Epilepsy: Effective Diagnosis & Treatment

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Epilepsy: the magnitude of the problem

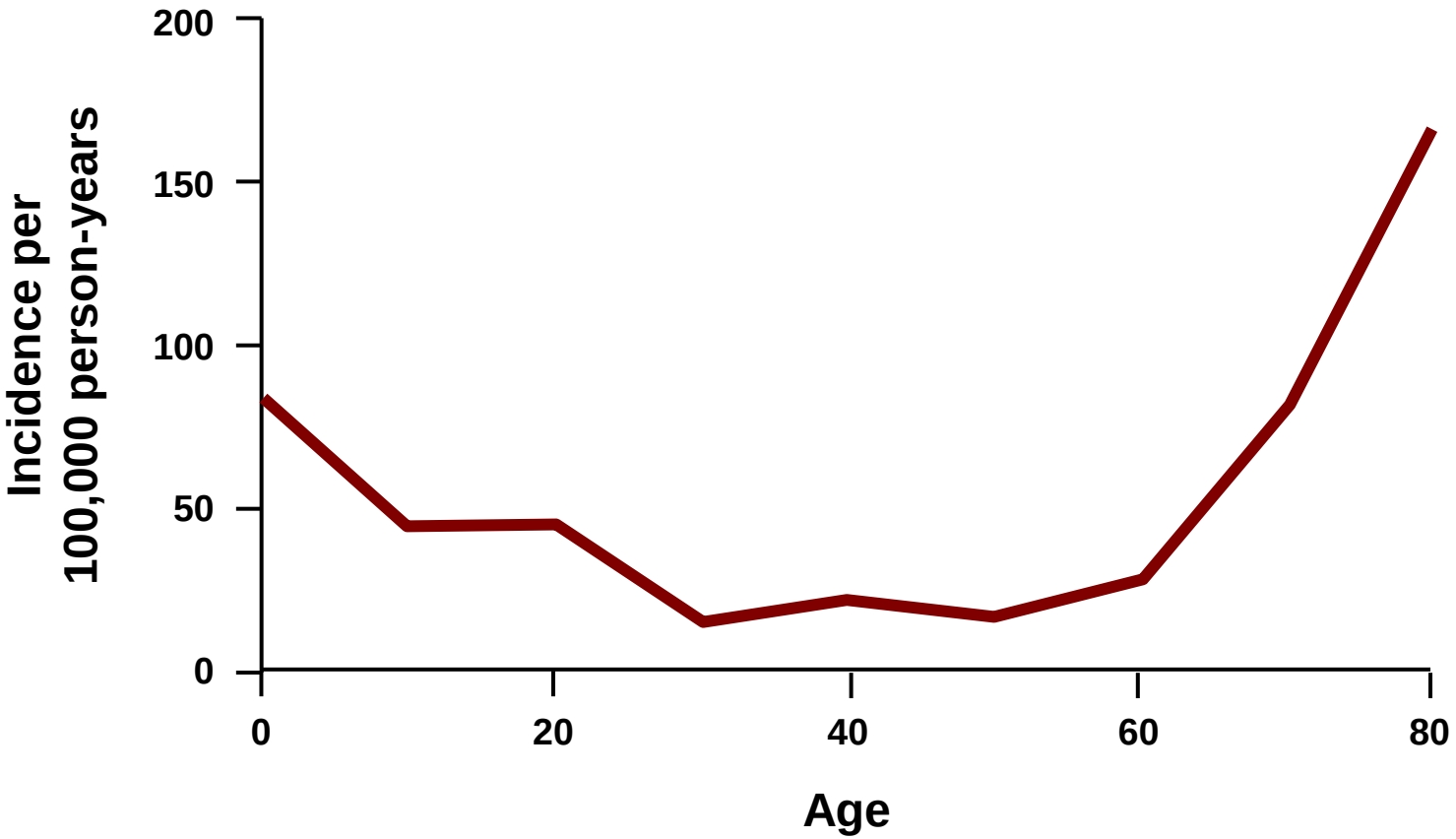
- Affects more than 3 million Americans
- At least 15% of the general population will have a seizure during their lifetime
- Annual direct and indirect costs: More than $15 billion (1995 estimates)
- If uncontrolled, 1/1000 patient death per year (SUDEP)

Sudden Unexpected Death in Epilepsy (SUDEP)

- SUDEP is a significant cause of mortality in patients with refractory epilepsy, accounting for up to 17% of all deaths in epilepsy
- SUDEP exceeds the expected rate of sudden death in the general population by nearly 24 times
- Incidence:
  - In all epilepsies: 1/1,000/year
  - In uncontrolled epilepsy: 3.5/1,000/year

Epidemiology

Age Specific Incidence of Epilepsy



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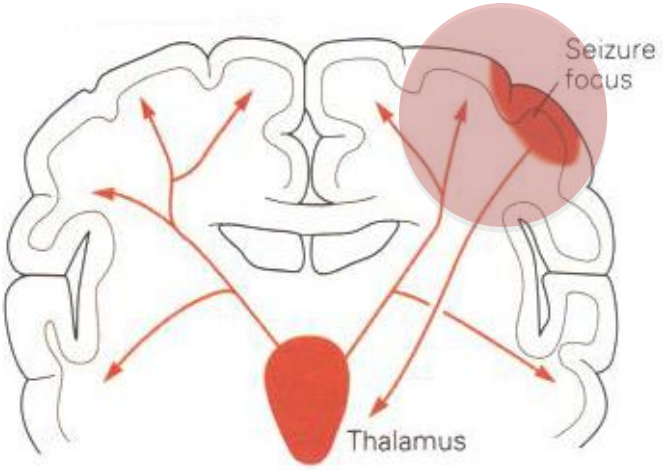
Hauser WA, et al. *Epilepsia*. 1993;34:453-468.

Epilepsy: Definitions

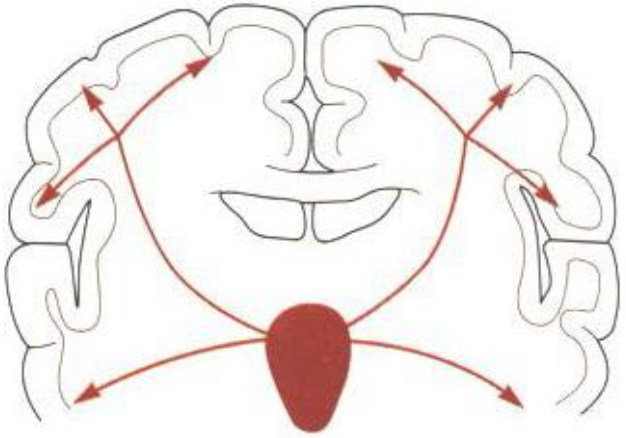
- **Clinical:** It is the occurrence of 2 or more spontaneous unprovoked epileptic seizures
- **Electrical:** It is the episodic occurrence of synchronized electrical activation of large areas of the brain or the whole brain at once (role of the electroencephalogram or EEG)

Epilepsy

- May start in small neuronal populations: **Focal epilepsy**



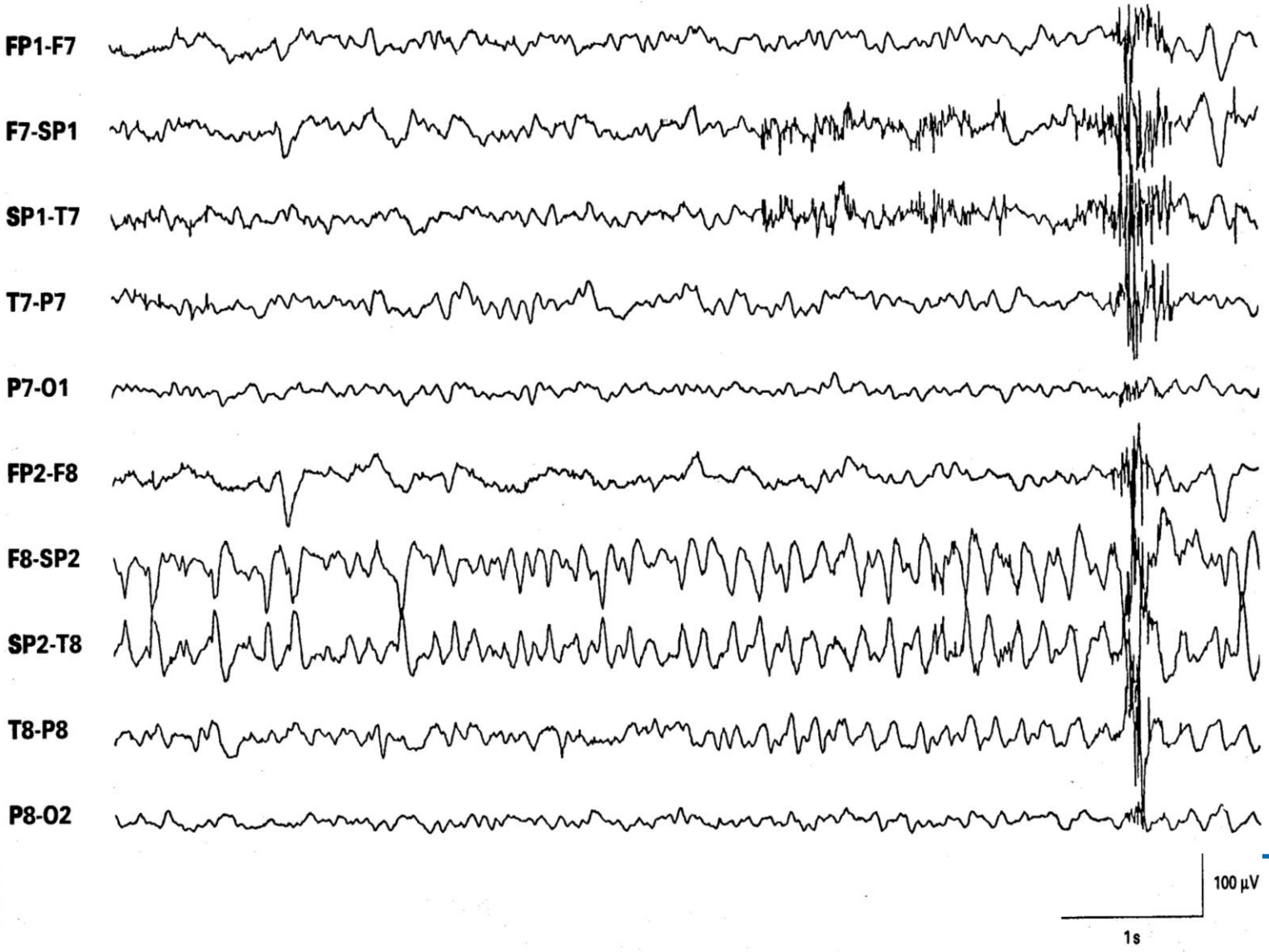
- May be recorded from the entire brain simultaneously: **Generalized epilepsy**



