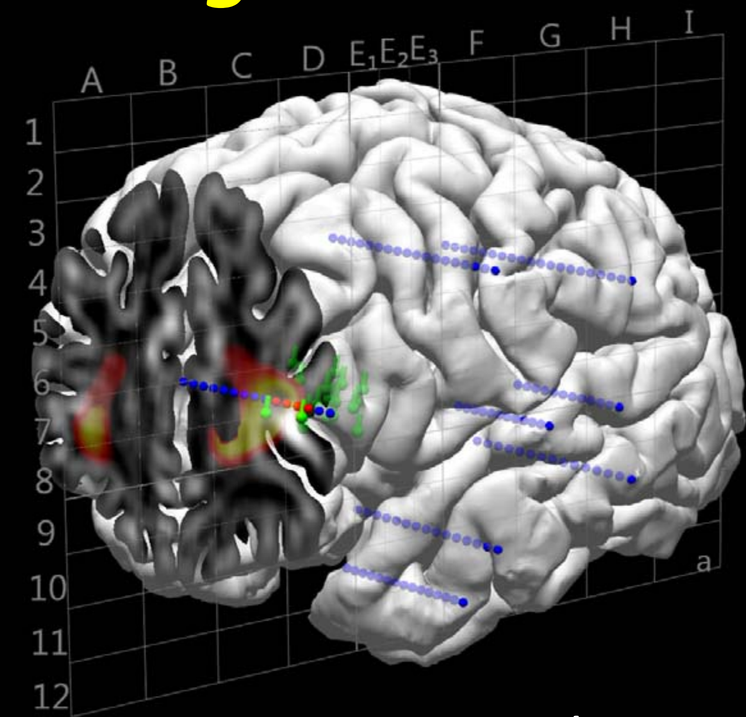
Brain MRI, PET, SPECT, Post-processing Tools and Multimodal Co-registration in Pre-surgical evaluation



Irene Wang, PhD
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2020.9.22

Outline

- MRI in Epilepsy (TLE, ETLE, Post-processing tools)
- PET in Epilepsy
- SPECT in Epilepsy
- Why?
  - To help formulate hypothesis
  - To optimize intracranial implantation
  - To improve seizure outcomes
- Multi-modal Integration

MRI in Epilepsy

Seminar in Epileptology

Epileptic Disord 2020; 22 (4): 421-37

MRI essentials in epileptology: a review from the ILAE Imaging Taskforce

Irene Wang [1], Andrea Bernasconi [2], Boris Bernhardt [3], Hal Blumenfeld [4], Fernando Cendes [5], Yotin Chinvarun [6], Graeme Jackson [7], Victoria Morgan [8], Stefan Rampp [9], Anna Elisabetta Vaudano [10], Paolo Federico [11]

Cleveland Clinic

Epilepsy MRI protocol

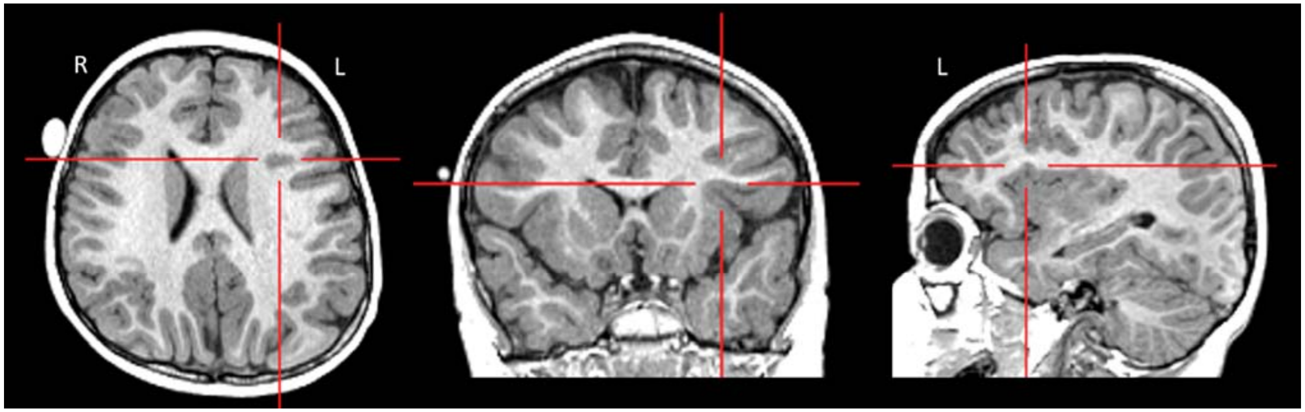
Table 2. Mandatory and optional sequences of the HARNESS-MRI protocol (Bernasconi *et al.*, 2019).

Name (abbreviation/vendor)			Advantages
Mandatory sequences – HARNESS MRI protocol			
Magnetization-prepared rapid gradient-echo (MPRAGE, Siemens), Spoiled gradient-echo (SPGR, GE), Turbo field echo (TFE, Phillips)	T1-weighted	3D	High-resolution images that can be reformatted to be viewed on coronal, axial and sagittal planes Optimal visualization of brain anatomy and morphology
3D fluid attenuation inversion recovery (FLAIR) ax/cor 2D FLAIR also commonly used	T2-weighted	3D	3D high-resolution images that can be reformatted to any plane Cerebrospinal fluid nulling enhances visibility of epileptic pathologies such as focal cortical dysplasia, hippocampal sclerosis, tubers, hamartomas, glial scars, *etc.*
Coronal spin echo (acquisition plane perpendicular to the long axis of the hippocampus)	T2-weighted	2D	High in-plane resolution Optimal visualization of hippocampal internal structure on coronal cuts
Optional sequences			
Gadolinium-enhanced MRI	T1-weighted	3D	Best for assessing tumor-like lesions, vascular malformations, or infectious processes
Susceptibility weighted imaging	T2*-weighted	3D	Sensitive to iron deposits, blood products and calcifications

(Bernasconi 2019; Wang 2020)

MRI Basic Reading Guidelines

- Provide as much clinical information as possible
- Reviewer should have expertise in epilepsy imaging
- Repeated review often necessary
- View T1- and T2-weighted images side-by-side to assess whether a putative abnormality is seen on both
- Be aware of partial volume effects, use all 3 planes



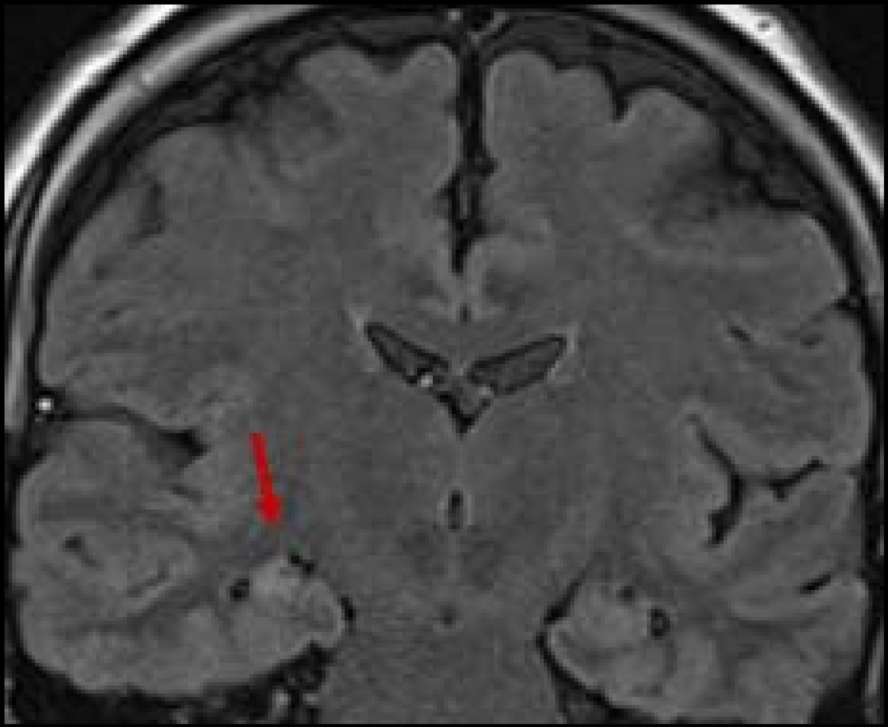
(Wang et al., Epileptic Disord 2020)

MRI Basic Reading Guidelines - TLE

- Before comparing L/R volume and shape, ensure brain is symmetrically positioned
- Pay special attention to coronal images acquired perpendicular to the long axis of hippocampus
- Coronal T2-weighted turbo spin echo (TSE) optimal for comparison of volume, shape and signal
- Coronal FLAIR particularly suited to evaluate signal asymmetry
- Sagittal images from 3D FLAIR provide a complete antero-posterior view of signal distribution along the length of the hippocampus and surrounding regions

(Wang et al., Epileptic Disord 2020)

Hippocampal Sclerosis



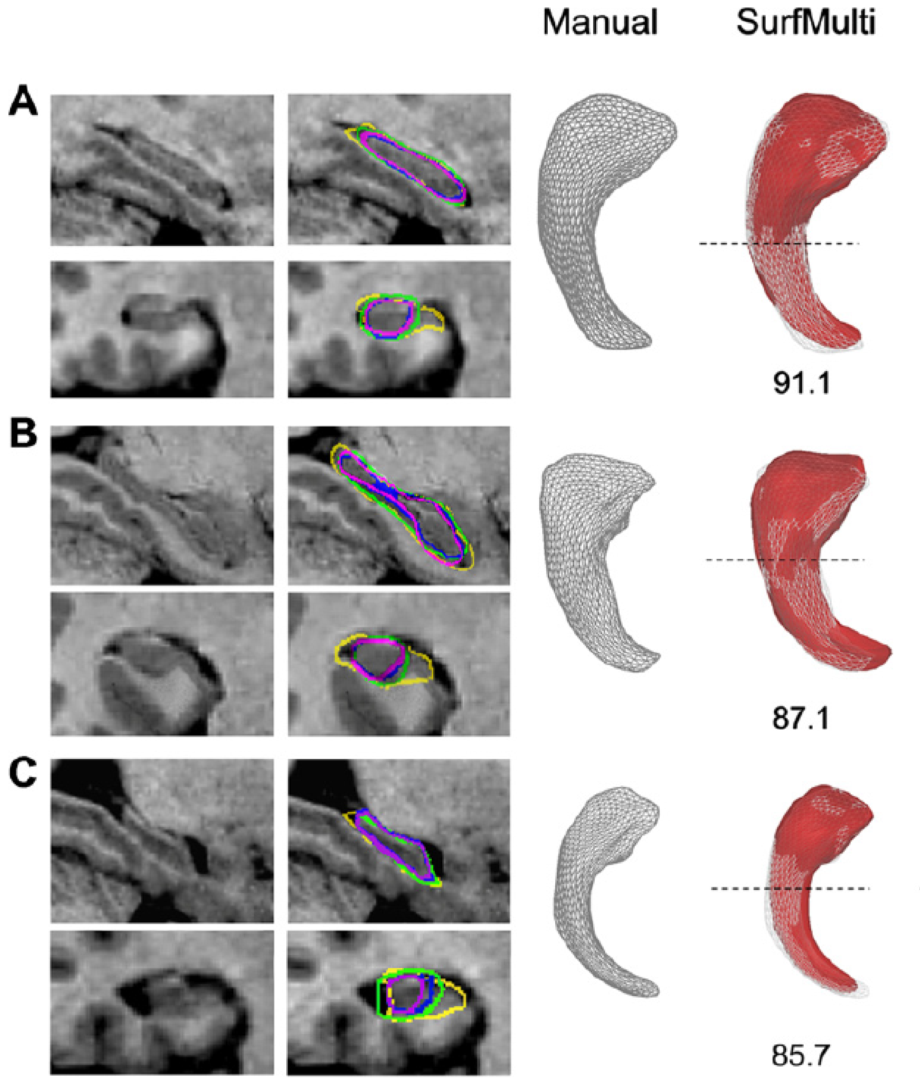
- Loss of volume
- Loss of internal architecture
- Hyperintensity on FLAIR/T2

Hippocampal Volumetry

- Manual segmentation accurate but time-consuming
- Atlas-based automated segmentation
  - Healthy controls OK
  - TLE patients challenging
  - Malrotation
    - TLE 43%
    - ETLE (FCD) 49%
    - Normal controls 10%

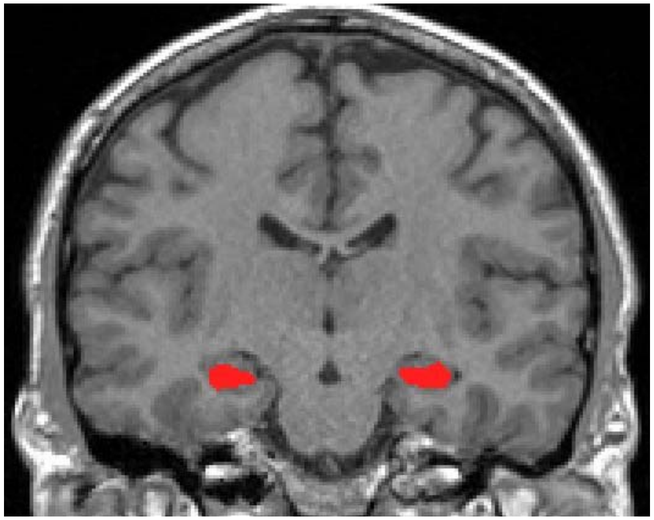
(Bernasconi et al., Brain 2005)

