Lesion Detection on Structural Imaging

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Presenter Disclosure

- Faculty: Dewi Schrader
- Relationships with commercial interests: none
- Honoraria: none
- Consulting Fees: none
- Other: none

Disclosure of Commercial Support

- none to disclose

Mitigating Potential Bias

- not applicable

MRI in epilepsy

high resolution T1

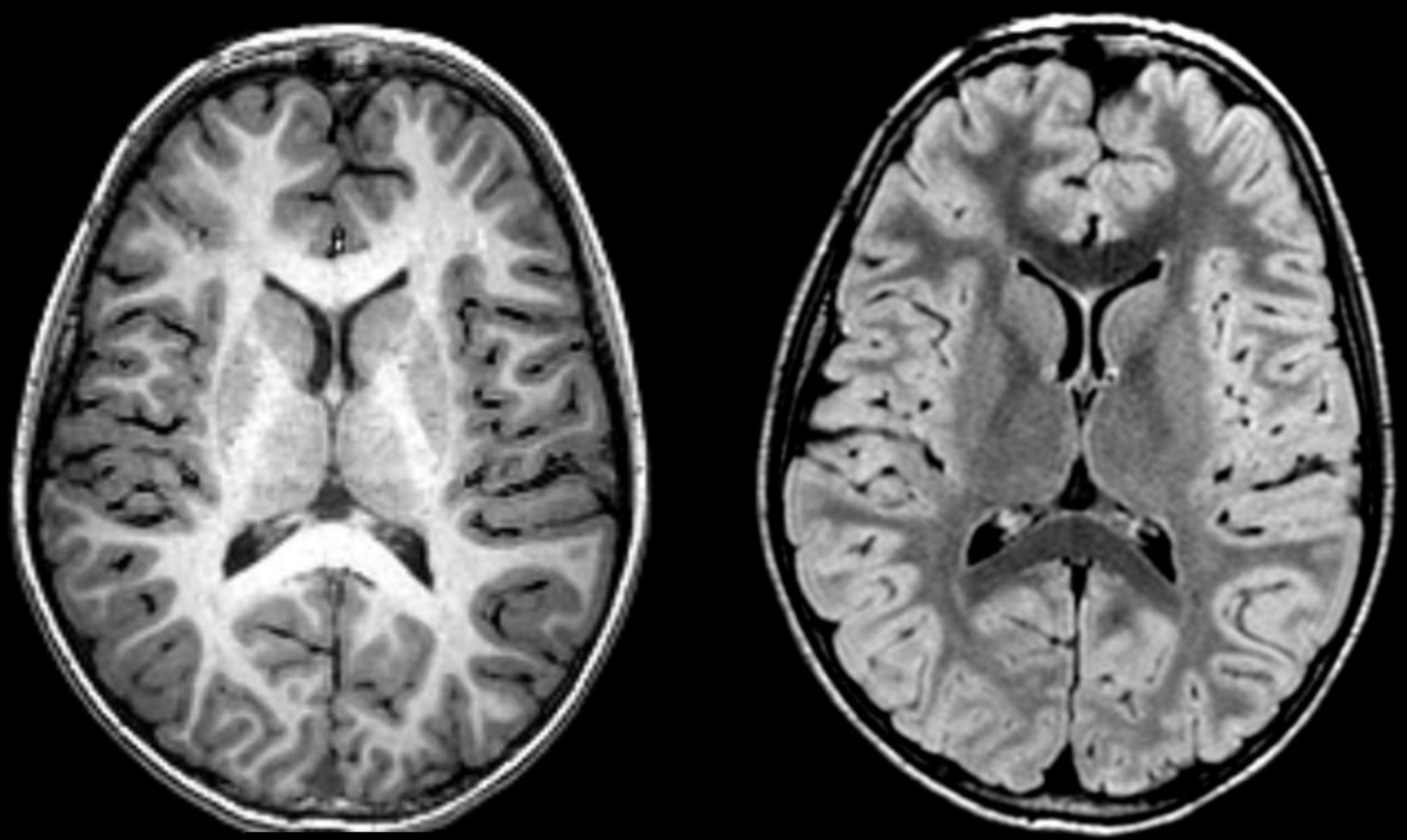
T2

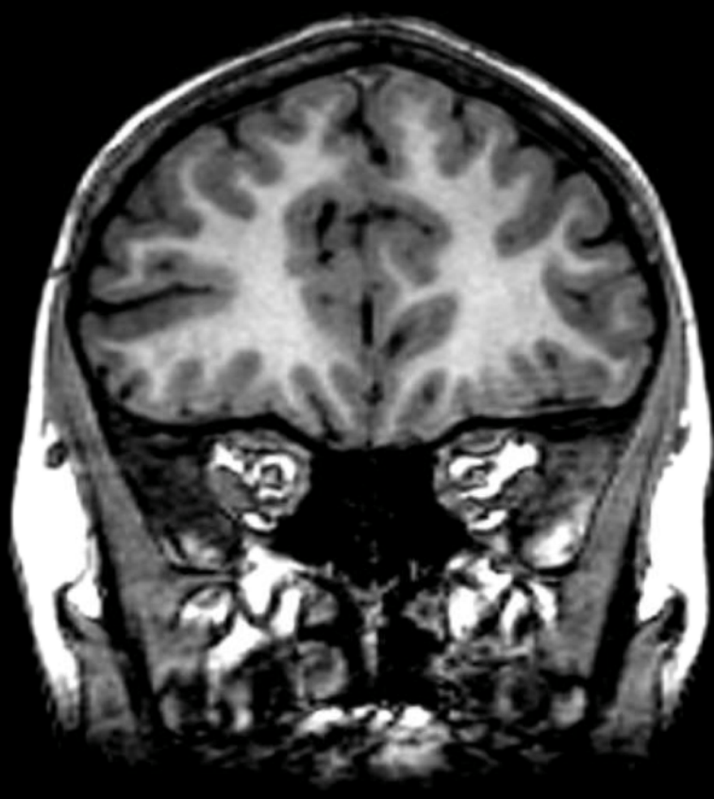
FLAIR

ideally 3D with
isotropic voxels

susceptibility weighted
imaging

Explosive onset of epilepsy at 3 years





2 year old with epilepsy and a history of febrile status and meninigitis at 6 months

MRI lesion

Best predictor of post surgical outcome

35 studies

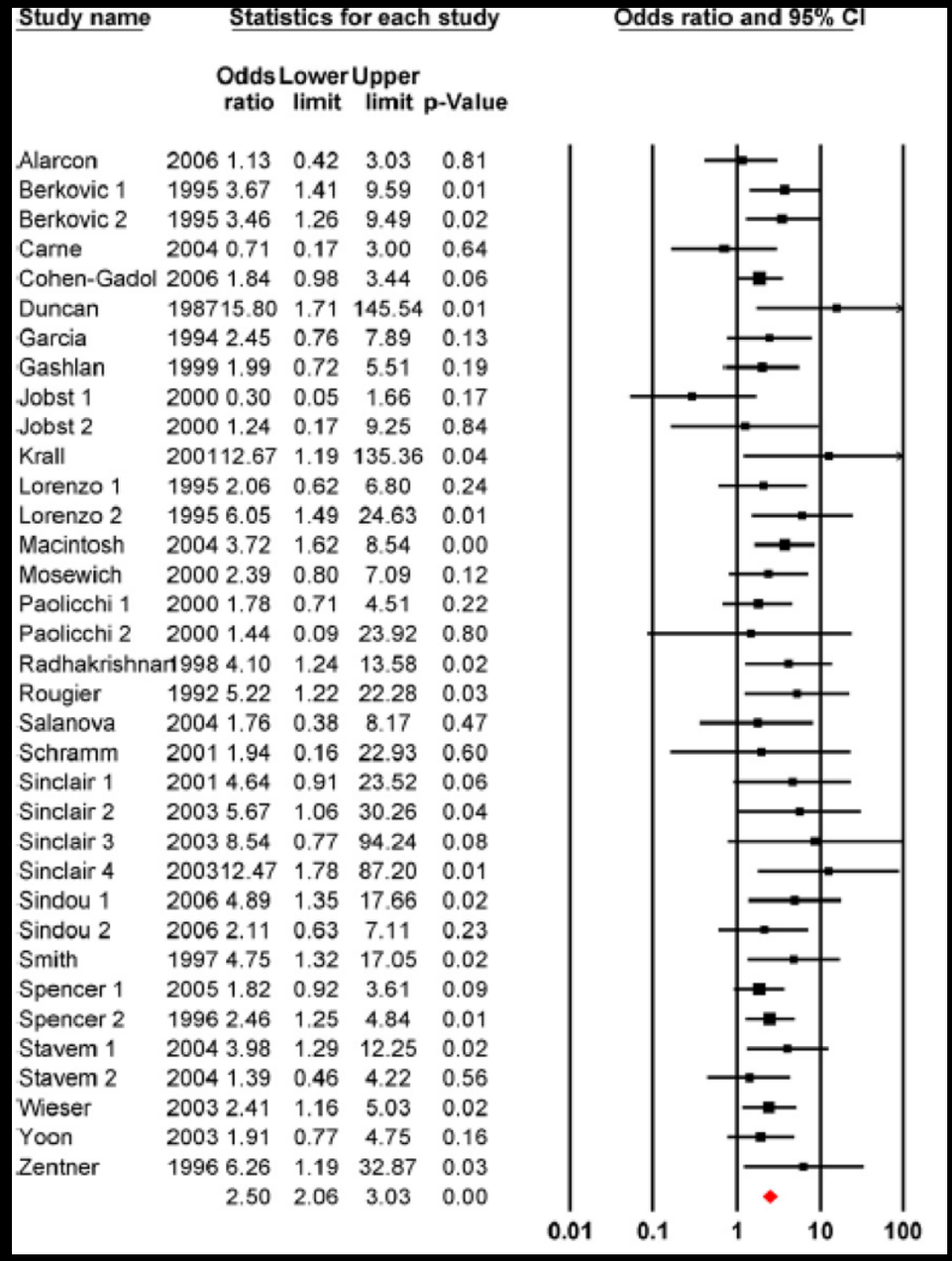
2860 patients with lesions

697 patients non-lesional

OR for seizure freedom based on MRI 2.4 (95%CI 1.8, 3.2, p < 0.001)

TLE OR 2.63 (95%CI 1.79, 3.85, p < 0.001)

extraTLE OR 2.6, 95%CI 1.3, 5.4 (p < 0.001)



Téllez-Zenteno et al Epilepsy Res. 2010

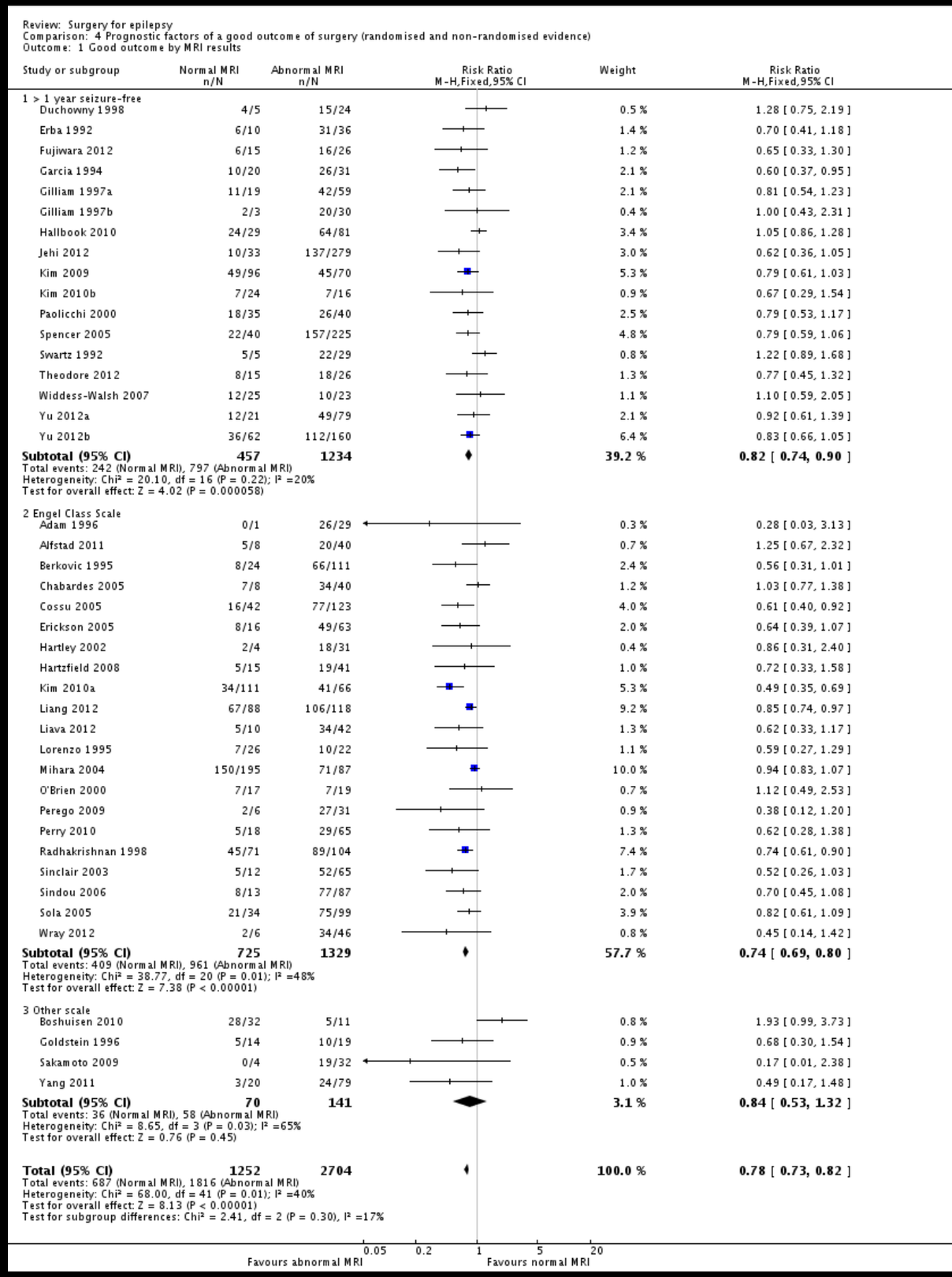
2015 Cochrane review

identified 177 studies investigating surgical outcome

42 studies 3956 participants reported data on pre-operative MRI results

abnormal pre-operative MRI predictive of good outcome

RR 0.78 (95% CI 0.73 to 0.82, P value < 0.00001)



