Phramongkutklao Comprehensive
Pediatric Epilepsy Center of Excellence
Integration • Passion • Wisdom

Epilepsy Surgery in Children: Why, When and How?

Assoc. Prof. Piradee Suwanpakdee, MD
Head of Pediatric Neurology Division
Phramongkutklao Hospital and College of Medicine, Thailand

- No disclosures

Outline

When to Consider Surgery

Identify appropriate surgical candidates and optimal windows for pediatric epilepsy surgery intervention

How to evaluate and techniques

Review comprehensive presurgical assessment protocols and surgical approaches

Why Surgery is Performed

Comprehend the neurodevelopmental and quality-of-life benefits of surgical management

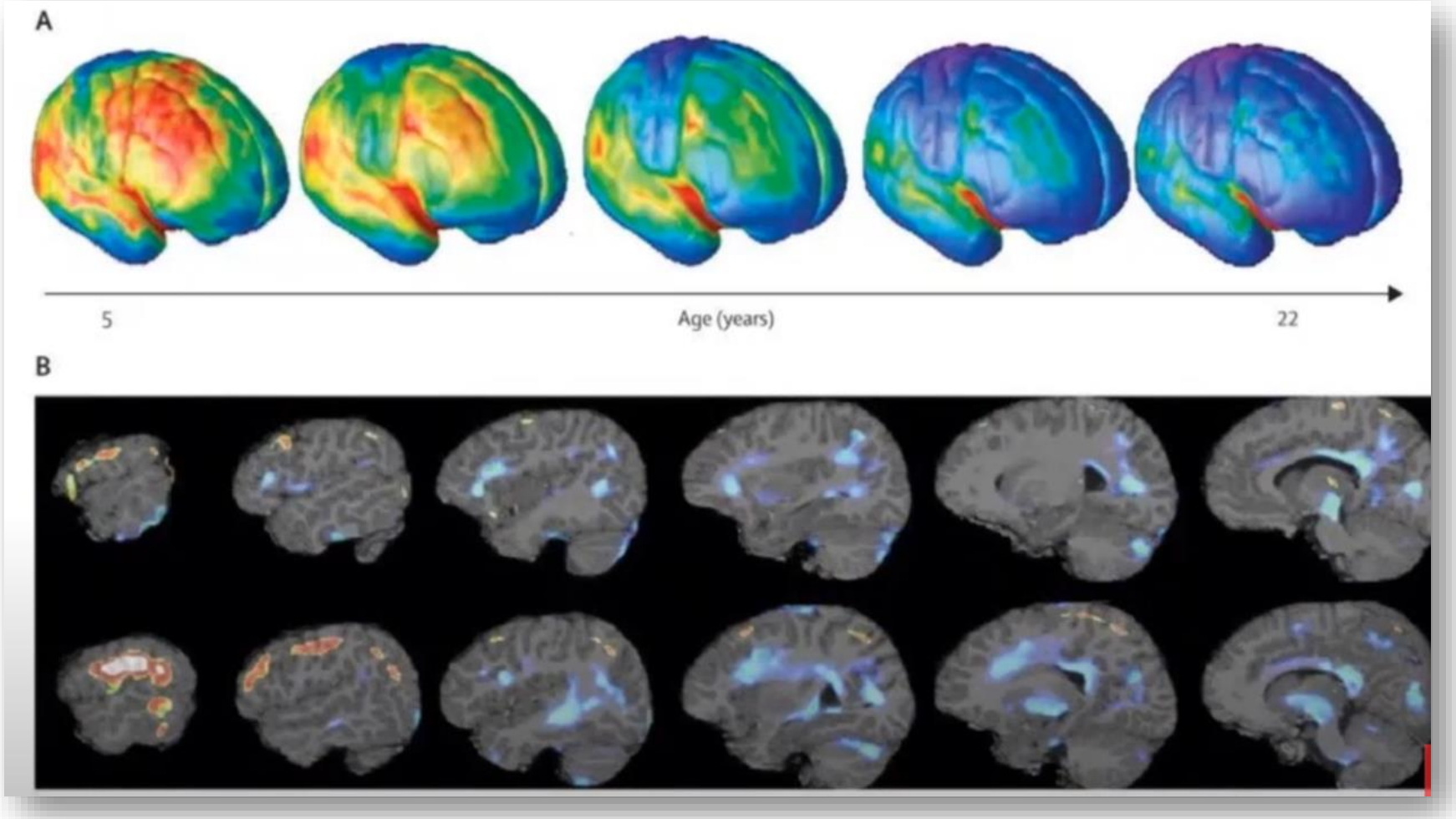
Why–Epilepsy Surgery?

- Incidence of new-onset seizures in children 4/1000
- Anti-seizure medications ≠ Anti-epileptogenic
- 30% of the epilepsy patients develop drug-resistant epilepsy (DRE) and need epilepsy surgery
- Excellent results after surgery with rare or no seizures have been shown in ever growing series of infants, children, and adolescents from a number of centers worldwide

Kwan P et al. 2000,Berg et al, 2001,
Duchowny M, et al. 1998, Wyllie et al, 1998.

Effects of seizures on the developing brain

- Healthy children show reduction in gray matter and expansion of white matter volumes with age (Fig A)
- Children with epilepsy show reduced white matter expansion and altered, region specific gray matter thinning (Fig B)



Lin et al, 2012

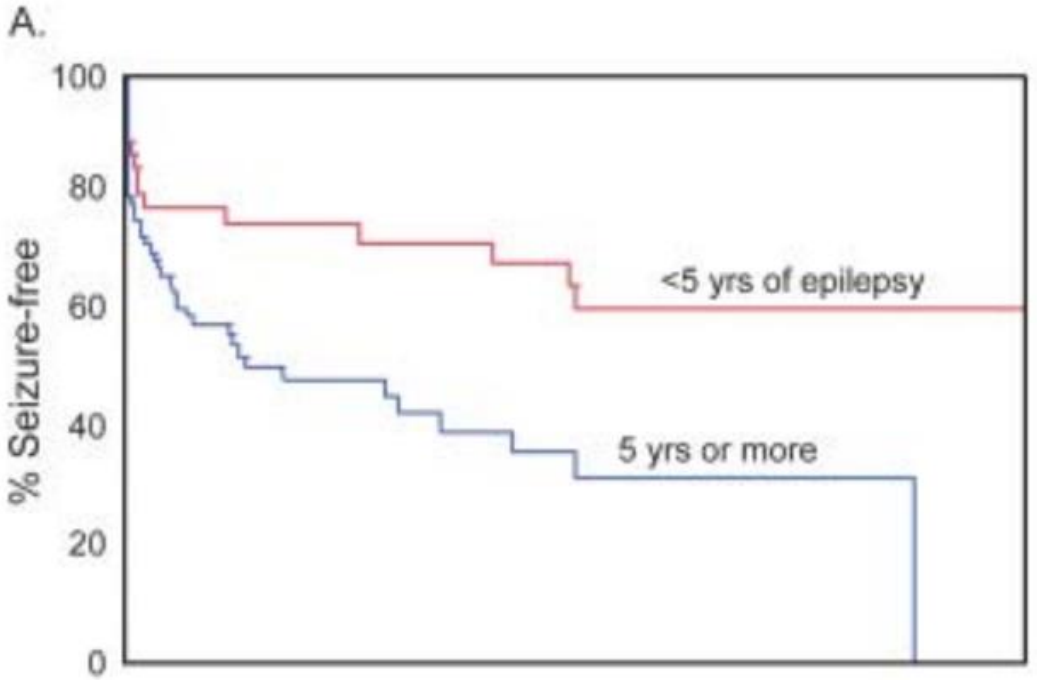
When to Consider Epilepsy Surgery?

- Drug-resistant epilepsy
- Seizures causing significant disability and impaired quality of life
- Epileptogenic zone can be localized
- Acceptable risks and benefits of epilepsy surgery

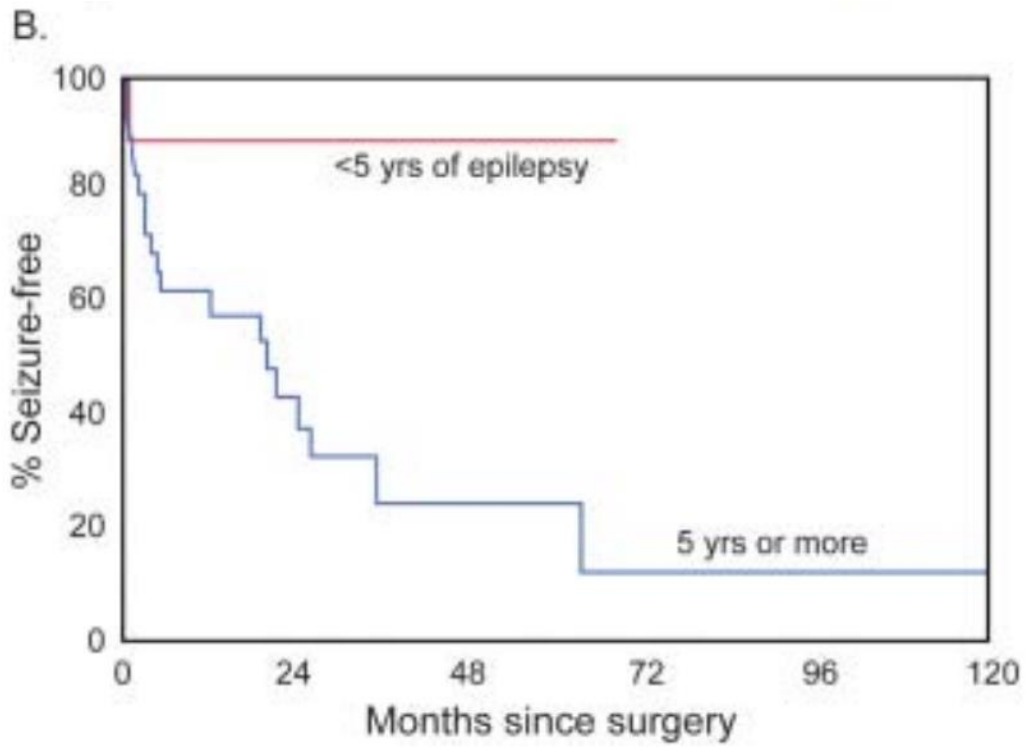
Epilepsia. 2010 Jun;51(6):1069-77

Improved Outcomes with Earlier Surgery for Intractable Frontal Lobe Epilepsy

" Sooner the epilepsy surgery in Children better is the prognosis for seizure outcome"



A) Lesional frontal lobe epilepsy



B) Non-lesional frontal lobe epilepsy

Simasatien T, et al. Ann Neurol 2013

Phramongkutklao Comprehensive
Pediatric Epilepsy Center of Excellence
Integration • Passion • Wisdom

Current approach to Presurgical Evaluation

Phase 1a
outpatient

Patient selection
History and neurological examination
EEG, MRI psychiatric evaluation

