



Traumatisme crânien grave

Apport des techniques avancées

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Le traumatisme crânien grave (TBI)

- = TC nécessitant une hospitalisation
- \pm 50 000 hospitalisations, 10 000 décès par an
- Principale cause de DC et handicap chez l'homme jeune
- Coût global se chiffrant en milliards d'€
- Pronostic imprévisible à la phase aiguë
- Aucun traitement efficace (autre que symptomatique) n'est actuellement disponible

Evolution favorable ou défavorable ?

- Aucun consensus sur le sujet
- Evalué par le **Glasgow Outcome Scale**
 - 1: Mort
 - 2: Etat Végétatif persistant
 - 3-: Etat Pauci Relationnel / Etat de Conscience minimale
 - 3+: Séquelles sévère (motrices/langage)
 - 4: Handicap modéré
 - 5: Bonne récupération

Evolution favorable ou défavorable ?

- Aucun consensus sur le sujet
 - Evalué par le Glasgow Outcome Scale
 - 1: Mort
 - 2: Etat Végétatif Persistant
 - 3-: Etat de conscience minimale
 - 3+: Severe Motor Disability
 - 4: Moderate Disability
 - 5: Good Recovery
- Evolution
Défavorable

Evolution favorable ou défavorable ?

- Aucun consensus sur le sujet
 - Evalué par le **Glasgow Outcome Scale**
 - 1: Death
 - 2: Persistent Vegetative State
 - 3-: Minimally Conscious State
 - 3+: Séquelles sévères (motrice/langage)
 - 4: Handicap modéré
 - 5: Evolution favorable
- Evolution Favorable

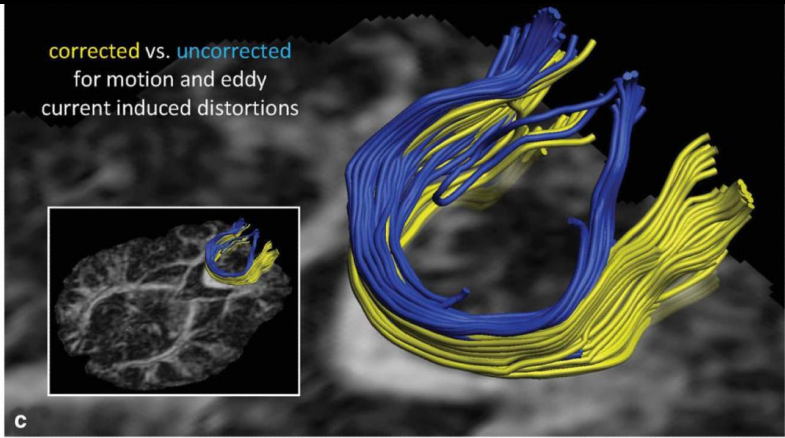
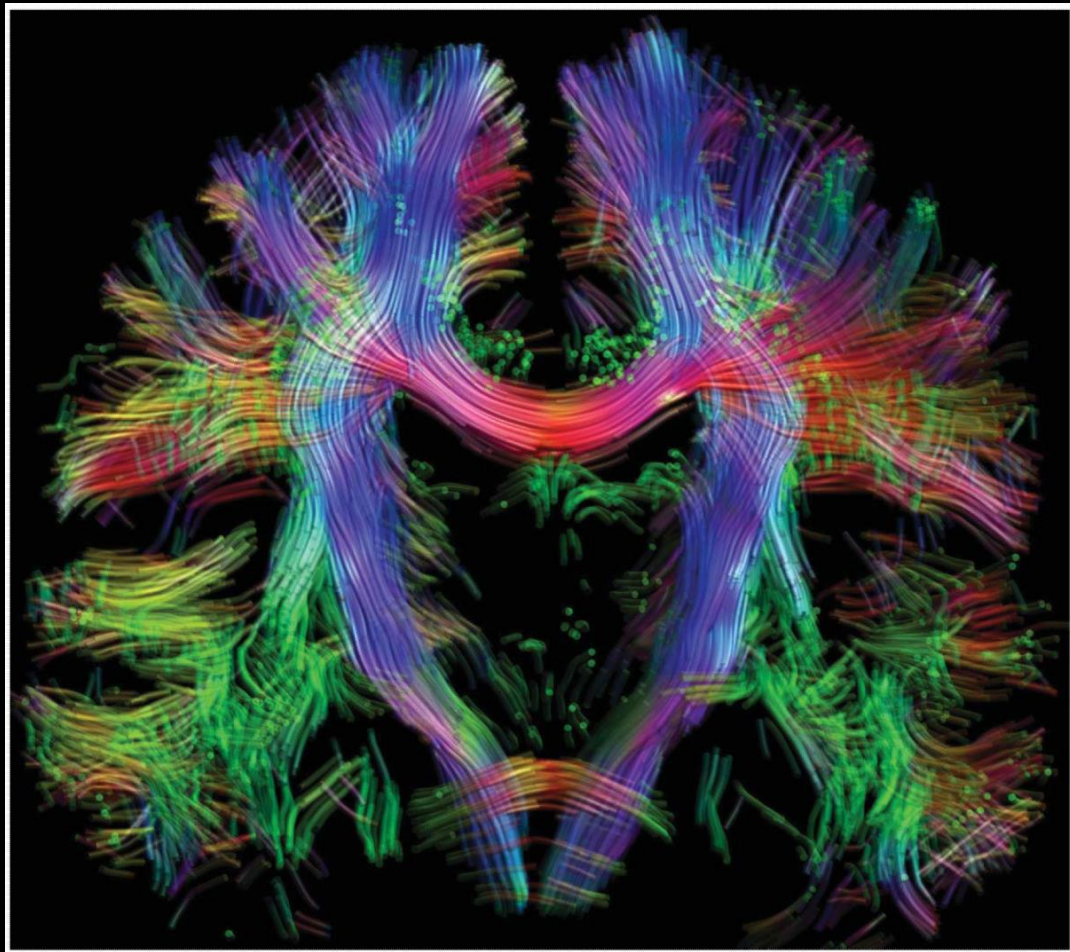
Etude "IRM et comas"

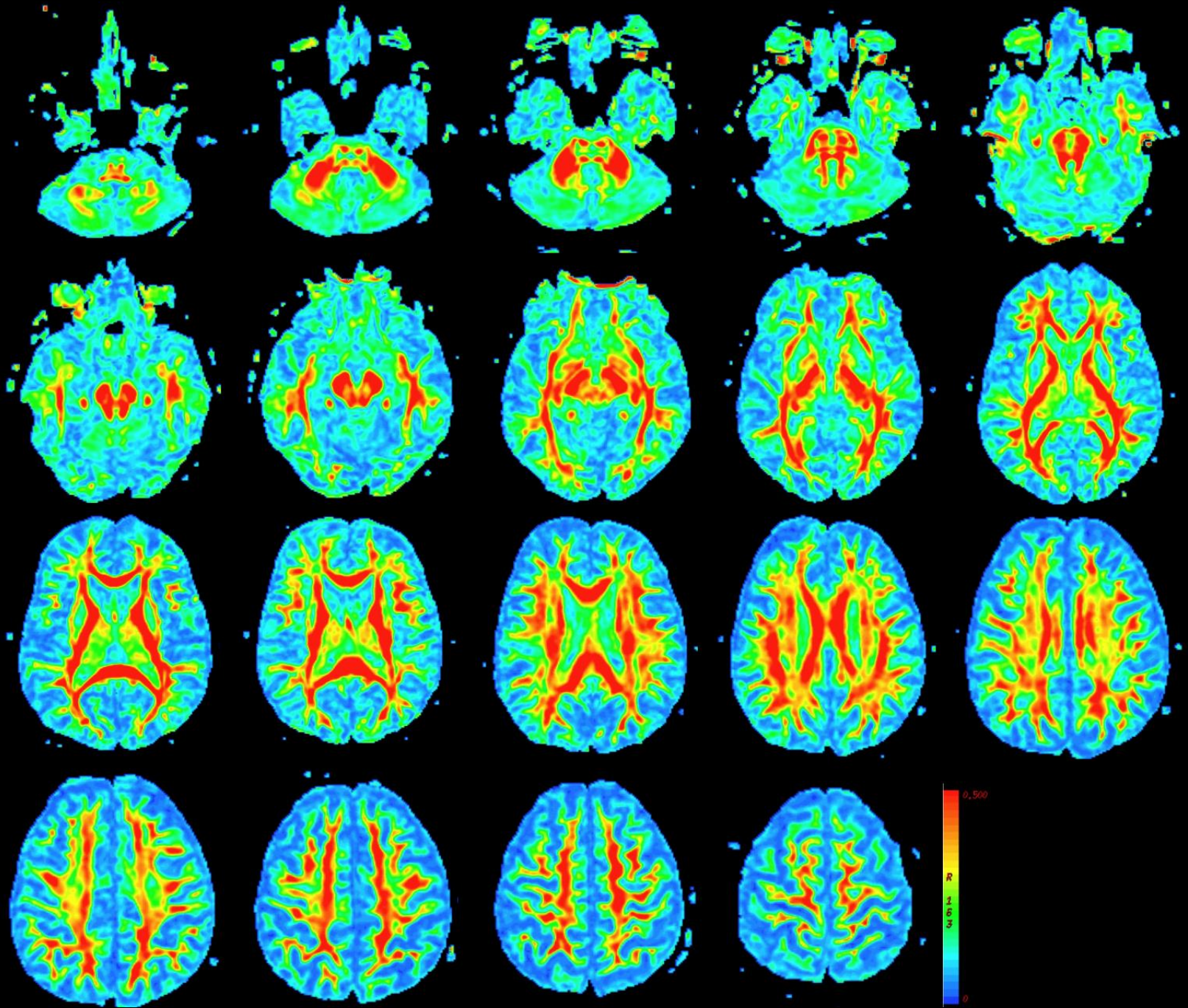
- **Objectif:** Créer une base de données d'IRM de patients comateux en utilisant un protocole standardisé
- Début en 2005, PHRC national
- **Etiologies:** TBI, arrêts cardiaques, Hgies méningées et contrôles
- Protocole adapté aux possibilités de chaque IRM mais doit comporter au minimum un tenseur de diffusion et de la spectroscopie sur les noyaux gris et le tronc cérébral
- Se poursuit sur le mode d'une base ouverte
- "open access" model
- > 400 patients et 100 contrôles inclus en 2013



DTI & coma Team

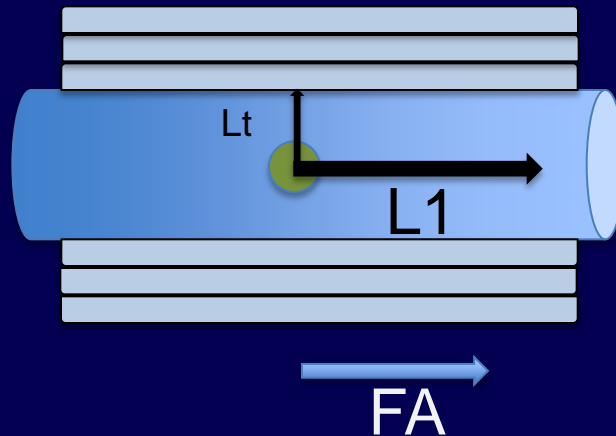
- **Paris Salpêtrière**: D Galanaud (neuroradiology), L Puybasset (neuro ICU), V Perlberg (CS lab), L Naccache (Physiology)
- **MGH**: R Gupta, O Khalilzadeh, J Dinkel (Radiology), J Giacino (rééducation)
- **Liège**: S. Laureys, A Vanhaudenhuyse (Cyclotron Research U)
- **JHU**: R Stevens (Neuro ICU), S Mori (Radiology)

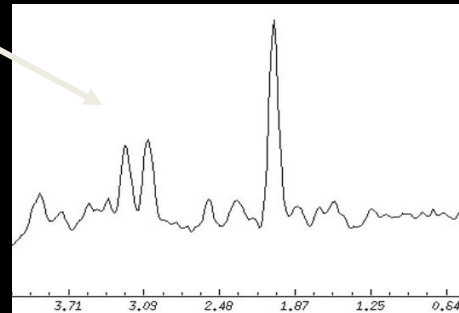
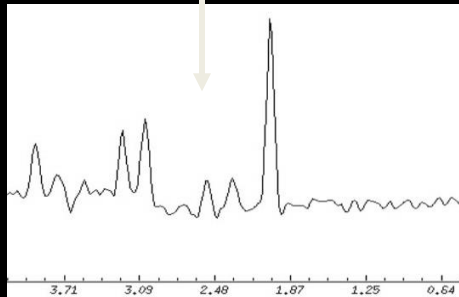
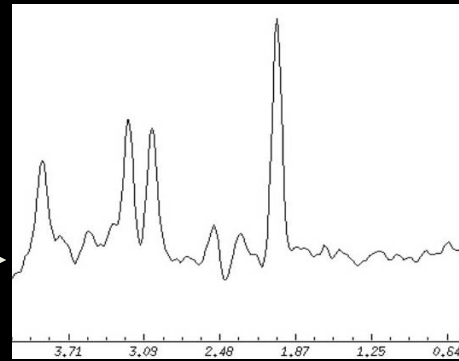
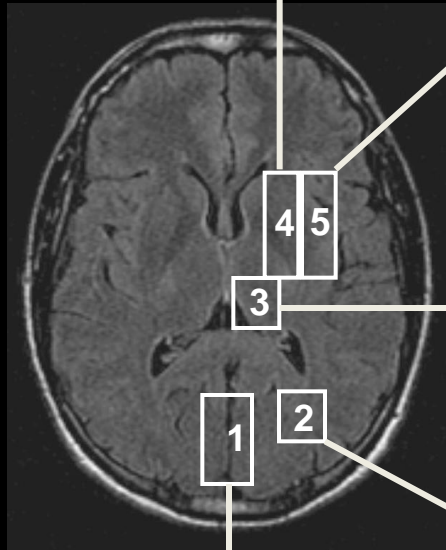
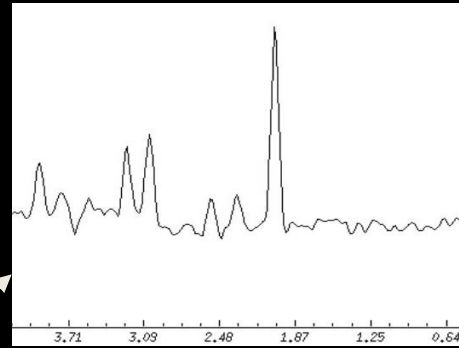
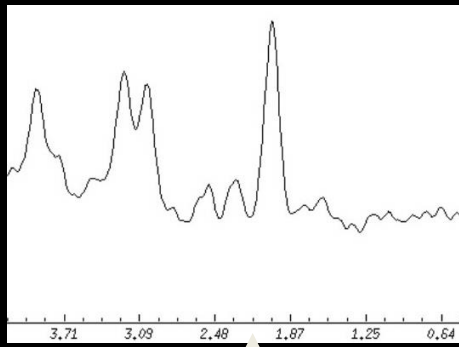