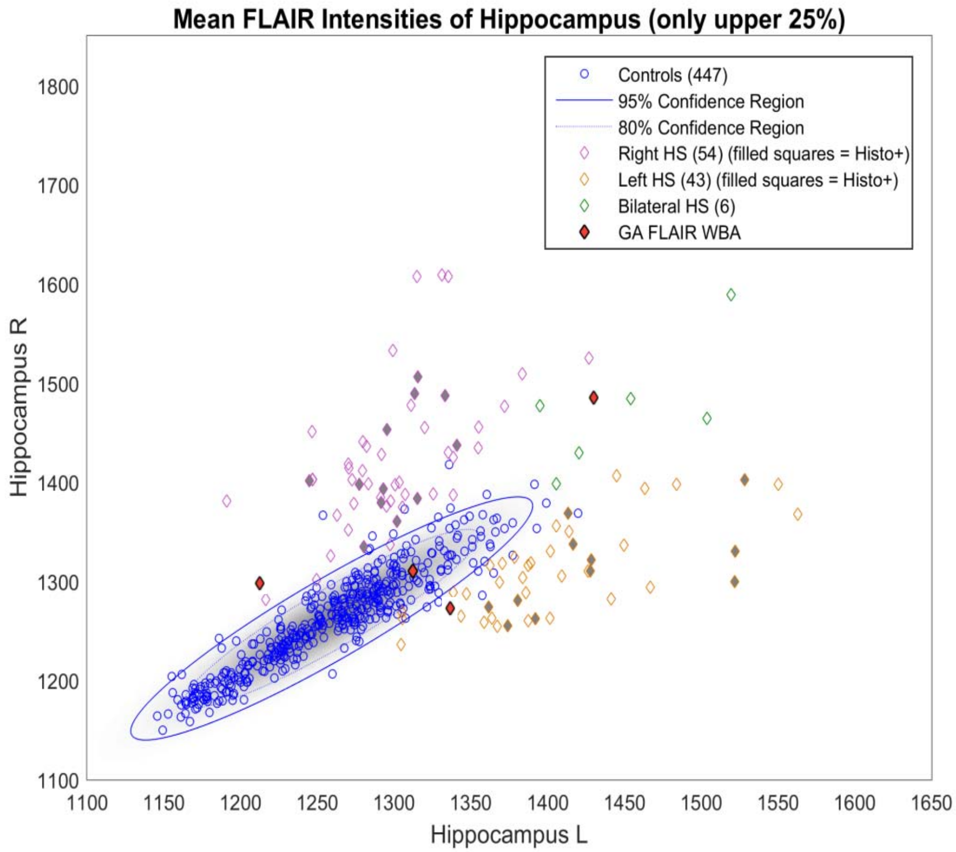
Hippocampal Volumetry



(Kim et al., NeuroImage 2012)

Hippocampal Signal Analysis



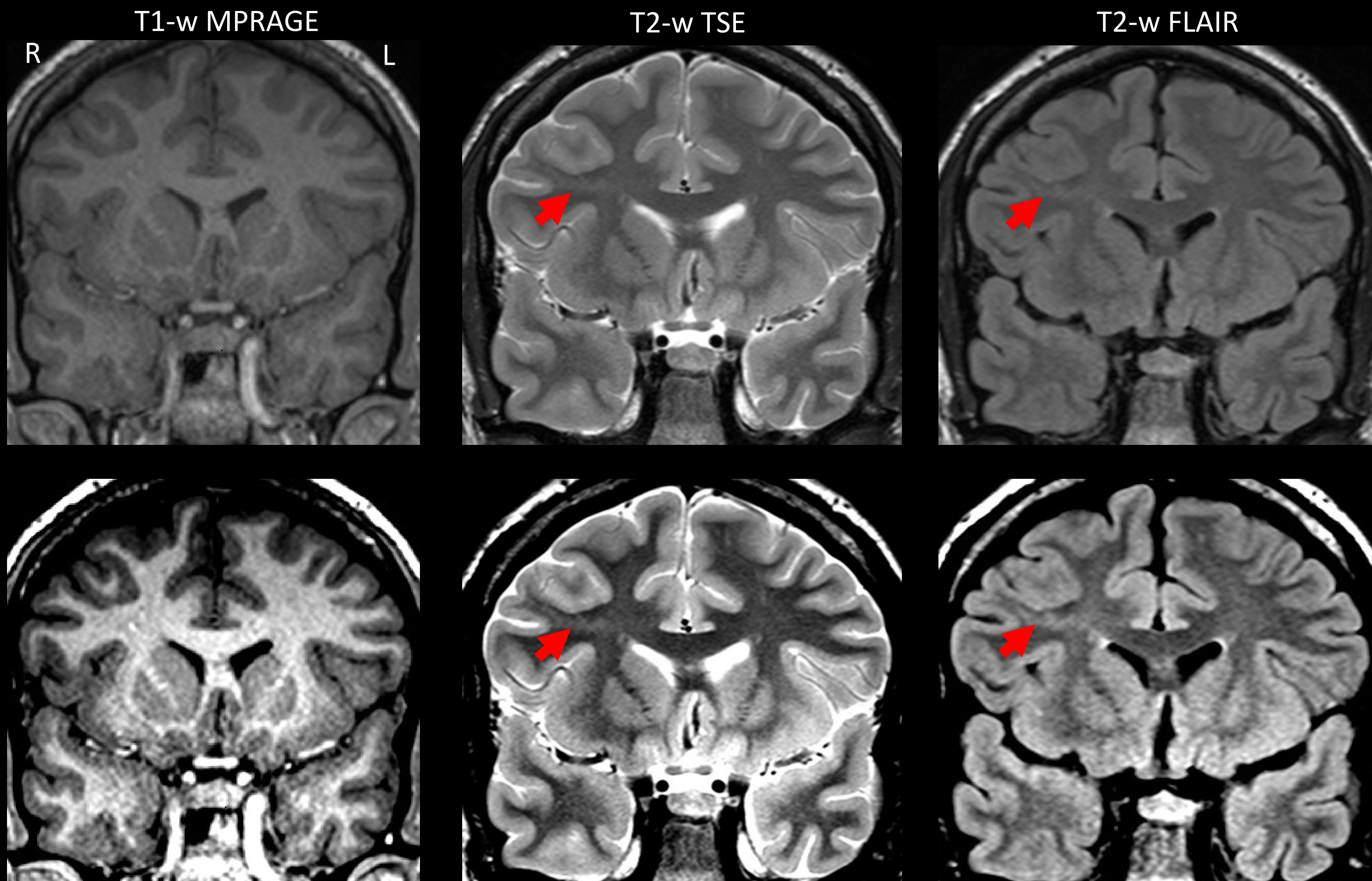


MRI Basic Reading Guidelines - ETLE

- Pay attention to the neocortical ribbon and white matter for underlying FCD
- Discovering a previously undetected lesion can drastically change the presurgical planning and outcome
- Look for transmantle sign, a funnel-shaped signal extending across the white matter, from the lateral ventricle to the cortex harboring the lesion
- Transmantle sign more evident on FLAIR, especially after properly adjusting the brightness and contrast of the images

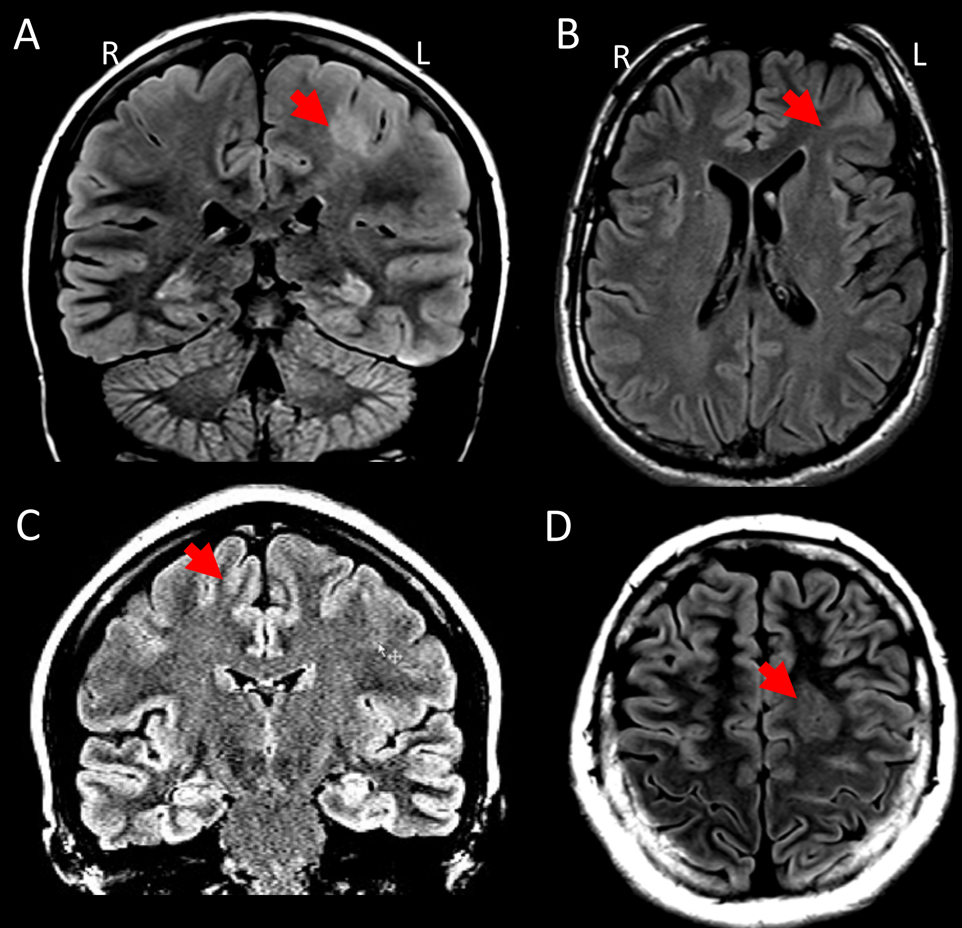
(Wang et al., Epileptic Disord 2020)

Transmantle Sign



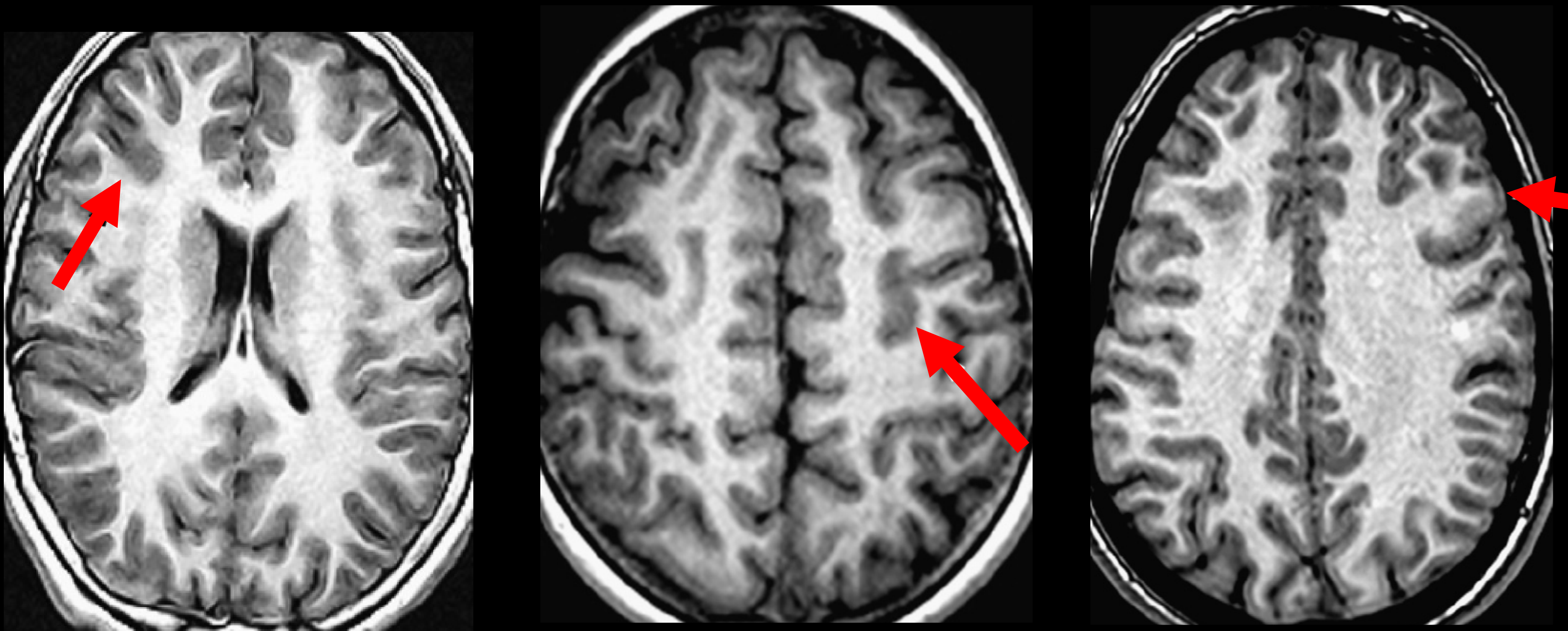
(Wang et al., Epileptic Disord 2020)

