

Characterization of Neurodegeneration Processes in Multiple Sclerosis using MRS and DTI

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Multiple Sclerosis

- **Clinical forms**

CIS : Clinically isolated syndrome

RR : Relapsing Remitting

SP : Secondary Progressive

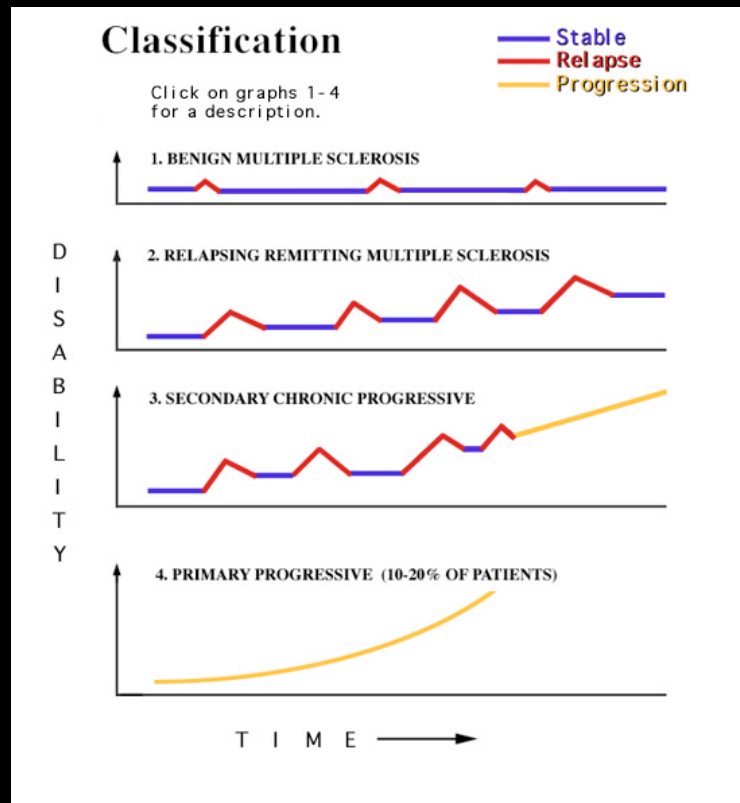
PP : Primary Progressive

- **Chronic disease**

- Inflammation
- Demyelination & remyelination
- Axonal damage
- Gliosis...

- **MRI evaluation**

- Lesion load
 - ➔ **inflammation**
- Poor correlation disability = “Clinical-MRI” paradox
 - ➔ **neurodegenerative**



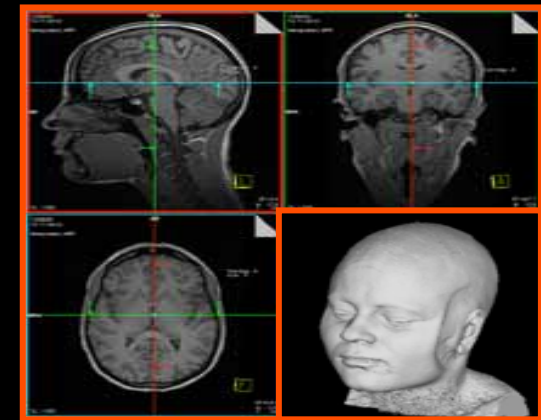
Objectives

- Characterization of inflammation and neurodegenerative processes with functional markers
 - Metabolism: NAA, Cho, Cr, Ins
 - Diffusivity: FA, ADC and λ_1 , λ_2 , λ_3
 - In different clinical forms
 - Relapsing Remitting (RR)
 - Secondary progressive (SP)
 - Primary progressive (PP)
- ➔ Predict patient evolution and adapt therapy

Multimodal & Longitudinal

100 patients (25 of each clinical form) examined every 6 months during 3 years

- **Population**
 - 30 patients : 10 RR, 10 SP, 10 PP
 - 10 controls
- **MRI protocol**
 - 3D-T1, T2, Flair
 - MR Spectroscopic Imaging
 - Diffusion Tensor Imaging
- **Sonata Siemens 1.5T**
 - Gradients 40 mT/m
 - 8 channel headcoil



