Scientific Symposium
Stereotactic Electroencephalography (sEEG) in the Pre-surgical Investigation of Refractory Focal Epilepsy

Symposium Co-Chairs:
Hans O. Lüders, M.D., Ph.D.
Epilepsy Center
Case Medical Center
University Hospitals Cleveland
Cleveland, OH

and

Philippe Kahane, M.D., Ph.D.
Neurology Department & INSERM U836
Grenoble University Hospital
Grenoble, France

Tuesday, December 4, 2012
Convention Center – Ballroom 6C, Upper Level
8:30 am – 10:00 am
OVERVIEW
A significant proportion of patients with refractory focal epilepsy who are being evaluated for resective surgery require invasive evaluations with subdural or depth electrode studies in order to better delineate the most likely epileptogenic zone. In most parts of the world that have the expertise and infrastructure to carry out intracranial electrode studies, the preferred method is subdural grid insertion with or without limited, non-stereotactic depth electrodes. A handful of centers in Europe and North America employ the use of stereotactically implanted, multiple-depth electrodes (stereotactic electroencephalography or sEEG), which have both advantages and potential limitations. Many centers have noted an increasing complexity of surgical cases presenting for presurgical evaluations, for example, patients who are MRI lesion negative, or who have dual or multiple epileptogenic pathologies. Such patients may be studied best using sEEG. This symposium will address the rationale, technology, advantages, risks and outcomes of sEEG usage in intractable focal epilepsy.

LEARNER OUTCOMES
- Recognize the usefulness of sEEG as an invasive evaluation technique for defining the epileptogenic zone in select patients who are candidates for epilepsy surgery and develop appropriate capacity to perform such studies
- Recognize the usefulness of sEEG as an invasive evaluation technique for defining eloquent cortex in select patients who are candidates for epilepsy surgery and develop the capacity for such studies.

TARGET AUDIENCE
Advanced: Symposium will address highly technical or complex topics (e.g., neurophysiology, advanced imaging techniques, advanced treatment modalities, including surgery)

AGENDA
8:30 – 8:35 am Introduction and Overview
Hans O. Lüders, M.D., Ph.D.

8:35 – 8:50 am Stereo-EEG methodology: the European Approach
Giorgio LoRusso, M.D.

8:50 – 9:05 am Stereo-EEG Methodology: the North American Approach
Jonathan P. Miller, M.D.

9:05 – 9:20 am Depth Electrodes vs. Stereo-EEG vs. Subdural Electrodes: Relative Advantages and Disadvantages
Jorge A. Gonzalez-Martinez, M.D.

9:20 – 9:35 am Mapping the Epileptogenic Zone with Stereo EEG
Philippe Kahane, M.D., Ph.D.

9:35 – 9:50 am Mapping the Eloquent Cortex with Stereo EEG
Samden Lhatoo, M.D.

9:50 – 10:00 am Round Table and Conclusions
Hans Lüders, M.D., Ph.D.
ACCREDITATION
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International Credits: The American Medical Association has determined that non-U.S. licensed physicians who participate in this CME activity are eligible for AMA PRA Category 1 Credit™.

ABPN Core Competencies
The American Board of Psychiatry and Neurology has reviewed the Annual Course and has approved this program as part of a comprehensive lifelong learning program, which is mandated by the ABMS as a necessary component of maintenance of certification.

Core Competencies: Medical Knowledge

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FACULTY / PLANNER BIO AND DISCLOSURES

Hans Luders, M.D., Ph.D. (Co-Chair)
Dr. Lüders is a neurologist with special training in clinical neurophysiology and epilepsy. His main research efforts are in semiology of seizures, classification of epilepsy, neurophysiology of epileptic seizures and surgical treatment of epilepsy. Throughout his career he has spent considerable time in training neurogists interested in clinical epilepsy and clinical neurophysiology.

Hans Luders, M.D., Ph.D. has nothing to disclose.