Transmantle Sign

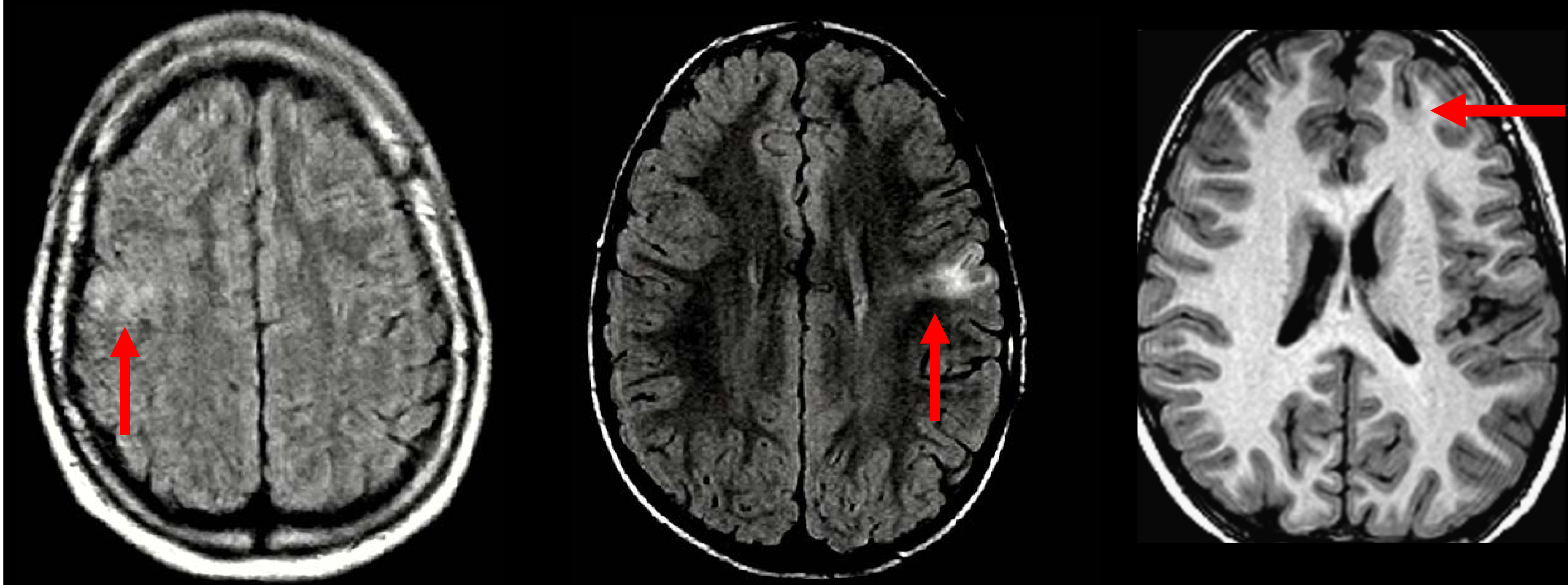


(*Wang et al., Epileptic Disord 2020*)

Focal Cortical Dysplasia
(Gray-white blurring)



Focal Cortical Dysplasia
(Signal abnormality)

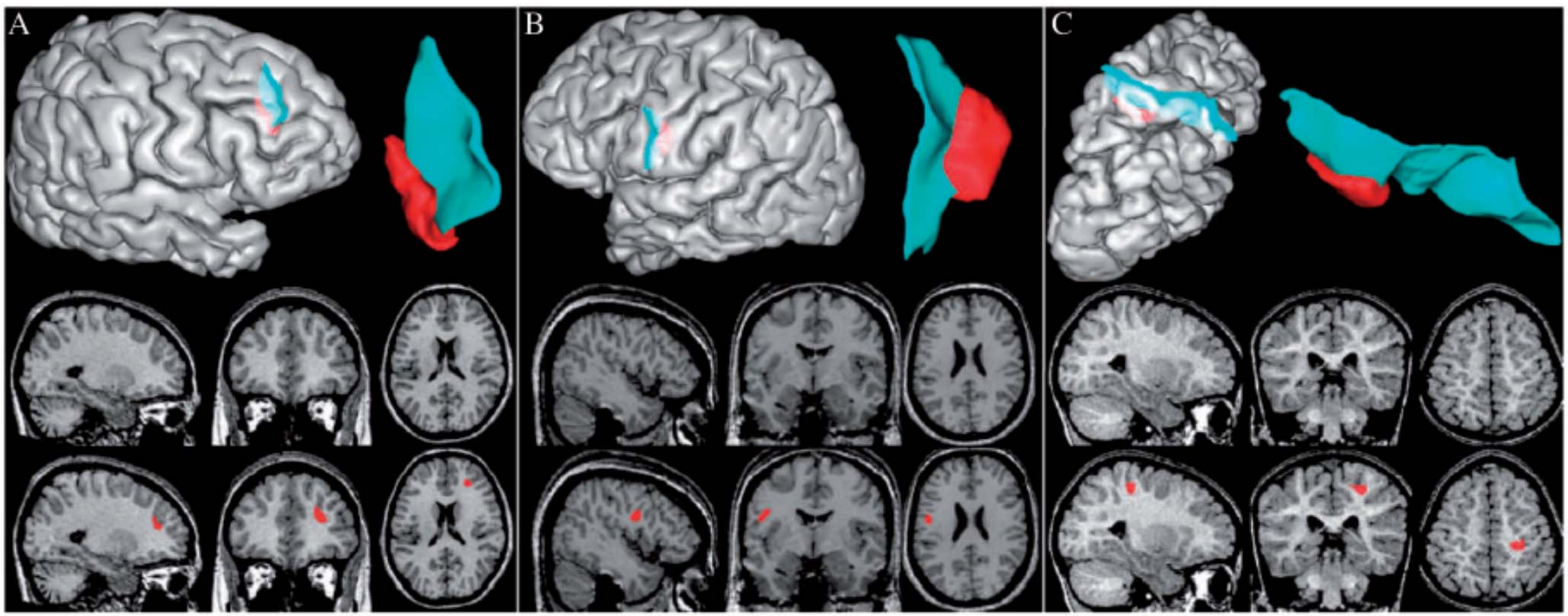


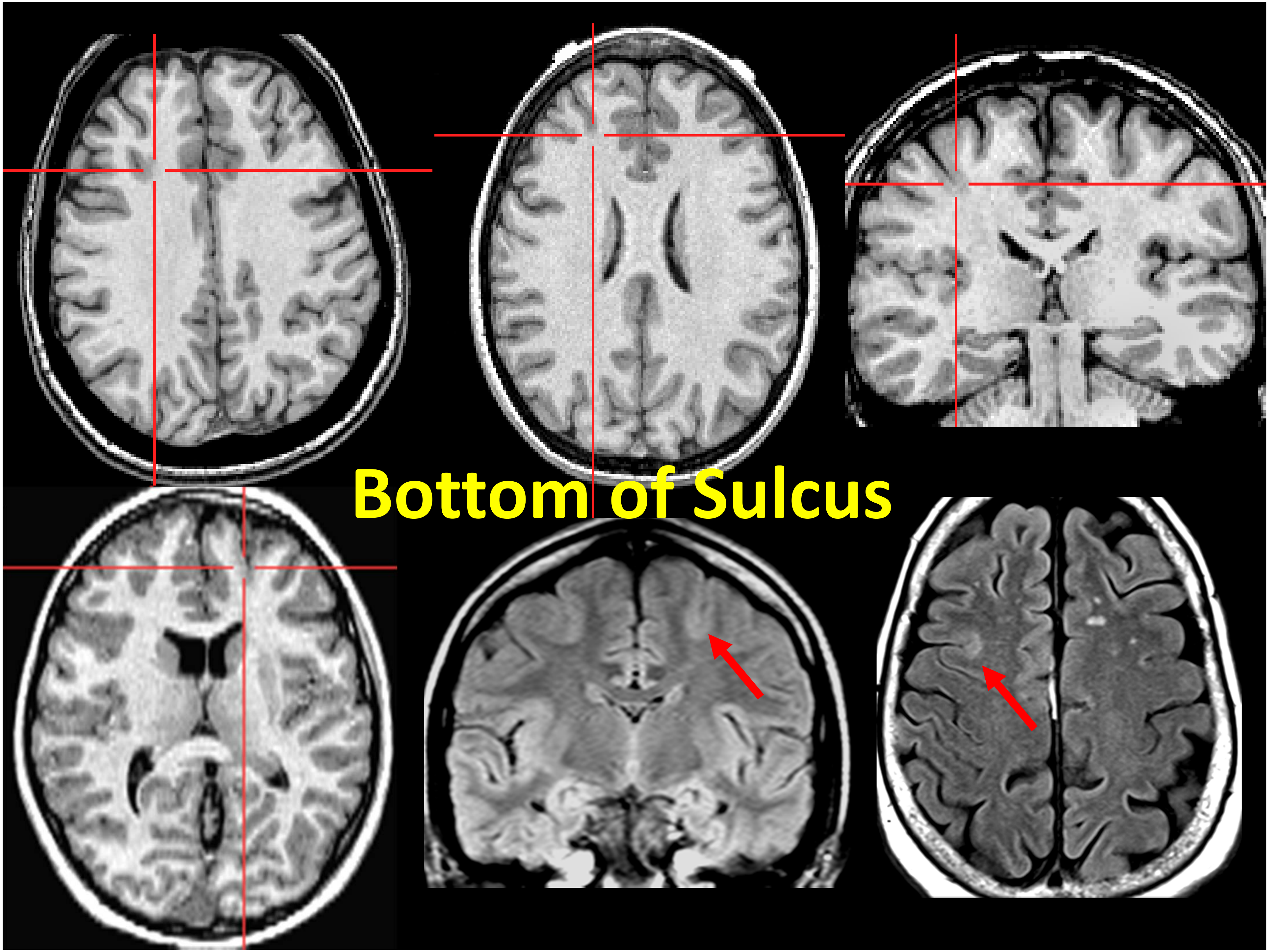
doi:10.1093/brain/awn224 *Brain* (2008), **131**, 3246–3255

Small focal cortical dysplasia lesions are located at the bottom of a deep sulcus

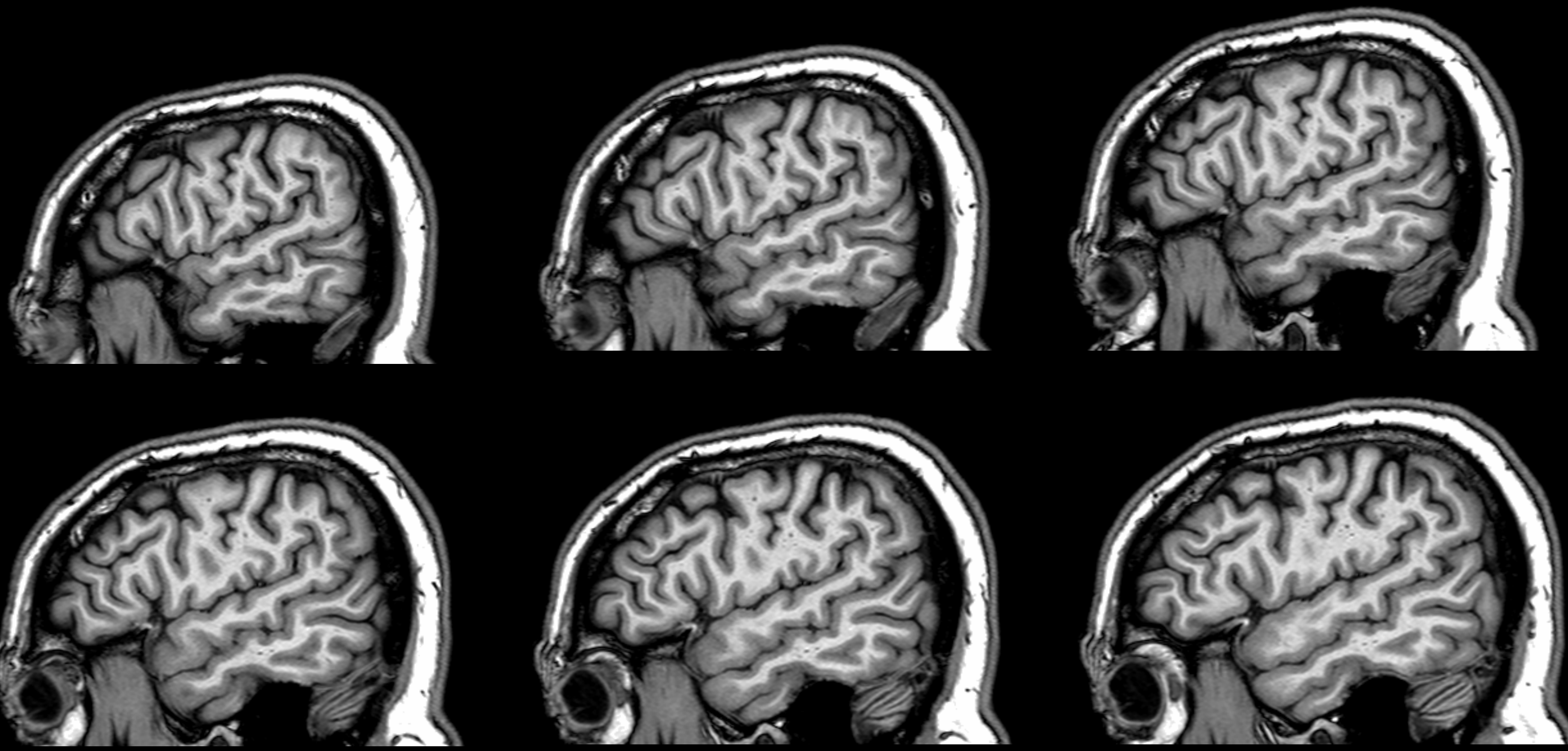
Pierre Besson, Frederick Andermann, Francois Dubeau and Andrea Bernasconi