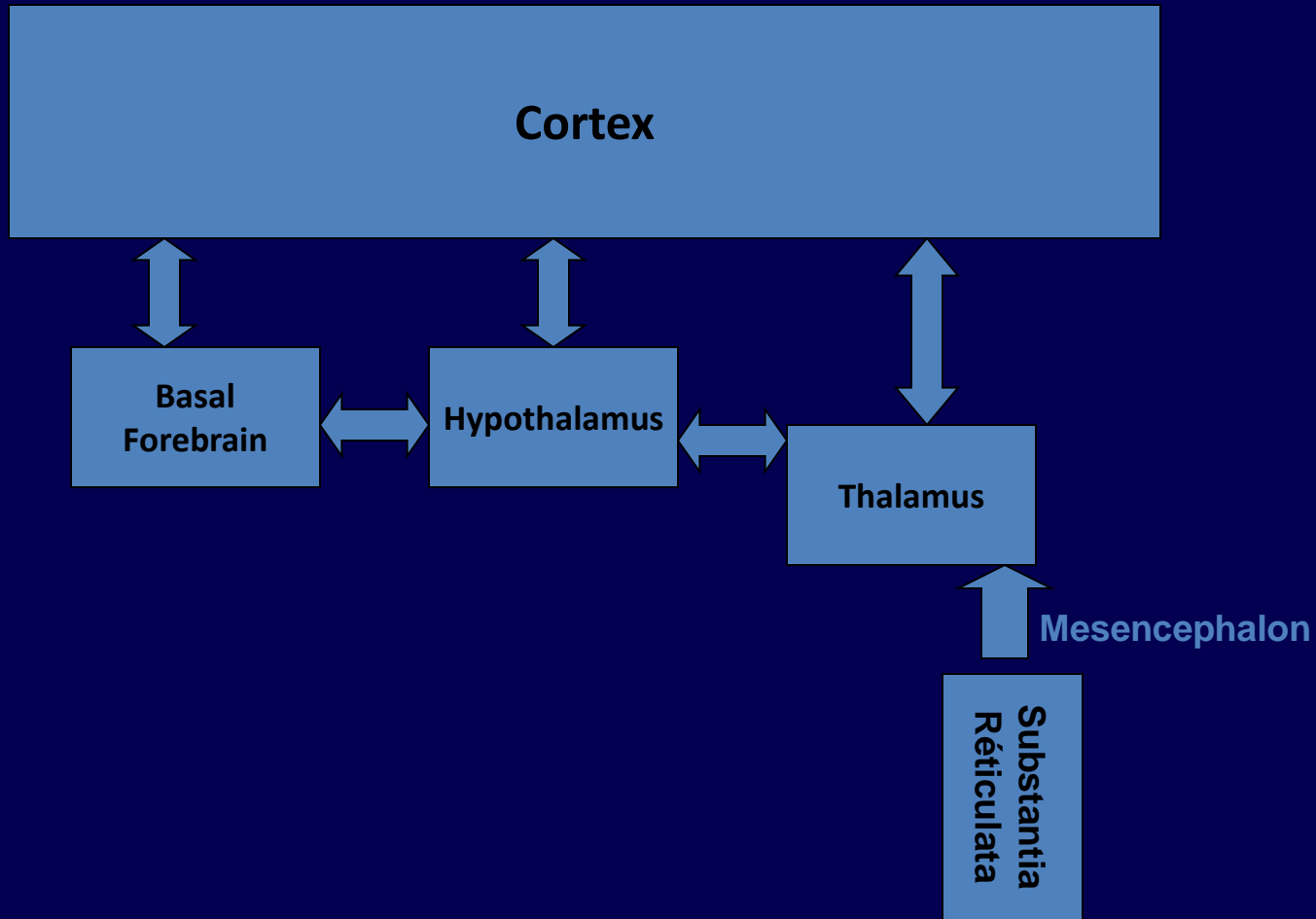
Tenseur de diffusion (II)

- Extraction de multiples paramètres
 - **MD/ADC**: “facilité globale de la diffusibilité”
 - **FA**: comment, globalement, est contrainte la diffusion (état de la SB)
 - **L1**: “grand axe” de la diffusibilité \approx axones
 - **Lt**: “axe orthogonal” de la diffusibilité \approx myéline



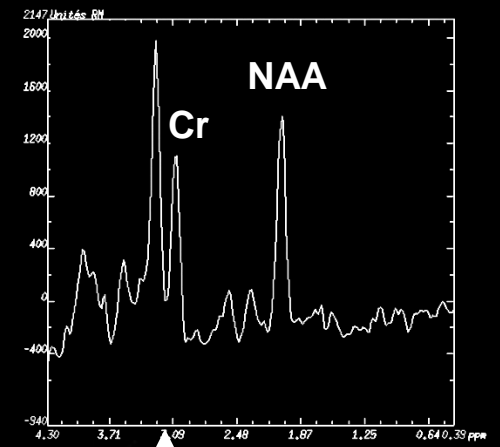
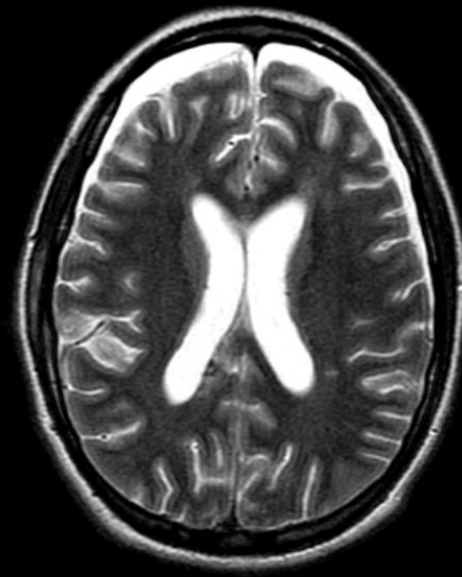
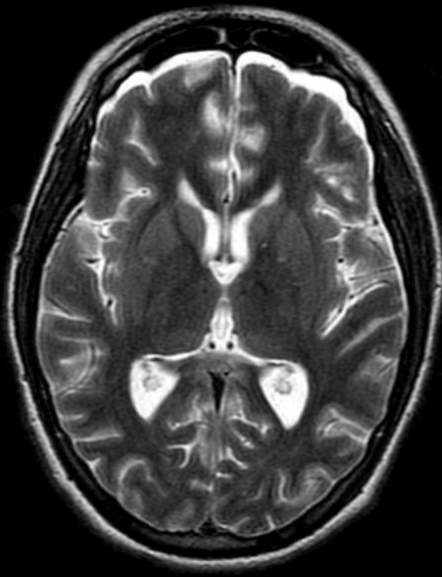


Les circuits de l'éveil

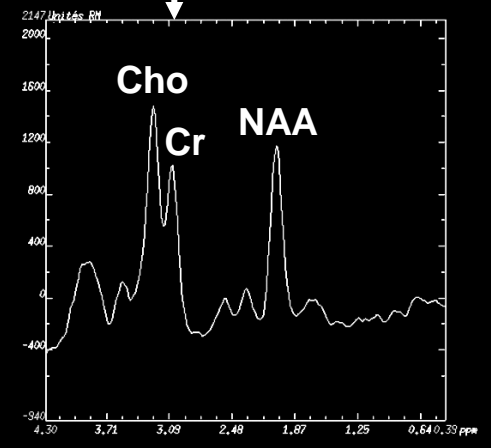
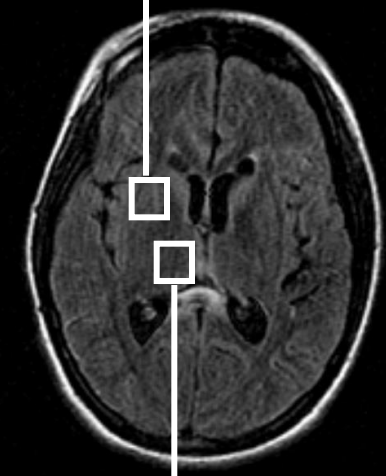
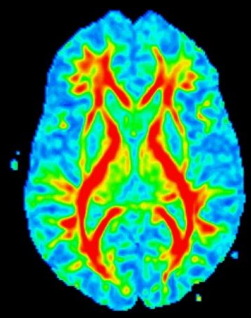
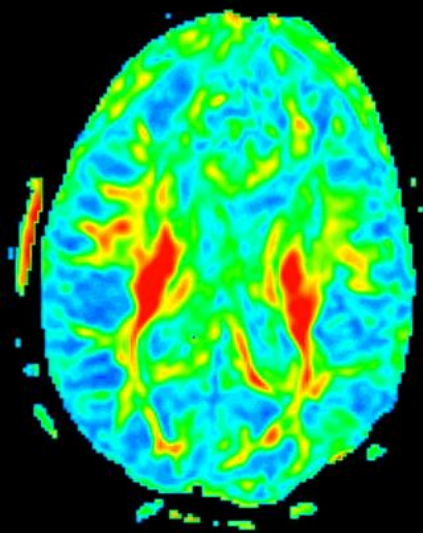
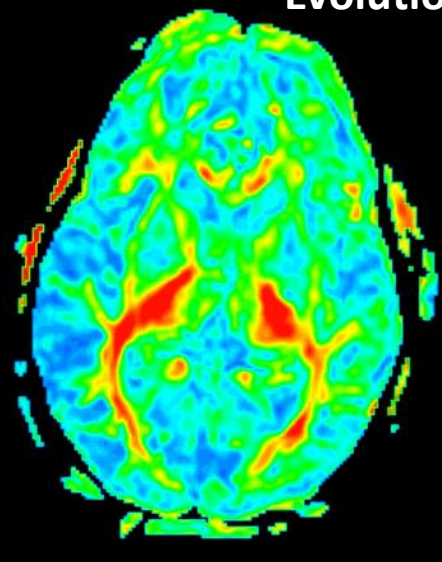


MRS

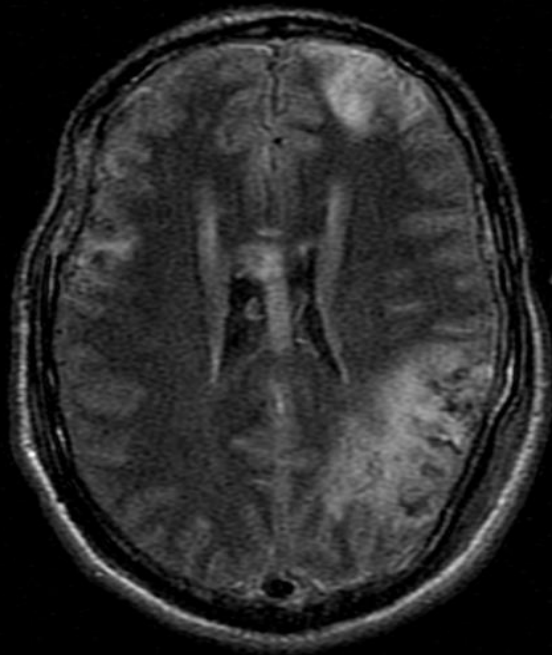
DTI



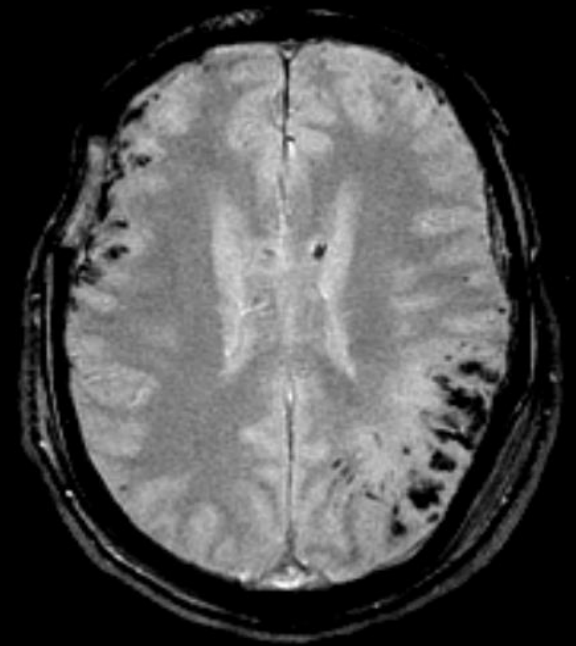
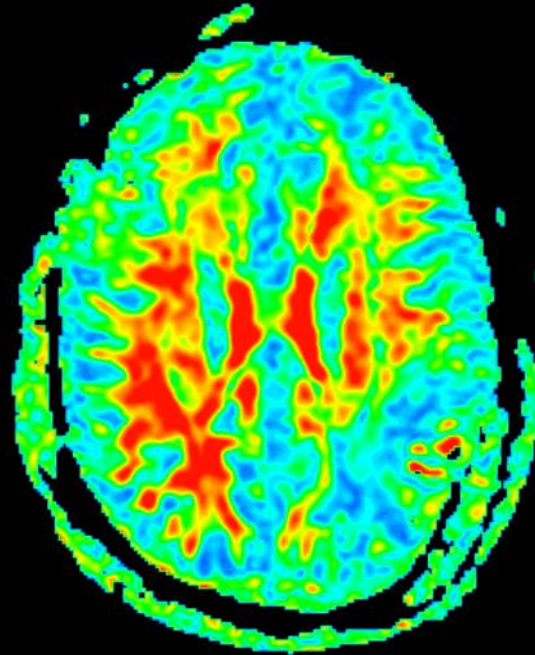
DAI graves
Evolution défavorable



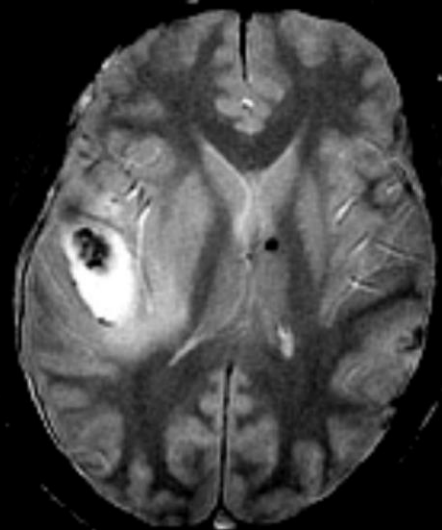
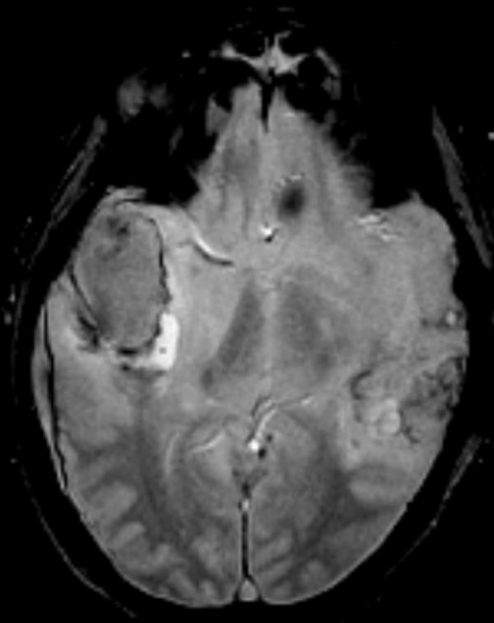
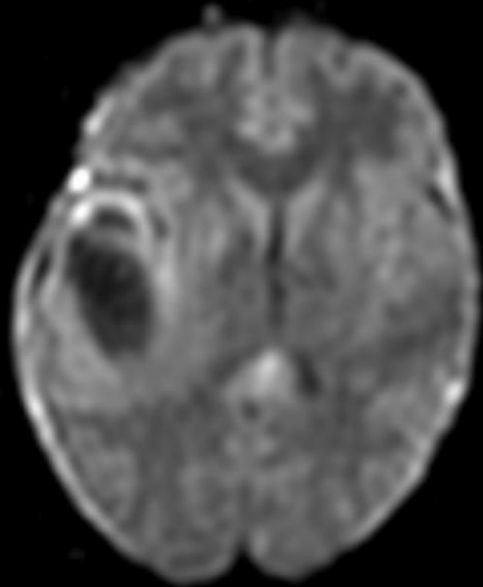
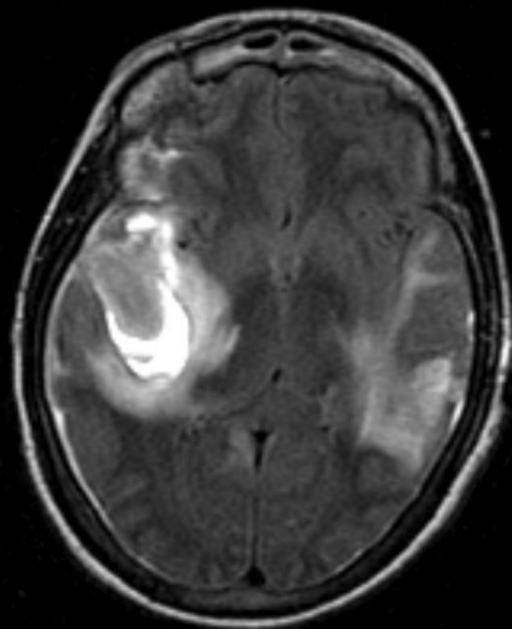
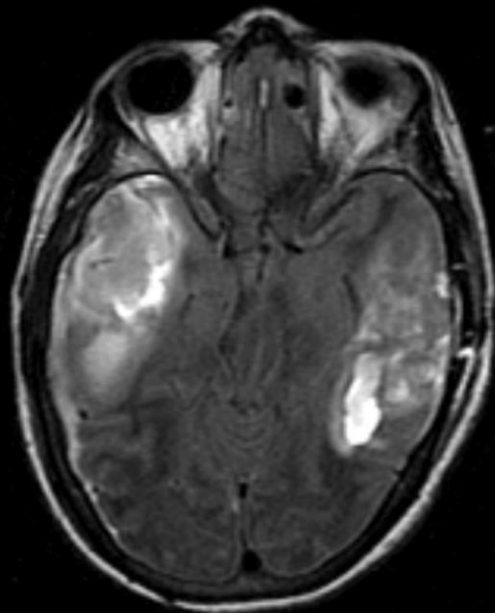
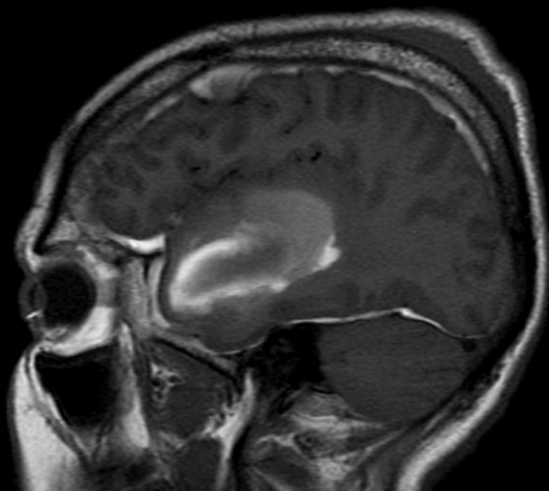
26 ans, TCG