Diagnosis

- Electroencephalogram (EEG): Gold standard
- Routine EEG (outpatient) is diagnostic in only one third of the patients
- The definitive diagnostic method is to **capture the seizure while recording both video and EEG**

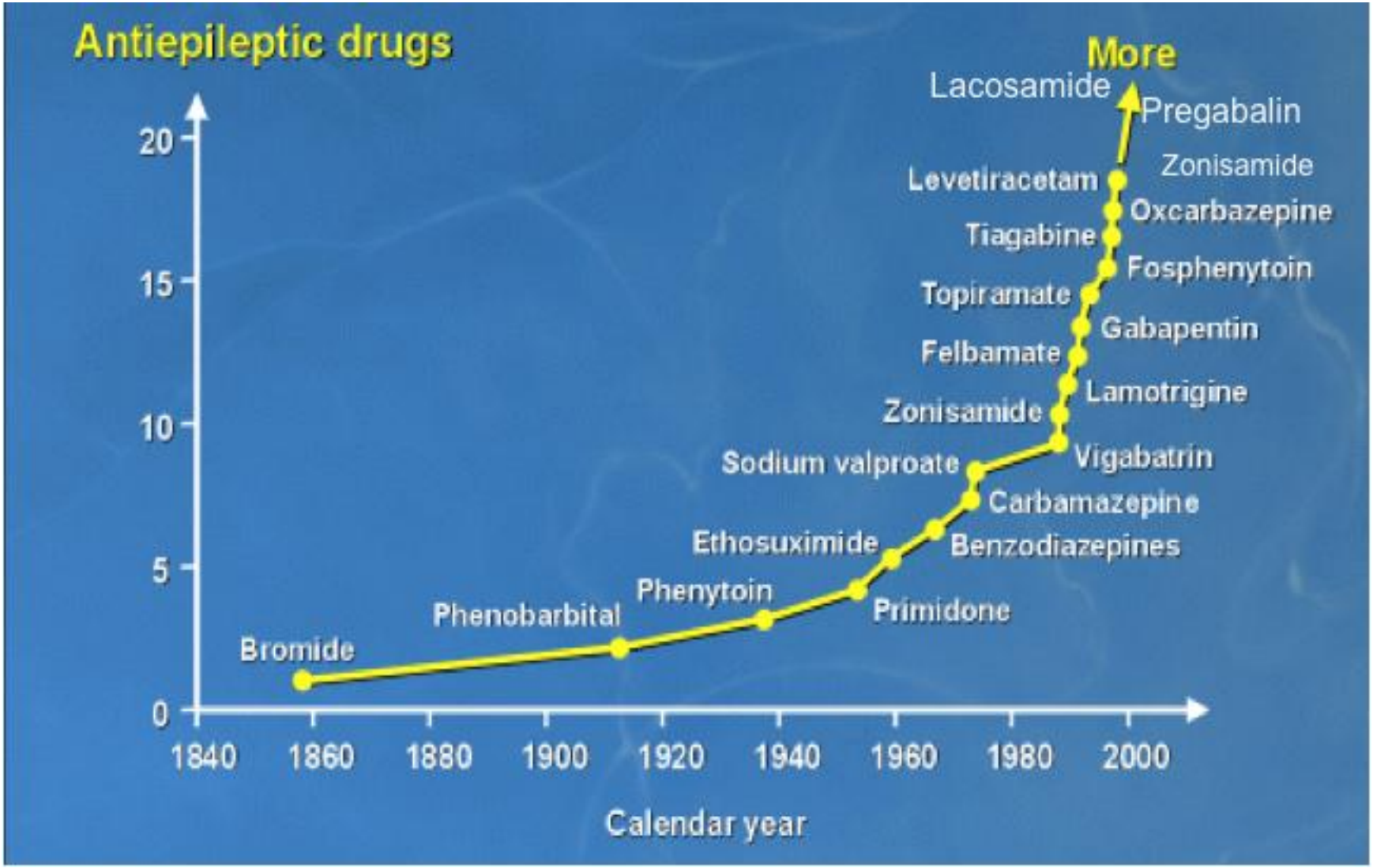
An epileptic EEG is a very well organized one: It is the “perfect storm”



Role of the Video-EEG evaluation in the Epilepsy Monitoring Unit (EMU)

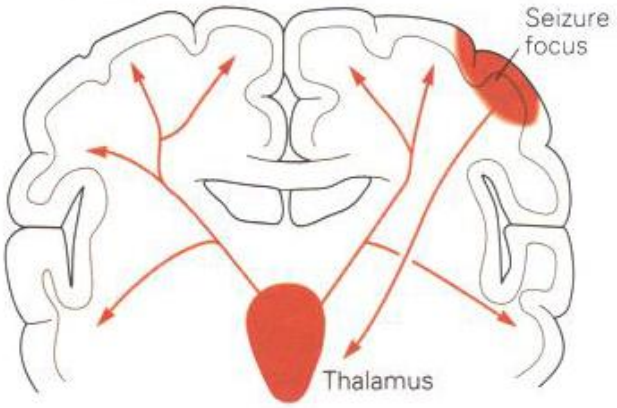
- Confirms the diagnosis of epilepsy (one third of the patients referred to the EMU have non epileptic seizures!)
- Characterizes the type of epilepsy and helps in the optimization of the medical and surgical treatment options

Medical treatment options for epilepsy: the good news!

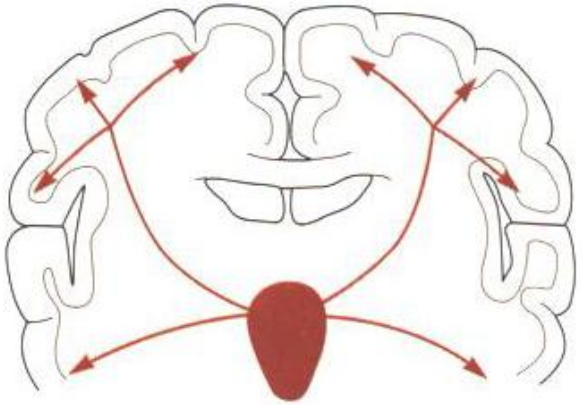


The Choice of the Antiepileptic medication depends on the Epilepsy type

- **Focal epilepsy:**
  - **Phenytoin**
  - **Carbamazepine**
  - **Levetiracetam…**

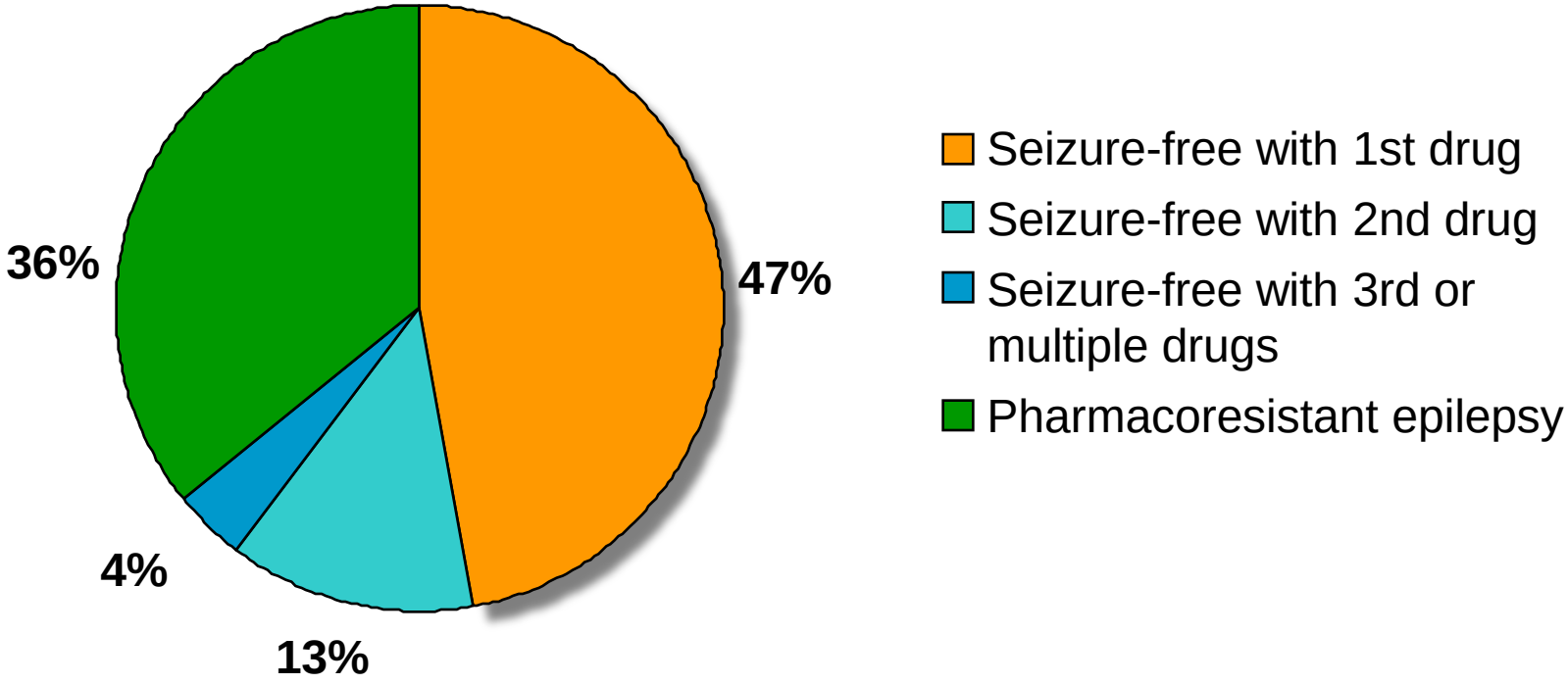


- **Generalized epilepsy:**
  - **Valproic acid**
  - **Lamotrigine**
  - **Ethosuximide**
  - **Topiramate**



Medical treatment options for epilepsy: the bad news!