Philippe Kahane, M.D., Ph.D. (Co-Chair)
Philippe Kahane, MD, PhD, born in 1962, is a neurologist and neurophysiologist, Hospital Practitioner and University Professor. He is responsible for the clinical epileptology program and the presurgical assessment of epilepsy at the Neurology Department of the Grenoble University Hospital (France). His area of research covers various fields in epileptology and physiology in humans, including the characterization of cognitive and epileptogenic networks using SEEG recordings and stimulation. He has published more than 130 articles in international journals.

Philippe Kahane, M.D., Ph.D. discloses receiving support as Consulting/Advisory Board Activity from GSK; consulting activity Actelion; as Honoraria from Commercial Sources from USB.

Jorge Gonzalez-Martinez, M.D., Ph.D.
Dr. Gonzalez-Martinez is a neurosurgeon specializing in Epilepsy Surgery. His main research efforts are related to surgical techniques in invasive monitoring (including subdural grids methodology and SEEG) and anatomical-electrophysiological connectivity in the epileptic brain. Currently, he is the director of the epilepsy surgery fellowship program at the Cleveland Clinic.

Jorge Gonzalez-Martinez, M.D., Ph.D. has nothing to disclose.

Samden Lhatoo, M.D. FRCP (Lon)
Dr. Lhatoo is an epileptologist engaged in clinical practice and in clinical epilepsy research. He is Director of the Epilepsy Center at University Hospitals Case Medical Center in Cleveland, Ohio which pioneers the use of stereotactic EEG in epilepsy surgery. He is Principal Investigator of the NINDS funded Prevention and Risk Identification of SUDEP Mortality (PRISM) Project (NINDS P20-NS-076965-01).

Samden Lhatoo, M.D. FRCP (Lon) discloses receiving support as Speakers Bureau Member (supported by for-profit entities) from Lundbeck Pharmaceuticals.

Giorgio Lo Russo, M.D.
Director Epilepsy Surgery Centre “C Munari” (2003-present) Niguarda Hospital Milano Italy.
Specialties: 1982 Neurosurgery, 1987 Neurology, Turin University. Trained in Paris (Neurosurgery, Hôpital S.te Anne, 1989-1990; Pr Talairach, Pr Bancaud) and Grenoble (Neurosurgery, Grenoble University 1991-1994; Pr Benabid) under the guide of his Mentor Pr Claudio Munari. He contributed to start the program of Epilepsy Surgery in Grenoble and to the founding of the Centre of Milano when Pr Munari went back in Italy. Experience acquired in the field of epilepsy surgery and particularly in invasive recordings with Stereo-EEG (more than 200 procedures).

Giorgio LoRusso, M.D. has nothing to disclose.
Jonathan Miller, M.D.
Jonathan Miller, MD, is Director of Functional and Restorative Neurosurgery and Director of Epilepsy Surgery at University Hospitals Case Medical Center/Case Western Reserve University. He completed residency training at University Hospitals and fellowship training in functional and epilepsy surgery under Kim Burchiel at Oregon Health & Science University. He has published over 50 peer-reviewed papers and has received 15 national awards. His research interests include development of novel methods of identifying epileptogenic tissue and brain stimulation for epilepsy.

Jonathan Miller, M.D. has nothing to disclose.

Paul Levisohn (Medical Content Specialist)
Dr. Levisohn is Associate Professor of Pediatrics and Neurology at the University of Colorado School of Medicine and Children’s Hospital Colorado. He is former medical director of the Epilepsy Monitoring Unit at The Children's Hospital. He has served as chair of the AES Practice Committee, is co-chair of the advisory committee for the National Center for Project Access at the Epilepsy Foundation and is a member of the EF Professional Advisory Board. He currently serves as consultant to AES on medical content of AES continuing medical education activities.

Paul Levisohn, M.D. has nothing to disclose.

Siddharth Kapoor, MD (Liaison Reviewer)
Siddharth Kapoor is an Asst. Professor of Neurology at the University of Kentucky College of Medicine. He completed his neurology residency at NYU, and epilepsy fellowship at University of Michigan. He serves as the Epileptologist for adult patients. He also directs the Headache program, including serving as the program director for an accredited fellowship. He is closely involved with resident education, serving on the RRC, involved with resident evaluation and progression through the various stages. His research interests include Post Ictal headache and the comorbidity of epilepsy and primary headaches.