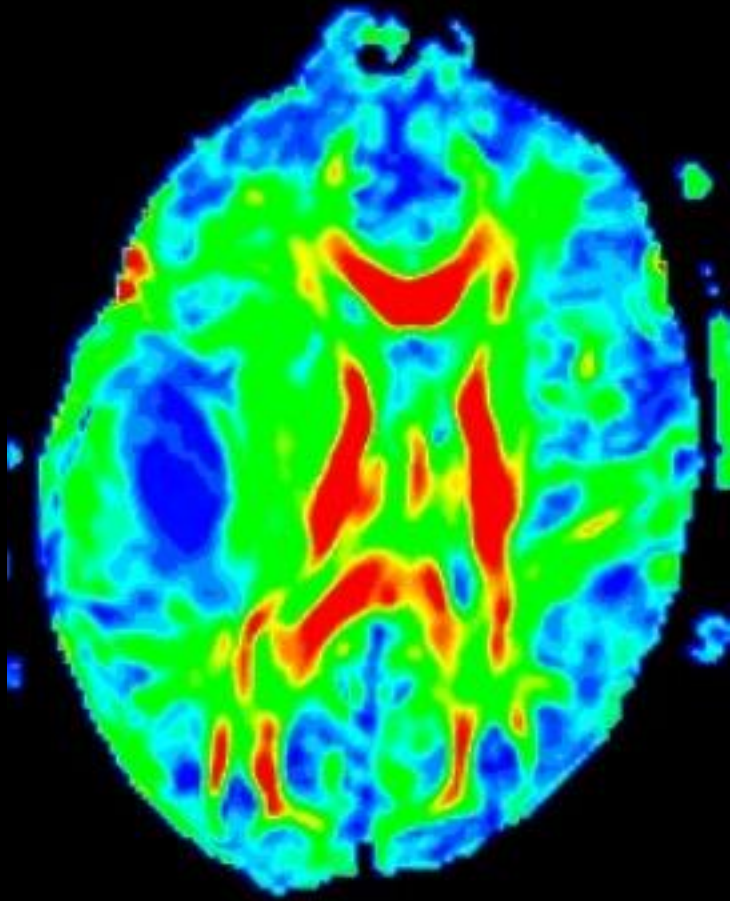
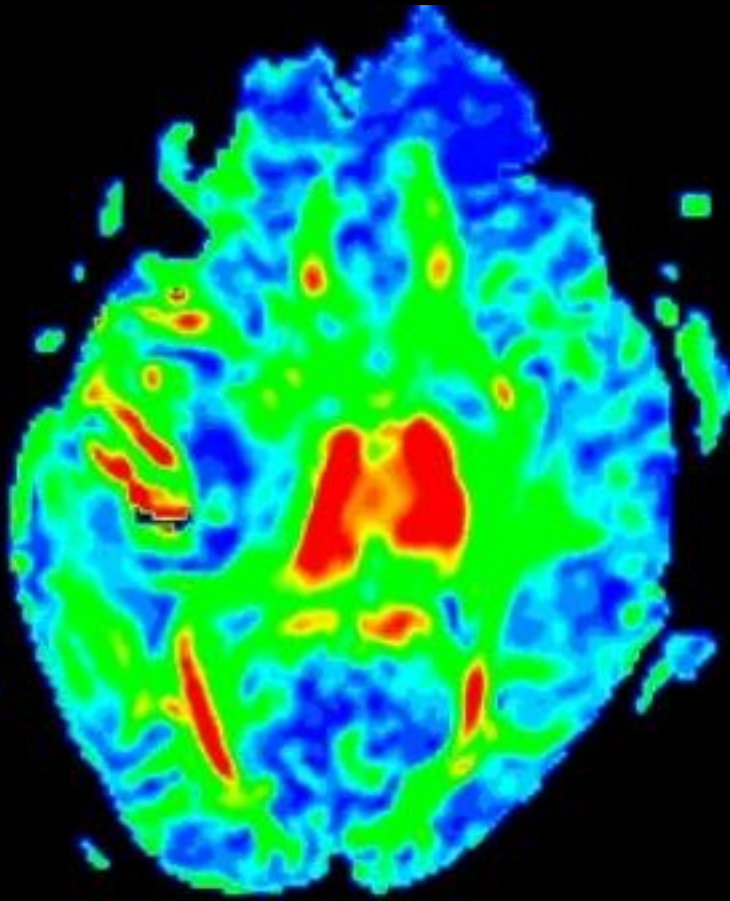
TCG



**DAI limitées
Evolution favorable**



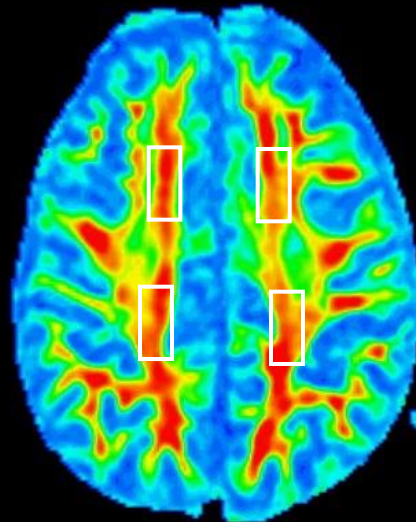
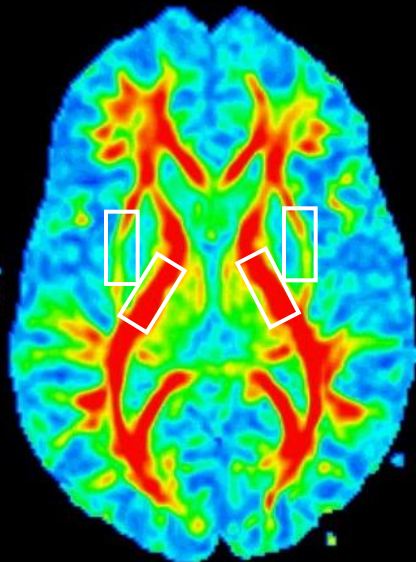
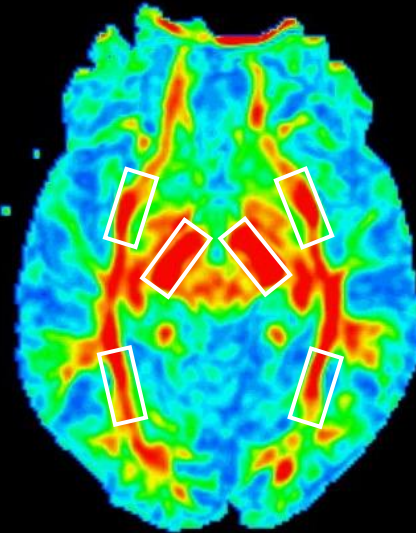
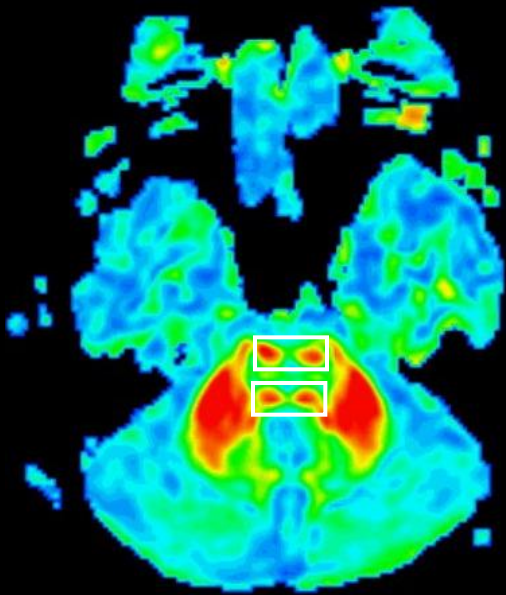
TCG

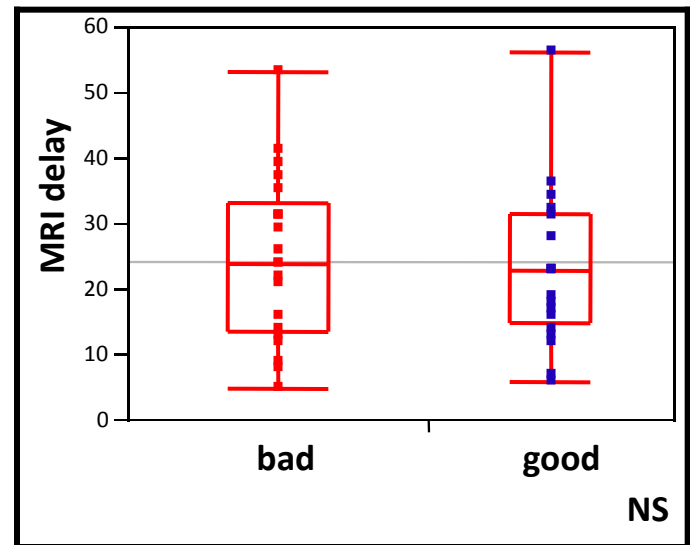
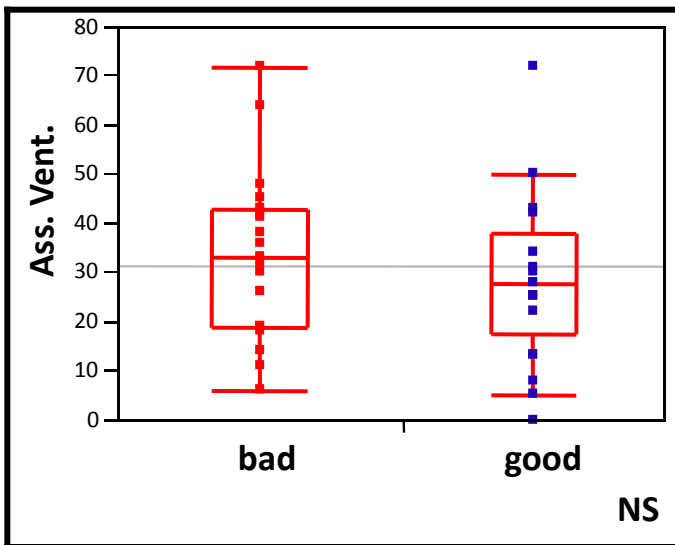
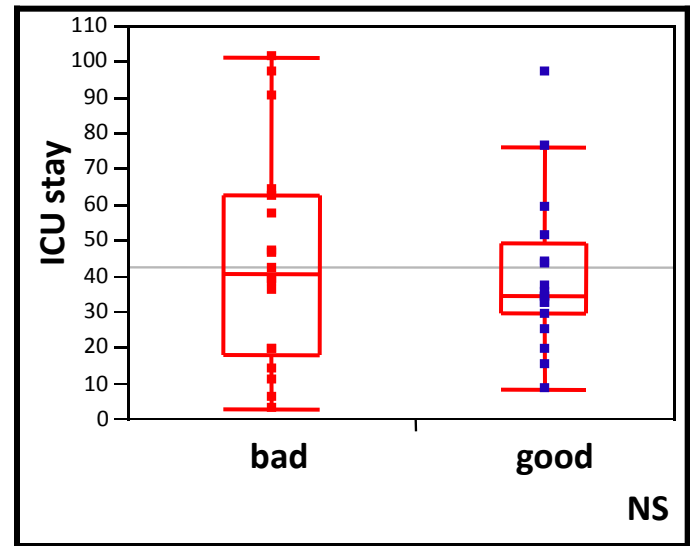
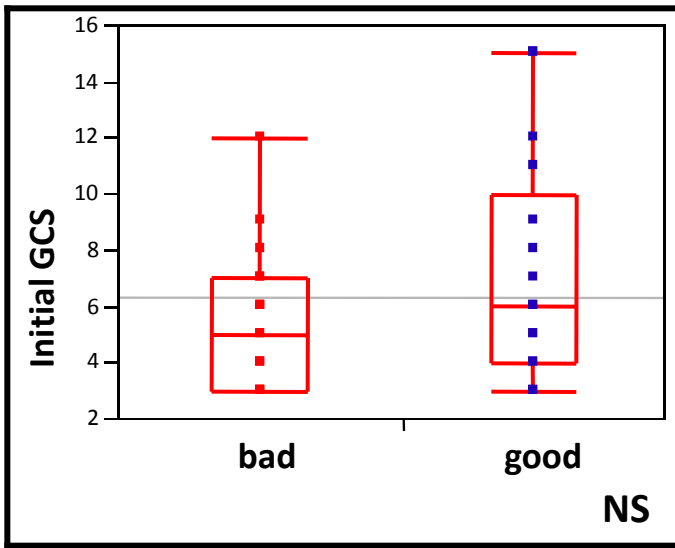


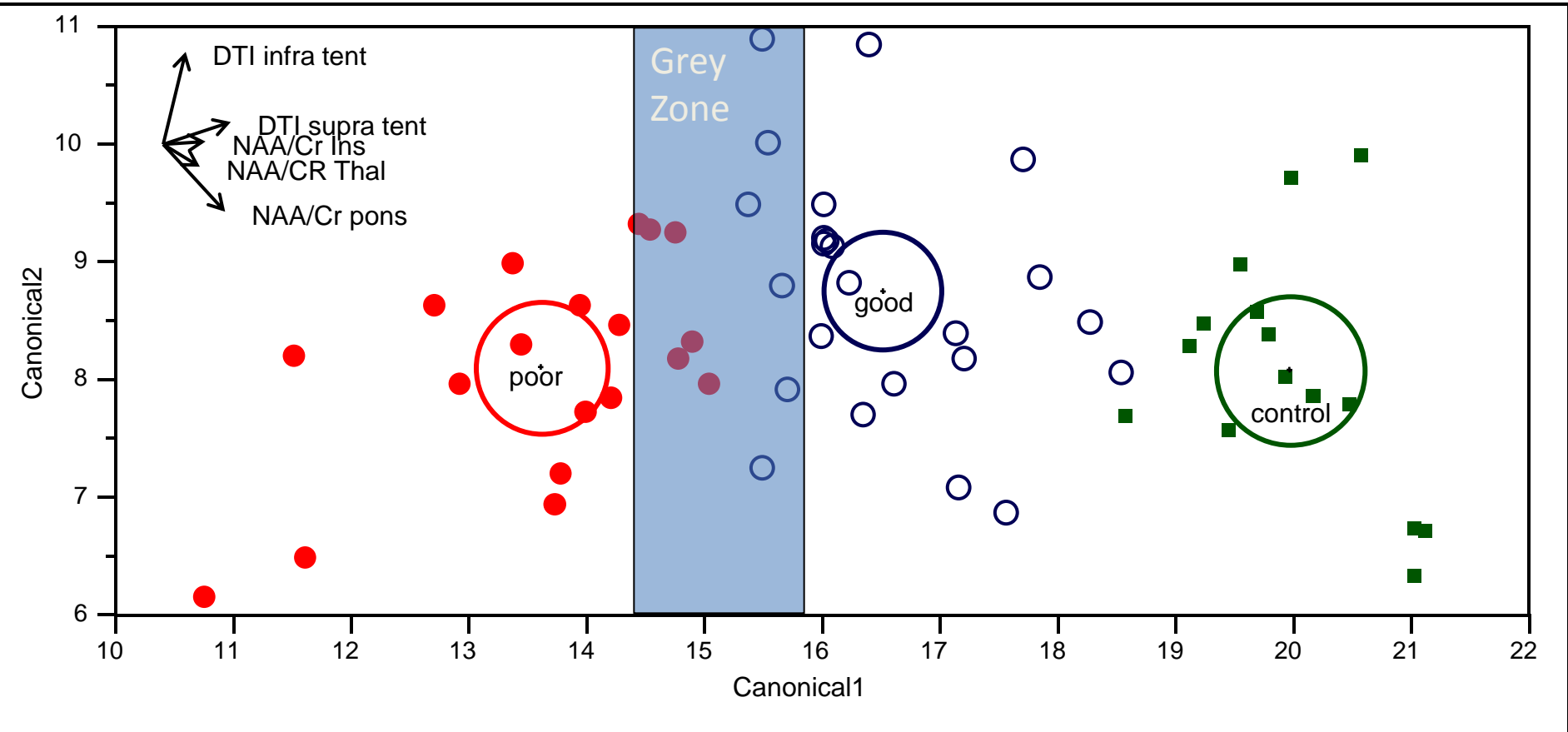
Compression du tronc sans lésions
Evolution favorable

Etude pilote PSL

- Evaluation systématique des patients comateux
- Protocole standardisé comportant
 - Imagerie conventionnelle FLAIR, T2*, T2
 - Spectroscopie
 - Tenseur de diffusion
- Analyse des résultats sur les patients TC (40 + 10 témoins)







2^{ème} analyse

Peut on automatiser l'analyse des images?