Phase 1b
Epilepsy-
monitoring unit

Video-EEG monitoring
iEEG and seizure semiology
SISCOM

Neuropsychology
fMRI, PET, VBM, MEG, ESI/MSI

Phase 2

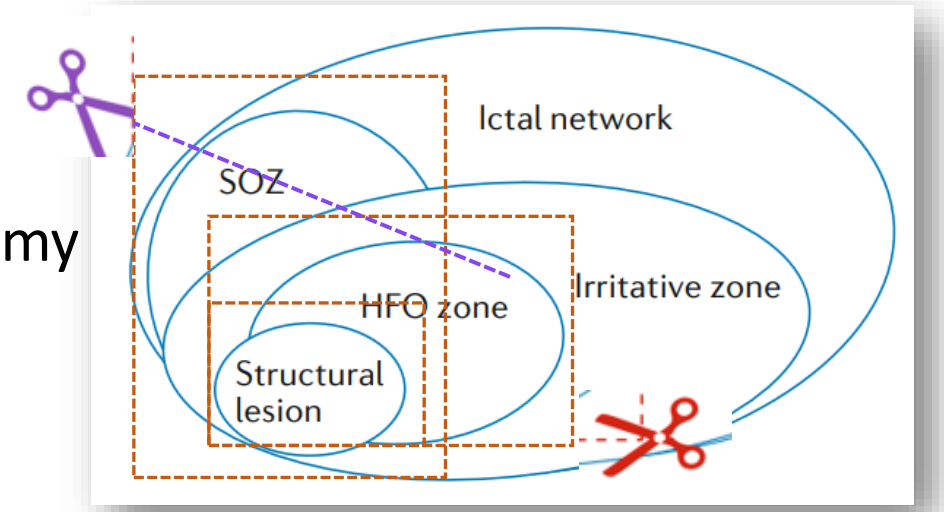
Invasive Video-EEG monitoring
Subdural grid, depth electrodes, Stereo-EEG

Modified after Rosenow et al. Epilepsia 2016

Epilepsy surgery

Resective surgery

- Lesionectomy
- Selective amygdalohippocampectomy
- Corticectomy
- Lobectomy
- Multilobar resection



Epileptogenic Zone

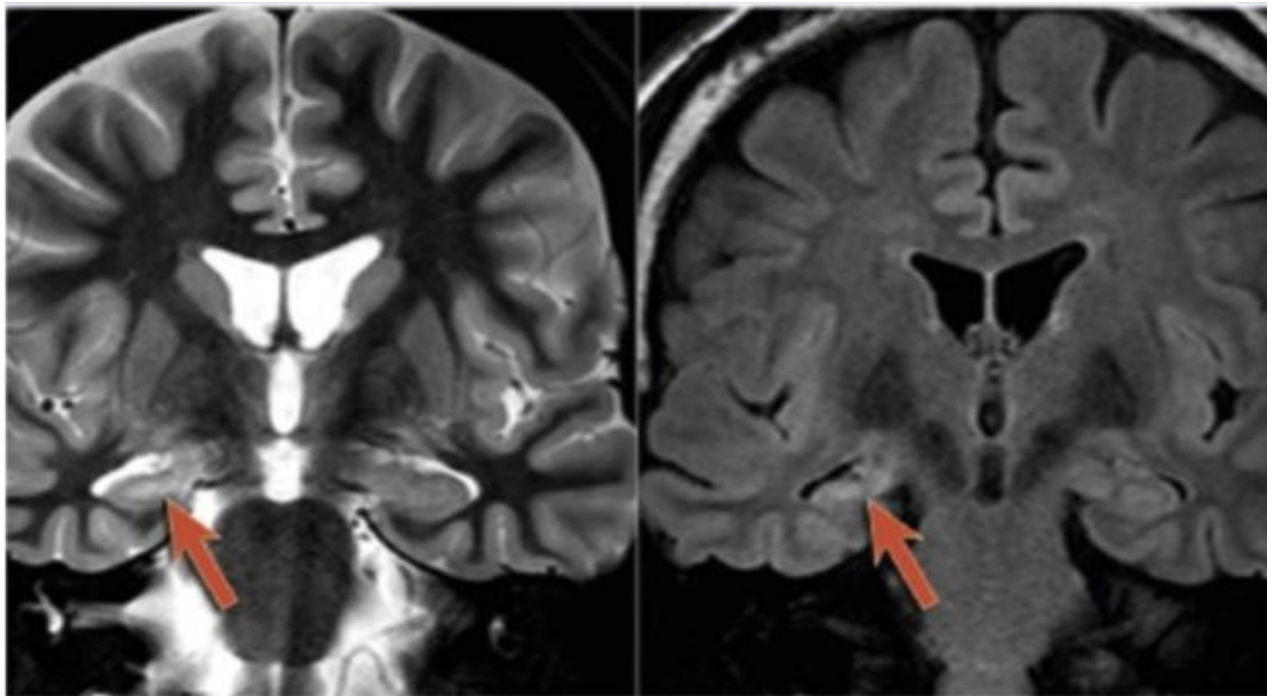
Other Surgery

- Corpus Callosotomy
- Multiple Subpial Transections
- LITT
- Neuromodulations:
  - VNS
  - DBS
  - RNS

Surgically remediable syndrome

- **Mesial temporal lobe epilepsy**
- Well circumscribed lesional partial epilepsy
- Hemispheric epilepsy syndrome
- Epilepsies in infants and young children due to large or diffuse lesions limited to one hemisphere

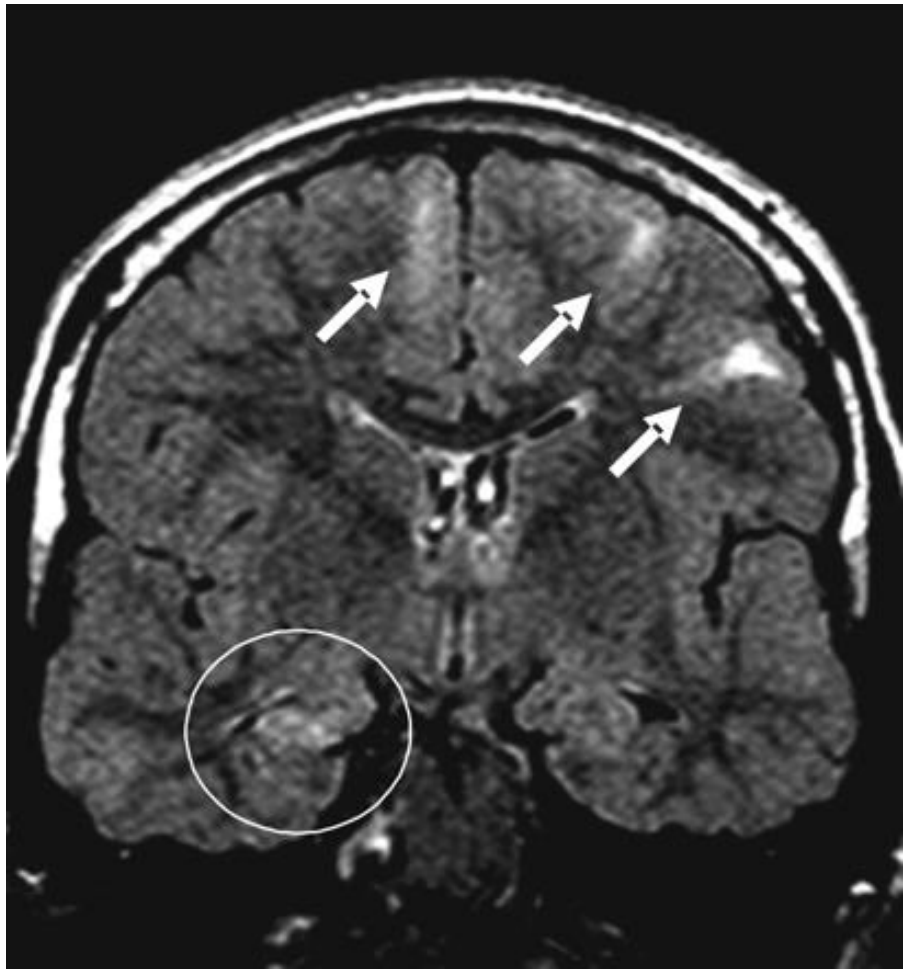
Hippocampal sclerosis (HS)



- HS is the most common lesion of epilepsy surgery, accounting for 33%–66%[1-3]
- Semiology: Aura-feeling butterfly in the stomach followed by oromotor automatism with impaired awareness, not frequent GTC
- History of febrile seizures is controversial but found 22%–67% of patients undergoing surgery[4-5]
- Drug resistant epilepsy
- MRI findings include:
  - Reduced hippocampal volume: hippocampal atrophy
  - Increased T2 signal
  - Abnormal morphology: loss of internal architecture (interdigitations of hippocampus)

[1]de Tisi et al., 2011; [2]Blümcke et al., 2012; [3]Blumcke et al., 2017
[4]Tezer et al., 2016; [5]Calderon-Garciduenas et al., 2018

Hippocampal sclerosis (HS)



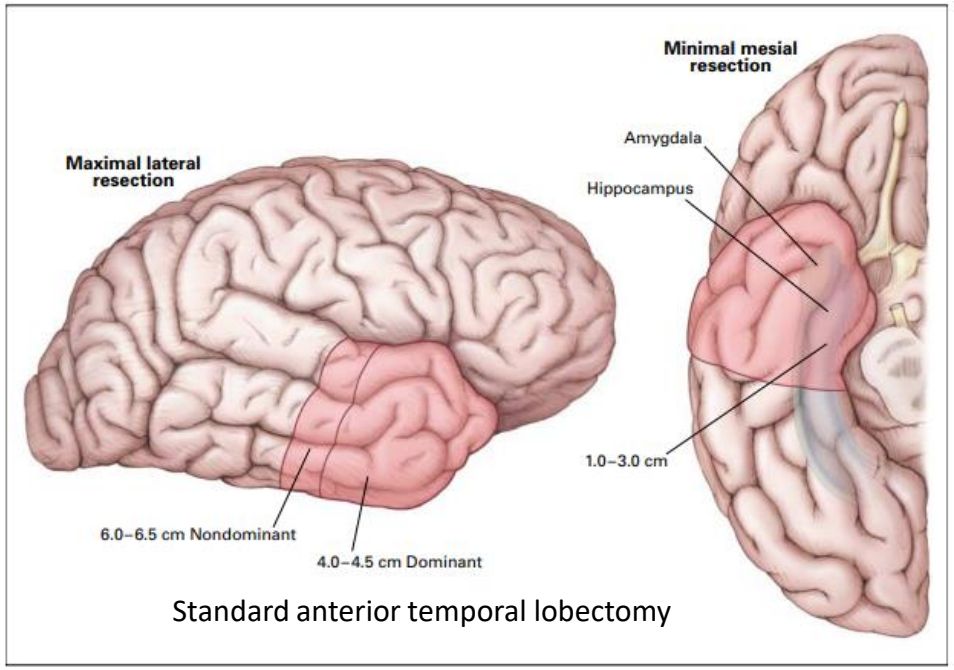
- How many lesions?
  - Unilateral HS
  - Bilateral HS
  - Duopathology- FCD IIIa
- Dominant vs. Nondominant
  - fMRI, WADA test, Neuropsychological testing
- Neuropsychological issue
- Patient characteristics

The New England
Journal of Medicine

VOLUME 345 AUGUST 2, 2001 NUMBER 5

A RANDOMIZED, CONTROLLED TRIAL OF SURGERY FOR TEMPORAL-LOBE EPILEPSY

SAMUEL WIEBE, M.D., WARREN T. BLUME, M.D., JOHN P. GIRVIN, M.D., PH.D., AND MICHAEL ELIASZIW, PH.D.,
FOR THE EFFECTIVENESS AND EFFICIENCY OF SURGERY FOR TEMPORAL LOBE EPILEPSY STUDY GROUP*