Previously Untreated Epilepsy Patients (n=470)



More than one third of patients with epilepsy fail to respond to antiepileptic medications

Kwan P, Brodie MJ. N Engl J Med. 2000;342:314-319.

What is Medical Intractability of Pharmacoresistance?

- It is the continuous occurrence of seizures despite the adequate trials of three or more antiepileptic medications in mono- or poly-therapy
- It is the failure of three medications or more to control the epileptic seizures

What are the Options when Epilepsy becomes Intractable or Pharmacoresistant?

Epilepsy Surgery: General Principles

- **Patient Candidates:**
  - Pharmacoresistant Epilepsy
  - Focal epilepsy (single and identifiable brain pacemaker)
  - Minimal risks from surgery induced deficits

Epilepsy Surgery: General Requirements

- Integrated and Comprehensive team approach (the concept of a true **Multidisciplinary Epilepsy Center**):
  - Subspecialty trained and board certified neurologists (13)
  - Subspecialty trained neurosurgeons (2)
  - Board certified neuroradiologists (2)
  - Board certified nuclear medicine specialist (1)
  - Board certified Neuropsychologists (5)
  - Board certified psychiatrists (2)
  - Licensed social workers (2)
  - Trained and certified EEG technologists (46)
  - Dedicated in patient nursing units (Adult and Pediatric)

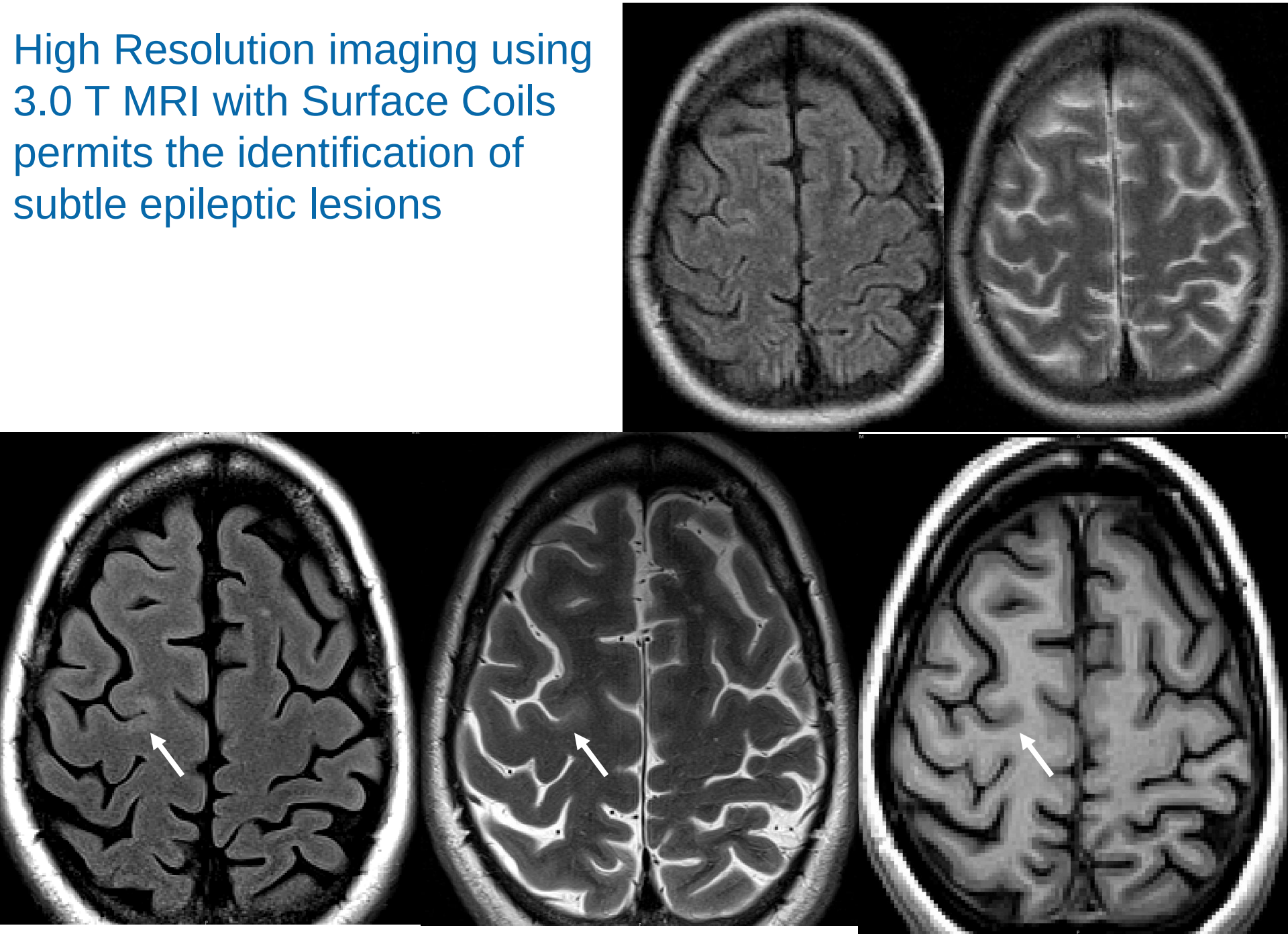
Epilepsy Surgery: General Requirements

- The technology:
  - State of the art digital video and EEG equipment:
    - Quality of recordings
    - Ability to apply post-processing localization techniques
  - Magnetic Resonance Imaging with dedicated Epilepsy Imaging Protocols for anatomic and functional imaging
  - Nuclear medicine facility with cyclotron: PET and ictal SPECT scanning
  - State of the art angiography suite and equipment
  - Magnetoencephalography (MEG)

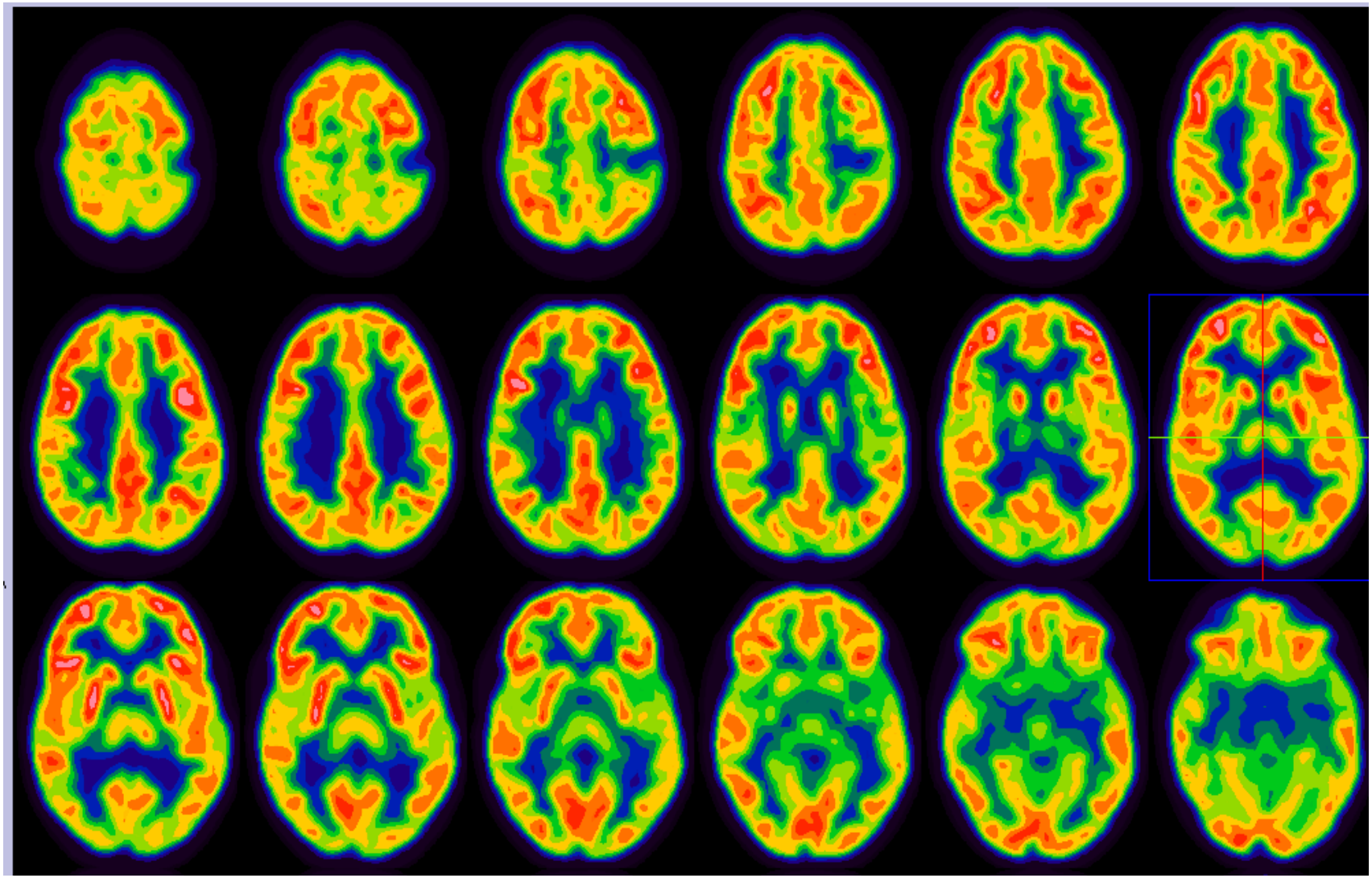
Epilepsy Surgery: General Requirements

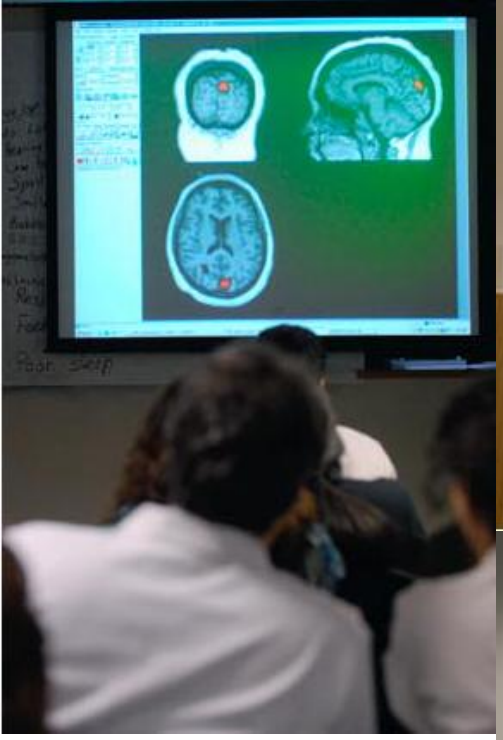
- The setting:
  - Dedicated **Epilepsy Monitoring Unit** for adults and another one for children with trained nurses, and technologists staffing the unit
  - Dedicated Neurointensive Care units for adults and children
  - Trained Neuroanesthesia staff