- Uniquement le tenseur
- Même groupe de patients
- Analyse par VBM et TBSS
- Détection automatique des régions critiques pour déterminer le pronostic
- LDA with bootstrap validation

Traumatic Brain Injury dataset from PSL

3 groups {
Control (n=10)
Good outcome (n=16) ~ [1 year GOS 4-5]
Poor outcome (n=15) ~ [1 year GOS 1-3]

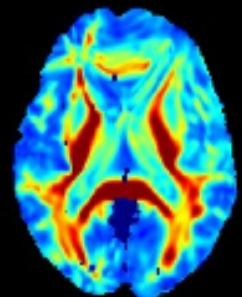
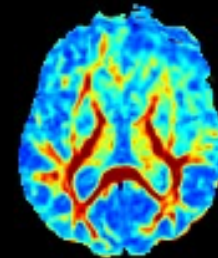
DTI acquisitions

23 directions, b value = 700 s/mm²

20 slices, voxel size 2.5 x 2.5 x 5 mm

DTI preprocessings

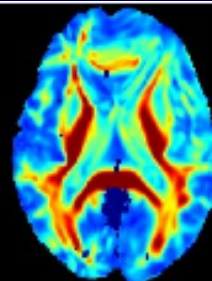
- 1- Distorsion and eddy current correction
- 2- Creation of FA (ADC) images from the diffusion tensor model
- 3- nonlinear registration in a 1x1x1 mm standard space



FA : Fractional Anisotropy

ADC : Apparent Diffusion Coefficient

TBSS : Tract-Based Spatial Statistics
VBM : Voxel-Based Morphometry



Registered FA (ADC) maps

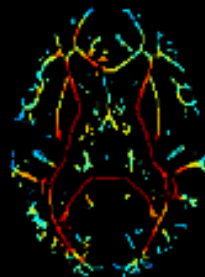
TBSS

VBM

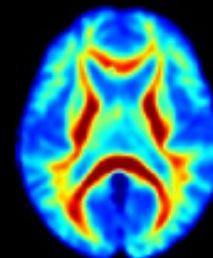
Creation of FA skeleton from the mean of all registered FA maps



Projection of FA (ADC) maps on the FA skeleton mask



Smooth the FA (ADC) maps
(FWHM = 3 mm)

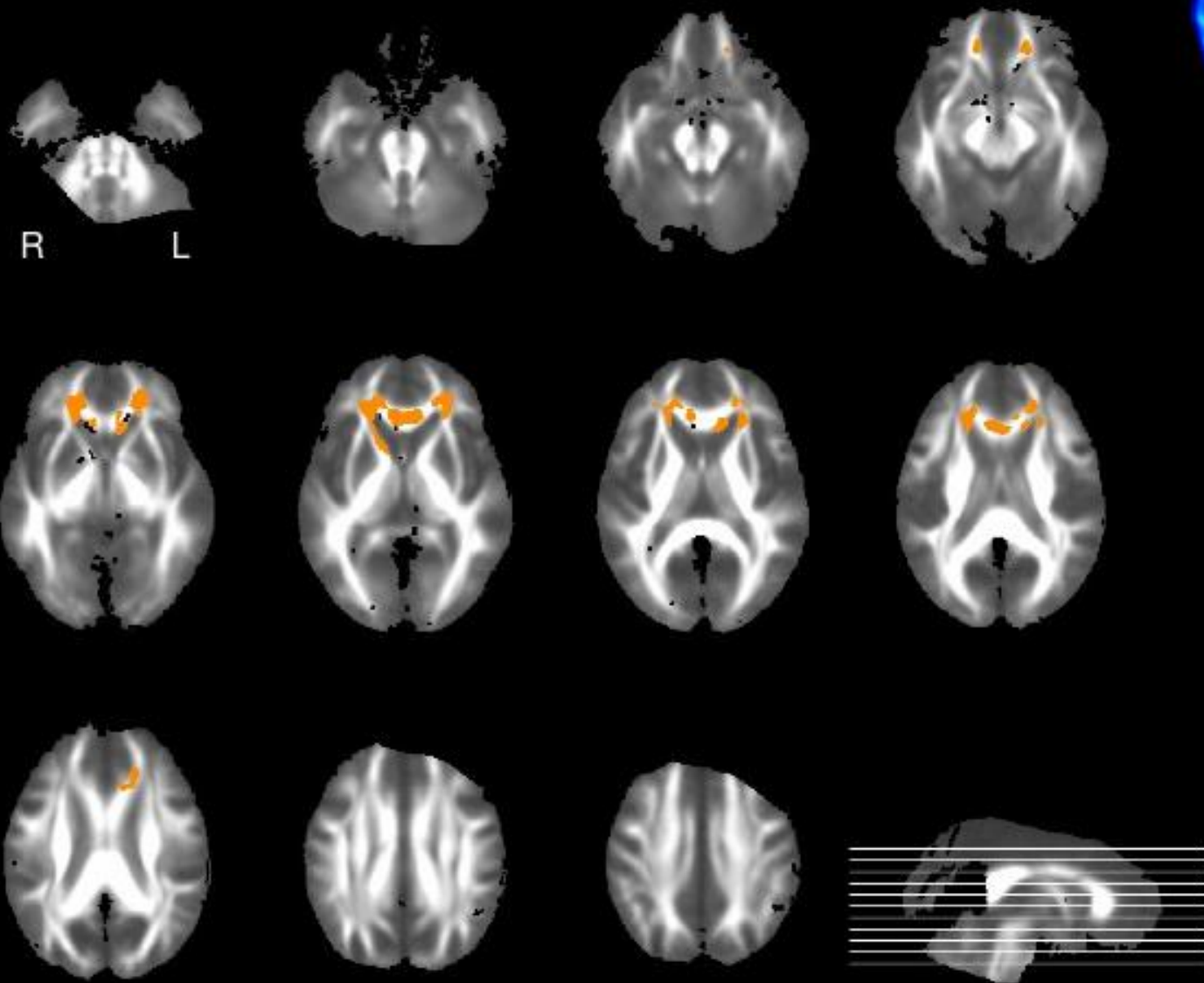


Voxelwise statistics to test significant difference in FA (ADC) values between two groups on the skeleton mask (TBSS) or on the whole brain (VBM)

FA

Voxelwise statistics on all FA data (VBM)

GOOD < CONTROL

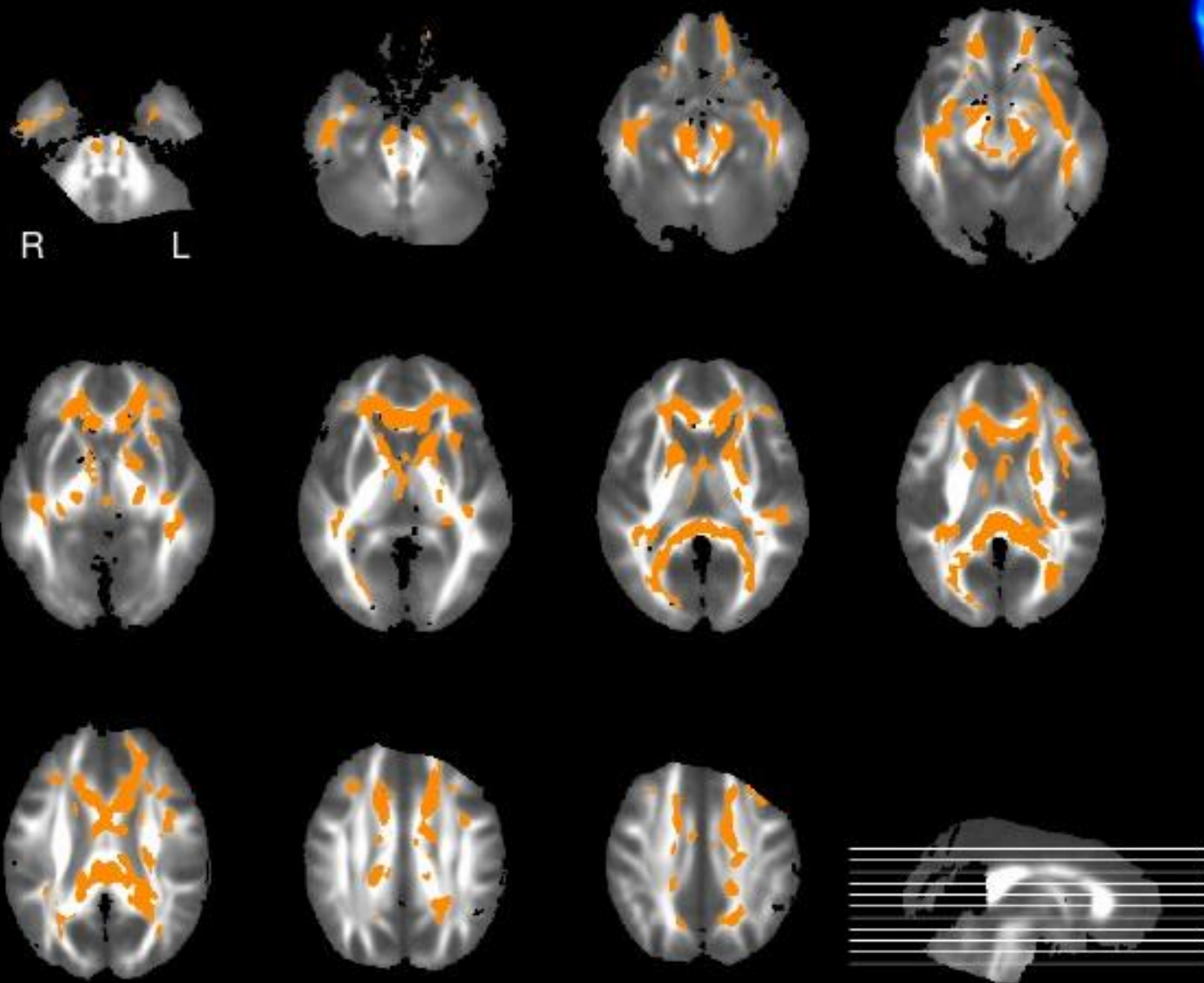


$P < 0.05$ (correction de Bonferroni)

FA

Voxelwise statistics on all FA data (VBM)

POOR < CONTROL

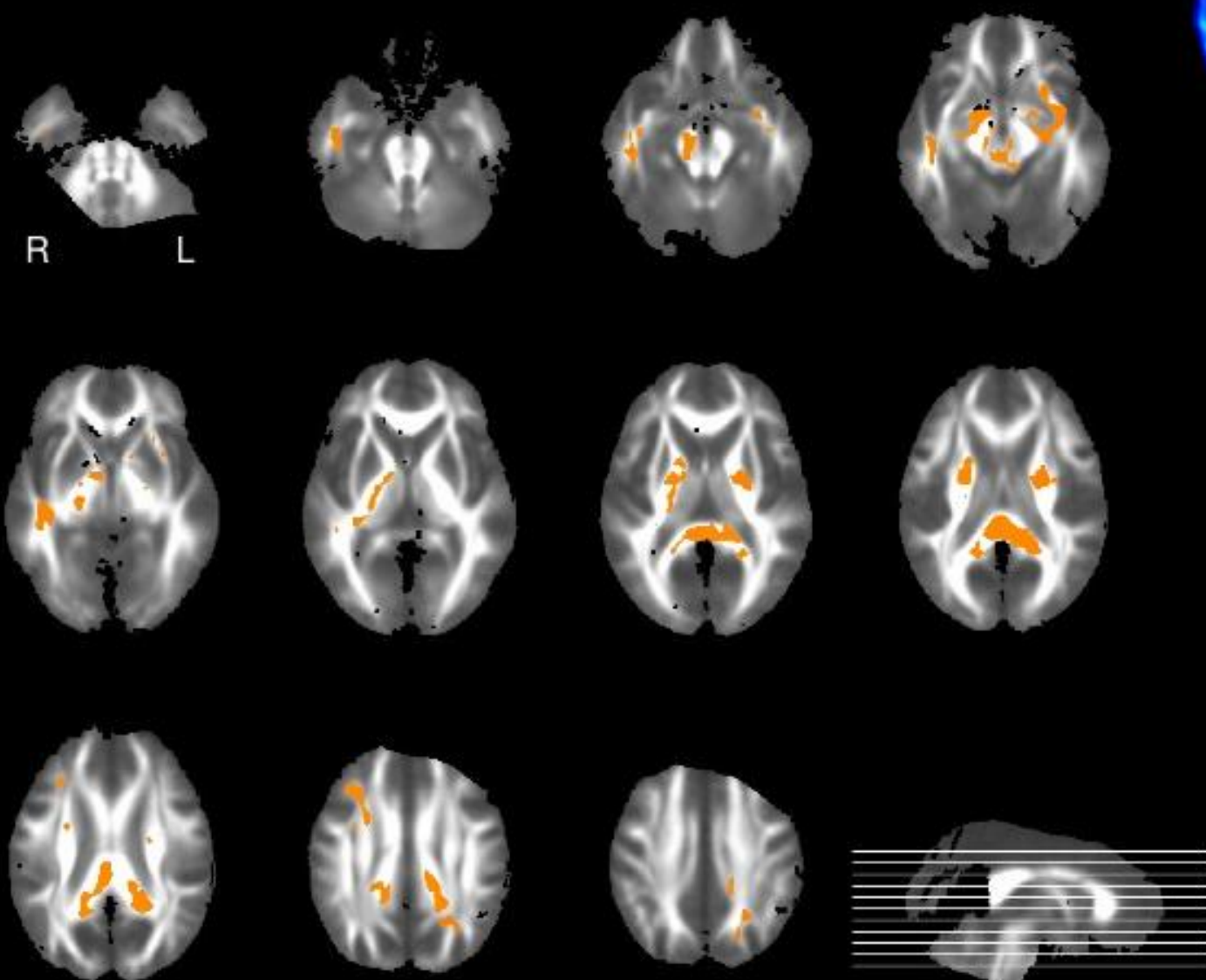


$P < 0.05$ (correction de Bonferroni)