Standard anterior temporal lobectomy

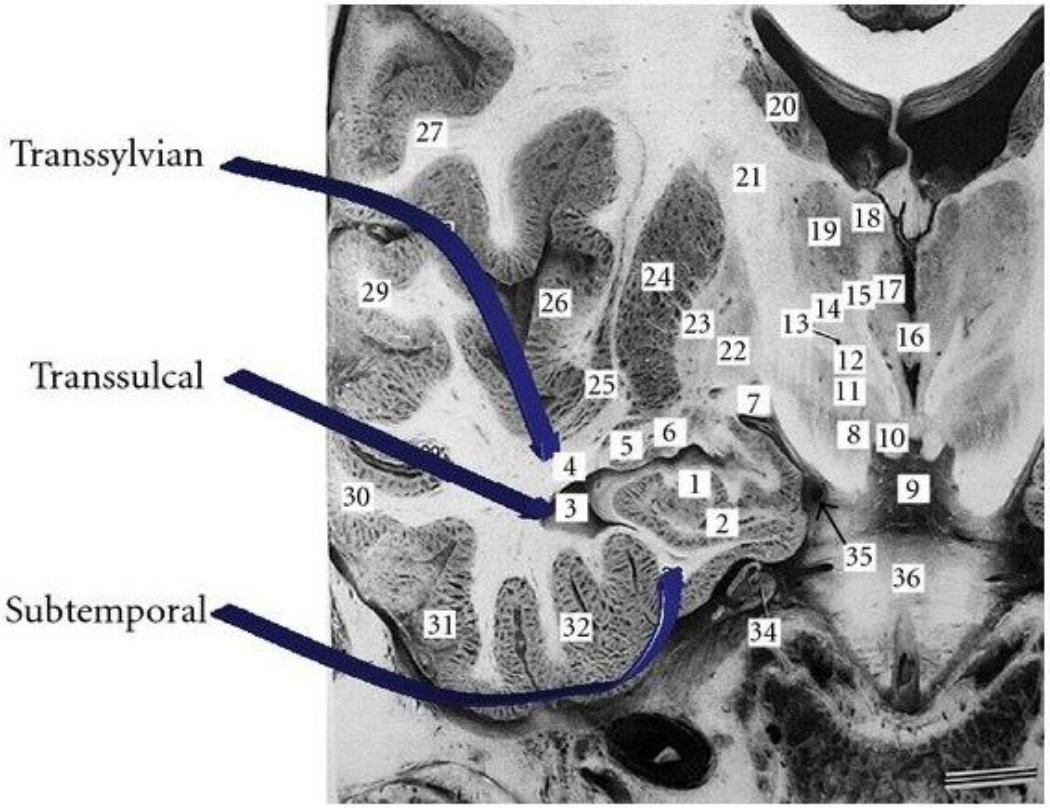
- A posterior incision at the lateral temporal gyri begins 5.5 cm from the temporal tip on the nondominant hemisphere
- 4.5 cm from the temporal tip on the dominant side at the level of T2

Methods: Eighty patients with temporal-lobe epilepsy were randomly assigned to surgery (40 patients) or treatment with antiepileptic drugs for one year (40 patients).

- The primary outcome: freedom from seizures that impair awareness of self and surroundings.
- The secondary outcomes: the frequency and severity of seizures, the quality of life, disability, and death.

Result: At one year, the cumulative proportion of patients who were free of seizures impairing awareness was 58 percent in the surgical group and 8 percent in the medical group (P<0.001).

The selective amygdalohippocampectomy (SAH)



- SAH was designed to preserve the temporal lobe neocortex while putatively offering seizure control equivalent to standard ATL and less verbal memory deficits than ATL
- **Adults**: SAH has shown excellent postoperative seizure outcomes in adults
- **Children**: Favorable results have also been observed in children with SAH. However, anterior temporal lobectomy (ATL) may be a more successful surgery for intractable TLE in children

Kell KM, et al. Epilepsy research and treatment 2011

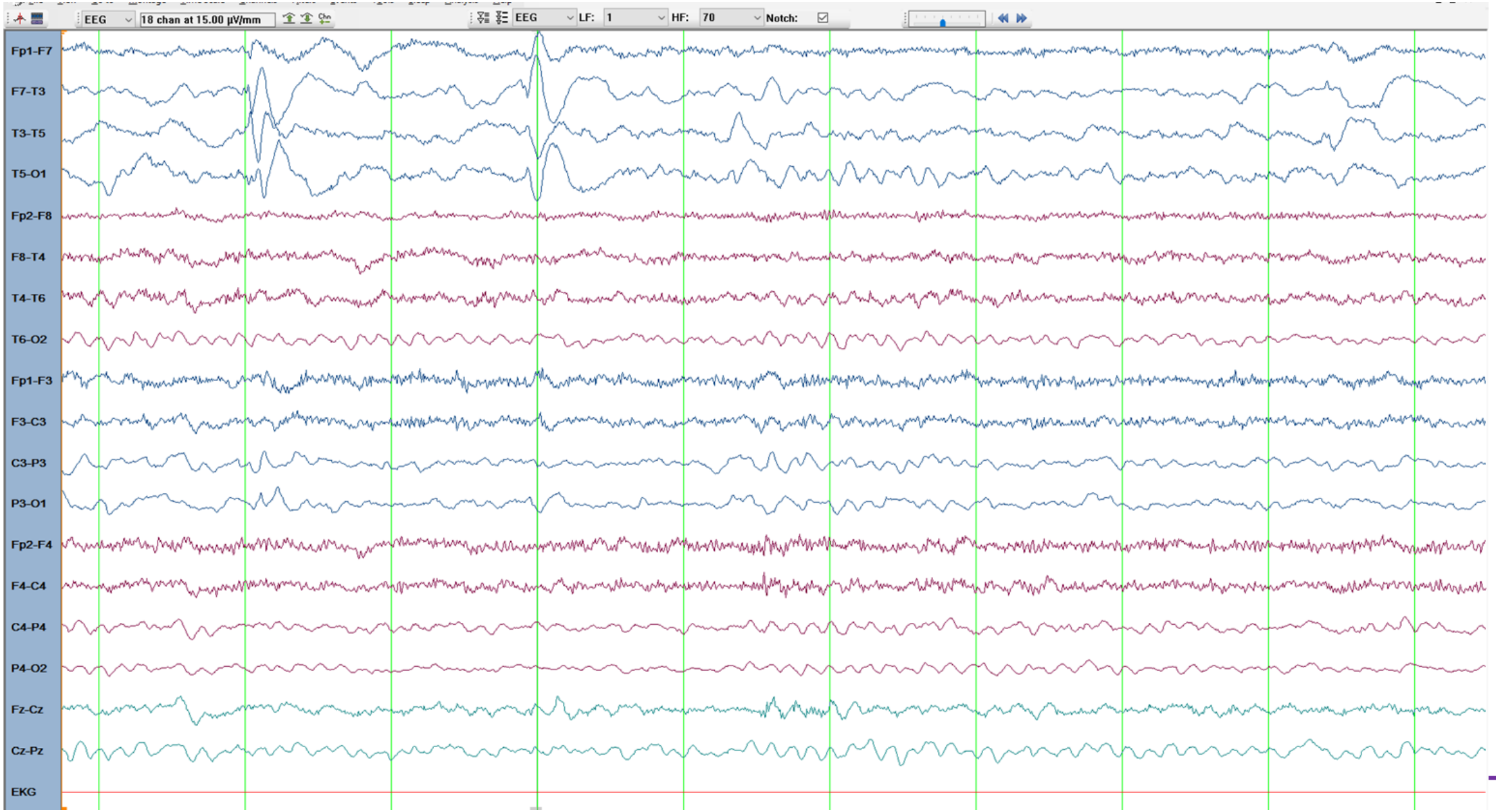
Surgically remediable syndrome

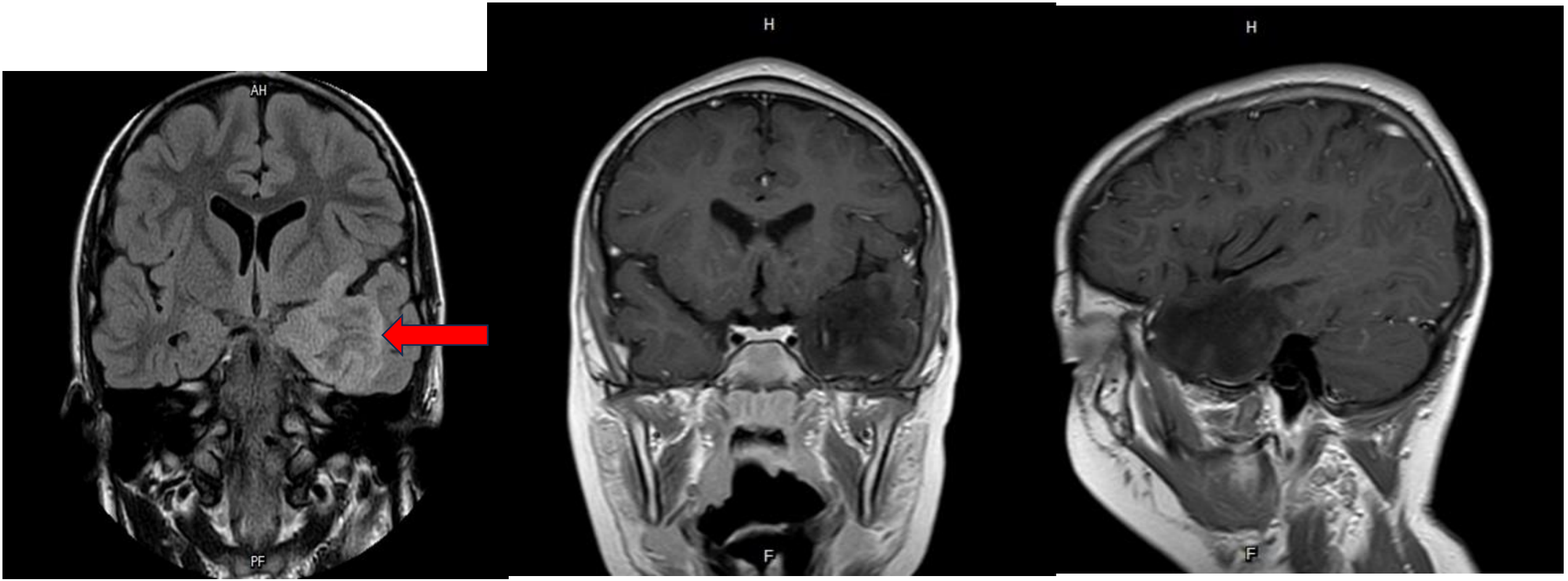
- Mesial temporal lobe epilepsy
- **Well circumscribed lesional partial epilepsy**
- Hemispheric epilepsy syndrome
- Epilepsies in infants and young children due to large or diffuse lesions limited to one hemisphere

Case a 6 years old boy, RH

- Seizure onset: 6 years old
- Seizure type:
- #1. Abdominal discomfort, nausea evolving to unresponsiveness with oral automatisms, lasting 1 minute
- #2. Fear of being caught, chest tightness followed by running around or jumping and hand automatisms lasting < 1 min
- Developmental History: normal
- EEG: Regional Left temporal (T3, T5 electrodes)
- ASMs: LEV, LCM, PER