West, S et al. Cochrane Database Syst Rev. 2015

MRI negative patients

only 50% of patients have lesion on conventional MRI

review of pathology results of MRI negative patients from 94 surgical studies from 2005-2015

most common pathology FCD, gliosis and HS

Pathology	n *(%)*
Focal cortical dysplasia	
ILAE Ib	9 (9)
ILAE Ic	28 (30)
ILAE IIb	4 (4)
ILAE IIIa	2 (2)
Palmini IA	26 (27)
Palmini IA+hippocampal sclerosis	2 (2)
Palmini IA+Nodular heterotopia	2 (2)
Palmini IB	9 (9)
Palmini IIB	4 (4)
Total	43 (45)
Gliosis only	21 (22)
Hamartia+gliosis	12 (13)
Hippocampal sclerosis only	9 (9)
No pathology identified	7 (7)
Dual osseous metaplasia	1 (1)
Hippocampal neuronal loss	1 (1)
Granular cell dispersion in hippocampus	1 (1)
Total	*95*

Wang 2013 Modern Pathology

Focal Cortical Dyplasia I

disordered radial or tangential lamination

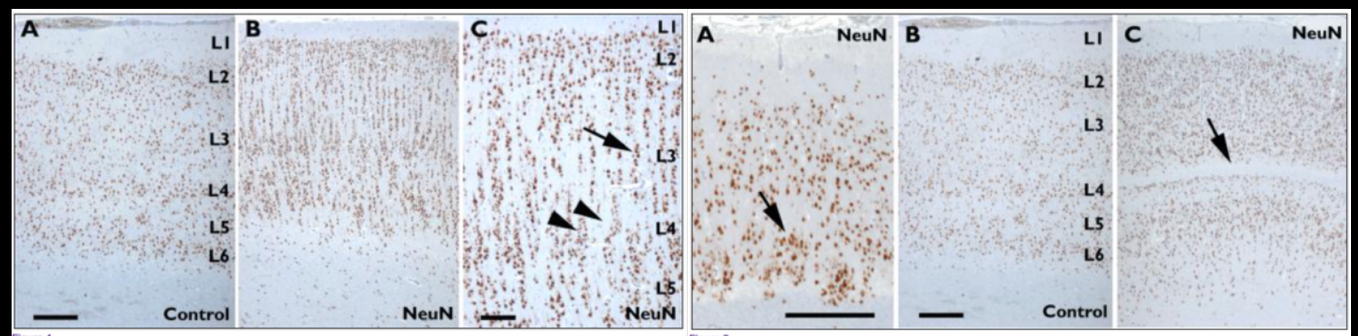
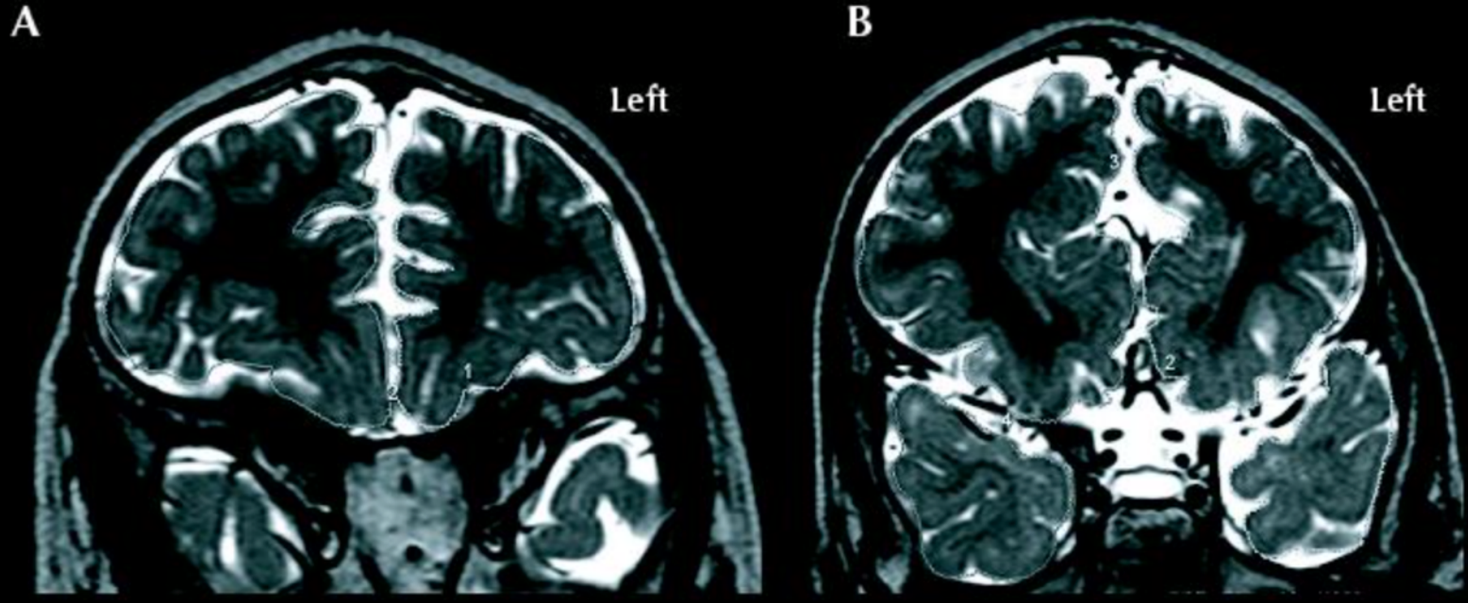


Figure 1
Histopathological findings in FCD Type Ia (abnormal radial lamination and abundant microcolumns)

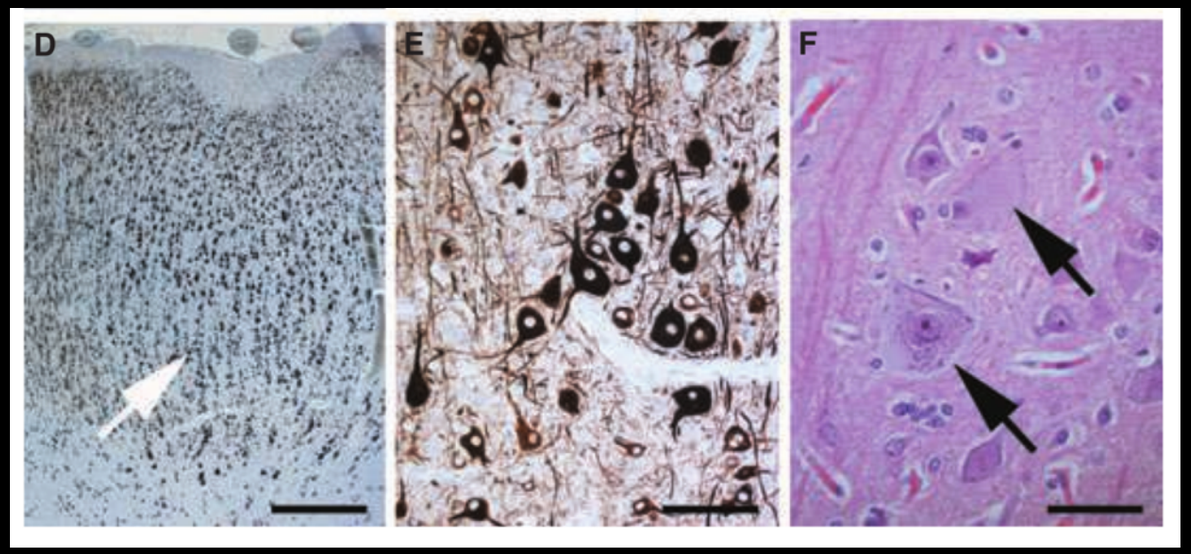
Figure 2
Histopathological findings in FCD Type Ib (abnormal tangential layer composition)

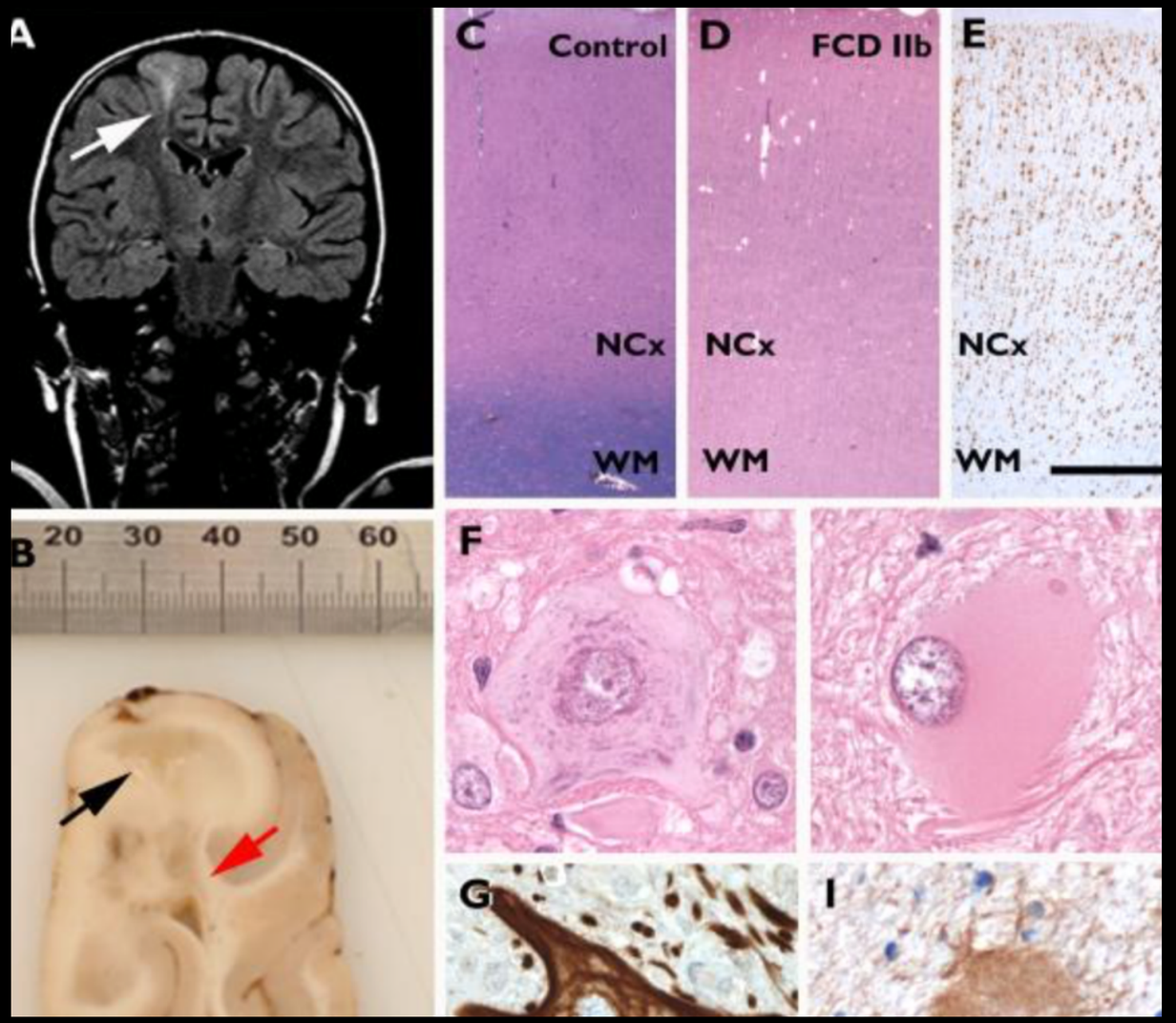
cortical thinning
intensitity changes
blurring
lobar hypoplasia



