

PRE-SURGICAL EVALUATION IN EPILEPSY AND EPILEPSY SURGERY

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TOPIC OUTLINES

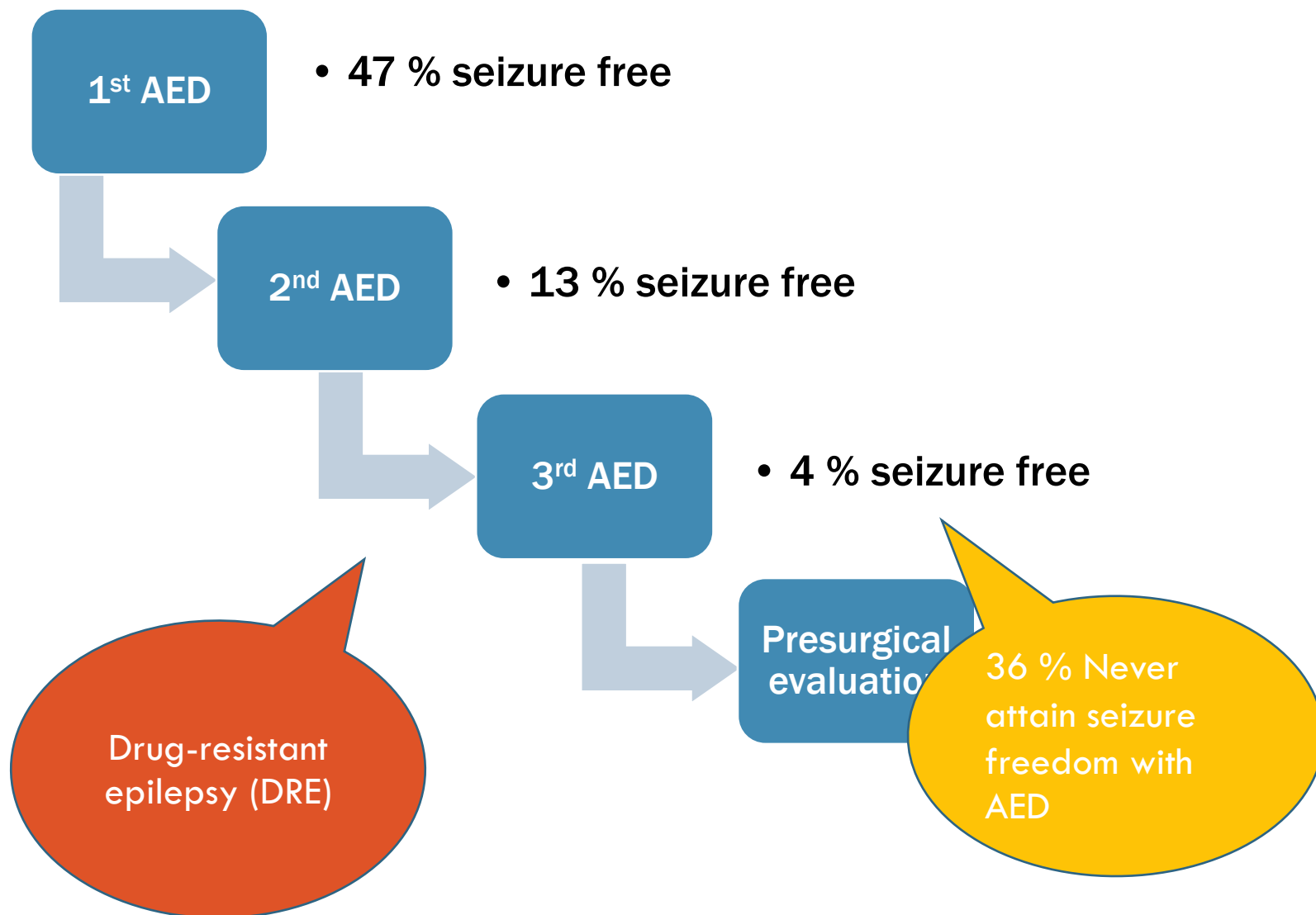
Identifying candidate for presurgical evaluation

Presurgical evaluation process in epilepsy

Type of epilepsy surgery

Outcome of epilepsy surgery

RESPONSE TO AED IN PATIENT WITH NEWLY DIAGNOSED EPILEPSY

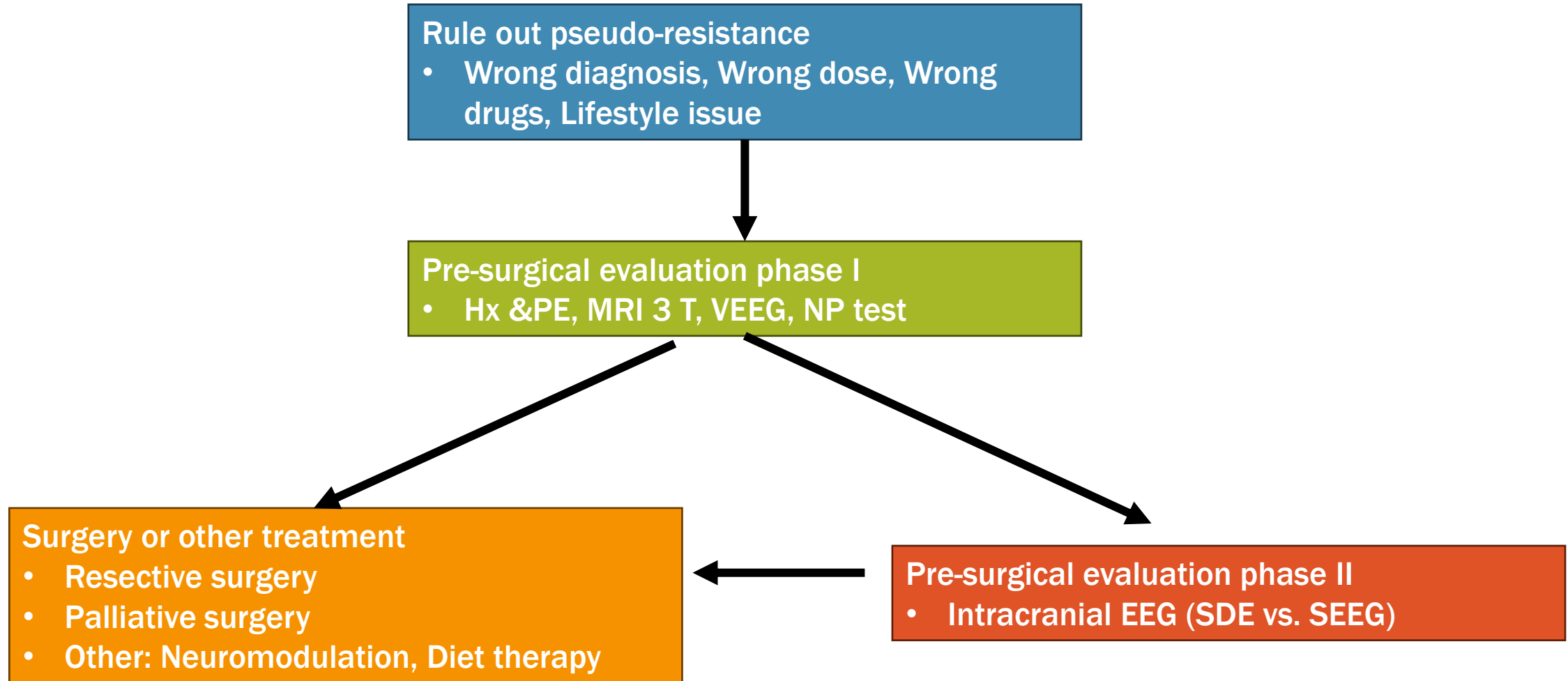


DRUGS RESISTANT EPILEPSY (DRE)

Defined as :

- **Failure of adequate trials of 2 Anti-seizure medication**
 - Tolerated
 - Appropriately chosen
 - Used AED schedules (whether as monotherapies or in combination)
- **To achieve sustained seizure freedom (Whichever is longer of:)**
 - 3 times the longest pre-intervention inter-seizure interval
 - 12 months

EVALUATION OF DRUGS RESISTANT EPILEPSY



PSEUDO-DRUGS RESISTANCE OF EPILEPSY

APPROACH TO ANTISEIZURE MEDICATION (ASM) PSEUDORESISTANCE

Incorrect Diagnosis

Review Epilepsy Diagnosis

- Exclude epileptic seizure mimics e.g., syncope, movement disorder, migraine

Incorrect/ inappropriate ASM

Review seizure type and epilepsy type/syndrome classification

Inadequate ASM dosing

Ensure optimal ASM dosage has been trialled
- Uptitration to maximal tolerated dose

ASM and concomitant medication (including over-the-counter medications) review
- drug-drug interaction affecting ASM efficacy

Adherence and Lifestyle Factors

ASM non-adherence


Sleep deprivation

Excessive alcohol use

Recreational drug use

SPECIAL REPORT

Timing of referral to evaluate for epilepsy surgery: Expert Consensus Recommendations from the Surgical Therapies Commission of the International League Against Epilepsy

Lara Jehi¹  | Nathalie Jette²  | Churl-Su Kwon³  | Colin B. Josephson⁴ |
Jorge G. Burneo⁵  | Fernando Cendes⁶  | Michael R. Sperling⁷  |
Sallie Baxendale⁸  | Robyn M. Busch¹  | Chahnez Charfi Triki⁹ |
J. Helen Cross¹⁰  | Dana Ekstein¹¹  | Dario J. Englot¹²  | Guoming Luan^{13,14,15} |
Andre Palmiini¹⁶  | Loreto Rios¹⁷ | Xiongfei Wang^{13,14,15} | Karl Roessler¹⁸ |
Bertil Rydenhag¹⁹ | Georgia Ramantani²⁰  | Stephan Schuele²¹ |
Jo M. Wilmshurst^{22,23}  | Sarah Wilson²⁴  | Samuel Wiebe⁴ 

WHEN TO CONSIDER EPILEPSY SURGERY

- All patients with drug resistant epilepsy (DRE)
 - Focal epilepsy → resective surgery
 - Multi-focal or generalized epilepsy → palliative surgery and neuromodulation
- Patient who are seizure free with 1 – 2 medications but has lesion on non-eloquent cortex.
- Epilepsy surgery can be offered to patients in all age group if no contraindication for surgery (Even infant or elderly)

TABLE 2 Factors supporting early surgery and consequences of delay.

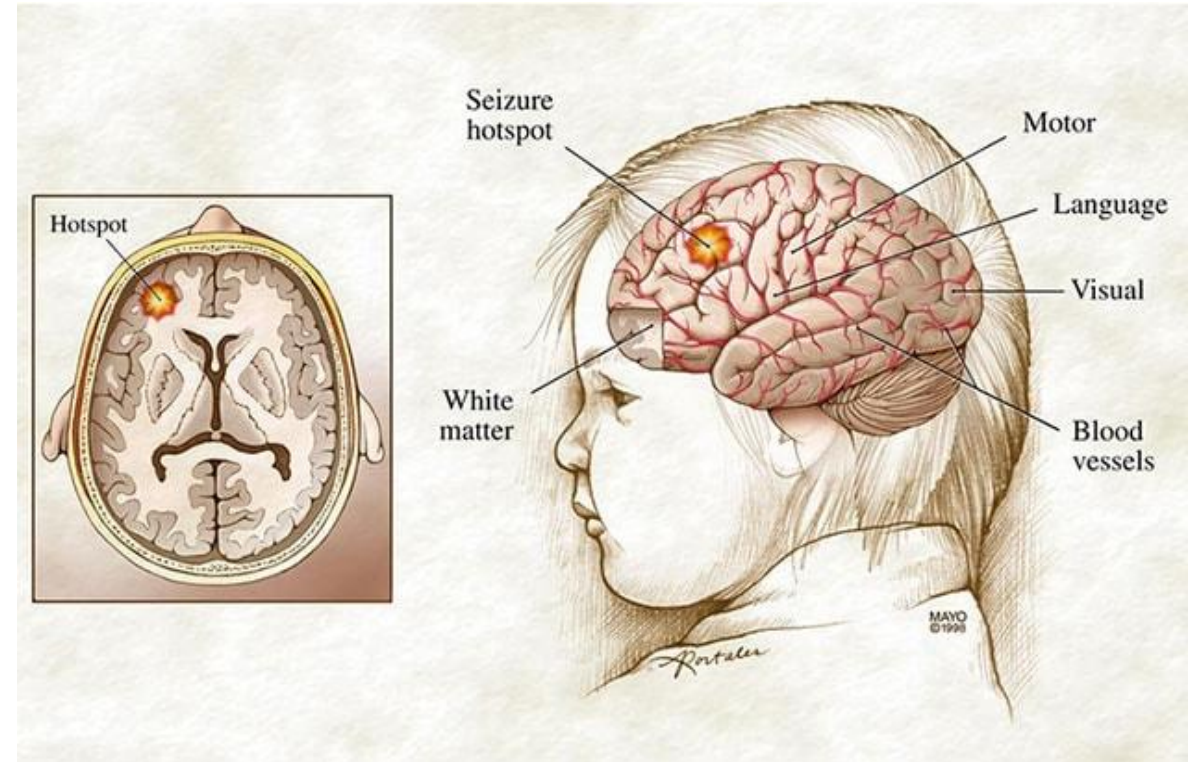
Factors supporting early surgery	Consequences of delay
Higher incidence of epilepsy in infants and toddlers	Decreased chances of surgical success due to ongoing epileptogenic processes
Epilepsy surgery proven safe and effective from a young age	Perpetuated cognitive decline related to seizures, epileptiform EEG discharges, and ASM, especially in developing brains
Higher rates of sustained seizure and ASM freedom in non-drug-resistant patients	Missed opportunity for superior reorganization and deficit compensation related to plasticity in early life
Improved quality of life (QoL) and developmental gains with early seizure freedom	Lifelong impact on cognition, behavior, socialization, education, and vocation
Early surgery viewed as disease-modifying with excellent outcomes in seizure and ASM freedom	Increased long-term epilepsy-related morbidity and mortality

SURGICAL REMEDIABLE EPILEPSY SYNDROMES

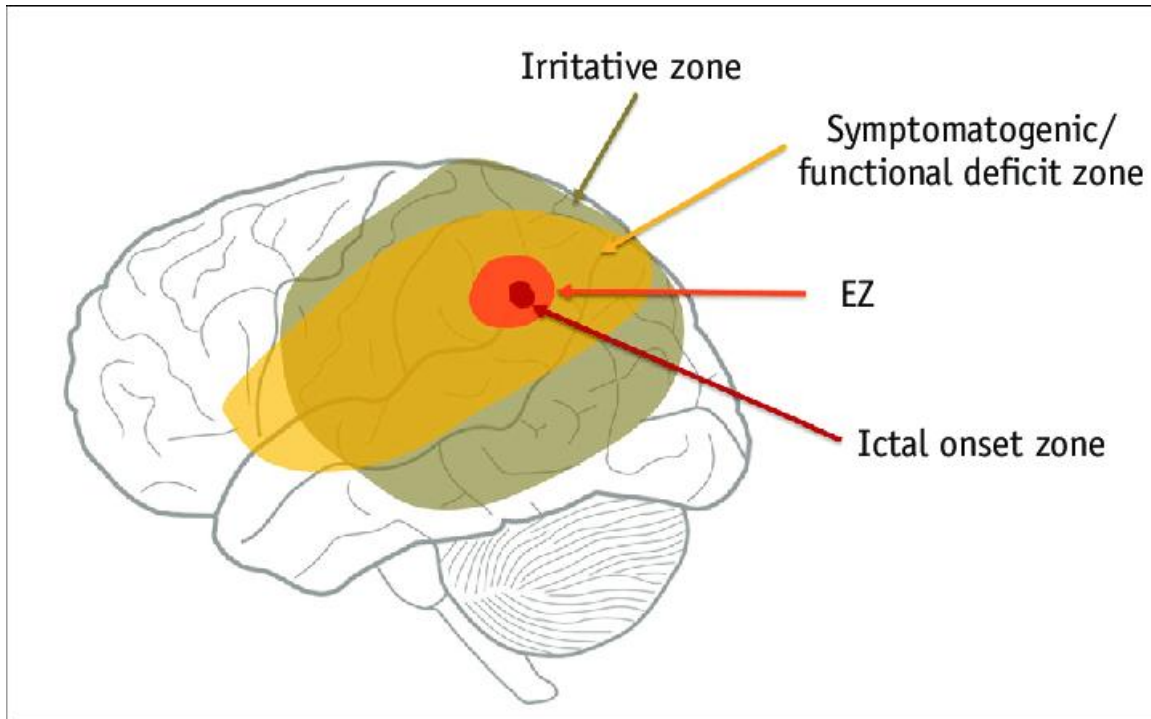
Can be selected by non-invasive	Required functional mapping or invasive evaluation
<ul style="list-style-type: none"> • Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS) 	<ul style="list-style-type: none"> • Malformation of cortical development
<ul style="list-style-type: none"> • Lesional epilepsy in non-eloquent cortex: <ul style="list-style-type: none"> • LEAT: DNET, Ganglioglioma • Vascular malformation: Cavernoma • Gliotic scar 	<ul style="list-style-type: none"> • Focal epilepsy with <ul style="list-style-type: none"> • MRI negative • Discordant electroclinical data • Adjacent to eloquent cortex • Multifocal pathology
<ul style="list-style-type: none"> • Hemispheric epilepsy <ul style="list-style-type: none"> • Hemimegalencephaly • Hemiconvulsion-Hemiplegia syndrome • Sturge-Weber syndrome • Rasmussen encephalitis 	

CONCEPTS OF PRE-SURGICAL EVALUATION IN EPILEPSY

- Identification of epileptic cortex → to resect → seizure free
- Preservation of functional cortex (Eloquent cortex) → to spare



CONCEPT OF EPILEPTOGENIC ZONE “EZ”



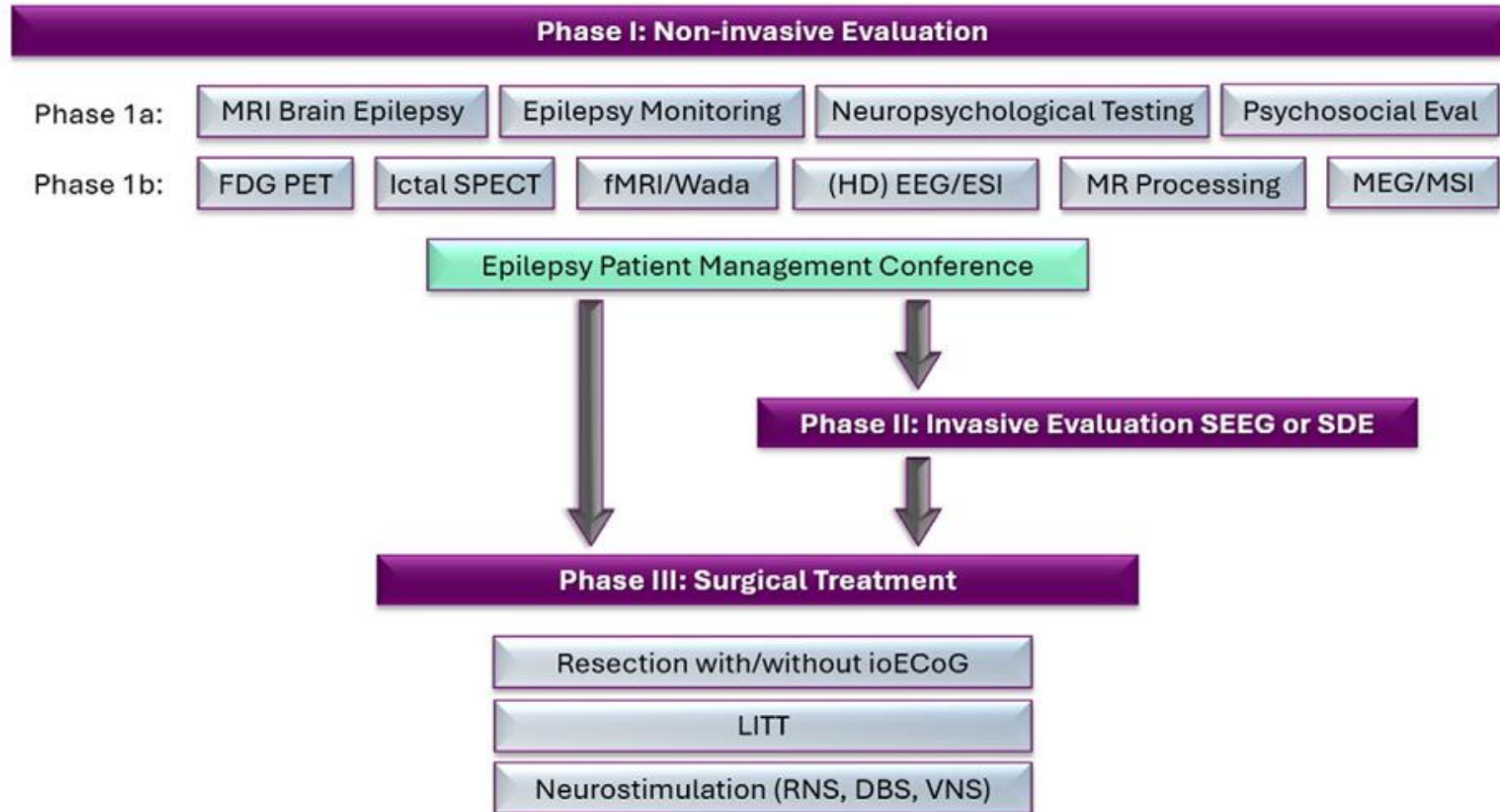
Epileptogenic zone (EZ)

- Zone whose resection is necessary and sufficient to render patient seizure free
- Is an imaginary zone but can be estimated using several data

Localization of EZ is done by

- History taking and Physical exam
- Clinical seizure (Semiology)
- EEG: Inter-ictal and Ictal (EEG onset)
- MRI: Epileptogenic lesion
- Neuropsychology test
- Etc.