FA

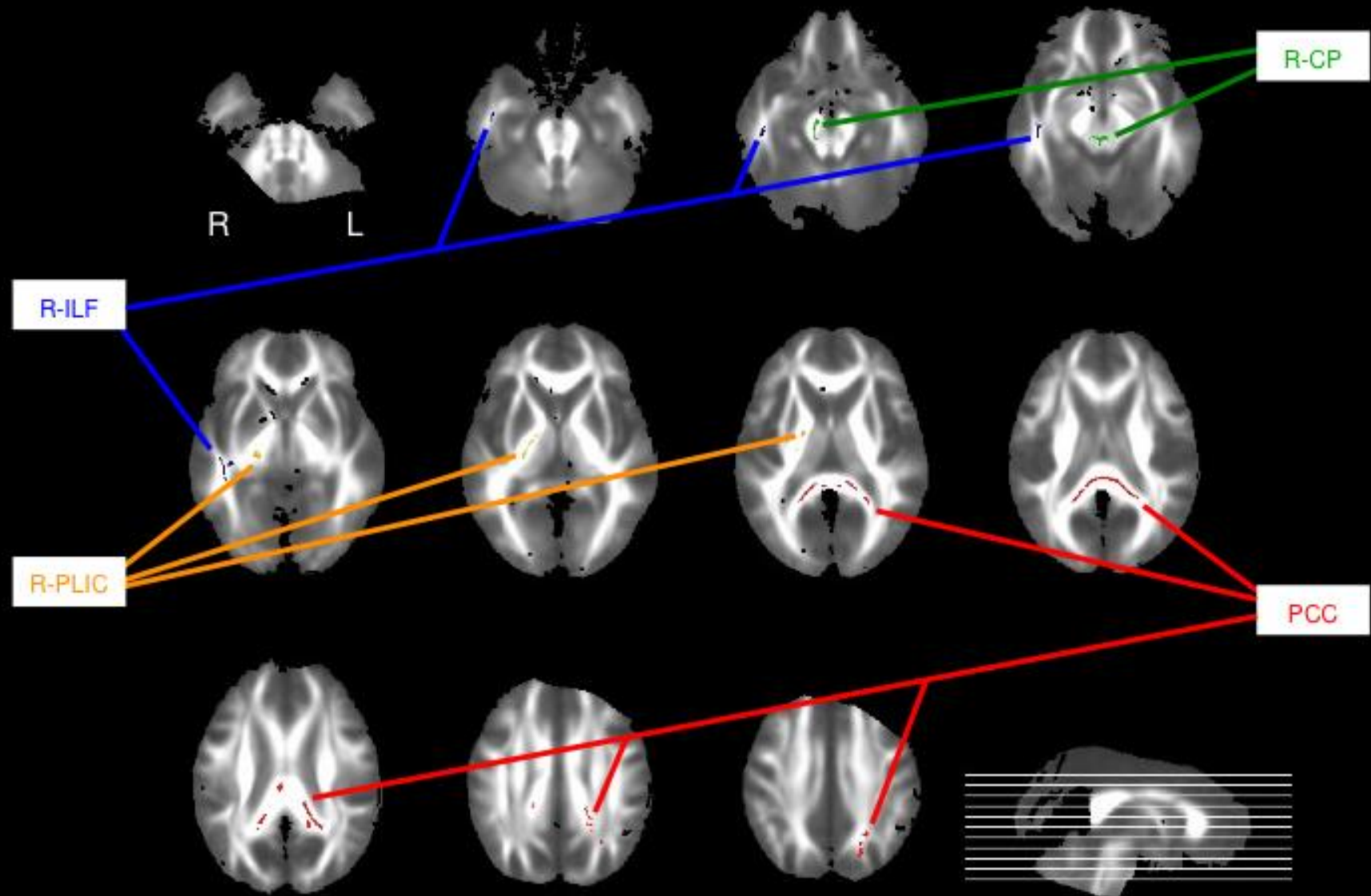
Voxelwise statistics on all FA data (VBM)

POOR < GOOD



$P < 0.05$ (correction de Bonferroni)

Regions where FA is significantly lower for poor outcome group than for good outcome group (TBSS results)



R-ILF : Right Inferior Longitudinal Fasciculus
R-CP : Right Cerebral Peduncle

R-PLIC : Right Posterior Limb of Internal Capsule
PCC : Posterior Corpus Callosum

Sn, Sp to predict poor outcome

Bootstrap analysis

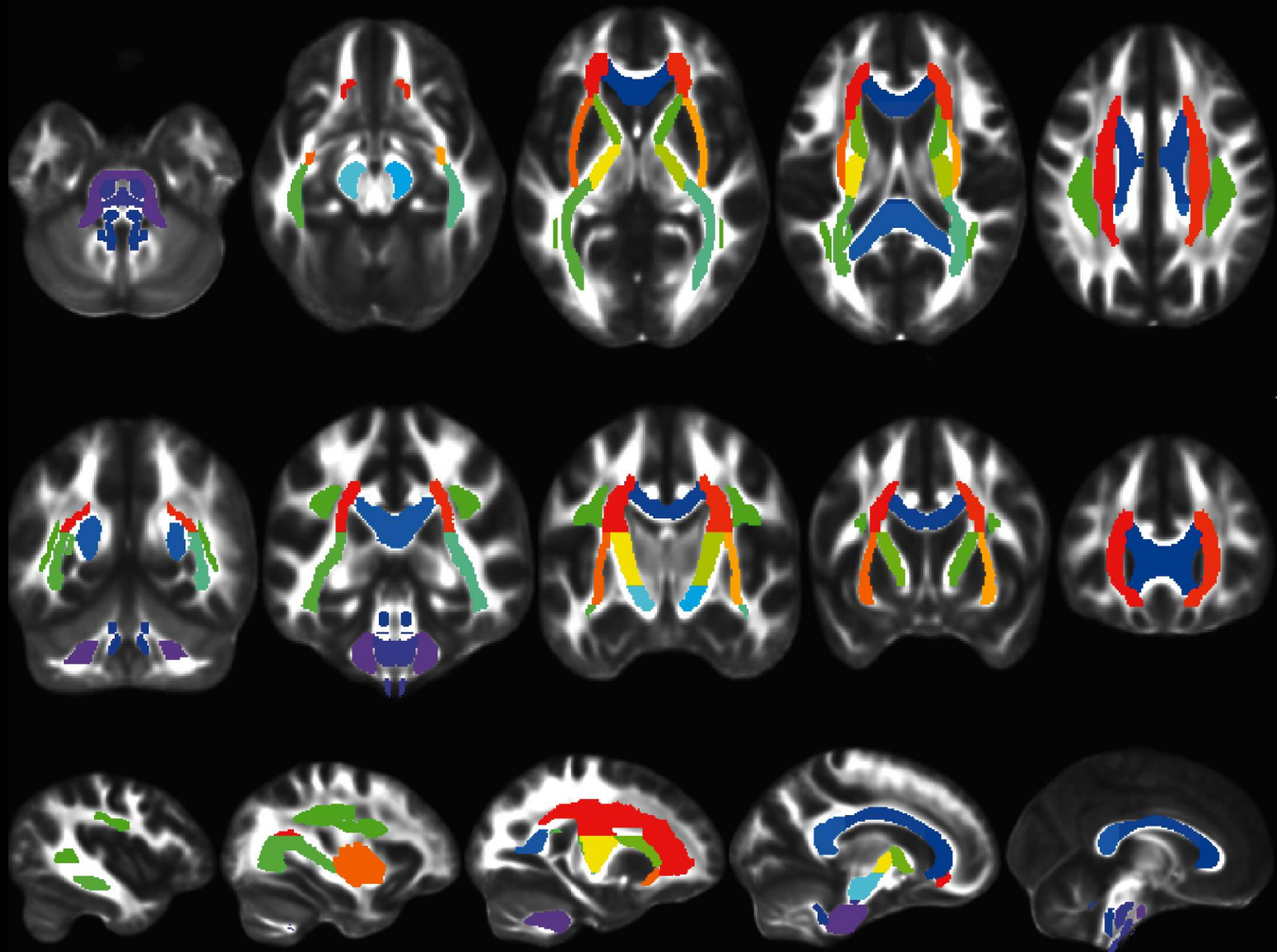
	threshold 0.5	threshold 0.95
Sn	86 %	49 %
Sp	86 %	97 %

Limites de ces études préliminaires

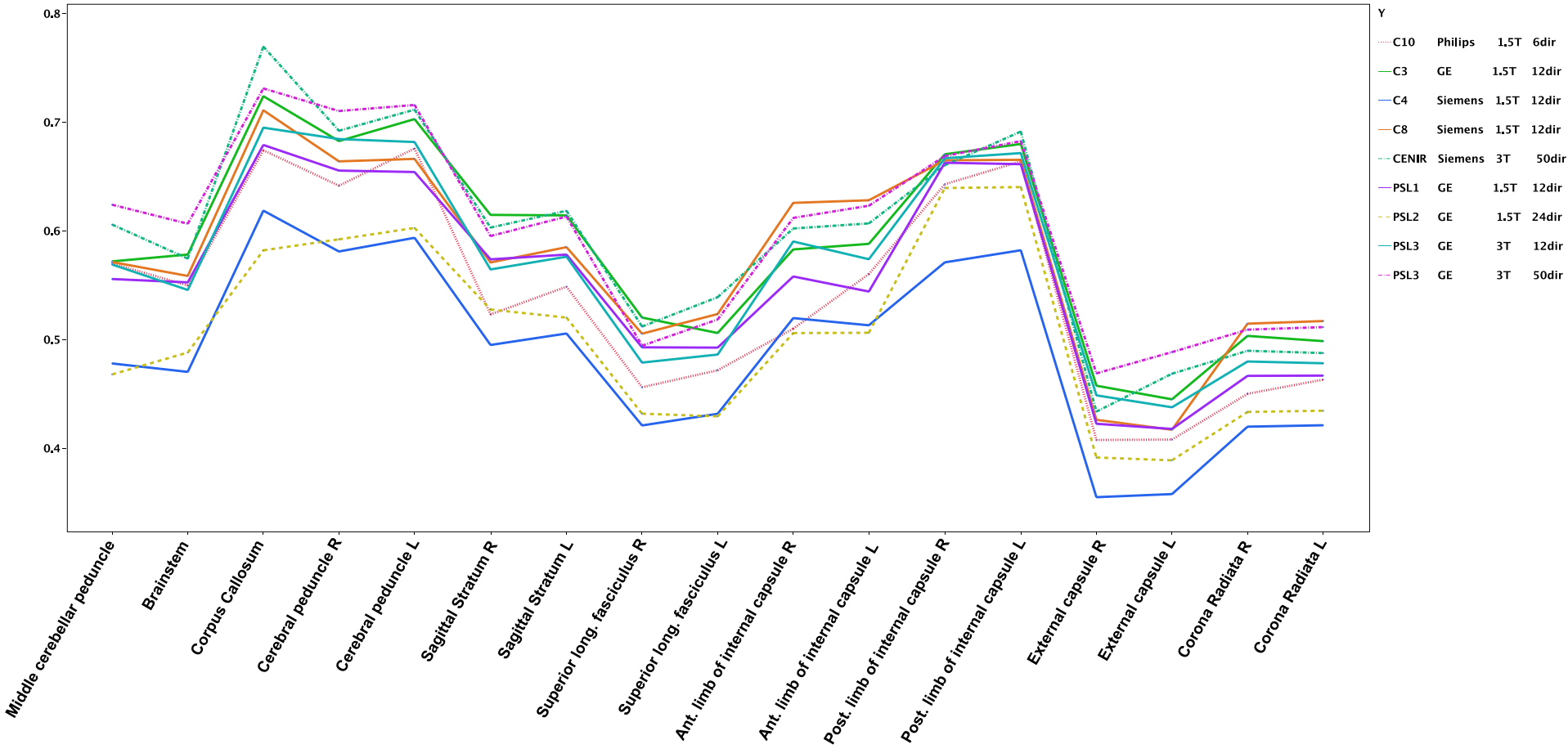
- Monocentrique
- Examens réalisés sur une seule IRM
- Nombre limité de patient
- *Prédiction limitée à une étiologie (TBI)*
- Prédiction limitée au retour à la conscience

Reproductibilité inter centres du tenseur de diffusion

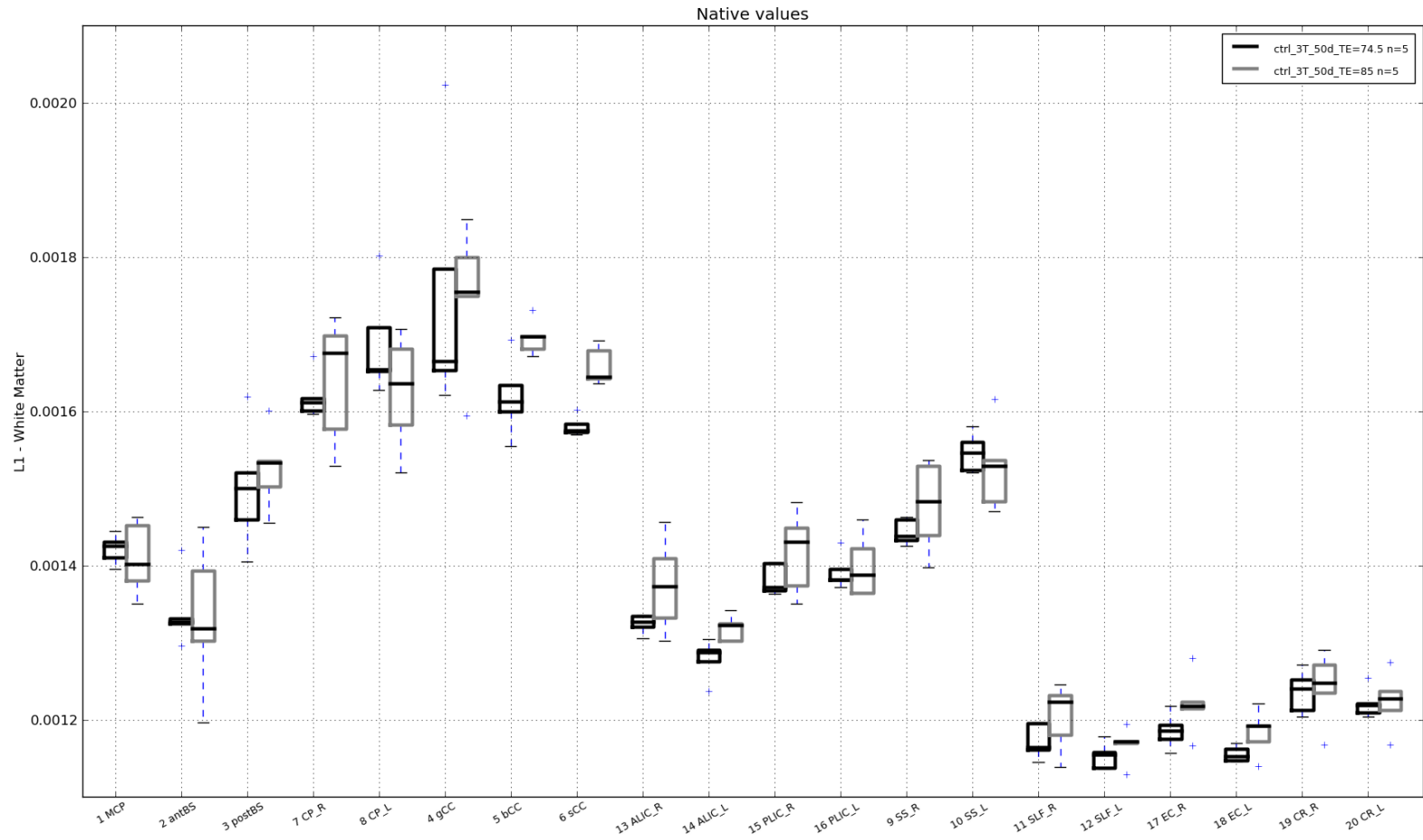
- 104 acquisitions chez 85 contrôles, 8 IRM différentes
- Siemens, GE, Philips
- 1.5T et 3T
- Epaisseur de coupe de 2 à 5 mm
- 6 à 50 directions
- Analyse automatisée de FA, MD, L1 et Lt dans 20 régions d'intérêt (logiciel développé à l'U678)