Interictal : SW T3T5





Operation: Tumor resection (23/05/2023)
Pathology : Low-grade glioma
Seizure outcome: Seizure free since surgery

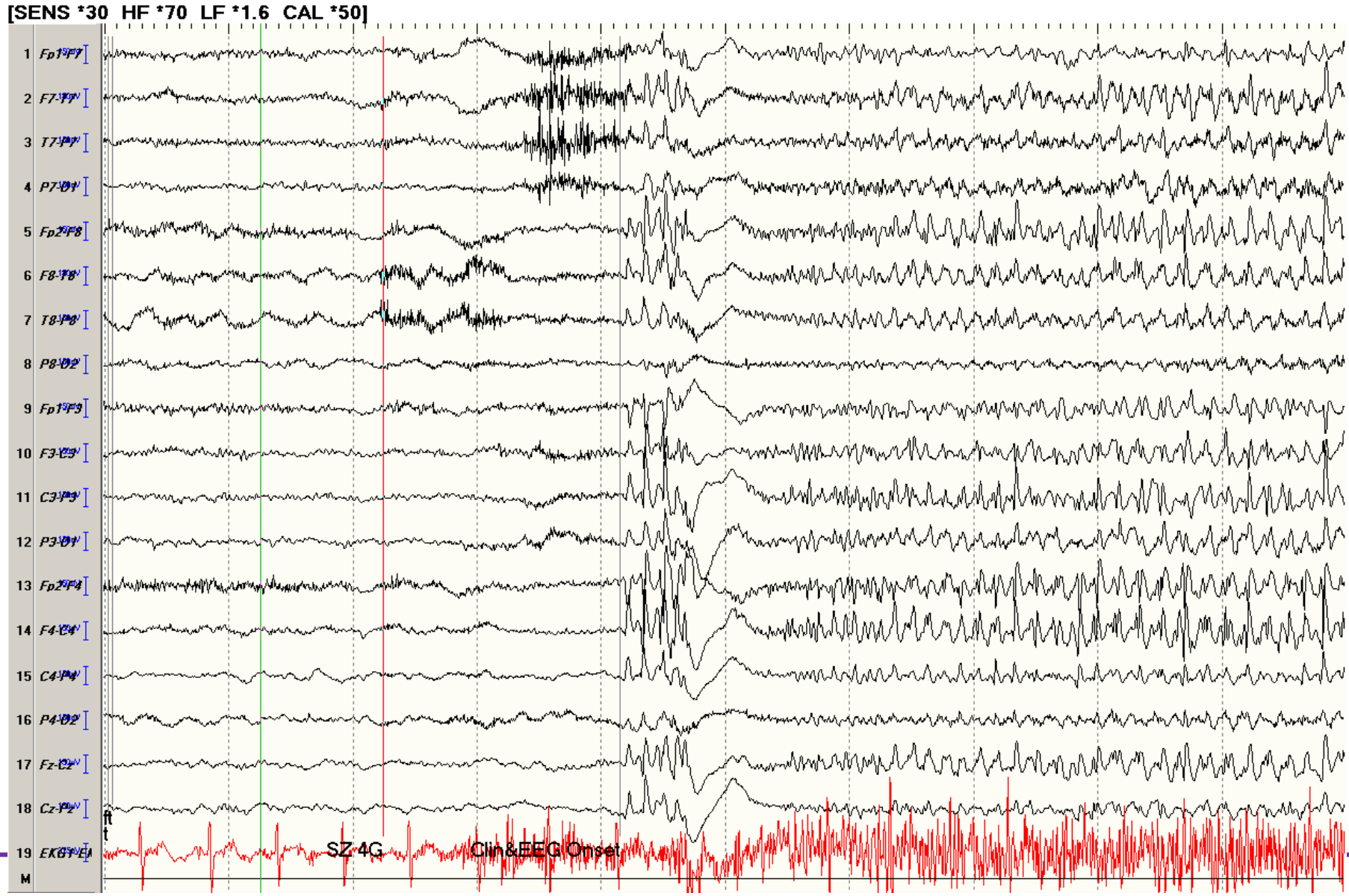
Surgically remediable syndrome

- Mesial temporal lobe epilepsy
- Well circumscribed lesional partial epilepsy
- **Hemispheric epilepsy syndrome**
- Epilepsies in infants and young children due to large or diffuse lesions limited to one hemisphere

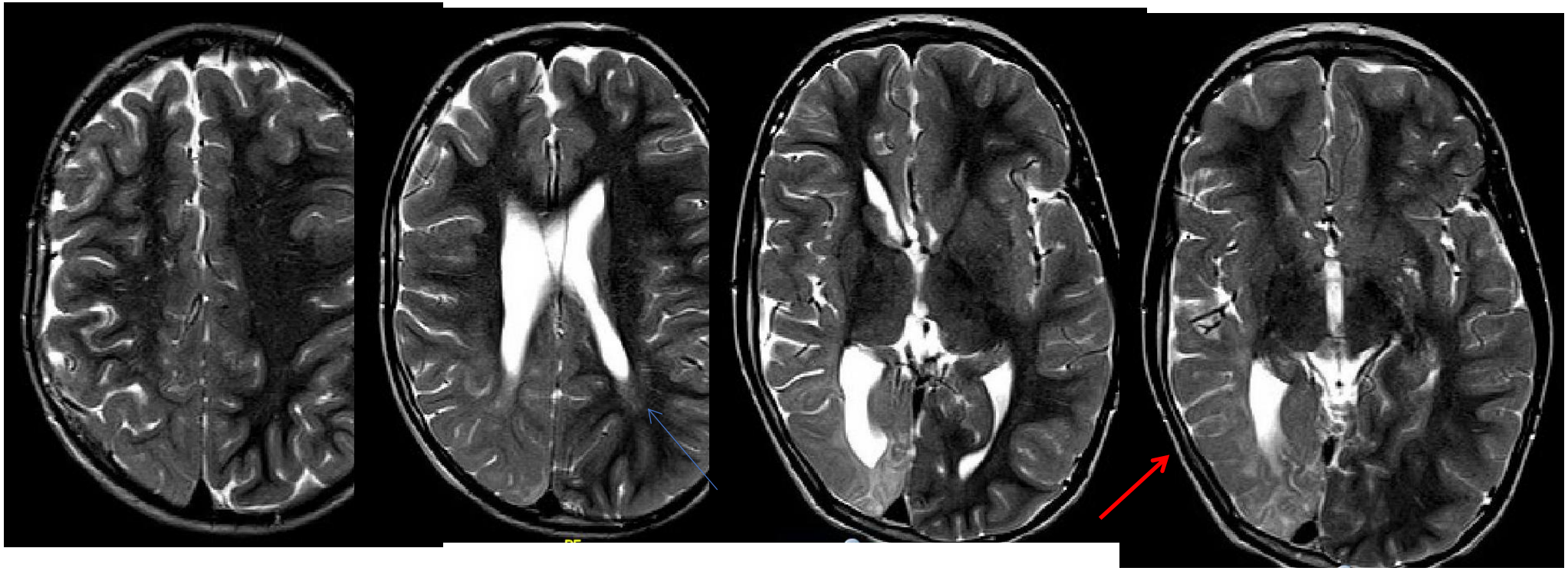
Case: 6 yr old boy, intractable epilepsy with developmental delay

- Seizures onset: 3 months
  - These were left arm tonic extension and left head deviation
  - Lasting 30-60 seconds, frequency: 5-10 per day.
- Current Seizures:
  - Tonic stiffening of all over the body, atonic
  - Frequent falls & injuries 3-5 per /day
- Current AEDs:
  - Clonazepam(0.5 MG) 1.5mg three times daily
  - Topiramate(25 MG) Take three (3) tablets twice a day
  - Failed: Carbamazepine, Clonazepam, Levetiracetam, Oxcarbazepine, Phenobarbital,Valproate, Zonisamide

Tonic Seizure: EEG onset

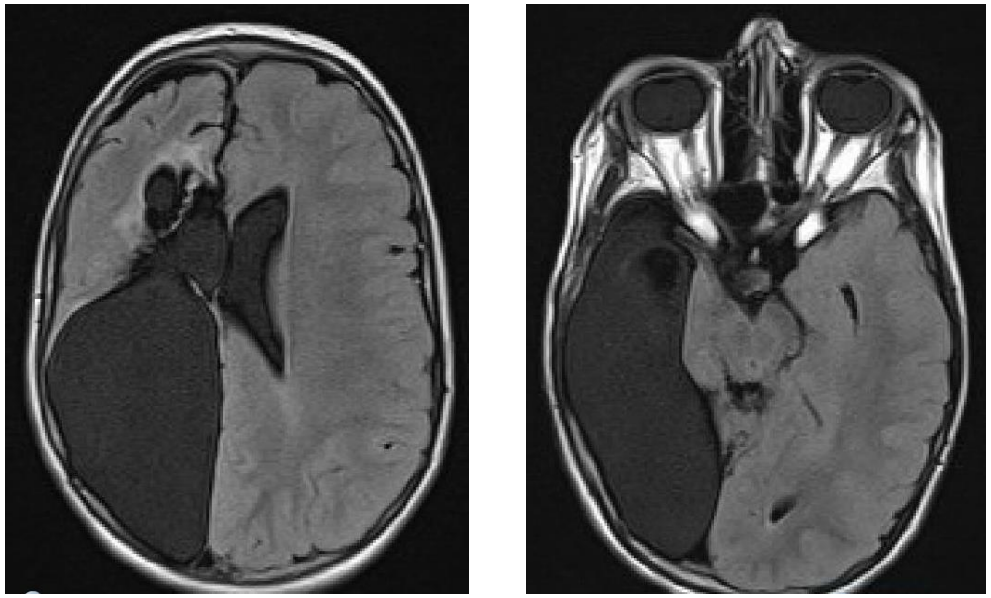


MRI-Axial



Right hemispheric hemiatrophy predominantly right posterior quadrant, mild signal abnormalities left posterior quadrant

Back to our case

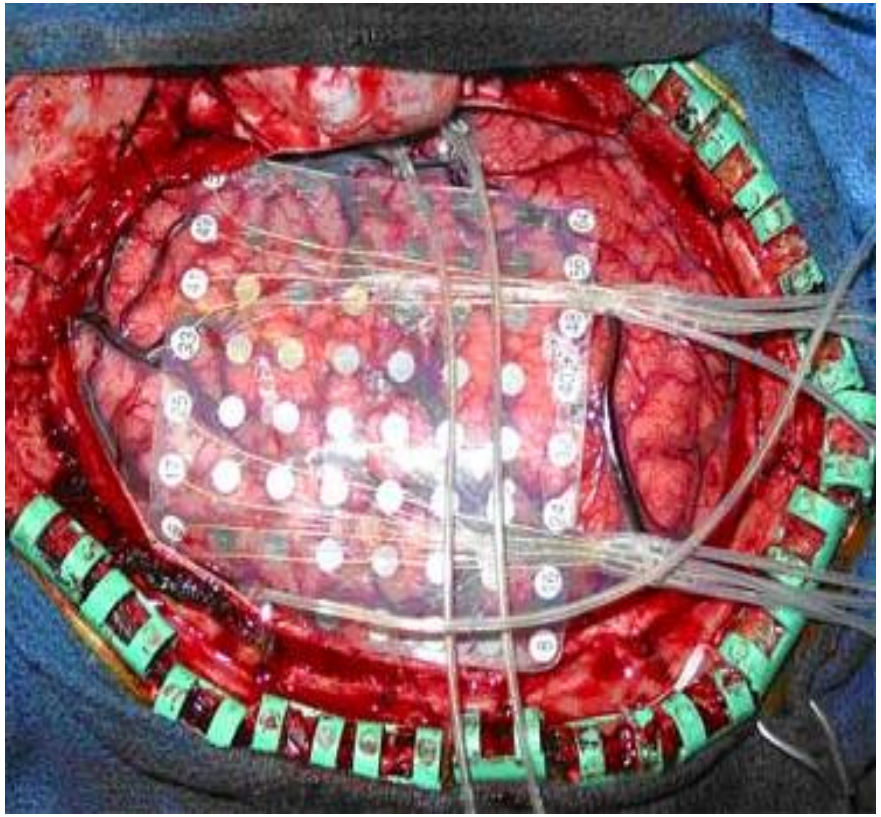


- Underwent right modified anatomic hemispherectomy with disconnected but residual frontal lobe
- Pathology : The malformation of cortical development is marked by architectural disorganization, neuronal cytomegaly, and dysmorphic neurons
- Seizure-free since surgery, markedly developmental improvement