PROCESS OF PRESURGICAL EVALUATION



PHASE IA: NON-INVASIVE PRESURGICAL EVALUATION

Detailed history taking & Physical examination

Admission to Epilepsy Monitoring Unit (EMU)
for Long term EEG monitoring (LVEEG)

MRI epilepsy protocol

Neuro-psychology test

DETAILED HISTORY TAKING AND PHYSICAL EXAM

Purpose of detailed history taking

- Established true drug resistant
- Obtain information regarding semiology
- Postulate possible etiology of epilepsy

Epilepsy

- Epilepsy onset
- Detailed description of semiology, Seizure type
- Frequency, chrono-rhythmicity, trigger
- Epilepsy risk factor
- ASM: current, previous, allergy, compliance
- Associated neurological deficit



EPILEPSY MONITORING UNIT (EMU)



LVEEG monitoring is conducted in EMU

- Designated bed for continuous monitoring of video and EEG
- Trained personnel to examine and assist patient during seizure

Presurgical evaluation

- ASMs are tapered to induce patient habitual seizure.
- Reviewed of EEG data include:
 - Interictal and background activity
 - Ictal EEG onset and clinical correlated
 - Detailed analysis of patient semiology

MRI EPILEPSY PROTOCOL

Gold standard for identifying epileptogenic lesion






MRI should be reviewed in the context of an electroclinical hypothesis to improve the yield of correctly identifying the often subtle abnormalities associated with DRE

An imaging protocol for people with epilepsy should provide both optimal volumes for visual assessment and ideal input data for postprocessing.

TABLE 3 MRI routine protocol optimized for individuals with epilepsy.

Sequence	Cut-plane orientation	Cut-plane angulation
3D T1	Three-dimensional	ac-pc
3D FLAIR	Three-dimensional	ac-pc
T2	Coronal	ac-pc ^a /lha ^b
FLAIR	Coronal	ac-pc ^a /lha ^b
T2	Axial	ac-pc ^a /lha ^b
FLAIR	Axial	ac-pc ^a /lha ^b
Hemo/Calc	Axial	ac-pc

Recommendations for the use of structural magnetic resonance imaging in the care of patients with epilepsy: A consensus report from the International League Against Epilepsy Neuroimaging Task Force

**Andrea Bernasconi¹  | Fernando Cendes²  | William H. Theodore³  |
Ravnoor S. Gill¹ | Matthias J. Koepp⁴ | Robert Edward Hogan⁵ | Graeme D. Jackson⁶ |
Paolo Federico⁷ | Angelo Labate⁸  | Anna Elisabetta Vaudano⁹ | Ingmar Blümcke¹⁰ |
Philippe Ryvlin¹¹  | Neda Bernasconi¹**

EPILEPSY PROTOCOL – 3D MRI

T1-weighted

Sequence type: gradient echo

Voxel size (mm): 1 x 1 x 1

Best to evaluate: anatomy and morphology
(volume, thickness, sulco-gyral shape, grey-white matter interface integrity)

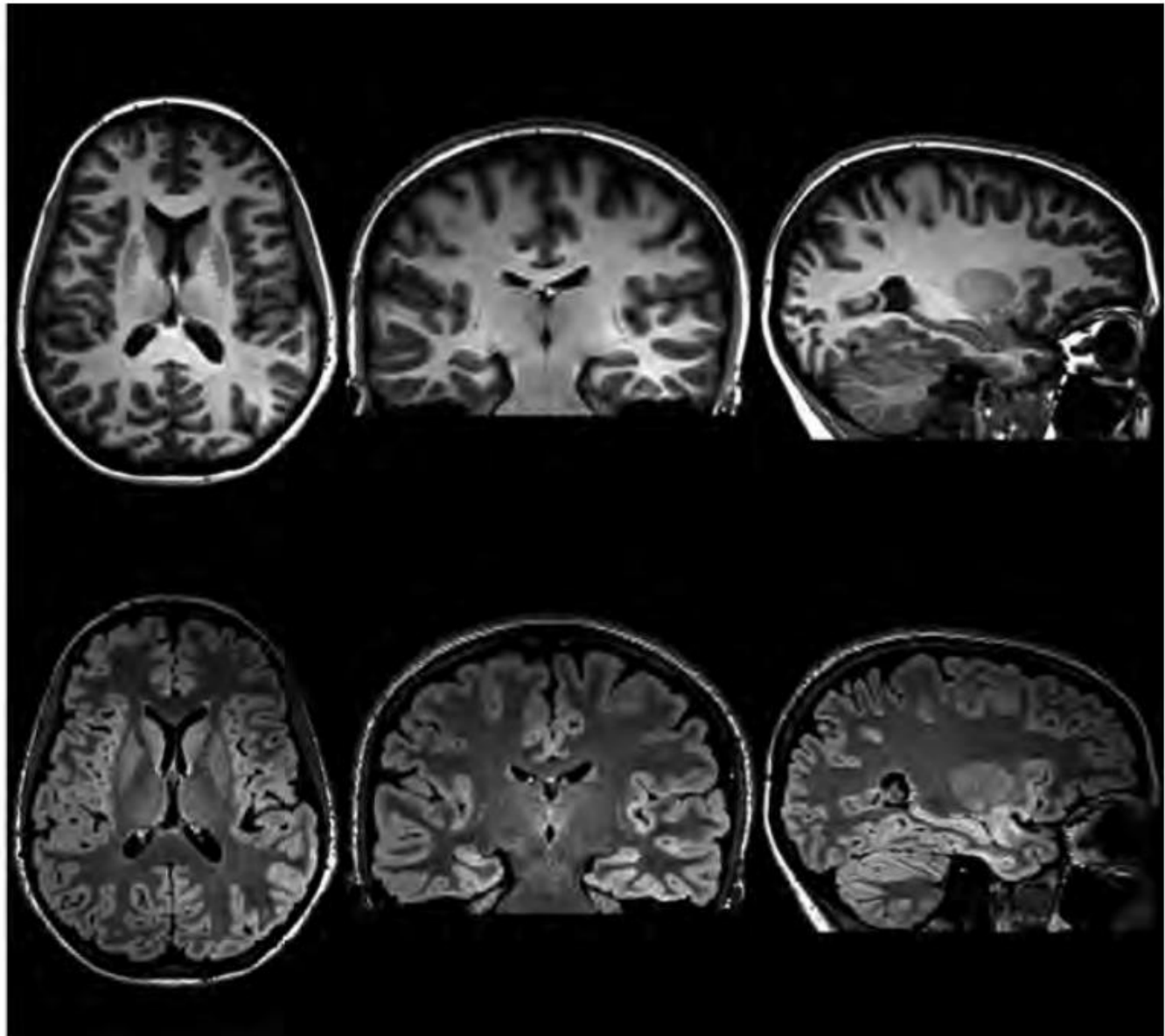
FLAIR

Sequence type: turbo spin echo

Voxel size (mm): 1 x 1 x 1

Best to evaluate: signal intensity

Caveat - Not sensitive in neonates and children <24 months of age due to incomplete myelination



EPILEPSY PROTOCOL – 2D MRI

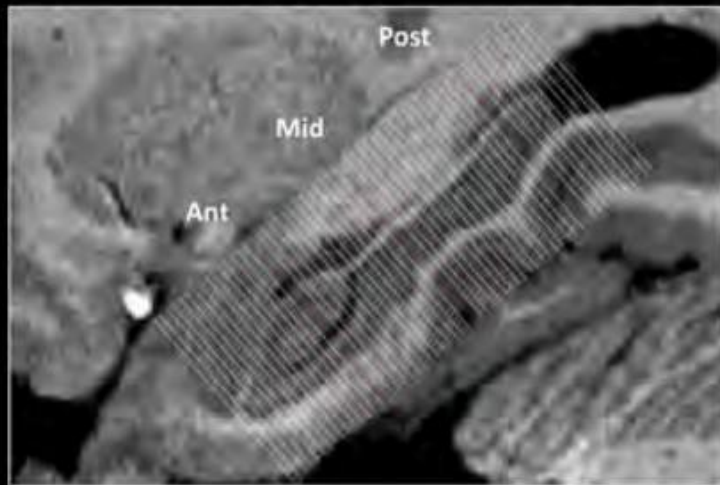
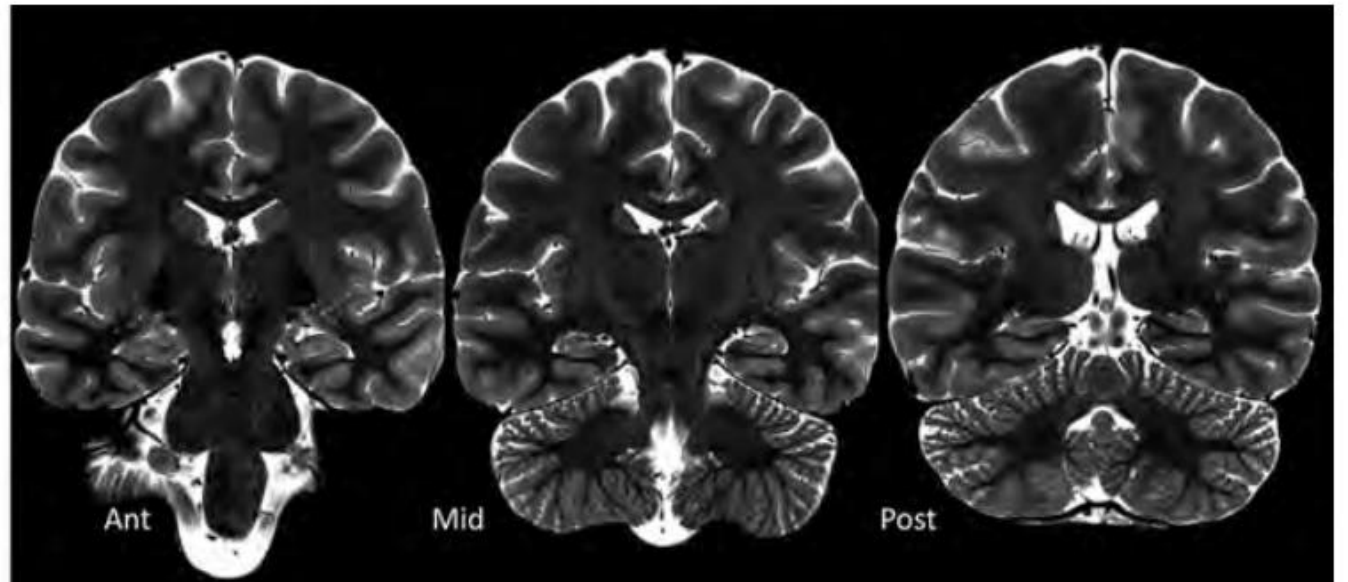
Coronal T2-weighted

Acquired perpendicular to hippocampal long axis

Sequence type: turbo spin echo

Voxel size (mm): 0.4 x 0.4 x 2; no inter-slice gap

Best to evaluate: Hippocampal internal structure (distinction of CA subfields, dentate gyrus), amygdala, and parahippocampal cortices



NEUROPSYCHOLOGICAL EVALUATION

Assessment of pre-operative cognitive deficit and psychosocial status of patient

Providing localization and lateralization, when take into account other data: (Electroclinical, imaging)

Prediction of post-operative cognitive decline

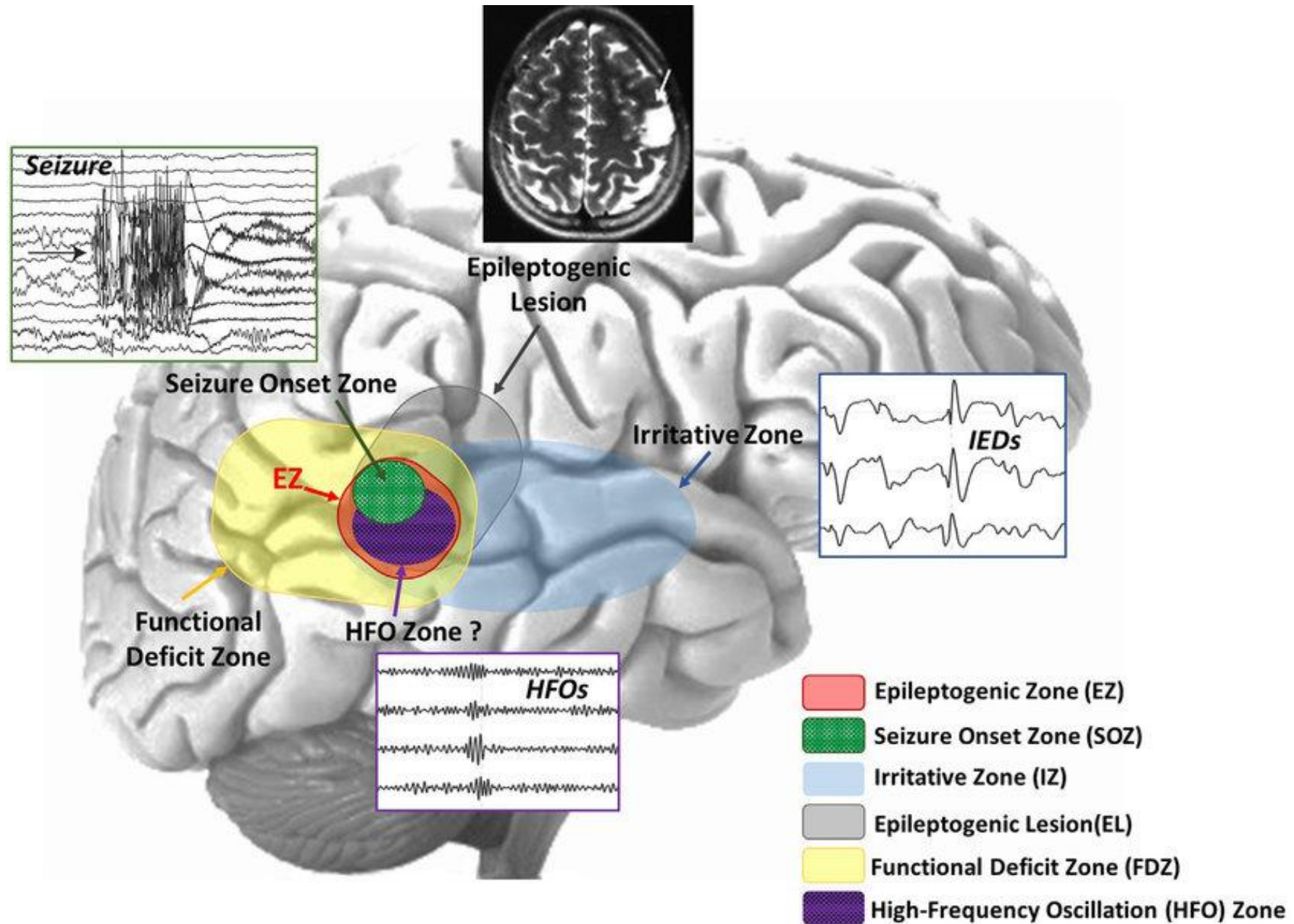
Identify and treat comorbid psychiatric disorder: depression, anxiety etc.

TABLE 4 Domains commonly assessed in a neuropsychological evaluation with test examples.

Domain	Abilities assessed	Test examples*
Intellectual ability	Estimate of premorbid function Verbal intellectual abilities Nonverbal intellectual abilities	Advanced Clinical Solutions Test of Premorbid Function, American National Adult Reading Test, Wide Range Achievement Test—Reading subtest Wechsler Verbal Comprehension Index or verbal subtests Wechsler Perceptual Reasoning Index or nonverbal subtests
Attention	Simple attention Complex attention/working memory Sustained attention	Wechsler Digit Span subtest Wechsler Letter-Number Sequencing subtest, Wechsler Arithmetic subtest Continuous Performance Test
Processing speed	Speeded mental/visuomotor skills	Wechsler Coding subtest, Wechsler Symbol Search subtest Trail Making Test – Part A
Language	Naming Verbal fluency	Boston Naming Test, Visual Naming Test Phonemic verbal fluency (e.g., Controlled Oral Word Association Test), Semantic verbal fluency (e.g., Animal Fluency)
Executive functioning	Problem-solving Planning Cognitive flexibility Response inhibition	Wisconsin Card-Sorting Test DKEFS Tower Test, Tower of London Trail Making Test—Part B DKEFS Color-Word Interference, Stroop
Visuospatial skills	Visuoperception Visuoconstruction	Judgment of Line Orientation Wechsler Block Design
Episodic memory	Verbal learning/recall/ recognition Visual learning/recognition	Rey Auditory Verbal Learning Test, California Verbal Learning Test, Wechsler Logical Memory Wechsler Visual Reproduction, Brief Visual Memory Test
Motor functioning	Motor speed Manual dexterity	Finger Tapping Grooved Pegboard
Performance validity	Stand-alone and embedded measures of test-taking effort	Various tests (e.g., Victoria Symptom Validity Scale, Word Memory Test, Advanced Clinical Solutions Word Choice, Reliable Digit Span)
Subjective cognition	Self- or caregiver report measures of subjective cognitive abilities (e.g., memory, language)	Memory Assessment Clinics Scale – Epilepsy, Everyday Memory Questionnaire, Everyday Verbal Memory Questionnaire
Social cognition	Theory of mind Social behavior Emotion recognition Empathy Sensitivity to moral and conventional rules	Various tests (e.g., Faux-Pas Test, Strange Stories Test, Reading the Mind in the Eyes Task, Facial Emotion Recognition, Empathy Questionnaire Social Situation Test, Moral/Conventional Distinction Test)
Emotional/Behavioral function	Self- or caregiver-report screening measures of mood, anxiety, behavior	Various tests (e.g., Beck Depression Inventory, Neurological Disorders Depression Inventory in Epilepsy, Patient Health Questionnaire Depression, Child Depression Inventory, Beck Anxiety Inventory, Patient Health Questionnaire Generalized Anxiety Disorder, Child Behavior Checklist)
Psychosocial status/ Function	Self- or caregiver report of adaptive functioning	Vineland Adaptive Behavior Scales
Quality of life	Self- or caregiver report measures of health-related quality of life	Quality of Life in Epilepsy, Quality of Life in Childhood Epilepsy

THE CORTICAL ZONES IN EPILEPSY

Cortical zone	Definition	Diagnostic tool	Notes
Epileptogenic zone	The zone which resection resulted in seizure free	-	Hypothetic zone estimate by using other zones
Symptomatic zone	The zone that generate semiology	History taking Video EEG	Non-eloquent cortex does not generate semiology. Non-primary cortex generates complex semiology, which hard to localize
Irritative zone	The zone that generate interictal discharge	Scalp EEG ESI, MEG	Deep source Area often wider than EZ
Ictal onset zone	The onset zone of EEG seizure	Scalp EEG ESI, ictal SPECT	Deep source Unclear onset in scalp
Functional deficit zone	The area that shows impairment in interictal period	NP test PET scan	-
Epileptogenic lesion	The lesion responsible for generating seizure	MRI brain VBM	Multifocal lesion Lesion negative MRI
Eloquent cortex	The zone which resection resulted in neurological deficit	NP test fMRI, WADA test	-

