สถาบันประสาทวิทยา
Neurological Institute of Thailand

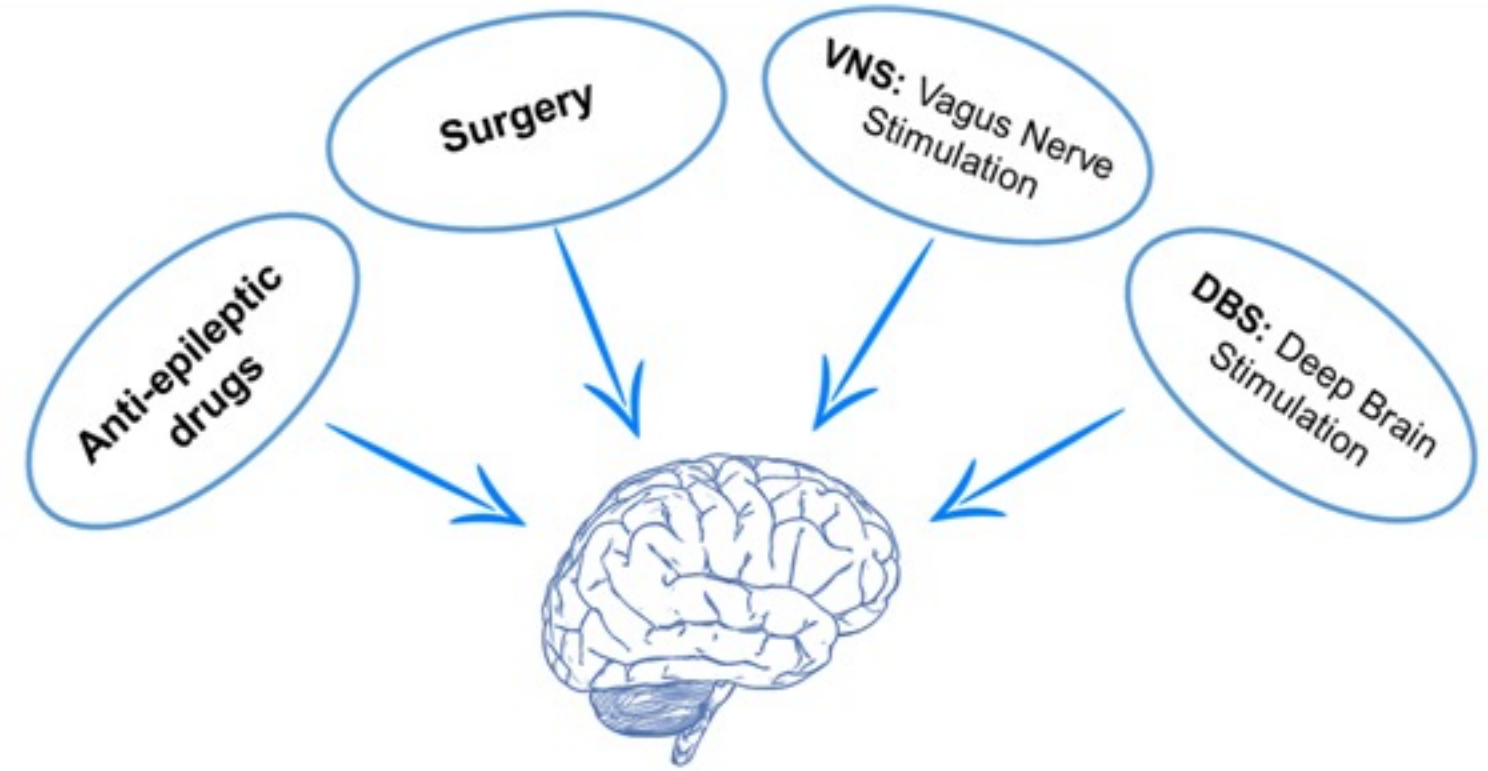
Presurgical Evaluation and Epilepsy surgery

Tinonkorn Yadee,MD
Neurological of Thailand

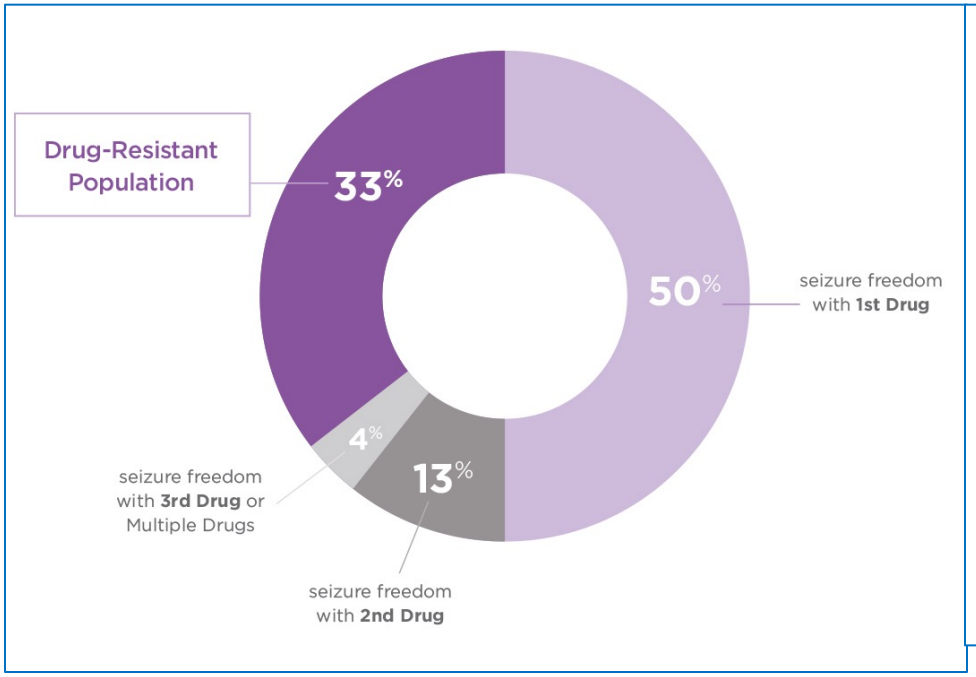
Outline

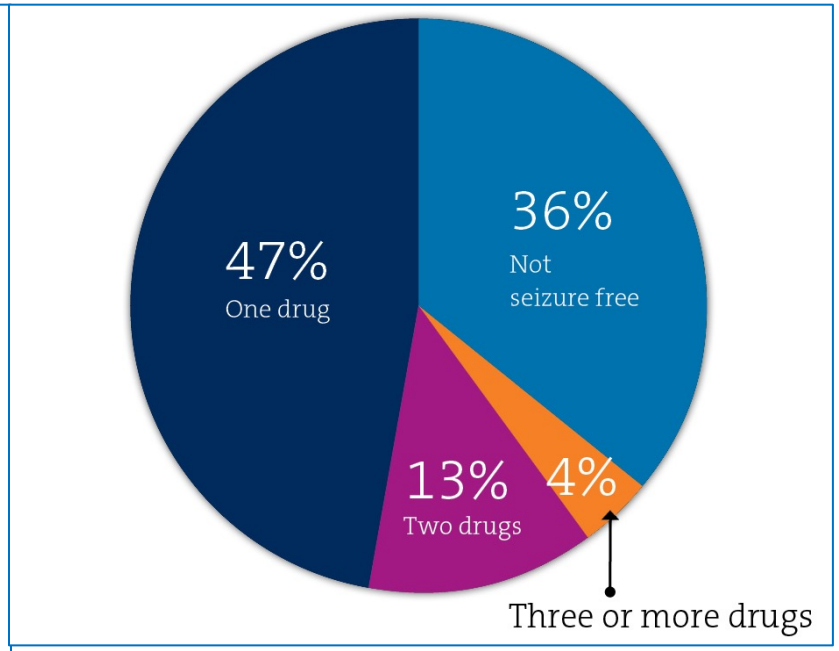
- Selecting patient for Epilepsy surgery
- Concept of presurgical evaluation
- Type of Epilepsy surgery
- Epilespy surgery outcome

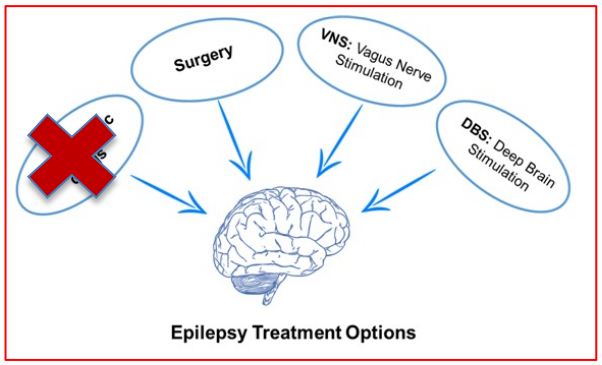
Epilepsy treatment



Drug resistance epilepsy







Kwan P, Brodie MJ. NEJM February 3, *2000; Vol. 342 No. 5*

Selecting patient for Epilepsy surgery

Recognizing Drug-Resistant Epilepsy

Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies

*[1] Patrick Kwan, †Alexis Arzimanoglou, ‡Anne T. Berg, §Martin J. Brodie, ¶W. Allen Hauser, #[2] Gary Mathern, **Solomon L. Moshé, ††Emilio Perucca, ‡‡Samuel Wiebe, and §§[2] Jacqueline French

- " Failure of adequate trials of two tolerated and appropriately chosen and used AED regimens whether as monotherapy or in combination to achieve sustained seizure freedom"