Blumcke et al Epileptic Disorders 2010, Blumcke et al, Epilepsia 2011

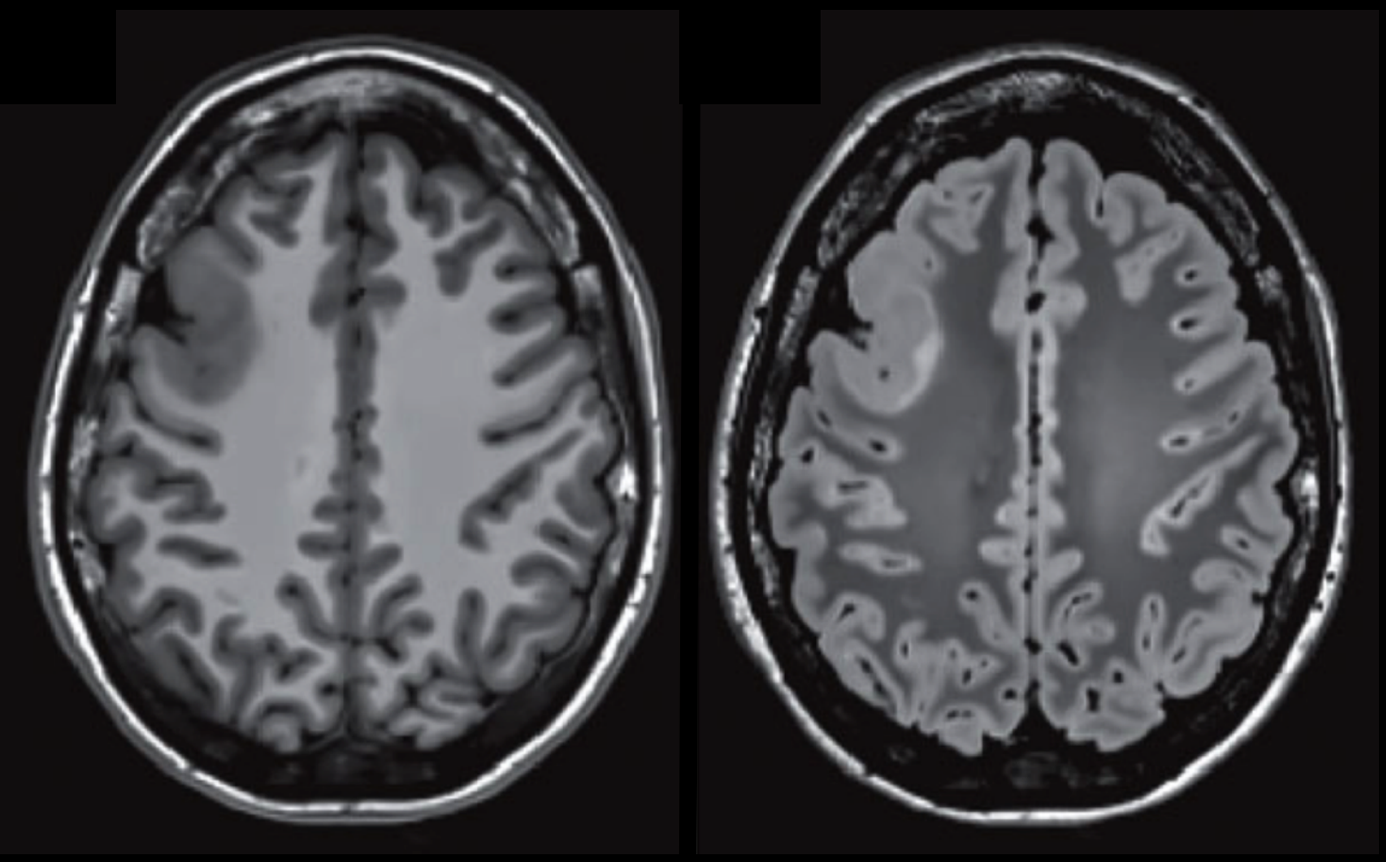
Focal Cortical Dysplasia II





Blumcke et al, Epilepsia 2011

Focal Cortical Dysplasia II



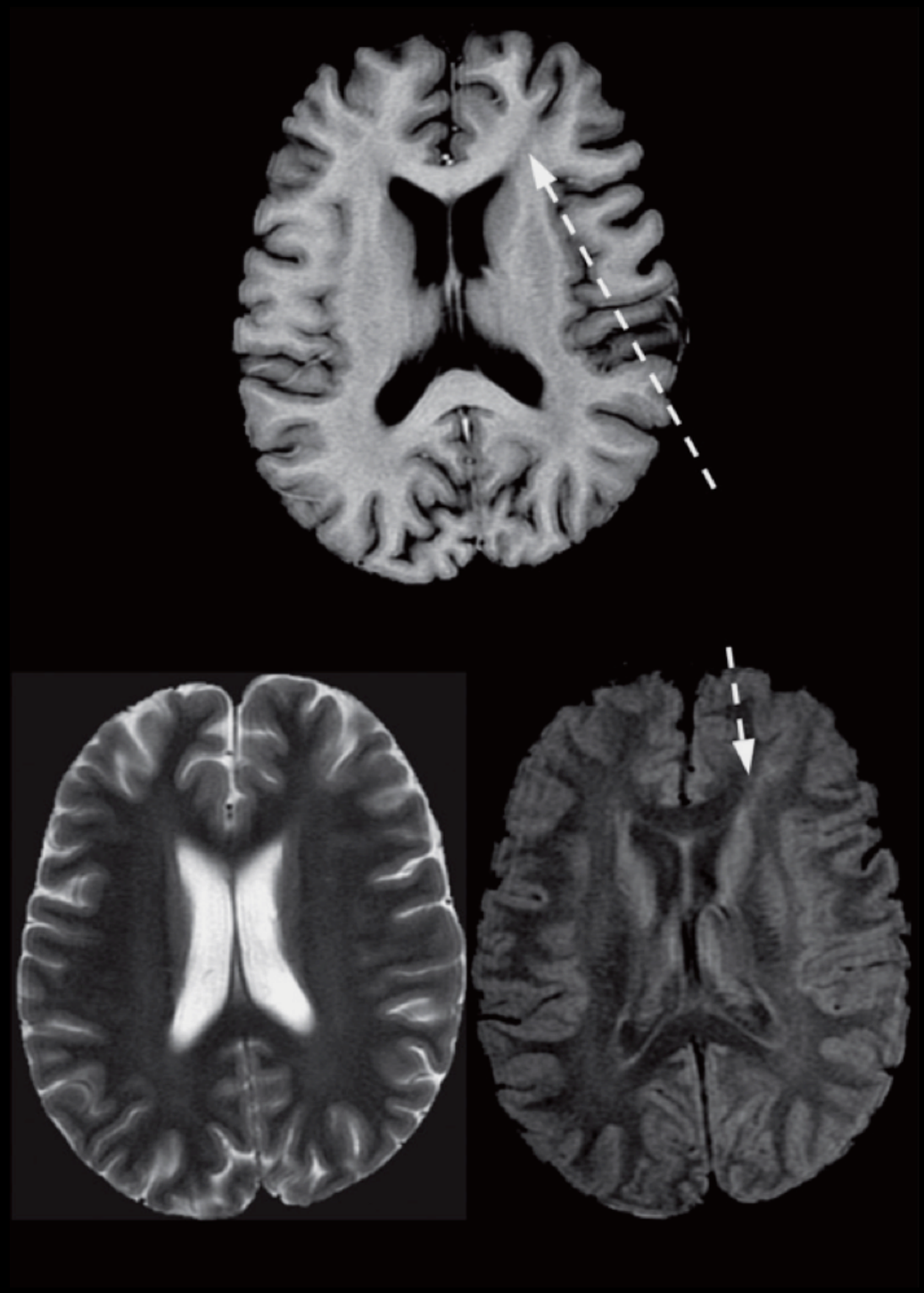
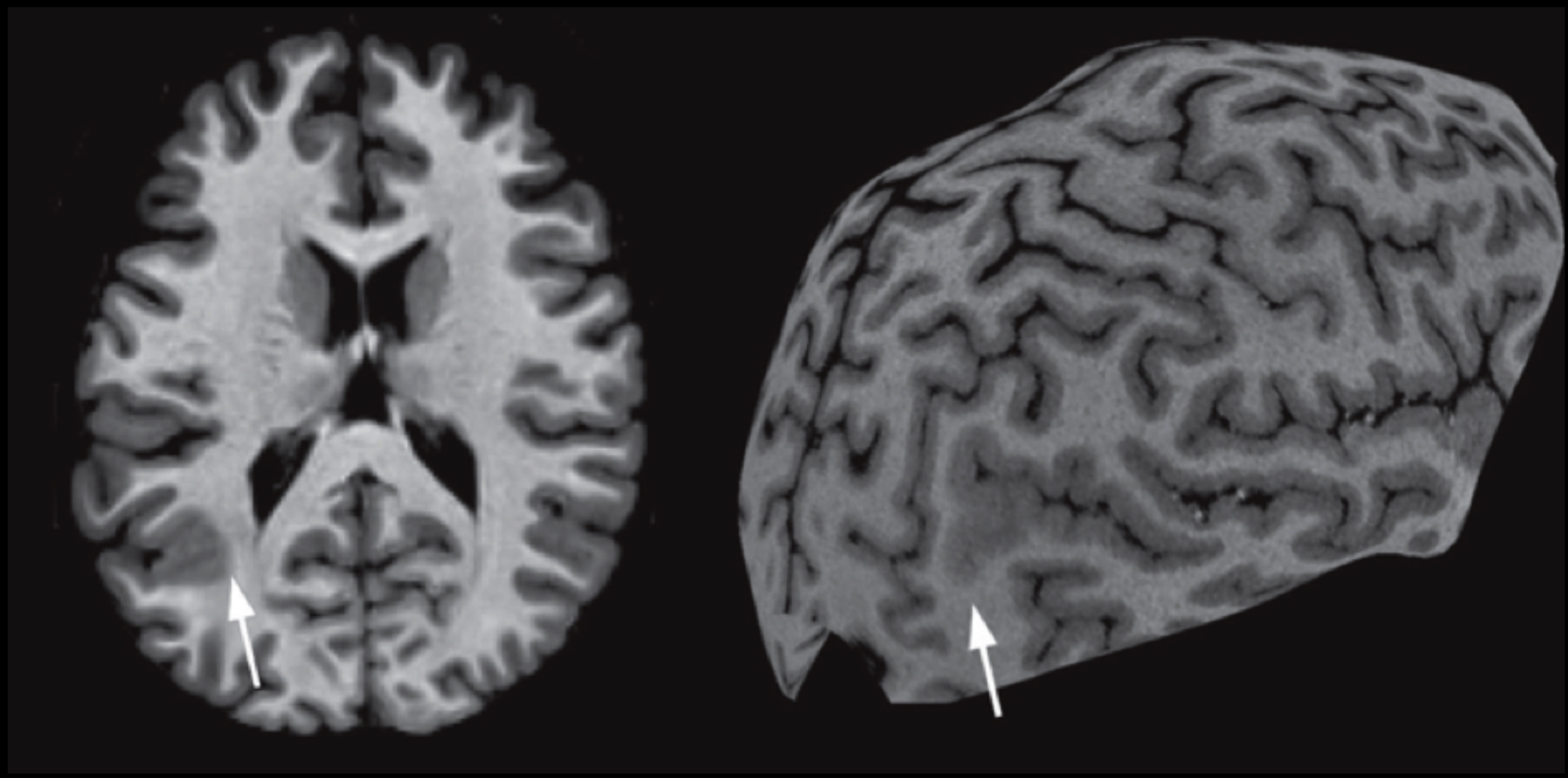


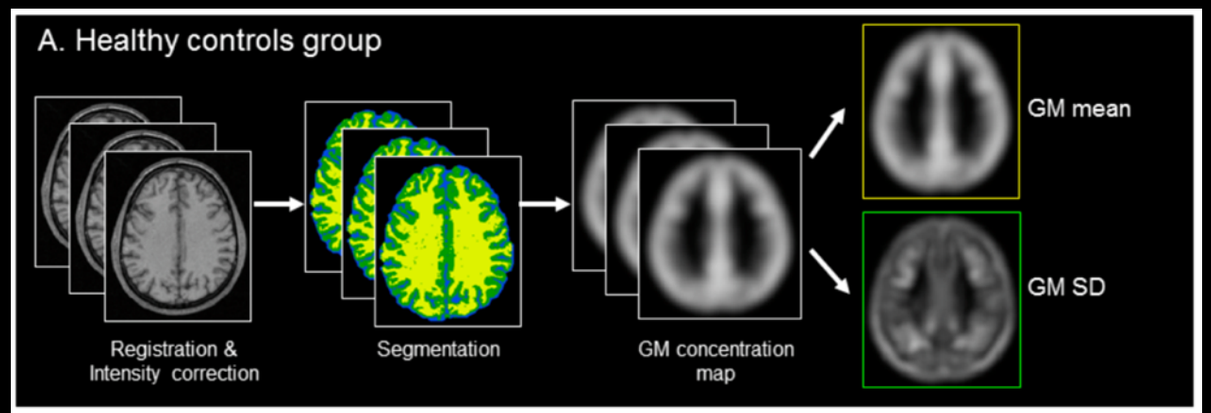
Image Processing

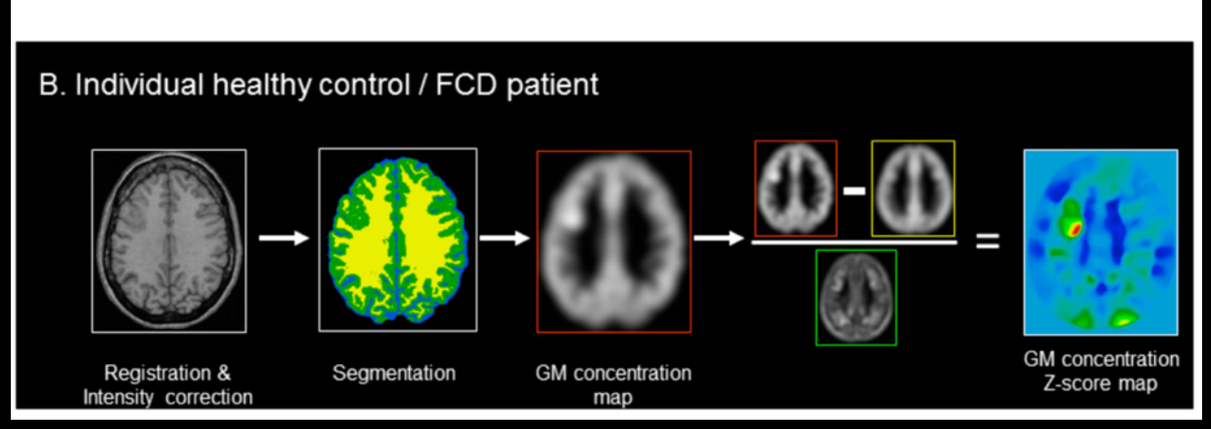
- model shape and folding complexity of tissue
- no a priori assumptions
- measure subtle changes in vivo
- no increase in scanner time or cost to patient