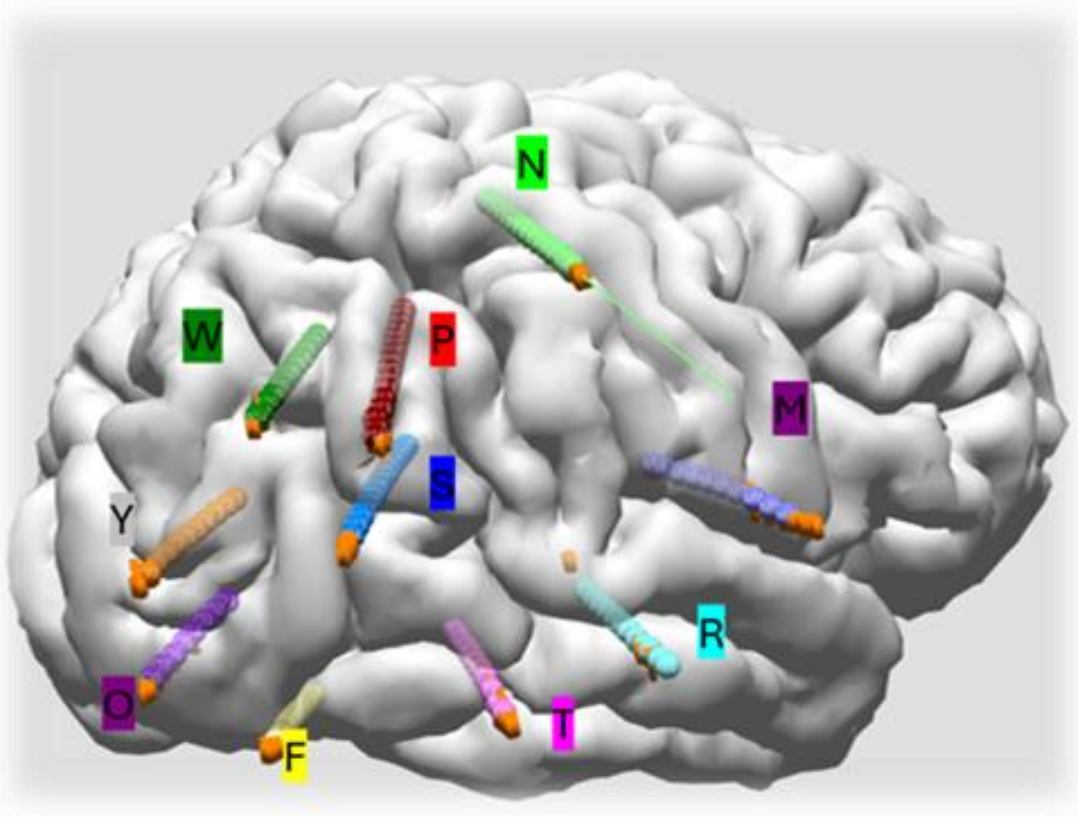
Who are the candidates for invasive monitoring?

- **Complex** focal drug-resistant epilepsy
- Discordant non-invasive investigations
- Normal or nonlocalizing MRI
- The possibility of an EZ that is deep-seated
- The need for bihemispheric explorations
- SEEG can be proposed for thermocoagulations

Invasive recording



Subdural Grid
Functional mapping
2D aspect of the epileptogenic zone

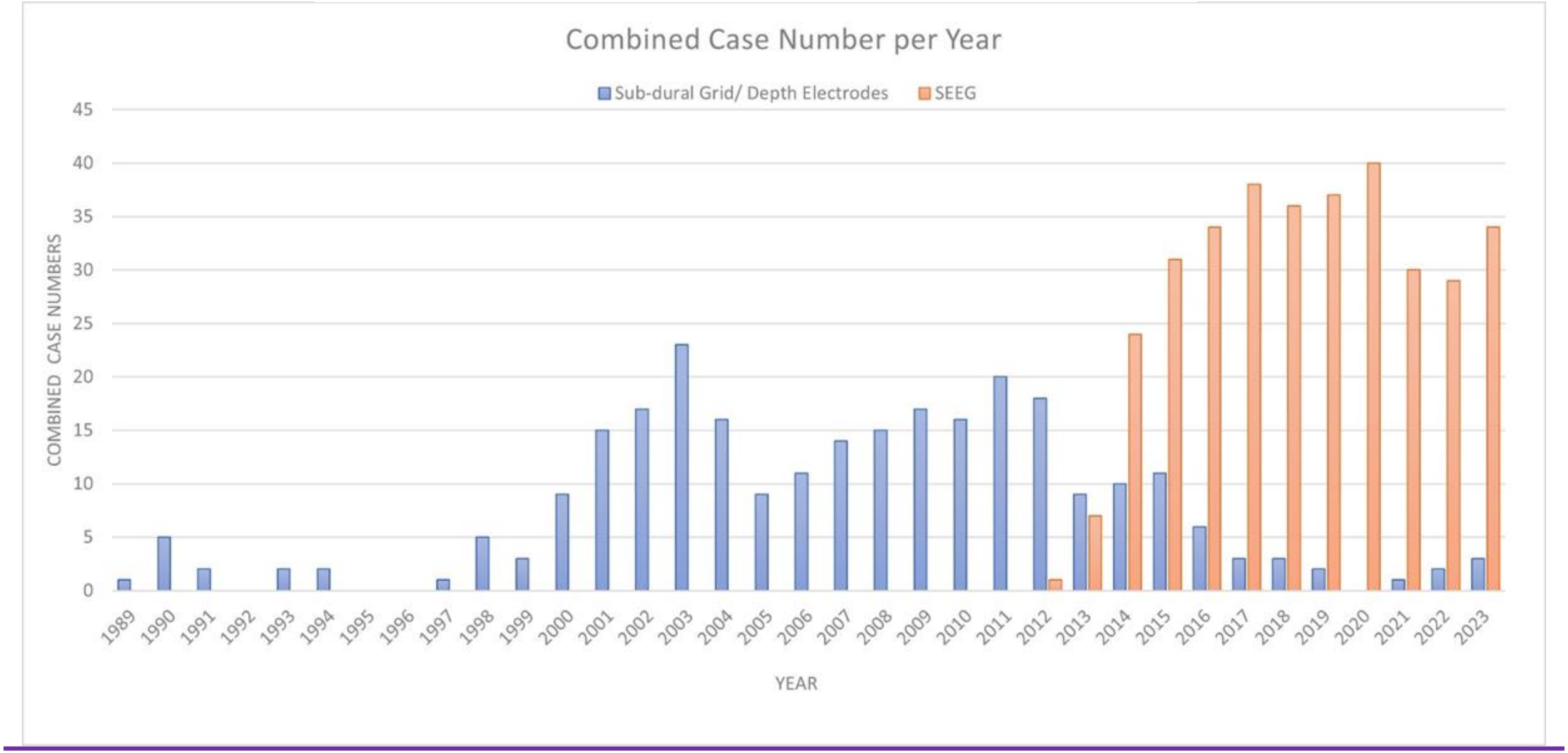


SEEG
AEC correlation
3D aspect of the epileptogenic zone

The development of Stereo-Electroencephalography (SEEG) in Southeast Asia and Oceania: Challenges to equity across the region.

Michael W.K. Fong [a,b,*], Kheng-Seang Lim [c], Si Lei Fong [c], Chien Chen [d], Shang-Yeong Kwan [d], Cheng-Chia Lee [e], Piradee Suwanpakdee [f], Charcrin Nagangchang [f,1], Minh-An Thuy Le [g,h], Yee-Mon Khine [i], Deepak Gill [a,b], Chong H. Wong [a,b]

Phramongkutklao Comprehensive Pediatric Epilepsy Center of Excellence
Integration • Passion • Wisdom



Michael W.K. Fong, et al. Neurophysiologie Clinique 2024

Where do we put the SEEG electrodes?

Phramongkutklao Comprehensive Pediatric Epilepsy Center of Excellence
Integration • Passion • Wisdom

Phase I noninvasive evaluation

Lesion
MRI/VBM
PET
Neurological exam
Neuropsychology

Ictal data
Video-EEG
Ictal SPECT
Ictal and post-ictal Neurologic and neuropsychologic examination

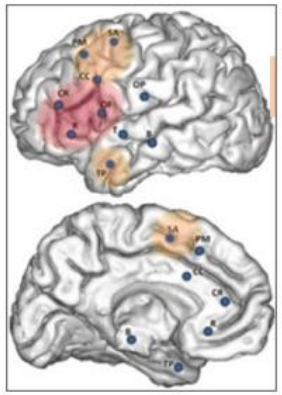
Interictal Data
Video-EEG
High density EEG
MEG
PET

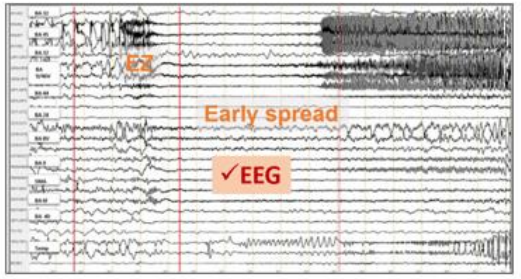
The gold standard techniques for the localization of the epileptogenic zone **(scalp EEG and video recordings of the seizure semiology)** are sufficient.