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Functional changes in MS

Metabolic
markers

Interpretation

Diffusivity
markers

↑↑ **Cho**

Demyelination

↑↑ **ADC**

↑↑ **Ins**

Inflammation

↓↓ **FA**

↑↑ **Lac**

Gliososis

↑↑ λ_a

↓↓ **NAA**

Axonal integrity

↑↑ λ_r

Neurodegenerative



In acute lesions

In normal appearing white matter

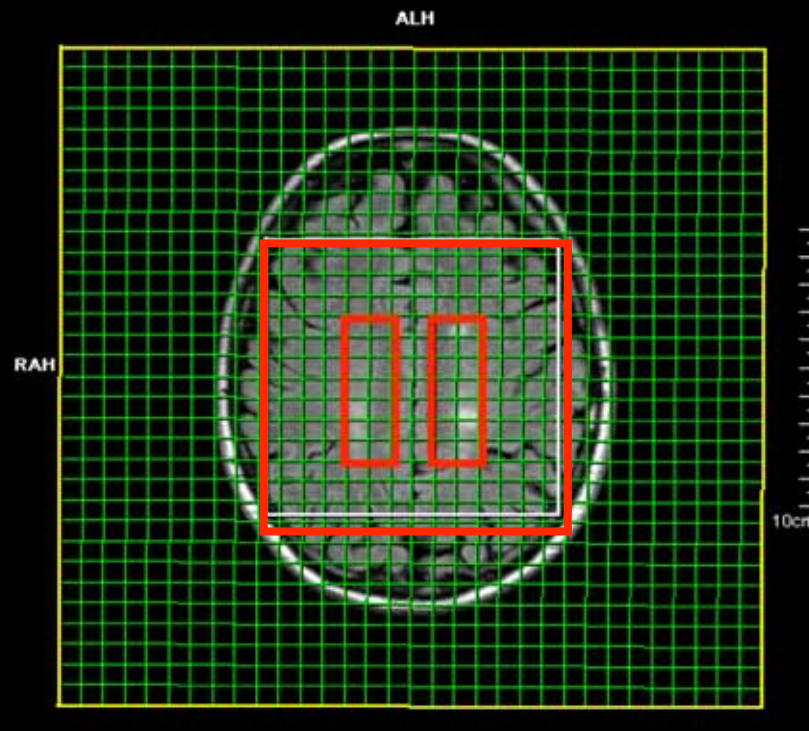
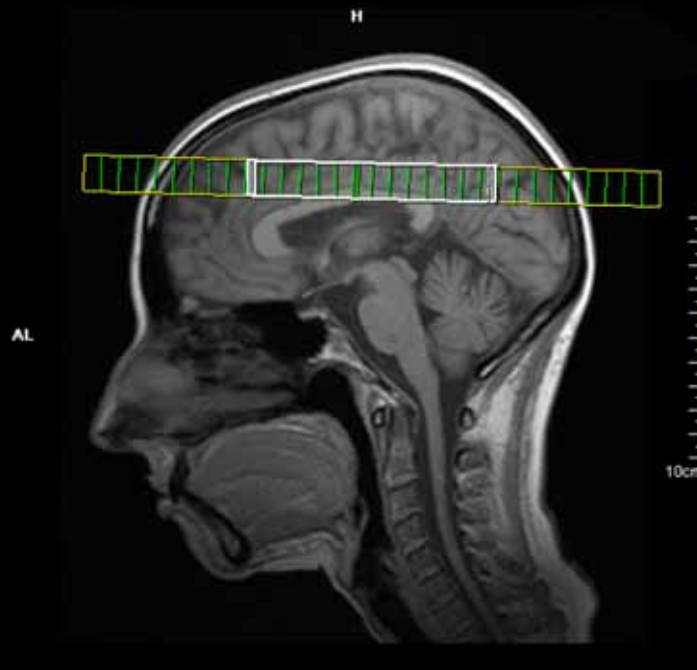
In normal appearing gray matter ...

cortical & subcortical

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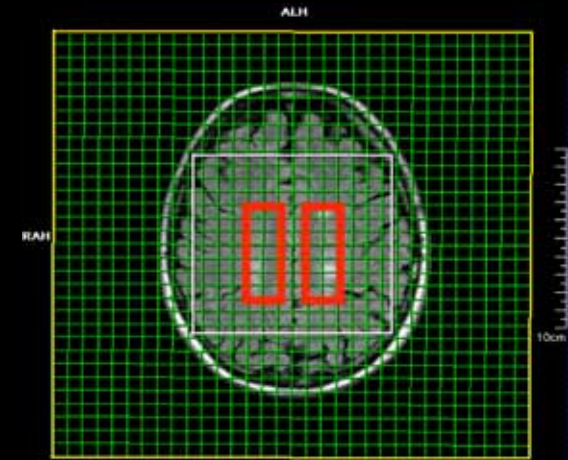
Spectroscopy protocol

- MR Spectroscopic Imaging
 - 2 slices with PRESS + 8 OVS
 - TR = 1570ms, TE = 135ms, VOI = 100x100x15mm³



MRSI processing

- Software: jMRUI
- Parameters
 - Water suppression by HSLVD
 - 1.4 Hz Lorentzian apodization

