Advanced Imaging Techniques—MRI, PET, SPECT, ESI-MSI, DTI

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## Disclosure

<table>
<thead>
<tr>
<th>Name of Commercial Interest</th>
<th>Type of Financial Relationship</th>
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<tbody>
<tr>
<td>None</td>
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</table>

American Epilepsy Society | 2013 Annual Meeting
Learning Objectives

• Audience participants will be able to define state-of-the-art neuroimaging available to support epilepsy diagnosis and localization today.

• Audience participants will know that advanced imaging tools can be applied in their respective centers with existing and additional available resources.
Introduction / Roadmap

- Diagnostic Imaging Rules
- MRI
- PET & SPECT
- Image Registration and Processing
- Combining Imaging and Neurophysiology
- EEG / ESI
- MEG / MSI

New Information?
## Lesional Partial Epilepsy (~56%) vs. Primary Epilepsies

<table>
<thead>
<tr>
<th>Identified lesion or cause</th>
<th>Cryptogenic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ MRI</td>
<td>- MRI</td>
<td>- MRI</td>
</tr>
<tr>
<td>- MRI</td>
<td>+/- MRI</td>
<td></td>
</tr>
</tbody>
</table>

**MRI Criteria:**
- **+ MRI (Identified lesion or cause)**: MRI is positive, indicating a lesion or cause.
- **- MRI (Cryptogenic)**: MRI is negative, indicating a cryptogenic cause.
- **+/- MRI**: MRI results are uncertain or mixed.
Diagnostic Accuracy

<table>
<thead>
<tr>
<th>Test</th>
<th>Truth</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>-</td>
</tr>
<tr>
<td>+</td>
<td>a</td>
</tr>
<tr>
<td>-</td>
<td>c</td>
</tr>
<tr>
<td></td>
<td>d</td>
</tr>
</tbody>
</table>
Towards Complete and Accurate Reporting of Studies of Diagnostic Accuracy: The STARD Initiative

For the STARD Group

[Diagram of diagnostic accuracy reporting process]
Hippocampal Sclerosis (HS)

Atrophy
Hyperintensity
Loss of internal architecture
MRI and TLE: Atypical HS

- End-folium sclerosis
- Isolated internal architecture disturbance
Evaluating hippocampal internal architecture on MRI: Inter-rater reliability of a proposed scoring system.

HIA Asymmetry and Surgical Outcome

<table>
<thead>
<tr>
<th>Concordant HIA Asym ≥ 0.5</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sz Free</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Not Sz Free</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Marginal Probability</td>
<td>0.83</td>
<td>0.53</td>
</tr>
<tr>
<td>Odds Ratio: 4.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p = 0.23</td>
<td></td>
</tr>
</tbody>
</table>

2005-2012: 272 Surgical Resections

2005-2012: 272 Surgical Resections

124 Extra-Temporal

148 Temporal lobe

84 HS+ MRI

44 other lesions

20 “normal” MRI

<table>
<thead>
<tr>
<th>Paradoxical HIA Asym</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sz Free</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Not Sz Free</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Marginal Probability</td>
<td>0.80</td>
<td>0.20</td>
</tr>
<tr>
<td>Odds Ratio: 16</td>
<td></td>
<td>p = 0.0317</td>
</tr>
</tbody>
</table>

Predictive value of hippocampal internal architecture asymmetry in temporal lobe epilepsy.
Tilt and Orientation
MRI and TLE: Besides HS

- Subtle parahippocampal abnormalities
- Hippocampal–incomplete inversion (aka “malrotation”)
- Temporal encephaloceles
- Hippocampal (choroidal fissure) cysts
- Temporal polar atrophy
The Parahippocampus
Hippocampal “Malrotation”—diagnostic significance?

Temporal Encephaloceles
Hippocampal Choroid Fissure Cysts
MRI and ExTLE: Detecting cryptic (occult) dysplasia

• Visual analysis
  – Base of the sulcus abnormalities
  – Surface visualization
  – Curvilinear reformatting

• Beyond visual analysis
  – Voxel based morphometry (VBM)
  – Machine learning strategies
  – White matter microabnormalities by DWI
Focal Cortical Dysplasia
Focal Cortical Dysplasia II
Focal Cortical Dysplasia III
PET

• Types / Ligands
  - $2-[^{18}\text{F}]$fluoro-2-deoxy-D-glucose (FDG)
  - $[^{11}\text{C}]$flumazenil
  - $\alpha[^{11}\text{C}]$methyl-L-tryptophan
  - $[^{18}\text{F}]$FCWAY (5-HT$_{1a}$ receptor ligand)
  - R-$[^{11}\text{C}]$verapamil

• Optimal visualization / analysis
  - Tilt and rotation correction
  - MRI coregistration
  - SPM analysis helpful
FDG-PET–Neocortical FCD Detection
PET-MRI Coregistration
PET-MRI Coregistration—partial volume correction
Ictal SPECT