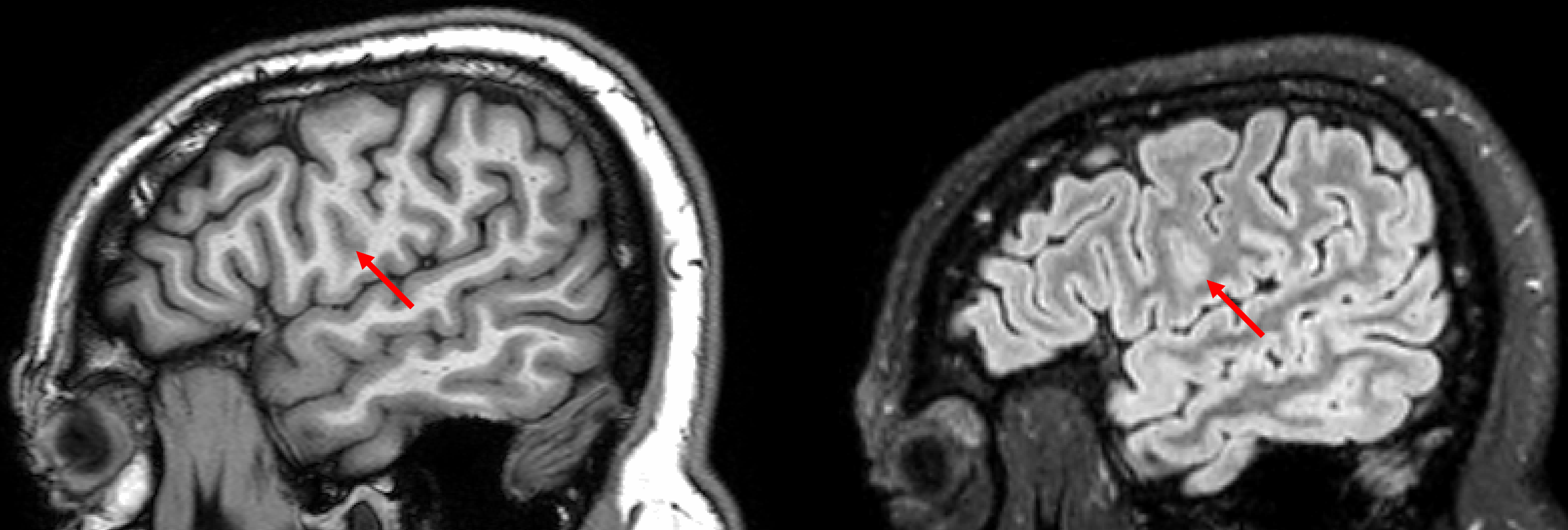
Department of Neurology and Neurosurgery and Brain Imaging Center, McGill University, Montreal Neurological Institute and Hospital, Montreal, Quebec, Canada




Bottom of Sulcus

Where is the Lesion?

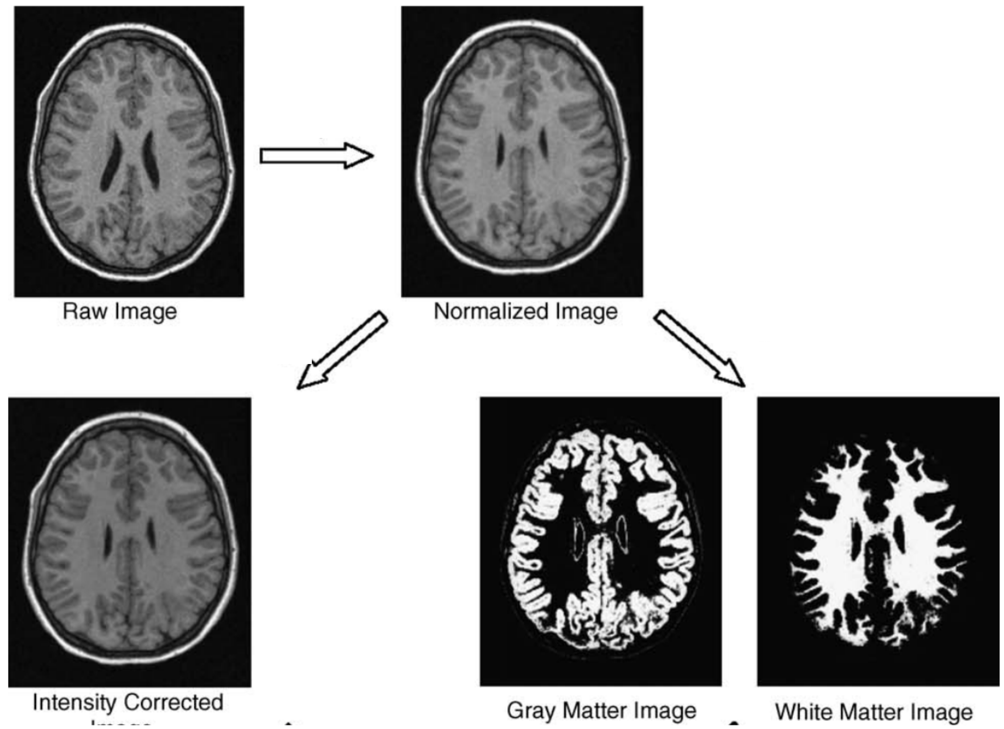




T1w 3D-FLAIR

Voxel-based Morphometry (VBM)

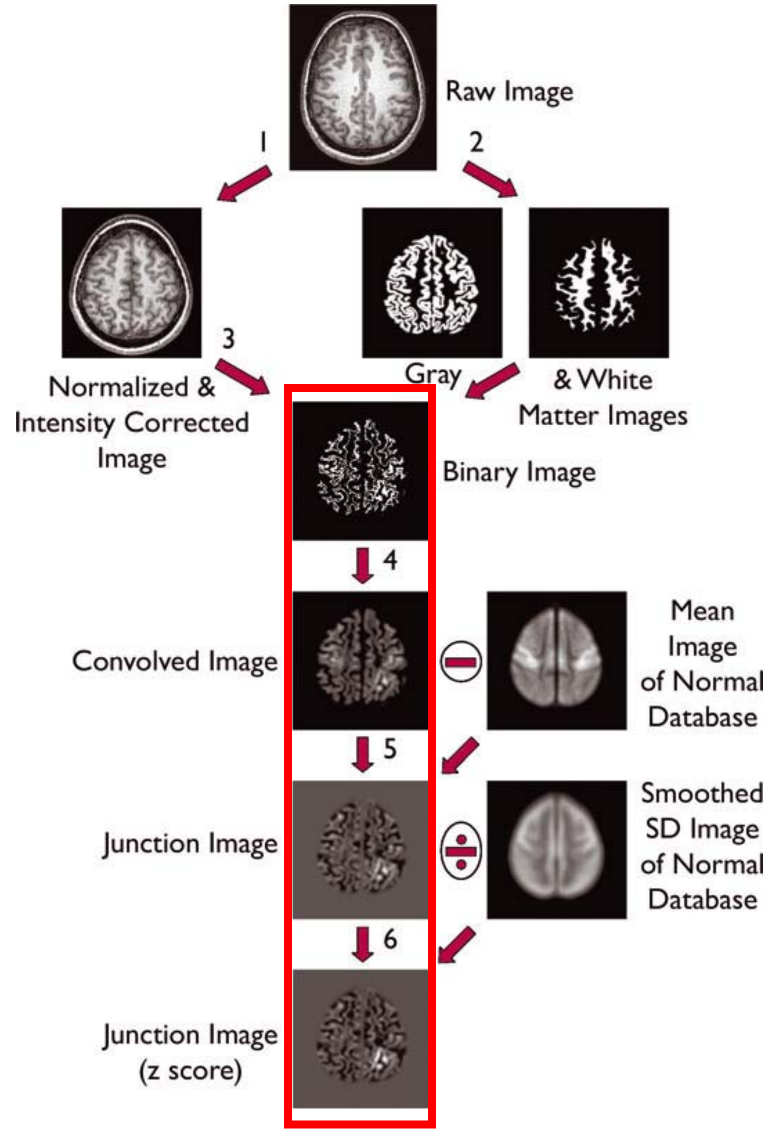
- Registration to a standard stereotaxic space
- Correction for intensity nonuniformity
- Tissue classification
- Comparison to control
- Can be optimized to be **applied on individual patients**



(Huppertz et al., Epi Res 2005)

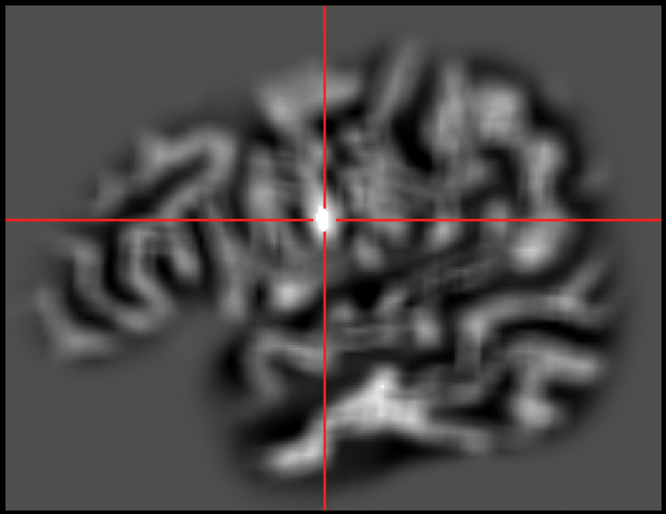
Morphometric Analysis Program (MAP)

- MAP is a specific VBM package optimized to be applied on an individual level.
- MAP is especially sensitive to subtle abnormalities associated with blurring in the gray-white matter junction.
- Such areas may be associated with an underlying cortical dysplasia.

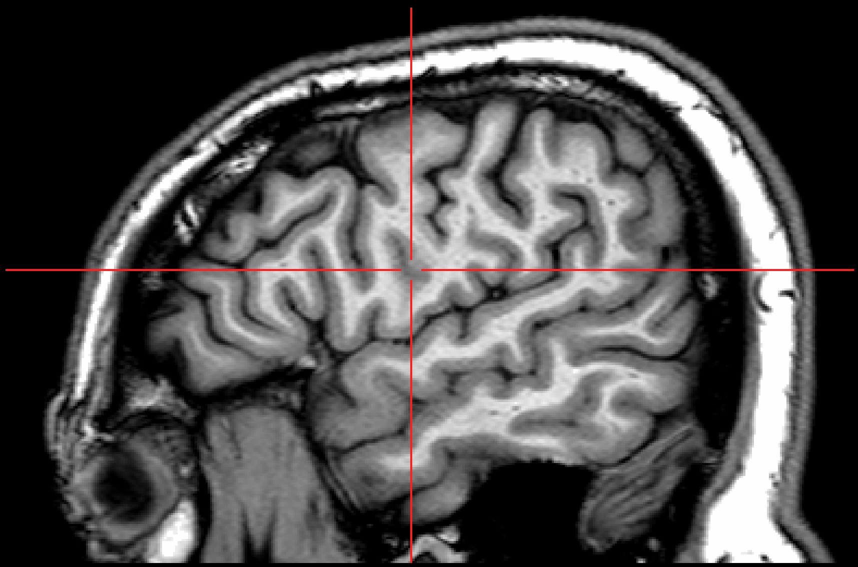


(Huppertz et al., Epilepsia 2008)

Where is the Lesion?