High Resolution imaging using 3.0 T MRI with Surface Coils permits the identification of subtle epileptic lesions



PET scan permits the identification of brain areas of abnormal dysfunction





The Patient Management Conference

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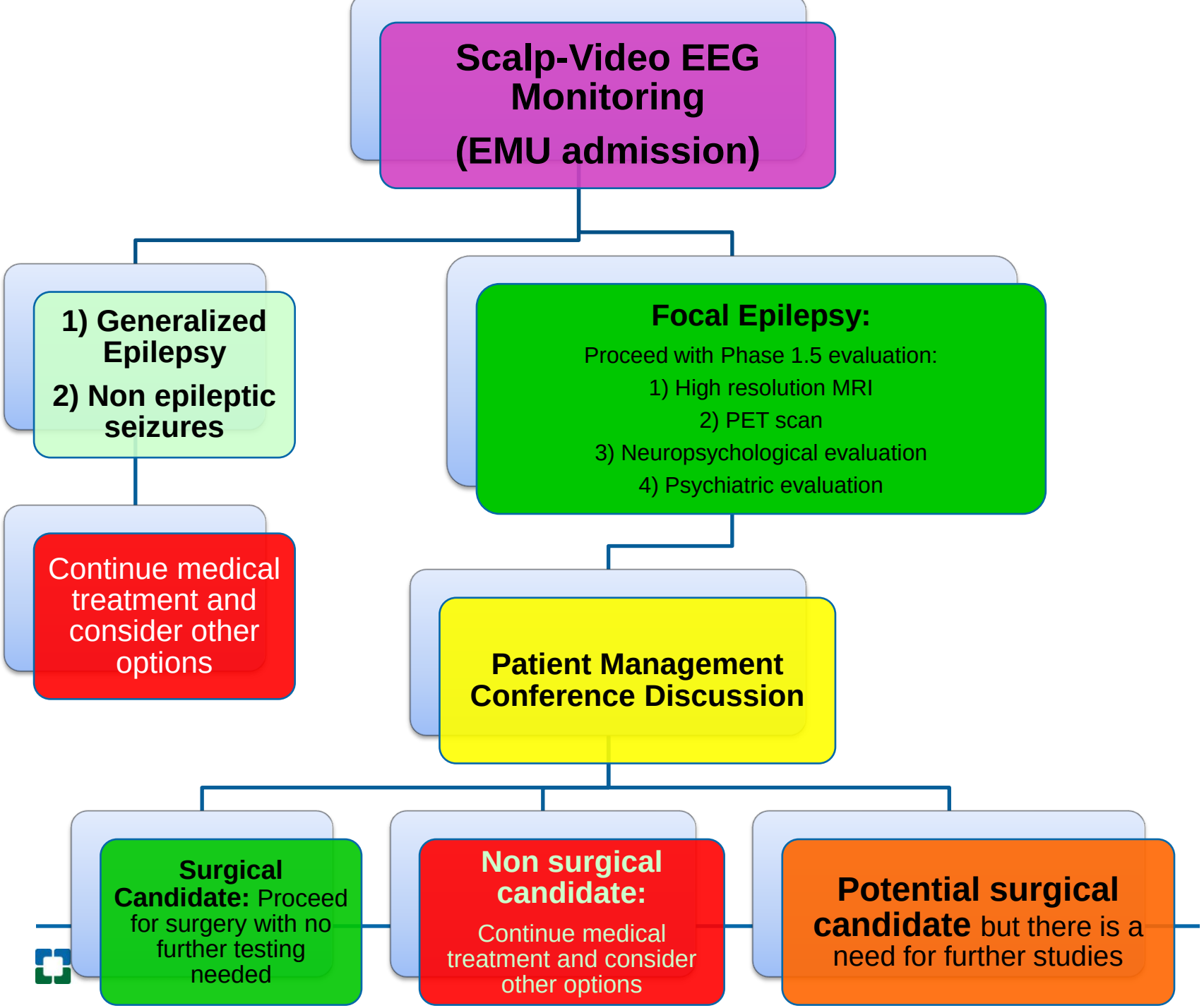

Scalp-Video EEG Monitoring
(EMU admission)
1) Generalized Epilepsy
2) Non epileptic seizures
Continue medical treatment and consider other options
Focal Epilepsy:
Proceed with Phase 1.5 evaluation:
1) High resolution MRI
2) PET scan
3) Neuropsychological evaluation
4) Psychiatric evaluation
Patient Management Conference Discussion
Surgical Candidate: Proceed for surgery with no further testing needed
Non surgical candidate:
Continue medical treatment and consider other options
Potential surgical candidate but there is a need for further studies

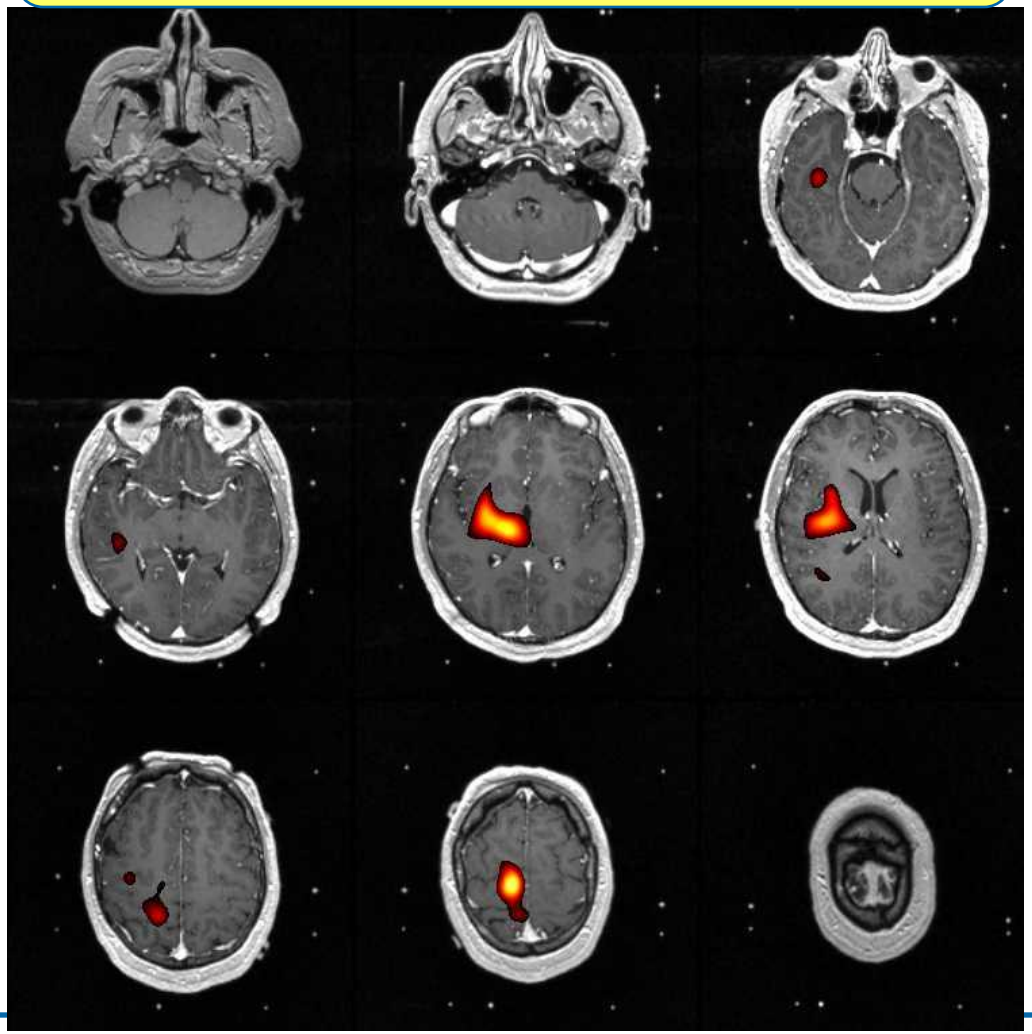
Based on PMC:
Patient is a potential surgical candidate but there is a need for further studies

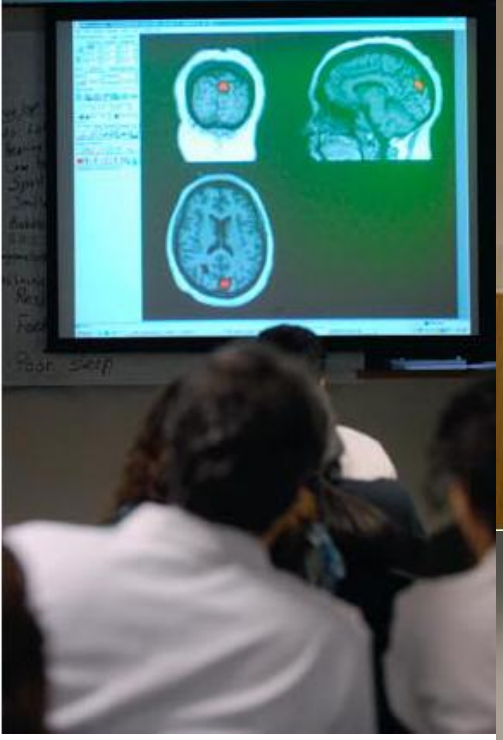
- The role of ictal SPECT
- Possibly other tests

Ictal SPECT

Requires another admission to the EMU.