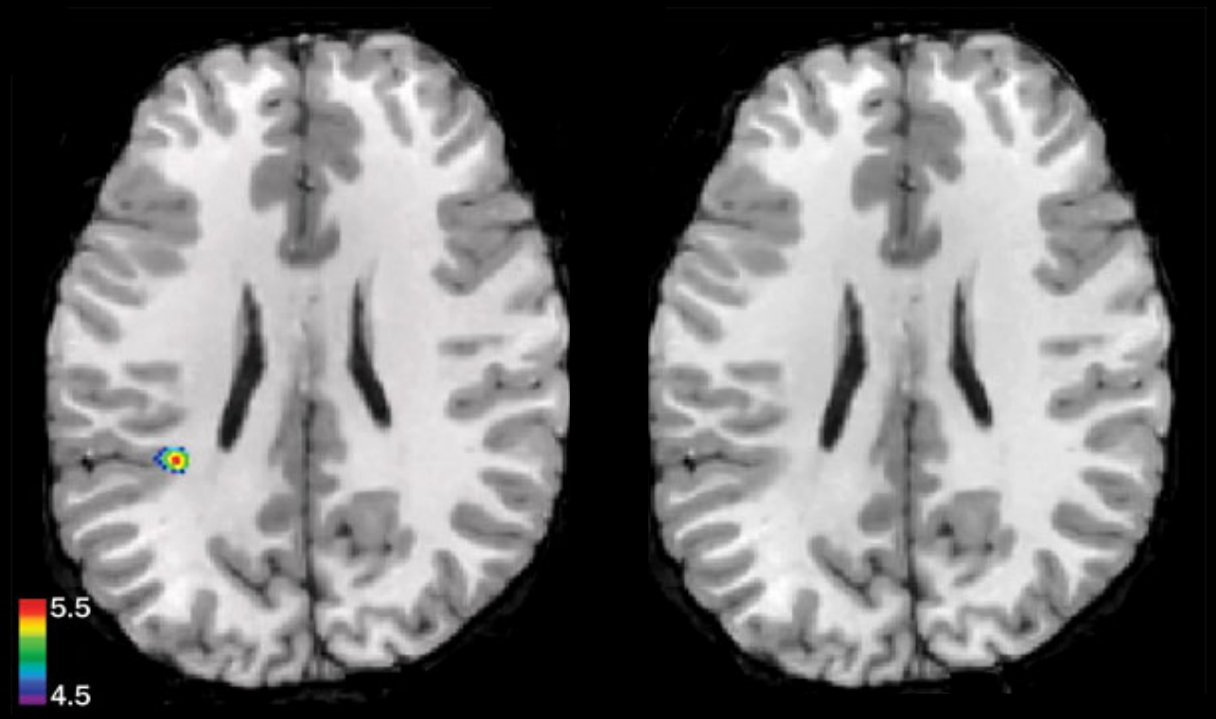
Curvilinear multiplanar reformatting



Voxel-based Morphometry







Identifies up to 86% of MRI visible lesions

Colliot et al, Neuroimage 2006,Bernasconi et al, Nature Reviews Neurology 2011

Voxel-based Analysis

FLAIR
Quantitative MRI

sensitive for MRI visible lesions

<30% sensitivity in MRI negative cases

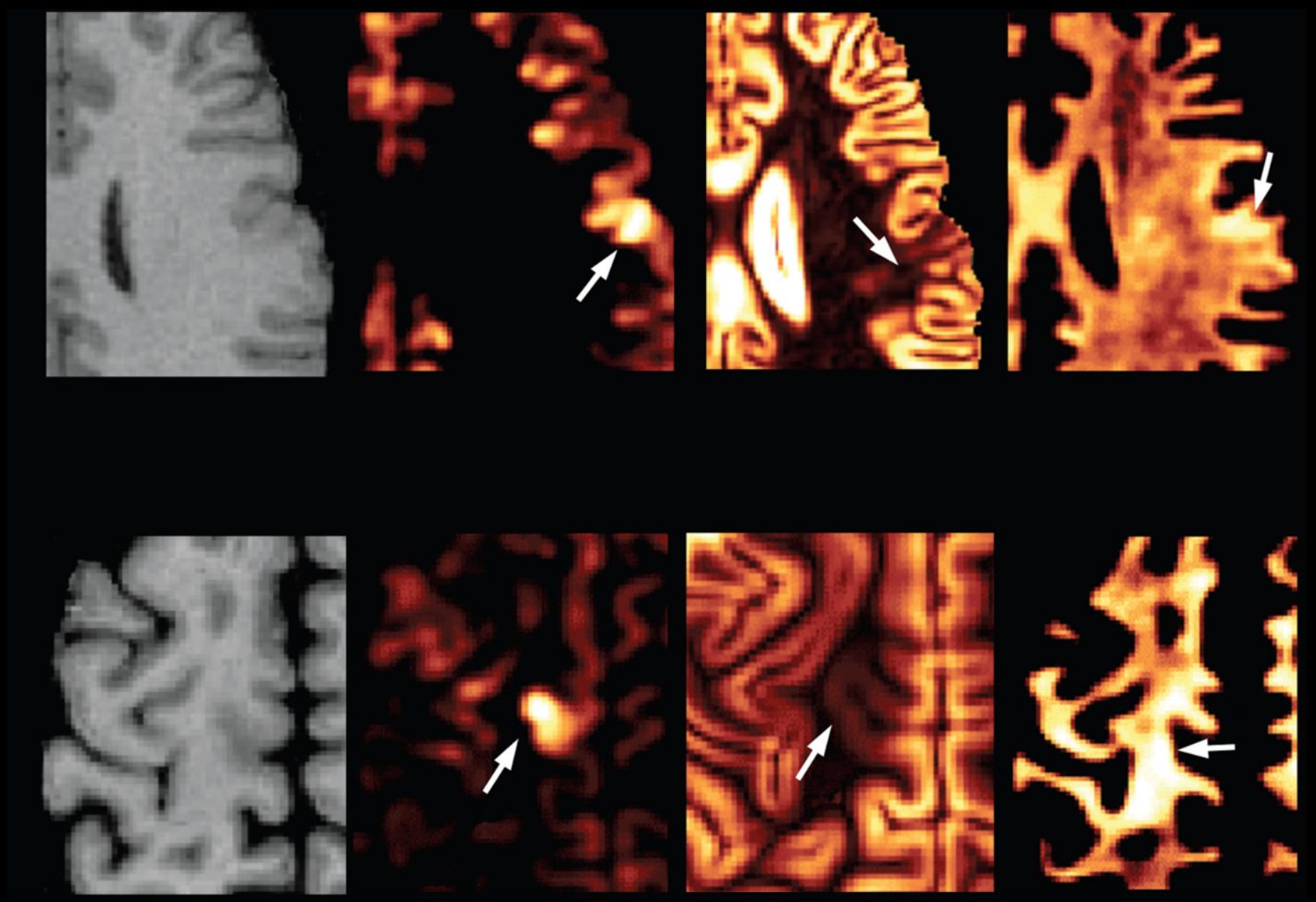
need multi-contrast framework

Table 2 | Voxel-based intensity analysis in MRI-visible cortical malformations

Reference	Contrast	Group (number of patients)	Sensitivity (%)*	Histopathology‡
Rugg-Gunn *et al.* (2003)[81]	MTI	MCD (15) Cryptogenic (19)	87 21	Not applicable
Rugg-Gunn *et al.* (2005)[80]	FLAIR	MCD (20; 5 FCD) Cryptogenic (17)	90 23	Not applicable
Rugg-Gunn *et al.* (2006)[83]	DIR	MCD (14; 5 FCD) Cryptogenic (14)	100 28	Not applicable
Salmenpera *et al.* (2007)[85]	FLAIR DIR MTI	Cryptogenic (49)	15 17 11	1 FCD, subtype not specified; 3 gliosis; 1 hamartoma
Focke *et al.* (2008)[82]	FLAIR	FCD (25)	88	2 Palmini IIb/ ILAE IIb; 1 FCD, subtype not specified; 1 gliosis
Focke *et al.* (2009)[86]	FLAIR	Cryptogenic (70)§	7	Not applicable

