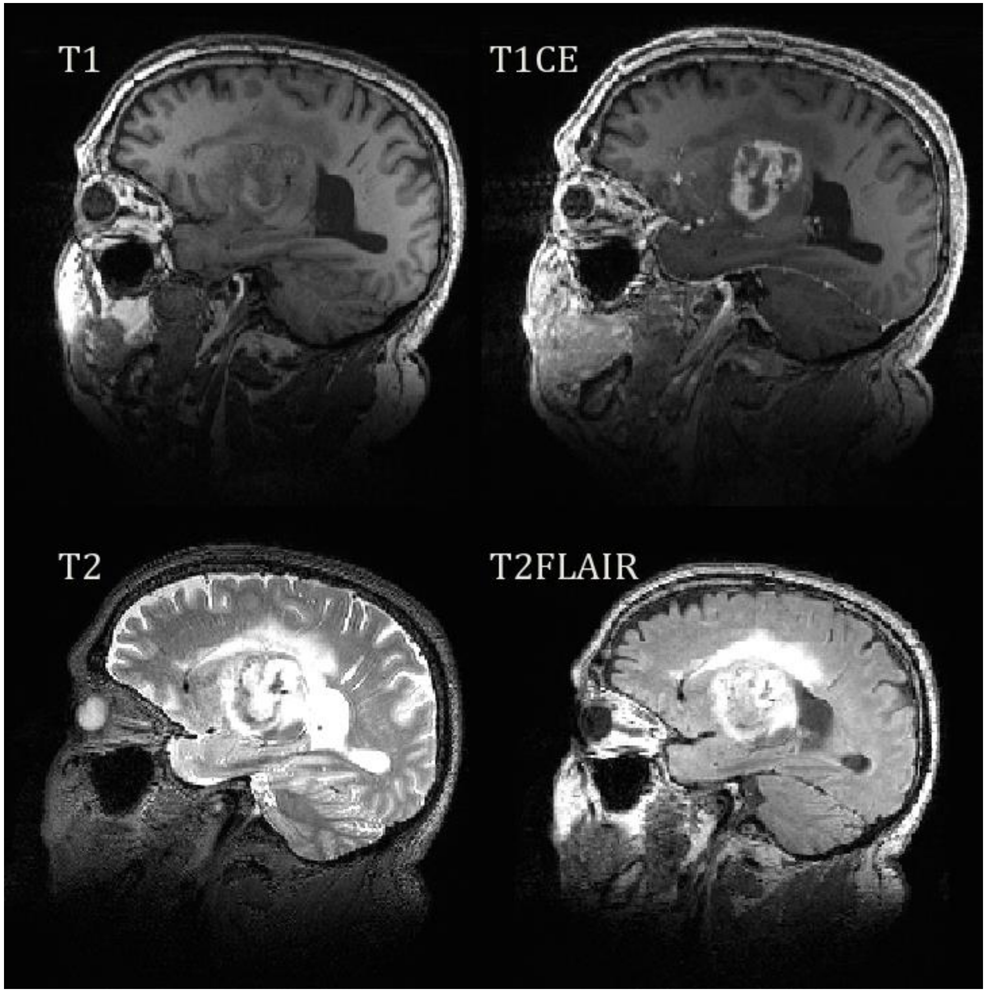
All metrics have shown high accuracies

Summary of first part

Gamma distribution function provides promising complementary metrics to a palette of maturation -sensitive MRI tools.