	Number	Abbreviation	Region
Posterior fossa	1	MCP	Middle cerebellar peduncle
	2	antBS	Anterior brainstem (pons, medulla oblongata)
	3	postBS	Posterior brainstem (pons, medulla oblongata)
	7	CP_R	Right cerebral peduncle
	8	CP_L	Left cerebral peduncle
Deep brain	4	gCC	Genu of the corpus callosum
	5	bCC	Body of the corpus callosum
	6	sCC	Splenium of the corpus callosum
	13	ALIC_R	Anterior arm of the internal capsule (right)
	14	ALIC_L	Anterior arm of the internal capsule (left)
	15	PLIC_R	Posterior arm of the internal capsule (right)
	16	PLIC_L	Posterior arm of the internal capsule (left)
Superficial regions	9	SS_R	Stratum sagittale (right)
	10	SS_L	Stratum sagittale (left)
	11	SLF_R	Superior longitudinal fasciculus (right)
	12	SLF_L	Superior longitudinal fasciculus (left)
	17	EC_R	External capsule (right)
	18	EC_L	External capsule (left)
	19	CR_R	Corona radiata (right)
	20	CR_L	Corona radiata (left)



Effet de la variation du TE



Variabilité inter centres du tenseur

- Variations importantes (surtout sur L1 et Lt)
- Même lorsque des séquences similaires sont utilisées
- Même sur des IRM “identiques”

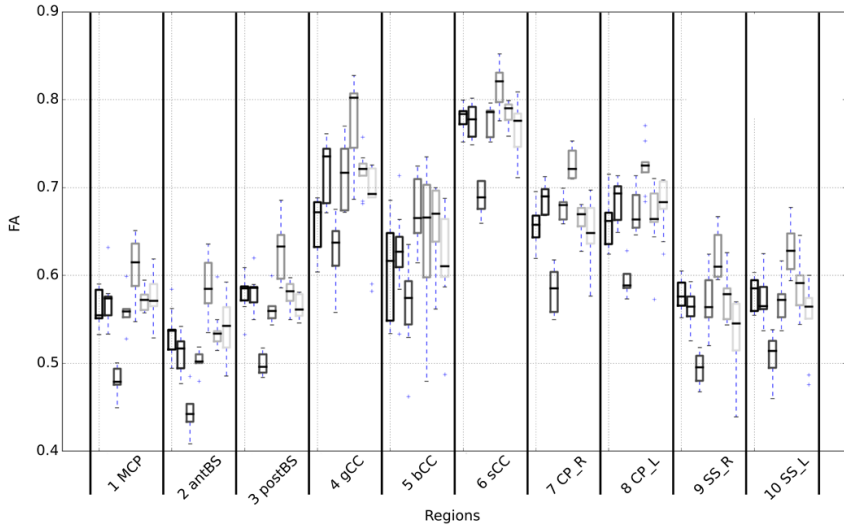
Explications possibles

- L'épaisseur de coupe et le TE jouent un rôle
- Séquences variables en fonction du constructeur
- Différences dans l'enregistrement des DICOM (Siemens vs GE&Philips)
- différentes versions de firmware

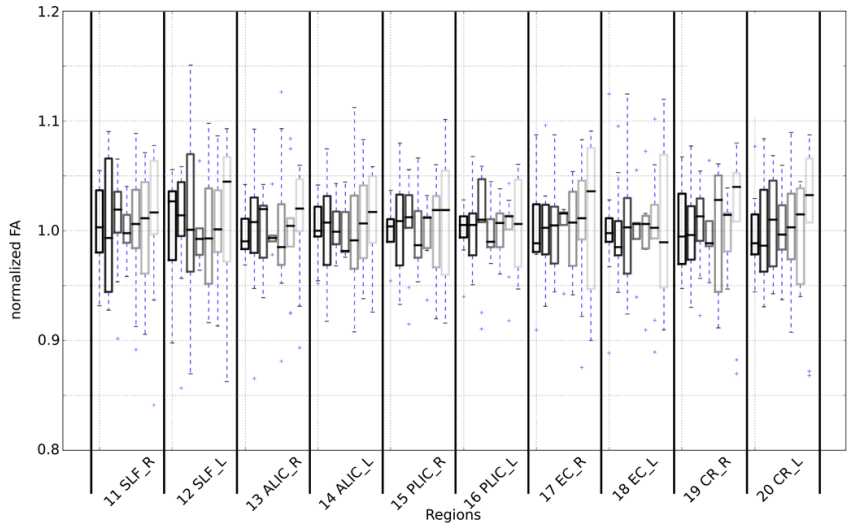
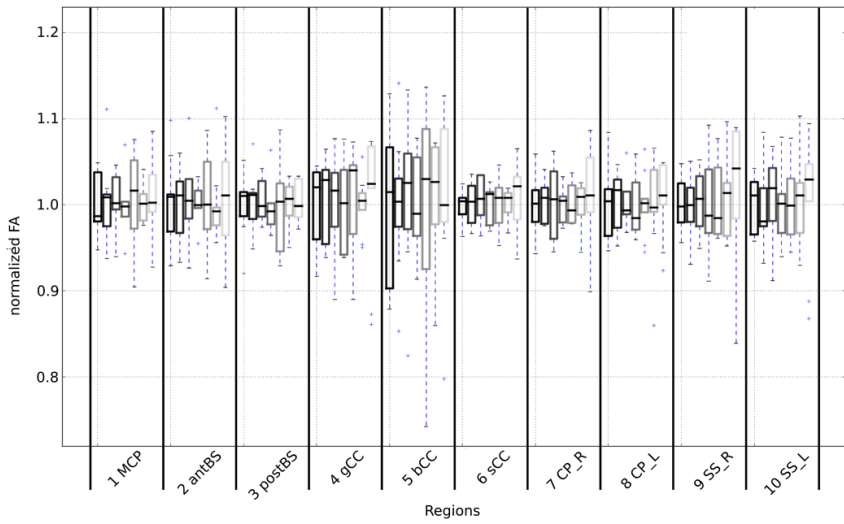
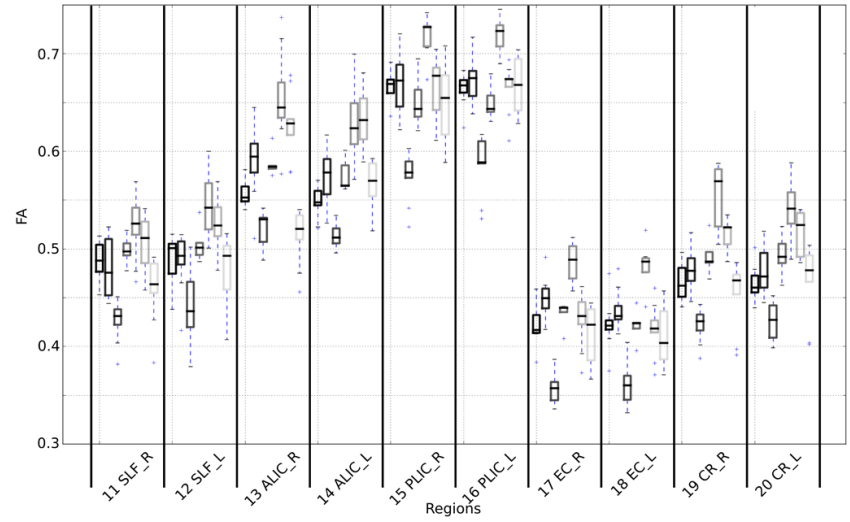
Solutions

- inclure des contrôles
- s'assurer de la stabilité des acquisitions
- développement d'un fantôme de tenseur de diffusion ?

— center 1 3T n=10
 — center 1 1.5T n=9
 — center 3 1.5T n=9
 — center 4 1.5T n=8

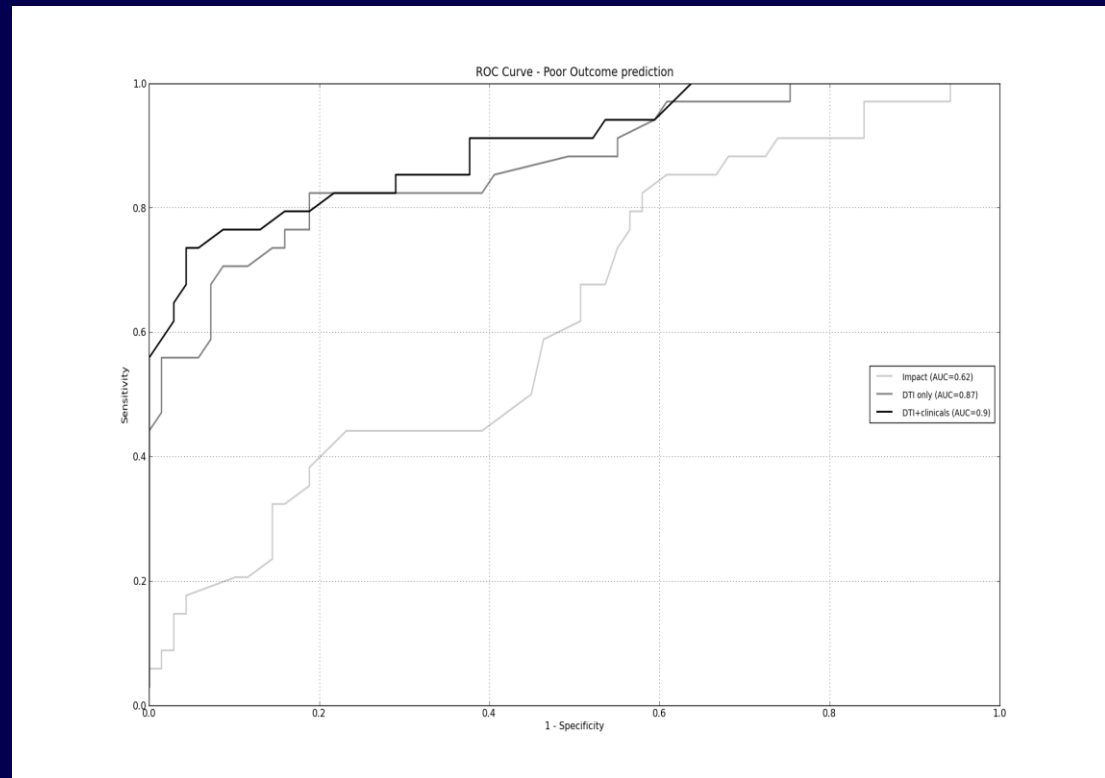


— center 5 1.5T n=5
 — center 6 1.5T n=10
 — center 8 1.5T n=10
 — center 10 1.5T n=8

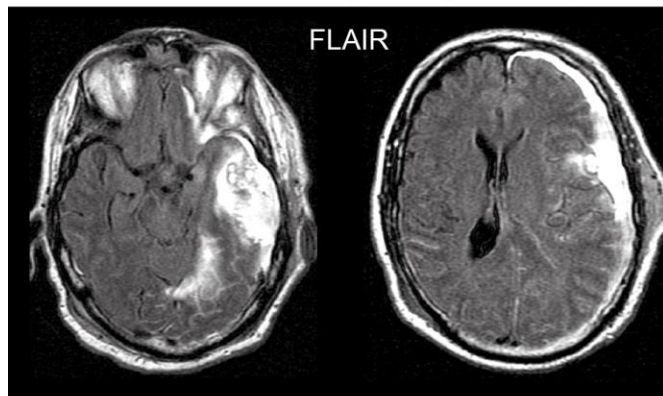


Résultats de l'étude multicentrique

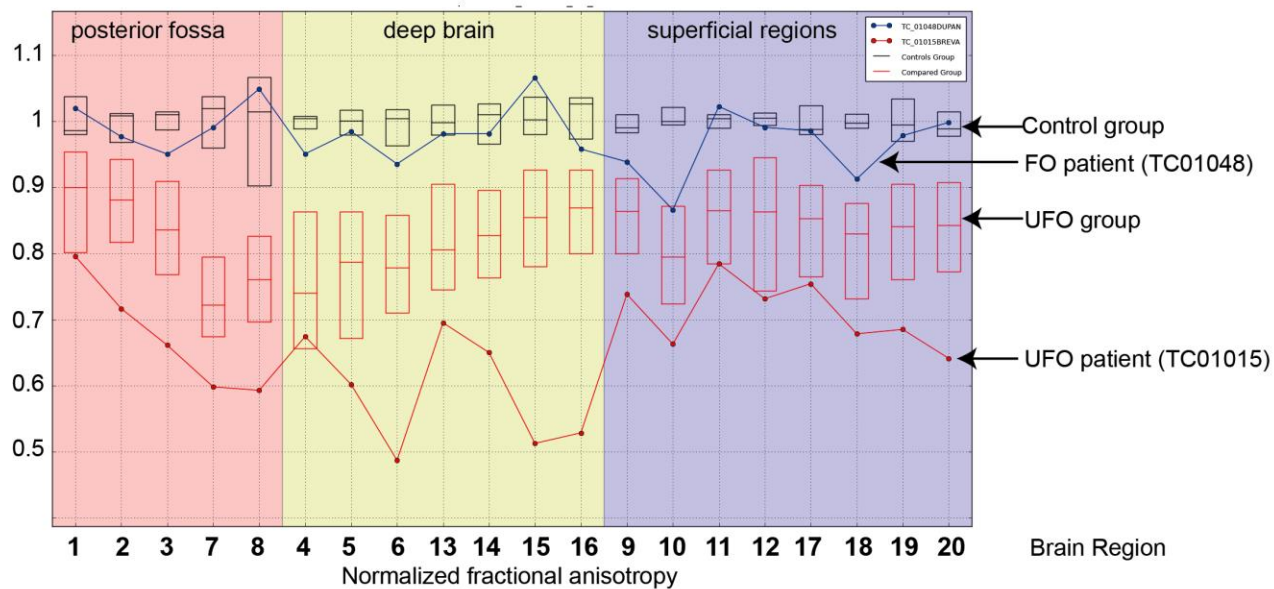
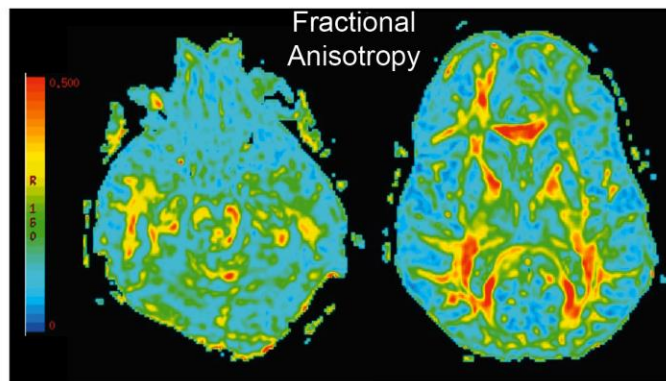
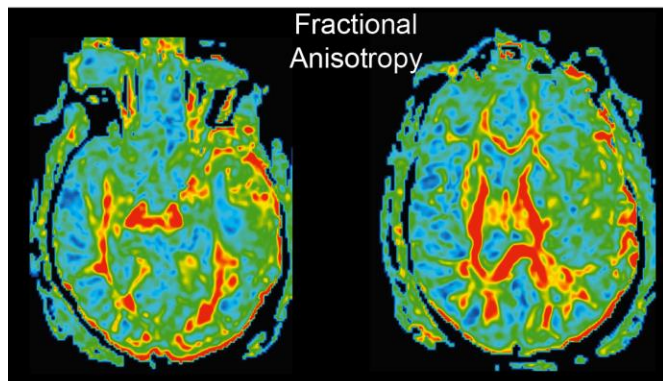
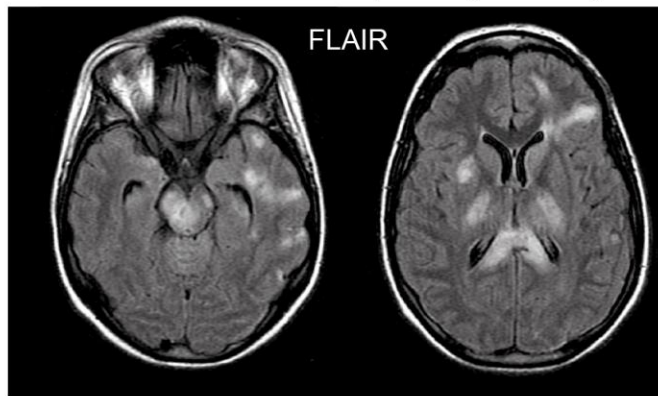
- 104 patients, 70 controls + 40 patients de la première étude utilisés comme base de validations
- 7 centres
- Prédiction de l'évolution défavorable avec une sensibilité de 64% (Sp 95%)