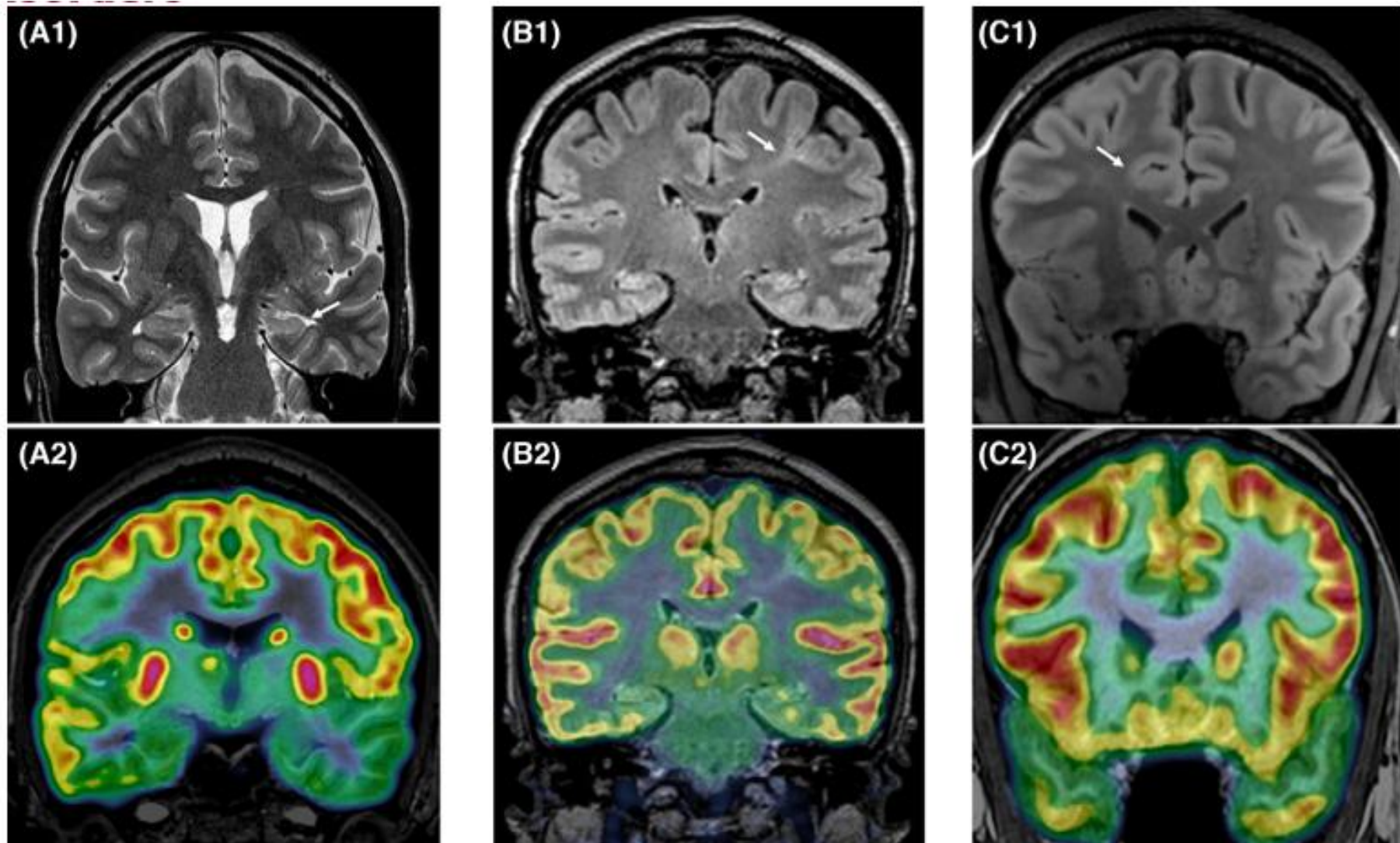


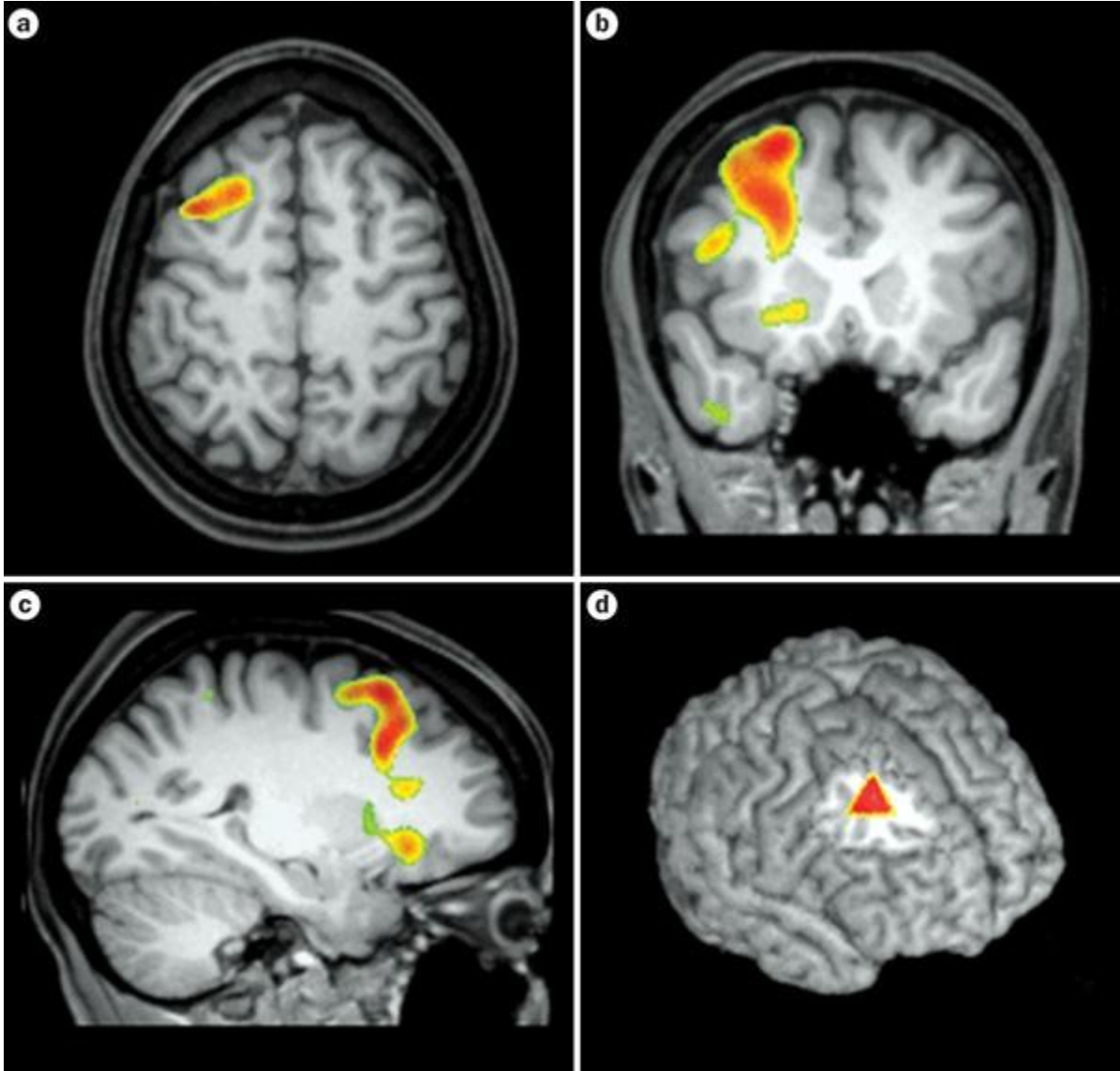
PHASE IB: (ADDITIONAL) NON-INVASIVE PRESURGICAL EVALUATION

Additional test done to complement the result of phase 1a and to generate hypothesis for phase 2

Test	Principle	Advantage	Disadvantage
FDG-PET	EZ demonstrated hypometabolism in PET during interictal period	<ul style="list-style-type: none"> • Provide the data of “Functional deficit zone” • Can be co-registered with MRI to search for epileptogenic lesion 	<ul style="list-style-type: none"> • Area of hypometabolism tend to be wider than primary EZ
Ictal SPECT	Hyper-perfusion in the area of ictal onset	<ul style="list-style-type: none"> • Provide the data of “Ictal onset zone” • Can be subtracted (Ictal – interictal) and reregistered with MRI (SISCOM) 	<ul style="list-style-type: none"> • The result depend on timing of injection, duration of seizure and generalization
MRI post-processing	Using voxel based morphometry to compare patient T1 MRI to large normative database and highlight abnormal in gray-white junction and abnormal cortical thickness	<ul style="list-style-type: none"> • Complement visual analysis of MRI • Can aid in detecting subtle MRI abnormality • Cheap and can be rapidly done can be integrated into routine practice 	<ul style="list-style-type: none"> • False positive result

FDG-PET CO-REGISTERED WITH MRI

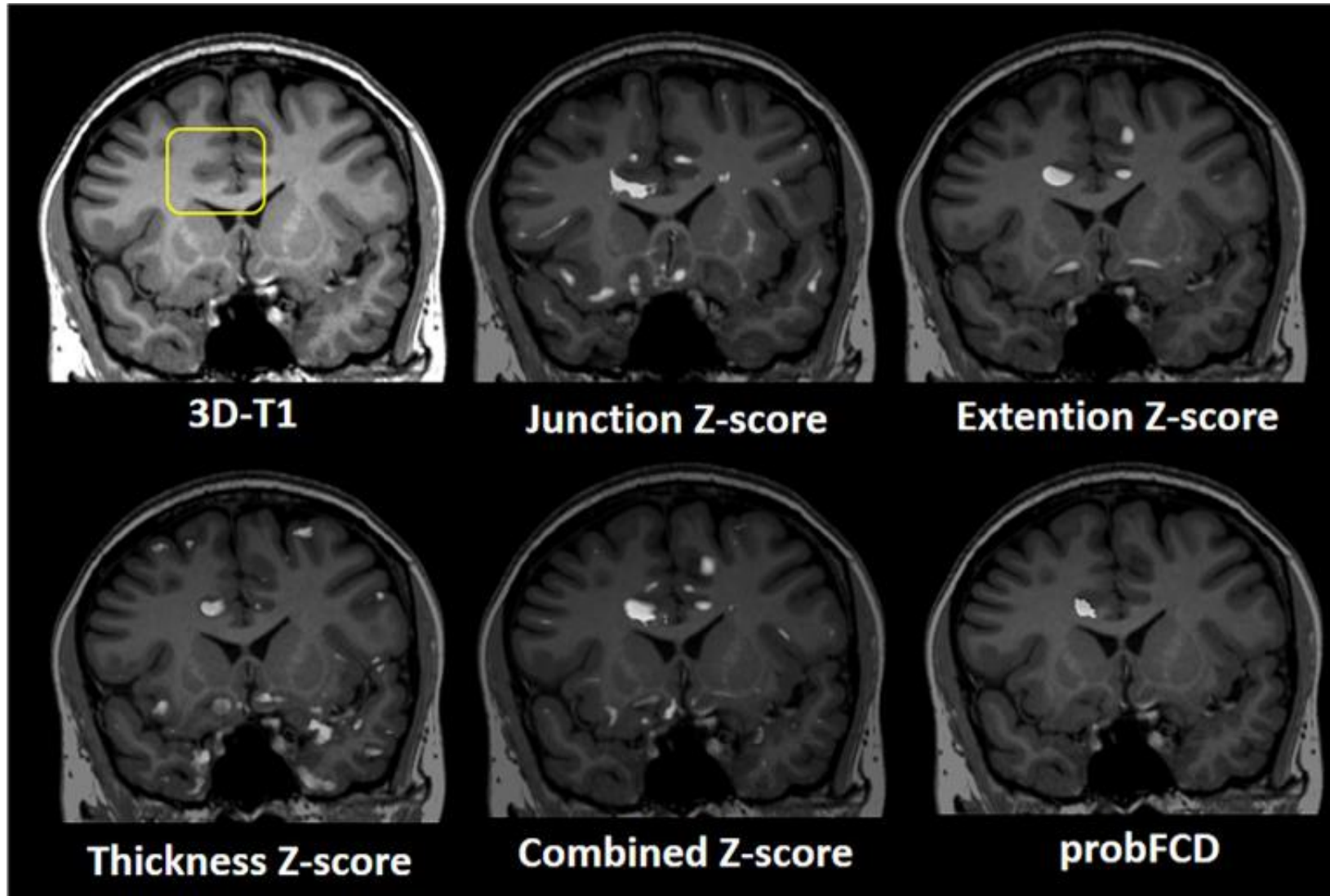




SISCOM

(‘subtraction ictal SPECT
coregistered to MRI’)

MRI POST-PROCESSING USING MAP18

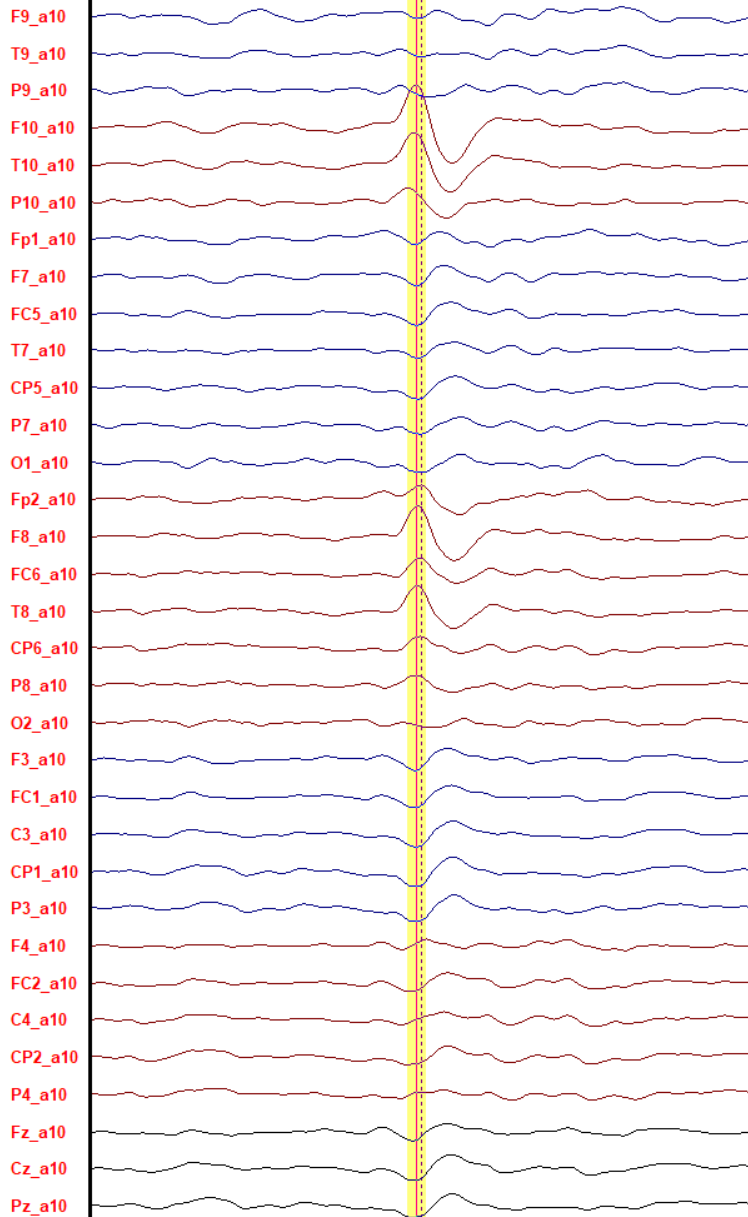


PHASE IB: (ADDITIONAL) NON-INVASIVE PRESURGICAL EVALUATION

Additional test done to complement the result of phase 1a and to generate hypothesis for phase 2

Test	Principle	Advantage	Disadvantage
Electrical source imaging	Mapping of electrical activity (interictal and ictal) to MRI brain	<ul style="list-style-type: none"> • Provide the data of “irritative zone” and “ictal onset zone” • Cheap and can be rapidly done can be integrated into routine practice 	
Functional MRI	Task-based: Detect BOLD signal upon neural activation of each stimulation paradigms	<ul style="list-style-type: none"> • Identification of eloquent cortex: Broca, Wernicke, hemispheric dominance, Motor cortex • Non –invasive test 	<ul style="list-style-type: none"> • Require cooperation of patient
WADA test	Performed by injecting anesthetic substances into the internal carotid artery in the interictal phase to temporarily inactivate the functions of one hemisphere.	<ul style="list-style-type: none"> • Determine the hemispheric lateralization of language function and the risk of postoperative memory impairment. 	<ul style="list-style-type: none"> • Invasive procedure required angiogram • Limitation in assessment of memory (hippocampus is supplied by posterior circulation)