Siddharth Kapoor, M.D. has nothing to disclose.

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The online Evaluator will be left open through February 28, 2013. You must complete the evaluations and credit tracking by that date.
By completing this information online, attendees greatly assist the Council on Education and Annual Meeting Committee with important needs assessment data whereby the AES can further plan and address educational gaps to meet the needs of our learners.

A meeting attendance certificate will be available for international meeting attendees at the registration desk.

SYLLABUS
Syllabi for the educational symposia are available to print in the AES Virtual Tote Bag. Paper handouts will not be provided on site.
Stereotactic Electroencephalography (sEEG) in the Pre-surgical Investigation of Refractory Focal Epilepsy
December 4, 2012
Hans O. Lüders
Epilepsy Center
Medical Center, University Hospitals, Cleveland

Learning Objectives
• Recognize the usefulness of sEEG as an invasive evaluation technique for defining the epileptogenic zone in candidates for epilepsy surgery

Invasive evaluation techniques in surgical candidates
• 5-10% of patients with epilepsy are candidates for epilepsy surgery and 25-50% of these patients will require invasive EEG studies (37,000 to 100,000 patients in USA alone)
• In the 1950th two “schools for invasive evaluation of surgical candidates with invasive electrodes emerged:
  – in Europe, Talairach and Bancaud developed the stereo EEG (s EEG) which analyses the brain in 3-D

Invasive evaluation techniques in surgical candidates
– in North America, however, Penfield and Jasper relied primarily on electrocorticography (ECoG) which led to the use of subdural electrodes, primarily a 2-D technique.

Disclosure
No commercial interest
Symposium overview

Drs. Giorgio LoRusso and Jonathan Miller are going to discuss respectively the European and the American approach to depth electrode insertion
Dr. Gonzalez-Martinez will compare depth and subdural electrodes
Drs. Philippe Kahane and Samden Lhatoo will present the use of depth electrodes for respectively mapping the epileptogenic zone and eloquent areas of the brain
We will conclude with a round table and answering questions from the audience

References

The Talairach’s methodology

• You have to know the
  
  **Stereo TAXIC**
  (three dimensional / arrangement)

• To perform a
  
  **Stereo TACTIC**
  – (three dimensional / touch)

approach

Jean Talairach’s methodology 1949

- **Cerebral commissures**
- **Vessels**
- **Ventriculography**
- **Angiography**

direct landmarks visualization

But how get the 3D............?

The Talairach’s proportional grid

- The “Quadrillage”

Learning Objectives

• Rationale of the original Talairach’s approach.

• Current 3D imaging-based SEEG methodology.

Disclosure

No Commercial Interest

“Stereo-EEG methodology: the European approach”

4th December 2012

Giorgio LoRusso, M.D.

Epilepsy Surgery Centre “C. Munari”

Niguarda Hospital, Milano Italy
Stereoscopic angiography

Current SEEG Implantation Technique
- Positioning of the guiding screw
- Positioning of the clip
- Positioning of the step up on the skull to reach the internal wall of the dura
- Drilling
- Completion of the dura mater with a manipulator-milling biocure
- Positioning of the screw
- Regulating the electrodes (under it key control)
- Temporary introduction of the tip
- Introduction of the electrode
- Tightening of the cap

Safety (May 1996 - November 2011)
500 SEEG procedures

Major morbidity

<table>
<thead>
<tr>
<th>Seizure freedom (reduction)</th>
<th>Seizure freedom (status)</th>
<th>Cerebritis</th>
<th>Hydrocephalus</th>
<th>Retained broken electrode</th>
<th>Psychotic event</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 (100%)</td>
<td>5 (100%)</td>
<td>2 (40%)</td>
<td>5 (100%)</td>
<td>2 (40%)</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
</tr>
</tbody>
</table>

Talairach, in my opinion, was the true father of what we now call image guided stereotactic surgery.

The original Talairach’s electrodes planning and implantation technique
- Simple and safe means for the introduction of tools without extensive calculations and with easy means of checking the safety of the penetrating track through a minimal opening, the size of the probe.

