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

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

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## Epilepsy MRI protocol

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

<table>
<thead>
<tr>
<th>Name (abbreviation/vendor)</th>
<th>Advantages</th>
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</thead>
<tbody>
<tr>
<td><strong>Mandatory sequences – HARNESS MRI protocol</strong></td>
<td></td>
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<tr>
<td>Magnetization-prepared rapid gradient-echo (MPRAGE, Siemens), Spoiled gradient-echo (SPGR, GE), Turbo field echo (TFE, Phillips)</td>
<td>T1-weighted 3D</td>
</tr>
<tr>
<td>3D fluid attenuation inversion recovery (FLAIR)</td>
<td>T2-weighted 3D</td>
</tr>
<tr>
<td><strong>ax/cor 2D FLAIR also commonly used</strong></td>
<td></td>
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<tr>
<td>Coronal spin echo (acquisition plane perpendicular to the long axis of the hippocampus)</td>
<td>T2-weighted 2D</td>
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<tr>
<td><strong>Optional sequences</strong></td>
<td></td>
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<tr>
<td>Gadolinium-enhanced MRI</td>
<td>T1-weighted 3D</td>
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<tr>
<td>Susceptibility weighted imaging</td>
<td>T2*-weighted 3D</td>
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</table>
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%
Hippocampal Volumetry

(Kim et al., NeuroImage 2012)
Hippocampal Signal Analysis

Mean FLAIR Intensities of Hippocampus (only upper 25%)

- Controls (447)
- 95% Confidence Region
- 80% Confidence Region
- Right HS (54) (filled squares = Histo+)
- Left HS (43) (filled squares = Histo+)
- Bilateral HS (6)
- GA FLAIR WBA

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

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Where is the Lesion?
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?
Voxel-Based Morphometric Magnetic Resonance Imaging (MRI) Postprocessing in MRI-Negative Epilepsies

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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.
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)


• 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

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

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

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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

<table>
<thead>
<tr>
<th>z score pairs</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 vs. 1</td>
<td>4.55</td>
<td>1.78</td>
<td>11.67</td>
</tr>
<tr>
<td>1.5 vs. 2</td>
<td>4.23</td>
<td>1.54</td>
<td>11.62</td>
</tr>
<tr>
<td>1.5 vs. 2.5</td>
<td>7.53</td>
<td>2.56</td>
<td>22.18</td>
</tr>
<tr>
<td>2 vs. 1</td>
<td>1.08</td>
<td>0.42</td>
<td>2.78</td>
</tr>
<tr>
<td>2 vs. 2.5</td>
<td>1.78</td>
<td>0.88</td>
<td>3.59</td>
</tr>
<tr>
<td>2.5 vs. 1</td>
<td>0.60</td>
<td>0.22</td>
<td>1.65</td>
</tr>
</tbody>
</table>
Multi-modal Integration
Presurgical evaluation tools
ICEEG Planning
Resection Planning
Summary
Thank you