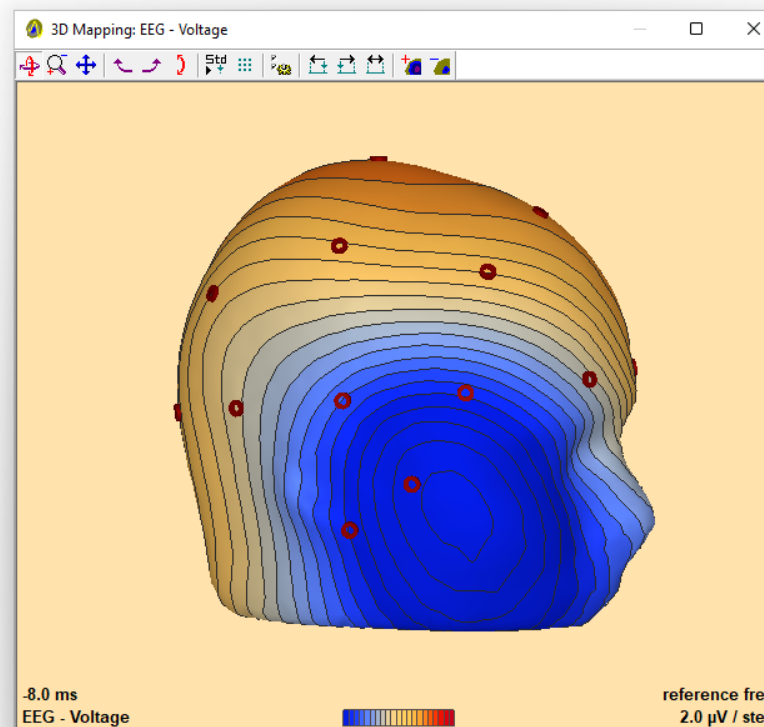
virtual Av33



Sp1: 10 avs

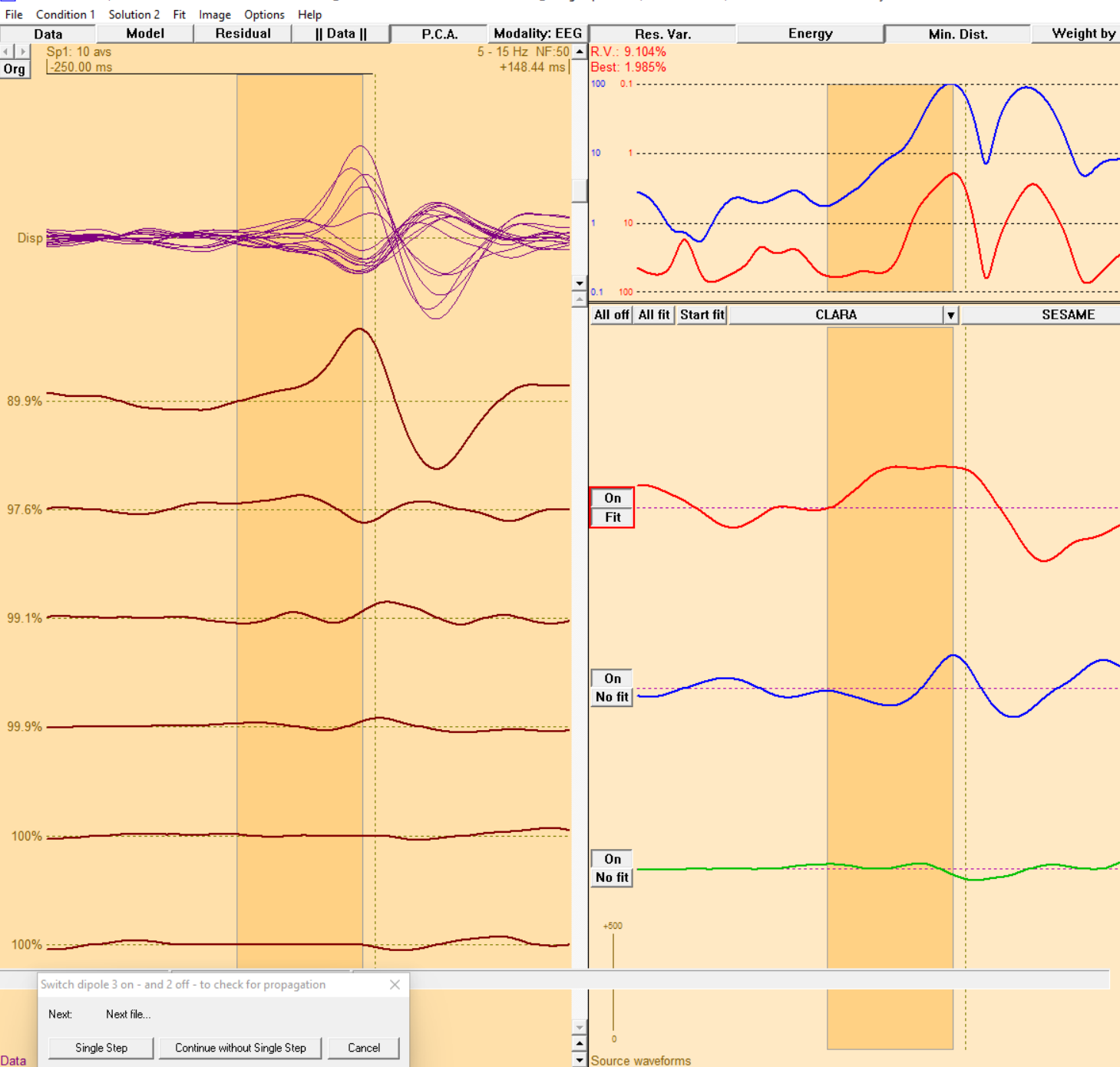
Add

Source localization: Interictal FT10

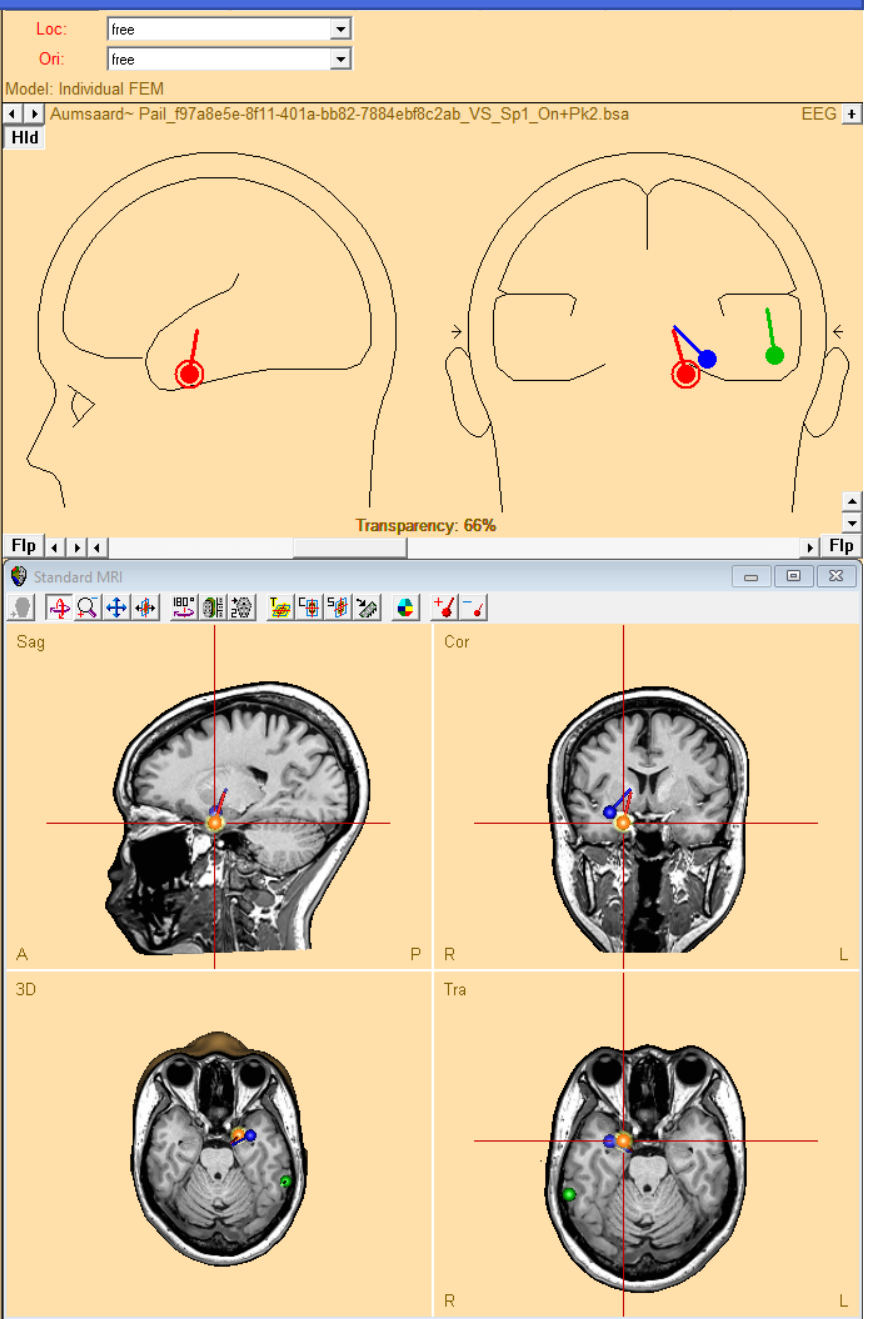
Scp
33/33

I

20
 μV



Source localization: Interictal FT10

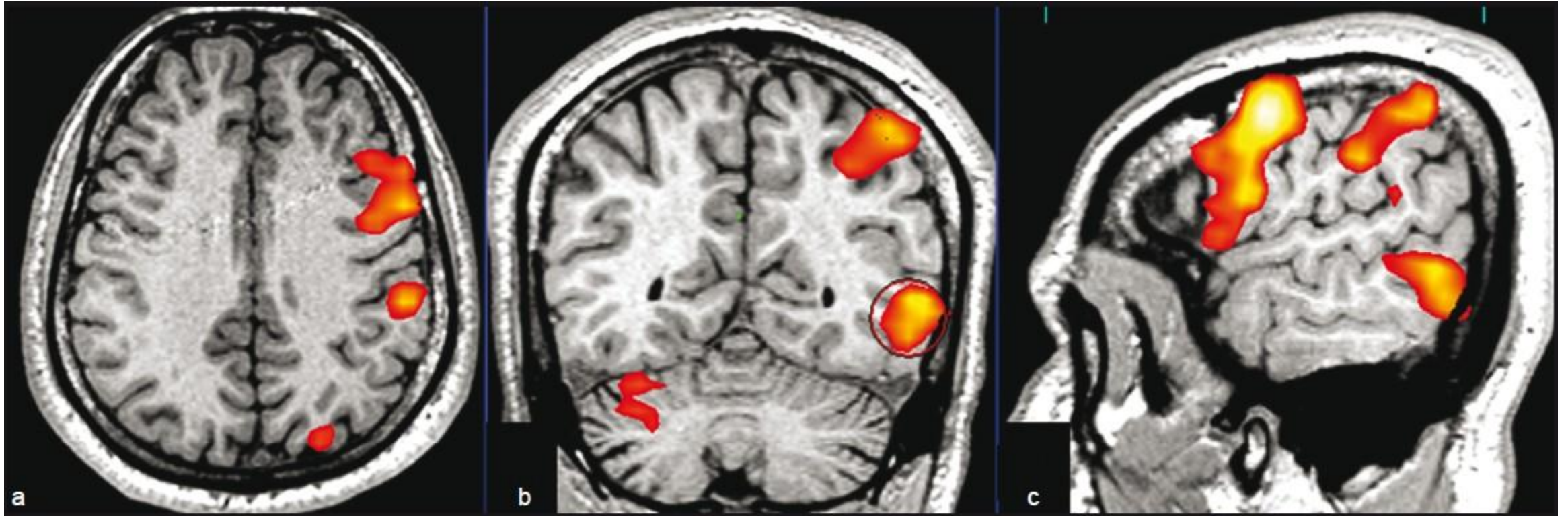


Switch dipole 3 on - and 2 off - to check for propagation

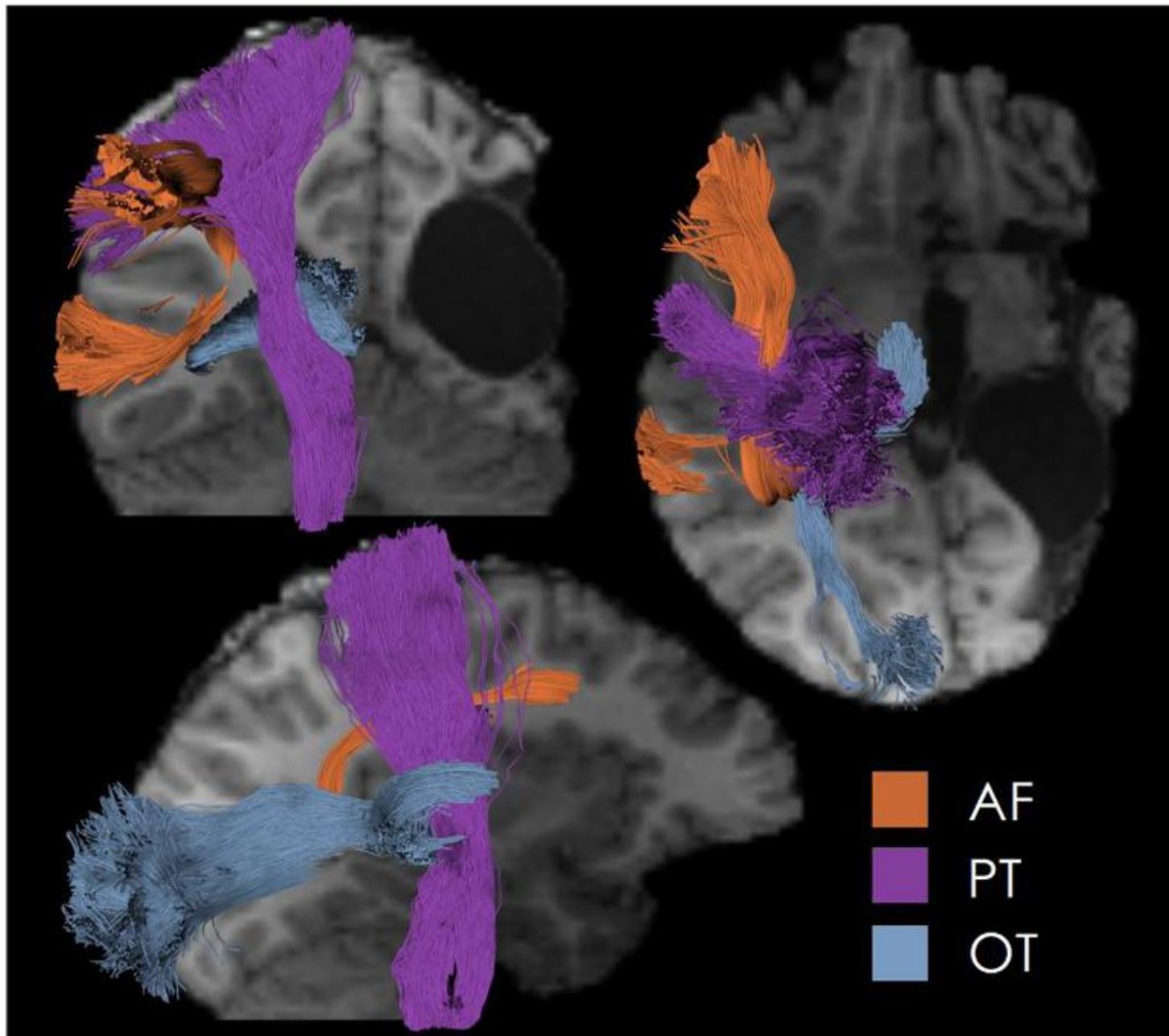
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Single Step Continue without Single Step Cancel

TASK-BASED FMRI



Left language lateralization on verbal fluency task: real-time fMRI processing



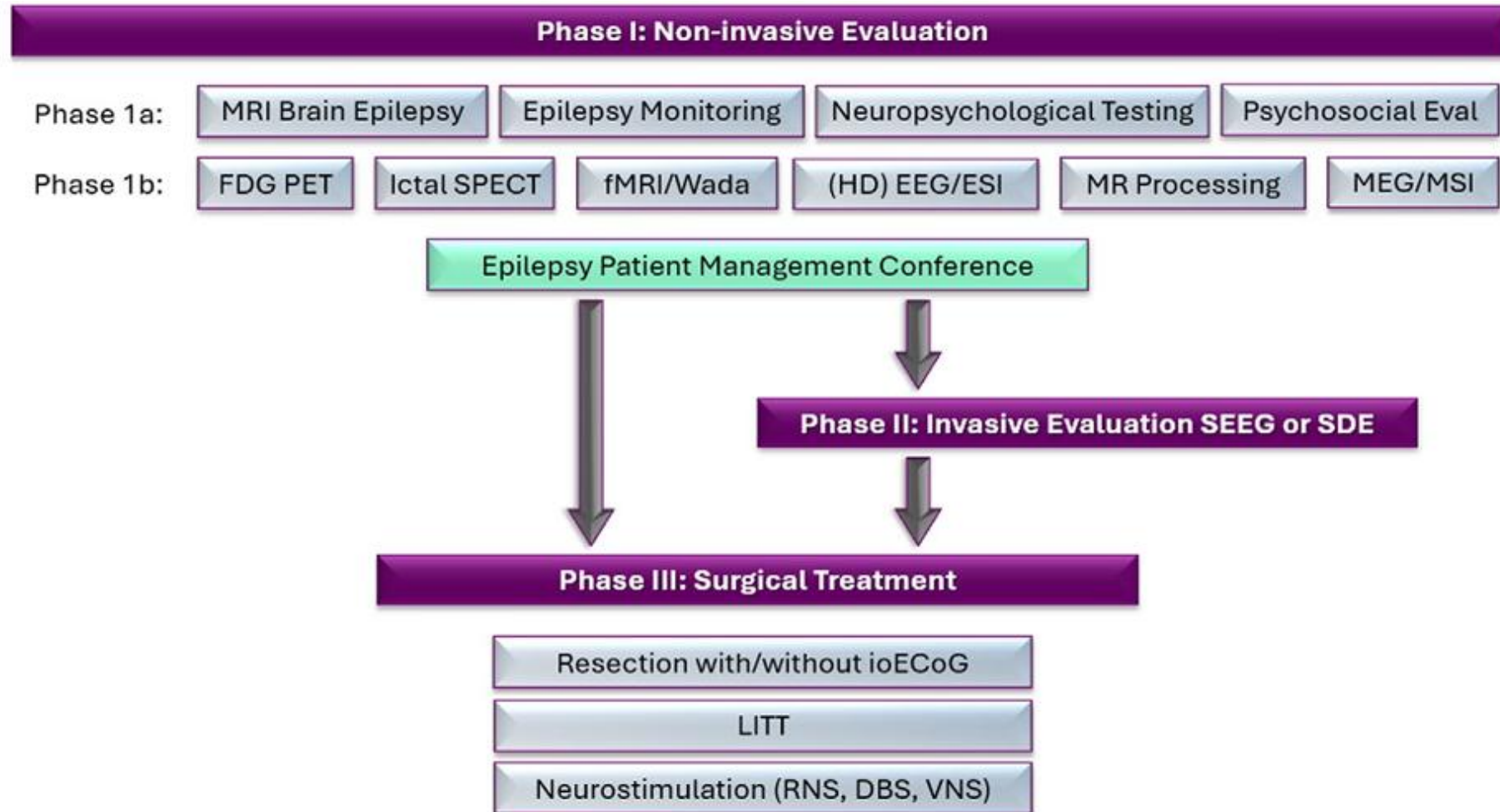
DIFFUSE TENSOR IMAGING (DTI)

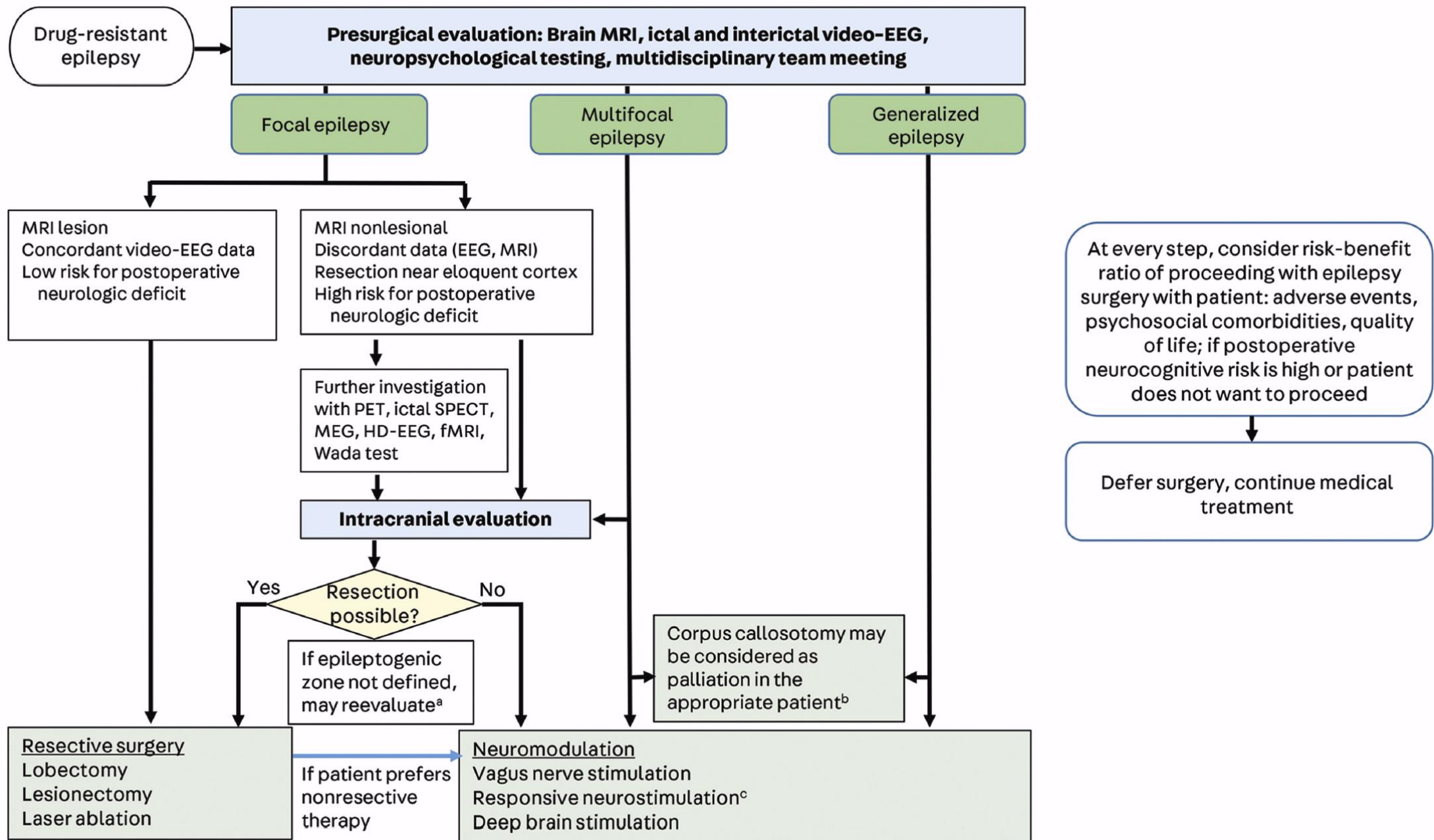
PATIENT MANAGEMENT CONFERENCE (PMC)

- Multi-disciplinary, presurgical conference to provide optimal, consensus based surgical management of individual patient
- The presurgical data of each patient are presented and discussed including: History, Video-EEG, Neuroimaging, Neuropsychological test (NP)
- The goal of the conference is to provide a consensus process determining if the patient is a **suitable surgical candidate**, identifying the **best procedure** given all available information, and estimating the **chance of success and potential risks** of the procedure.