Helps localize the area of seizure onset





Another Patient Management Conference

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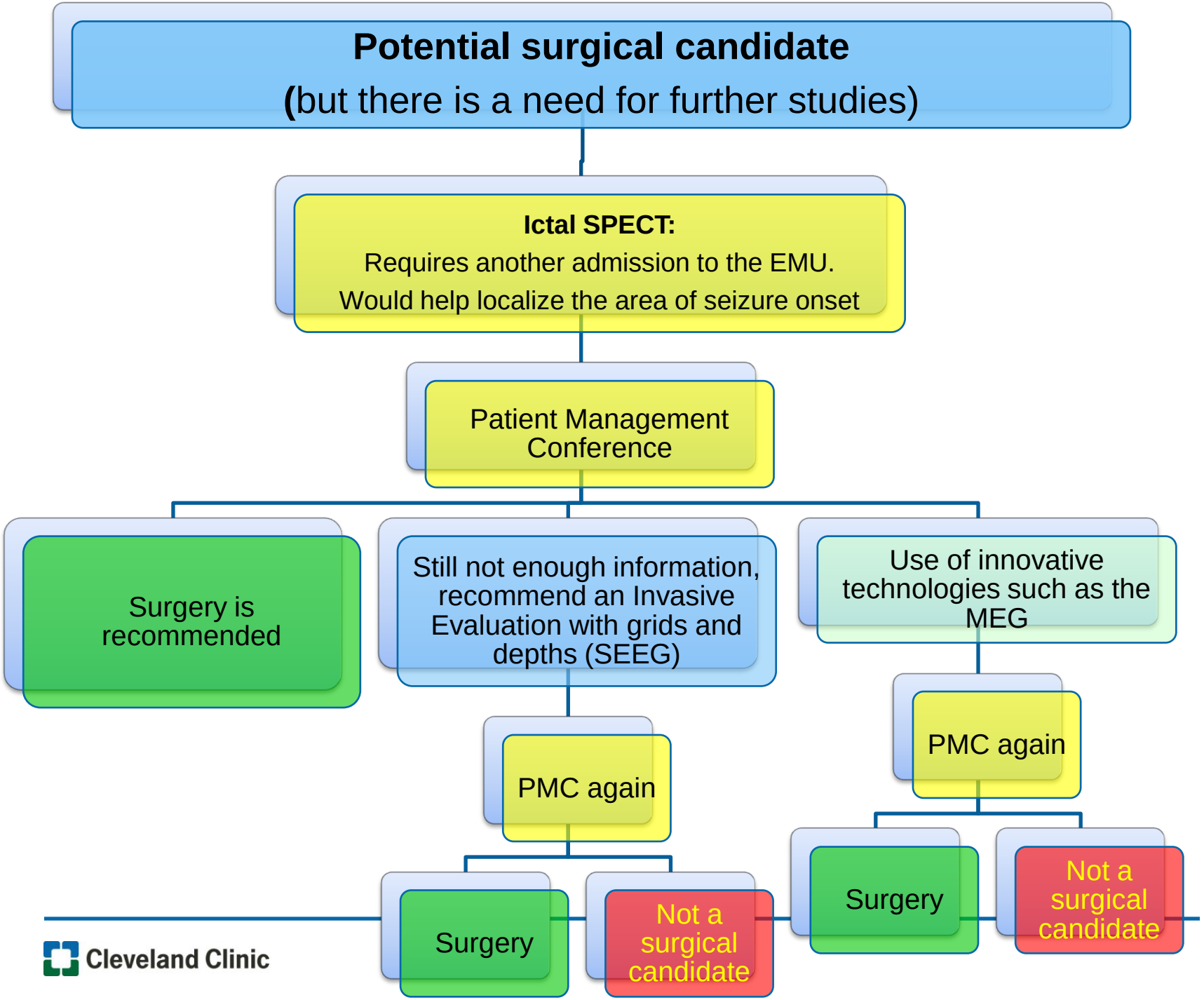
Potential surgical candidate
(but there is a need for further studies)
Ictal SPECT:
Requires another admission to the EMU.
Would help localize the area of seizure onset
Patient Management Conference
Surgery is recommended
Still not enough information, recommend an Invasive Evaluation with grids and depths (SEEG)
Use of innovative technologies such as the MEG
PMC again
PMC again
Surgery
Not a surgical candidate
Surgery
Not a surgical candidate
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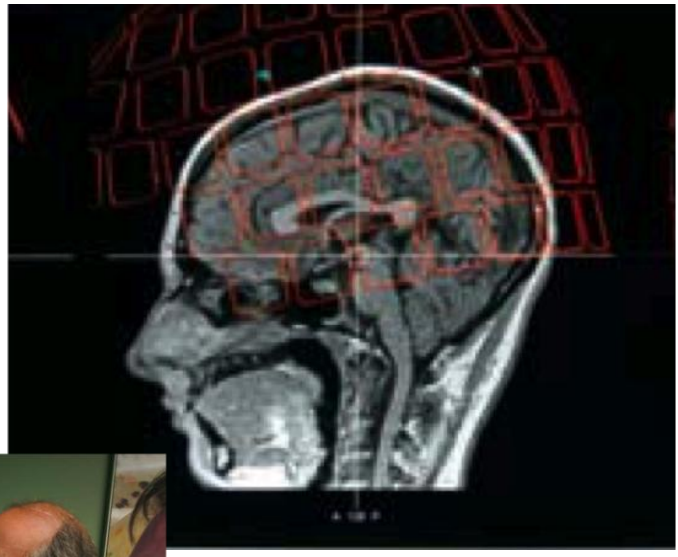
Cleveland Clinic Epilepsy Center State of the Art Technology: MEG scan

- Cleveland Clinic has the first Clinical machine in Ohio
- A team of physicians, physicists and Scientists led by Dr Richard Burgess and Dr John Mosher is taking the MEG application to a new height
- The first clinical MEG scans at the Epilepsy Center (49 procedures done so far) have been done on a small fraction of patients after PMC

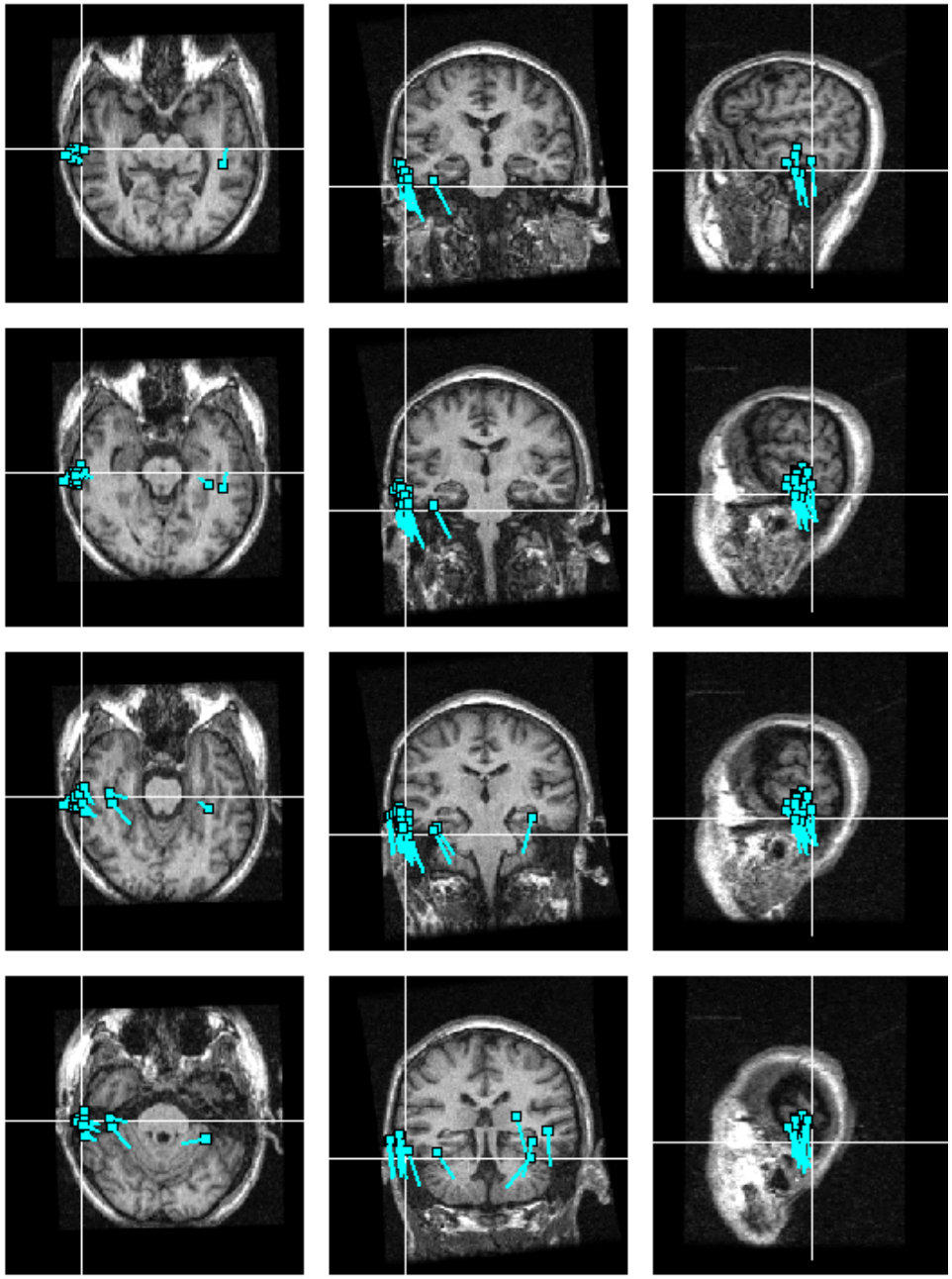
Cleveland Clinic MEG Program

MEG can evaluate the brain's spontaneous activity or its response to specific external stimuli.