Bernasconi, Nature Reviews Neurology 2011

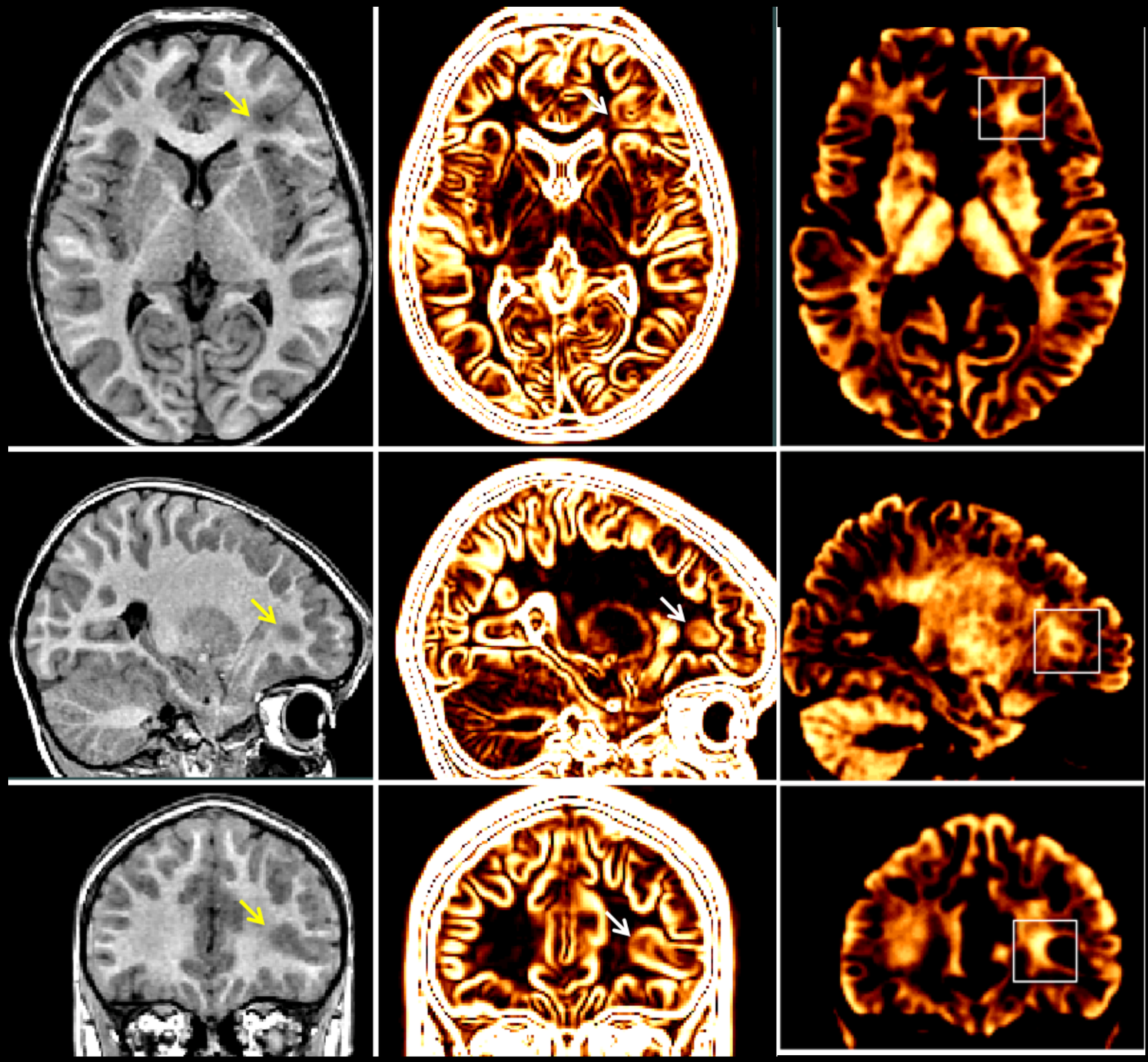
Computer-based models of FCD



combined feature map increases detection by 30%

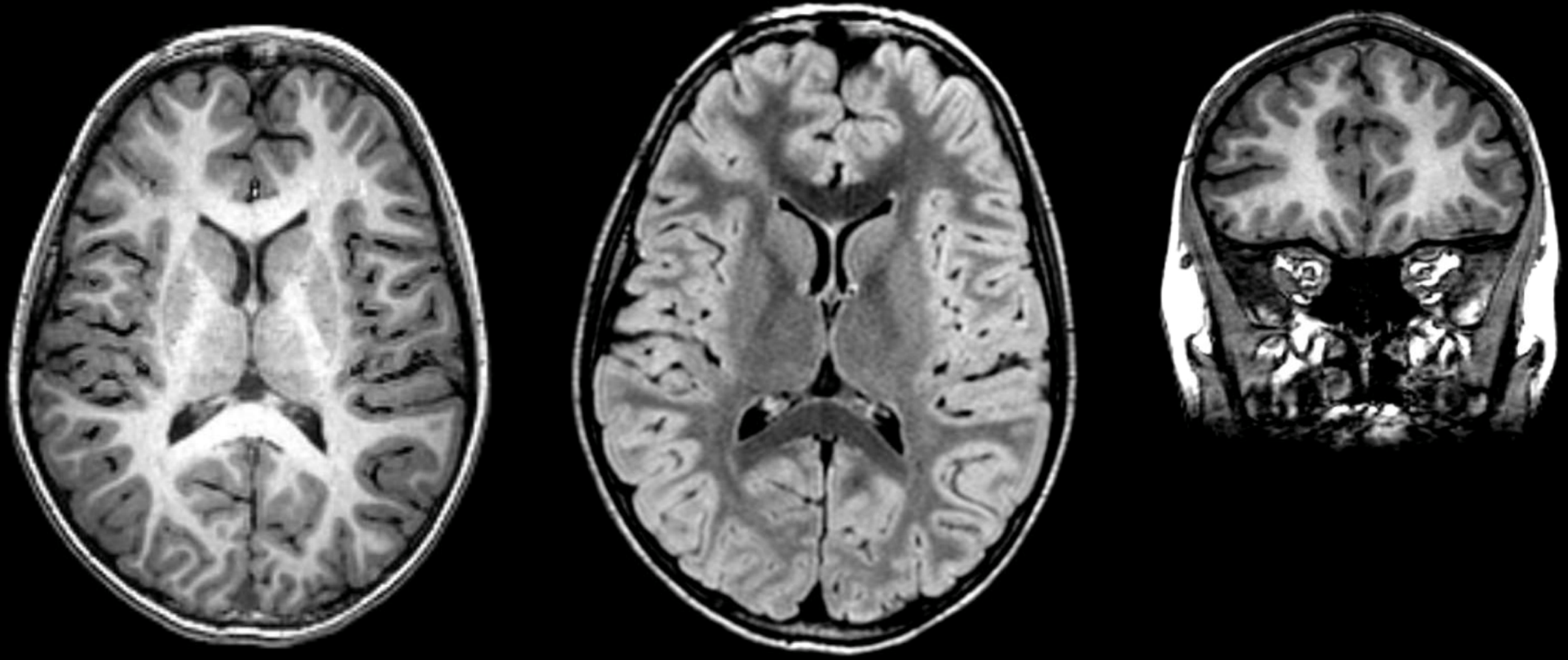
automated classifier incorporating higher-order textural features sensitivity 83% (including 4 /7 overlooked lesions)

Bernasconi 2001, Annals of Neurology, Antel et al 2003 Neuroimage



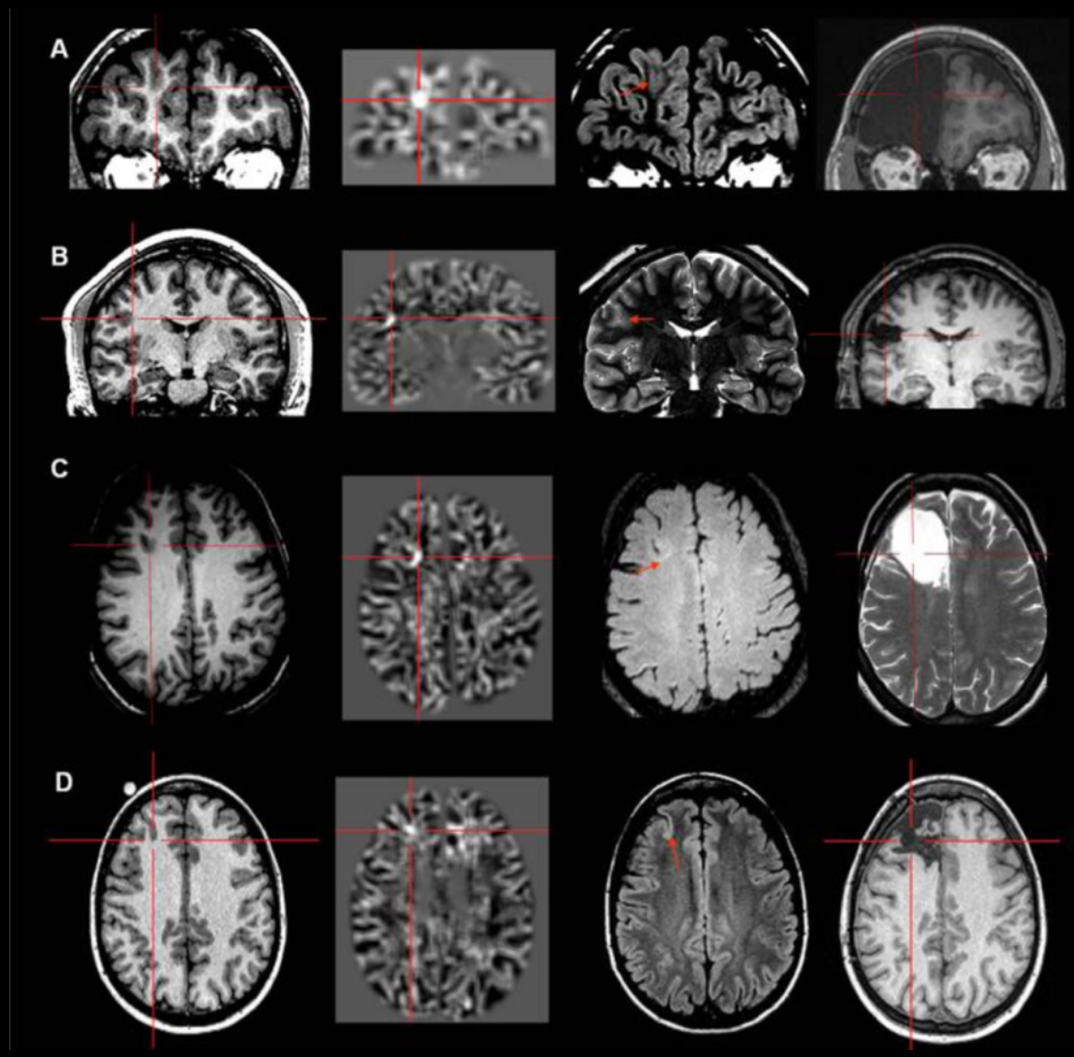
T1 Gradient Map Relative Intensity Map

BCCH patient processed at NOEL



voxel-based morphometric analysis

- software developed by Huppertz that models blurring at GM-WM junction
- series of MRI negative patients
- 150 MRI negative adult patients 43% positive rate, sensitivity of 0.9, and



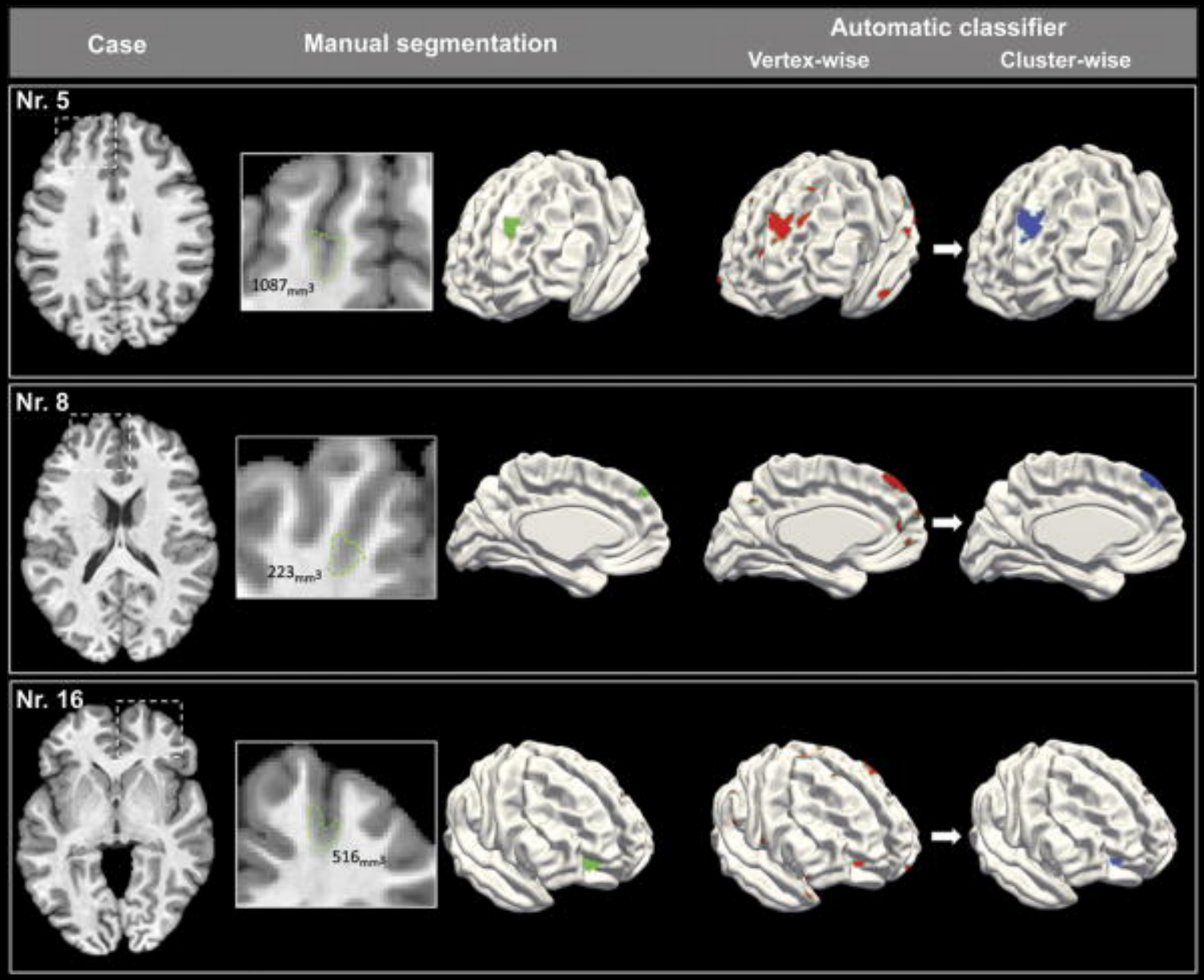
Wang et al, Annals of Neurology 2015

Surface-based models of FCD

morphologic features
- cortical thickness
- curvature
- sulcal depth

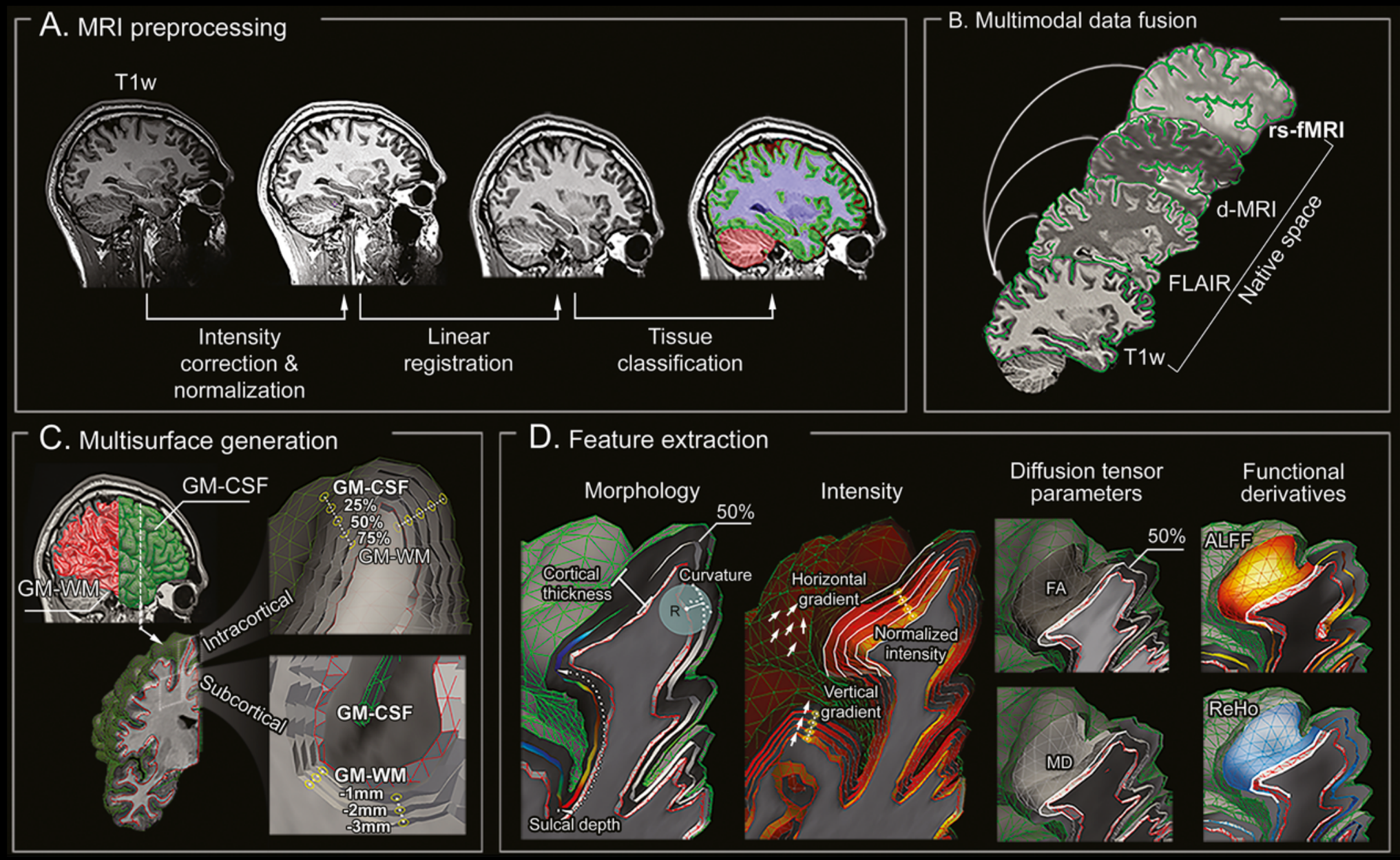
intensity features
- relative intensity
- blurring