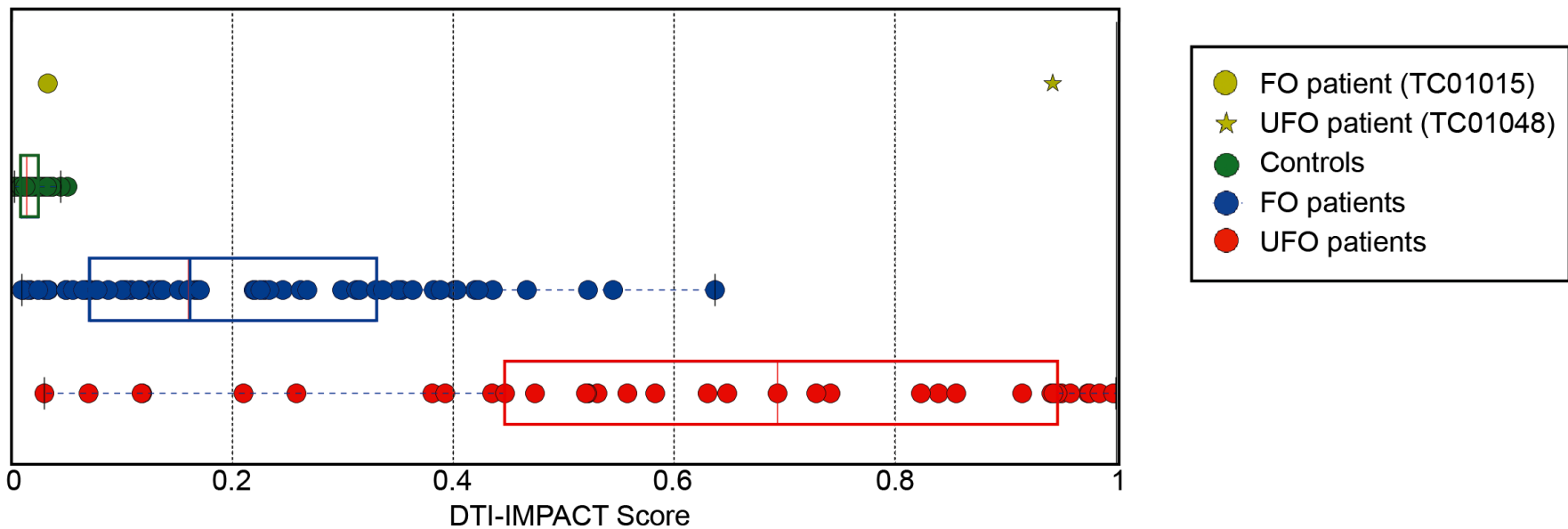
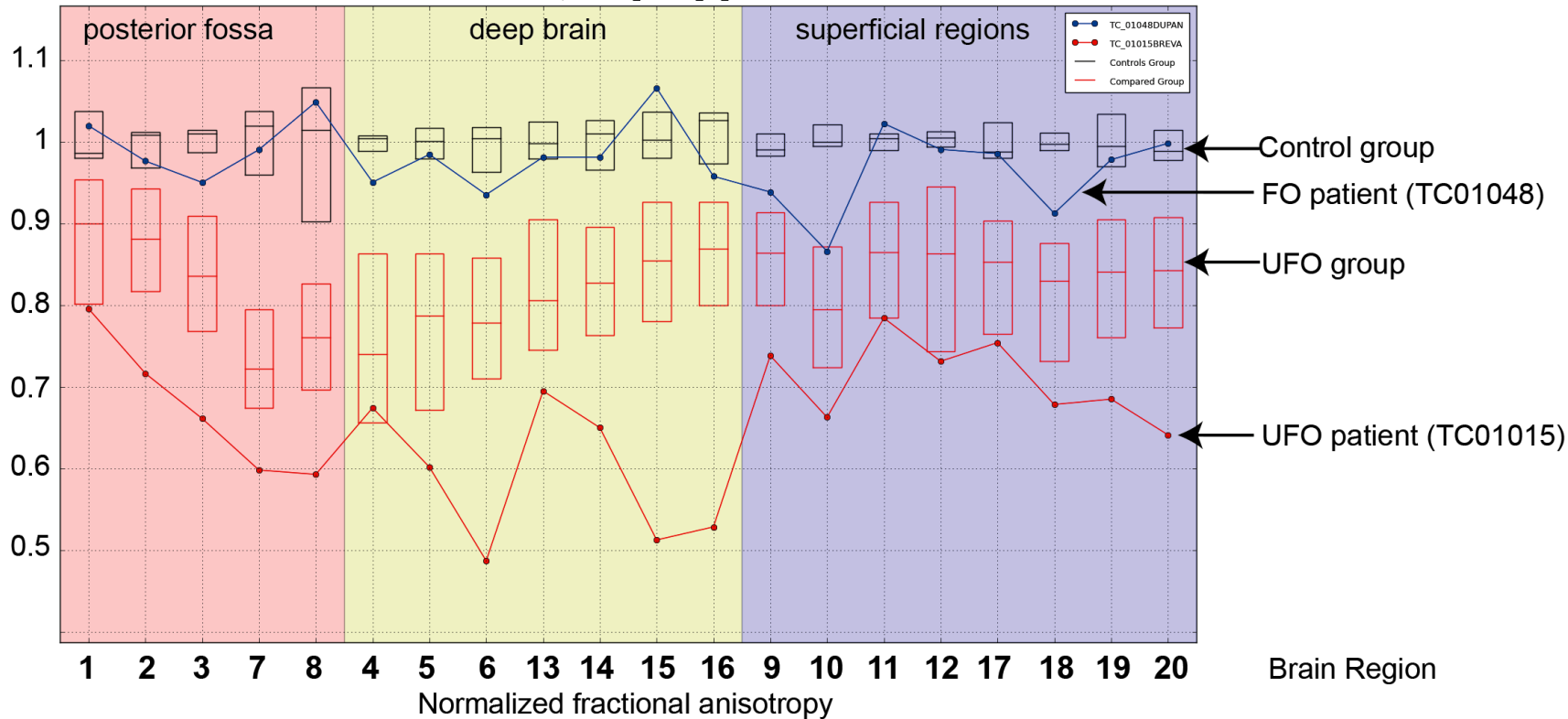


Favorable outcome patient (TC01048)

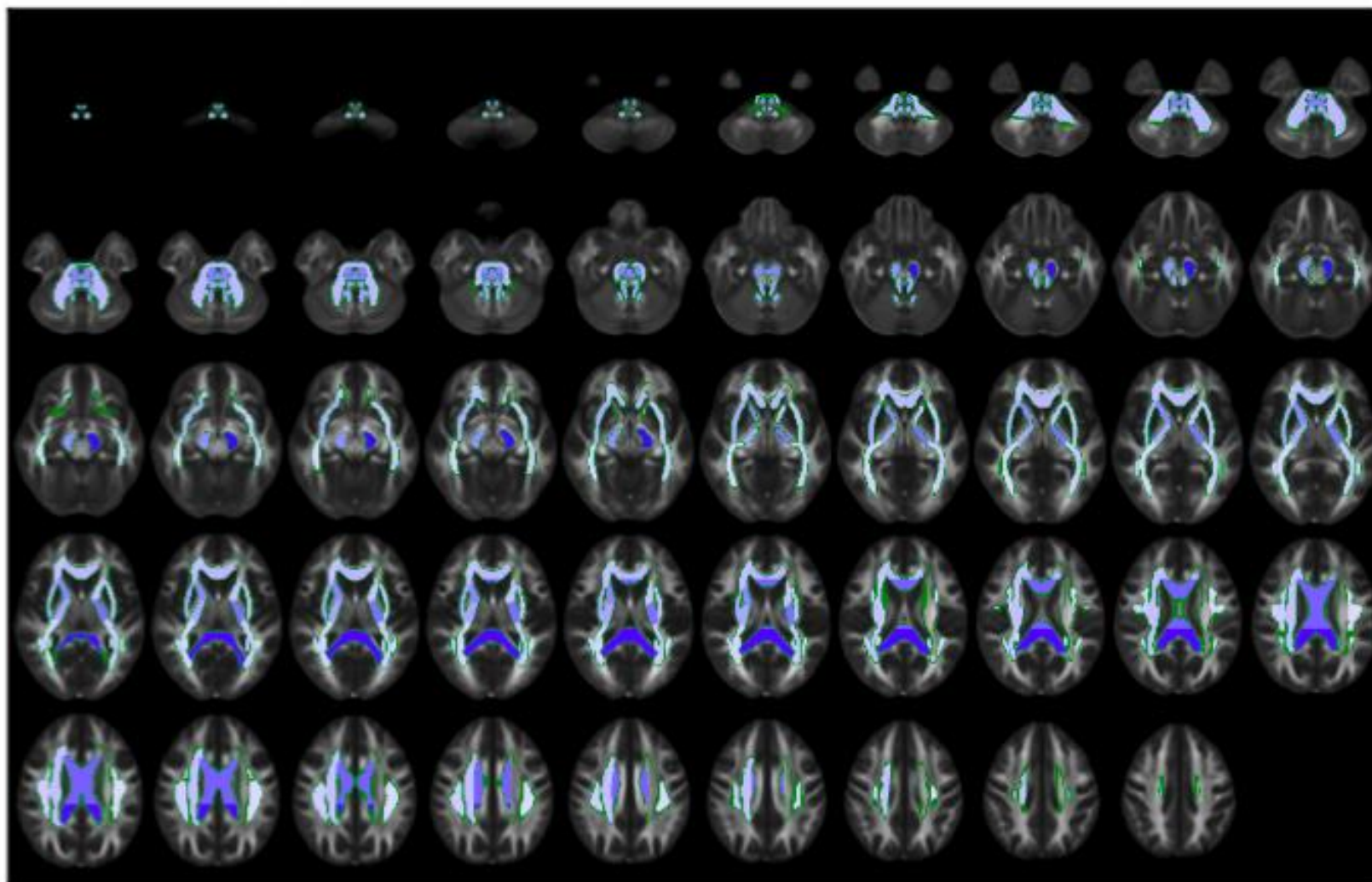


Unfavorable outcome patient (TC01015)