GW Junction Image



T1-w

RESEARCH ARTICLE

ANNALS of Neurology

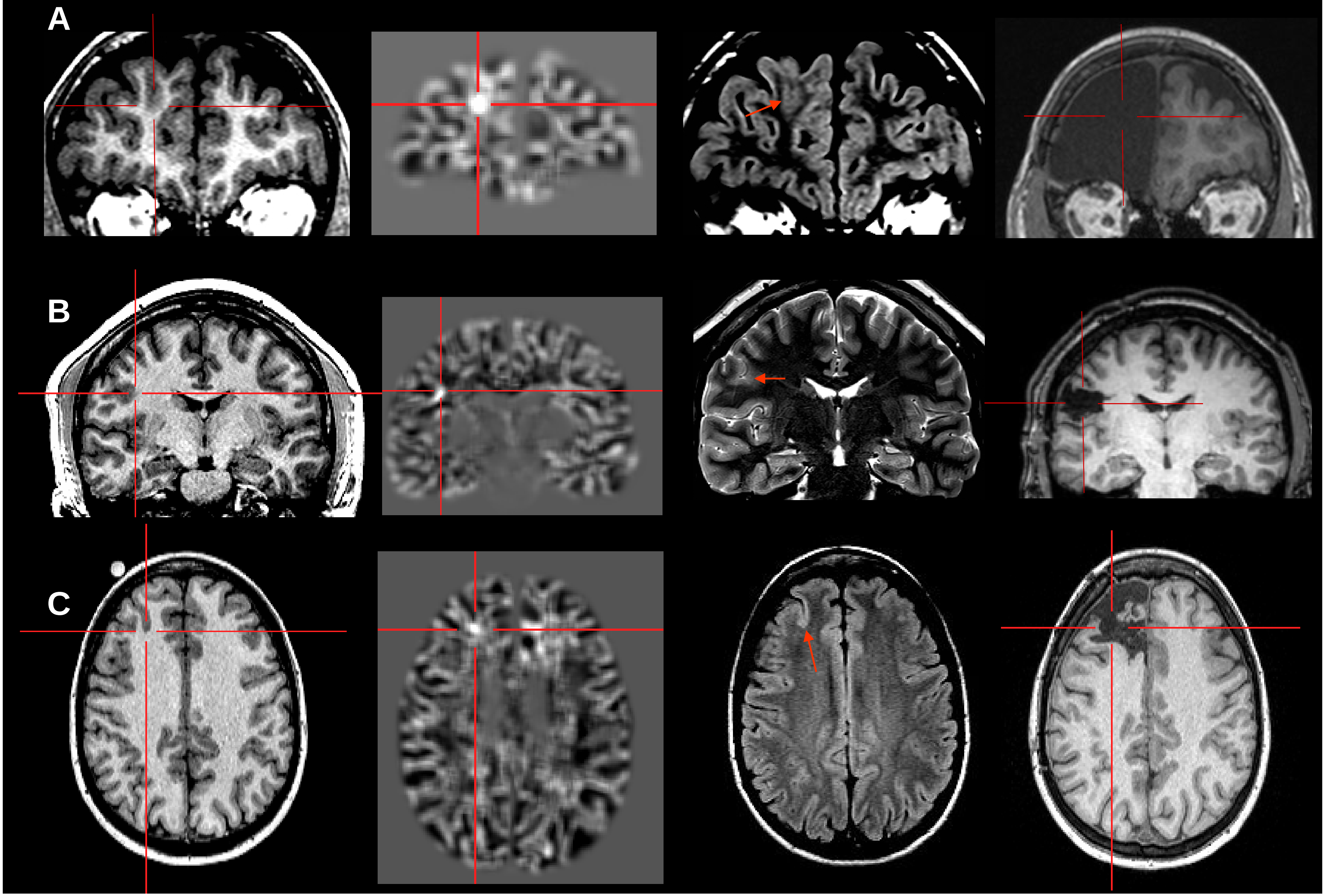
Voxel-Based Morphometric Magnetic Resonance Imaging (MRI) Postprocessing in MRI-Negative Epilepsies

Z. Irene Wang, PhD,[1] Stephen E. Jones, MD, PhD,[2] Zeenat Jaisani, MD,[3] Imad M. Najm, MD,[1] Richard A. Prayson, MD,[4] Richard C. Burgess, MD, PhD,[1] Balu Krishnan, PhD,[1] Aleksandar Ristic, MD,[5] Chong H. Wong, MD, PhD,[6] William Bingaman, MD,[7] Jorge A. Gonzalez-Martinez, MD, PhD,[7] and Andreas V. Alexopoulos, MD, MPH[1]

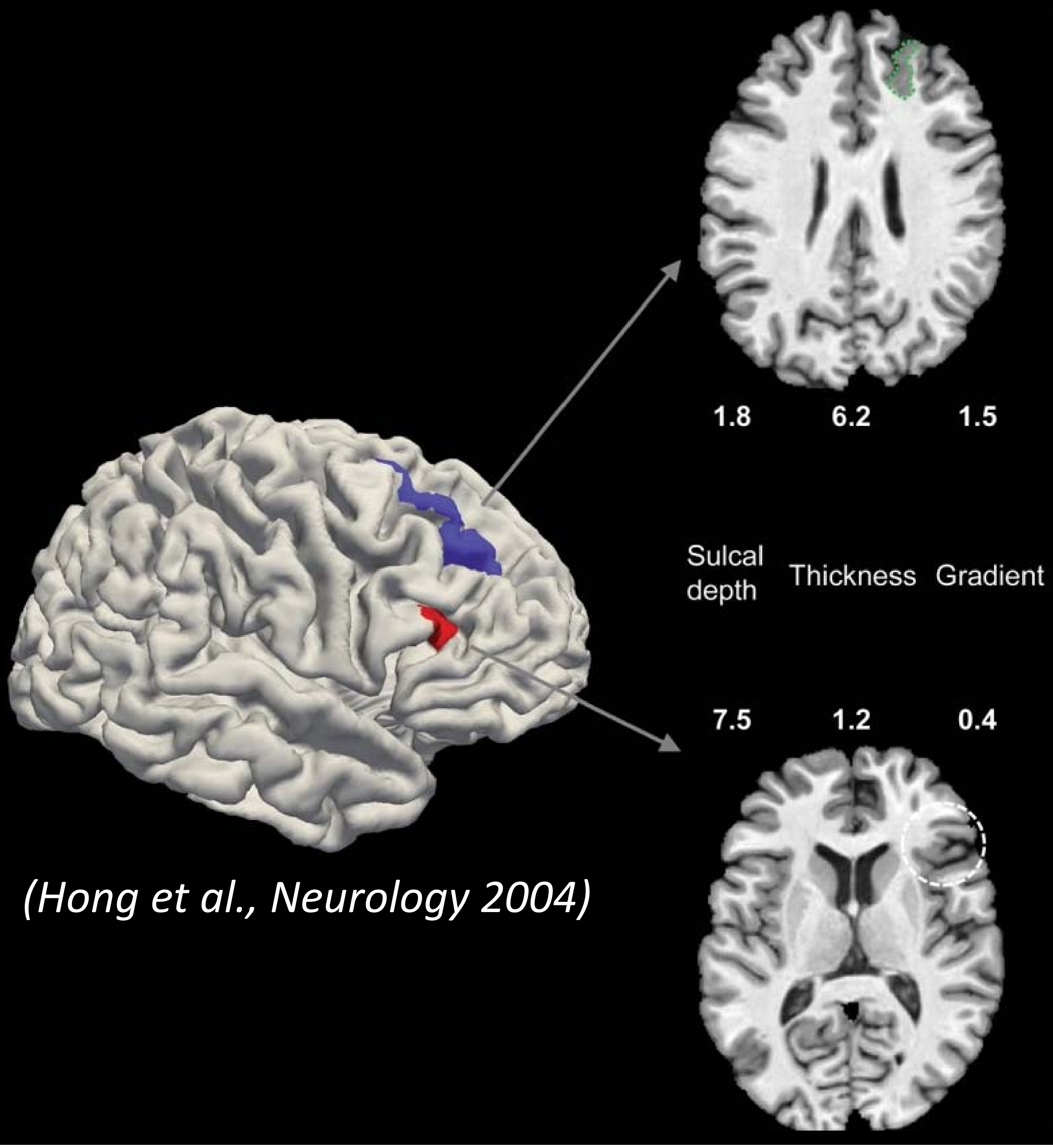
Objective: In the presurgical workup of magnetic resonance imaging (MRI)-negative (MRI^- or "nonlesional") pharmacoresistant focal epilepsy (PFE) patients, discovering a previously undetected lesion can drastically change the evaluation and likely improve surgical outcome. Our study utilizes a voxel-based MRI postprocessing technique, implemented in a morphometric analysis program (MAP), to facilitate detection of subtle abnormalities in a consecutive cohort of MRI^- surgical candidates.
Methods: Included in this retrospective study was a consecutive cohort of 150 MRI^- surgical patients. MAP was performed on T1-weighted MRI, with comparison to a scanner-specific normal database. Review and analysis of MAP were performed blinded to patients' clinical information. The pertinence of MAP^+ areas was confirmed by surgical outcome and pathology.
Results: MAP showed a 43% positive rate, sensitivity of 0.9, and specificity of 0.67. Overall, patients with the MAP^+ region completely resected had the best seizure outcomes, followed by the MAP^- patients, and patients who had no/partial resection of the MAP^+ region had the worst outcome ($p < 0.001$). Subgroup analysis revealed that visually identified subtle findings are more likely correct if also MAP^+. False-positive rate in 52 normal controls was 2%. Surgical pathology of the resected MAP^+ areas contained mainly non–balloon-cell focal cortical dysplasia (FCD). Multiple MAP^+ regions were present in 7% of patients.
Interpretation: MAP can be a practical and valuable tool to: (1) guide the search for subtle MRI abnormalities and (2) confirm visually identified questionable abnormalities in patients with PFE due to suspected FCD. A MAP^+ region, when concordant with the patient's electroclinical presentation, should provide a legitimate target for surgical exploration.

ANN NEUROL 2015;77:1060–1075

Frontal



Multiple

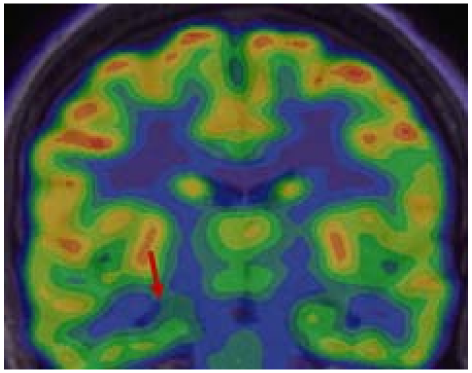


(Hong et al., Neurology 2004)

PET in Epilepsy

PET and TLE

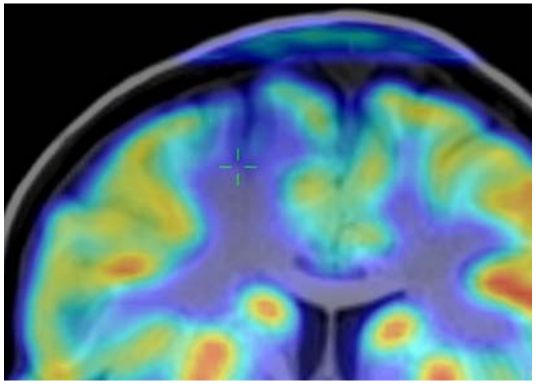
- PET is one of the most routinely used noninvasive modalities in presurgical evaluation.