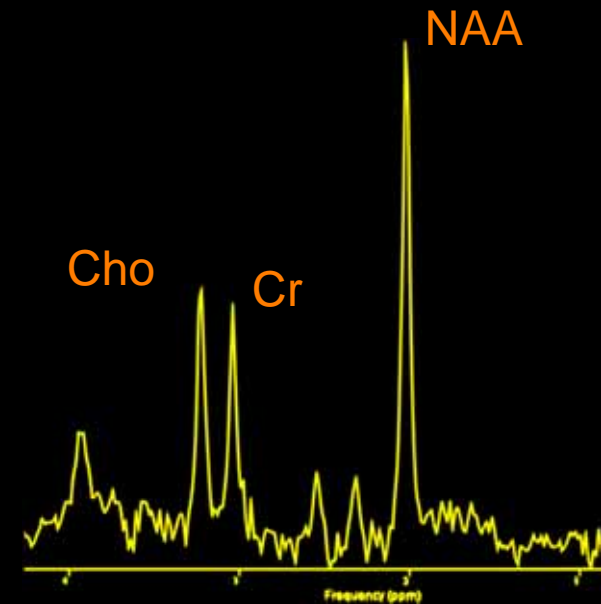


- Quantification by QUEST

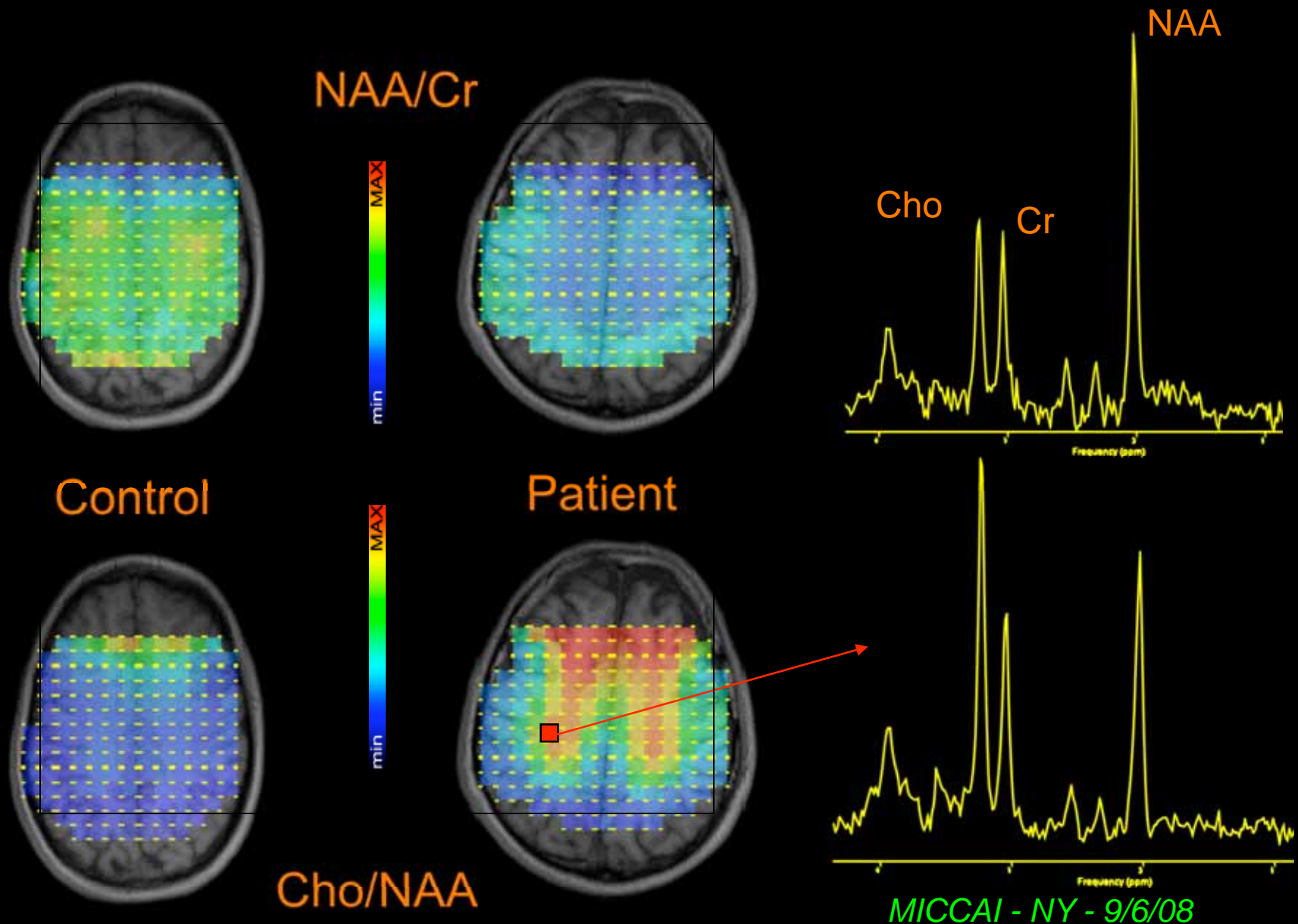
Semi-parametric time-domain algorithm with basis-set (NAA, Cho, Cr, Ins) from NMRScope quantum mechanic simulator

- Baseline estimation

by subtraction method (15 pts)



Metabolic Results



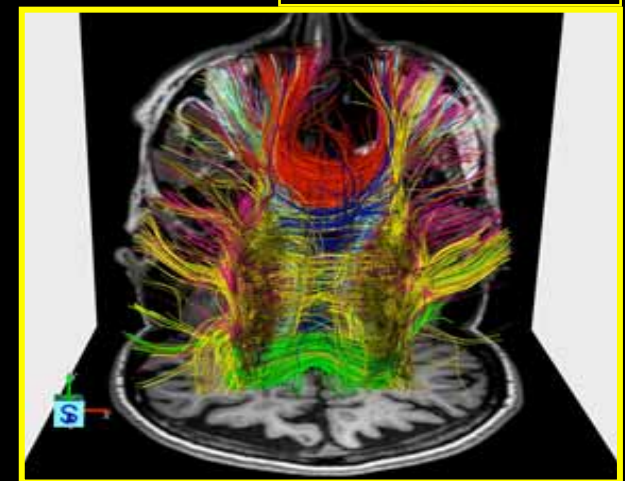
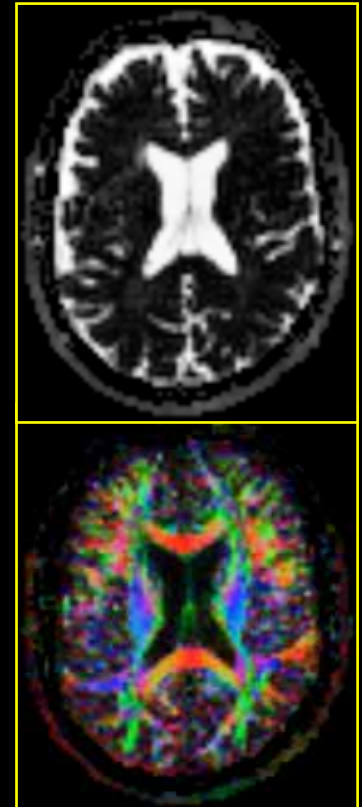
DTI protocol

- Acquisition

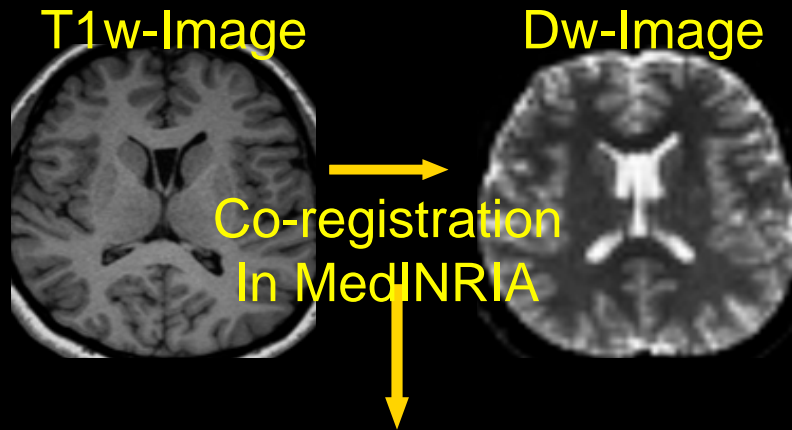
- EPI sequence 128 x 128
- 51 axial slices in AC-PC
- Isotropic resolution of 2.5 x 2.5 x 2.5 mm³
- 24 directions with b=1000 s/mm²

- Processing: MedINRIA

- Images of ADC & FA
- Fiber tracking on all brain and ROIs



DTI pre-processings

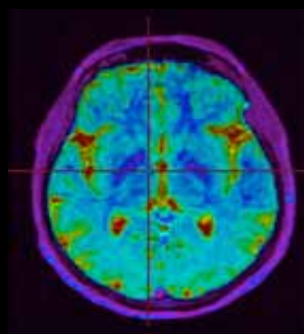


Affine Transformation *Translation Vector*

$$A = \begin{bmatrix} A_{11} & A_{21} & A_{31} \\ A_{12} & A_{22} & A_{32} \\ A_{13} & A_{23} & A_{33} \end{bmatrix} \quad T = \begin{bmatrix} t_1 \\ t_2 \\ t_3 \end{bmatrix}$$