Sensitivity 74% in MRI negative patients



Hong et al, 2014 Neurology

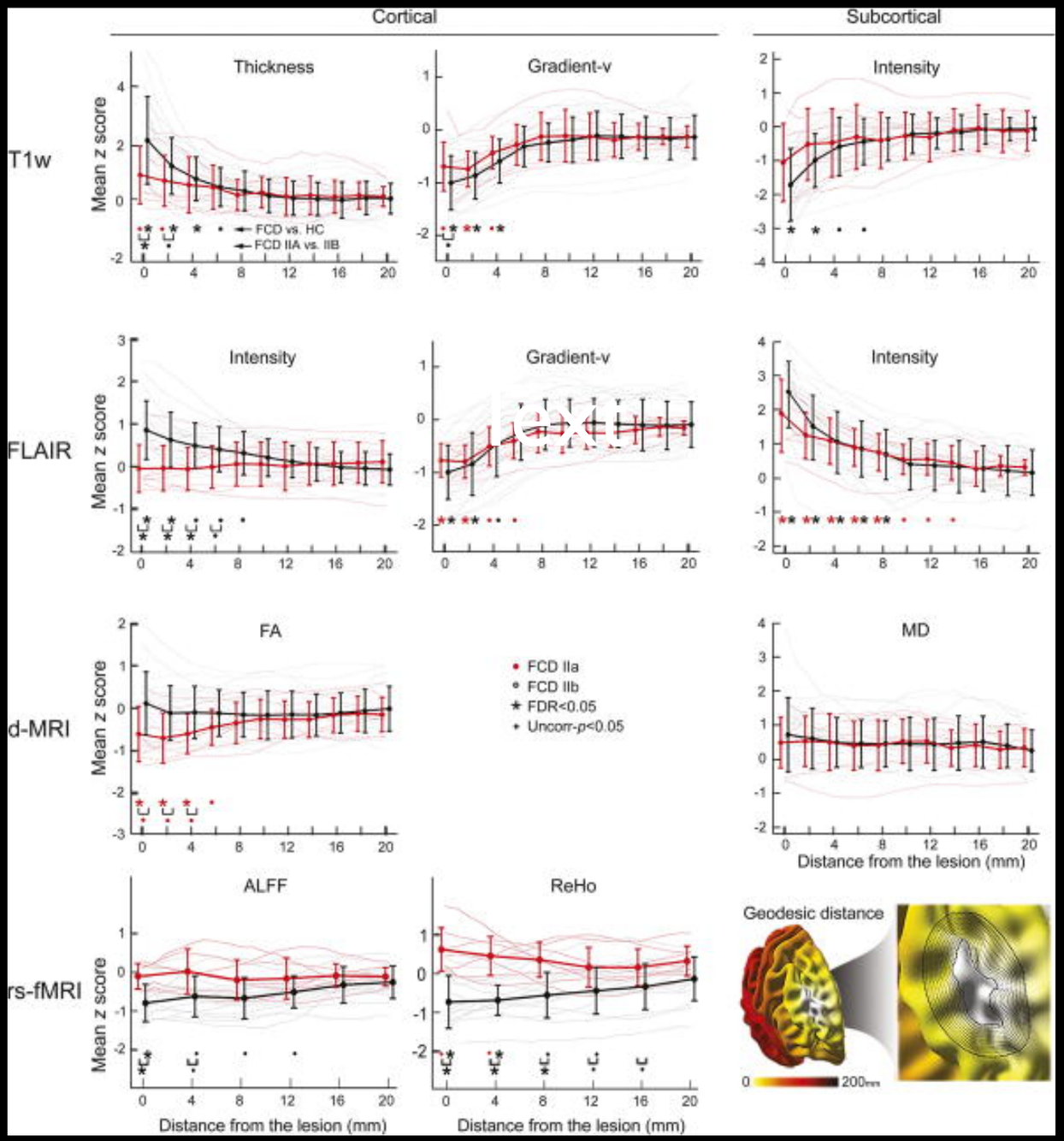
Surface-Based Multimodal Lesion Profiling



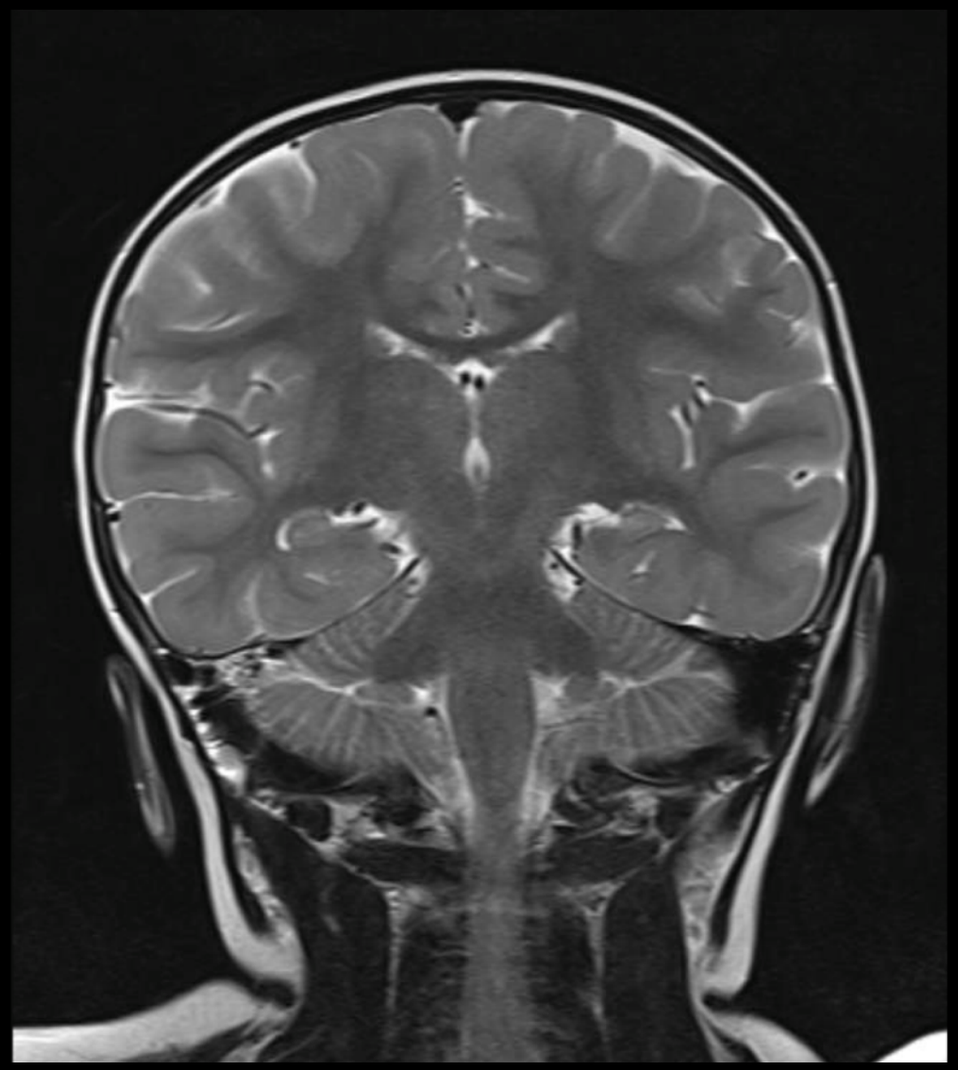
predicted FCD II subtype 85% with 94% specificity

2017 Neurology Hong et. al.

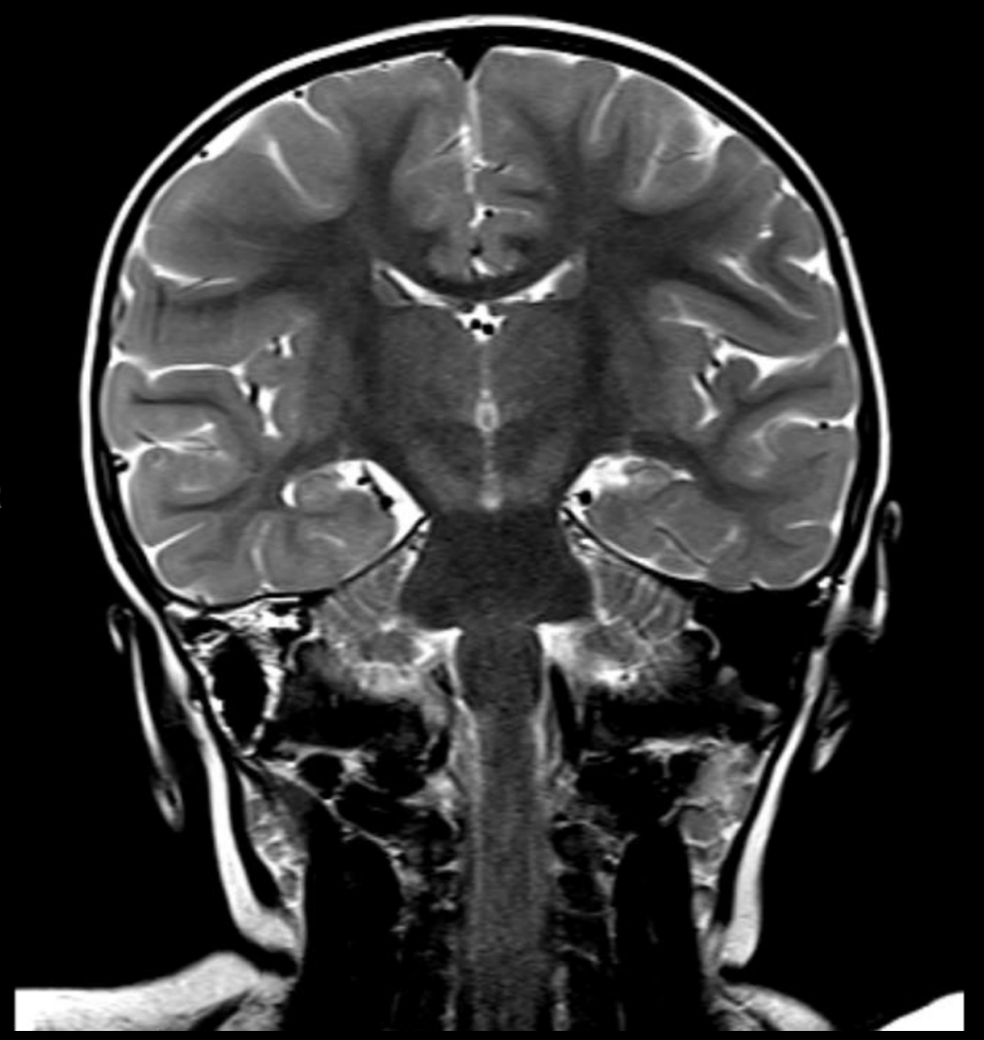
Perilesional mapping



2017 Neurology Hong et. al.



17 mo



2.5 years

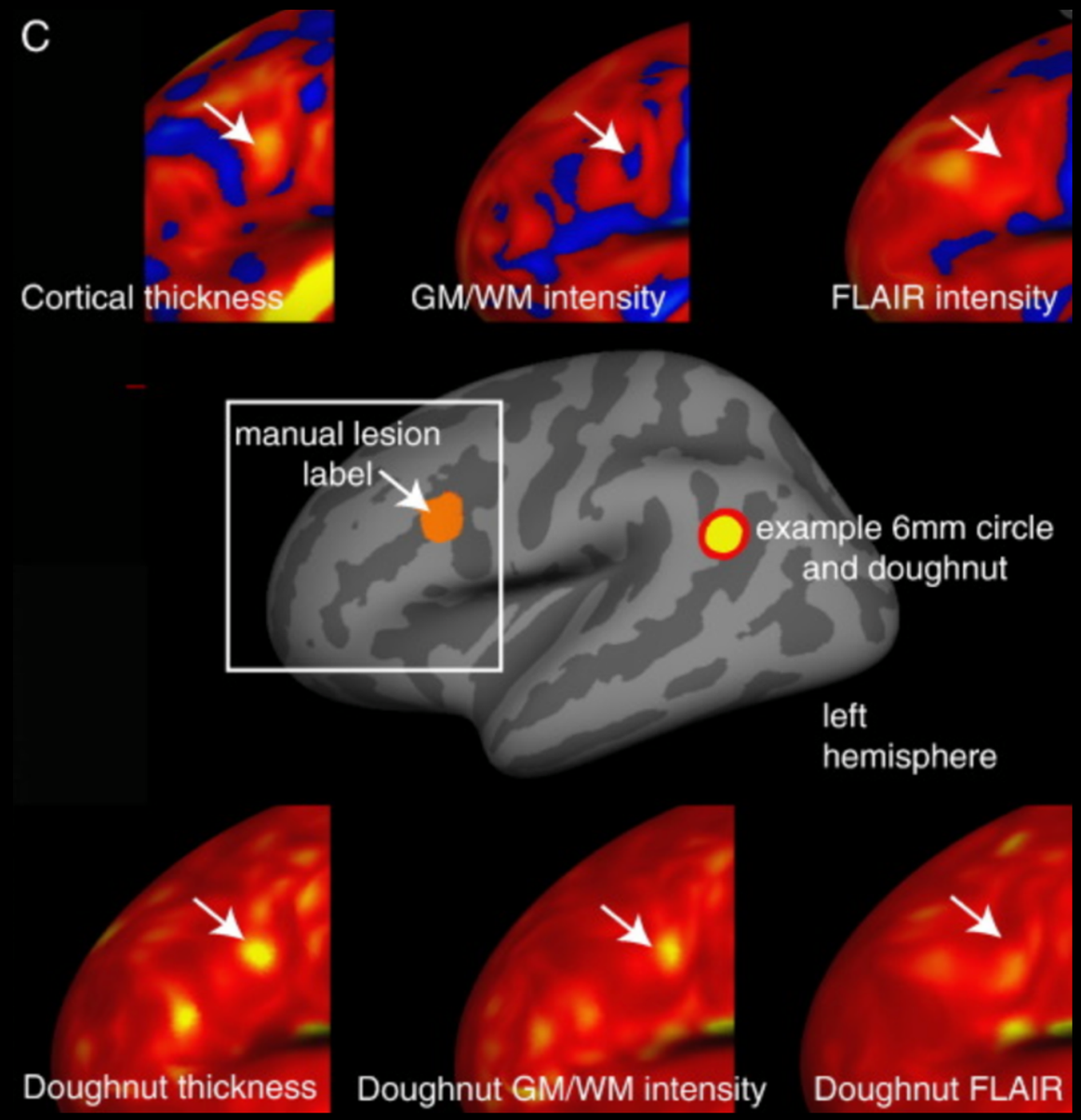
2 yo

14 yo

Pediatric FCD lesion detection

developmental changes in myelination, cortical thickness and gyrification during development