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

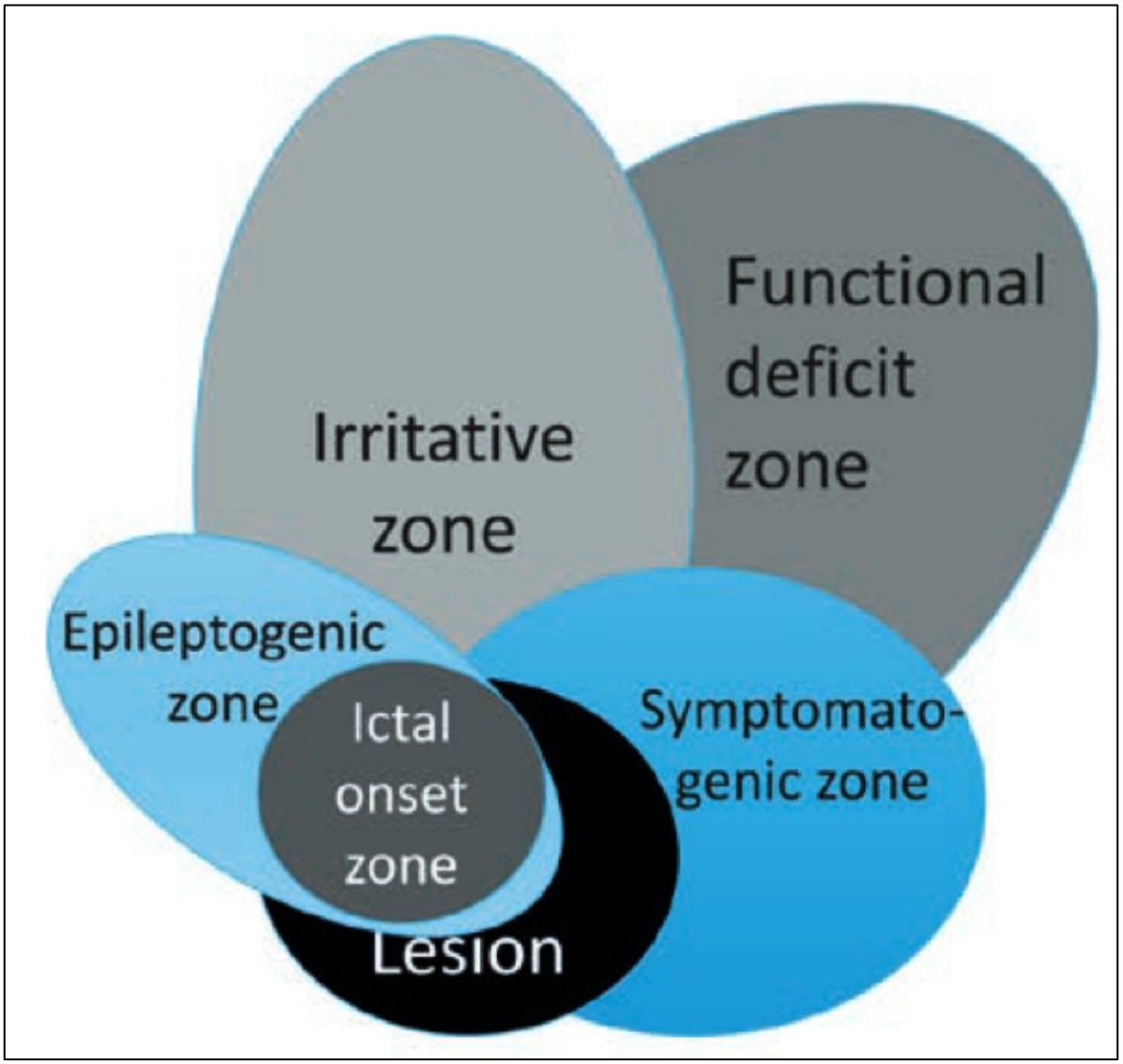
Selecting patient for Epilepsy surgery

Other causes consider to surgical intervention

- Cognitive decline accruing due to recurrent epilepsy
- Depression
- Vocational issues impeding employment
- Social stigma associated with epilepsy
- Better long term economic feasibility in the patient under- going early surgery

M. Tripathi et al. / International Journal of Surgery 36 (2016) 405e410

Using the Presurgical Evaluation to Select Epilepsy Surgery Candidates



Lara Jehi, Epilepsy Currents,2018

Using the Presurgical Evaluation to Select Epilepsy Surgery Candidates

Zone	Tests Used to Define It
Irritative zone: area of cortex that generates interictal spikes	EEG, MEG, EEG-fMRI
Seizure-onset zone: area of cortex that initiates clinical seizures	EEG, ictal SPECT and, to a lesser degree, f-MRI and MEG
Symptomatogenic zone: area of cortex that, when activated, produces the initial ictal symptoms or signs	Initial seizure symptomatology
Epileptogenic lesion: macroscopic lesion that is causative of the epileptic seizures because the lesion itself is epileptogenic (e.g., cortical dysplasia) or by secondary hyperexcitability of adjacent cortex)	MRI
Functional deficit zone: area of cortex that is not functioning normally in the interictal period	Neurological examination, neuropsychological examination and functional imaging (interictal SPECT and PET)

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

From the American Epilepsy Society 2009 Annual Course

Localizing and lateralizing features of auras and seizures

Nancy Foldvary-Schaefer [a,*], Kanjana Unnwongse [b]

[a] Cleveland Clinic Neurological Institute, Cleveland, OH, USA
[b] Prasat Neurological Institute, Bangkok, Thailand

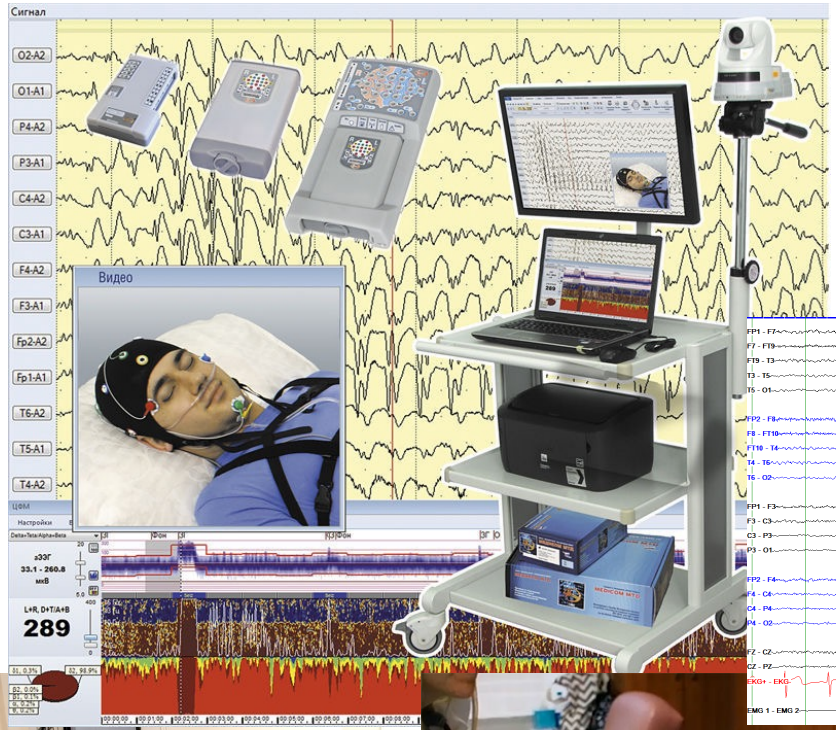
Localization and lateralization of epileptic signs and symptoms.
Source. Modified from Rona [61].

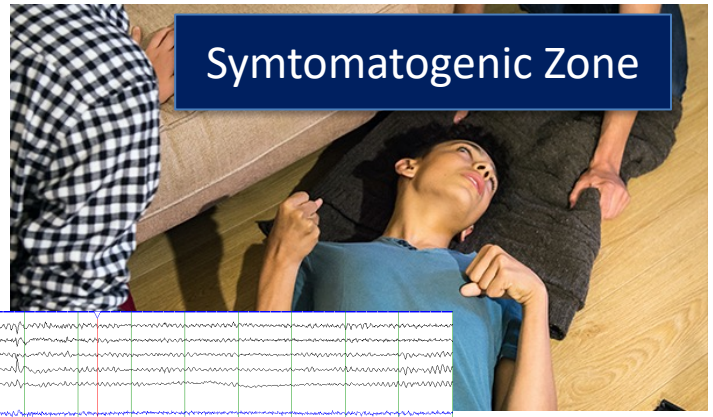
Seizure type	Subtype	Symptomatogenic zone[a]	Lateralization	Epilepsy syndrome[b]
Auras	Somatosensory	Primary somatosensory cortex (areas 1,2, and 3b)	CL[c]	PLE
		Secondary somatosensory areas (parietal operculum/SSII)	IPSI (if unilateral)	PLE, TLE
		SSMA	CL (mostly)	PLE, FLE
	Simple visual	Primary visual cortex (areas 17, 18, and 19)	CL	OLE
	Complex visual	Temporo-occipital junction and basal temporal cortex	CL (if unilateral)	TLE, OLE
	Simple auditory	Primary auditory cortex (area 41)	CL (if unilateral)	TLE
	Complex auditory	Auditory association cortex (areas 42 and 22)	CL (if unilateral)	TLE
	Vertiginous	Temporo-occipital junction	NonLAT (often right)	TLE
	Olfactory	Orbitofrontal region, amygdala, and insula	NonLAT	MTLE, FLE
	Gustatory	Parietal operculum and basal temporal cortex	NonLAT	TLE
	Autonomic	Insula, amygdala, anterior cingulum, and SSMA	NonLAT	TLE, FLE
	Abdominal	Anterior insula, frontal operculum, mesial temporal lobe, and SSMA	NonLAT	MTLE
	Fear	Amygdala, hippocampus, and mesial frontal lobe	NonLAT	TLE, FLE
	Déjà vu/jamais vu	Uncus, entorhinal cortex, and temporal neocortex	NonLAT (often ND)	TLE
	Multisensorial	Mesiobasal limbic cortex, temporal neocortex, TPO junction	NonLAT	TLE, PLE
	Cephalic/whole body	Amygdala, entorhinal cortex, and temporal neocortex/SSII and SSMA	NonLAT	NTLE, FLE
Simple motor	Myoclonic/negative myoclonus	Primary motor cortex (area 4) and premotor cortex (area 6)/primary somatosensory area	CL (if unilateral)	FLE
	Clonic	Primary motor cortex, premotor cortex, and SSMA	CL	FLE
	Tonic	Primary motor cortex and SSMA	CL (if unilateral)	FLE
Complex motor	Hypermotor	Anterior cingulum, orbitofrontal region, frontopolar region, opercular–insular cortex, and medial intermediate frontal area	NonLAT	FLE
	Automotor	Mesial temporal and anterior cingulum	NonLAT	TLE, FLE
	Gelastic	Hypothalamus, anteromesial frontal region, and basal temporal area	NonLAT	FLE, TLE
Dialeptic		Limbic temporal structures, cingulum, intermediate frontal (area 8) and orbitofrontal areas	NonLAT	
Autonomic	Tachycardia/ hyperventilation	Amygdala, insula, anterior cingulum, and medial prefrontal cortex	NonLAT (often right)	TLE
	Pilorection		IPSI	TLE
	Mydriasis		IPSI (if unilateral)	TOLE

Lateralizing signs of focal seizures.
Source. Modified from Bianchin and Sakamoto [62].

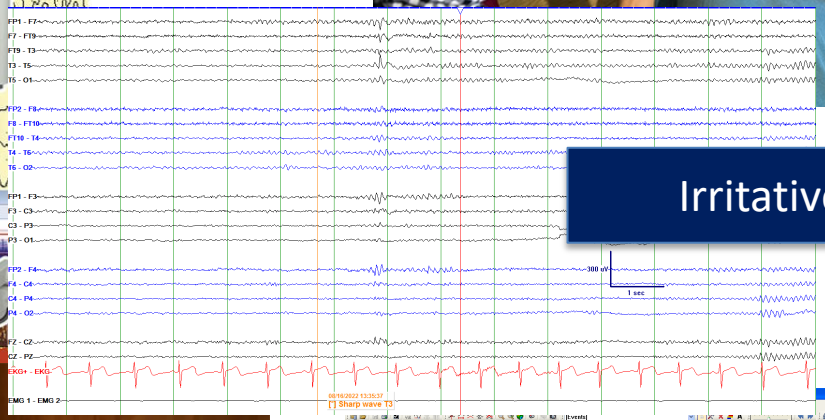
Ictal sign	Subtype	Symptomatogenic zone or mechanism[a]	Lateralization	Epilepsy syndrome[b]
Motor signs in complex motor seizures	Dystonic limb posturing	Activation of basal ganglia	CL[c]	TLE, FLE
	Tonic posturing	Activation of SSMA, basal ganglia, cingulum, and primary motor cortex	CL	FLE, TLE
	Immobile limb	Activation of negative motor areas or exhaustion of primary motor or premotor cortex	CL	TLE
	Head turning	Exhaustion of epileptogenic hemisphere, seizures propagate to basal ganglia, or neglect of CL space	IPSI	TLE
	Facial alterations	Activation of emotional network (amygdala, prefrontal cortex, hypothalamus, orbitofrontal region, insula) or emotional facial movements in cingulum	CL (if facial weakness)	TLE
	Eye version	Frontal eye fields (area 8) and extrastriate cortex (area 19)	CL	
	Unilateral eye blinking	Mesial temporal structures	IPSI	
	Nose wiping	Ictal olfactory hallucinations, increased nasal secretions, or CL postictal immobile limb	IPSI	MTLE
Nondominant temporal signs	Automatisms with preserved responsiveness	Non-speech-dominant temporal lobe and anterior cingulum	ND	TLE, FLE
	Ictal vomiting	Mesial temporal structures, insula, and mesial frontal regions	ND	TLE
	Ictal splitting	Complex automatisms, excessive salivation, or bad mouth sensations	ND	TLE
	Ictal urinary urge	Activation of central bladder control	ND	TLE
	Peri-ictal water drinking	Hypothalamic involvement	ND	TLE
	Ictal/postictal cough	Increased secretions or direct activation of central autonomic system	ND	TLE
	Unilateral ear plugging	Superior temporal gyrus	CL	TLE
Signs during secondary generalized tonic–clonic seizures	Head version	Premotor area (areas 6 and 8)	CL	FLE, TLE
	Asymmetric tonic limb posturing	SSMA and precentral area	CL	TLE, FLE
	Asymmetric ending of clonic jerks	Exhaustion of hemisphere of seizure onset	IPSI	
Language manifestation	Ictal/postictal aphasia	Anterior and posterior language areas	D	TLE
	Ictal speech	Inhibition of D hemisphere or overexcitement of ND hemisphere	ND	TLE