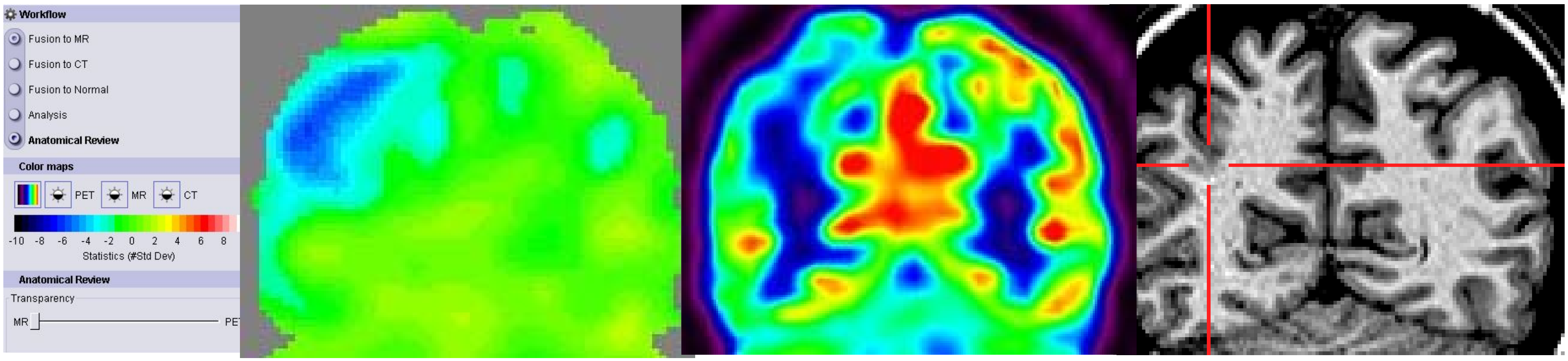
- ^{18}F-FDG is the most used tracer
- Helpful for lateralization of TLE
- MRI-negative PET-positive TLE (Carne et al., Brain 2004)
- Simultaneous EEG important

PET and ETLE

- Coregistration with MRI improves detection of FCD. (Salamon, 2008)
- MRI-negative ETLE cases: sensitivity varies from 19%-86%. (Lee 2005, Kim 2002, Chassoux 2005, Knowlton 2008)
- Post-processing can increase the yield of visually "normal" PET scans. (Mayoral, 2016)

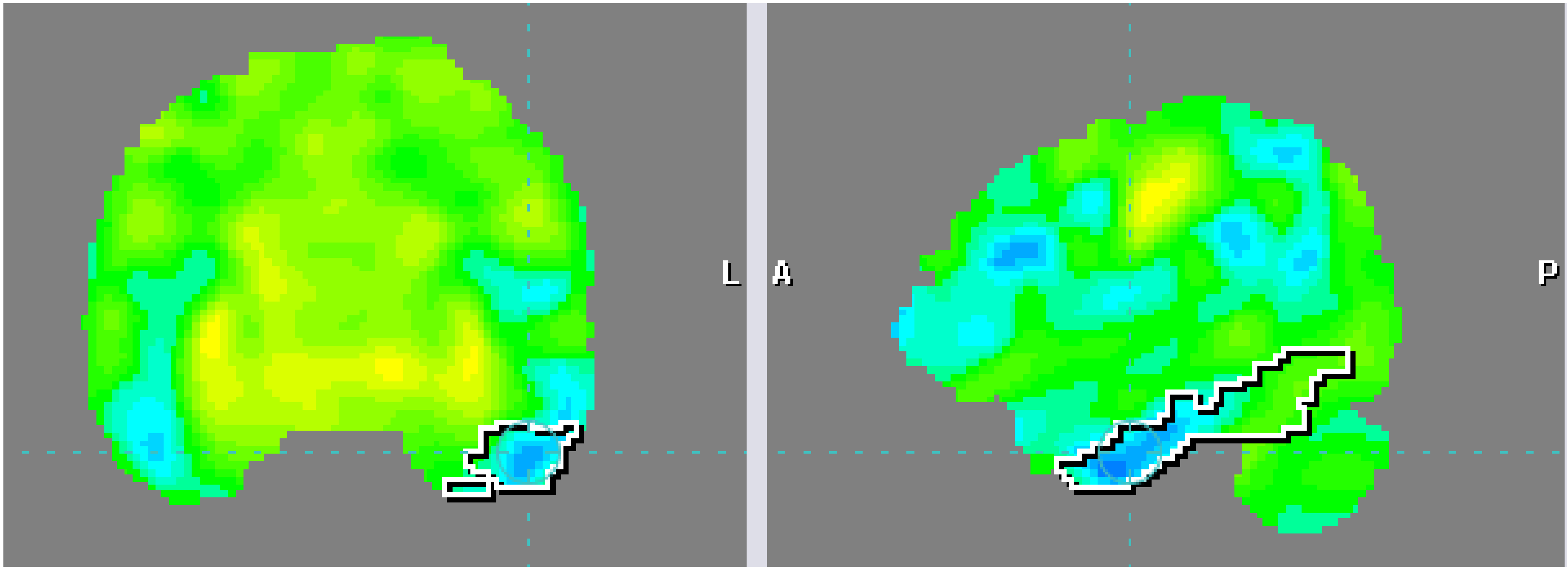


Post-processing of PET



- Database comparison
- Normalization: whole-brain, cerebellum?
- Be aware of artifacts
- Metabolism can be affected by medication, smoking
- Always re-affirm on raw data

A network phenomenon



Always interpret with the patient's electroclinical profile

SPECT in Epilepsy

SPECT in Epilepsy

- Ictal single photon emission computed tomography (SPECT)
- Tracers: Tc-99m ECD, Tc-99m HMPAO
- Measuring regional cerebral blood flow
- SPECT co-registered to magnetic resonance imaging (SISCOM)
  - Ictal acquisition (within in 2 hrs after injection)
  - Interictal (24 hrs of no seizures)
  - Subtraction

SPECT/SISCOM

- A picture of ictal onset + seizure propagation
- Remember the delay in tracer uptake (approximately 30 sec)
- Early injection extremely important

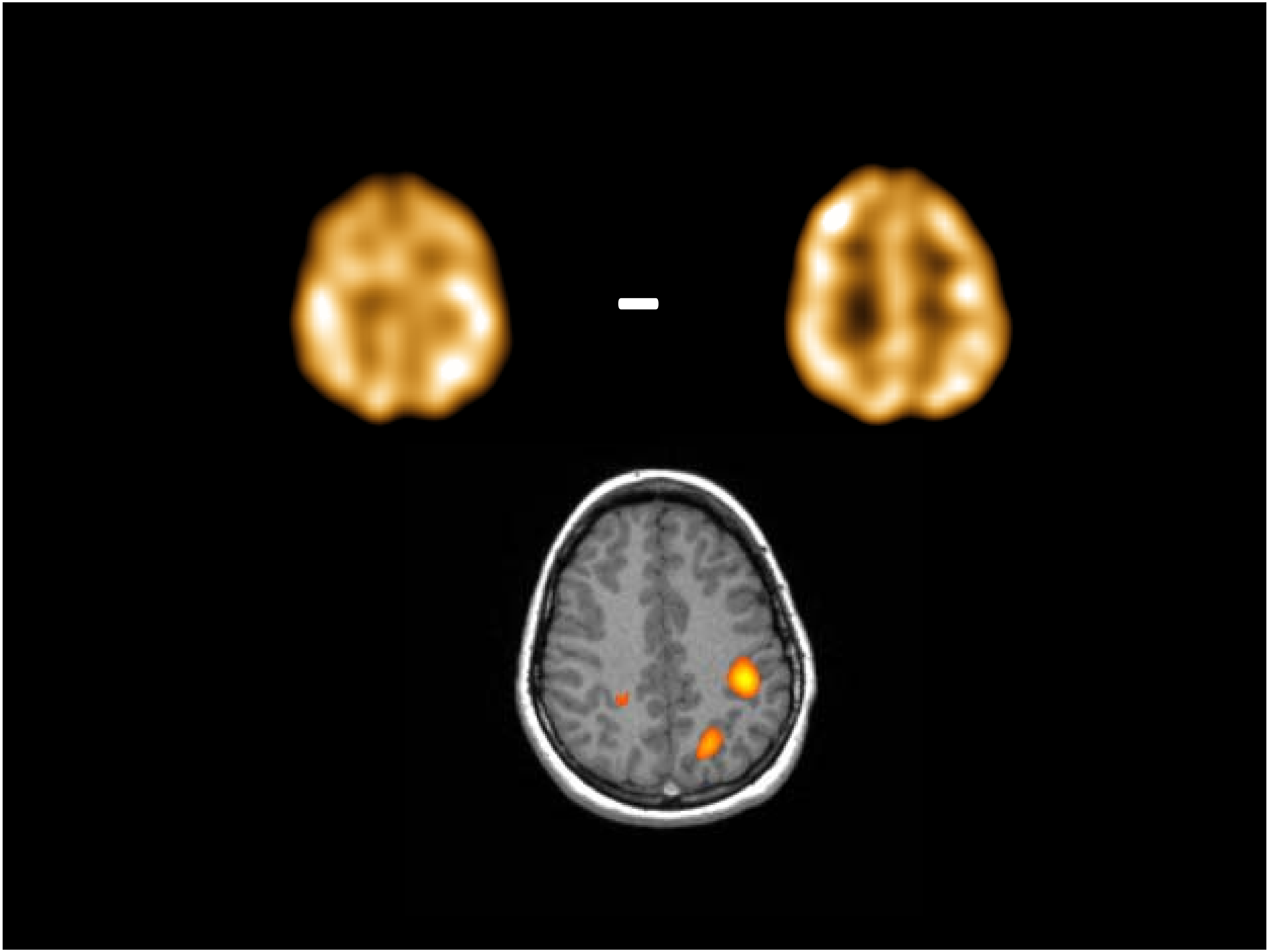
Neuroradiology (2006) 48: 678–684
DOI 10.1007/s00234-006-0106-z

FUNCTIONAL NEURORADIOLOGY

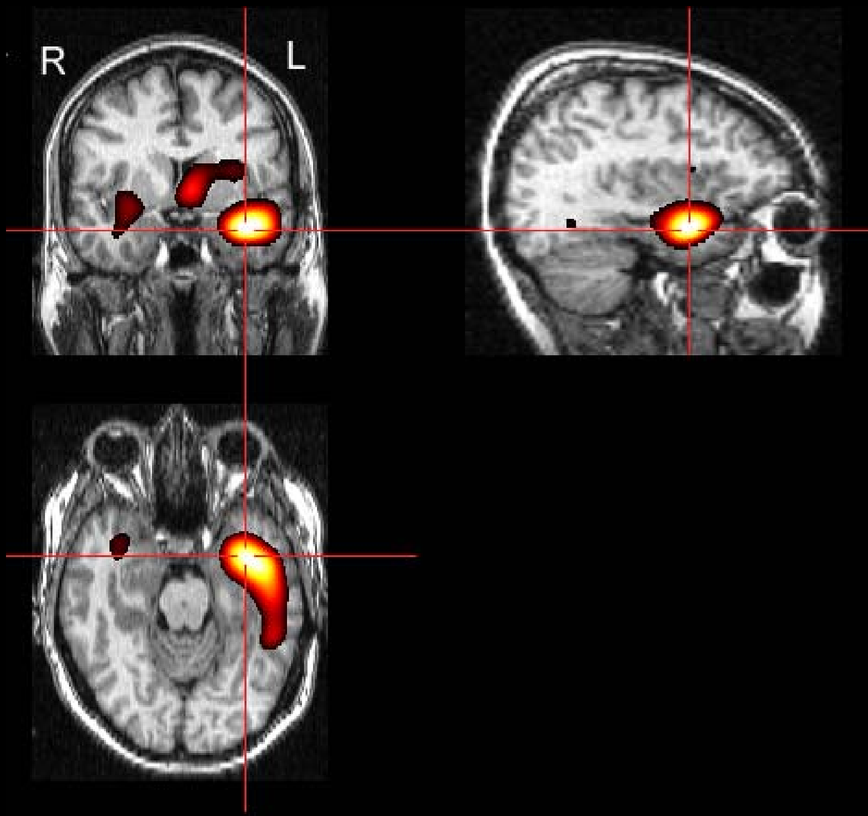
Sang Kun Lee
Seo-Young Lee
Chang-Ho Yun
Ho-Young Lee
Jae-Sung Lee
Dong-Soo Lee

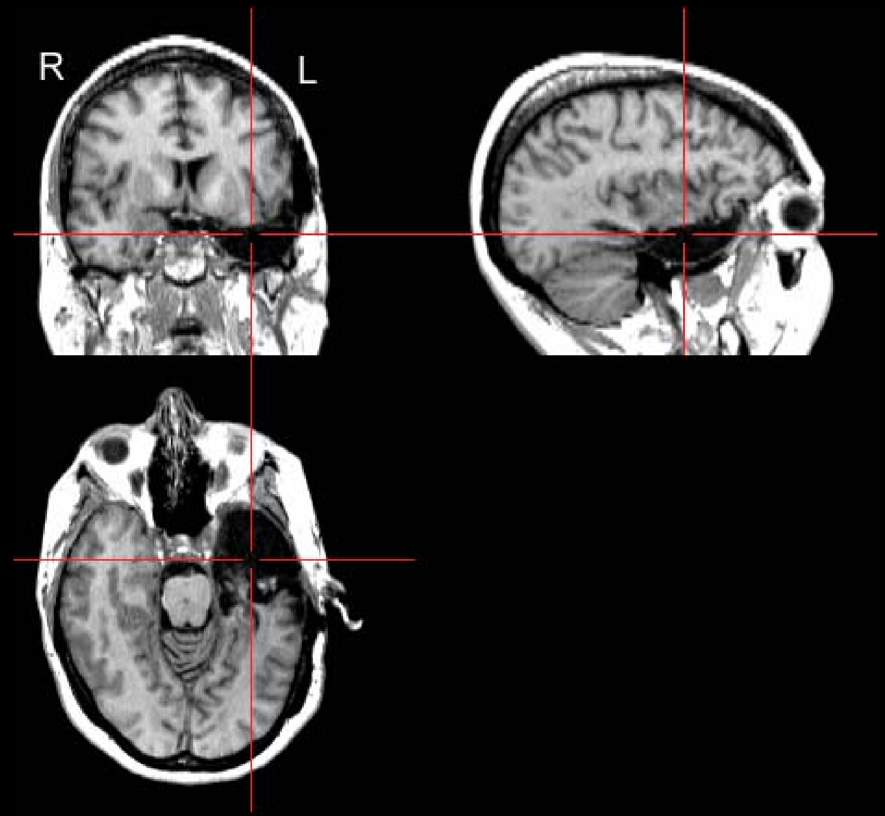
Ictal SPECT in neocortical epilepsies: clinical usefulness and factors affecting the pattern of hyperperfusion