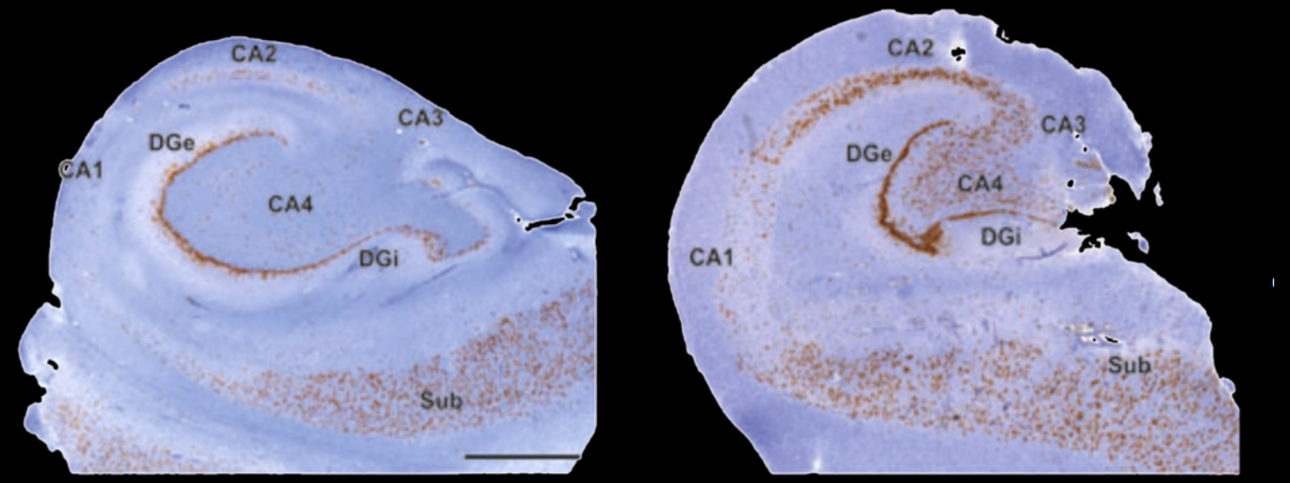
motion artifact



Adler et al Neuroimage Clin. 2017

Temporal Lobe Epilepsy

- most common form of drug-resistant epilepsy
- most commonly Hippocampal sclerosis
- variable pattern of cell loss and/or gliosis



Blumcke 2013, Epilepsia

Temporal lobe epilepsy

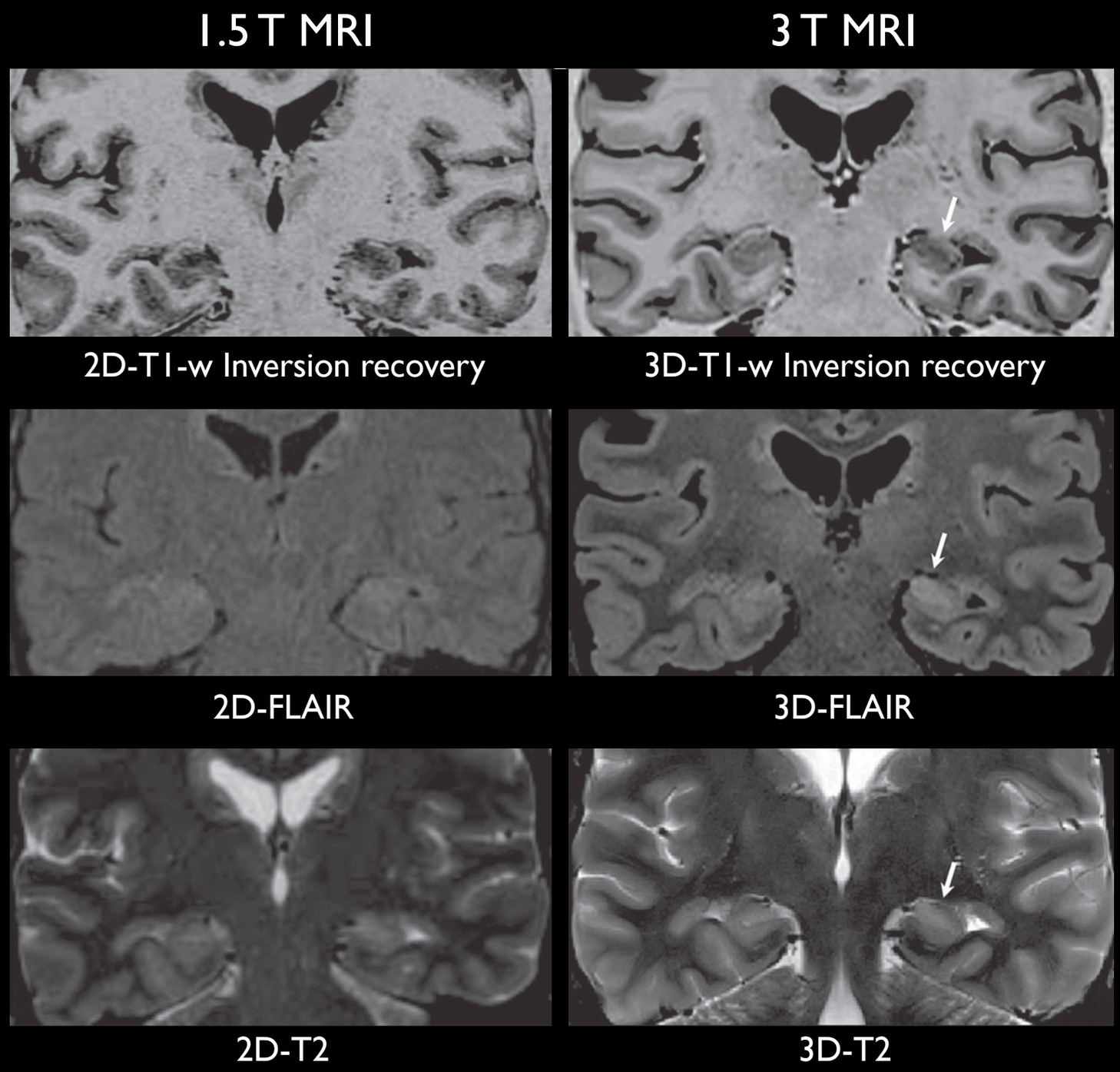
Hippocampal atrophy

decreased T1 signal

increased T2 signal

loss of internal structure

best seen at 3T 3D images with millimetric or sub-millimetric isotropic voxels



Schrader et al 2015, Oxford Textbook of Neuroimaging

Volumetry

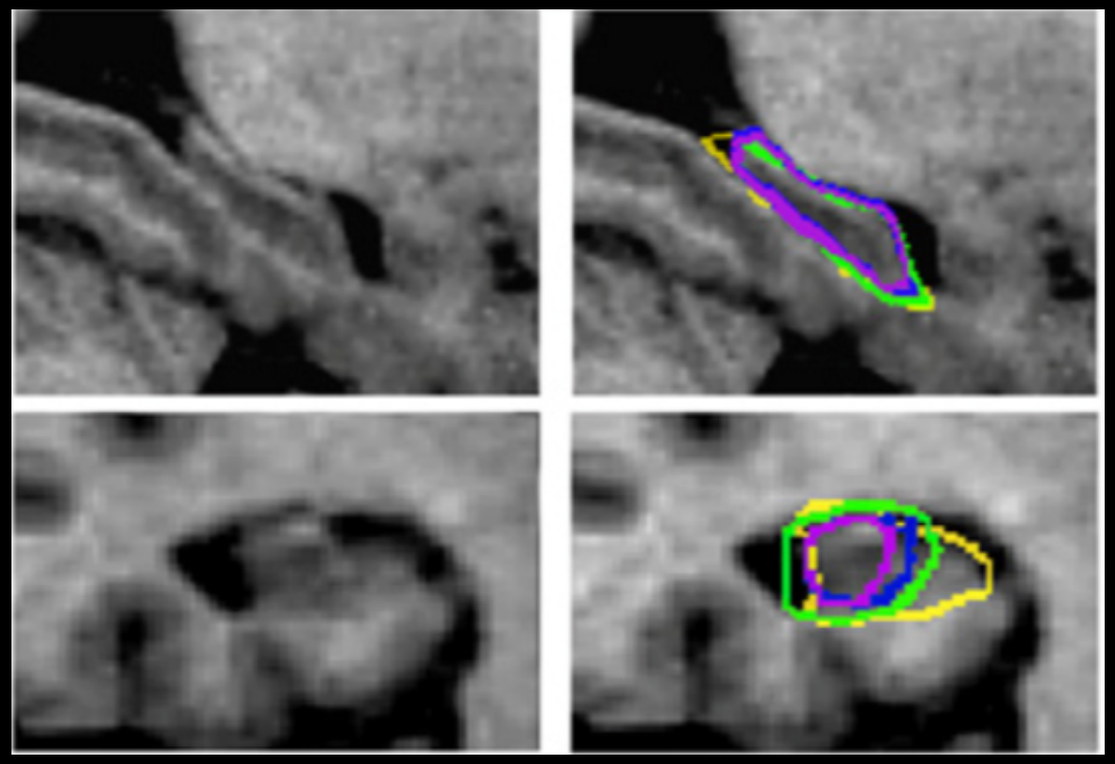
increases sensitivity to atrophy of hippocampus

lateralize seizure focus in 90% TLE

correlates with cell loss

entorhinal cortex, temporal pole, amygdala

automated hippocampal segmentation algorithms available

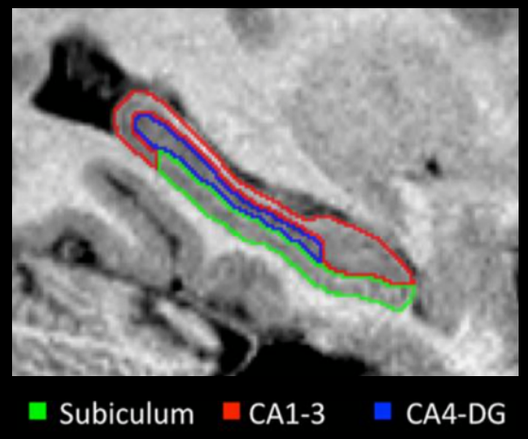


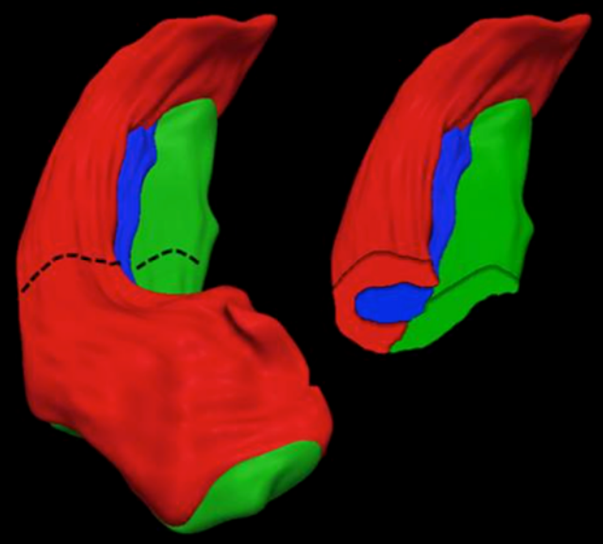
Kim et al 2012, Medical Image Analysis

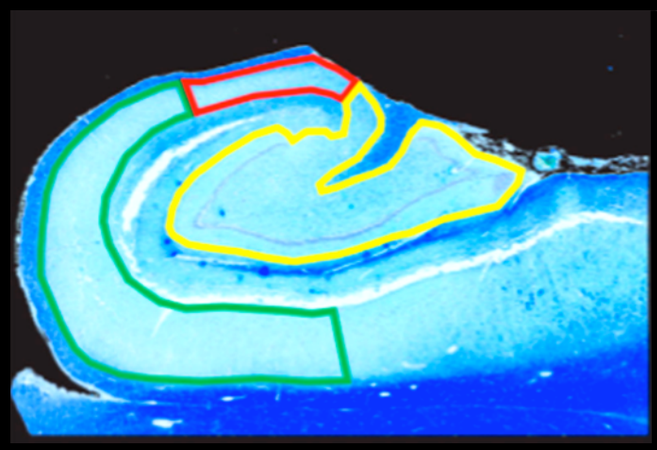
Subfield analysis

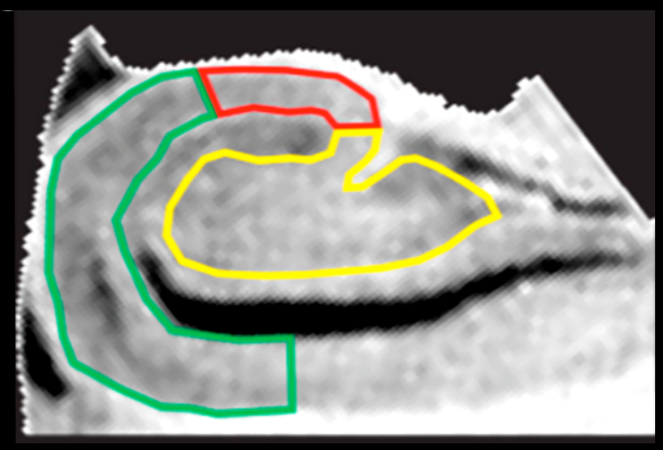
- 40% of patients with TLE have normal hippocampal volumes