Visualization and Difference Analysis

– Intensity normalization
– Image alignment (registration)
– Subtraction
– Coregistration to MRI
– SISCOM\(^1\) versus SPM\(^2\) techniques

\(^1\) Subtraction Ictal SPECT with Coregistration on MRI (SISCOM)
\(^2\) Statistical Parametric Mapping (SPM)
Ictal SPECT analysis with SPM

Statistical ictal SPECT coregistered to MRI (STATISCOM)

Ictal-interictal SPECT analyzed by SPM (ISAS)
http://spect.yale.edu
SPM (STATISCOM) vs SISCOM

Adapted from:
Paige et al. Comparison of Ictal SPECT Analysis Methods. AES Platform 2010
ISAS vs SISCOM
iSPECT–MRI + (large lesion)
EEG / MEG Source Localization (EEG / MEG Source Imaging)

• Improving pre intracranial EEG (ICEEG) hypothesis—increase proportion of patients that can proceed to surgery
  – TLE—mesial versus lateral
  – Delineate focal epileptogenic tissue amongst larger MRI abnormalities
  – Increase detection of cryptic focal cortical dysplasia
• Prediction of ICEEG yield and surgery outcome
ESI / MSI Sublobar Localization
MEG Prediction of ICEEG Yield and Surgical Outcome

- Subdural grids and strips
    n=11 ICEEG cases, 10/11 concordant ICEEG ictal onset
    n=23 ICEEG cases, 17 were localized, 11/17 (70%) had greater than 6 or more densely clustered spikes.
    n=22 ICEEG children cases (MRI negative).
    *MEG single clusters agree with localized ICEEG and surgical outcome.*
# MEG Prediction of ICEEG Yield and Surgical Outcome

<table>
<thead>
<tr>
<th>Diagnostic Values</th>
<th>MSI (n = 72)</th>
<th>Diagnostic MSI⁴ (n = 58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, % (CI)</td>
<td>62.7 (48.1–75.5)</td>
<td>80.0 (63.9–90.4)</td>
</tr>
<tr>
<td>Specificity, % (CI)</td>
<td>75.0 (47.4–91.7)</td>
<td>69.2 (38.9–89.6)</td>
</tr>
<tr>
<td><strong>PPV, % (CI)</strong></td>
<td><strong>88.9 (78.0–96.4)</strong></td>
<td><strong>88.9 (73.0–96.4)</strong></td>
</tr>
<tr>
<td>NPV, % (CI)</td>
<td>38.7 (22.4–57.7)</td>
<td>52.9 (28.5–76.1)</td>
</tr>
<tr>
<td>Discordant cases, n</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

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*Table 3. Magnetic Source Imaging Diagnostic Measures Based on Intracranial Electroencephalography Localization*

<table>
<thead>
<tr>
<th>Diagnostic Value</th>
<th>MSI, (CI) (n = 62)</th>
<th>Diagnostic MSI (CI)* (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>55% (44.2–63.7)</td>
<td>72% (59.1–82.7)</td>
</tr>
<tr>
<td>Specificity</td>
<td>75% (57.4–88.4)</td>
<td>70% (50.8–84.8)</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td><strong>78% (62.1–89.7)</strong></td>
<td><strong>78% (63.5–88.8)</strong></td>
</tr>
<tr>
<td>NPV</td>
<td>51% (39.4–60.6)</td>
<td>64% (46.1–77.1)</td>
</tr>
</tbody>
</table>

*Nondiagnostic MSI (no spikes) cases excluded.
MSI = magnetic source imaging; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value.
MEG Prediction of ICEEG Yield and Surgical Outcome

• Stereo-electroencephalography (SEEG)
  – Jung et al. *Brain* 2013: **136**; 3176-3186

  N=21 MRI negative cases—using *volumetric imaging* of spike source generators, unequivocal spikes in 17 (81%)

<table>
<thead>
<tr>
<th>MEG spike volume extent and ictal SEEG localization</th>
<th>SEEG Localized</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEG</td>
<td>Yes</td>
</tr>
<tr>
<td>Loc</td>
<td>8</td>
</tr>
<tr>
<td>Lateralized</td>
<td>3</td>
</tr>
<tr>
<td>Non-localized</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
</tr>
</tbody>
</table>

Fisher's Exact *p* < 0.05
Nonlesional Epilepsy Imaging

Optimal visualization is critical—take control of image processing and confirm with your own visual analysis

– MRI—scrutinize appropriate sequences for subtle, but *established* epileptogenic abnormalities; refrain from temptation to over-read.

– PET—ignore all interpretation but your own.

– SPECT—perform either ISAS or STATISCOM.

– ESI/MSI—use your EEG expertise to interpret.
Impact on Clinical Care and Practice

• Extracting the maximum amount of information from imaging tests may increase the proportion of patients that can proceed to epilepsy surgery.
• Many techniques for acquiring and extracting more information from established tests are available and can be implemented at most centers.
• Diagnostic accuracy and reliability of new tests/information should be confirmed before being given much weight in clinical decision-making.