Continuous VEEG monitoring

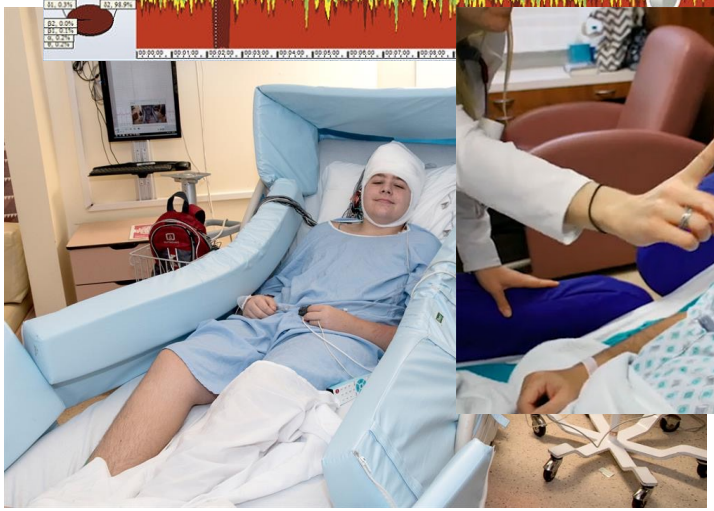




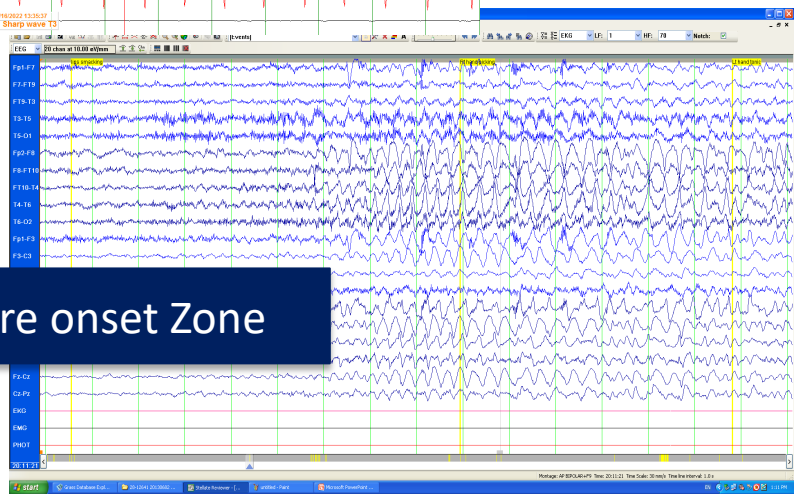
Symtomatogenic Zone



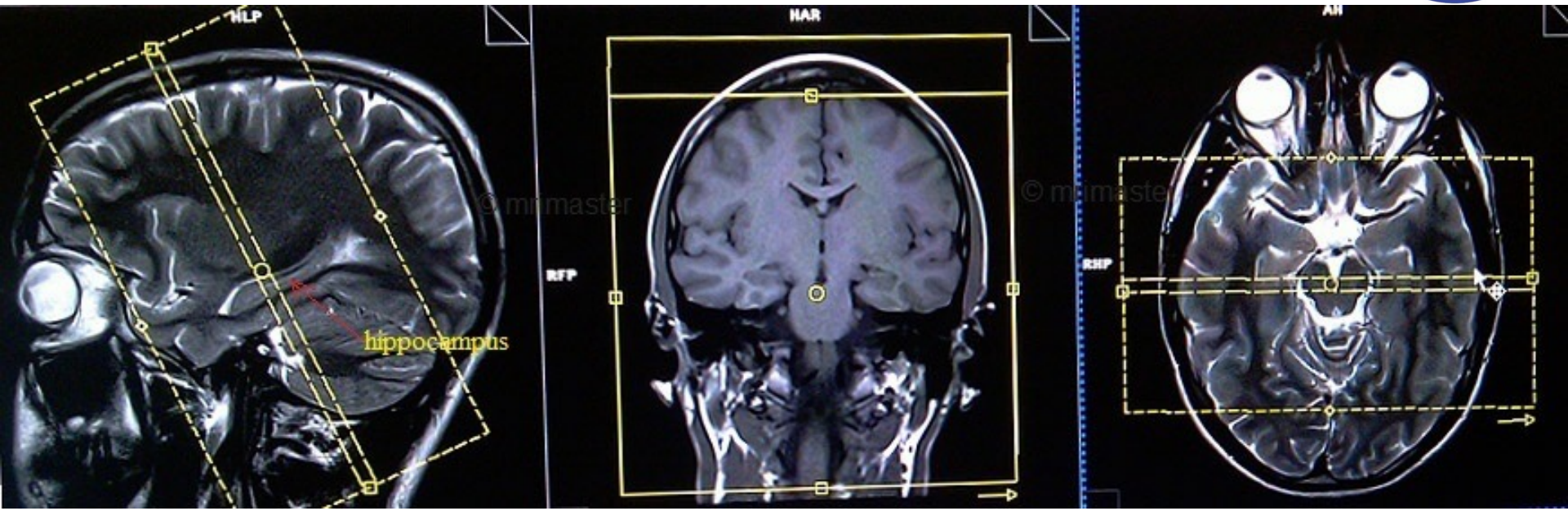
Irritative Zone



Seizure onset Zone



MRI

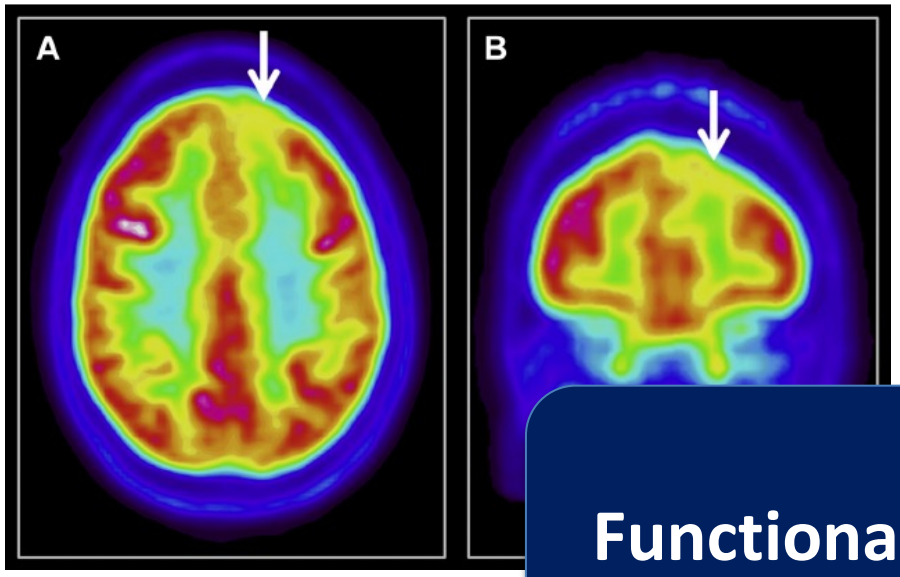


MRI protocol epilepsy

T1WI	isotropic 3D-sequence
FLAIR	Axial Coronal = perpendicular to temporal lobe
T2* or SWI	Susceptibilty artefacts
CE T1WI	Brain tumor - Sturge Weber

Epileptogenic Lesion

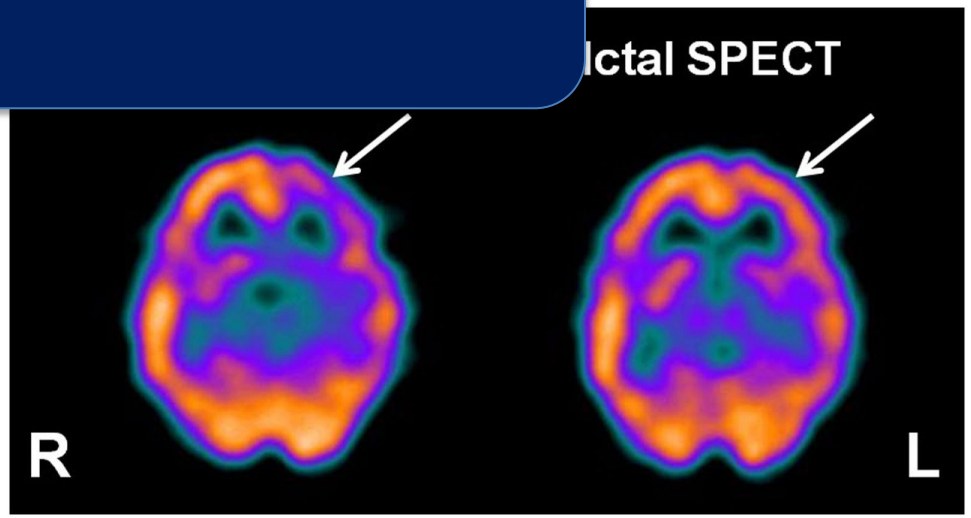
Neuclear radiology



PET Scan

Functional Deficit Zone

Ictal SPECT



Neuropsychology test

ILAE commission report

Epileptic Disord 2019; 21 (3): 221-34

Indications and expectations for neuropsychological assessment in epilepsy surgery in children and ad

Report of the ILAE Ne

Task Force Diagnostic

Commission: 2017-2021

Neuropsychological assessment in epilepsy surgery

Sallie Baxendale [1], Sarah J. Wilson [2], Gus A. Baker [3], William Barr [4], Christoph Helmstaedter [5], Bruce P. Hermann [6], John Langfitt [7], Gitta Reuner [8], Patricia Rzezak [9], Séverine Samson [10], Mary-Lou Smith [11]