Today from 2D to 3D
- Today the main diagnostic acquisition are 3D

But... THE SONG REMAINS THE SAME
- First think stereotaxic and then stereotactic
The problem of Source Localization

Fronto peritral SEEG exploration: multiplanar view and 3D reconstruction

Neurophysiological individual localization

DTI-FT of the Cortico Spinal Tract
SEEG stimulation and motor evoked potentials

The relevance of the 3D exploration

The deep seated lesions

White-Grey matter boundary with FDG-PET overlay

The "inflated" representation
The neurophysiological label of the FCD

Periventricular Nodular Heterotopia

Case 1: 24 yrs.

SEEG exploration

Periventricular Nodular Heterotopia

Case 2: 9 yrs.

SEEG exploration
Periventricular Nodular Heterotopia

Case 2: 9 yrs. ♫
SEEG exploration

Red: the nodule
Violet-Green: the CST

Impact on Clinical Care and Practice

• SEEG is a methodology for invasive EEG recording
  • definition of the Epileptogenic Zone
  • functional cortical and subcortical mapping
  • thermocoagulation of the Epileptogenic Zone
• Accurate visualization of contact location (both cortical and subcortical) by multimodal imaging.
• Limited patient’s discomfort.
• After the removal of the electrodes, all the collected SEEG data are available for an accurate and thoughtful interpretation before surgery.
The American Approach to Depth Electrode Insertion
December 4, 2012

Jonathan Miller, MD
Director, Epilepsy Surgery
University Hospitals Case Medical Center/Case Western Reserve University
Cleveland, Ohio

The Goal of SEEG
Localization of the
Epileptogenic Zone

Learning Objectives
• After this session, participants will gain an understanding of SEEG technique and indications

The Goal of SEEG

Disclosure
None
The Goal of SEEG

Localisation of the Symptomatogenic Zone

Irritative Zone

Seizure Onset Zone

Eloquent Tissue

SEEG Localization of the Symptomatogenic Zone

Epileptogenic Zone

Lesion

The Goal of SEEG

EEG vs. SEEG

EEG vs. SEEG

EEG vs. SEEG

EEG vs. SEEG

EEG vs. SEEG

EEG vs. SEEG

Subdural Grids

Subdural Grids

Depth Electrodes

No activity

Ictal/interictal activity

Eloquent cortex
History of SEEG

Modern Era: MRI Targetting

SEEG Strategies

1. Multi-target SEEG
   – Identify epileptic structures

2. 3D-SEEG
   – Delineate epileptogenic & eloquent zones
11/14/2012

**SEEG Strategies**

1. **Multi-target SEEG**
   - Identify epileptic structures
   - Identify epileptic structures

2. **3D-SEEG**
   - Delineate epileptogenic & eloquent zones
   - Delineate epileptogenic & eloquent zones

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**Multi-Target SEEG**

- Choose entry point to cover area of interest
- Can enter from any direction to sample tissue of interest
- Additional depth electrodes may be added in second stage

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**3D-SEEG**

- Surround area of interest using "three-dimensional grid"
- Can enter from any direction; parallel electrodes may be easier to interpret

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**Framed Stereotaxy**
Framed Stereotaxy

Ring less limited than arc
(-30º to 210º)        (30º to 150º)

Positioning

Supine (Prone) = from front (back)

Lateral = from side

Positioning

Ring perpendicular to electrode path

Frame Placement

Placed low to maximize trajectory options
Frame Placement

Simultaneous bilateral placement: tilt frame toward dependent side

Fluoroscopy

Verify correct placement
Determine depth of placement

Implantation

- 3 mm stab incision, 2.7 mm drill
- Open dura with monopolar cautery
- Advance stylet to target under x-ray
Implantation
• 3 mm stab incision, 2.7 mm drill
• Open dura with monopolar cautery
• Advance stylet to target under x-ray
• Place anchor bolt
• Place electrode

Postoperative Processing
• Postoperative volumetric CT (1 mm)
  – Fused with preoperative MRI
• Contour electrodes
  – Anatomic definition of EZ
  – Can import into frameless stereotaxy for resection