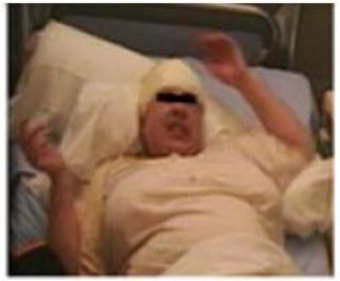
(Siegel AM. Neurosurg Rev. 2004)

Generate an Anatomo-Electro-Clinical (AEC) network hypothesis

Anatomical | Electrical | Clinical







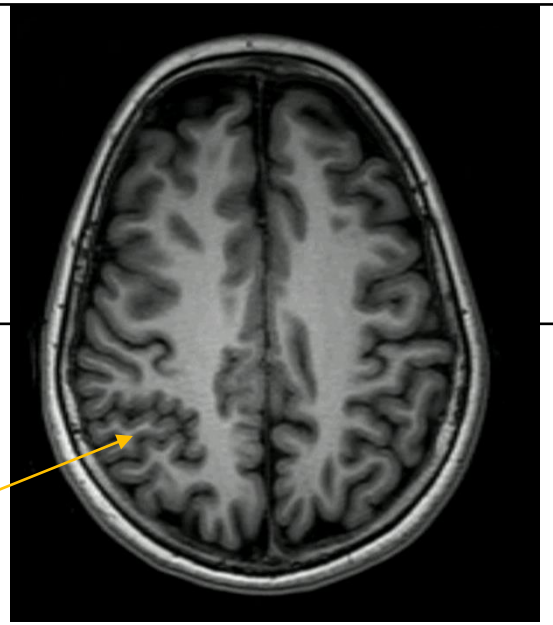
Bonini F, Epilepsia 2014

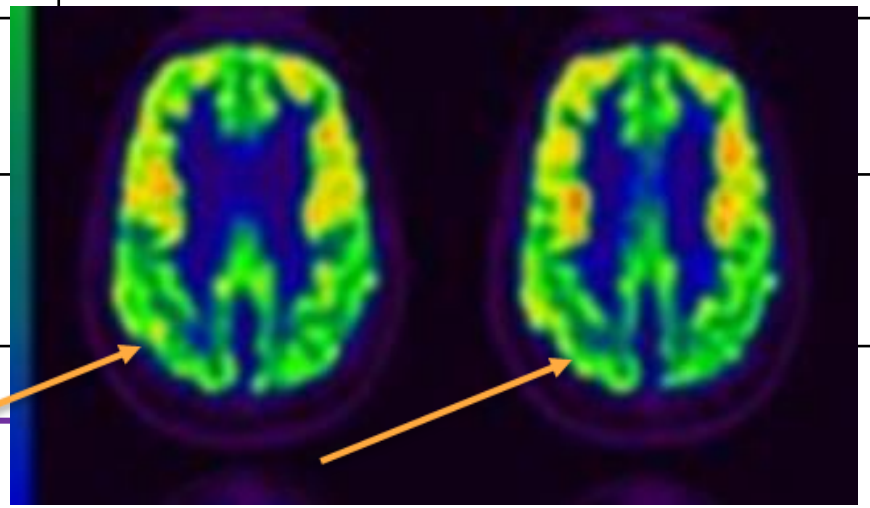
SEEG Electrode implantation

Yield of SEEG depends on where electrodes are placed:
***clear hypotheses

Case a 12-year-old girl, RH

	Right	Left	Non-lateralized
Semiology	numbness around the left face, tongue, excessive salivation, followed by focal clonic movements of the left side of the mouth (frequency 3-4 times/day)		
VEEG	-Epileptiform discharges was seen in the Rt. centro-temporal head region(s). -Intermittent rhythmic slowing was seen in the Rt. centro-parieto-temporal head region.		
MRI	Increased small gyration at Rt. post central gyrus and Rt. high parietal lobule, Possible polymicrogyria		
PET	Hypometabolism of Rt. inferior post central gyrus and Rt. superior parietal lobule reflect functional deficit zones.		

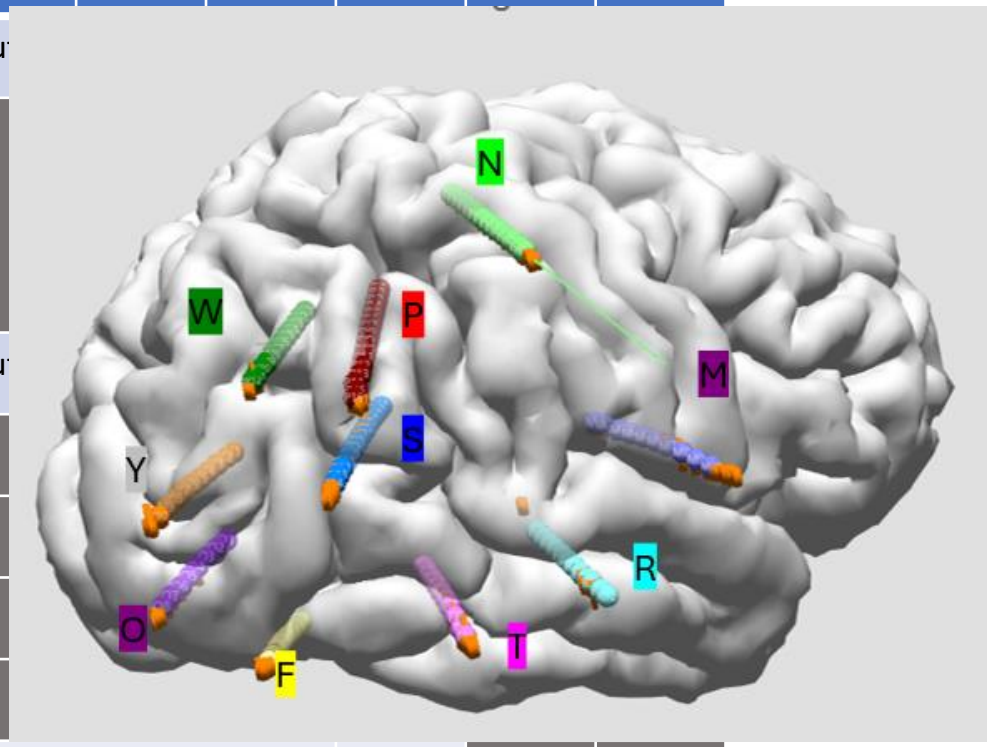




Reconstruction map

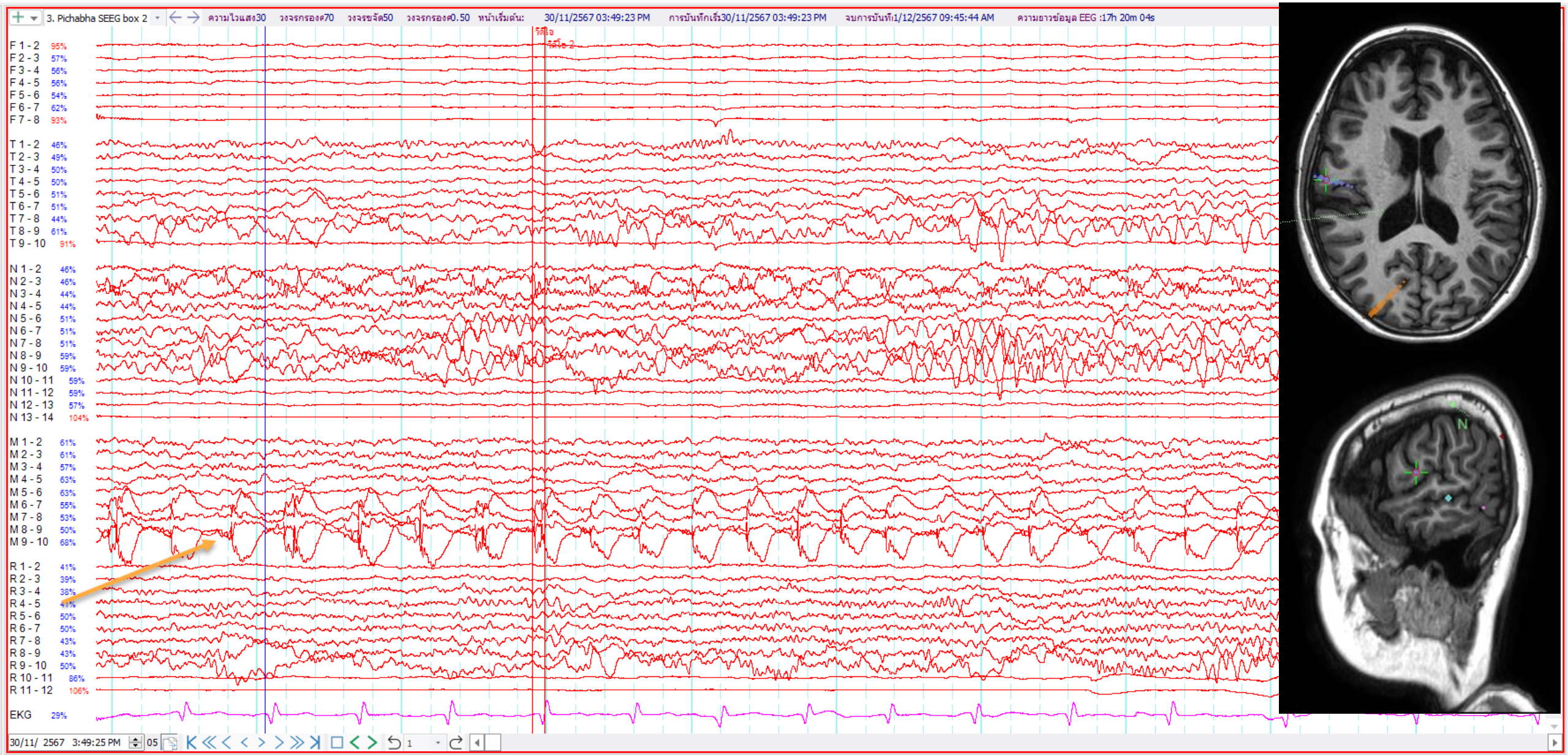
Phramongkutklao Comprehensive Pediatric Epilepsy Center of Excellence
Integration • Passion • Wisdom

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
N	SFG			SFS		Sup. Parietal cortex				Out	Out					
M	Post. insula	Parietal operculum														
R	STG/ STS								Out	Out	Out					
T	WM	WM	MTG							Out						
F	Occipital gyrus			ITG												
O	Occipital gyrus															
Y	Cuneus			WM	WM	WM	Occipital gyrus									
S	WM	WM	WM	WM	WM	WM	Inferior parietal lobule							Out		
P	WM	WM	Superior parietal lobule (polymicrogyria)											Out	Out	Out
W	WM	WM	WM	SPL		IPL				Out	Out	Out				