PROCESS OF PRESURGICAL EVALUATION





PHASE II: INVASIVE EVALUATION

Indication for invasive evaluation

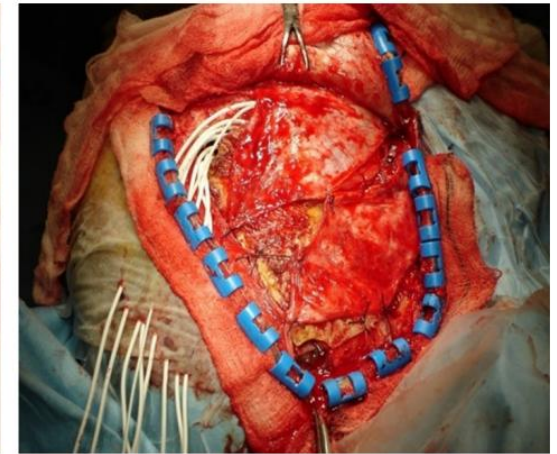
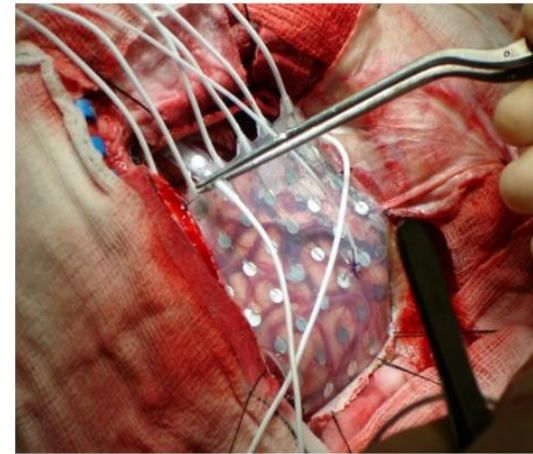
- Phase I data can generate strong hypothesis of single epileptogenic focus but data is insufficient to proceed directly to surgery
 - MRI negative
 - Discordant electroclinical or imaging features
 - Resection close to eloquent cortex
- Invasive EEG is used to confirm hypothesis regarding the epileptogenic zone

Types of invasive evaluation

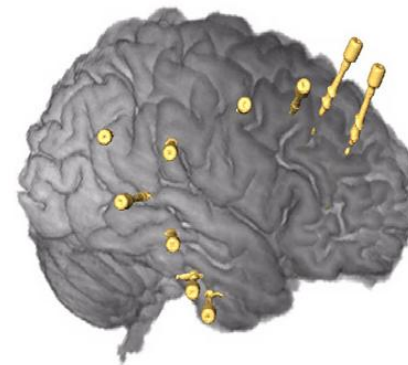
1. Subdural grid (SDG)
2. Stereo-electroencephalography (SEEG)

Process during invasive monitoring

1. EEG: Background activity, inter-ictal activity
2. Anatomic-electro-clinical-correlation (AEC) of patient habitual seizure
3. Electrical stimulation and mapping



Subdural grid (SDG)



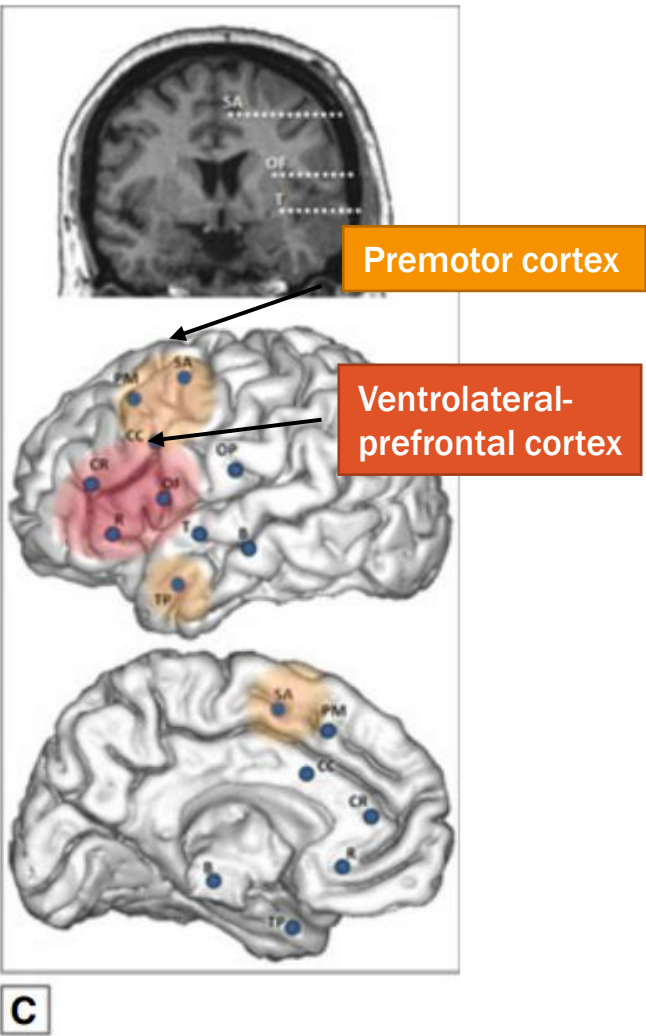
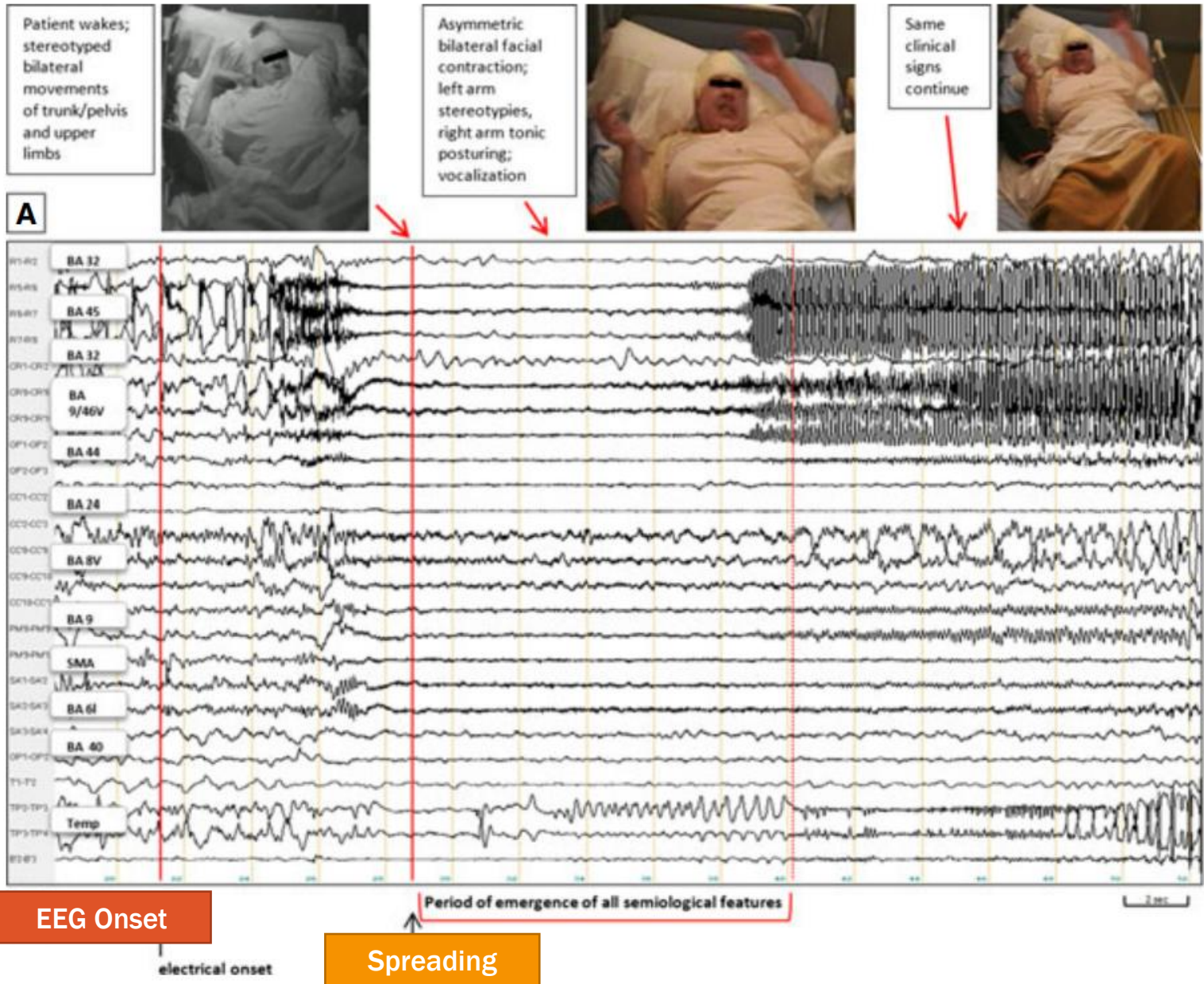
Stereo-electroencephalography (SEEG)

COMPARISON: SDG VS. SEEG

	Advantages	Disadvantages
Stereo-EEG	<p>Maps three-dimensional epileptogenic networks, including easier sampling of spatially distinct and deep regions (eg, periventricular gray matter heterotopia, insular, depth-of-sulcus regions)</p> <p>Easily samples bilateral hemispheres</p> <p>No craniotomy, decreased perioperative pain, and shorter recovery time</p> <p>Lower rate of serious adverse events</p>	<p>Limited spatial sampling of electrical activity from tissue directly around each electrode</p> <p>Does not map spatially continuous coverage of brain surface gyri</p> <p>Less feasible in young children (requires bone thickness > 2 mm)</p>
Subdural grid electrodes	<p>More precise functional mapping when the epileptogenic zone involves cortical regions adjacent to eloquent cortex</p> <p>Craniotomy has been performed, and resection can occur when electrodes come out</p> <p>Depth electrodes may be added to sample deep structures of interest; however, the accuracy may be affected because of shifting of the brain after craniotomy</p>	<p>Higher rates of serious adverse events</p> <p>Sampling of insula is difficult and high risk</p> <p>Sampling bilateral hemispheres is challenging (ie, bilateral craniotomies)</p> <p>Cannot sample gray matter in sulci (eg, depth-of-sulcus lesions)</p>

EXAMPLE OF AEC (ANATOMO-ELECTRICO-CLINICAL CORRELATION)

Ventrolateral-prefrontal cortex



ELECTRICAL STIMULATION AND MAPPING

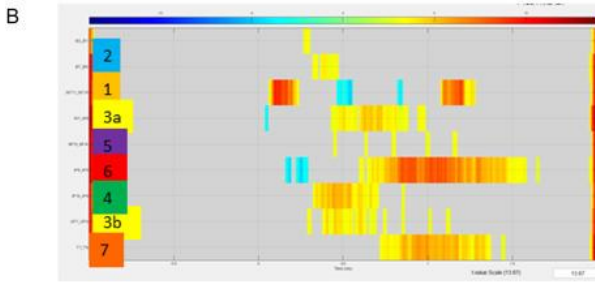
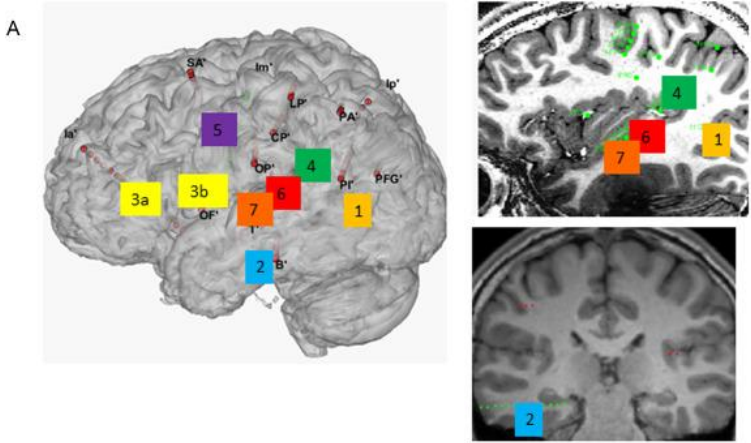
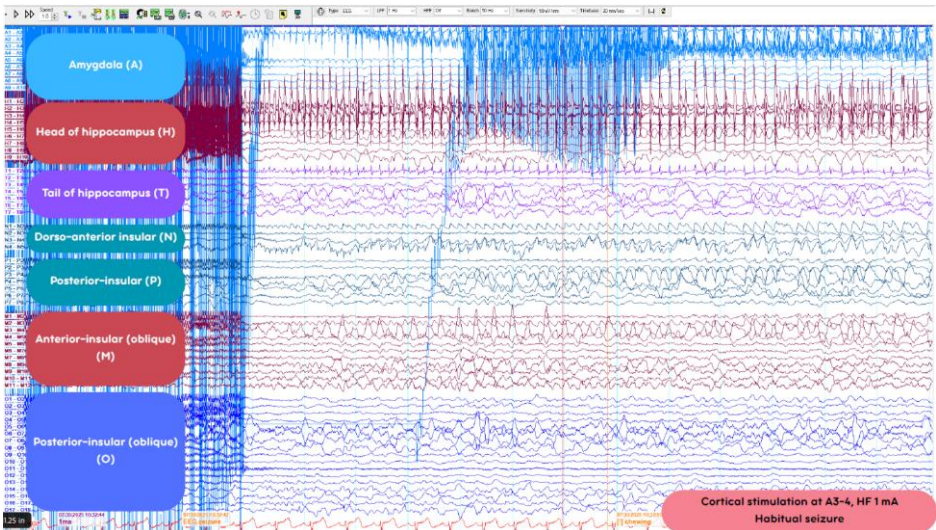
Electrical stimulation delivered via invasive electrodes.

Objective

- Mapping of eloquent cortex: Language, Motor, Visual etc.
- Eliciting seizure
- To assess overlapping of EZ and functional cortex

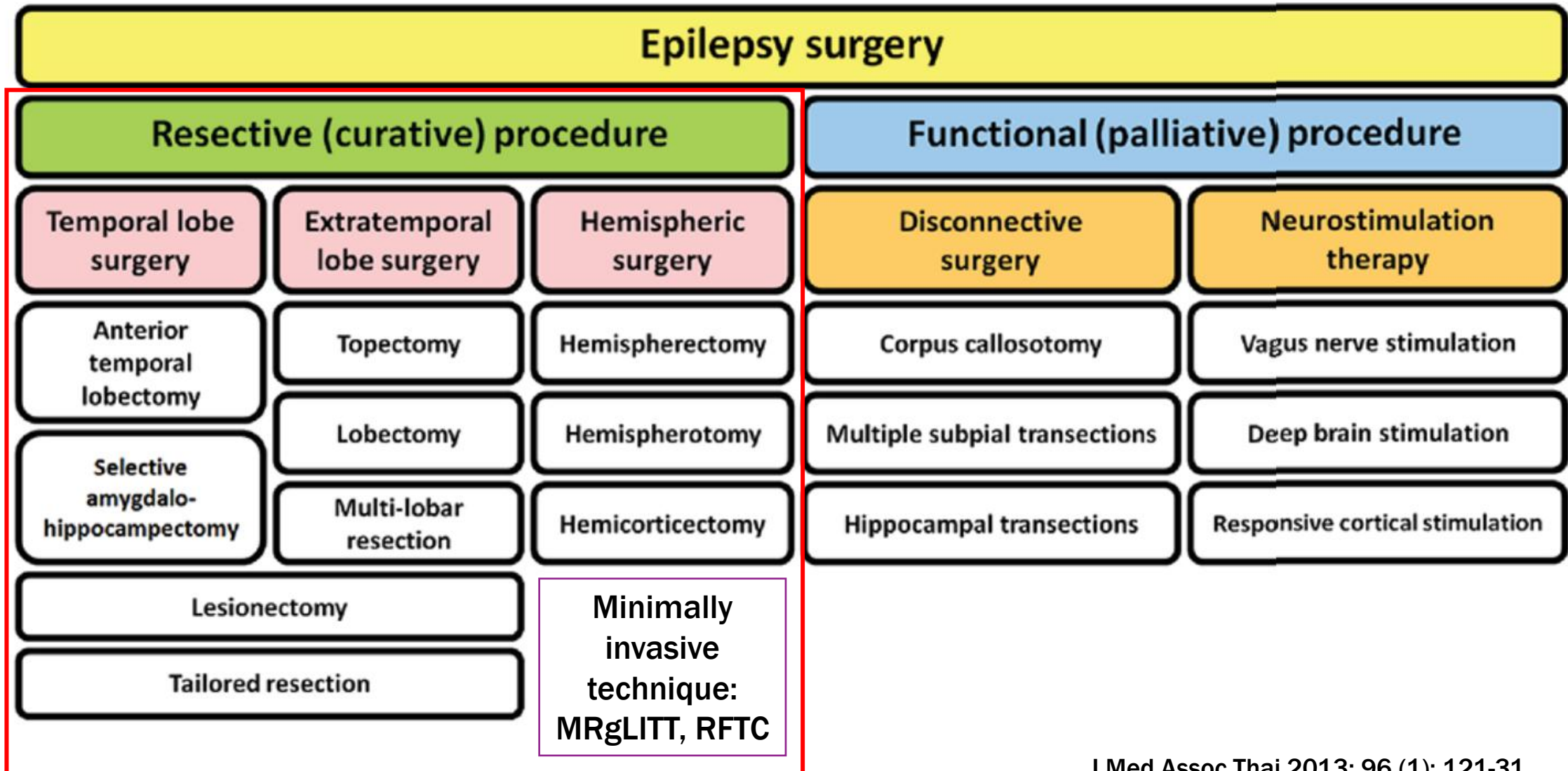
Perform at the end of invasive EEG recording

ASM should be resumed prior to stimulation.



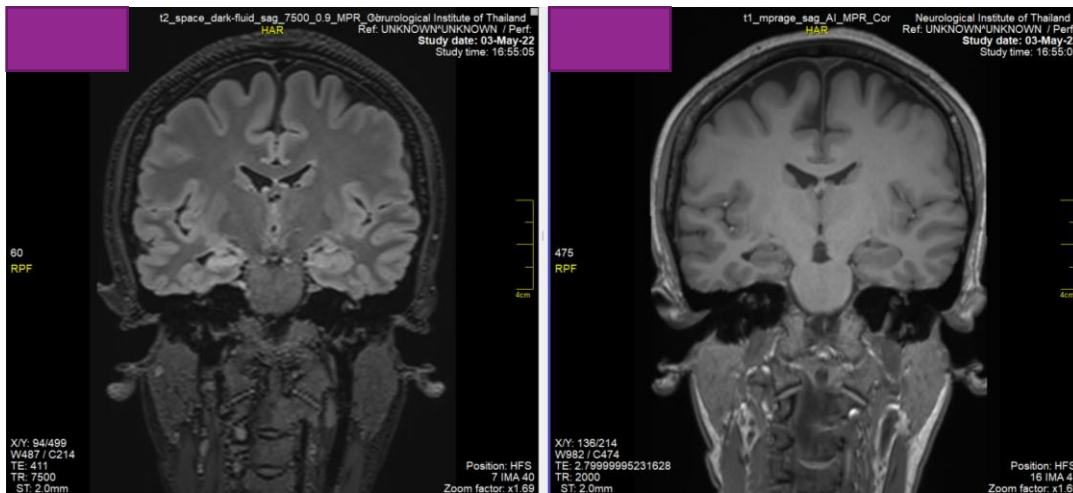
C	Anatomical	N°	s	mA	AD	Task
	Occipital Lateral	1	5	1,5	0	Naming
	aBTA	2	5	1,5	0	Naming
	IFG (PreC)	3b	5	1,5	0	Naming
	IFG (pars Tri)	3a	5	1,5	0	Naming
	sTPJ	4	5	1,5	0	repetition
	sTPJ	4	5	1,2	0	Pataka
	Pre Motor	5	5	1,5	0	speech
	Auditory Cortex (PAC)	6	5	1	0	Words
	Auditory Cortex (AAC)	7	5	1,5	0	repetition

TYPE OF EPILEPSY SURGERY

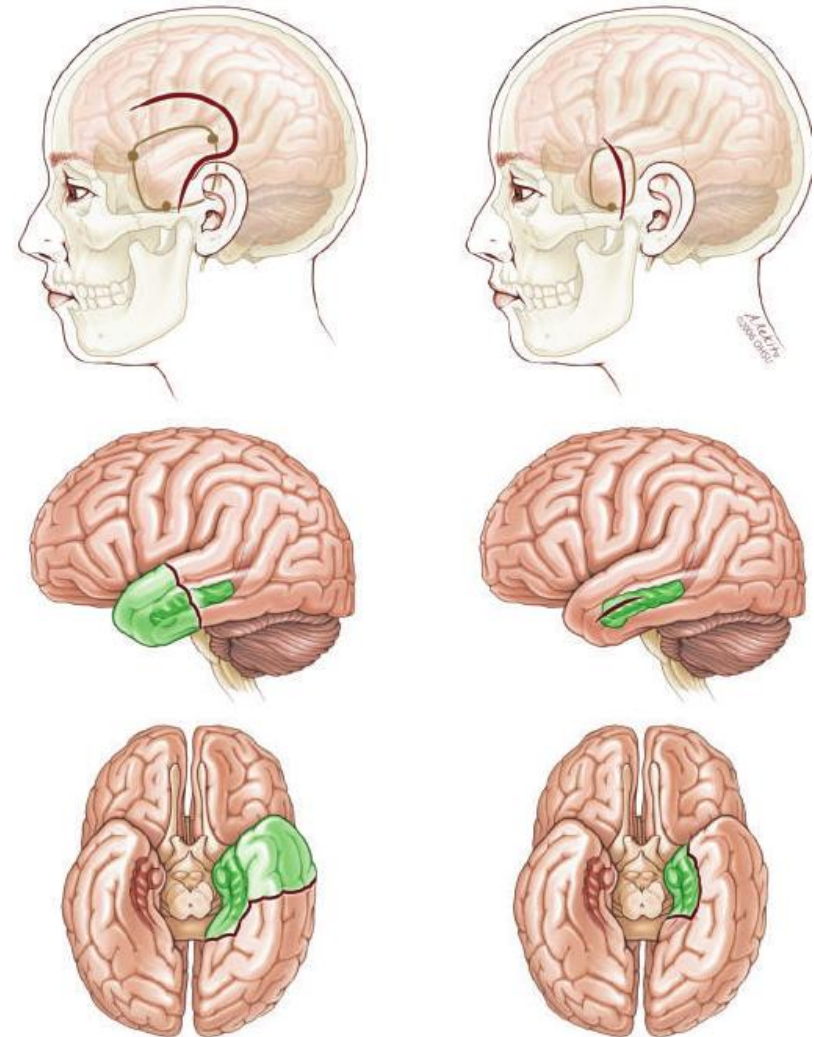


TEMPORAL LOBE SURGERY

- Substrate: Hippocampal sclerosis (HS)
- Choice of surgery
 - Anterior temporal lobectomy (ATL)
 - Selective amygdalo-hippocampectomy (SAH)
 - Minimally invasive technique:
 - MRI-guided Laser interstitial thermal therapy (MRgLITT)
 - Radiofrequency Thermocoagulation (RFTC)