Case Example
| 32 year old RH man | Seizures: déjà vu aura, dialeptic, automotor | Etiology: unknown (imaging normal) | Location: left temporal (Sp1>P7) | Related medical conditions: bipolar disorder |
### Case Example

*32 year old RH man*

**Seizures:** déjà vu aura, dialeptic, automotor  
**Etiology:** unknown (imaging normal)  
**Location:** left temporal (Sp1-P7)  
**Related medical conditions:** bipolar disorder

---

### Case Example

*57 year old RH woman*

**Seizures:** visual aura, aphasia  
**Etiology:** cavernous angioma  
**Location:** left temporal (Sp1)  
**Related medical conditions:** migraine

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**Pathology:** Cortical Dysplasia
Conclusions

- Standard stereotactic techniques are used for implantation
- Goal is improved anatomic delineation of epileptogenic zone; hypothesis is important
- Provides anatomic information that can be helpful to guide surgical resection
Indications for Subdural Grids versus SEEG versus Depth Electrodes
December, 2012
Jorge Gonzalez-Martinez MD PhD
Epilepsy Center
Cleveland Clinic

Learning Objectives

• Discuss specific indications for subdural grids/strips and SEEG in the diagnosis and treatment of refractory focal epilepsy

Subdural Method Advantages

• "Standard procedure" in North America.
• Optimal coverage of the subdural space adjacent cortex.
• Anatomical relation between cortex and electrode is easily understood.
• Adequate functional mapping capabilities.
• Open procedure, better management of possible intra-operative complications.
• Resection planning is simple to understand.
• Mapping and resections are performed during the same hospital admission.

Disclosure

None
CORTICAL STIMULATION

Hand Motor
Hand Sensory
Face motor
Face sensory
Ictal onset

Subdural Method Disadvantages

- Poor coverage of deep located cortex.
- Precise anatomical placement in basal and mesial cortex is unpredictable.
- Invasive method (complications can reach 10-15% in some series).
- Poor 3D view.
- Bilateral implantations are more challenging.

SEEG after Subdursals

Follow up: 20 months
SF: 6/10

SEEG Method Advantages

- Precise and accurate mapping of deep cortical areas.
- 3D aspect of the hypothetical EZ.
- “less invasive”. 3-5% complication rate.
- Electrode implantation is predictable.
- Intra-cortical recordings.
- Bilateral implantations are straightforward.

Gonzalez-Martinez et al., 2012; Cossu et al., 2005; Talairach et al., 1972
SEEG Disadvantages

- Contiguous superficial coverage is poor.
- Superficial functional mapping is challenging, requiring speculation of the anatomical limits of a specific functional area.
- Imprecise interface between the hypothetical EZ and functional areas (mainly speech).
- Imprecise interface between the hypothetical EZ and functional areas.
- Anatomical-electrophysiological correlation and the 3D aspect of the EZ are difficult to understand.
- “Blind” procedure. Poor control of IC bleedings.

Impact on Clinical Care and Practice

<table>
<thead>
<tr>
<th>Clinical scenario</th>
<th>Method of Choice</th>
<th>Second Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesional MRI: lesion is superficially located, near or in eloquent cortex.</td>
<td>SEEG</td>
<td>SBG</td>
</tr>
<tr>
<td>Lesional MRI: lesion is deep located. Normal MRI: hypothetical EZ located in the proximity of eloquent cortex (mainly speech).</td>
<td>SEEG</td>
<td>SBG with depths</td>
</tr>
<tr>
<td>Lesional MRI: lesion is deep located. Normal MRI: hypothetical EZ is deep located or located in non-eloquent area.</td>
<td>SEEG</td>
<td>SBG with depths</td>
</tr>
<tr>
<td>Need for bilateral explorations/reoperations</td>
<td>SEEG</td>
<td>SBG with depths</td>
</tr>
<tr>
<td>After SBG failure</td>
<td>SEEG</td>
<td>SBG with depths</td>
</tr>
<tr>
<td>Need for epileptogenic network mapping</td>
<td>SEEG</td>
<td>SBG with depths</td>
</tr>
</tbody>
</table>
Mapping the Epileptogenic Zone with SEEG
December 4, 2012
Philippe KAHANE, M.D., Ph.D.
Neurology Department & INSERM U836
Grenoble University Hospital, France

The epileptogenic zone
The minimum amount of cortex that must be resected (inactivated, completely disconnected) to produce seizure freedom (Lüders et al. 2006).