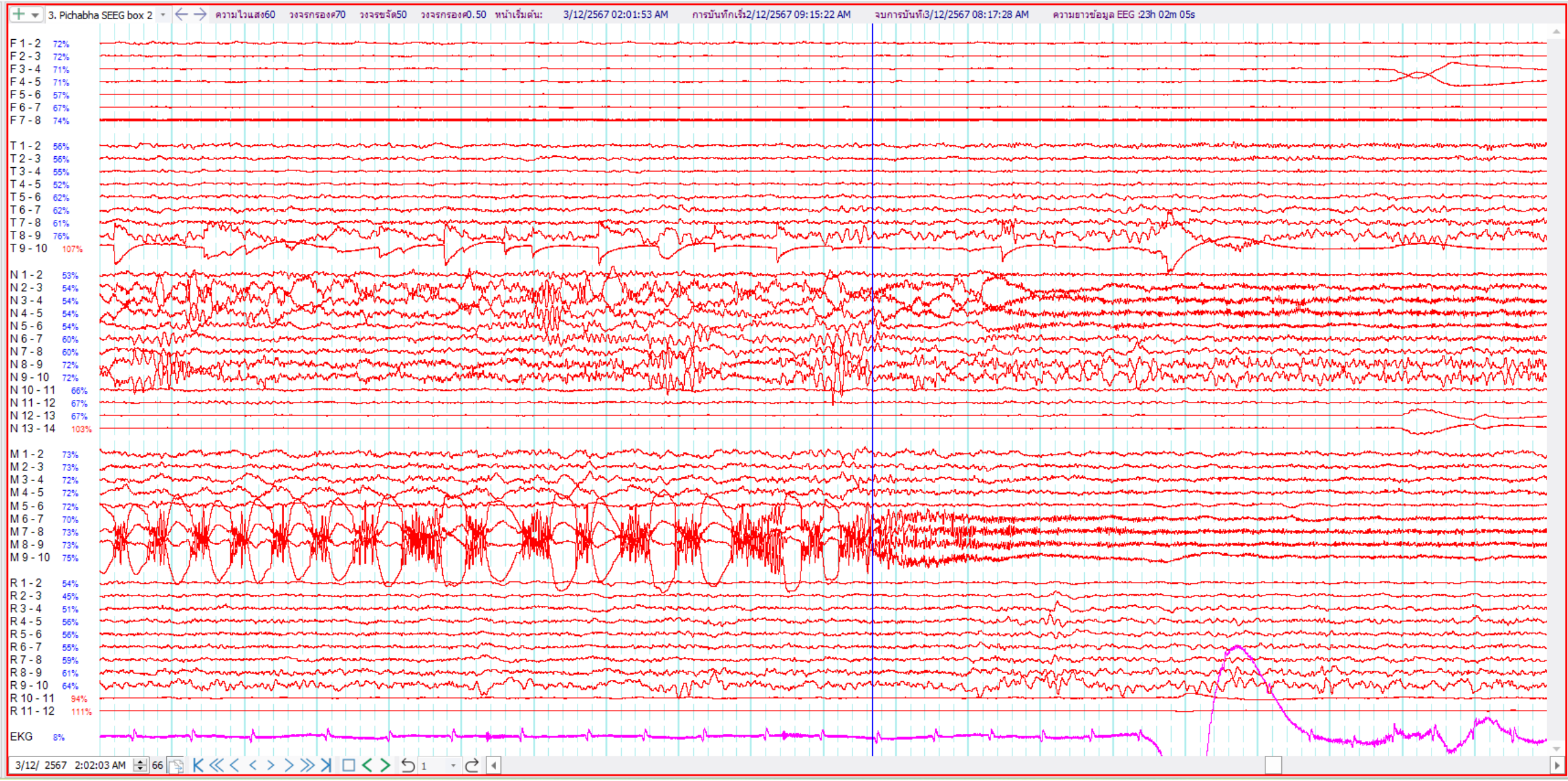
SPK #1 M 6-10 (80%) R parietal operculum

Phramongkutklao Comprehensive
Pediatric Epilepsy Center of Excellence
Integration • Passion • Wisdom

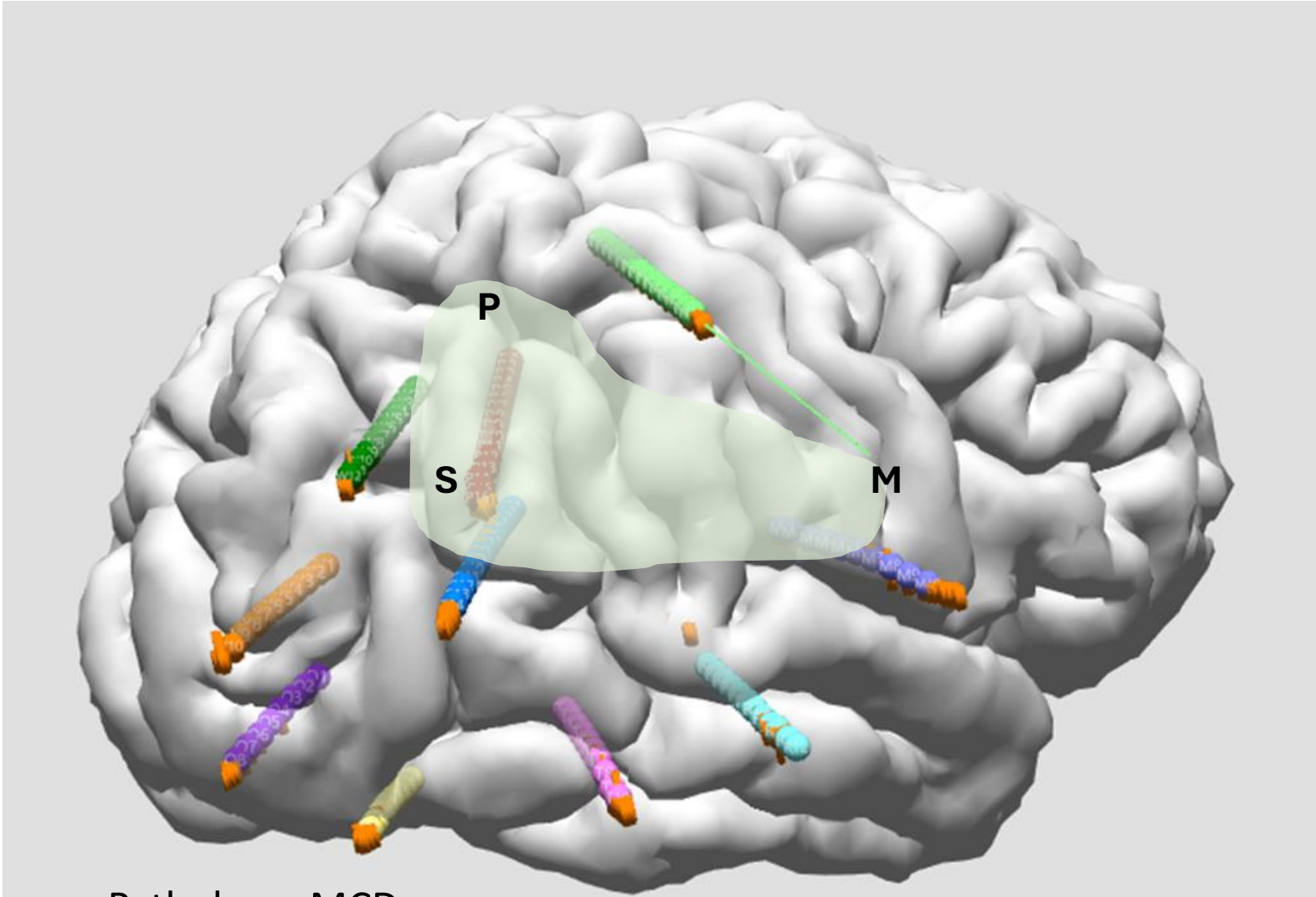


SZ onset: Zoom-in (EEG onset M6-10)

Phramongkutklao Comprehensive
Pediatric Epilepsy Center of Excellence
Integration • Passion • Wisdom



Resection (M 6-10, P 9-13, S 10-13)



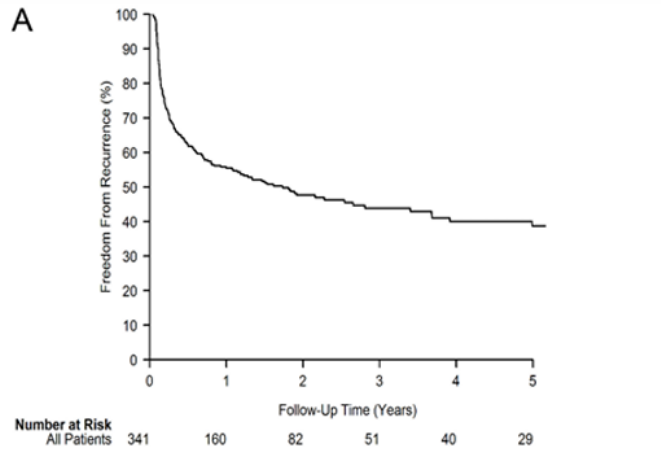
Pathology: MCD

Seizure outcome: Rare aura 1 time/month

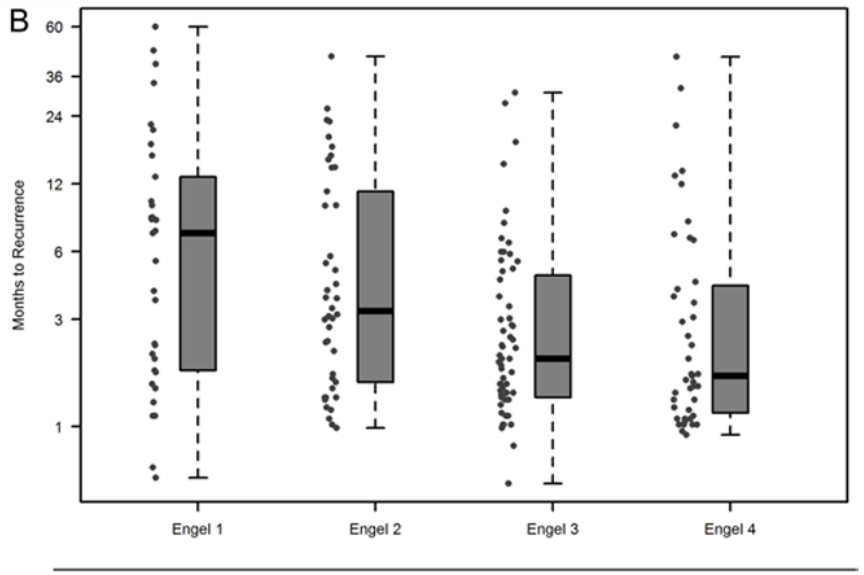
Determinants of seizure outcome after resective surgery following stereoelectroencephalography

Juan C. Bulacio, MD,[1] James Bena, MS,[2] Piradee Suwanpakdee, MD,[1] Dileep Nair, MD,[1] Ajay Gupta, MD,[1] Andreas Alexopoulos, MD,[1] William Bingaman, MD,[1] and Imad Najm, MD[1]

[1]Epilepsy Center, Neurological Institute, Cleveland Clinic, Cleveland; and [2]Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio



Follow-up Time	1y	3y	5y
Sz Free (%)	55.5 (50.2,61.8)	43.9 (37.7, 50.0)	39 (31.8, 45.7)