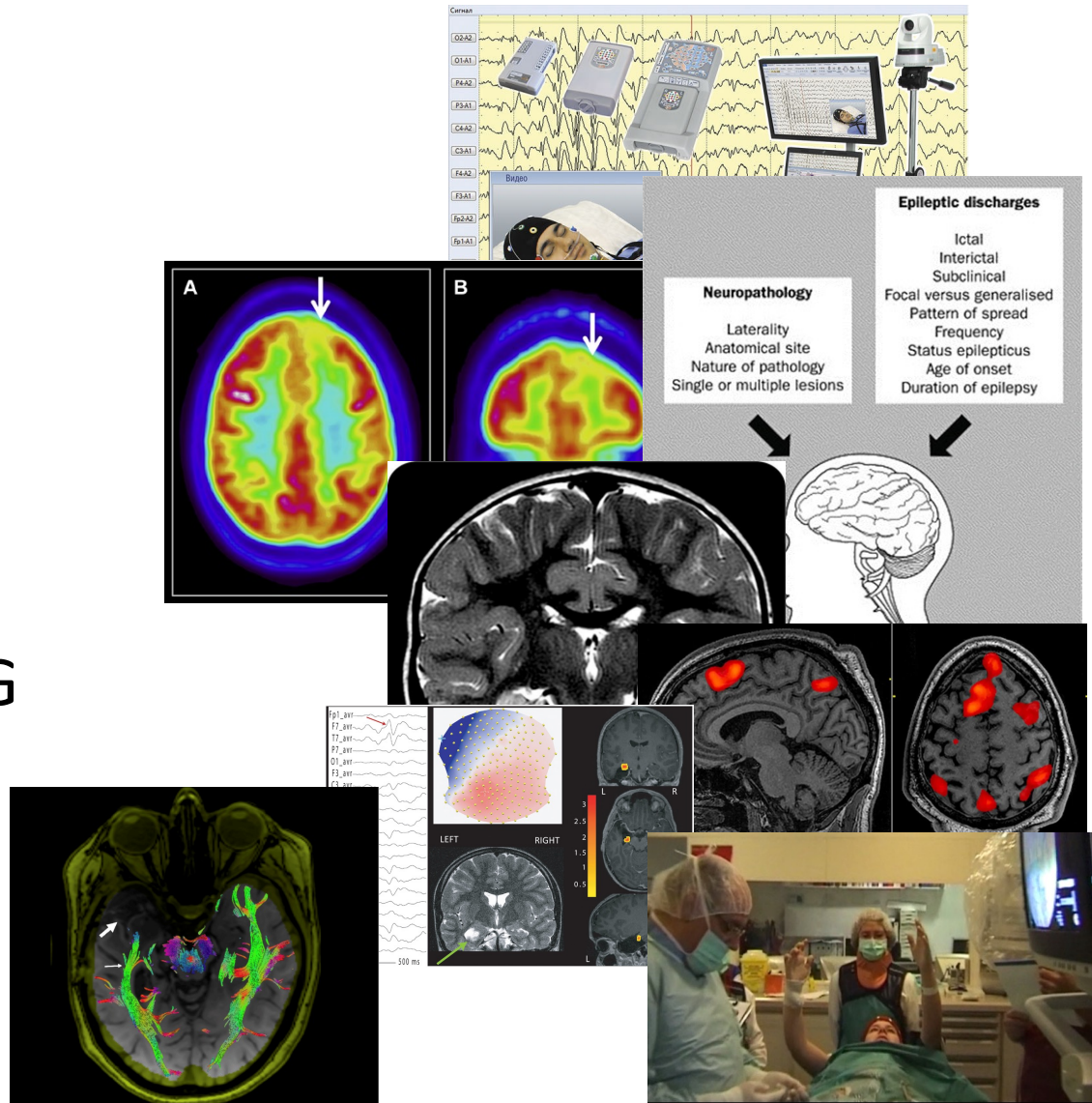
[1] Department of Clinical and Experimental Epilepsy, Institute of Neurology, UCL, London, UK

Functional Deficit Zone

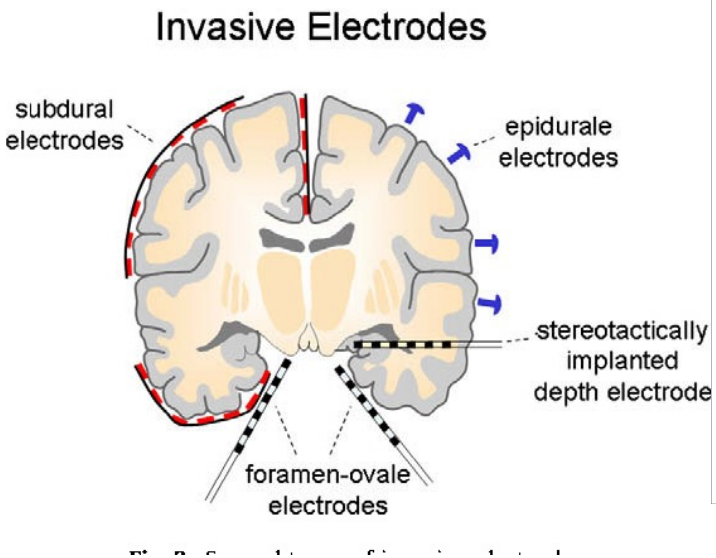
Function	Considerations
Pre surgical assessment	Must be up-to-date. Function in all cognitive domains should be assessed. Should include objective & subjective measures of cognitive function. Should include formal measures of psychosocial function and health-related quality of life. Must also include parental/caregiver evaluations of behaviour and ability in paediatric populations. Teacher/educator evaluations may also be helpful in some cases in paediatric populations.
1. Baseline for outcome comparison	The timing of the formal assessment with respect to the proximity to the last …edication effects will impact on the stability of the baseline …nd must be considered in the interpretation of results.
	…interpreted in a developmental context. …non-organic, static and dynamic influences on function must …he interpretation of results from the preoperative
	…e baseline data should be used to predict the likely cognitive …entify the primary cognitive risks associated with the …ls and nomograms may aid these predictions in adults …dardised operations. …ust be identified in temporal lobe surgery candidates.
4. Feedback and preoperative counselling	Should include explanation of the results of the pre-surgical assessment and education about the aetiology of cognitive and functional deficits identified. Must include detailed discussion of any predicted cognitive changes following surgery. Must include discussion of the patients' (and their families') expectations of surgery. May include prehabilitation for anticipated cognitive losses or psychosocial difficulties.
Post-surgical assessment	Should evaluate all aspects of cognitive and behavioural function assessed prior to surgery. Change must be identified using reliable methods. The nature of the surgery and postoperative seizure outcome must be considered in the interpretation of the postoperative results. The timing of the postoperative assessment will have a significant impact on the results and must be considered in the interpretation of the results. The longer the follow-up, the more accurate the picture of postoperative outcome that emerges. It may take at least 5 years after the surgery for quantifiable changes in HRQoL to become evident in adults and for cognitive changes to emerge in children. Psychotherapeutic input may be required in some cases to help surgical candidates maximise their postoperative potential.

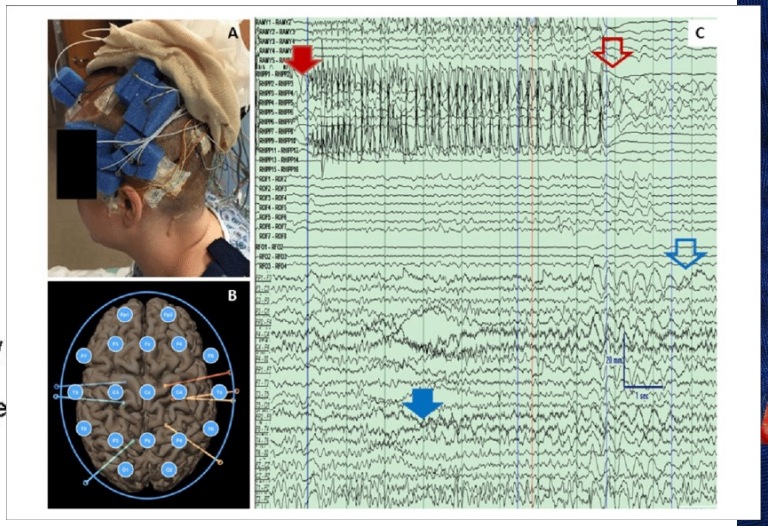
Presurgical evaluation : Phase I

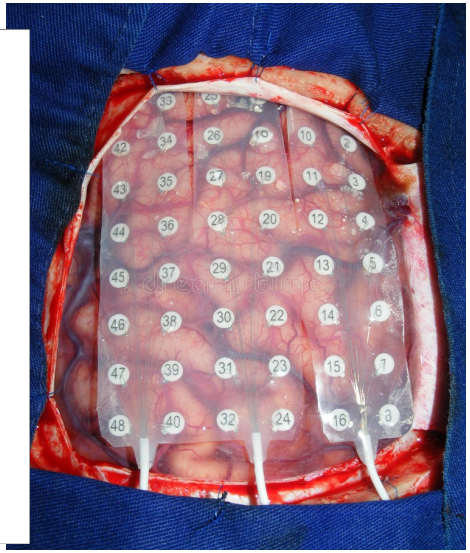
- VEEG
- MRI
- Nuclearradiology
- Neuropsychology
- Complementary
  - fMRI, Wada, MEG
  - Tractography

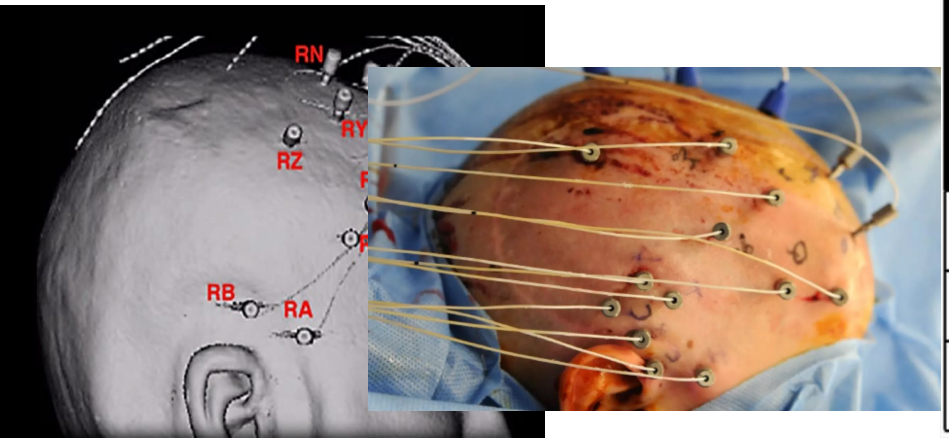


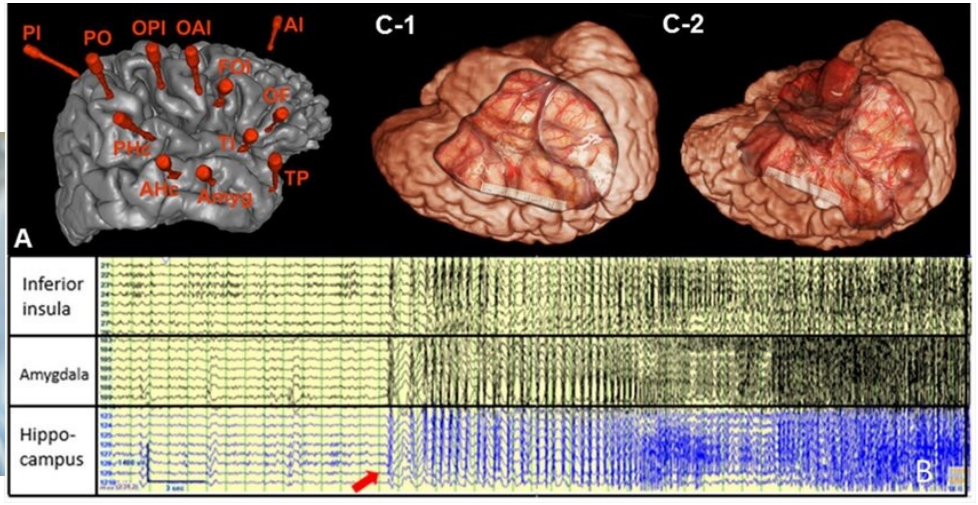
Phase II


Invasive Electrodes
subdural electrodes
epidurale electrodes
stereotactically implanted depth electrode
foramen-ovale electrodes

