Multimodal Imaging in Epilepsy Surgery

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Disclosure

I have no actual or potential conflict of interest in relation to this program

Outline

1. Introduction
2. Clinical Applications
3. Concepts of multi-modality use in SEEG
4. Clinical Workflow
5. Selected Studies
6. Future Directions
Concept of multimodal integration

A precise orientation of the brain is a basic condition in the attempt at a 3-dimensional synthesis from 2-dimensional morphologic data – anatomy itself being volume and space

Gábor Szikla
Hungary 1928 – 1983 Paris
Angiography of the Human Brain Cortex. Springer 1977

Image coregistration

- Process of transforming disparate imaging modalities
- Allows for integration in the same coordinate space
- Computational formula to account for differences
- Spatial coregistration margins of error & validation
- Relationship to electrophysiology (SEEG seizures/mapping)

* Presupposes that each individual imaging approach is performed as intended both technically and clinically


Multi-Modality Image Registration for Pre-Operative planning and Image Guided Neurosurgical Procedures

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Keywords:
Stereotactic registration, functional information, tumor

Introduction

Image registration is the process of transforming images acquired at different time points, or with different imaging modalities, to the same coordinate space. It is an essential part of any neurosurgical planning and navigational system because it facilitates overlaying images with important anatomic, vascular, and functional information to improve the information base on which a surgeon makes critical decisions.

Magnetic resonance imaging (MRI) can be used to provide both structural and functional neuroanatomical information that is important in planning neurosurgical procedures. Optimal identification and localization of the motor and sensory cortex, and the motor and sensory cortex of the face, can be achieved using the functional data of the images. In cases where the area of interest is in the motor and sensory cortex, MRI can help to identify the exact location of the neuron. In addition, the information can be used to plan the incision and to ensure that the surgical technique is accurate.
Talairach stereotactic apparatus

Contrast Ventriculogram showing AC & PC lines of reference

Proportional Grid System

Szikla Stereotactic Tele-Angiography

...allowing for superimposition of all radiologic documents (encephalograms, ventriculograms, arteriograms)...

The “cartoon era”

Cortical Surface & Talairach Grid

Cleveland Clinic SEEG platform
**Why multimodality coregistration?**

- A single modality only reveals limited number of tissue features
- Modality-specific advantages and **intrinsic limitations**
- Visual interpretation of each modality in isolation is **subjective** and dependent on the interpreter’s experience
- Synergistic use of modalities to establish **concordance**
- Advance accuracy of epileptic focus **localization** and advance our SEEG pre-implantation hypothesis
- Facilitate **spatio-temporal** understanding of SEEG data
- Guide completeness of surgical resection

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**Superimposing Imaging Modalities**

![Figure 2](Image)

Unusual Gyral pattern  Visual Analysis

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**Importance of superimposing PET/MRI**

![Figure 2](Image)

Unusual Gyral pattern  Visual Analysis  PET/MRI fusion

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*Chassoux F. et al. Neurology 2010*
Improved postoperative seizure outcome with or without intracranial EEG

Coregistration of multimodal imaging is associated with favourable two-year seizure outcome after paediatric epilepsy surgery

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Conclusions: Coregistration of multimodal imaging is associated with favourable two-year seizure outcome after paediatric epilepsy surgery. Coregistration may be useful for improving surgical planning and increasing the success of surgical procedures.

Change in SEEG implantation strategy

Utility of 3D multimodality imaging in the implantation of intracranial electrodes in epilepsy

*(John Dunec, a)Roman Rodosthenes, (George Zambani, (Rachel Spano, (Gavin Winsten, (Jane Kinghorn, (Bread Dufft, (Tim Walker, (Anna Mitrichchi, (Andrew MeVay, (Sebastian Orselli, and (John Dunec

Objective: We present a single-center prospective study, validating the use of 3D multimodality imaging (SMII) in patients undergoing intracranial electroencephalography (IC-EEG).

Methods: IC-EEG implantation preparation entails first designing the overall strategy of implantation (strategy) and around the precise details of implantation (planning). For each case, the multidisciplinary team reviews decision on strategy and planning before the disclosure of multimodal imaging results. Any changes to the strategy or planning are considered at this point. Results: Disclosures of SMII led to a change in strategy in 16 (46%) of 35 individuals. The changes included addition and repositioning of electrodes, addition of grids, and going directly to resection. For the detailed surgical planning, SMII led to a change in 19 (54%) of 36 individuals. Twenty-five (72%) of 35 patients undergoing surgery-BRS (SMII) underwent a change in electrode placement, with 18 (51%) of 35 electrode trajectories being altered. Significance: The use of SMII makes substantial changes in clinical decision making.