How to map it with SEEG?

The epileptogenic zone
Bancaud and Talairach view

Seizure was the symptom to be cured: it was the region of the cortex generating seizures that had to be defined electrophysiologically, and translated into anatomical terms.

SEEG definition (Munari and Bancaud, 1987):
the site of the beginning and of the primary organization of epileptic seizures

ZE: ictal onset zone + early seizure spread

Ictal onset

Imaging the seizure onset zone with SEEG (David et al. 2011)
Imaging the seizure onset zone with SEEG (David et al. 2011)

**Ictal onset**

- View of EEG and fMRI images during ictal onset.

**Seizure spread**

- Delay AND Fast discharge
- Electrically-induced seizures
  - 1 Hz ES [3ms / 0.2-3mA / 40s]
  - 50 Hz ES [1ms / 0.2-3mA / 5s]
- Seizure spread due to different frequencies.

**Seizure spread**

- Electrical involvement of different brain regions:
  - Mesial-T to Lateral-T
  - Insula to Orb-F to FP
  - Amygd to Ant Hc to T-basal to T-O to 2dTG to 1stTG

**Seizure spread**

- Electro-clinical seizure onset (mouth tingling).
Seizure spread
Can we go further?

Mapping the EZ with SEEG
Mapping Eloquent Cortex with Stereotactic EEG
12-04-2012

Sam Lhatoo, MD FRCP (Lon)
University Hospitals Case Medical Center,
Cleveland OHIO
Disclosure

Lundbeck USA

NIH-NINDS

CDC

Speakers Bureau

PI – NS076965-01

C3U48DP001930
Learning Objectives

• To gain perspectives on the feasibility of Stereotactic EEG in mapping eloquent cortex

• To understand the advantages and disadvantages of Stereotactic EEG in the mapping of eloquent cortex
• The human brain is extensively convoluted into sulcii and gyrii
• 2/3\textsuperscript{rd}s of the human cortex lies in sulcii deep to the cortical surface
• The ventral and mesial surfaces of the brain are relatively inaccessible
• Precisely placed stereotactic depth electrodes render areas accessible to recording as well as to stimulation
• In practice?
Stimulation Parameters

To avoid tissue damage, the critical measurement is charge density measured in \( \mu \text{Coulombs/cm}^2/\text{phase} \). Safe maximum is considered to be 50 to 60 \( \mu \text{C/cm}^2/\text{phase} \) (Gotman 2012, Gordon & Lesser 1989).

- 1 \( \mu \text{C} = 1 \text{mA} \times 1\text{ms} 
- 1 \text{electrode is approximately } 0.1 \text{ cm}^2

- Mono-polar or bi-polar
- Bi-phasic
- Pulse width = 0.2ms – 1ms
- Pulse frequency = 1 Hz – 50Hz
- Pulse duration = 5s – 40 s

American Epilepsy Society | Annual Meeting 2012
Stimulation of Motor Cortex
Stimulation of language areas
Stimulation of Frontal Eye Fields

Video
Stimulation of other areas

Stimulation induced Mirth and laughter
1. Arroyo S. Brain 1993; 116:757-780. Patient 2; 1A and 1B

Video
Conclusions

• Stimulation of cortex using SEEG electrodes is feasible, safe and localizes eloquent cortex
• Stimulation parameters are similar to those using subdural electrodes
• Eloquent motor, sensory and language cortex can be well identified
• “Novel” brain areas can be accessed for stimulation
With thanks

• AliReza Bozorgi MD
• Guadalupe Fernandez BacaVaca MD
• Hans Lüders MD PhD
• Jean Gotman PhD
• Kitti Kaiboriboon MD
• Shahram Amina MD