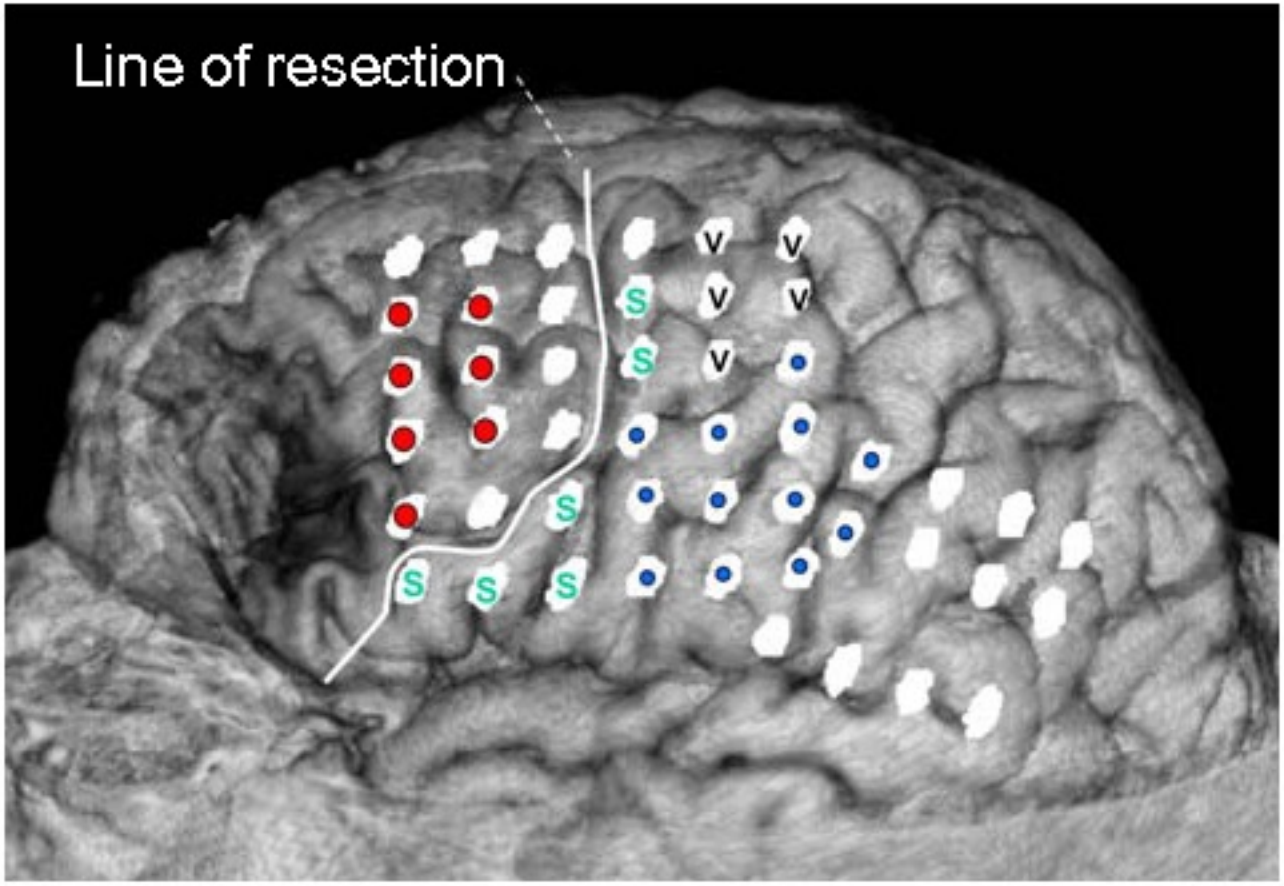

A
B
C

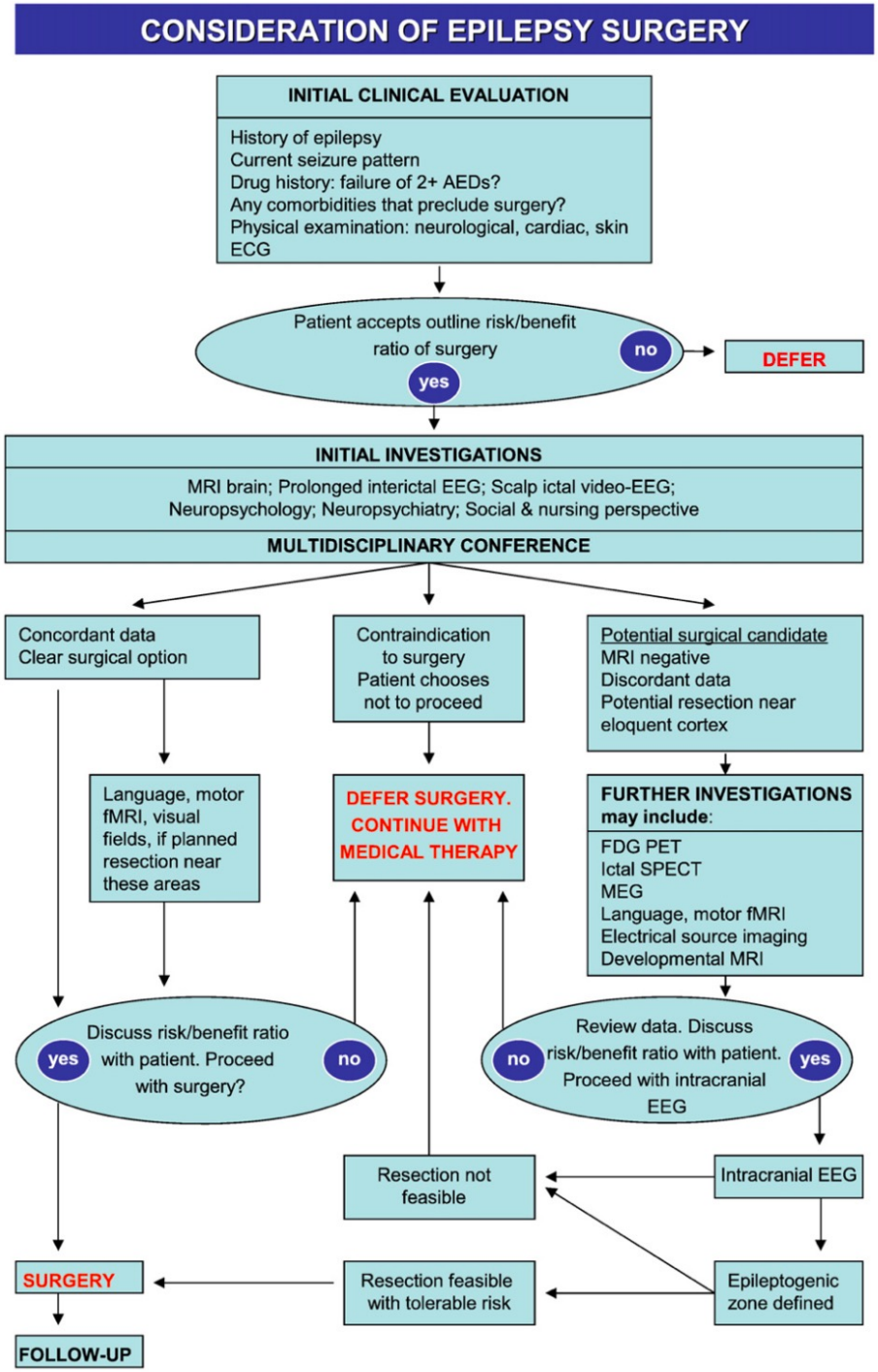



RN
RY
RZ
RB
RA


PI
PO
OPI
OAI
AI
FOI
OF
PHC
TI
AHC
Amyg
TP
A
C-1
C-2
Inferior insula
Amygdala
Hippo-campus
B

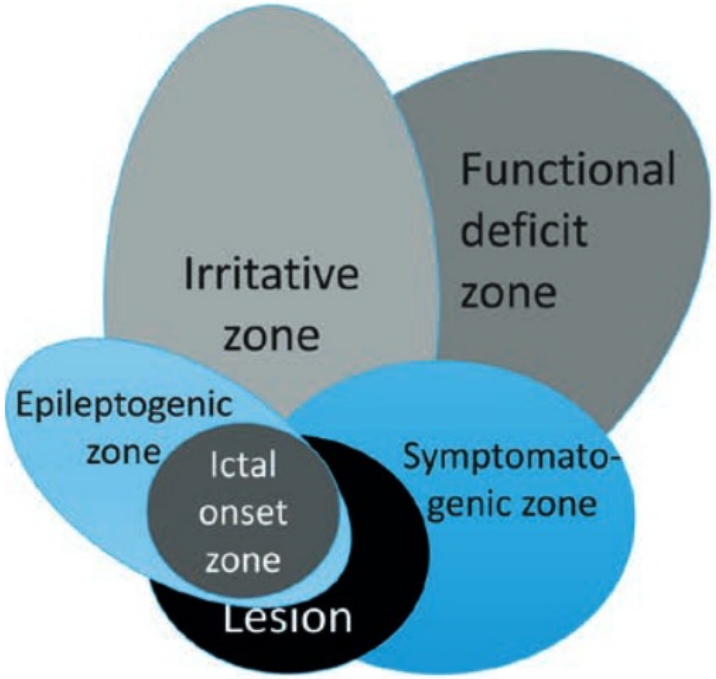
Phase II : Cortical stimulation





J.S. Duncan / Epilepsy & Behavior 20 (2011) 230–232

Epileptogenic Zone concept



Implications:

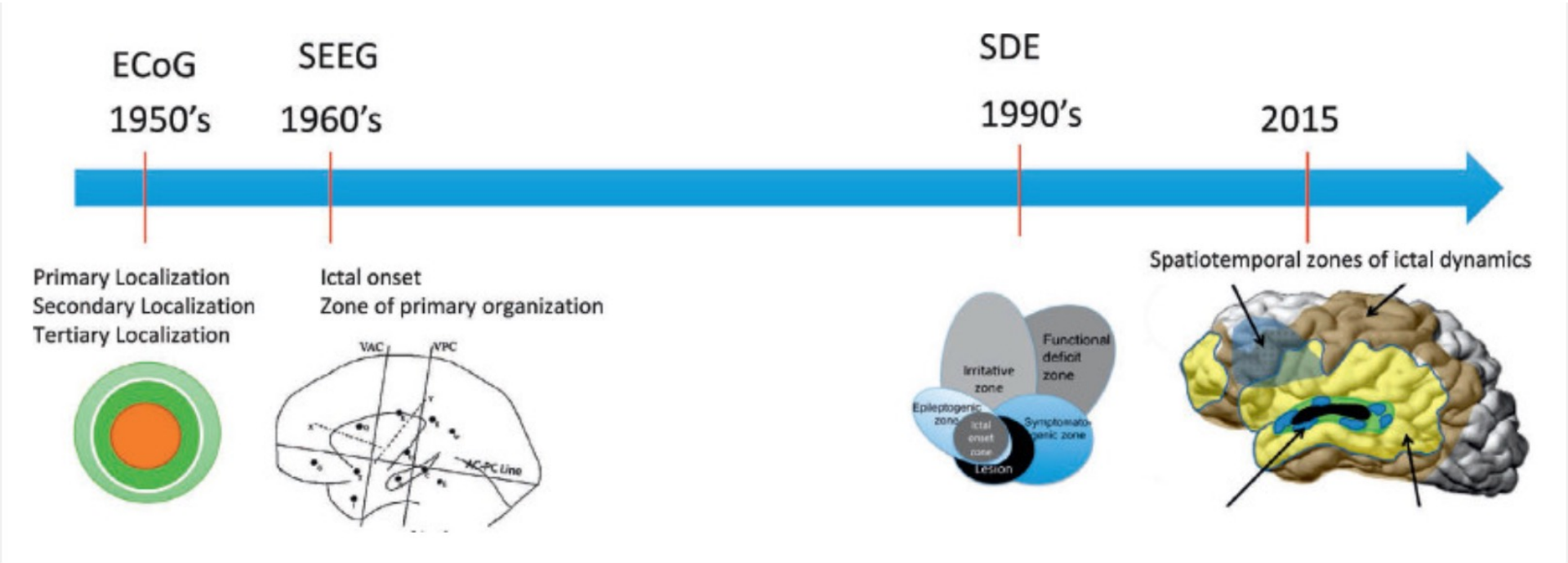
1)- No single zone is equivalent to the EZ

2)- No single TEST allows measurement of the EZ

3)- Specifically, defining the IOZ is not the same as defining the EZ.