81 consecutive neocortical patients with surgery (36 normal MRI)
Injection time < 20s significantly correlated with correct localization

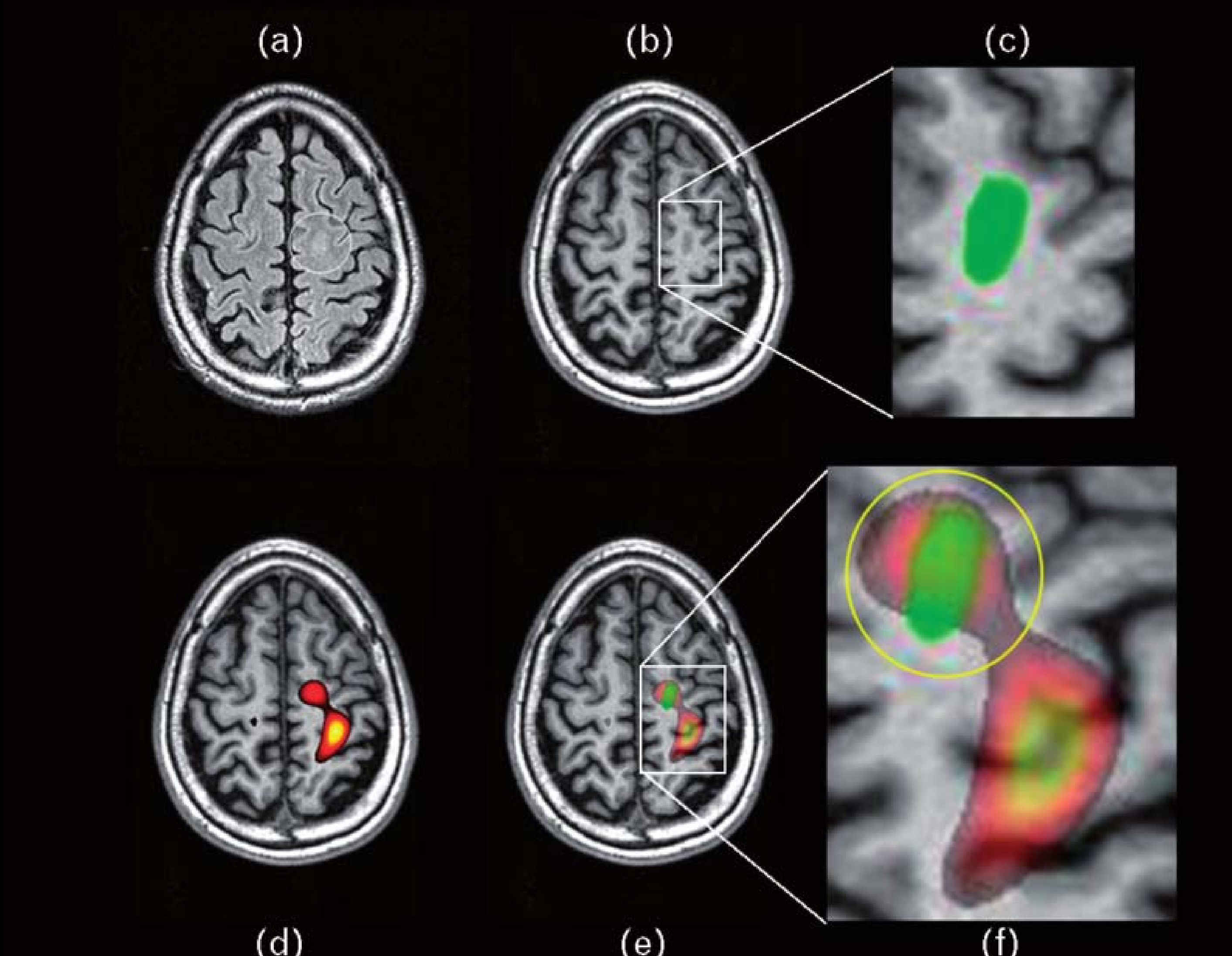


Common Practice





The hour-glass pattern



(Van Paesschen et al., 2007)

Varying z-score Strategy

Epilepsia, 54(5):793–800, 2013
doi: 10.1111/epi.12139

FULL-LENGTH ORIGINAL RESEARCH

Optimizing SPECT SISCOM analysis to localize seizure-onset zone by using varying z scores

*Christopher R. Newey, †‡Chong Wong, †Z. Irene Wang, §Xin Chen, †¶Guiyun Wu, and †Andreas V. Alexopoulos

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26 patients, seizure-free, z=1, 1.5, 2, 2.5

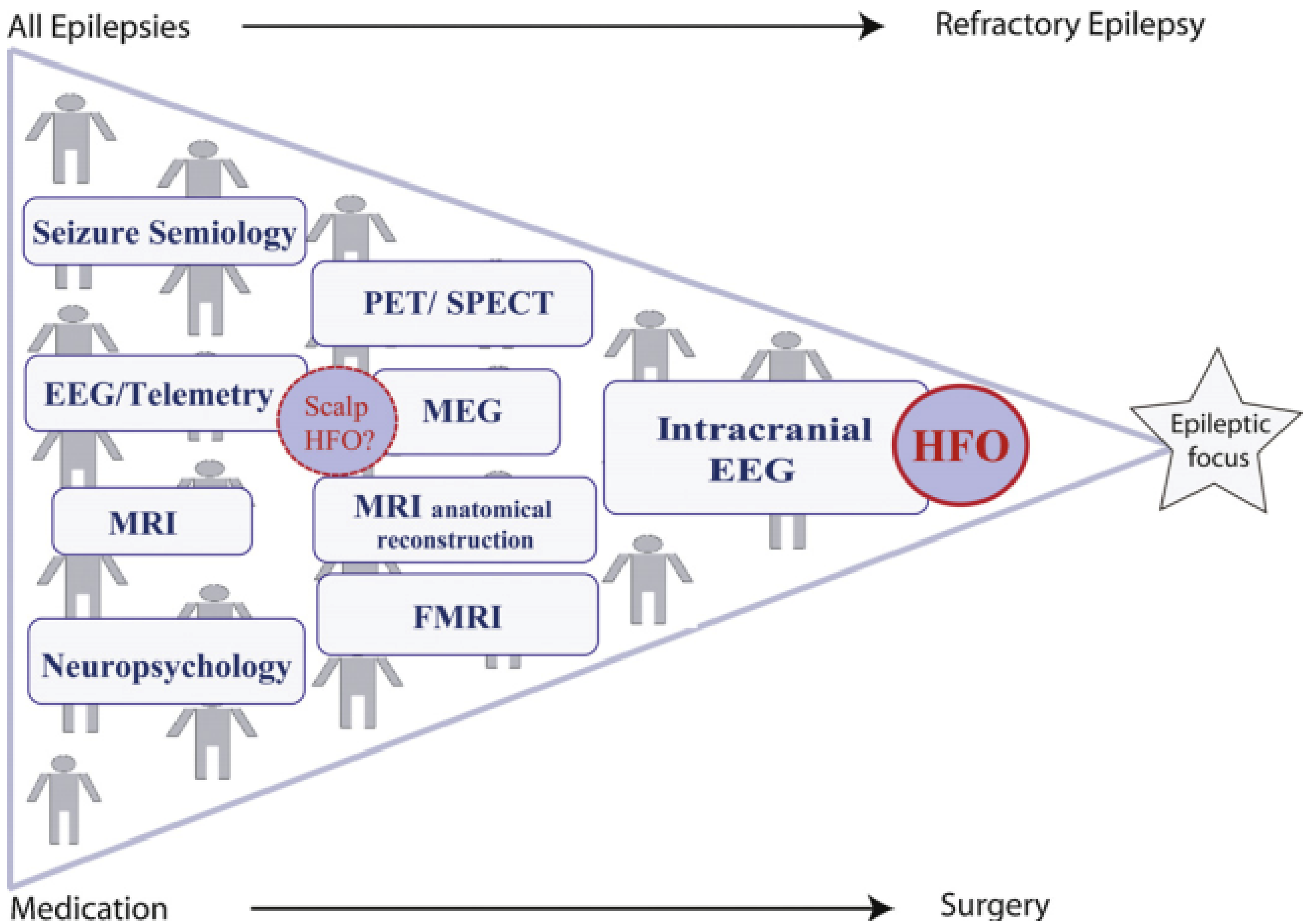
Table 1. Pair-wise comparisons of each z score with regards to its localization accuracy

	z score pairs	Odds ratio	95% CI	p-Value
1.5 vs. 1	4.55	1.78	11.67	0.002
1.5 vs. 2	4.23	1.54	11.62	0.005
1.5 vs. 2.5	7.53	2.56	22.18	0.0002
2 vs. 1	1.08	0.42	2.78	0.88
2 vs. 2.5	1.78	0.88	3.59	0.11
2.5 vs. 1	0.60	0.22	1.65	0.33