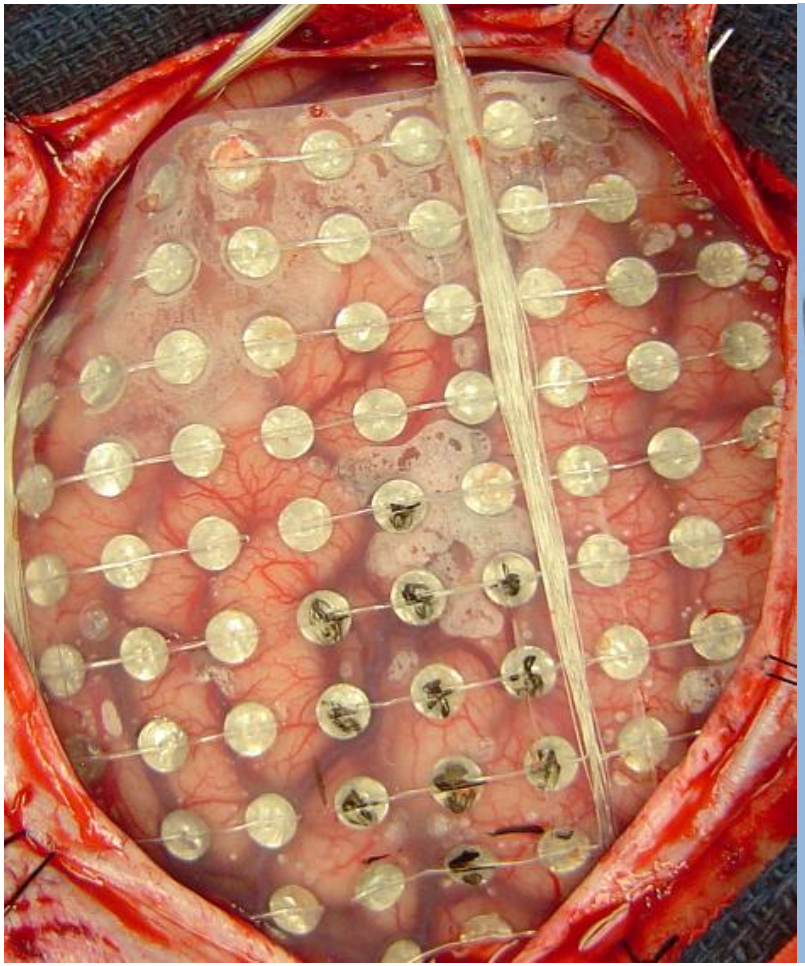


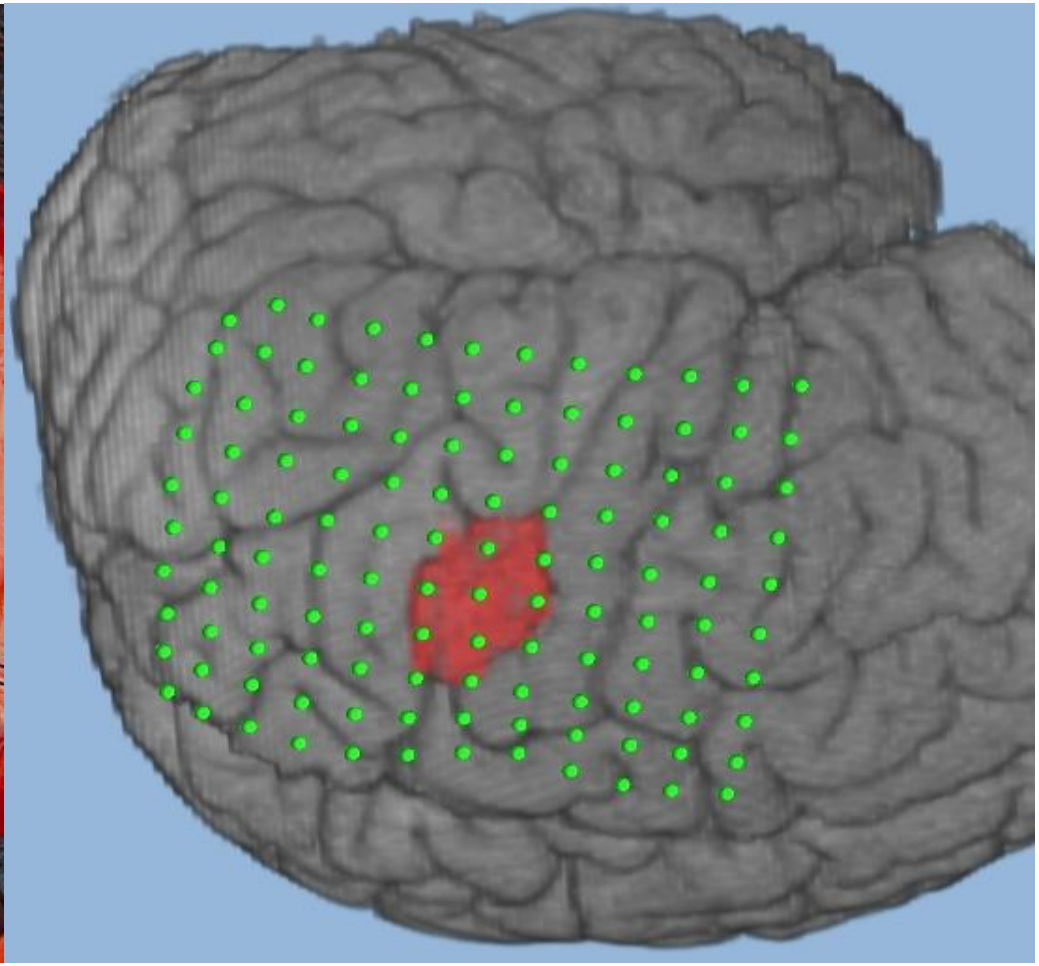
Like PET and fMRI, MEG "lights up" the brain areas that are activated by a task. However, PET and fMRI measure the changes in blood flow over seconds, while MEG measures electrical activity on a millisecond by millisecond basis.

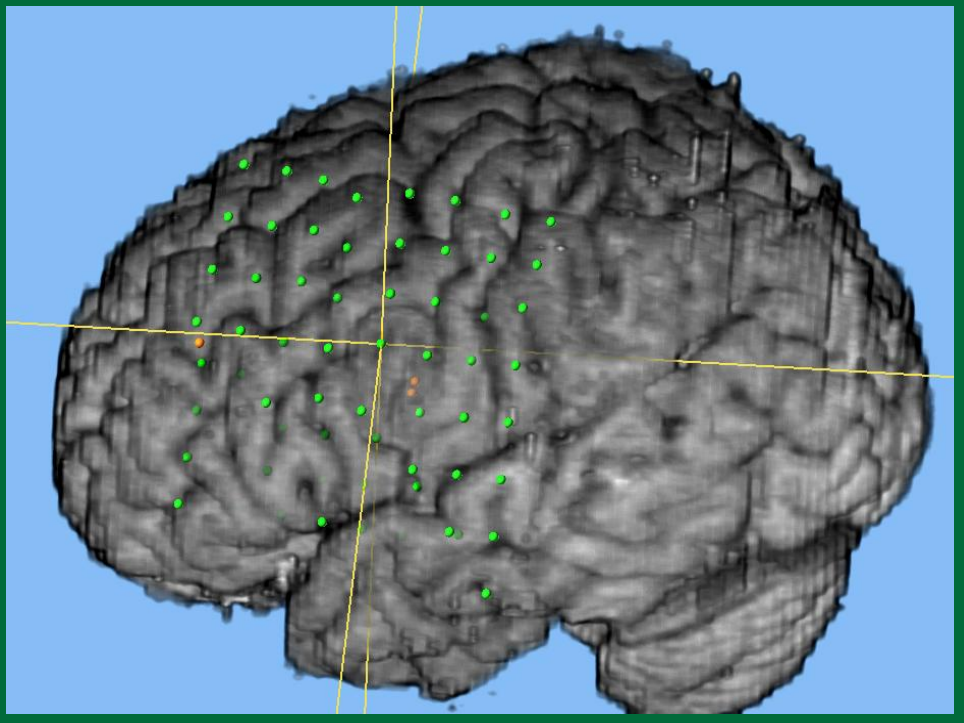
MagnetoEncephalography (MEG) permits the non invasive localization of the seizure onset zone