- up to 50% of patients have gliosis only









Kulaga-Yoskovitz et al, 2015 Scientific Data, Steve et al 2017 Neuroimage

Subfield analysis

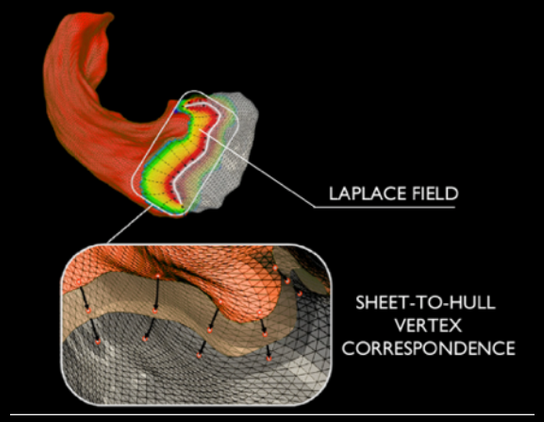
HS

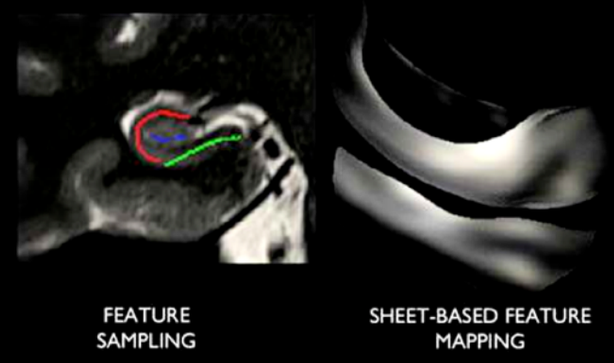
ipsilateral atrophy,
widespread increased T2 and MD

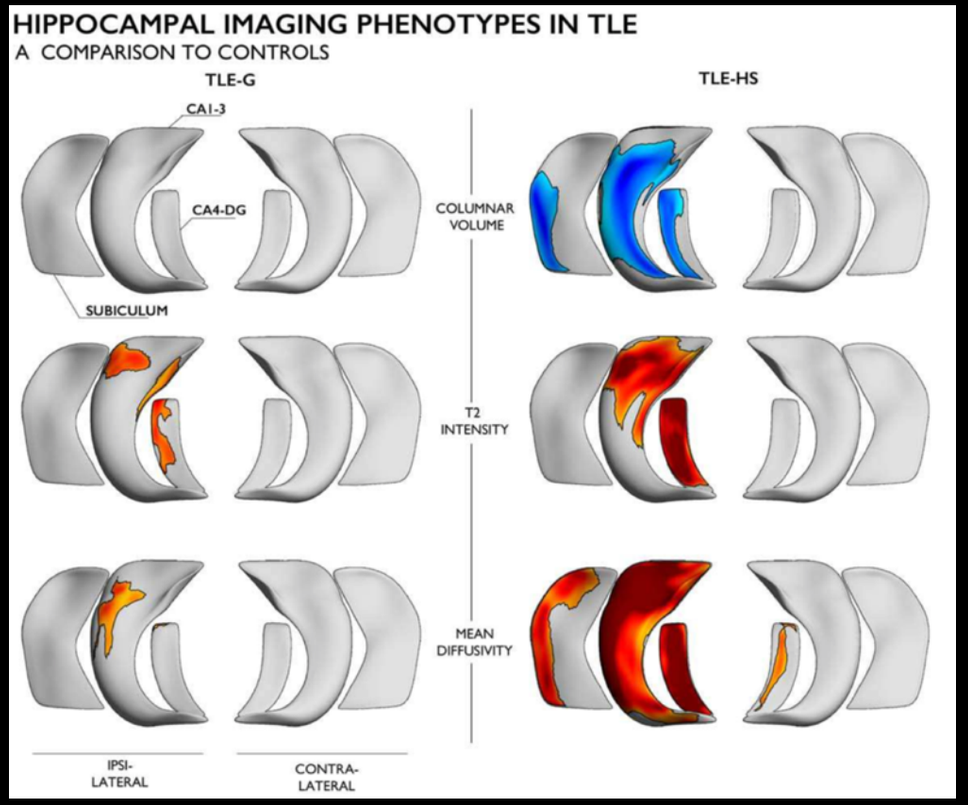
gliosis only

dentate gyrus hypertrophy
focal T2 and MD increases

multivariate automated classifier
lateralized seizure focus in 85%
(vs 59% clinical)







Bernhardt et al Annals of Neurology 2016

final frontiers

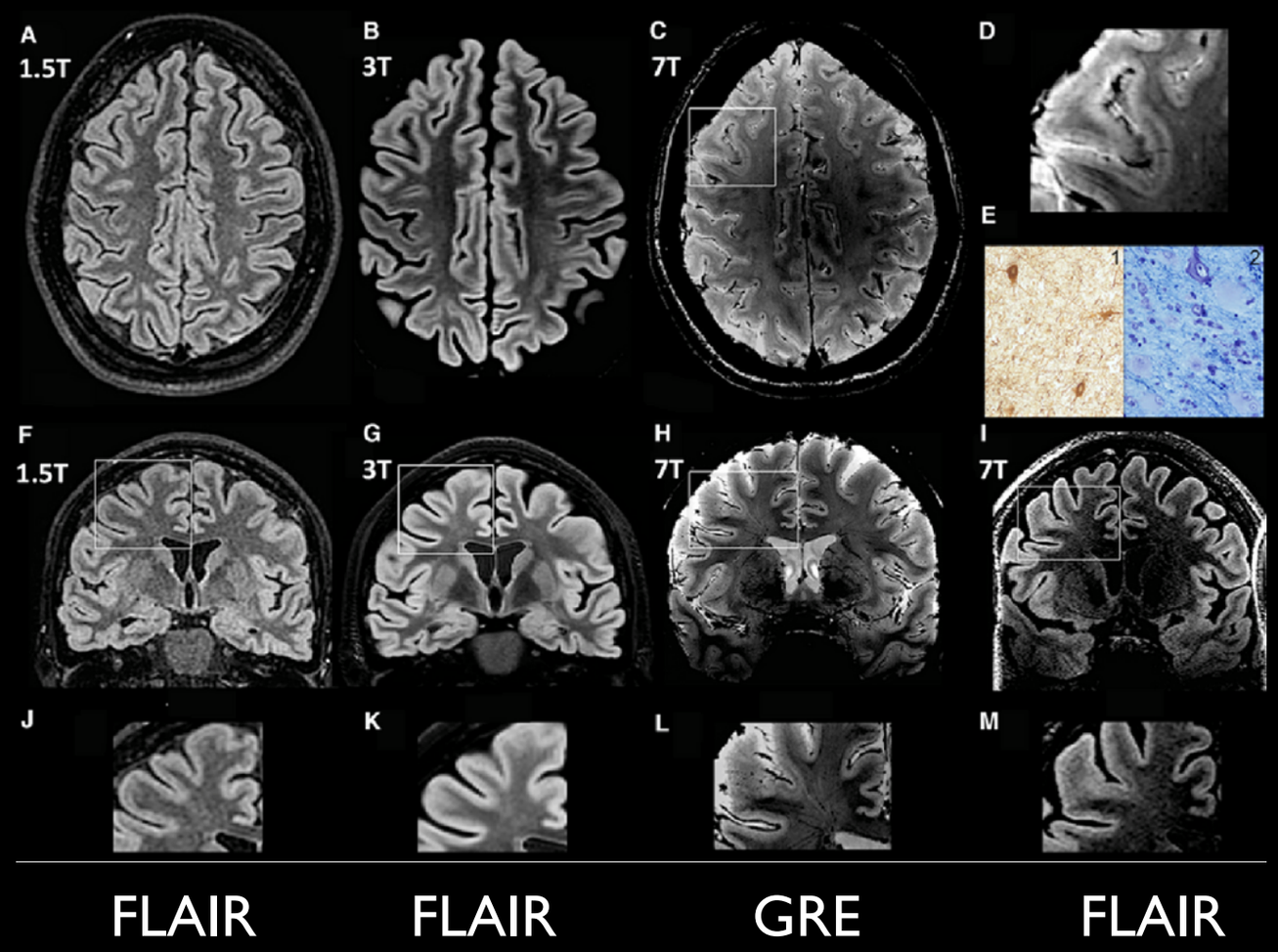
- FCD I
- lesion detection
  below 2 years
  - beyond lesion
    detection
    - surgical outcome
      prediction

Ultra-High Field strength

21 children and adults with normal MRI at 1.5 or 3T

6 revealed lesions

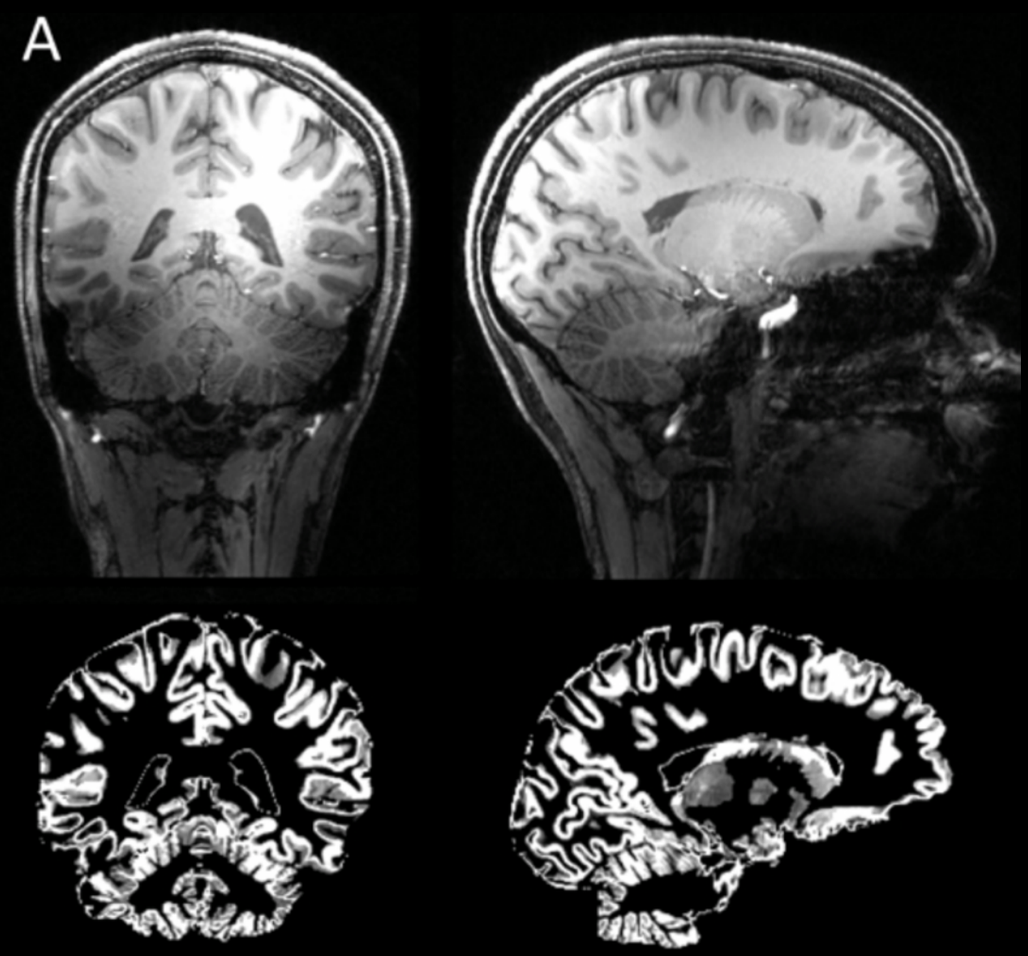
4 had surgery and had FCD



De Ciantis, Epilepsia 2016

Ultra-High Field strength

- better signal to noise
- higher resolution
- worsening intensity inhomogeneities
- need to adapt post-processing



Seiger et al, Neuroimage 2015

Future directions

- multi-modal lesion detection algorithms
- quantitative correlation of MRI features with histology and genetics
- higher field strengths
- evaluation of algorithms on larger data sets
- integration with other modalities

Neuroimaging of Epilepsy Laboratory
- Andrea Bernasconi
- Neda Bernasconi
- Seok-Jun Hong

Multimodal Imaging and Connectome Analysis Lab, MNI
- Boris Bernhardt
- Sara Lariviere

BC Children's Hospital Epilepsy Team
- Mary Connolly
- Kelly Anderson

BC Children's Hospital MRI Research Facility
- Bruce Bjornson
- Kevin Fitzpatrick
- Danny Kim
- Lynn Williams

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

SickKids