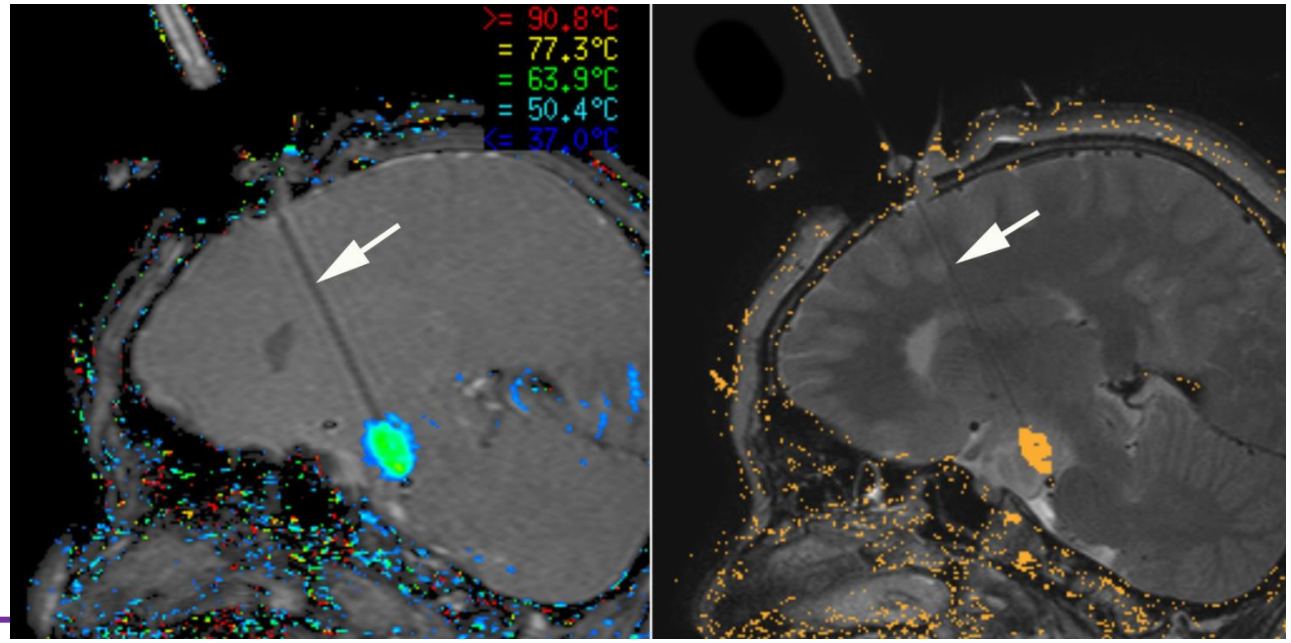


- Of 527 patients satisfying study criteria, 341 underwent resective surgery.
- Complete and continuous seizure freedom after surgery was achieved in 55.5% of patients at 1 year postoperatively, 44% of patients at 3 years, and 39% of patients at 5 years.
- As a secondary outcome point, 58% of patients achieved Engel class I seizure outcome for at least 1 year at last follow-up

Bulacio J et al, J Neurosurg, 2021

Laser Interstitial Thermal Ablation (LITT)

- MRI-guided controlled burn of tissue by a laser
- Minimally invasive travel through the brain to target tissue
- Must have well-defined MRI lesion or depth electrode confirmed well-circumscribed target
  - Mesial temporal sclerosis
  - Hypothalamic hamartoma
  - Tumor
  - Cavernous malformation



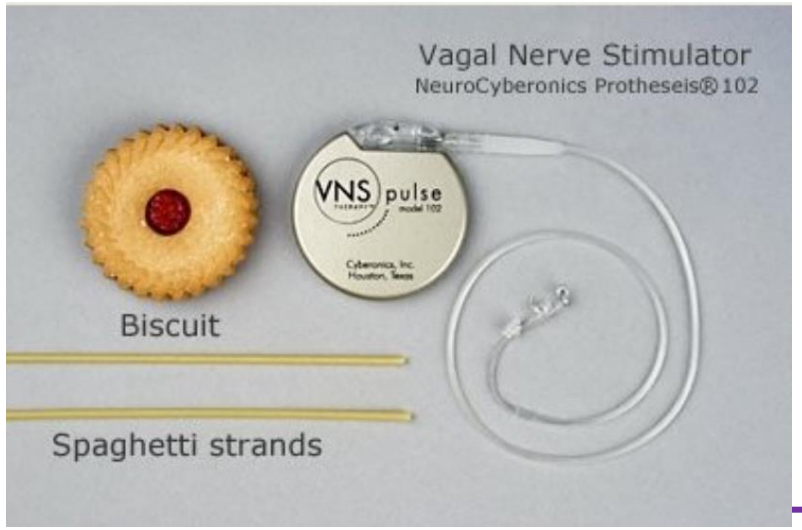
Outcomes after LITT for temporal lobe epilepsy: a systematic review and meta-analysis

- The study included 836 patients
- Seizure outcomes were categorized as follows:
  - Engel I outcome: Achieved in 56% of patients
  - Engel II outcome: Seen in 19.2% of patients
  - Engel III outcome: Observed in 17.3% of patients
  - Engel IV outcome: Present in 10.5% of patients
- Neurocognitive outcomes:
  - Verbal and visual memory decline: Approximately 24.2%
  - Naming decline: About 13.4%
- Comparing LITT outcomes with those after temporal lobectomy, LITT was slightly inferior in terms of seizure control
- However, data on cognitive outcomes after LITT remain scarce and heterogeneous

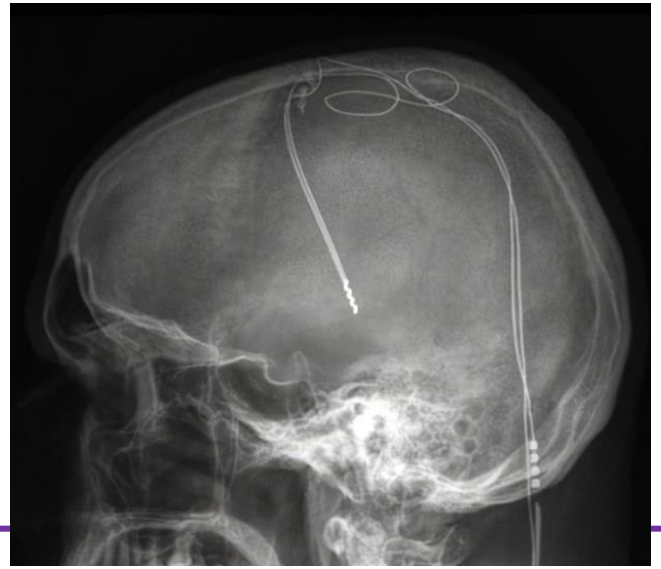
Alomar SA, et al. Neurosurg Rev. 2023

Neuromodulation

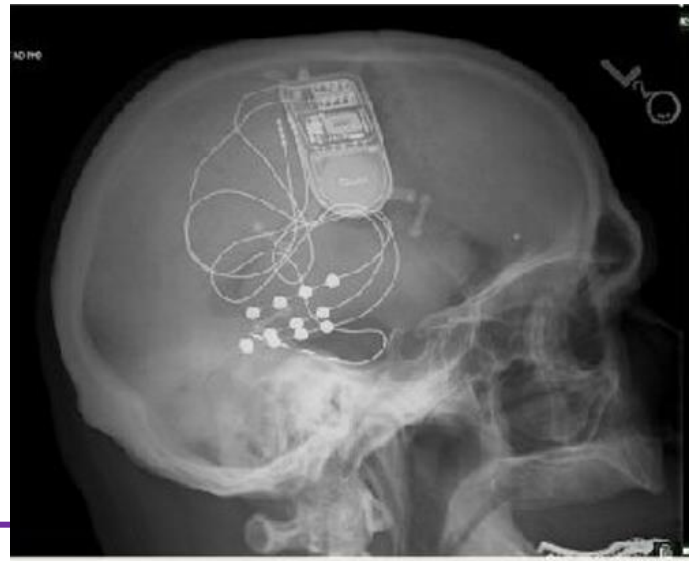
- If the seizure focus is unresectable
  - Bilateral TLE
  - Overlap with the eloquent cortex
- VNS: Vagal nerve stimulation
- DBS: Deep brain stimulation
- RNS: Responsive neurostimulation



VNS



DBS



RNS

VNS vs RNS in Patients with Temporal Lobe Epilepsy

	VNS group (n = 11)	RNS group (n = 12)	p value
Postoperative seizure frequency, month, mean ± SD	16.3±18.9	11.8±18.4	
Change in seizure frequency	−17.2±34.3	−24.5±48.8	0.69
Responder rate, % (n)*	45.5 (5)	66.7 (8)	0.318
Seizure reduction, % (n)	46.3±40.9	58.1±38.7	0.49
Engel score, mean ± SD**	3.2±0.9	3.2±0.4	0.57
Engel I, % (n)	9.1 (1)	0.0 (0)	
Engel II, % (n)	0.0 (0)	0.0 (0)	
Engel III, % (n)	54.5 (6)	83.3 (10)	
Engel IV, % (n)	36.4 (4)	16.7 (2)	
Postoperative meds, mean ± SD	3.1±0.8	2.9±0.6	
Change in medications, mean ± SD	0.1±0.5	0.3±0.5	0.50
Underwent future resective surgery, % (n)*	27.3 (3)	8.3 (1)	0.23

Wang, AmyÂ J et al. Stereotact Funct Neurosurg 2020

Deep Brain Stimulation and Drug-Resistant Epilepsy: A Review of the Literature

Author/year	Mean age (years)	Type of study	n	Seizure type (s)	Follow up (months)	Average seizure reduction (range)
HC						
Velasco et al. (113, 114)	24	Open label	10	(TLE) CPS, SGTC	2 weeks	100% after 6 days
Vonck, 2002 (115)	33	Open label	3	(MTLE) CPS, GTC	5 (3–6)	77% (50–94%)
Vonck et al. (116)	NR	Open label	7	(TLE) NR	14 (5.5–21)	43% (0–100%)
Tellez-Zenteno et al. (98)	32	Clinical trial (Double blind, cross over)	4	(MTLE) CPS, SGTC	6 blind	26% (ON) vs. −49% (OFF)
Boon et al. (105)	NR	Open label	10	(MTLE) CPS, SPS, SGTC	31 (15–52)	50% (<30–100%)
Velasco et al. (109, 117)	29	Clinical trial	9	(MTLE) CPS, SGTC	18 (1 blind)	83% (50–100%); 9/9 RR
McLachlan et al. (106)	45, 54	Clinical trial (Double blind, cross over)	2	NR	3	33% (ON) vs. 4% (OFF)
Boex et al. (110) Bondallaz et al. (118)	34	Open label	8	(MTLE) CPS, SGTC	44	67% (0–100%); 6/8 RR
Tyrand, 2012 (119)	32	Open label	12	(TLE) NR	0	58.1%*
Morrell et al. (53) (RNS trial) Heck et al. (54) (RNS trial)	34.9 (18–66)	Clinical trial	95 of 191	SPS, CPS, SGTC	3 blind 48	38% (ON) vs. 17% (OFF) 53%, 55% RR
Vonck et al. (107)	NR	Open label	11	(MTLE) CPS, SPS, SGTC	96 (67–120)	70% (0–100%); 8/11 RR;
Cukiert et al. (57)	37	Single blind	9	(TLE) CPS, SPS, SGTC	30.1	61% (−50–100%); 7/9 RR
Jin et al. (120)	NR	Open label	3	CPS, SGTC	35	93% (91–95%)
Lim et al. (121)	35	Open label	5	CPS, SGTC	38	45% (22–72%); 3/5 RR
Cukiert et al. (108)	38.4	Clinical trial (Double blind, randomized)	16	SPS, CPS	8 (6 blind)	3/14 RR in CPS, 7/16 RR in SPS

Zangiabadi N, Frontier in Neurology 2019

Common misconceptions about epilepsy surgery

- All anti-seizure medications need to be tried
- Not a good candidate for surgery if:
  - bilateral interictal epileptiform discharges
  - Neuroimaging
    - normal brain MRI
    - multiple or diffuse lesions on MRI
    - lesions on the dominant cerebral hemisphere

Take home message

Epilepsy Surgery in Children:

- **Why?**
  - Epilepsy surgery offers a chance for seizure freedom or significant reduction in seizures when medications fail.
  - Early intervention can improve cognitive, and developmental outcomes
- **When?**
  - Surgery should be considered **early** in the course of DRE
  - Timely referral is crucial to avoid prolonged exposure to seizures
- **How?**
  - Through a **multidisciplinary approach** involving clinical evaluation, advanced neuroimaging,long-term EEG monitoring.
- Surgical techniques vary depending on the seizure substrate.