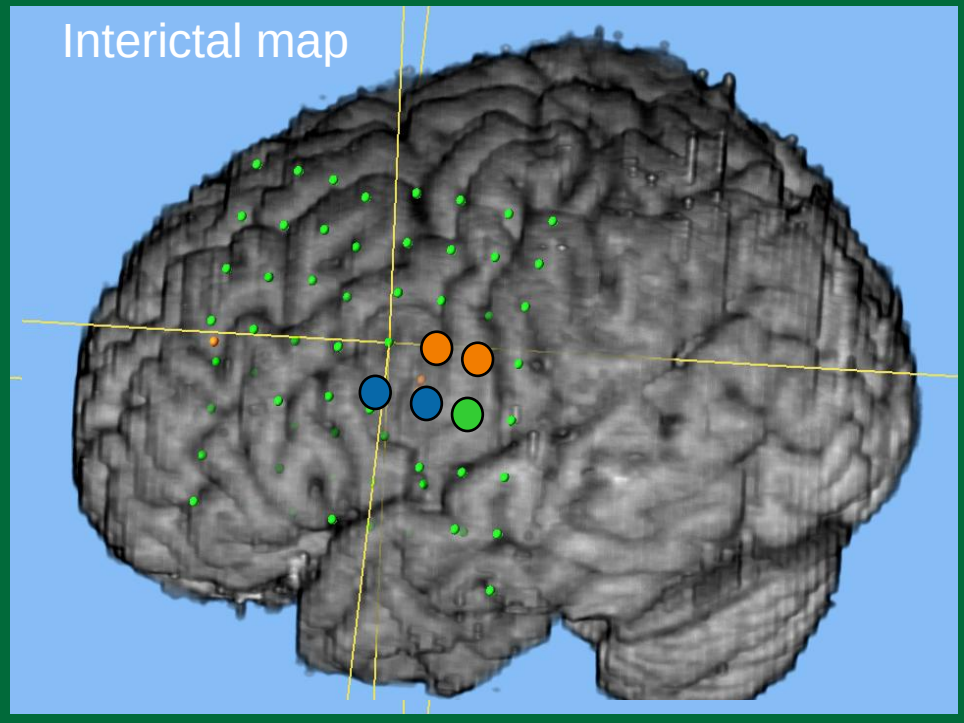


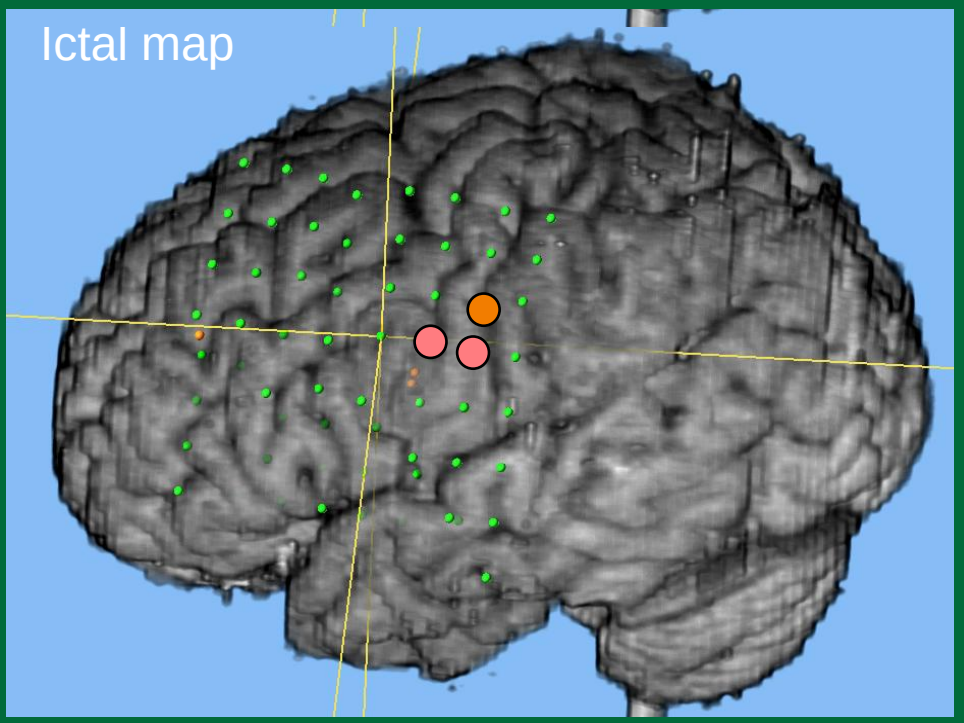
Cleveland Clinic was one of the first to introduce subdural grids for the localization of epilepsy and functional mapping