Tumour

24 untreated tumour patient
Whole body 3T Siemens MAGNETOM Tim-Trio scanner



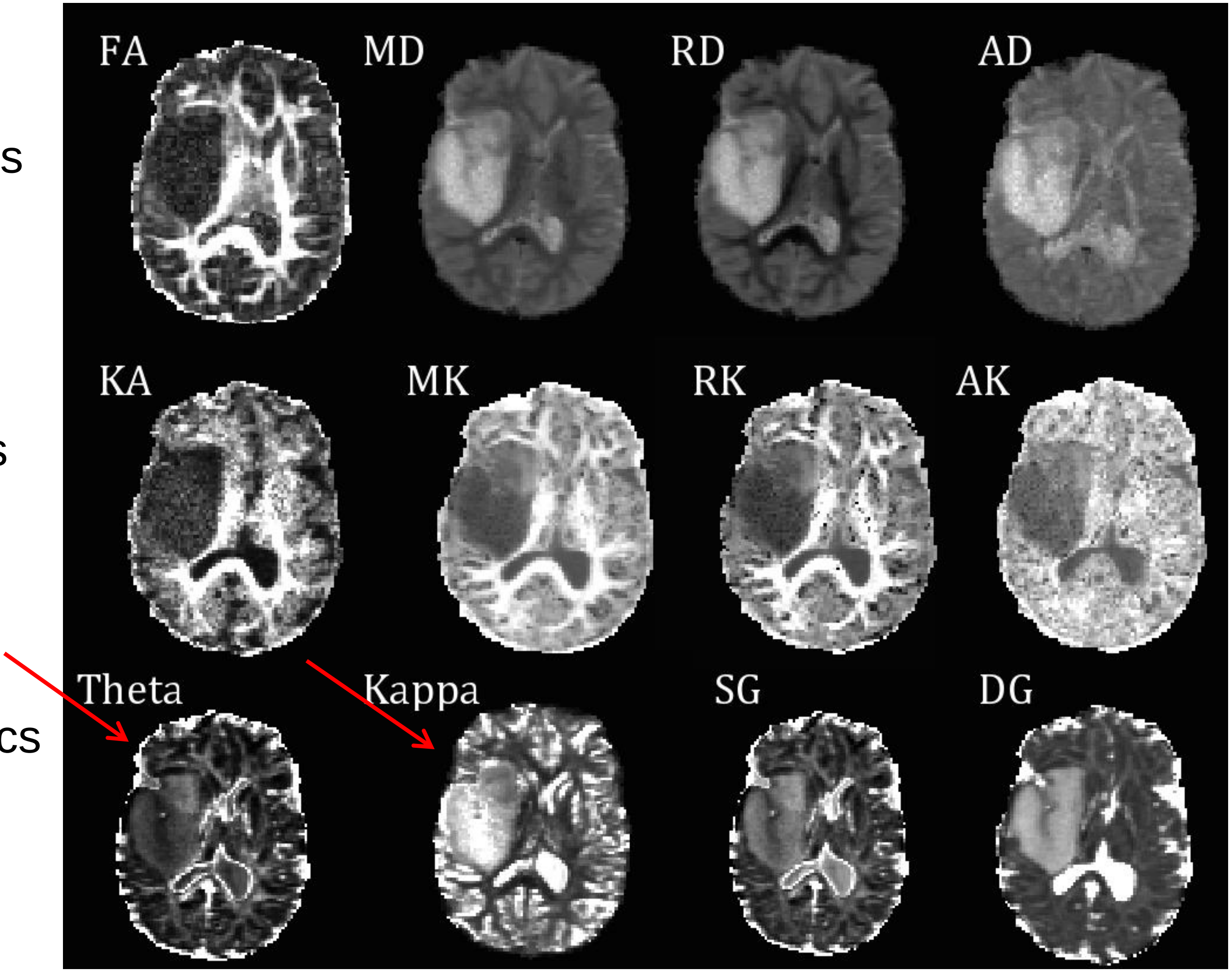
T1-weighted images

T1-weighted images with contrast enhanced

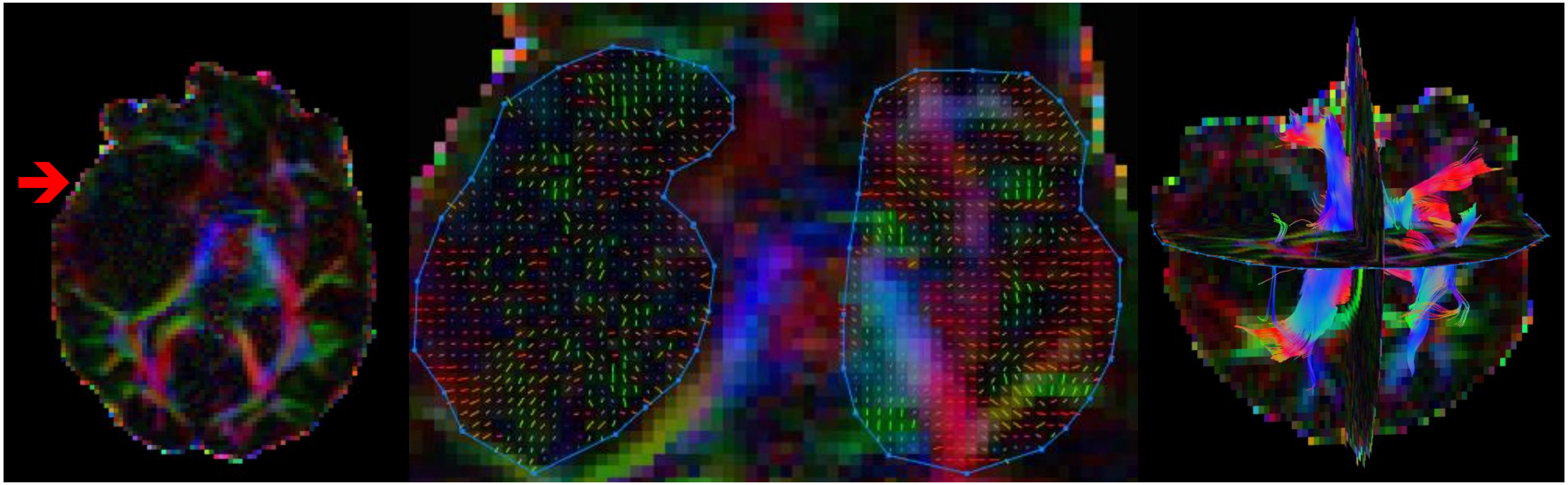
T2-weighted image

T2FLAIR (Fluid attenuated Inversion Recovery)

Diffusion parameters



Color-encoded FA and fiber tracking for a tumor human brain in axial plane



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Diffusion MRI gives a lot of complementary information to tumor assessment

This project is on going process and future work provide more results!

Conclusions

- Novel diffusion models provide information about tissue conditions, which is not attainable with conventional DMRI.
- The results show the efficiency of the gamma parameters, it can show the tumor heterogeneity
- All non-Gaussian models shown to provide valuable information regarding the tissue microstructure and conditions.

Acknowledgements

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Thank you
for
your attention !