Matrix :

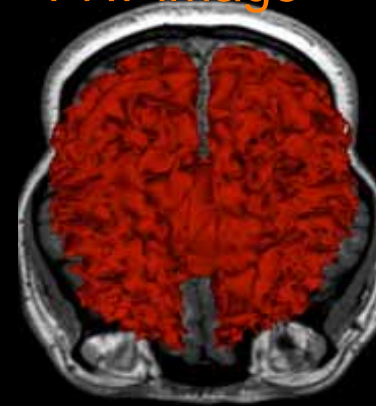
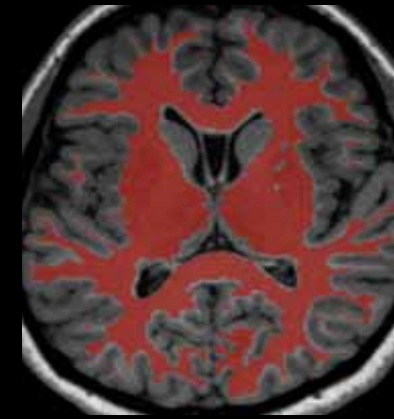
$$[A_{11} \ A_{12} \ A_{13} \ A_{21} \ A_{22} \ A_{23} \ A_{31} \ A_{32} \ A_{33} \ t_1 \ t_2 \ t_3]$$



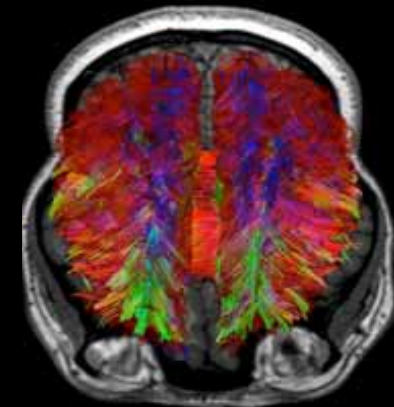
Fusion of T1w- and Dw- images co-registered

Global WM analysis

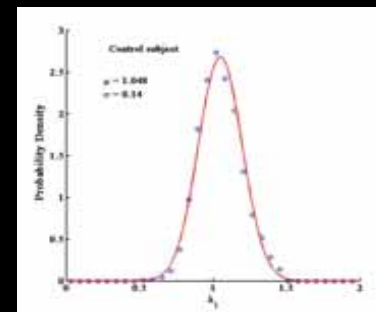
Segmentation with FAST-FSL of WM tissue on T1w-image