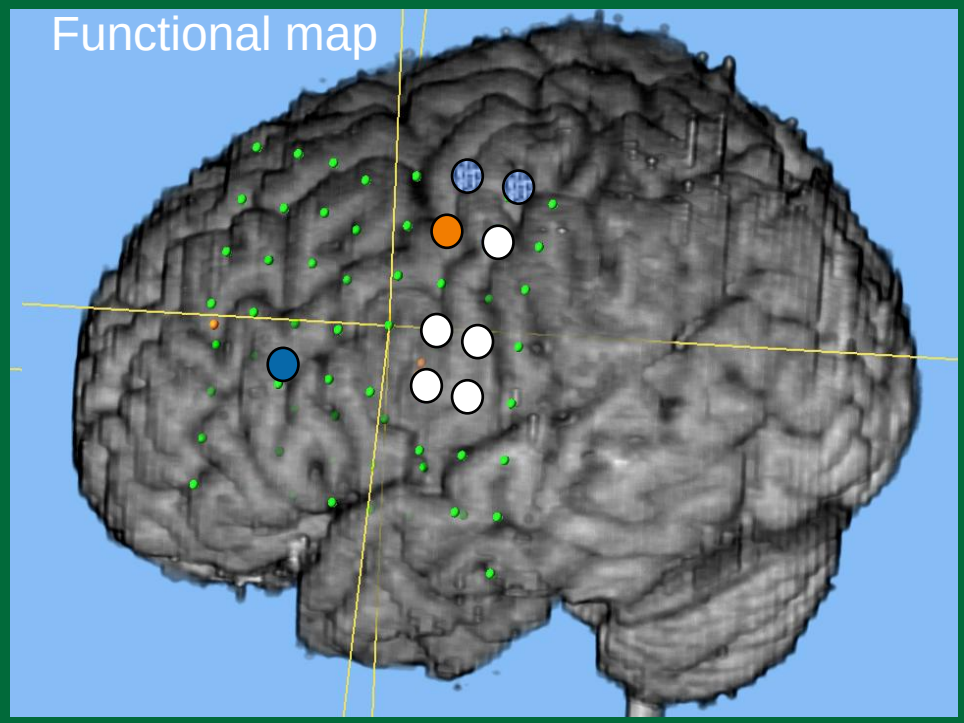




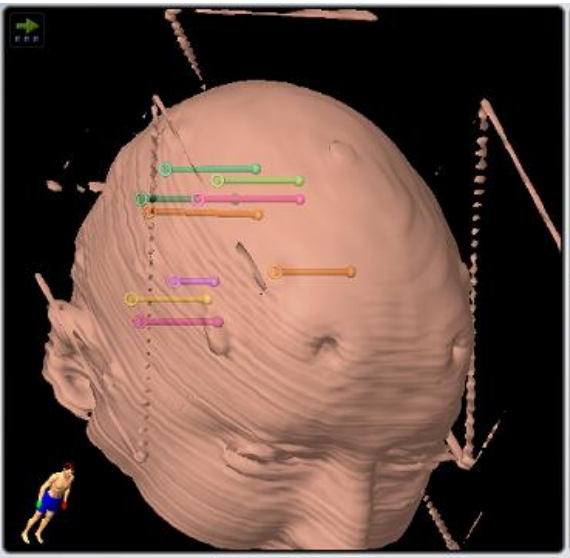


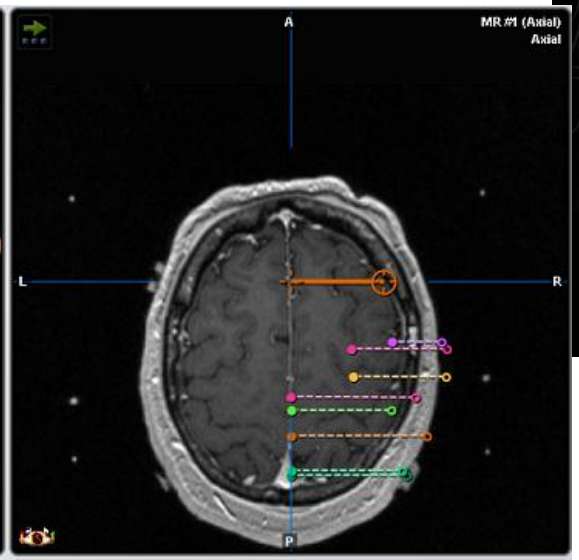

Interictal map

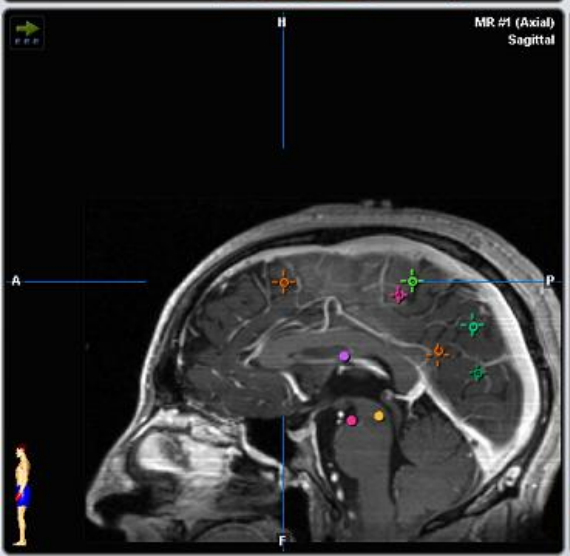

Ictal map

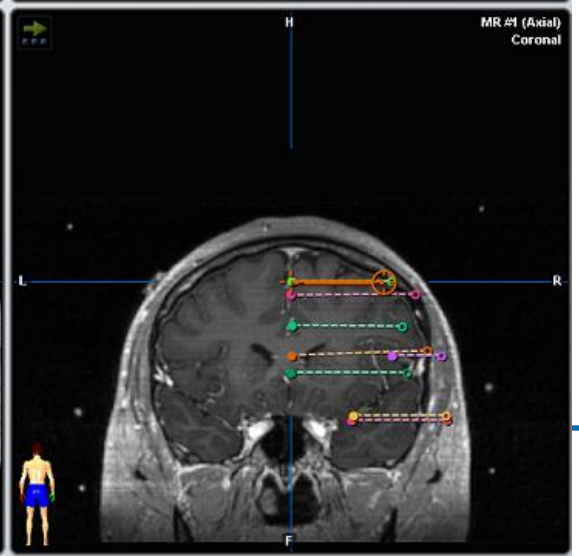

Functional map

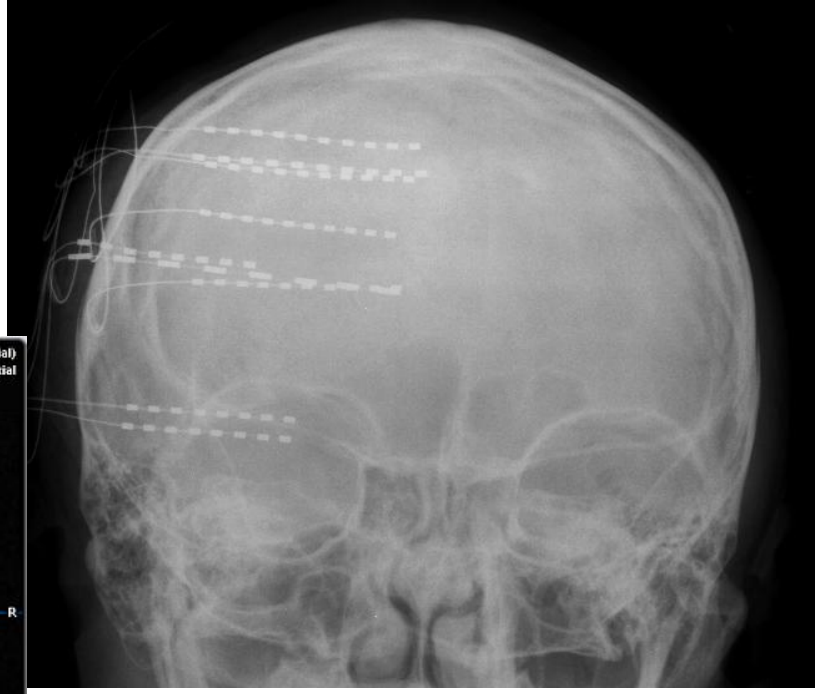
Cleveland Clinic is the first to introduce minimally invasive EEG evaluation in the United States



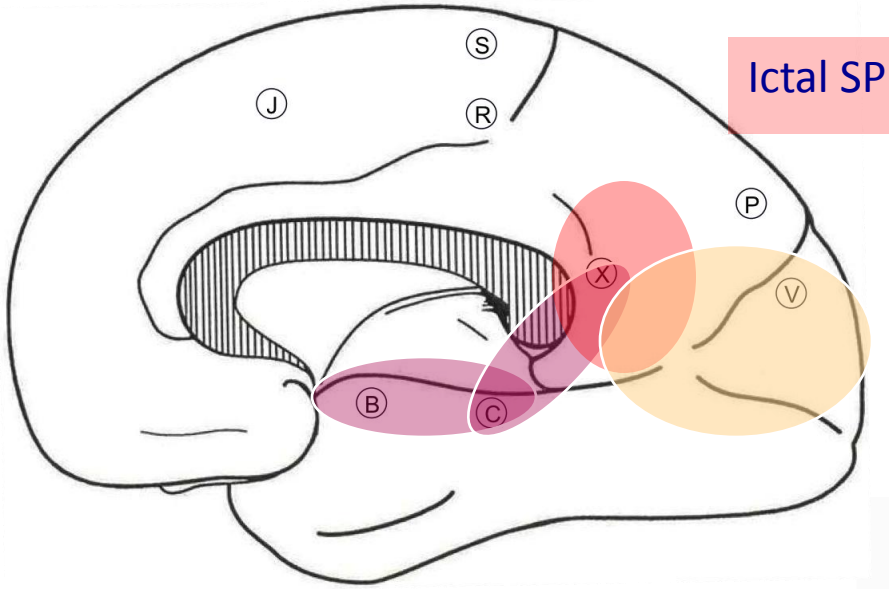








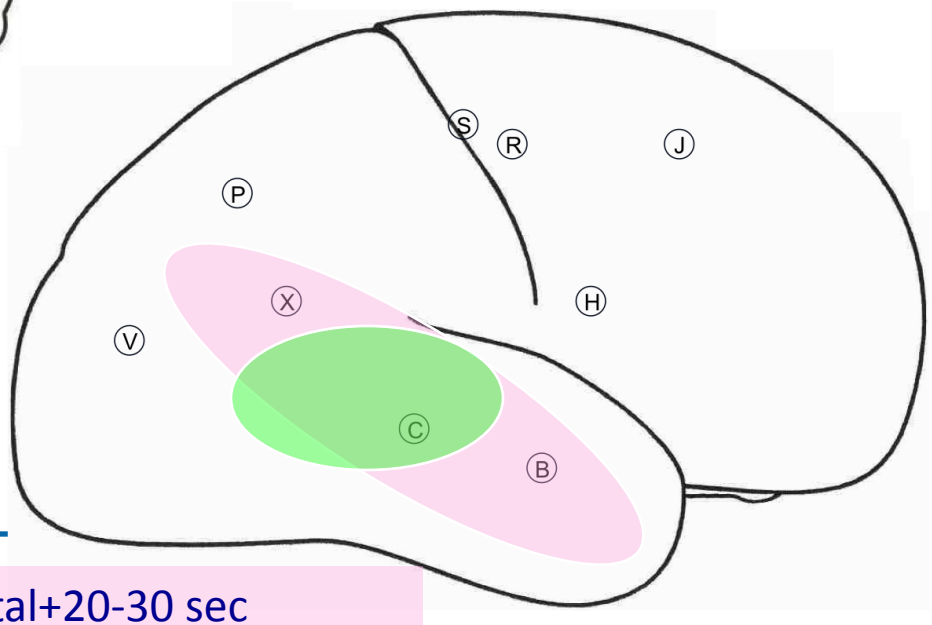
Non invasive and SEEG Evaluation permits the localization of epilepsy in patients with normal MRI



Ictal SPECT: Mesial Parietal

Aura: Right occipital

SEEG:
Onset and electrical stimulation



MEG: Interictal and ictal

SEEG: Ictal+20-30 sec

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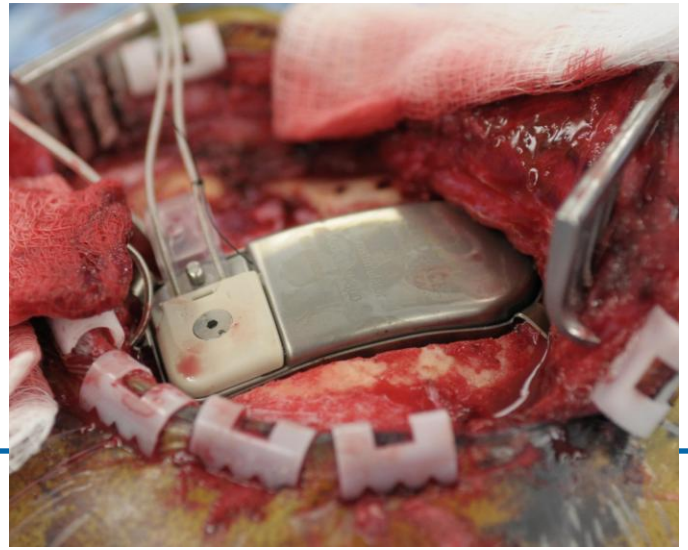
Non Resective Surgical Options

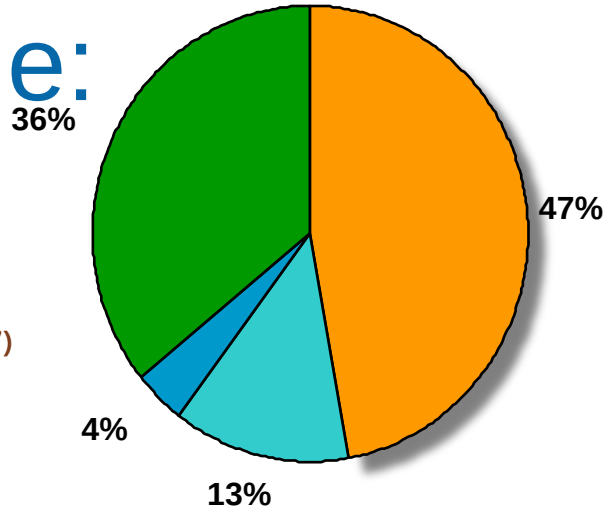
Vagus Nerve stimulation: only FDA approved modality (Cyberonics®)

Deep Brain Stimulation (various targets, experimental)

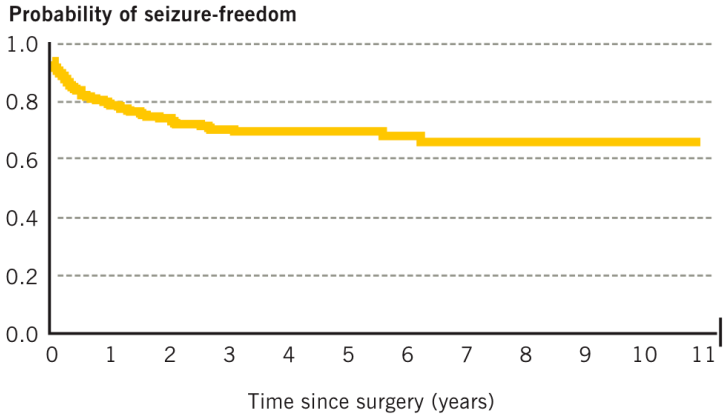
Responsive neurostimulation (RNS, Neuropace®)



Epilepsy Surgery Outcome: Seizure freedom



Seizure-freedom following temporal lobectomy for epilepsy (N=474 surgeries from 1997-2007)



Time since surgery	1 year	2 years	5 years	10 years
% seizure-free (Cleveland Clinic)	81%	75%	71%	68%
% seizure-free (national)	72%	54%	59%	51%

Epilepsy Surgery Outcome: Mortality

- Incidence 2.4/1,000 person years after epilepsy surgery in 596 Swedish patients. None of 6 SUDEPs seizure free
  - *Nilsson Epilepsia 2003;44:575*
- No SUDEP among 256 seizure free US patients with a follow-up of ~ 5 years after surgery
  - *Sperling Epilepsia 2005;46(Suppl.11):49*
- SUDEP incidence (Cleveland Clinic Series):
  - 2/141 who were not seizure free died, and both were SUDEP.
  - None of the 230 patients who were seizure free died.
    - *Jehi et al, Neurology 2006*

Epilepsy Surgery Outcome: Cost savings

- Decrease number of Emergency admissions
- Decrease number of lab expenses
- Decrease number of medication related costs
- Decrease number of ancillary tests done

Questions and Answers…