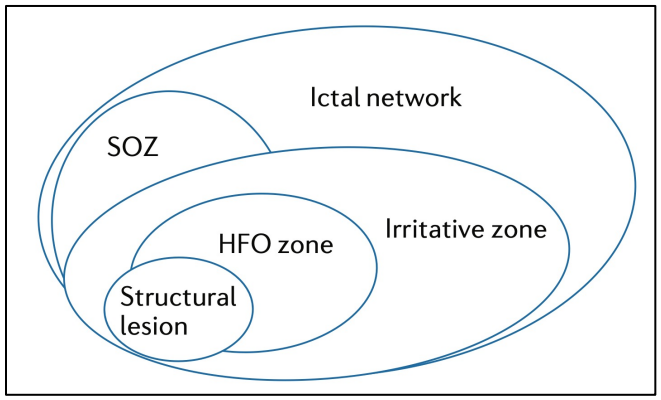
Lara Jehi, Epilepsy Currents,2018

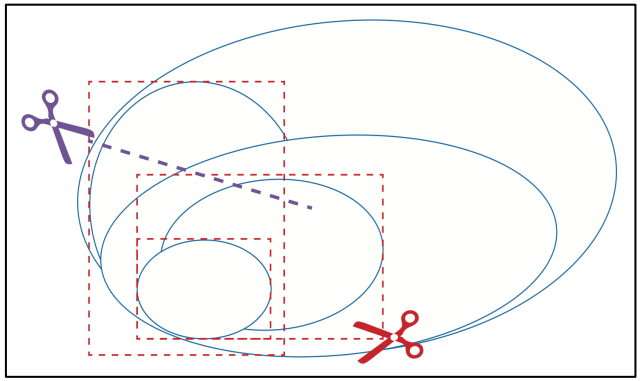
Network Epilepsy: 2000s to Present – SEEG/Depth Recordings

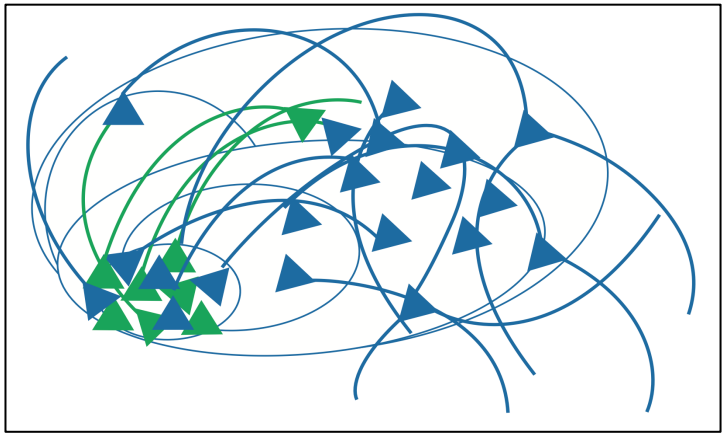


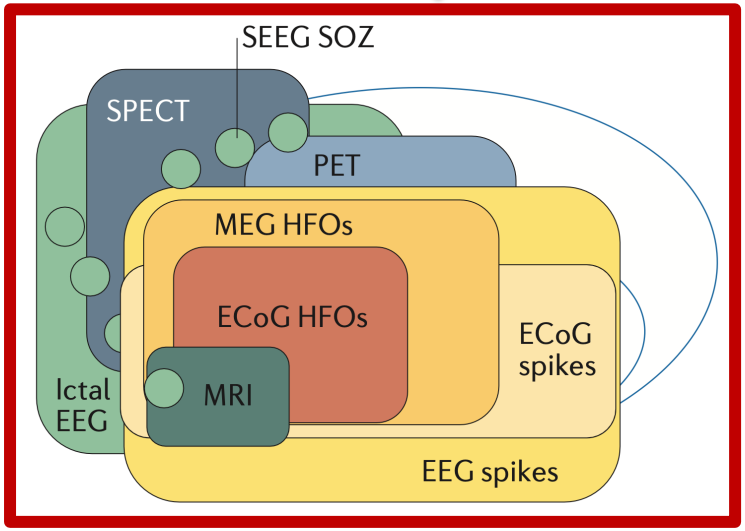
Lara Jehi, Epilepsy Currents,2018

Change in concept









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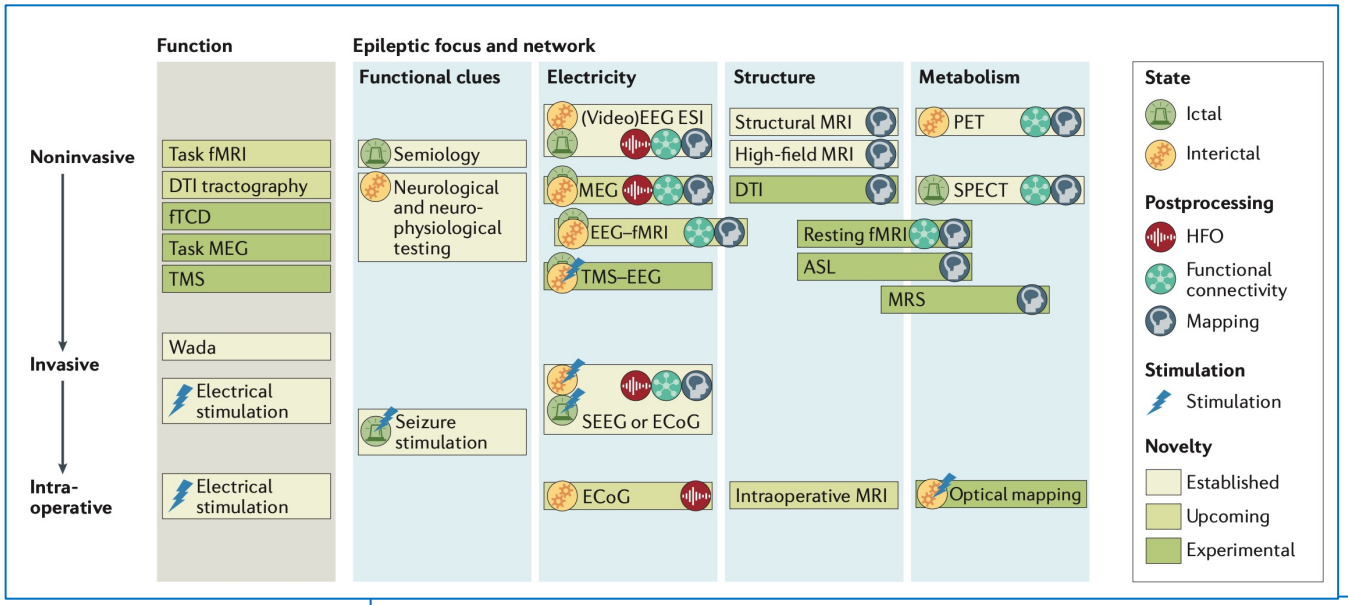
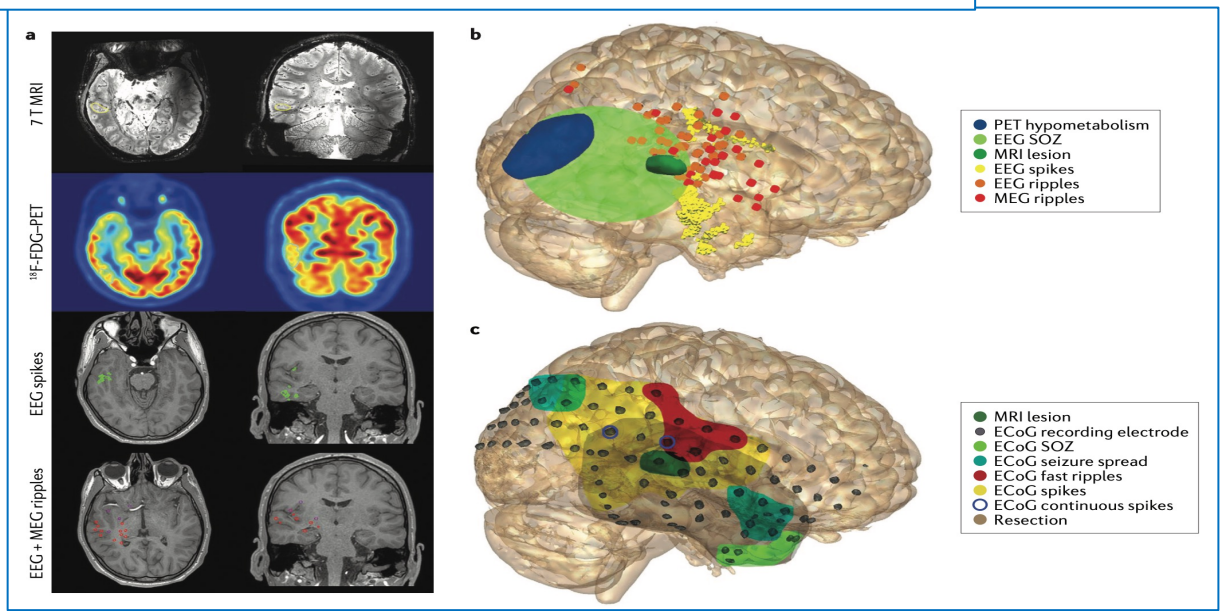
Multimodal Presurgical Evaluation of Medically Refractory





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Types of Epilepsy Surgery

สถาบันประสาทวิทยา
Neurological Institute of Thailand
65th year NIT

Resective Surgery

surgery which the most common type of epilepsy surgery where a small part of the brain that triggers the attack is removed.

Corpus callosotomys

MST

is usually performed in children who experience abnormal brain activity that speeds from one side to the other side of the brain.

Laser interstitial thermal therapys

therapy is a minimally invasive technique guided by MRI.

Hemispherectomy

Hemispherectomy in this procedure the gray matter of one hemisphere of the brain is removed.