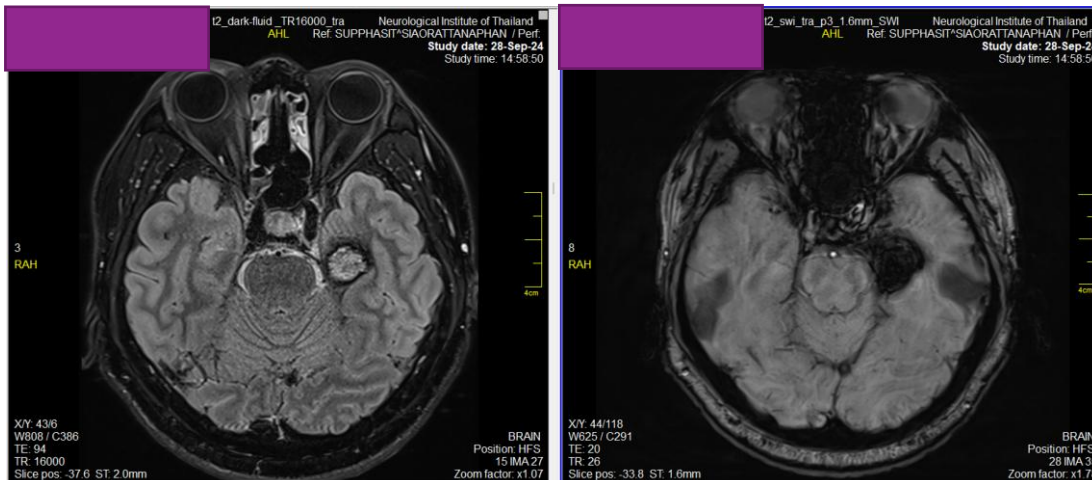


Right mesial temporal sclerosis

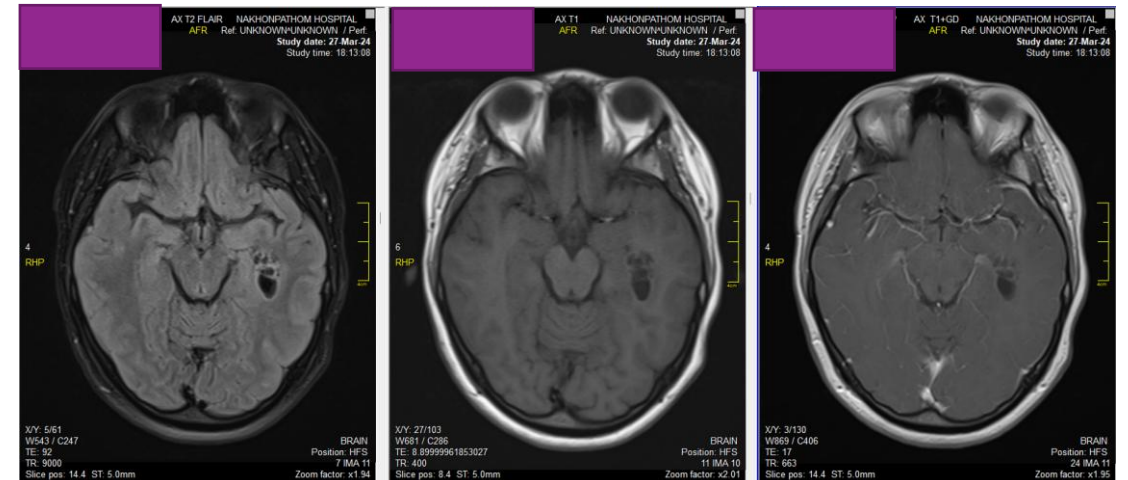


LESIONECTOMY

- Surgical resection of epileptogenic lesion
- May guided by intraoperative electrocorticography
- Substrate
 - LEAT (Long term epilepsy associated tumor: DNET, Ganglioglioma)
 - Vascular malformation (Cavernoma)
 - Gliotic scar
 - Malformation of cortical development



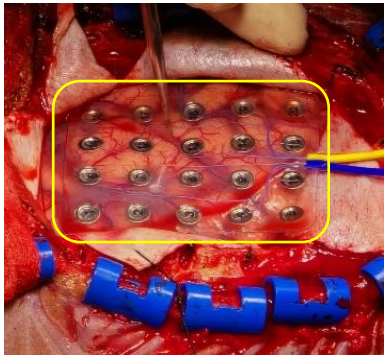
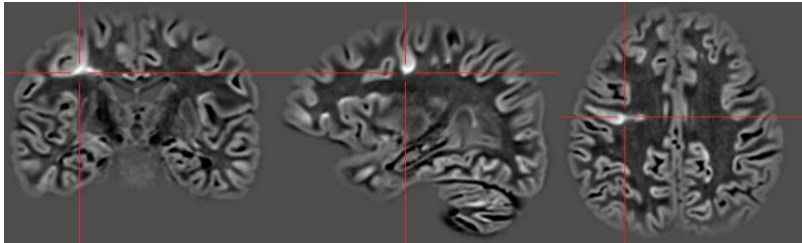
Left mesial temporal cavernoma



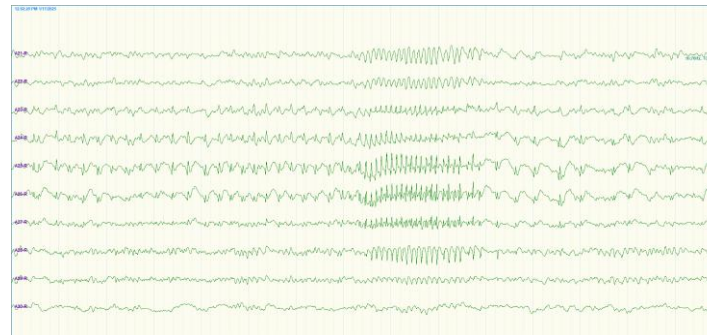
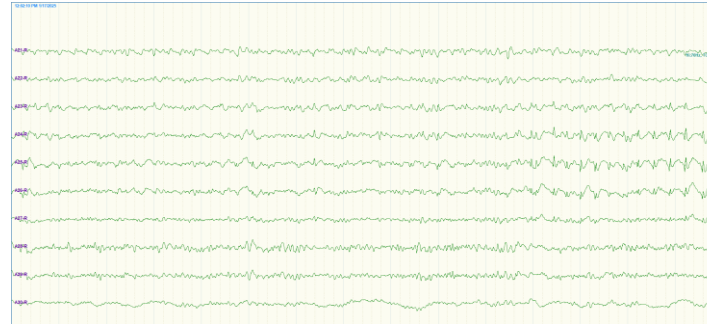
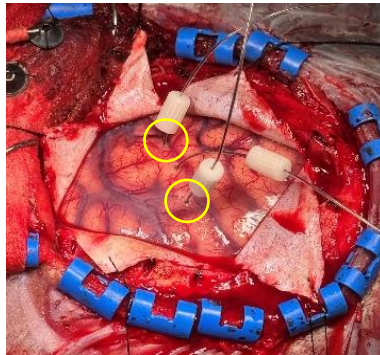
Ganglioglioma at left parahippocampal gyrus

INTRAOPERATIVE ELECTROCORTICOGRAPHY (ECoG)

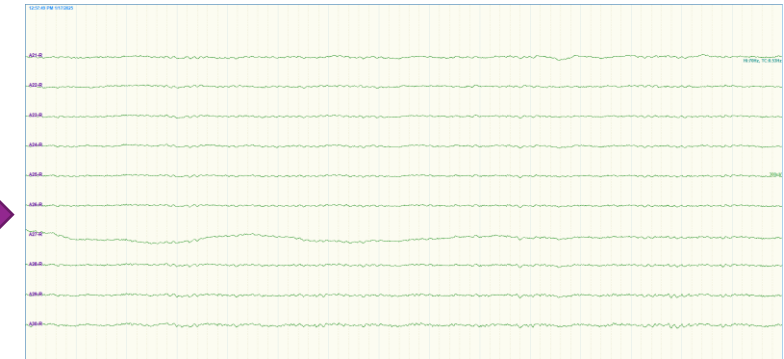
- Placing of electrodes (SDG) during surgery
- Allow instantaneous assessment of irritative zone and guided resection of epileptogenic lesion
- Especially useful in superficial lesion: FCD, cortical based tumor
- Can identify epileptiform discharge post-resection



SDG + Depth electrode



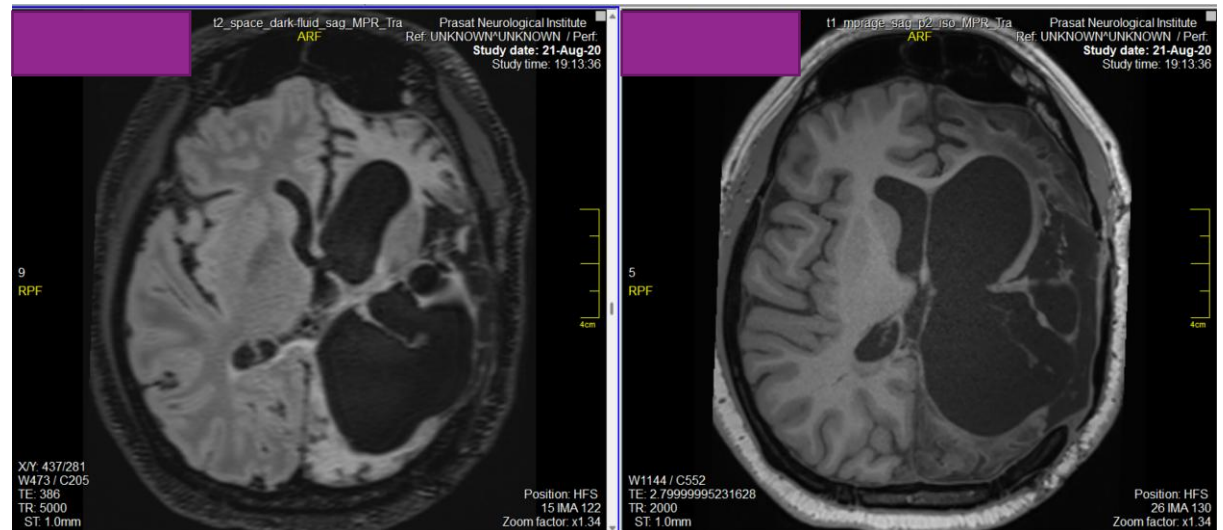
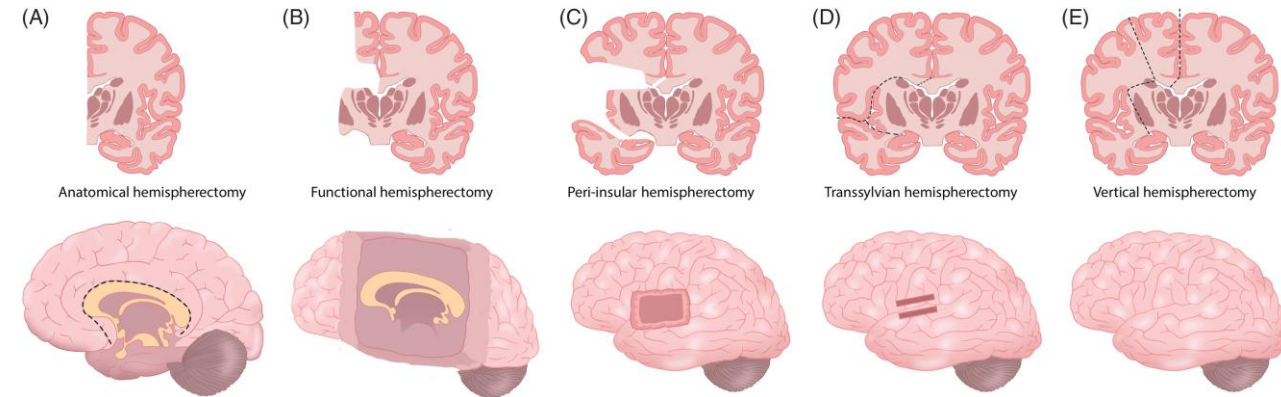
Pre-resection



Post-resection

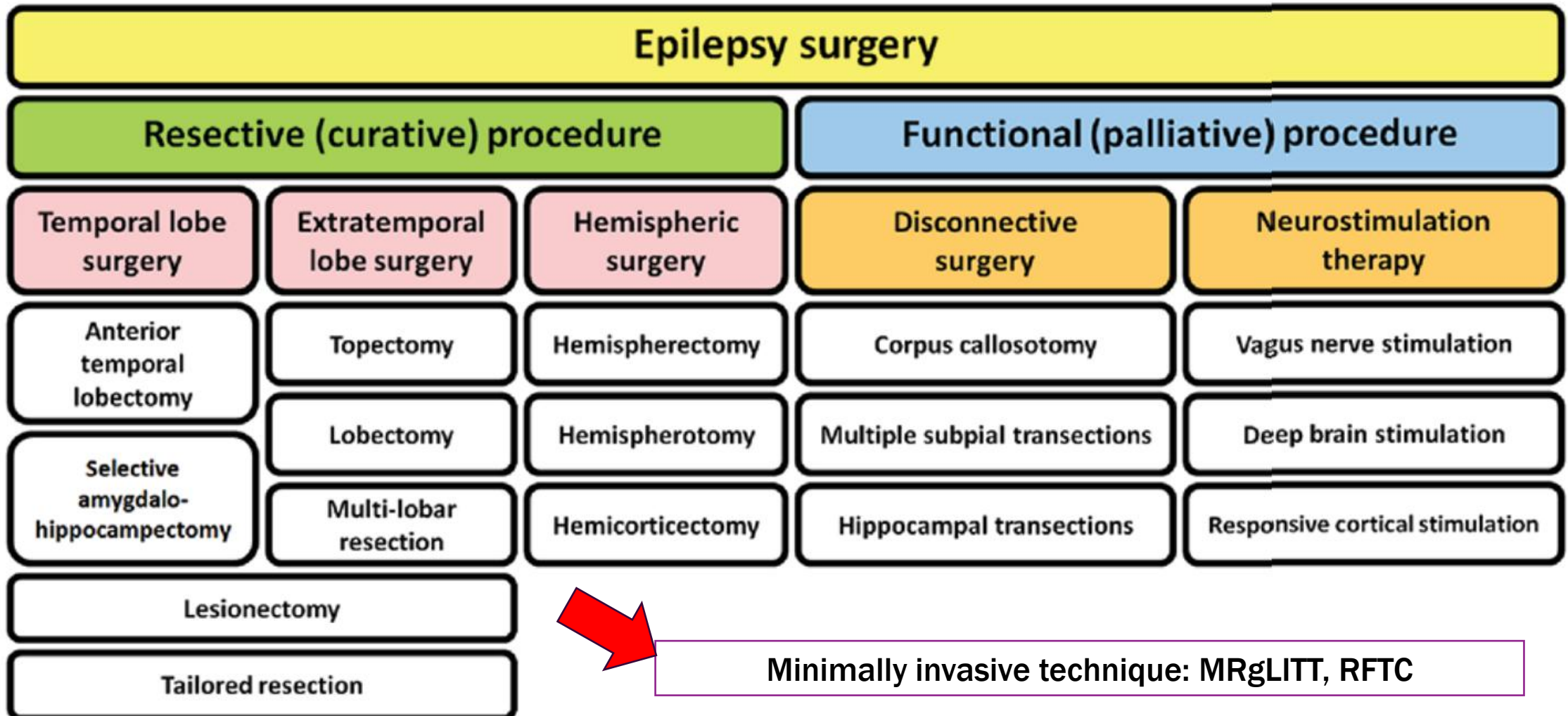
HEMISPHERECTOMY

- Anatomical hemispherectomy:
 - Anatomical removal of one hemisphere
- Functional hemispherectomy
 - Disconnecting the hemisphere from brainstem and contralateral hemisphere
- Candidate for hemispherectomy
 - Large hemispheric lesions:
 - Hemimegaloencephaly
 - Rasmussen encephalitis
 - Sturge weber syndrome
 - Hemi-convulsion-hemiplegia syndrome etc.
 - Pre-existing neurological deficit related to hemispheric dysfunction
 - Minimal to no risk for new acceptable deficit



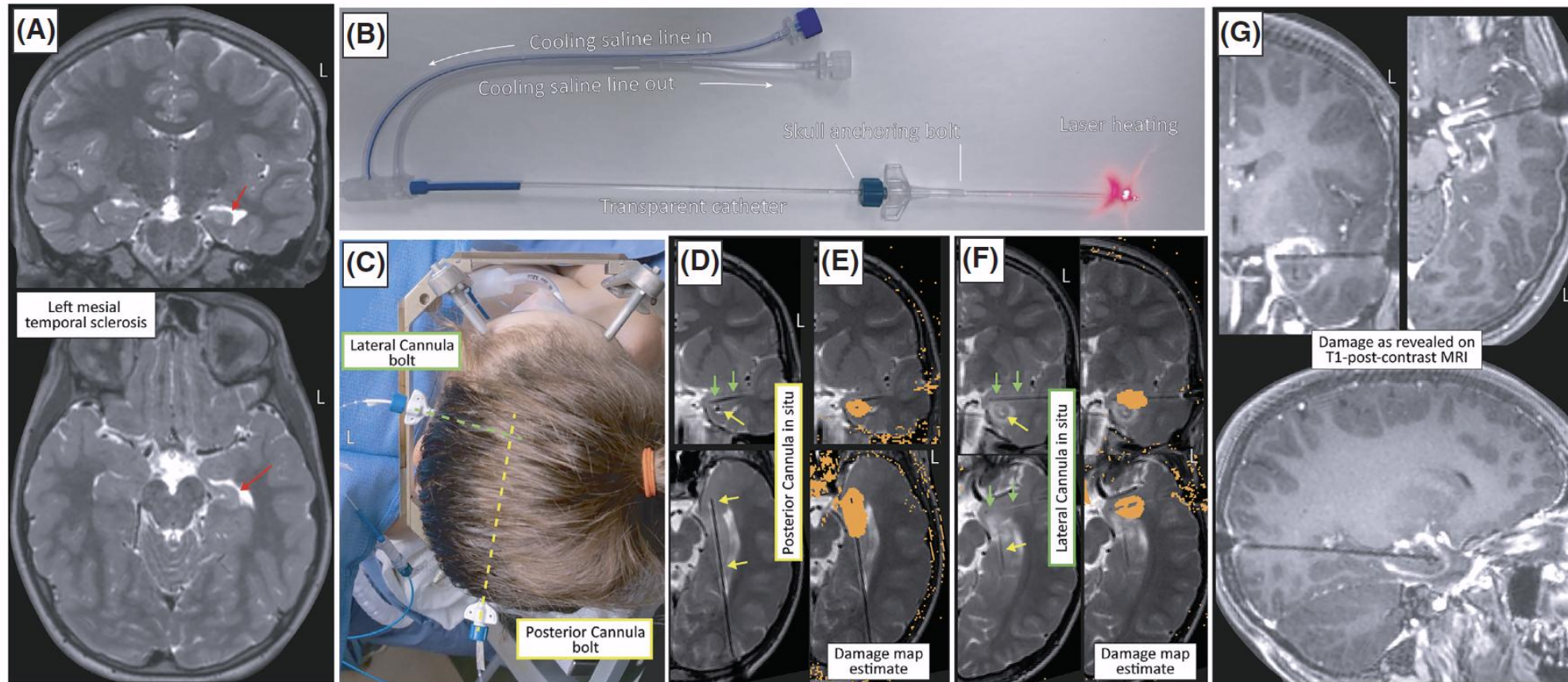
Cystic encephalomalacia of entire left hemisphere