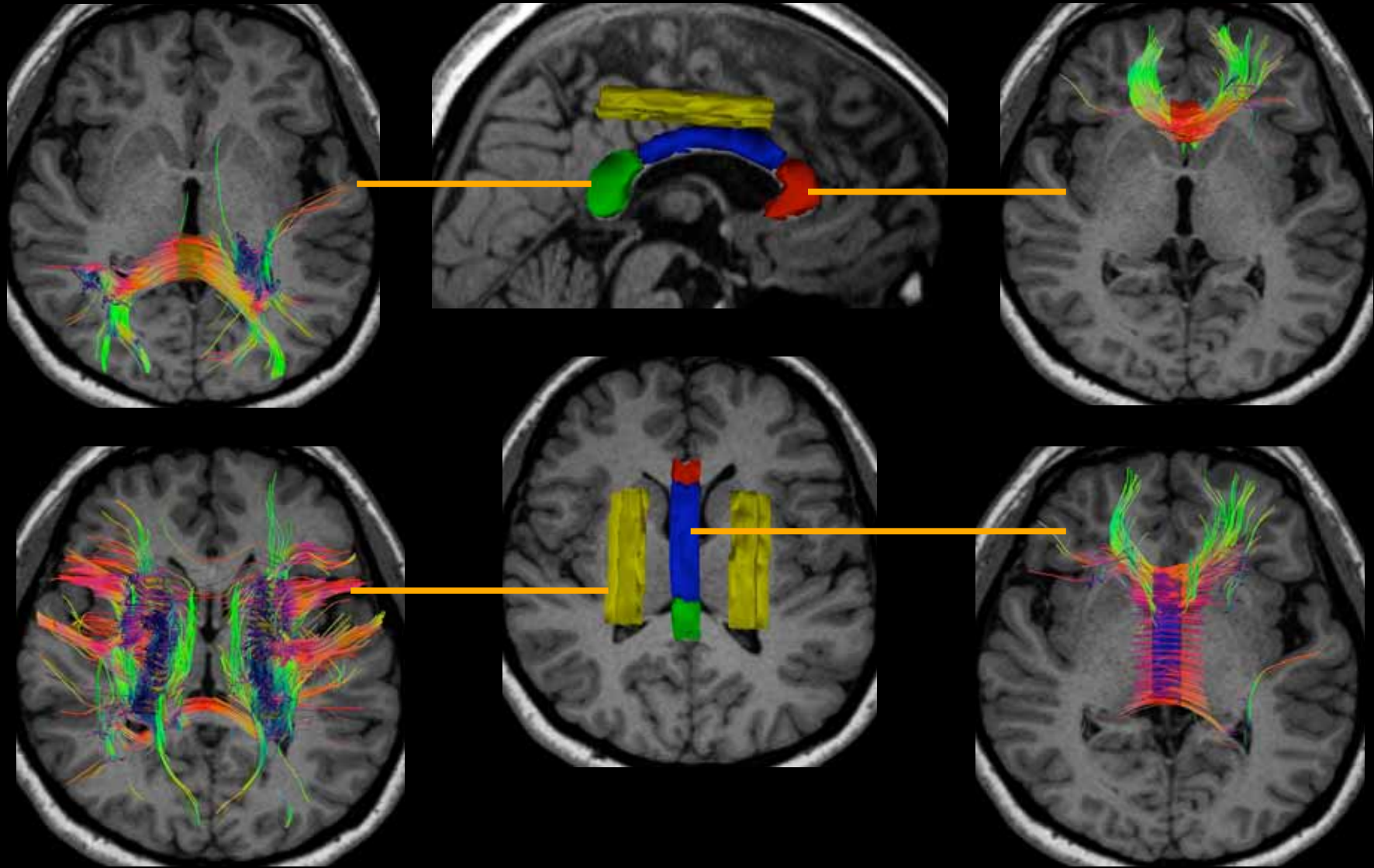
Import of ROI in MedINRIA



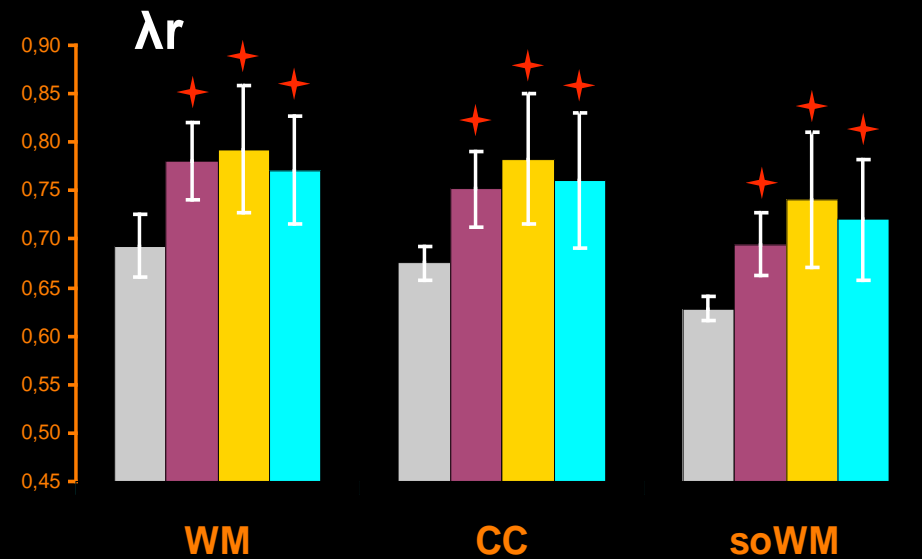
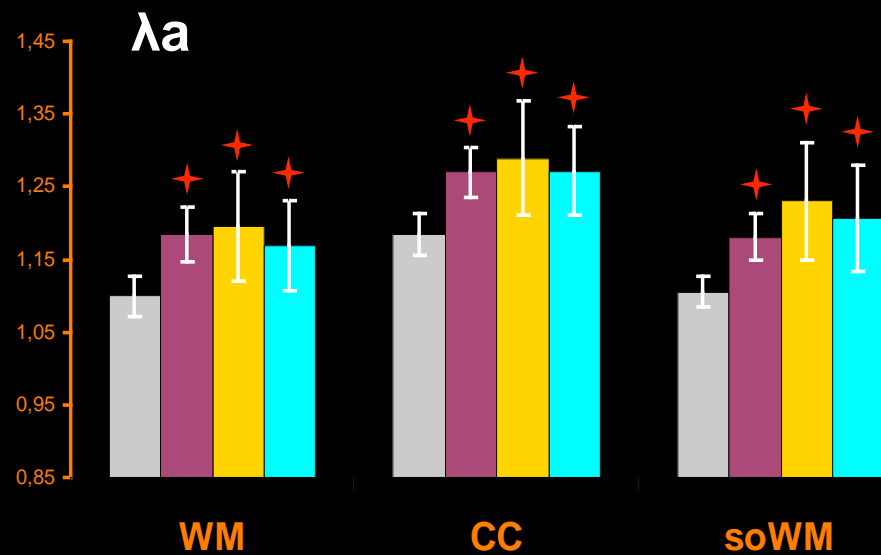
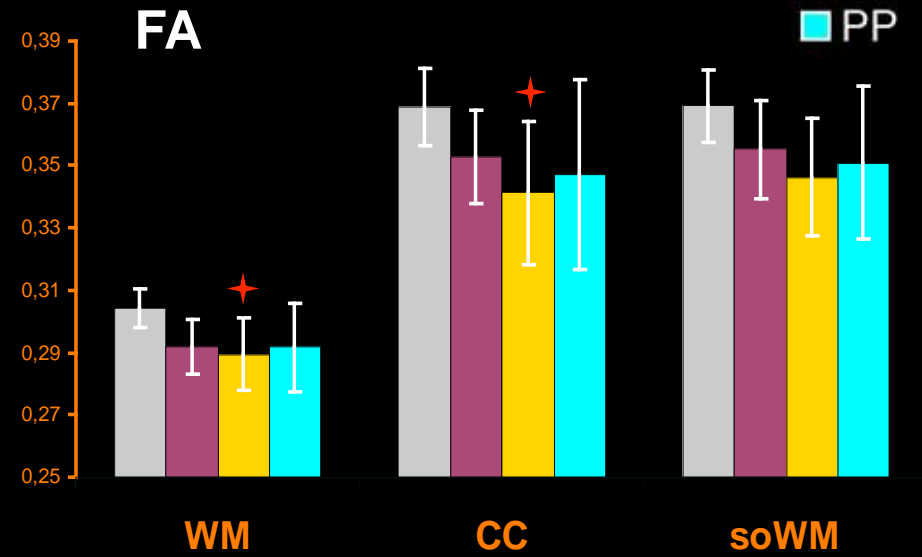
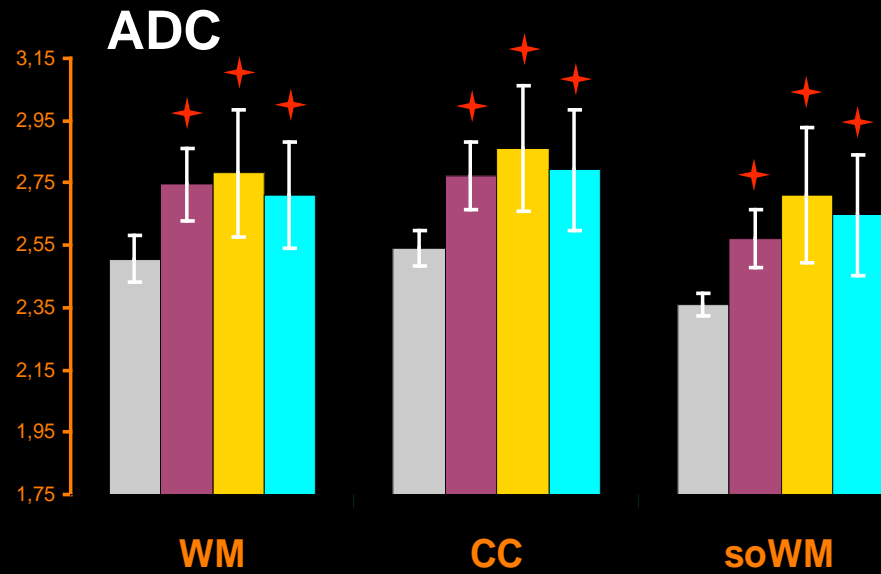
Fit of FA, ADC, & λ histogram values in Matlab