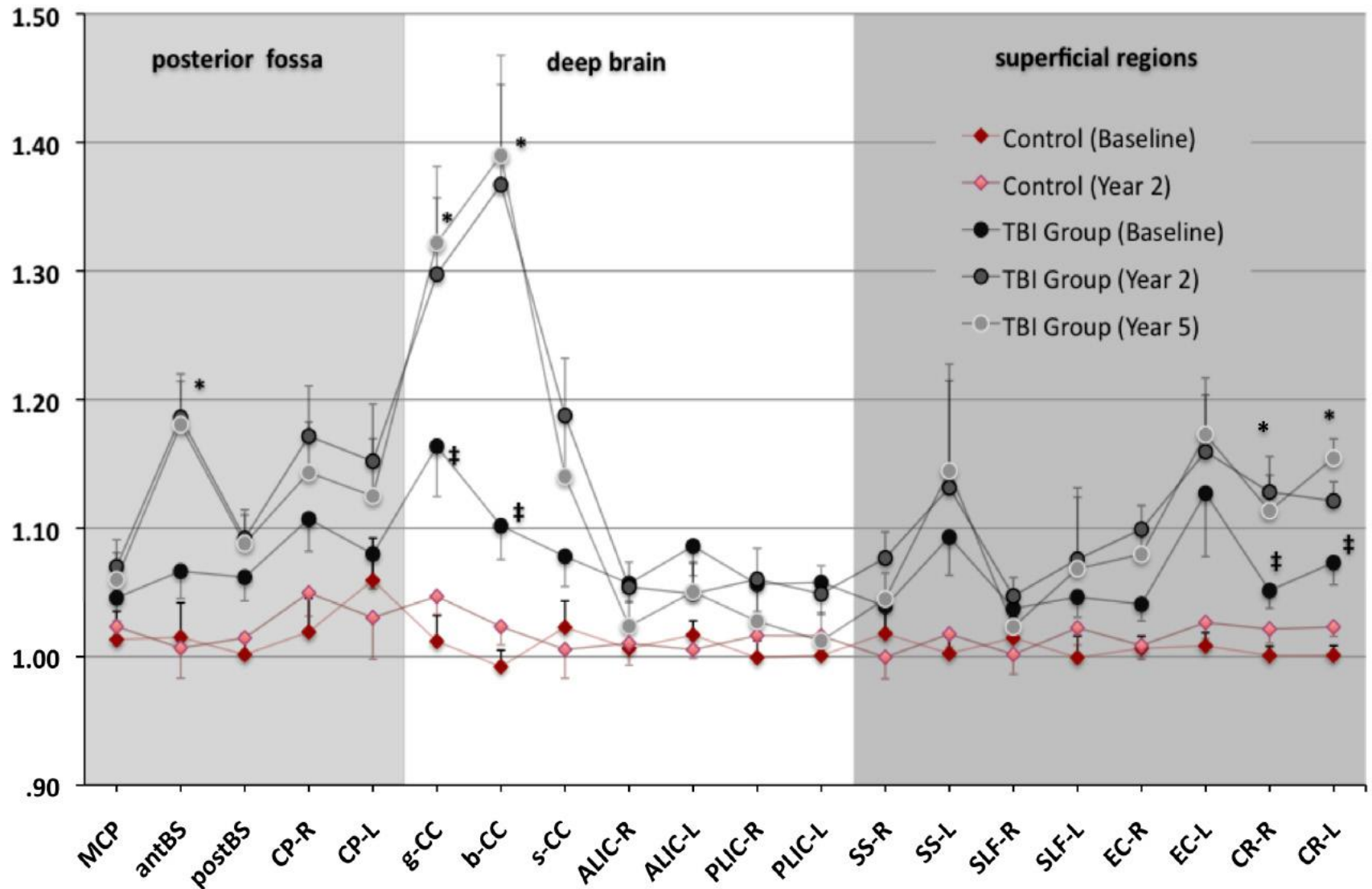




Regional FA differences relative to normal values

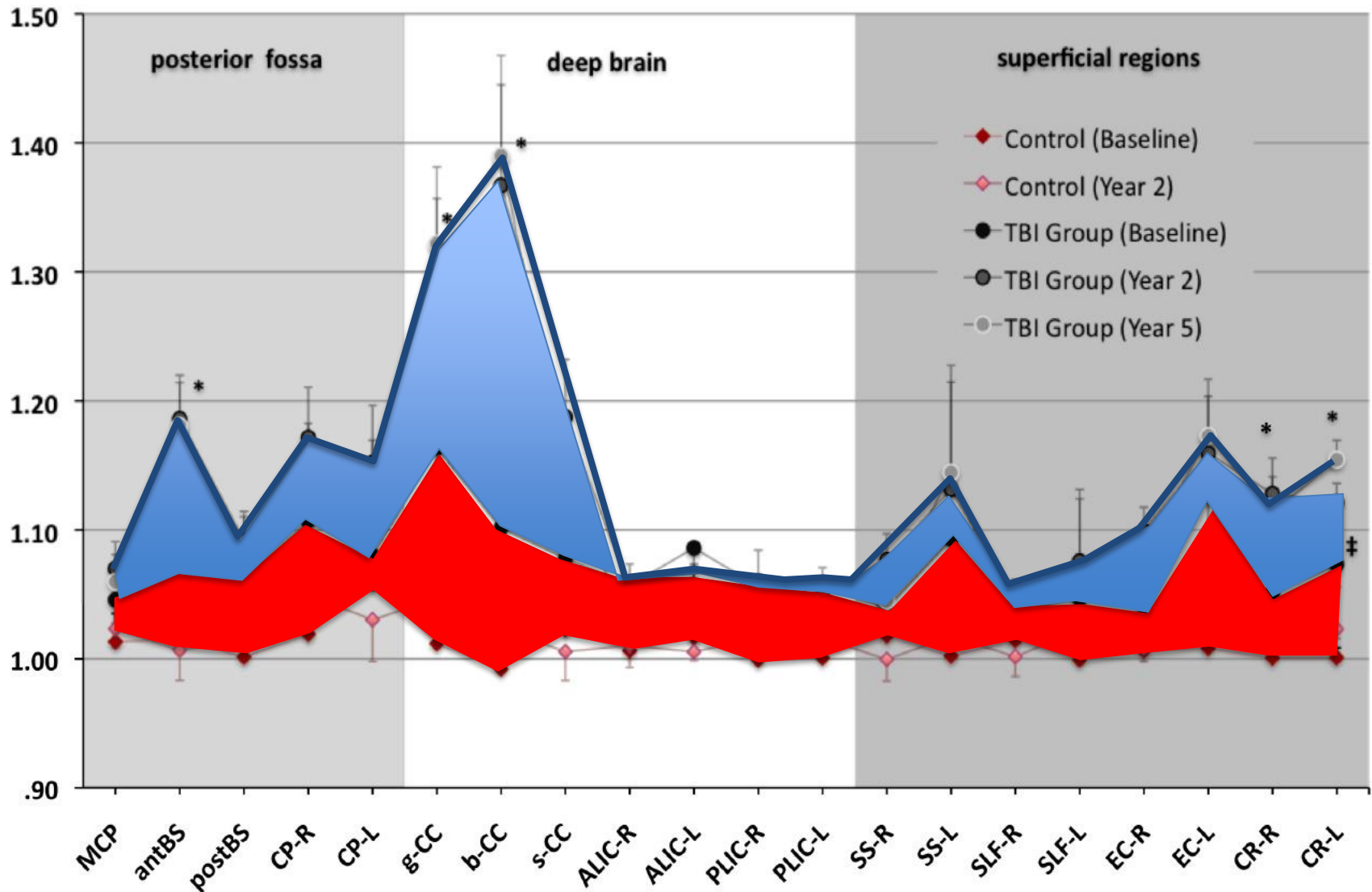


Radiological Convention <-Right|Left->



Suivi à 5 ans de TCG. Diffusibilité radiaire

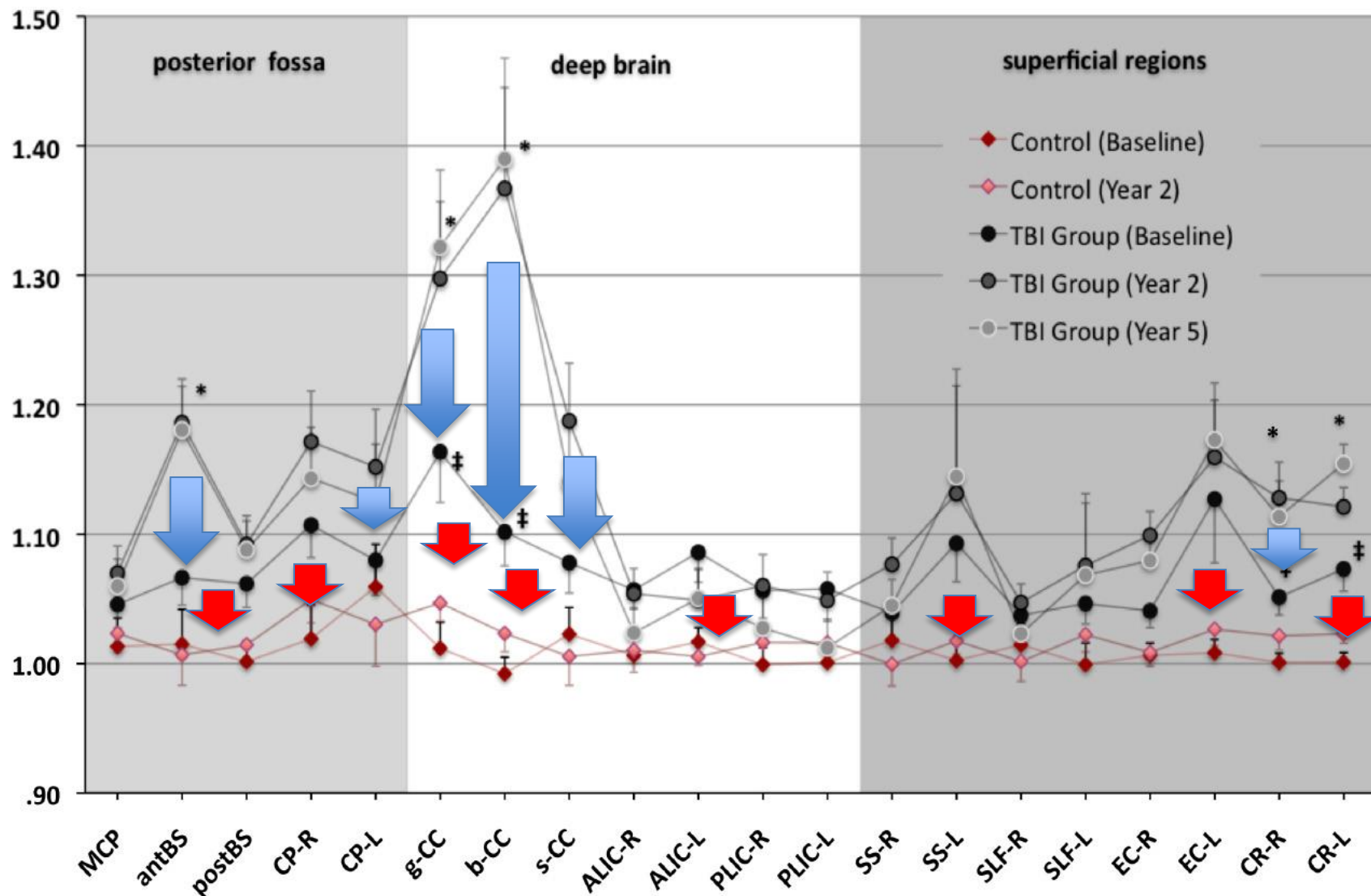
Lésion primaire **Neurodégénérescence secondaire**



Suivi à 5 ans de TCG. Diffusibilité radiaire

Drug for primary insult

Stimulation of neuroregeneration

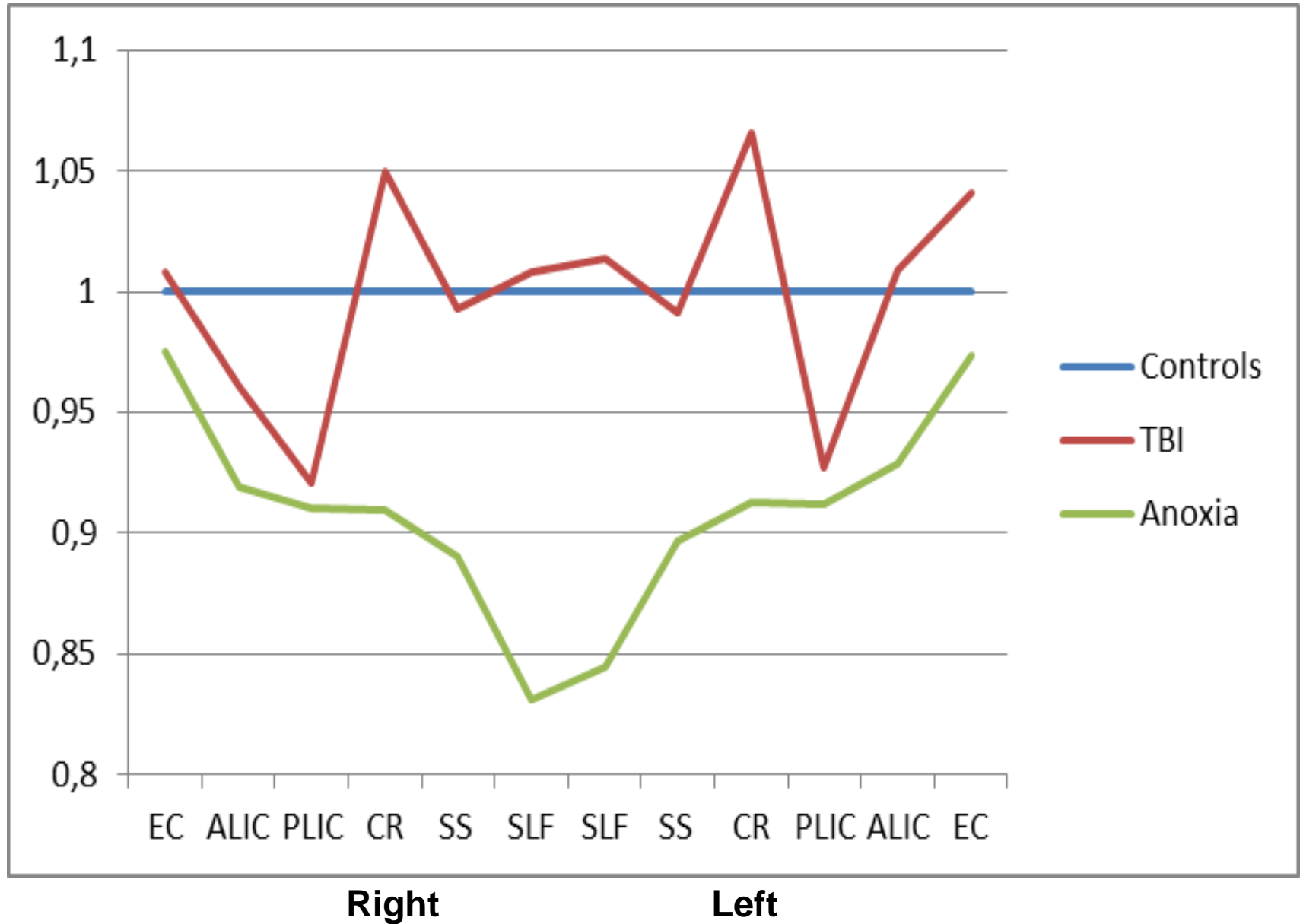


Suivi à 5 ans de TCG. Diffusibilité radiaire

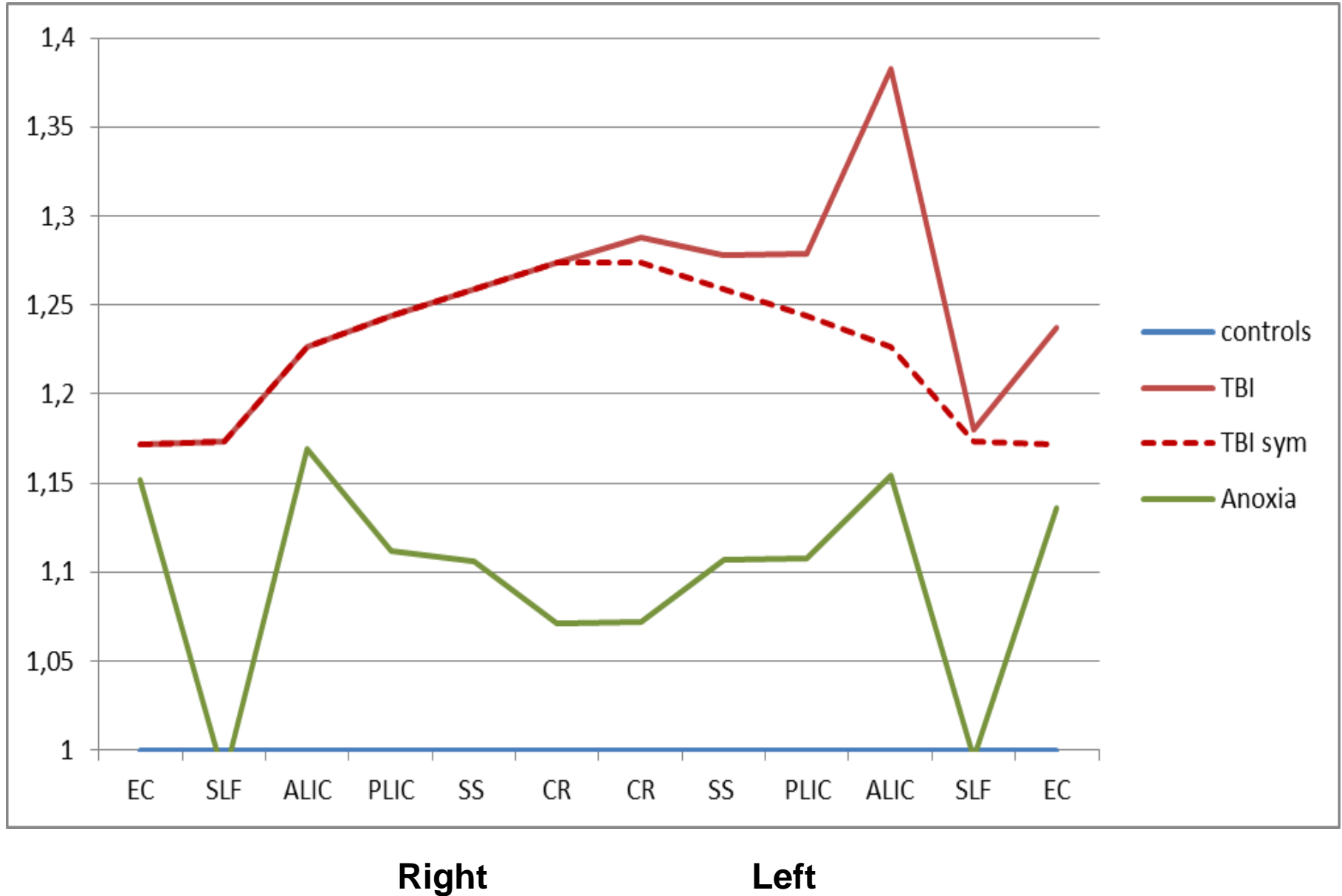
Quelles sont les différences entre AC et TBI ?

- Généralement poolés dans les études en IRMf des patients végétatifs et pauci relationnels
- Mécanismes des maladies très différents
- Etude comparative des malades d'évolution défavorable
 - Arrêt cardiaque N=49
 - TBI N=40

Unfavorable outcome : Hemispheres, axial

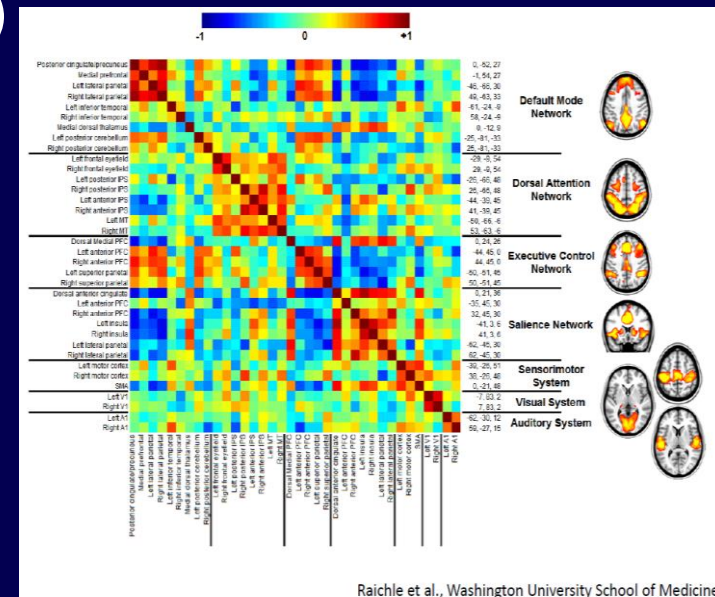


Unfavorable outcome : Hemispheres, radial



Conclusion

- Intérêt du tenseur de diffusion dans le bilan des traumatismes crâniens grave
- Permet une évaluation quantitative de l'atteinte
- Intérêt théorique potentiel pour l'évaluation pharmacologique et l'exploration physiopathologique
- Autres séquences ? (spectro, IRMf)



Merci