Functional Hemispherectomy

Hemispherectomy is usually performed for children in which a seizure-inducing hemisphere is undercut thereby there is no loss of brain tissues.

Deep brain stimulation

VNS

RNS

stimulation is also an MRI guided procedure where an electrode is permanently implanted deep in the brain and generator to send electrical pulse is implanted in the chest.

Epilepsy surgery outcome classification

Table 1
Engel classification of epilepsy surgery outcome.

Class I (free of disabling seizures (excludes early post-op seizures))
- 1A: Completely seizure-free since surgery
- 1B: Non-disabling simple partial seizures only since surgery
- 1C: Some disabling seizures after surgery, but free of disabling seizures for at least 2 years
- 1D: Generalized convulsion with AED withdrawal only

Class II (rare disabling seizures "almost seizure-free")
- 2A: Initially free of disabling seizures but has rare seizures now
- 2B: Rare disabling seizures since surgery
- 2C: More than rare disabling seizures after surgery, but rare seizures for at least 2 years
- 2D: Nocturnal seizures only

Class III (worthwhile improvement)
- 3A: Worthwhile seizure reduction
- 3B: Prolonged seizure-free intervals amounting to greater than half the follow-up period, but not less than 2 years

Class IV (no worthwhile improvement)
- 4A: Significant seizure reduction
- 4B: No appreciable change
- 4C: Seizures worse

TABLE 1: ILAE classification of surgical outcome with respect to epileptic seizures.

Outcome classification	Definition
1	Completely seizure-free; no auras
2	Only auras; no other seizures
3	One to three seizure days per year; ±auras
4	Four seizure days per year to 50% reduction of baseline seizure days; ±auras
5	Less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; ±auras
6	More than 100% increase of baseline seizure days; ±auras

Therapeutics and Clinical Risk Management

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ORIGINAL RESEARCH

Efficacy and Safety of Epilepsy Surgery for Older Adult Patients with Refractory Epilepsy

Table 4 Detailed Seizure Outcomes Using the ILAE Seizure Outcome Scale and Histopathology of Surgical Specimens

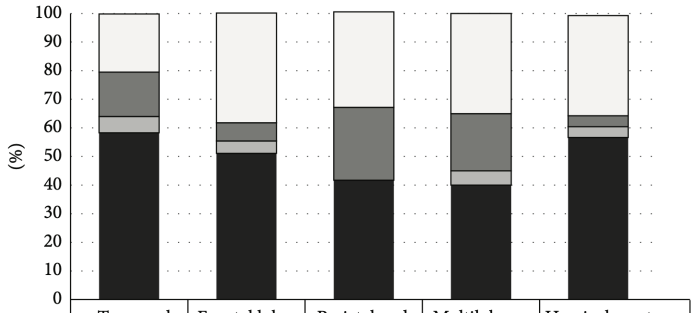
N=16	Temporal	Frontal	Multilober	Total
ILAE Class I	8		1	9 (56.3%)
Class II	1			1 (6.3%)
Class III	1		1	2 (12.5%)
Class IV	2	1	1	4 (25%)
	12 (75%)	1 (6.3%)	3 (18.8%)	
Histopathology				15
HS				3 (20%)
HS+AVM				1 (6.7%)
AVM				1 (6.7%)
FCD				3 (20%)
Gliosis				1 (6.7%)
Non specific				6 (40%)

Table 3 Neurological Deficits and Complications

Total 6 Cases (n=6/52: 11.5%)	
Permanent deficits	2 (3.8%)
Transient deficits & asymptomatic	4 (7.7%)
Intracranial hematoma	4
Hematoma removal	(2)
Observation	(2)
Cerebral infarction	1
Hydrocephalus	1
Invasive procedures	
Electrodes insertion	4
Resective epilepsy surgery	1
Wada test	1

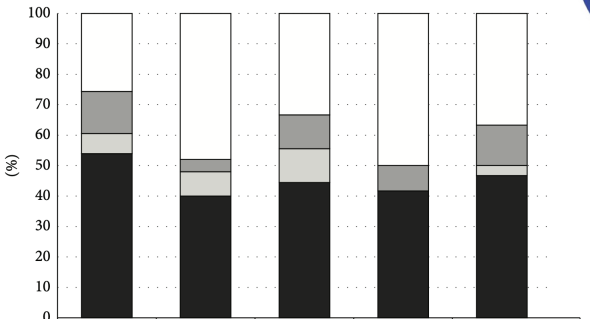
Conclusion: These results suggest that epilepsy surgery may represent a valuable approach in selected adult patients.

Epilepsy surgery outcome



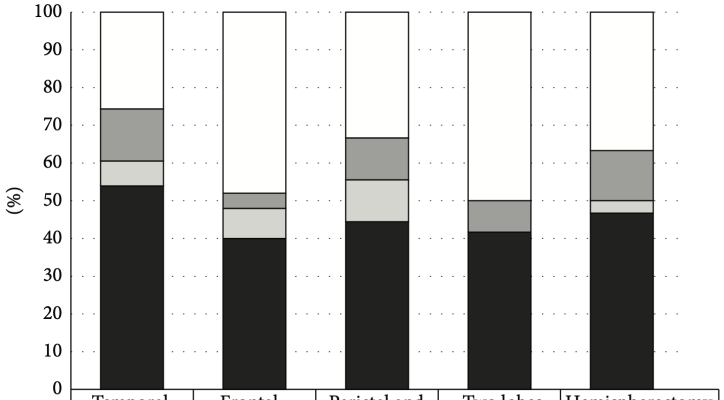
	Temporal lobe surgery	Frontal lobe surgery	Parietal and occipital lobes surgery	Multilobar surgery	Hemispherectomy
More than 3 seizures	20.30%	38.30%	33.30%	35.00%	35.00%
1–3 seizures	15.50%	6.40%	25.50%	20.00%	3.80%
Seizure-free with aura	5.70%	4.30%	0	5%	3.80%
Seizure-free with no aura	58.30%	51.10%	41.70%	40.00%	56.60%

FIGURE 1: first-year epilepsy surgery outcome according to procedure.



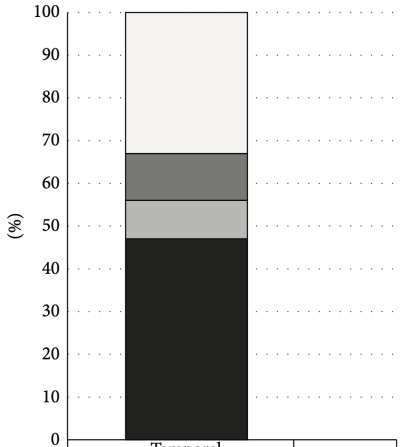
	Temporal lobectomy/ lesionectomy	Frontal lobectomy/ lesionectomy	Parietal and occipital lobectomy/ lesionectomy	Two lobes surgery	Hemispherectomy
More than 3 seizures	25.60%	48.00%	33.30%	50.00%	36.70%
1–3 seizures	13.80%	4.00%	11.10%	8.30%	13.30%
Seizure-free with aura	6.60%	8.00%	11.10%	0	3.30%
Seizure-free with no aura	53.80%	40.00%	44.40%	41.70%	46.70%

FIGURE 2: The third-year epilepsy surgery outcome according to procedure.



	Temporal lobectomy/ lesionectomy	Frontal lobectomy/ lesionectomy	Parietal and occipital lobectomy/ lesionectomy	Two lobes surgery	Hemispherectomy
More than 3 seizures	25.60%	48.00%	33.30%	50.00%	36.70%
1–3 seizures	13.80%	4.00%	11.10%	8.30%	13.30%
Seizure-free with aura	6.60%	8.00%	11.10%	0	3.30%
Seizure-free with no aura	53.80%	40.00%	44.40%	41.70%	46.70%

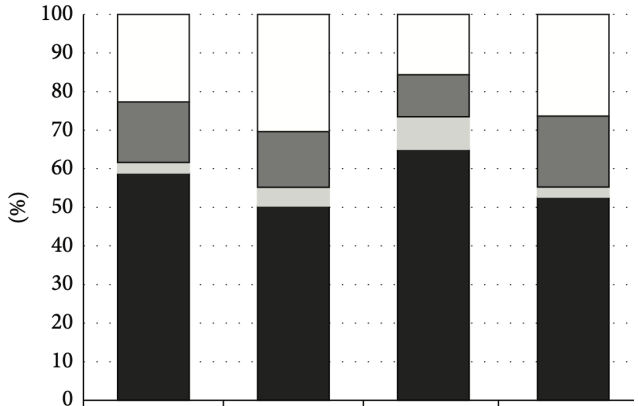
FIGURE 2: The third-year epilepsy surgery outcome according to procedure.



	Temporal lobectomy/ lesionectomy	
More than 3 seizures	33.00%	
1–3 seizures	11.00%	
Seizure-free with aura	9.00%	
Seizure-free with no aura	47%	

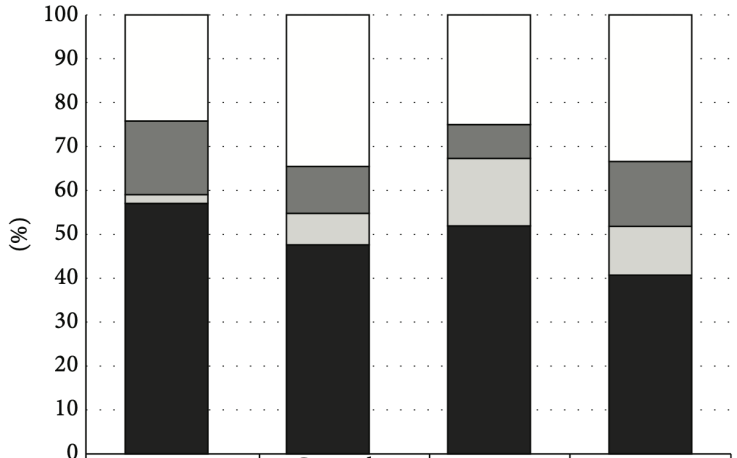
FIGURE 3: The fifth year epilepsy outcome temporal lobe surgery.

Epilepsy surgery outcome



	Mesial temporal sclerosis	Cortical dysplasia/ heterotopia	CNS tumors	Dual patholog
More than 3 seizures	22.70%	30.40%	15.66%	26%
1–3 seizures	15.67%	14.40%	10.84%	18.40%
Seizure-free with aura	2.70%	4.80%	8.43%	2.60%
Seizure-free with no aura	58.90%	50.40%	65.06%	52.60%

FIGURE 5: The first-year epilepsy surgery outcome according to histopathology.



	Mesial temporal sclerosis	Cortical dysplasia /heterotopia	CNS tumors	Dual pathology
More than 3 seizures	24.00%	34.52%	25.00%	33.40%
1–3 seizures	17%	10.72%	7.70%	14.80%
Seizure-free with aura	2.00%	7.14%	15.40%	11.10%
Seizure-free with no aura	57%	47.62%	51.90%	40.70%

FIGURE 6: The third-year epilepsy surgery outcome according to histopathology.