KEY WORDS: Epilepsy surgery, Image Integration, Preoperative evaluation.

Spatial vs. Temporal Domain

#### Invasiveness

<table>
<thead>
<tr>
<th>EEG</th>
<th>MEG</th>
</tr>
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<tbody>
<tr>
<td>ECoG</td>
<td>sEEG</td>
</tr>
</tbody>
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#### Spatial Resolution (mm)

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<tr>
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<th>10</th>
<th>10²</th>
<th>10³</th>
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<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>10</td>
<td>20</td>
<td>30</td>
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#### Temporal Resolution (msec)

<table>
<thead>
<tr>
<th>1msec</th>
<th>&gt;10sec</th>
</tr>
</thead>
</table>

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*Reference: Cleveland Clinic*
Concept of SEEG planning & interpretation

SEEG should not be considered as a technique rather a method that is deeply rooted in anatomo-functional-electro-clinical correlations

The “gold-standard” intracranial EEG

“I’m right there in the room, and no one even acknowledges me.”

The “gold-standard” problem

• Well-localized ICEEG but poor outcome
• Non-localized ICEEG but resection helps
• Systematic sampling bias
• Aborted without conclusive information
• Importance of concordance of electroclinical analysis and noninvasive studies
Pitfalls of Intracranial EEG recordings

- Inherently limited sampling
- Inadequate coverage
- Erroneous coverage
- Edge discharges
- Intra-ictal activation
- Ambiguous interpretation
- Yield unclear
- Risky
- Costly

Localization of Seizure Foci: Pitfalls and Caveats
Prerna Juyal, Michel Duchowny, Teresa J. Renick, and Lori A. Alzate

From noninvasive to invasive recordings

- The indication and planning for placement of invasive electrodes is based on systematic electroclinical analysis with semiology playing a central role, and results of all presurgical noninvasive testing followed by a thorough multidisciplinary discussion in patient management conference

- There is a need for a solid, well-defined hypothesis derived from all non-invasive studies before placing any electrodes

- There is a limit on what can be covered
Current Clinical Workflow
Multimodality Coregistration
in daily practice (SEEG)
at the Cleveland Clinic Epilepsy Center

Multi-modal Integration for ICEEG Planning

• Image Fusion: MRI (T1, T2, FLAIR, post-processing), PET, SISCOM, MEG, vasculature
• Realistic rendering of cortical surface
• Talairach grid
• Same platform includes electrode planning
• Electrode trajectories exported to neuro-navigation system

Image Fusion: MRI

Jin, Wang et al.
Image Fusion: Vasculature

Multimodal visualization patient management discussion

Multimodal visualization patient management discussion
Other modalities

Lesion side

Normal side

Image Fusion: Talairach Grid

Jin et al, in preparation

SEEG Implantation Planning
Image fusion: post-SEEG CAT scan

3-Dimensional SEEG analysis

Resection planning
Image fusion: post-resection MRI
Reoperation after SEEG

Cortical Surface (prior surgery)

Challenging RNS implantation
Amygdala lead
From Clinical Observation to systematic study

Illustrative Case: Clinical Synopsis

- 30yo male with “nonlesional” epilepsy since 12yo
- Semiology: tingling sensation in the throat, drooling and garbled speech (no loss of awareness) up to 10/day
- Interictal VEEG: **No Interictal Epileptiform abnormalities**
- Ictal Video-EEG: Nonlocalizable

Noninvasive data

- Scalp EEG:
  - no interictal abnormalities
  - non-localizable EEG seizure patterns
- PET and SPECT: non-localizing
- MRI:
  - 2003 MRI: Normal
  - 2008 MRI: Normal
  - 2009 MRI: Normal

Wang ZI, Jones SE, Alexopoulos AV et al. Epilepsy Research 2012
Morphometric Analysis Program (MAP)

- A specific Voxel-Based Morphometry package optimized for application to individual patients
- MAP is especially sensitive to subtle abnormalities associated with *blurring in the gray-white matter junction*
- Such areas may be associated with an underlying (occult) focal cortical dysplasia

Stereo-EEG depth electrode implantation targets this area
Linking MRI Postprocessing with Magnetic Source Imaging in MRI-negative Epilepsy

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Objective: MRI-negative (MRI-) pharmcoresistant focal epilepsy (PTE) patients are an enigma challenging for optimal surgical management. This study utilizes a voxel-based MRI postprocessing technique, implemented using a morphometric analysis program (MAP), aiming to facilitate detection of subtle focal cortical dysplasia (FCD) in MRI- patients. Furthermore, the study examines the concordance between MAP-identified regions and localisation from magnetic source imaging (MSI).