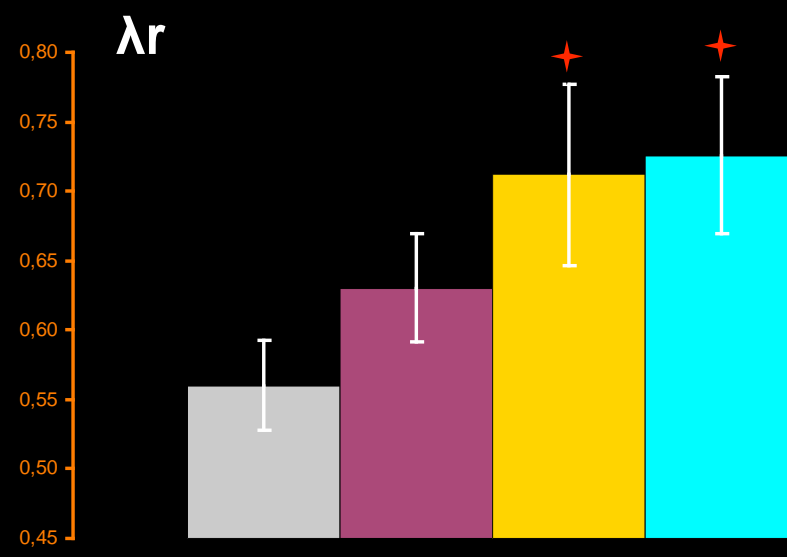
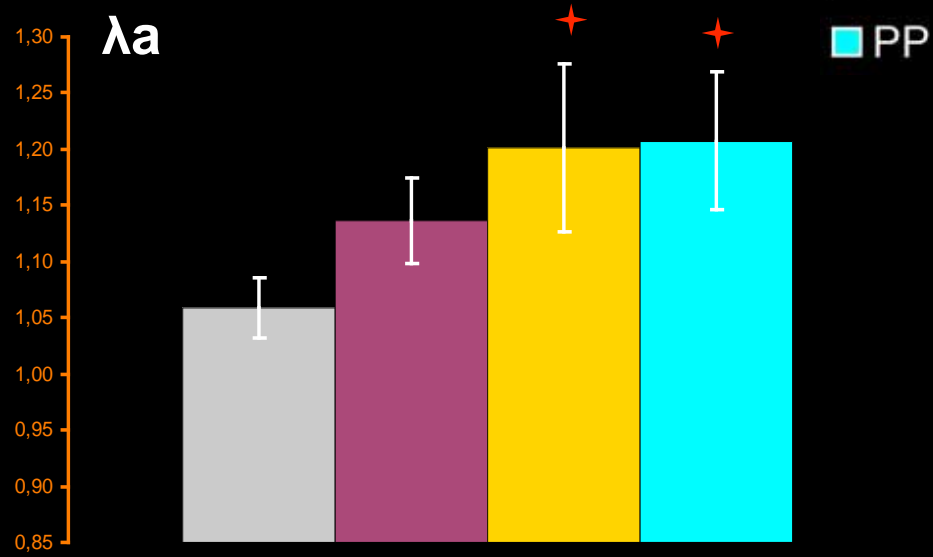
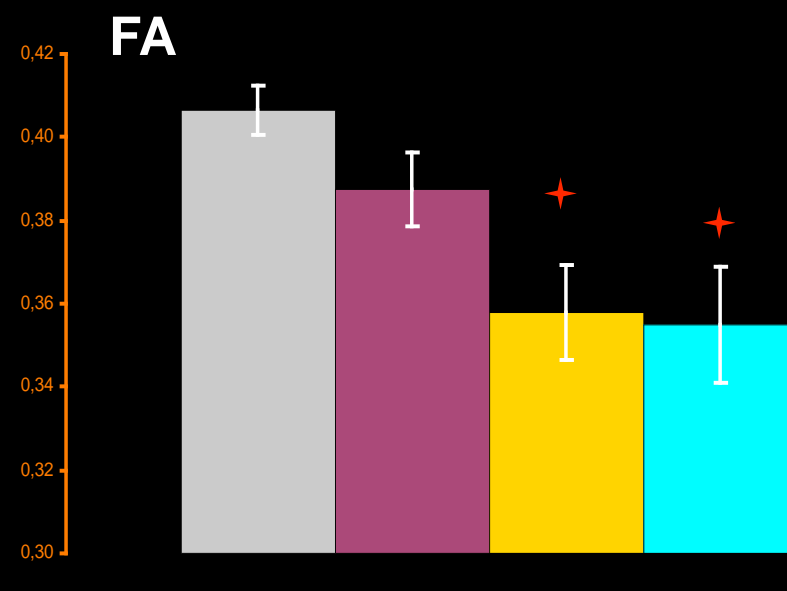
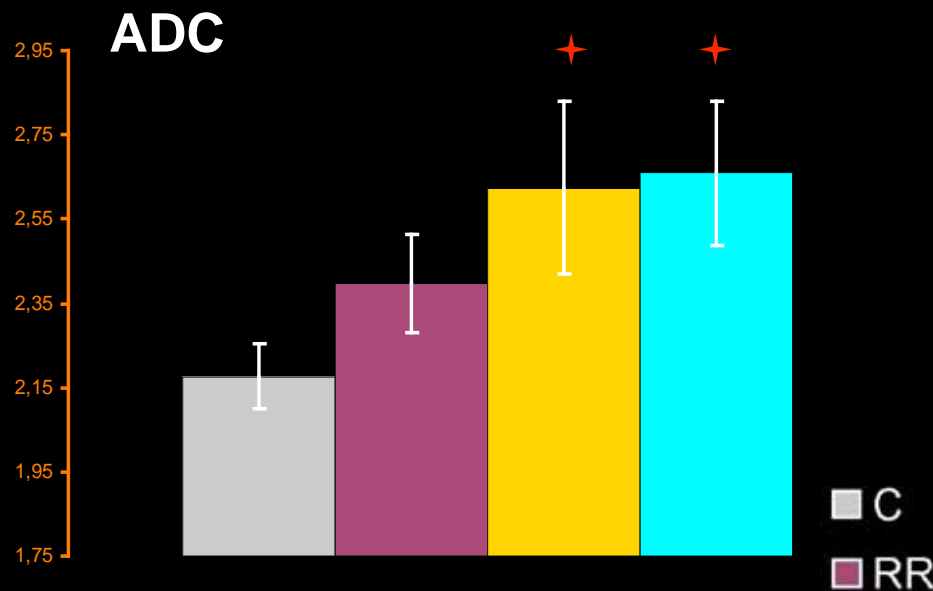
Manual selection of Corpus Callosum & SoWM ROIs