TYPE OF EPILEPSY SURGERY



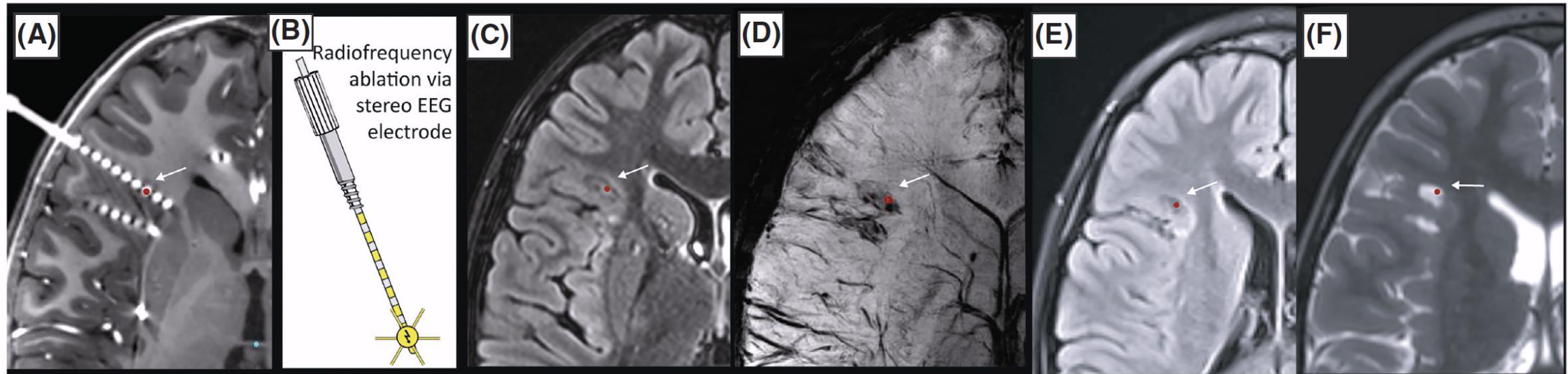
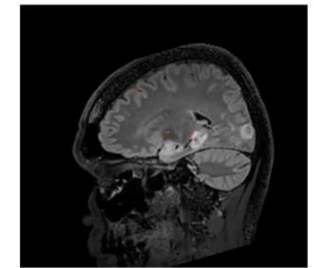
MGLITT

- Using Laser catheter inserted by stereotactic to burn brain tissue of interest
- Real-time damage estimation using continuous MRI
- Perform after SEEG identification of SOZ

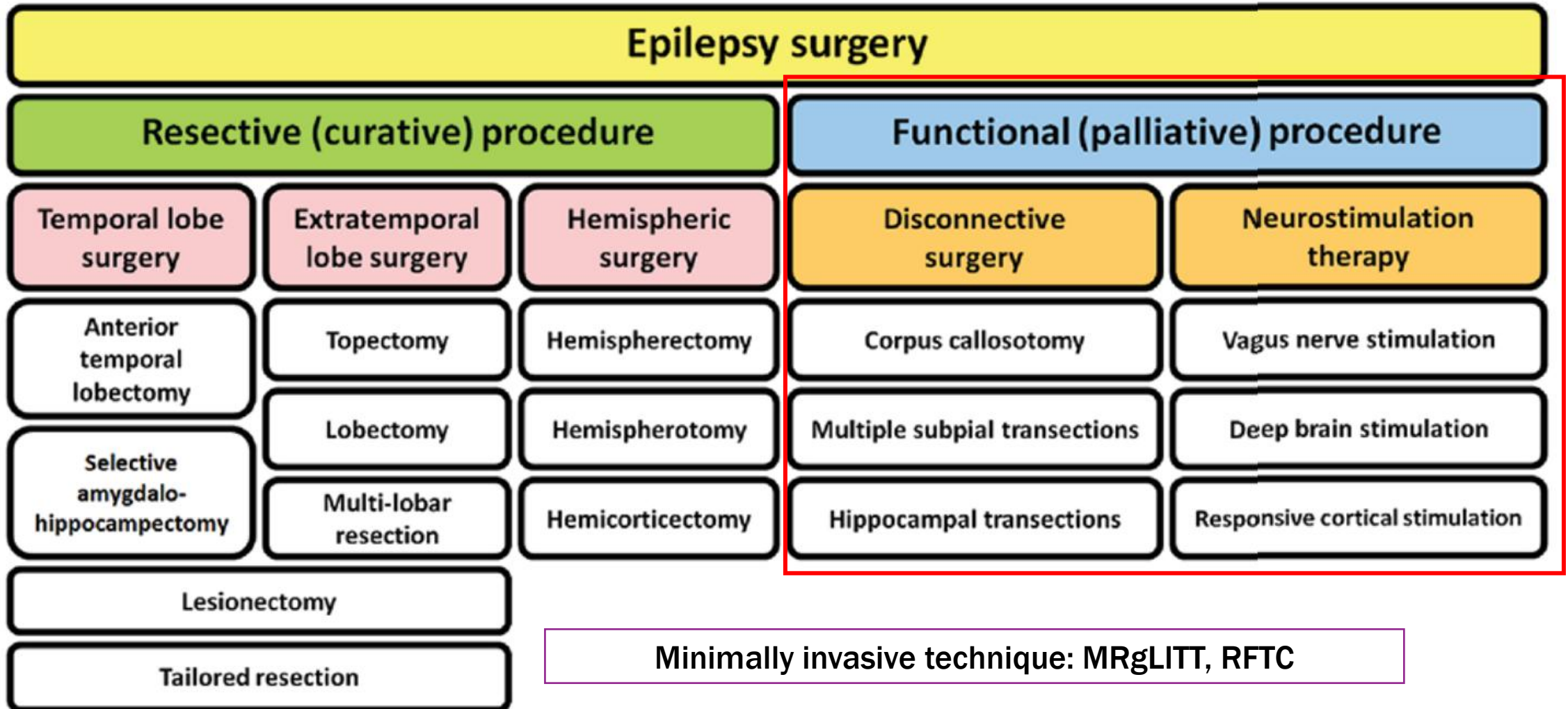


RADIOFREQUENCY THERMOCOAGULATION (RFTC)

- Delivering high levels of electrical current through the implanted SEEG leads to burn adjacent epileptogenic tissue
- Performed at the bedside, typically with a neurosurgeon attaching RF cables to the SEEG leads and delivering high-power (typically ~5 W) current sequentially through a set of predetermined contacts using a clinical RF generator

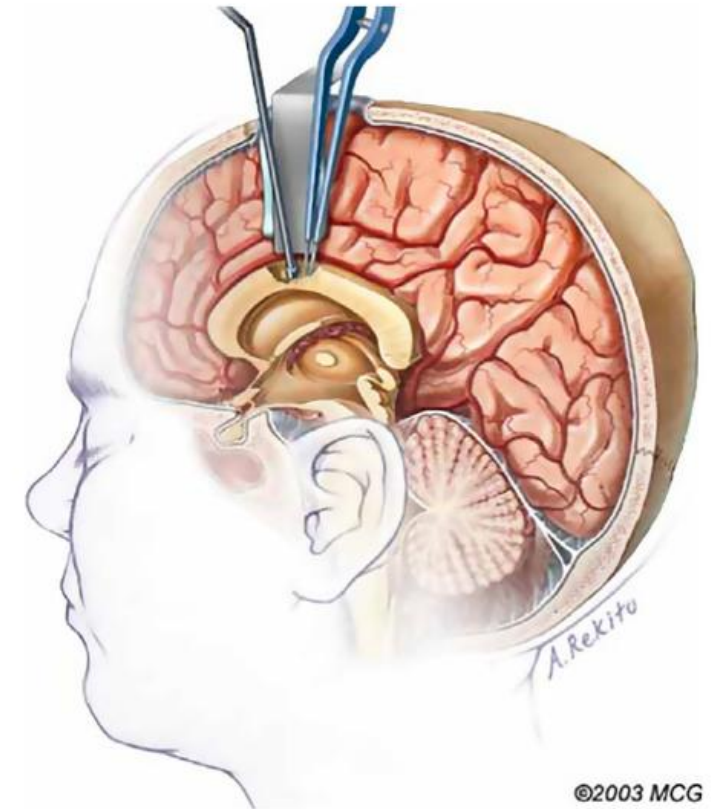
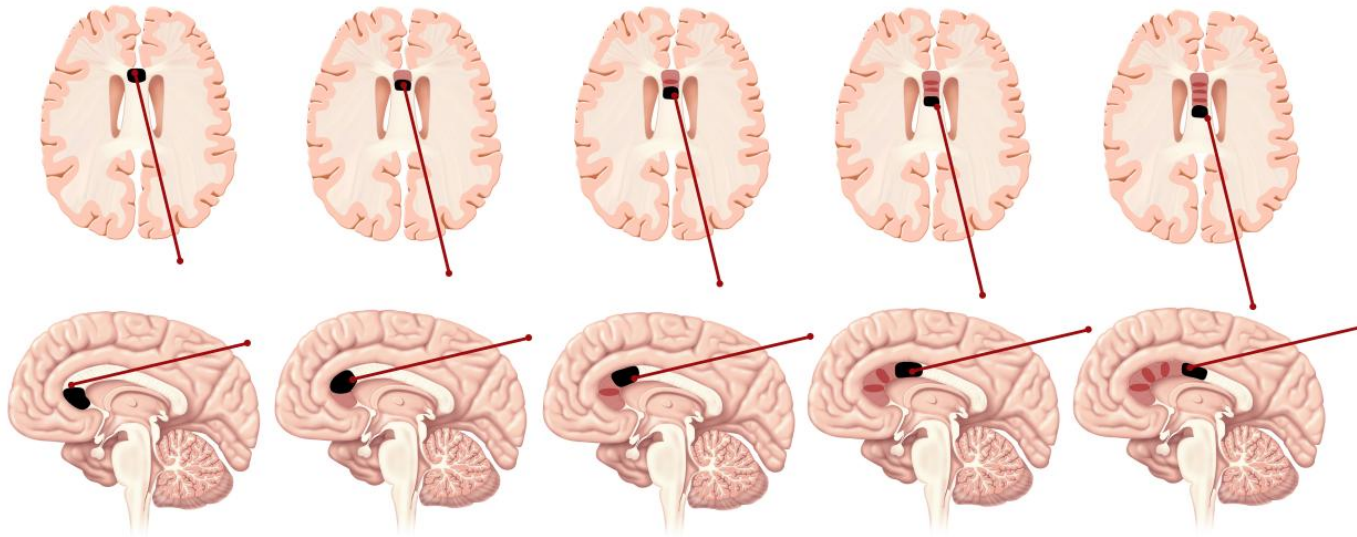


TYPE OF EPILEPSY SURGERY



CORPUS CALLOSOTOMY (CC)

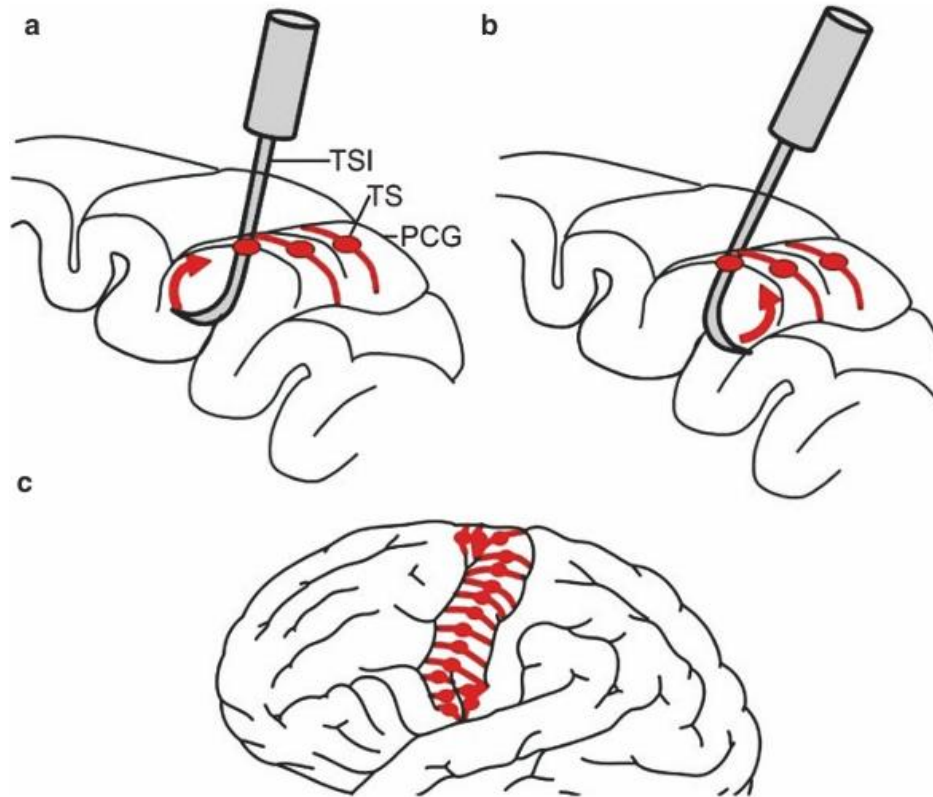
- Use in patient with intractable drop attacks such as LGS
- Decrease drop attacks by prevent interhemispheric spreading of seizure activity



©2003 MCG

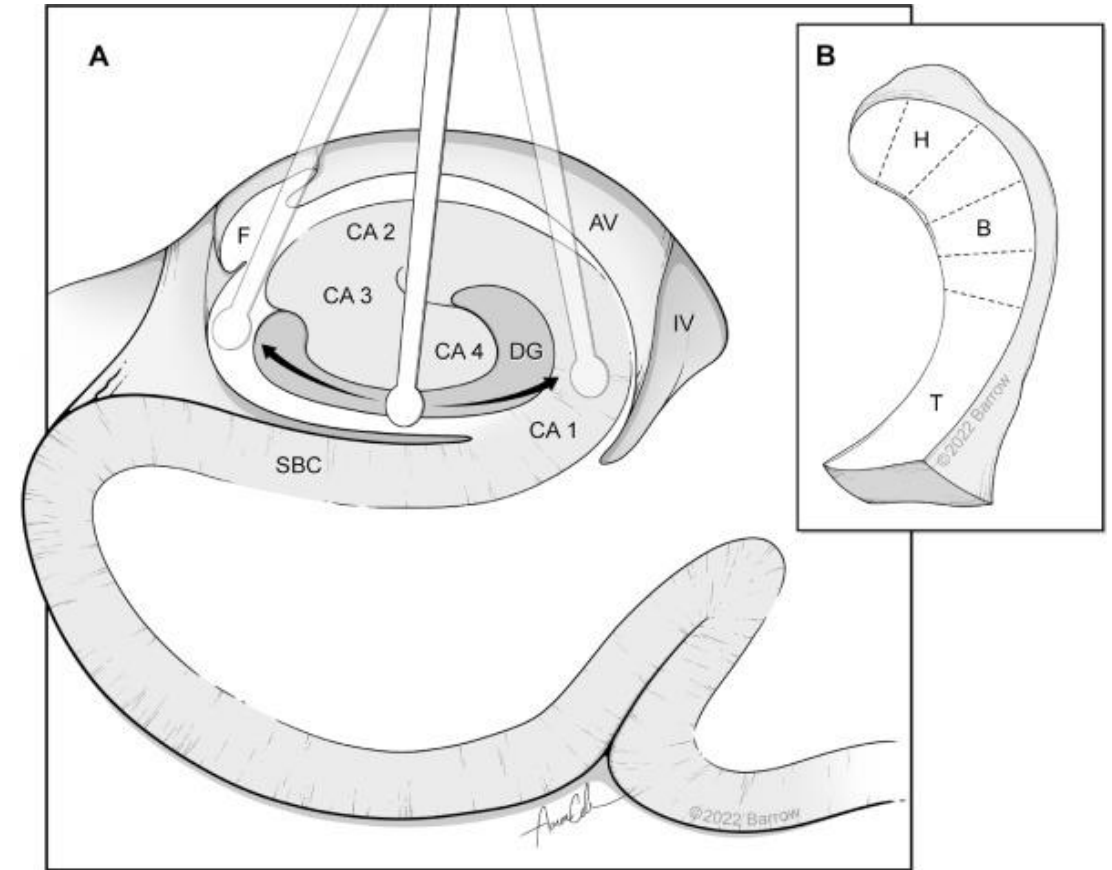
MULTIPLE SUBPIAL TRANSECTION (MST)

- Disconnective surgery used in patient with EZ localized to eloquent cortex
- Based on the observation that a neuronal functional unit is organized vertically while the seizures spread horizontally, and that a minimal contiguous cortical surface area is necessary for the maintenance of cortical activity
- Have been shown effective in patient with Landau kleffner syndrome

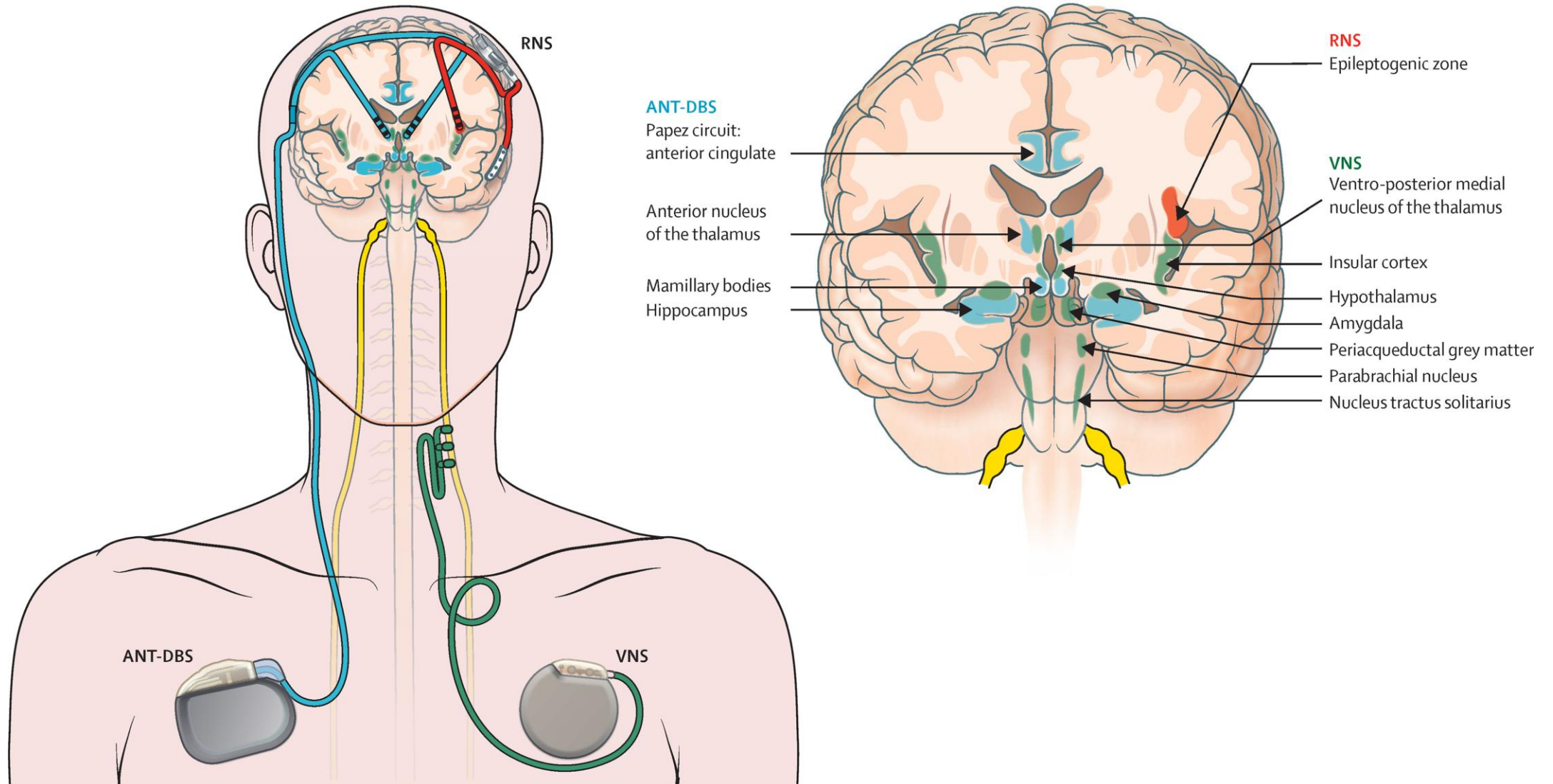


MULTIPLE HIPPOCAMPAL TRANSECTION (MHT)

- Disconnective surgery used in patient with EZ localized to dominant hippocampus to preserve verbal memory
- MHT aims to interrupt the longitudinal fibers responsible for seizure spread while preserving the transverse memory circuits, with the goal of minimizing memory impairment.