Methods: A retrospective study was conducted on 20 MRI- surgical patients. MAP was performed on T1-weighted MRIs, with comparison to a normal database. The performance of MAP- areas was confirmed by MSI, surgical outcome and pathology. Analysis of MAP and MSI were performed blindly from patients’ clinical information and established epilepsy from each other.

Results: The detection rate of subtle changes by MAP was 89% (12/13). Once MAP- areas were reased, patients demonstrated a significantly higher chance to achieving a seizure-free outcome following complete resection of the area (p = 0.006). In the 9 confirmed MAP- areas, pathology revealed FCD type IIb in 7 and type I in 2.

Interpretation: MAP shows promise in identifying subtle FCD abnormalities and increasing the diagnostic yield of clinical assessment. Furthermore, comparison between MRI and MSI analysis may lead to the noninvasive identification of a structurally and electrically abnormal seizure foci that can be surgically targeted.

AJNR Neuroradiol 2014;73:5-775
Improving noninvasive localization in MRI-negative pts

Low cost MRI post-processing (MAP) approach

Concordant MAP and MEG uncovers a structurally and electrically abnormal brain tissue

This localized abnormality can be surgically targeted

Complete resection of the MAP/MEG area is associated with favorable outcome

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Linking MEG with MRI post-processing in Focal Cortical Dysplasia

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Correlating magnetoencephalography to stereo-electroencephalography in patients undergoing epilepsy surgery
Table 2  Correlation between sampling of MEG cluster and outcome

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total Seizure-free (12m)</th>
<th>Not seizure-free (12m)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete sampling</td>
<td>26</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>Partial sampling</td>
<td>17</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>No sampling</td>
<td>7</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

P-values were generated by Fisher’s Exact test. The partial sampling and no sampling subgroups were combined to perform the test.

Figure 2: Schematic of a 3-dimensional view of MEG and fMRI. Green: electrodes contacts; yellow: MEG contacts on the scalp. Red contacts are not visible on the scalp where MEG is located. Red contacts indicate the MEG contacts cannot be reliably or safely

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Single SEEG Spike note the progression of amplitude decrease across electrode contacts (distance)

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"Where the telescope ends, the microscope begins. Which of the two has the grander view?"

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Concordance between interictal MEG and stereo-EEG predicts seizure freedom after epilepsy surgery

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Victor Hugo Les Misérables
Future Directions

Practical Directions

• Individual level: Prospective use to assist surgical planning
• Group level: Summarize/compare across patients and modalities

Focal Cortical Dysplasia “visualization” Toolbox

Algorithm 1 Raycasting multi-volumes

```plaintext
Input: Reference volume \( F_r \) and floating volume \( F_f \)
Output: Multi-modal image
1. Determine entry \( j \) and exit \( i \) positions of \( F_f \)
2. Compute ray direction \( d \)
3. \( x_n \leftarrow 0 \)
4. \( m \leftarrow 0 \)
5. \( \text{while} \ x_n < \text{distance}(0,0) \) \( \text{do} \)
6. \( x_{n+1} \leftarrow x_n + d \)
7. \( P \leftarrow r \left( x_n \right) \)
8. \( P \leftarrow F_f \left(X_n \right) \)
9. \( \text{if} \ P \neq 0 \) \( \text{then} \)
10. \( \text{Get the data value of } P \text{ at } P \)
11. \( \text{Color} (R,G,B) \text{and accumulate in } F_r \)
12. \( \text{end if} \)
13. \( x \leftarrow x_n \)
14. \( \text{end for} \)
15. \( x \leftarrow x + \Delta x \)
16. \( \text{end while} \)
```

Toward a Multimodal Diagnostic Exploratory Visualization of Focal Cortical Dysplasia

Future directions

• Automated machine learning “lesion” detection
• Obviate need for intracranial recordings
• Allow for targeted surgical or other therapies
• Facilitate interpretation of complex SEEG results
• Clinically-relevant connectivity information
• “4D” Multimodal Integration
  - Seizure itself being volume and space and time...

Thank you for your attention