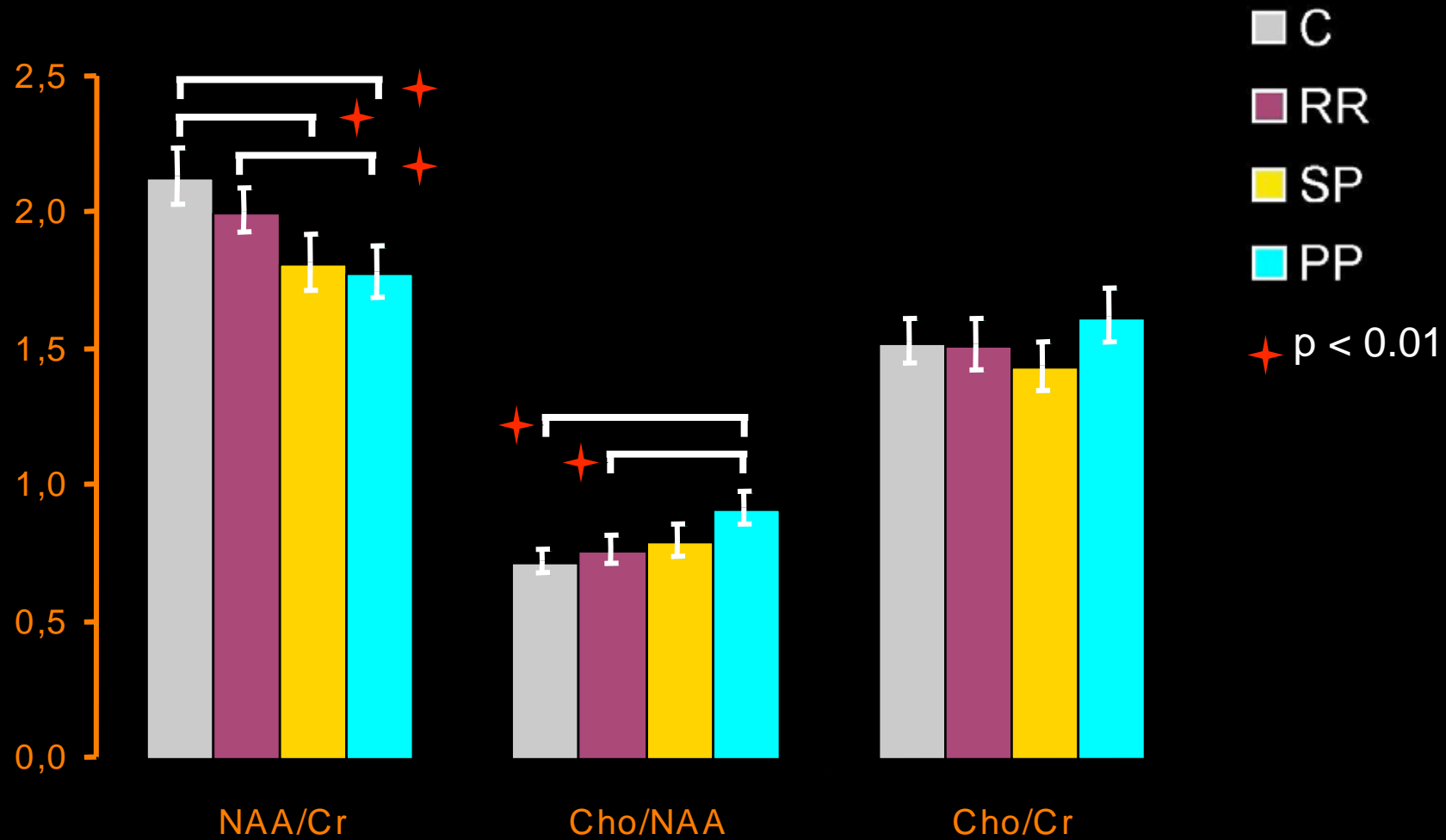
Diffusivity Results in Fibers



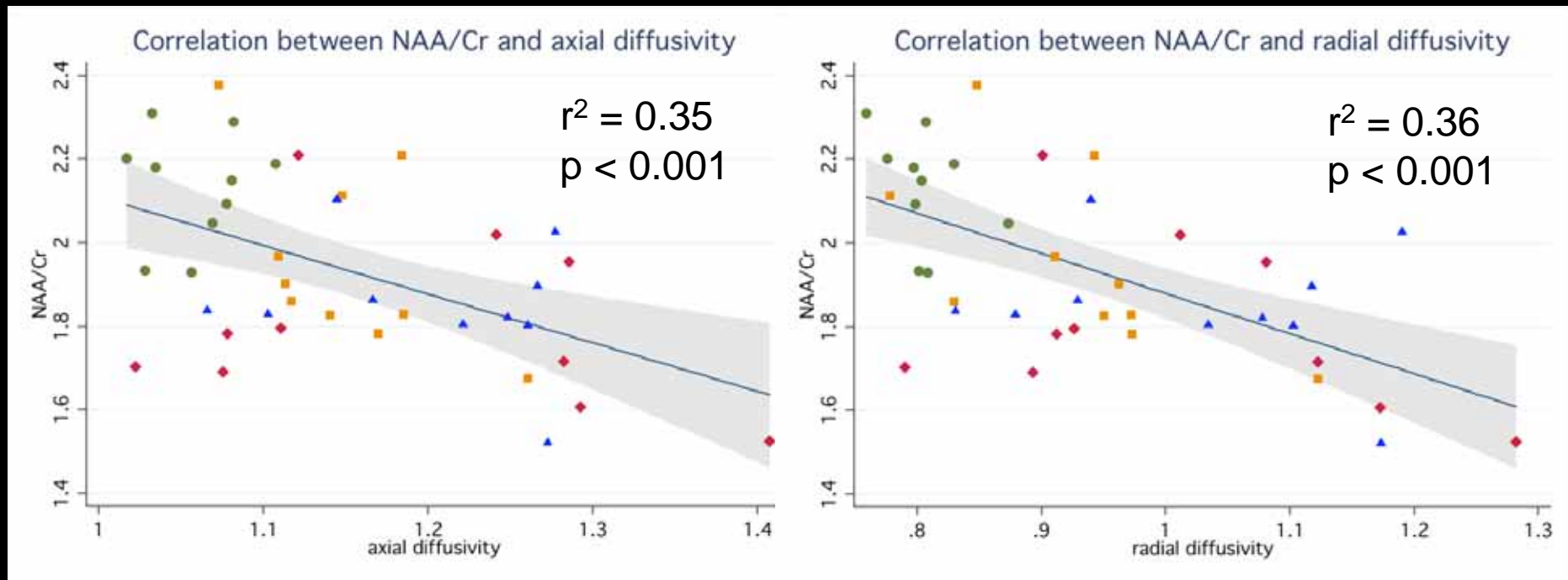
Diffusivity Results in SoWM ROI



Metabolic Results

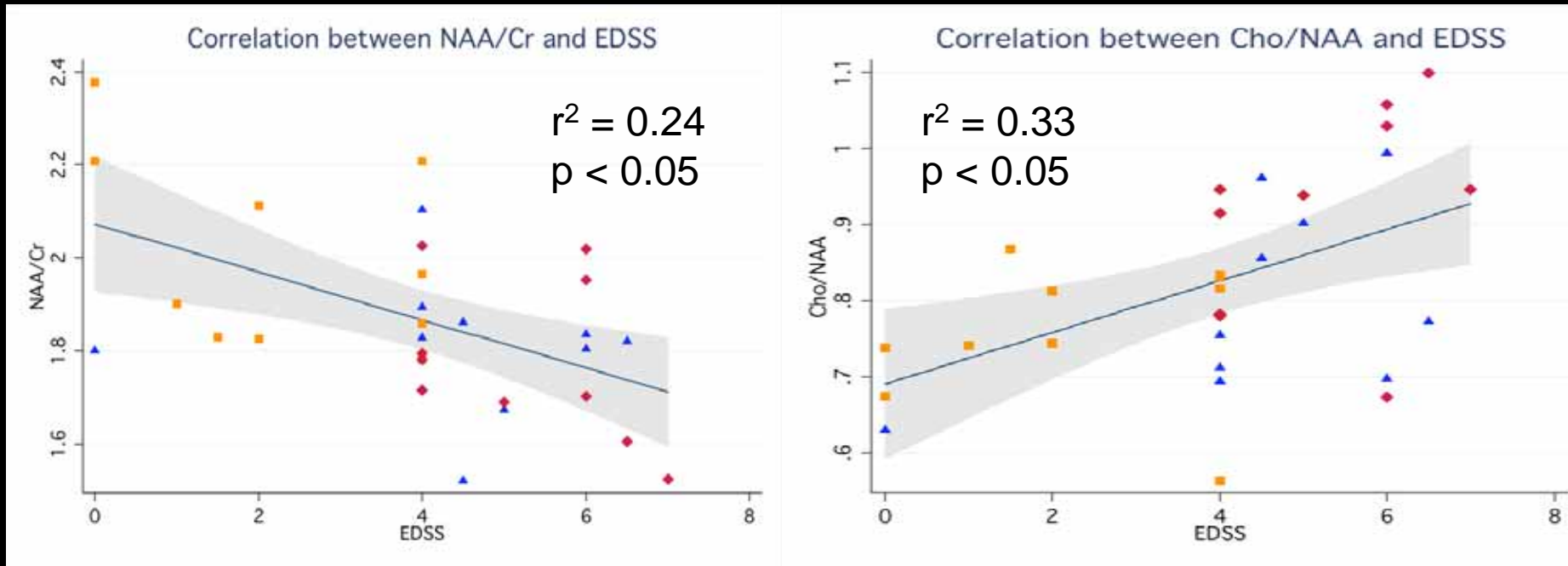


Correlation between metabolism and diffusivity



- Controls
- RR
- ▲ SP
- ◆ PP

Correlation between metabolism and clinical handicap



- Controls
- RR
- ▲ SP
- ◆ PP

Discussion

- **Correlation** between metabolic and diffusivity markers reflecting both inflammatory and neurodegenerative processes
- **MRSI confirm** \uparrow **Cho** and \downarrow **NAA** in **SP** and **PP**
 - Significant correlation between metabolism and disability
 - Significant increase of Cho/NAA ration in PP form being more specific marker of severe inflammation process
- **DTI shows** \uparrow **ADC**, \downarrow **FA**, \uparrow λ_a & \uparrow λ_r in **RR**, **SP** & **PP**
 - At different extents between clinical forms
 - No correlation with disability
 - Larger increase in λ_r than λ_a that may reflect greater changes in membrane porosity than in axonal integrity

Conclusion

- MRSI & DTI provide markers :

- Sensitive to inflammatory and neurodegenerative processes
- Correlate or not with disability

➔ Investigation of clinical status (EDSS & MSFC) and its correlation with functional markers

- Analyze in each patient

- Longitudinal changes
- Correlation between functional markers and disability

➔ Measure the evolution rate in each patient
Predict its clinical form for a better therapeutic approach

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