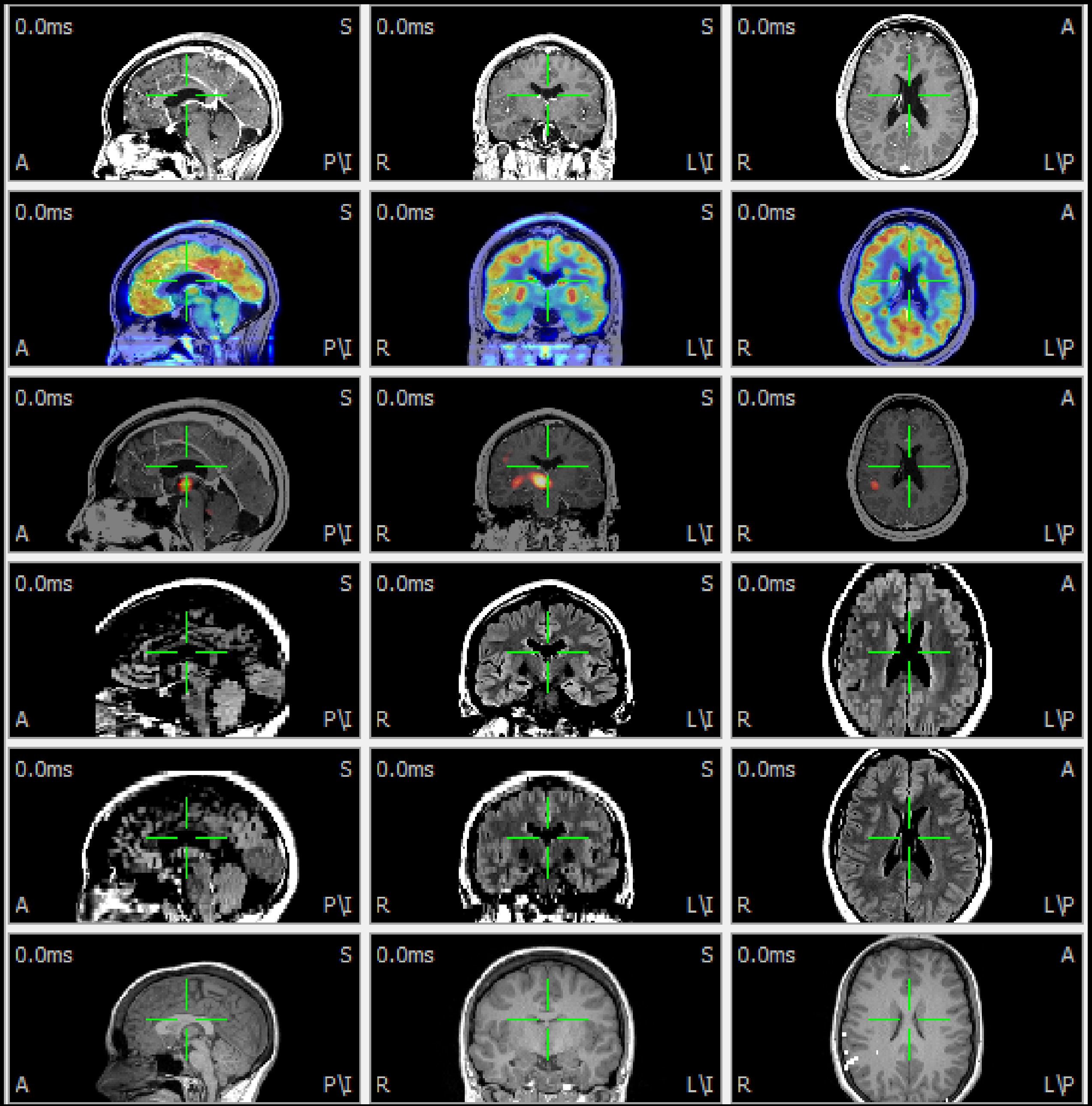
Multi-modal Integration

Presurgical evaluation tools

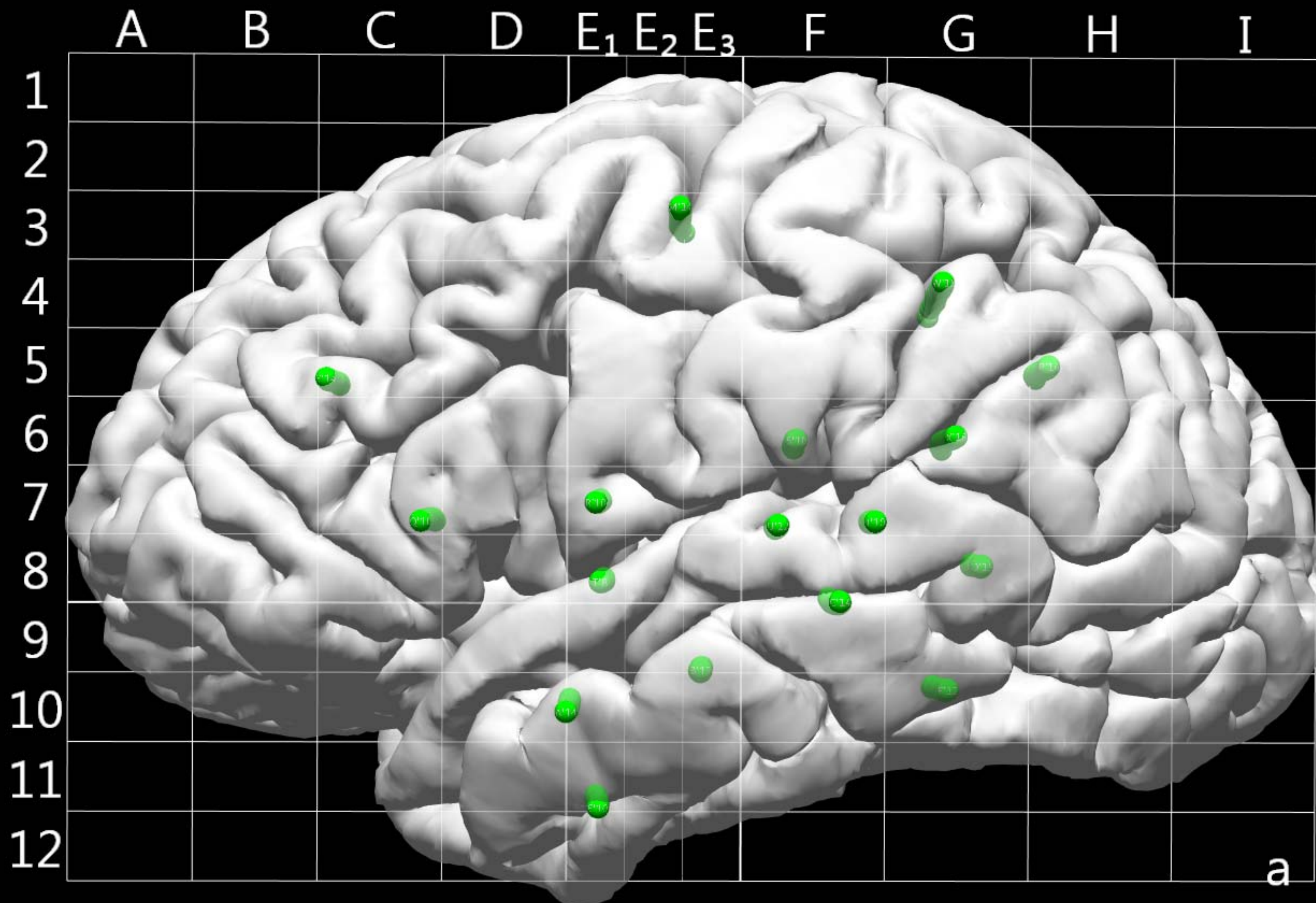
J. Jacobs et al. / Progress in Neurobiology 98 (2012) 302–315



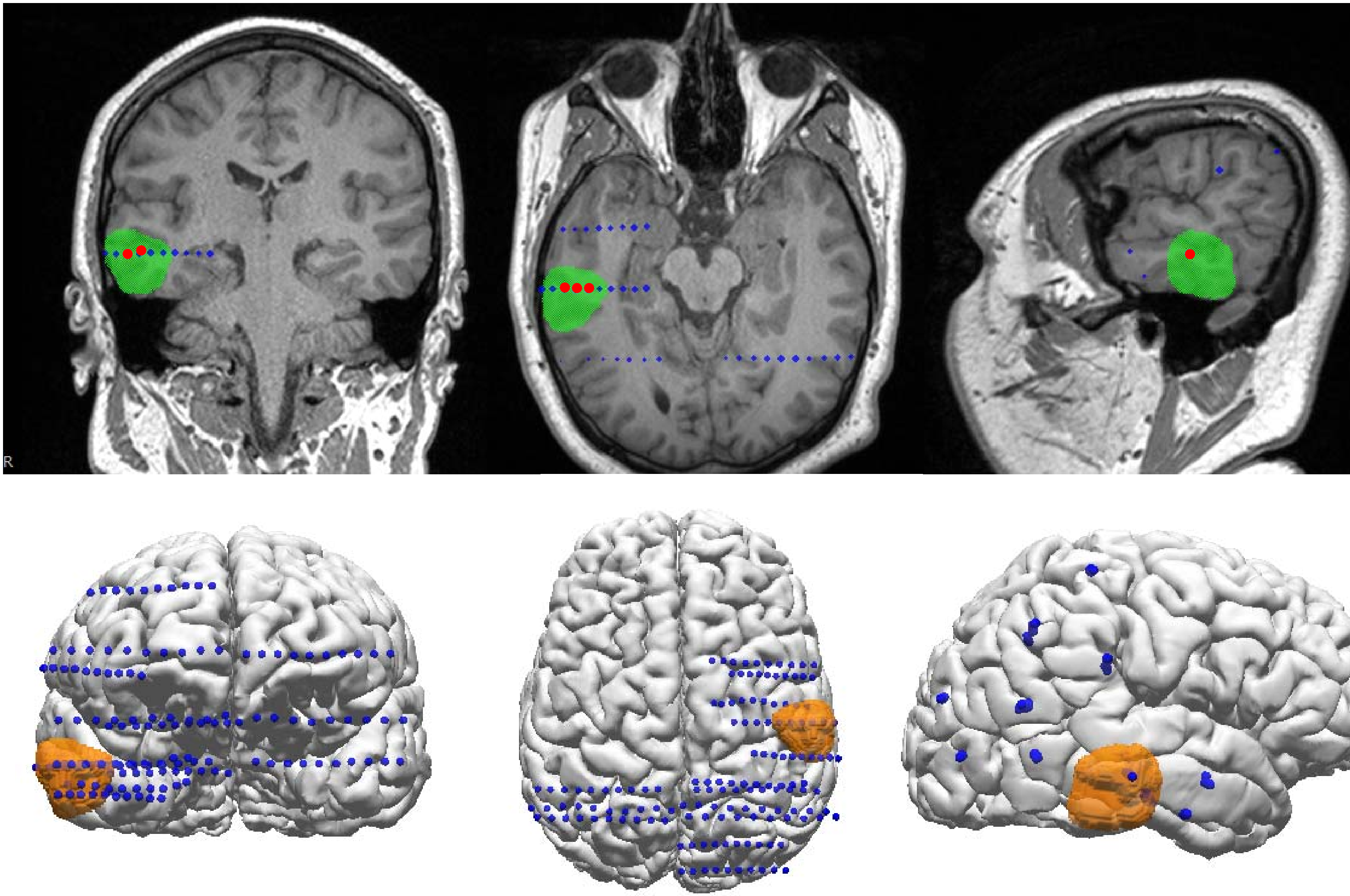
ICEEG Planning



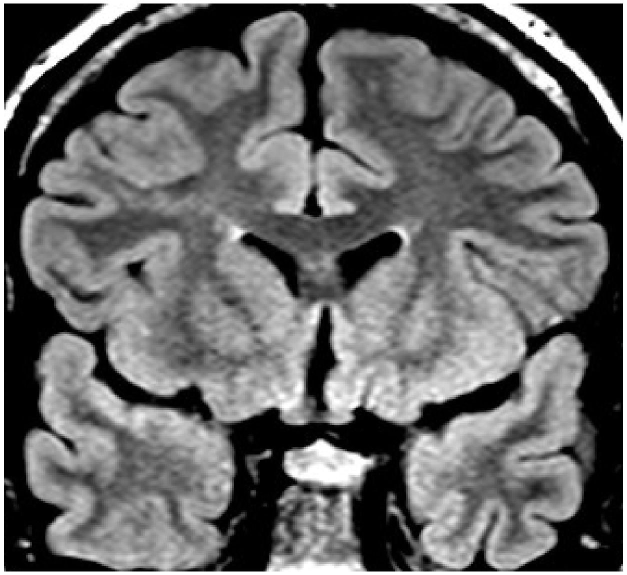
ICEEG Planning

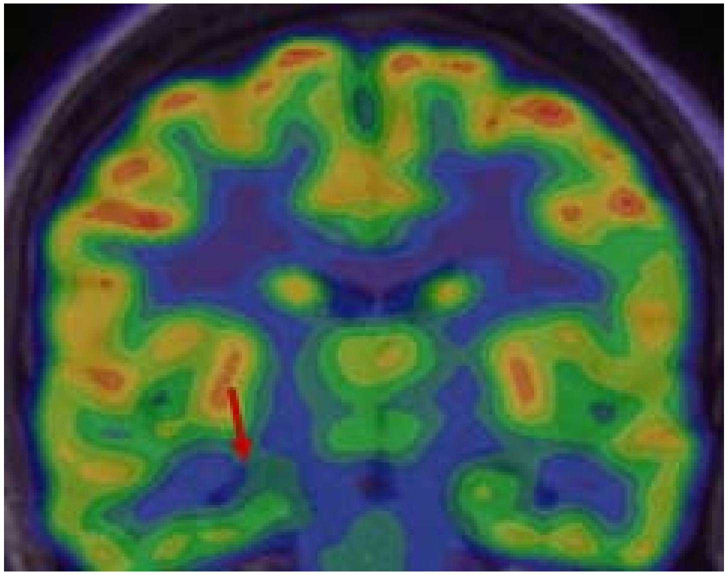


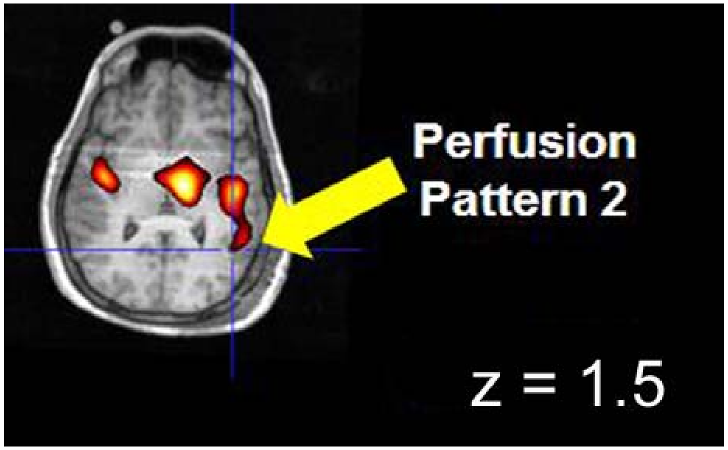
Resection Planning

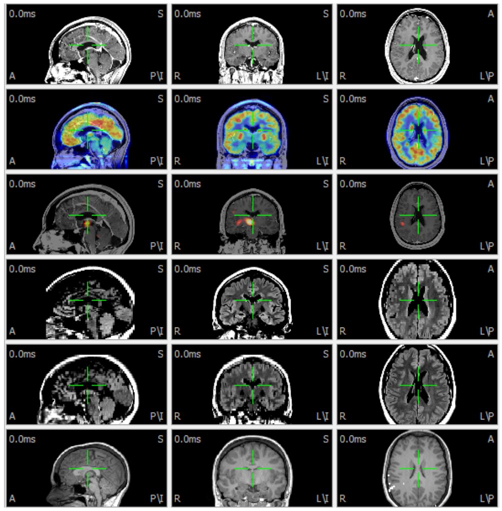


Summary










Thank you