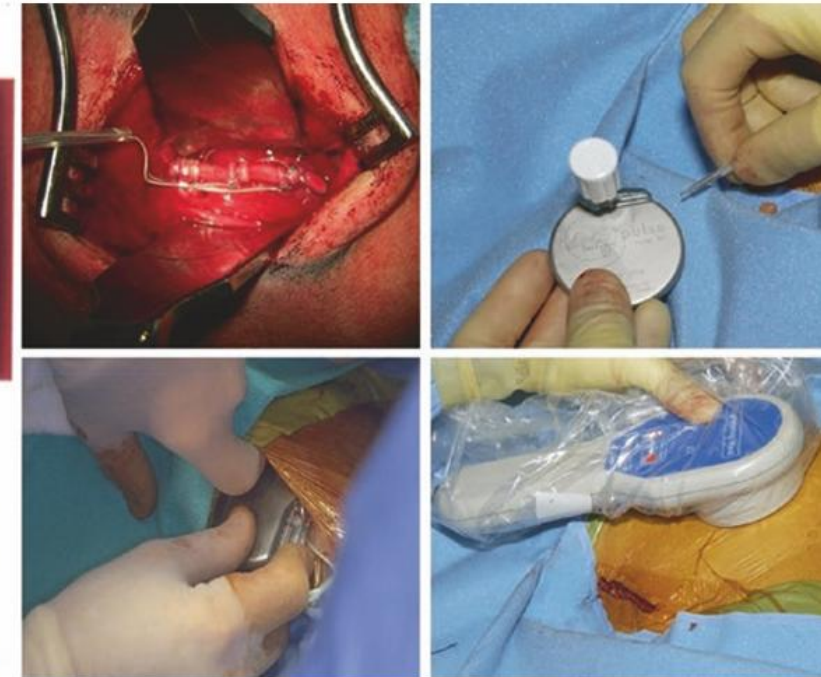
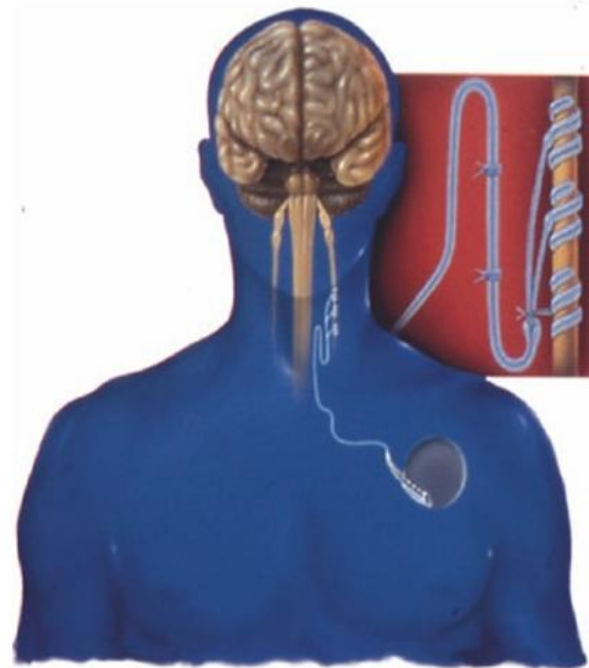


NEUROMODULATION

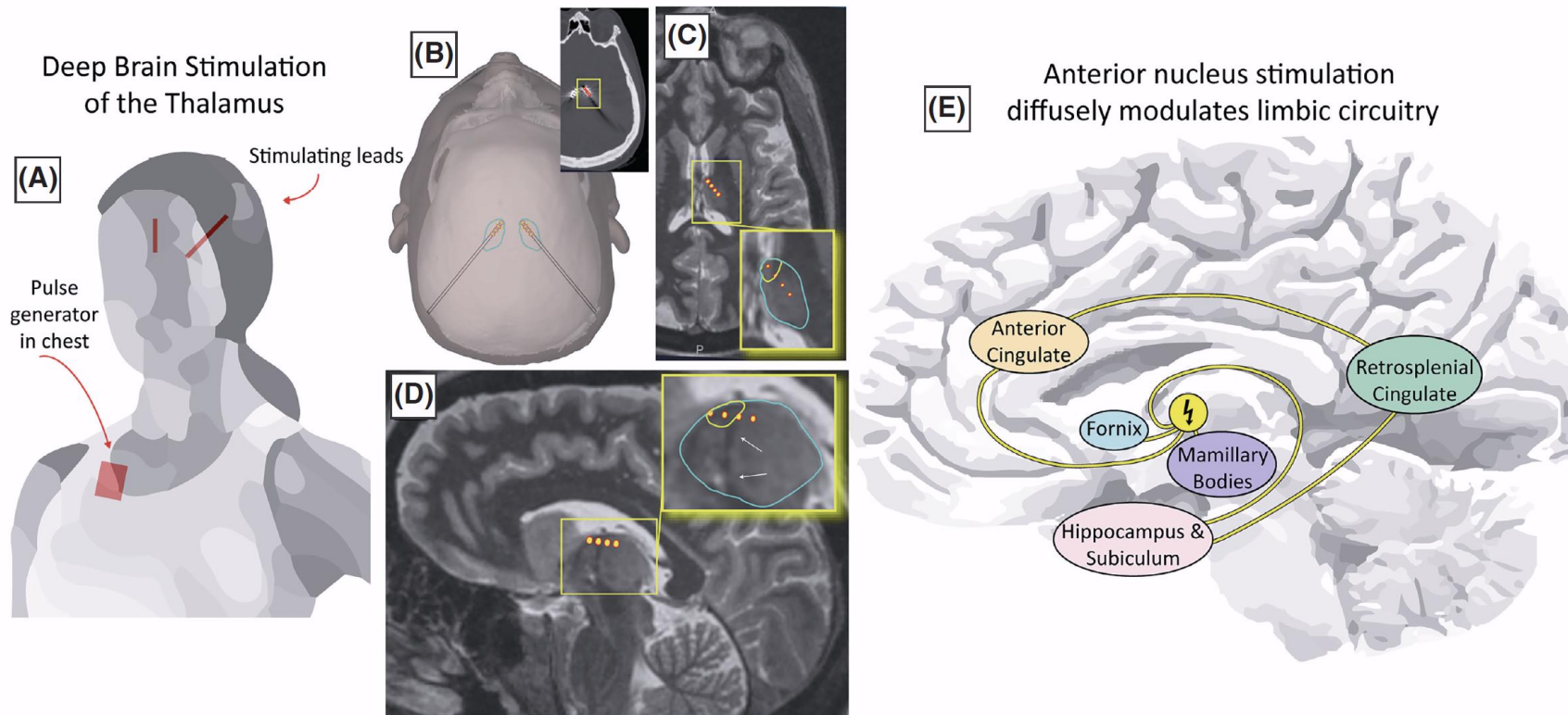


VAGAL NERVE STIMULATION (VNS)

- Open loop stimulation of left vagal nerve
- The device resembles a cardiac pacemaker and delivers intermittent electrical impulses to the left vagus nerve
- Reduce seizure by modulate brainstem, thalamic, and cortical afferent projections, including catecholaminergic nuclei and limbic regions.
- Newer generation of VNS
 - Closed-loop VNS: deliver shock upon detection of heart rate increase
 - On-demand: patient or their relative can use magnet to deliver shock upon having seizure



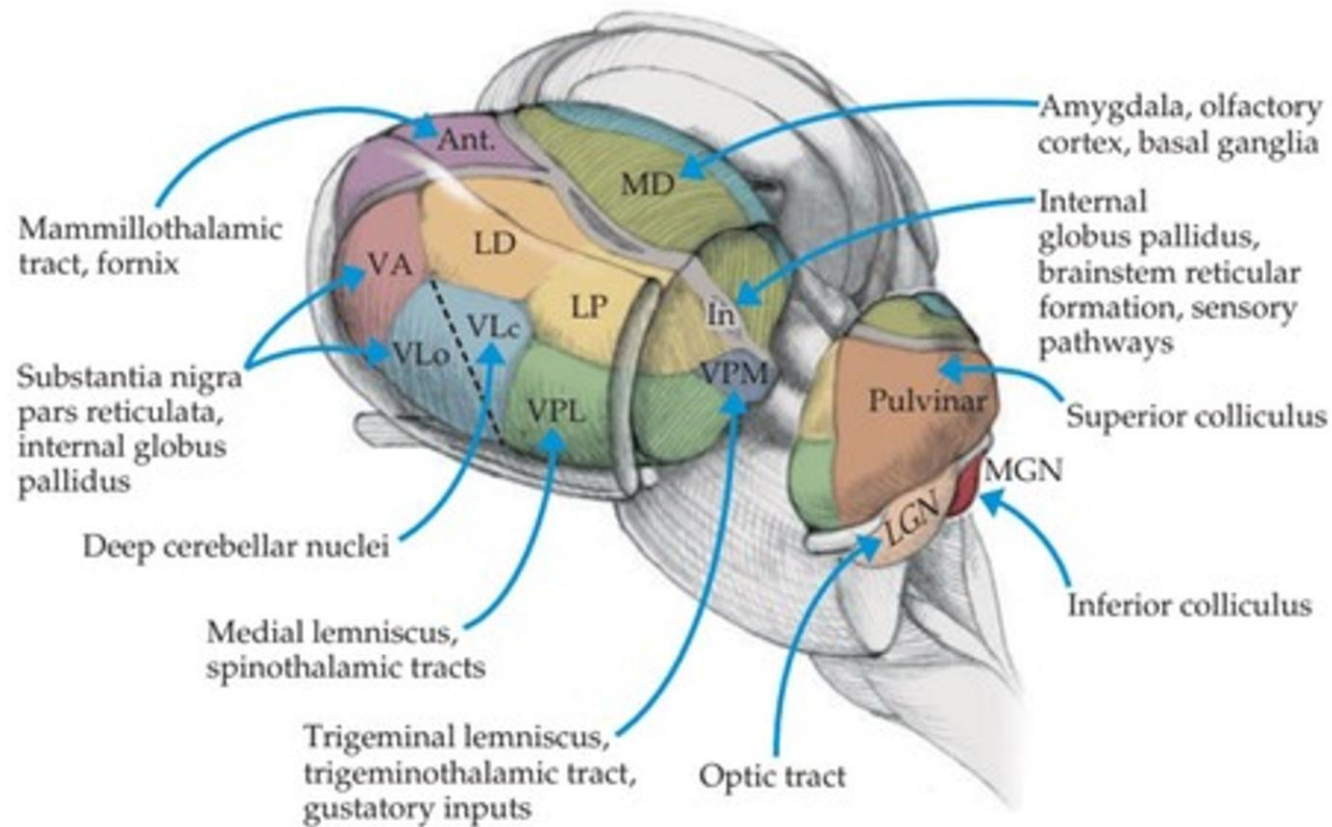
DEEP BRAIN STIMULATION (DBS)



- Open loop stimulation of possible to target central brain nodes (thalamus) where propagating seizure activity converges
- The device delivers continuous therapy to the nuclei of the thalamus.
- Currently, Anterior Nuclear of Thalamus (ANT) is only FDA approved target
- However, the ANT is a component of limbic circuitry and is not a universal node in all seizure networks

DEEP BRAIN STIMULATION (DBS) TARGET

Anterior :
Limbic system



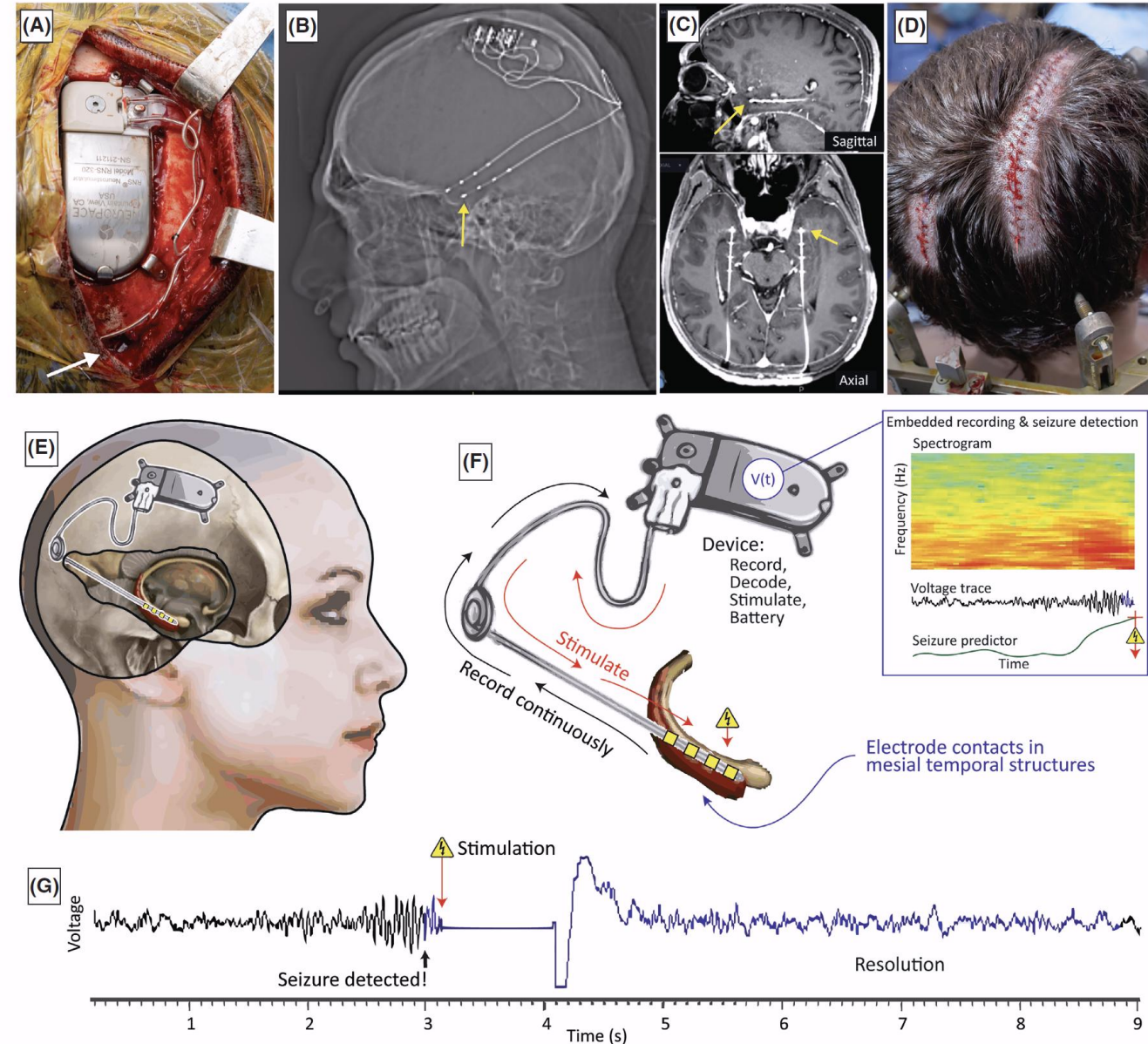
Centromedian :
Basal ganglia, motoric and
generalized epilepsy

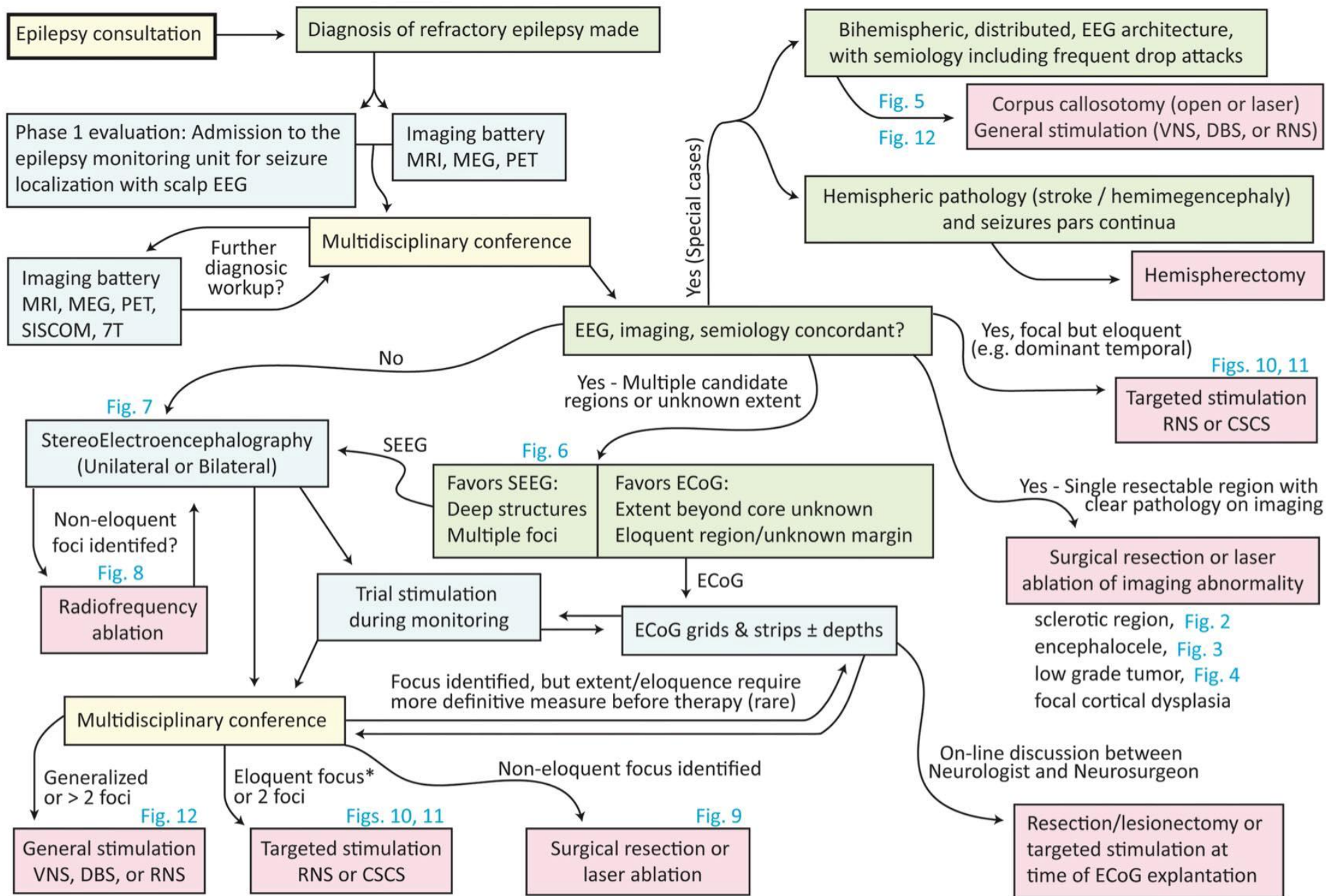
Intralaminar :
Seizure with impaired
awareness

Pulvinar :
Occipital lobe epilepsy,
seizure with eye
movement semiology

RESPONSIVE NEUROSTIMULATION (RNS)

- Closed loop neurostimulation with continuous EEG monitoring at SOZ
- Detected seizure and delivered short burst of electrical stimulation to terminate seizure
- A device implanted in the skull and two subdural or depth four-contact leads electrodes for recording and stimulation.
- The closed-loop RNS system can treat two foci simultaneously including those in opposite hemispheres





SURGICAL OUTCOME AFTER EPILEPSY SURGERY

Engel Epilepsy Surgery Outcome Scale³³

- ◆ Class I: free of disabling seizures (Ia); nondisabling focal aware seizures or auras only (Ib); some disabling seizures after surgery but free of disabling seizures for ≥ 2 years (Ic); convulsions with seizure medication withdrawal only (Id)
- ◆ Class II: initially seizure free (IIa) but had rare disabling seizures (IIb) in the past 2 years (IIc); nocturnal seizures only (IIId)
- ◆ Class III: worthwhile seizure reduction (IIIa); prolonged seizure-free periods last less than 2 years but $>50\%$ of follow-up period (IIIb)
- ◆ Class IV: no worthwhile improvement; significant seizure reduction (IVa); no change (IVb); worsened seizures (IVc)

International League Against Epilepsy Classification³⁴

- ◆ Class 1: completely seizure free (if since surgery, 1a); no auras
- ◆ Class 2: only auras; no other seizures
- ◆ Class 3: 1-3 seizure days per year; with or without auras
- ◆ Class 4: 4 seizure days per year to 50% reduction in baseline number of seizure days; with or without auras
- ◆ Class 5: $<50\%$ reduction in baseline number of seizure days to 100% increase in baseline number of seizure days; with or without auras
- ◆ Class 6: $>100\%$ increase in baseline number of seizure days; with or without auras

TAKE HOME MESSAGE (1)

- All patient with DRE should be considered for presurgical evaluation
- Goal of presurgical evaluation: identify epileptogenic cortex + preservation of eloquent cortex
- Mandatory tool for presurgical evaluation:
 - Long-term EEG, MRI epilepsy, Neuropsychology test
- Indication for invasive evaluation:
 - MRI negative, discordant electroclinical data, EZ near eloquent cortex, Multifocal pathology

TAKE HOME MESSAGE (2)

- **PMC: multidisciplinary approach to provide consensus based surgical management for patient with epilepsy**
- **Types of epilepsy surgery: Resective surgery vs. palliative surgery**
- **Resective surgery is selected based on epileptic substrate**
- **Palliative surgery aim to reduce seizure frequency of patient**