Effectiveness of Epilepsy Surgery

Systematic Reviews

Study	Research Question	Years, Sources Searched	Number of Studies Included	Pooled Seizure Outcome
Englot et al, 2011 (6)	What are the predictors of seizure freedom in the surgical treatment of supratentorial cavernous malformations?	1985–2011, PubMed	31 (1,226 patients)	75% seizure-free
Seiam et al, 2011 (7)	What are the preoperative, operative, and postoperative variables that influence HRQOL after epilepsy surgery in adults?	1950–2008; MEDLINE, EMBASE, Cochrane	39 (3,373 patients)	58.1% seizure-free 35.4% seizure improvement 6.5% no improvement
Tellez-Zenteno et al, 2010 (8)	What are the seizure outcomes in patients undergoing epilepsy surgery and how consistent are the results across studies?	1995–2007, MEDLINE, EMBASE, Cochrane	40 (3,557 patients)	**TL + XTL** 68% seizure-free (lesional) (95% CI, 66–70) 43% seizure-free (nonlesional) (95% CI, 39–46) **TL** 69% seizure-free (lesional) (95% CI, 66–70) 45% seizure-free (nonlesional) (95% CI, 40–49)
Schmidt & Stavem, 2009 (5)	What are the long-term seizure outcomes of surgery versus no surgery for drug-resistant partial epilepsy?	1947–2007, MEDLINE, EMBASE, Index Medicus, Cochrane	20 (1,621 patients)	Surgical: 44% seizure-free; control: 12 % seizure-free (RR 4.26; 95% CI, 3.03–5.98)
Tellez-Zenteno et al, 2005 (9)	What are the long-term (> 5 years) seizure outcomes following epilepsy surgery?	1991–2003, MEDLINE, Index Medicus, Cochrane	76 (7,343 patients)	**TL** 66% seizure-free (95% CI, 62–70) **TL + XTL** 59% seizure-free (95% CI, 56–62) **Frontal** 27% seizure-free (95% CI, 23–30)
Tonini et al, 2004 (10)	What are the predictors of epilepsy surgery outcome?	1984–2001, MEDLINE	47 (3,511 patients)	63% 'good outcome' 21% 'improved outcome' 12% 'poor outcome'

Health Quality Ontario. Epilepsy surgery: an evidence summary. Ont Health Technol Assess Ser [Internet]. 2012

Study or Subgroup	Surgical patients Events	Total	Non-surgical patients Events	Total	Risk Ratio M-H, Random, 95% CI
Altshuler 1999	34	49	4	13	2.26 [0.98, 5.20]
Bien 2006	68	131	31	253	4.24 [2.93, 6.12]
Derry 2001	22	30	2	9	3.30 [0.95, 11.42]
Engel* 2012	11	15	0	23	34.50 [2.18, 545.02]
Gillam 1999	81	125	0	71	93.14 [5.86, 1479.28]
Jones 2002	39	61	1	23	14.70 [2.14, 100.92]
Kumlien 2002	26	36	11	47	3.09 [1.77, 5.38]
Markand 2000	32	53	0	33	40.93 [2.59, 646.55]
McLachlin 1997	17	40	0	13	11.95 [0.77, 185.99]
Mikati 2006	17	20	6	17	2.41 [1.23, 4.70]
Mikati 2010	15	19	4	19	3.75 [1.52, 9.23]
Picot 2008	64	82	16	104	5.07 [3.19, 8.08]
Stavem 2008	33	69	13	69	2.54 [1.47, 4.39]
Vickrey 1995	61	202	3	46	4.63 [1.52, 14.11]
Wiebe* 2001	23	40	3	40	7.67 [2.50, 23.51]
Yasuda 2006	19	26	9	75	6.09 [3.16, 11.73]
Total (95% CI)		**998**		**855**	**4.30 [3.14, 5.87]**
Total events	562		103		

Heterogeneity: Tau² = 0.16; Chi² = 30.50, df = 15 (P = 0.01); I² = 51%

Test for overall effect: Z = 9.15 (P < 0.00001)

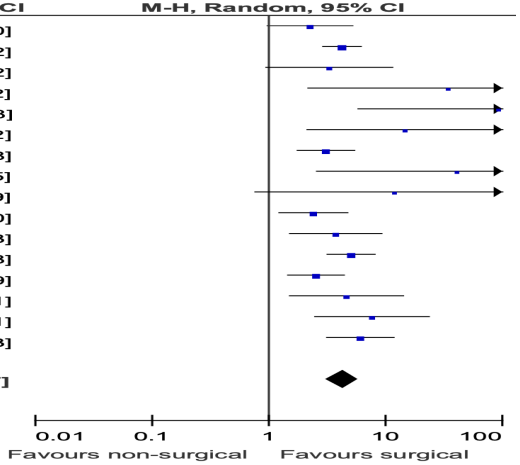


Figure 2: Forest Plot of All Studies Comparing Epilepsy Surgery to No Surgery Since 1995

Abbreviations: CI, confidence interval; M–H, Mantel–Haenszel.

* Randomized controlled trials (11;12)

Study or Subgroup	Surgical patients Events	Total	Non-surgical patients Events	Total	Risk Ratio M-H, Random, 95% CI
Engel* 2012	11	15	0	23	34.50 [2.18, 545.02]
Gillam 1999	81	125	0	71	93.14 [5.86, 1479.28]
Markand 2000	32	53	0	33	40.93 [2.59, 646.55]
McLachlin 1997	17	40	0	13	11.95 [0.77, 185.99]
Wiebe* 2001	23	40	3	40	7.67 [2.50, 23.51]
Yasuda 2006	19	26	9	75	6.09 [3.16, 11.73]
Total (95% CI)		**299**		**255**	**13.99 [4.61, 42.44]**
Total events	183		12		

Heterogeneity: Tau² = 0.94; Chi² = 12.09, df = 5 (P = 0.03); I² = 59%

Test for overall effect: Z = 4.66 (P < 0.00001)

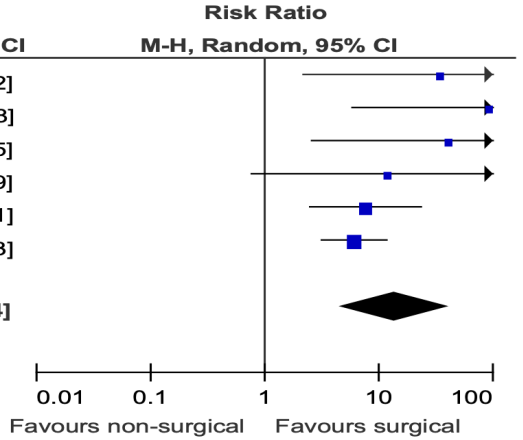


Figure 3: Forest Plot of Studies Comparing Epilepsy Surgery to No Surgery With 1 to 2 Years' Follow-up

Abbreviations: CI, confidence interval; M–H, Mantel–Haenszel.

* Randomized controlled trials (11;12)

	Surgical patients		Non-surgical patients		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI
Altshuler 1999	34	49	4	13	2.26 [0.98, 5.20]
Bien 2006	68	131	31	253	4.24 [2.93, 6.12]
Derry 2001	22	30	2	9	3.30 [0.95, 11.42]
Jones 2002	39	61	1	23	14.70 [2.14, 100.92]
Kumlien 2002	26	36	11	47	3.09 [1.77, 5.38]
Mikati 2006	17	20	6	17	2.41 [1.23, 4.70]
Mikati 2010	15	19	4	19	3.75 [1.52, 9.23]
Picot 2008	64	82	16	104	5.07 [3.19, 8.08]
Vickrey 1995	61	202	3	46	4.63 [1.52, 14.11]
Total (95% CI)		**630**		**531**	**3.82 [3.08, 4.73]**
Total events	346		78		

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.06$, df = 8 (P = 0.43); $I^2 = 1\%$

Test for overall effect: Z = 12.18 (P < 0.00001)

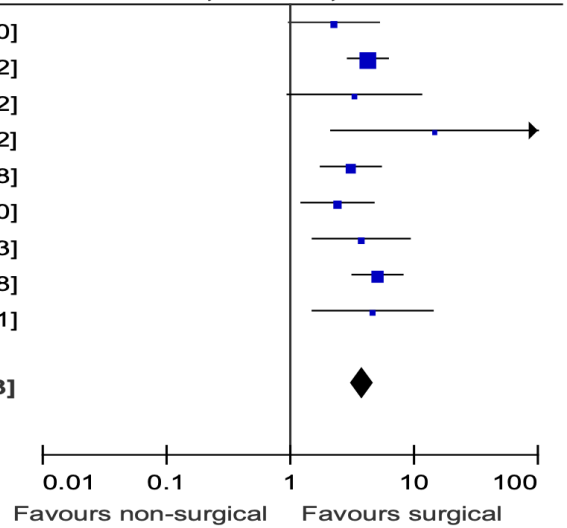


Figure 4: Forest Plot of Studies Comparing Epilepsy Surgery to No Surgery With 3 or More Years' Follow-up

Safety of Epilepsy Surgery

Systematic Reviews

Study	Study Design	Years	Number of Patients	Patient Population	Duration of Follow-up	Complications
Terra et al, 2010 (28)	Retrospective cohort	1995–2008	267	Children (< 18 years)	Mean [SD] = 5.5 [3.7] years	Only mortality data reported 2 deaths due to acute surgical complications 7 deaths in 2–10 years postsurgery (5 pneumonia, 1 sudden death, 1 status epilepticus)
Koubeissi et al, 2009 (27)	Retrospective cohort (inpatient health administrative data)	2000–2005	484	Inpatients	Duration of in-hospital stay	No surgical mortality Depression (n = 34) Intracerebral hemorrhage (n = 13) Visual field defect (n = 3)
Kim et al, 2008 (29)	Retrospective cohort	1993–2005	134	Children (8 months to 18 years)	62.3 months (range, 12–168 months)	No surgical mortality Brain swelling leading to removal of grid (n = 2) Subdural hematoma (n = 1) Visual field defect (n = 13) Permanent hemiparesis (n = 3)
Sindou et al, 2006 (30)	Retrospective cohort	1994–2003	100	Adults (18–58 years)	Mean 4.5 years (range, 1–10 years)	No surgical mortality Permanent mild hemiparesis (n = 2) Durable depressive state (partial recovery) (n = 3) Transient complications (n = 14)
Clusmann et al, 2004 (31)	Retrospective cohort	1995–2000	442	All ages	Unclear	No surgical mortality Symptomatic postoperative hemorrhages (n = 17) Permanent mild deficits (n = 33)
Salanova et al, 2002 (32)	Retrospective cohort	1984–1999	215	All ages (8 – 57 years) Patients with TLE	Mean 7 years (range, 1–15 years)	No surgical mortality Mortality—3 deaths during seizures, 3 deaths unexplained, 2 suicide, 2 accidents, 1 breast cancer (n = 11) Mild hemiparesis (n = 2) Infections (n = 3) Transient cranial nerve palsies (n = 7) Verbal memory loss (n = 19)
Rydenhag and Silander, 2001 (33)	Retrospective cohort (data from Swedish National Epilepsy Surgery Register)	1990–1995	654 (205 invasive electrode procedures, 449 therapeutic procedures)	All ages (6 months to 67 years) All surgery types	< 2 years	Invasive electrode procedures: Infection (n = 4) Hematoma (n = 7) Dislocation of electrode (n = 2) Therapeutic procedures: **Hematoma causing death (n = 1)** Hemiparesis (major) (n = 10) Hemianopia (major) (n = 2) Infection (minor) (n = 23) Other minor (n = 17)
Behrens et al, 1997 (34)	Retrospective cohort	1987–1992	429	All ages (4 months to 67 years)	Mean 3 years (range, 1–7.3 years)	No surgical mortality Transient surgical complications (n = 33) Permanent surgical complications (hydrocephalus) (n = 3) Transient neurological complications (n = 13) Permanent neurological complications (hemiparesis, dysphasia, disconnection syndrome) (n = 10)

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