Surgical Treatment for DRE

Resection or Neuromodulation

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Outline

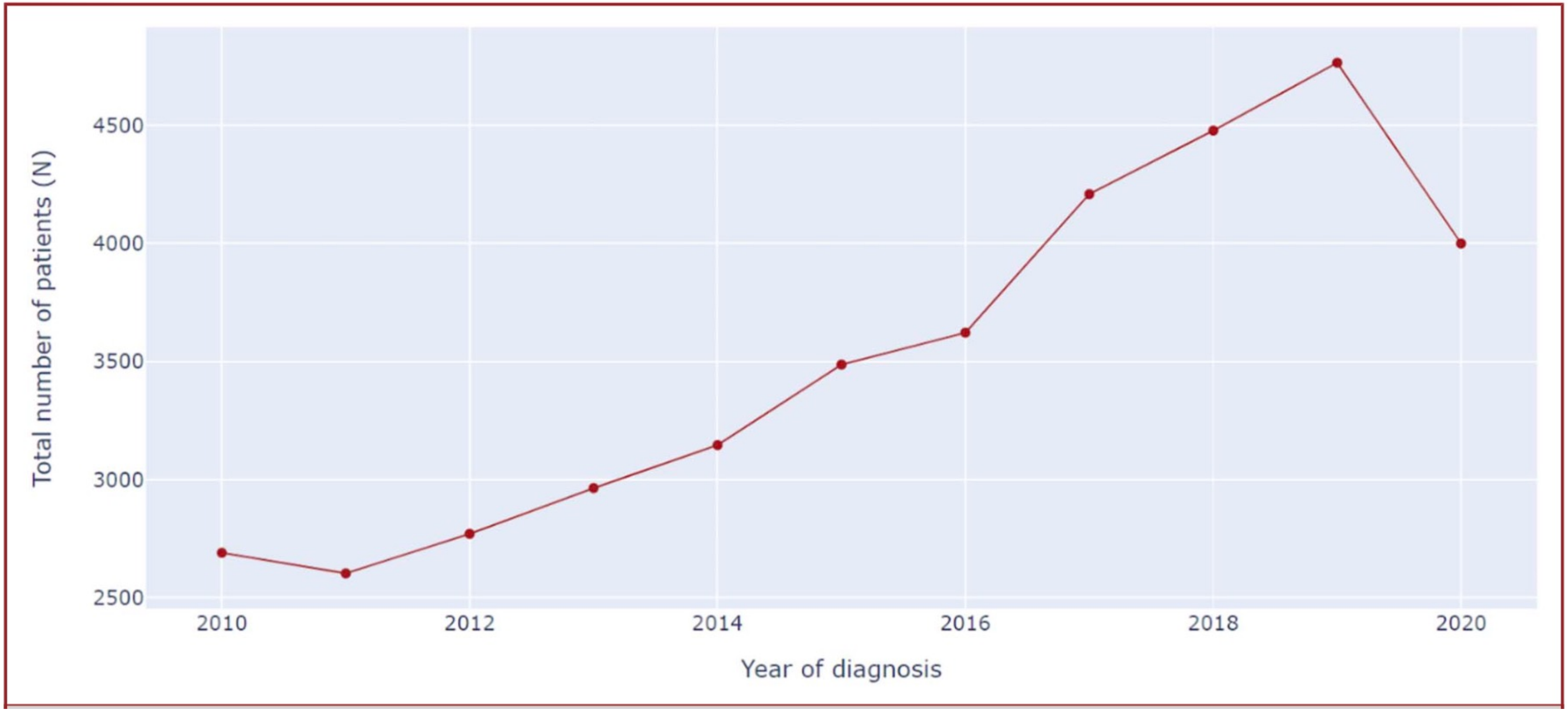
- Introduction
- Evolution & current concept of Epileptogenic zone.
- Decision making in Epilepsy Surgery in 2020s.
- Presurgical assessment of Epilepsy Surgery in 2020s.
- Treatment alogrithm & Surgical Tools for Epilepsy.
    - Resection, Ablation, Neuromodulation
- Case: What’s your opinion?
- Conclusion

Drug-resistance epilepsy (DRE)

- **Failure** of **adequate trials of two or more** tolerated, appropriately chosen and used **AEDs** to achieve sustained seizure-free outcomes. (Kwan P2010, Scheffer IE 2017)

- Prevalence: **30-40%** (36.3%) **of epilepsy patients** (50.4-81.7 / 100,000 people annually) (Sultana B 2021)

- Surgery is currently the primary treatment.



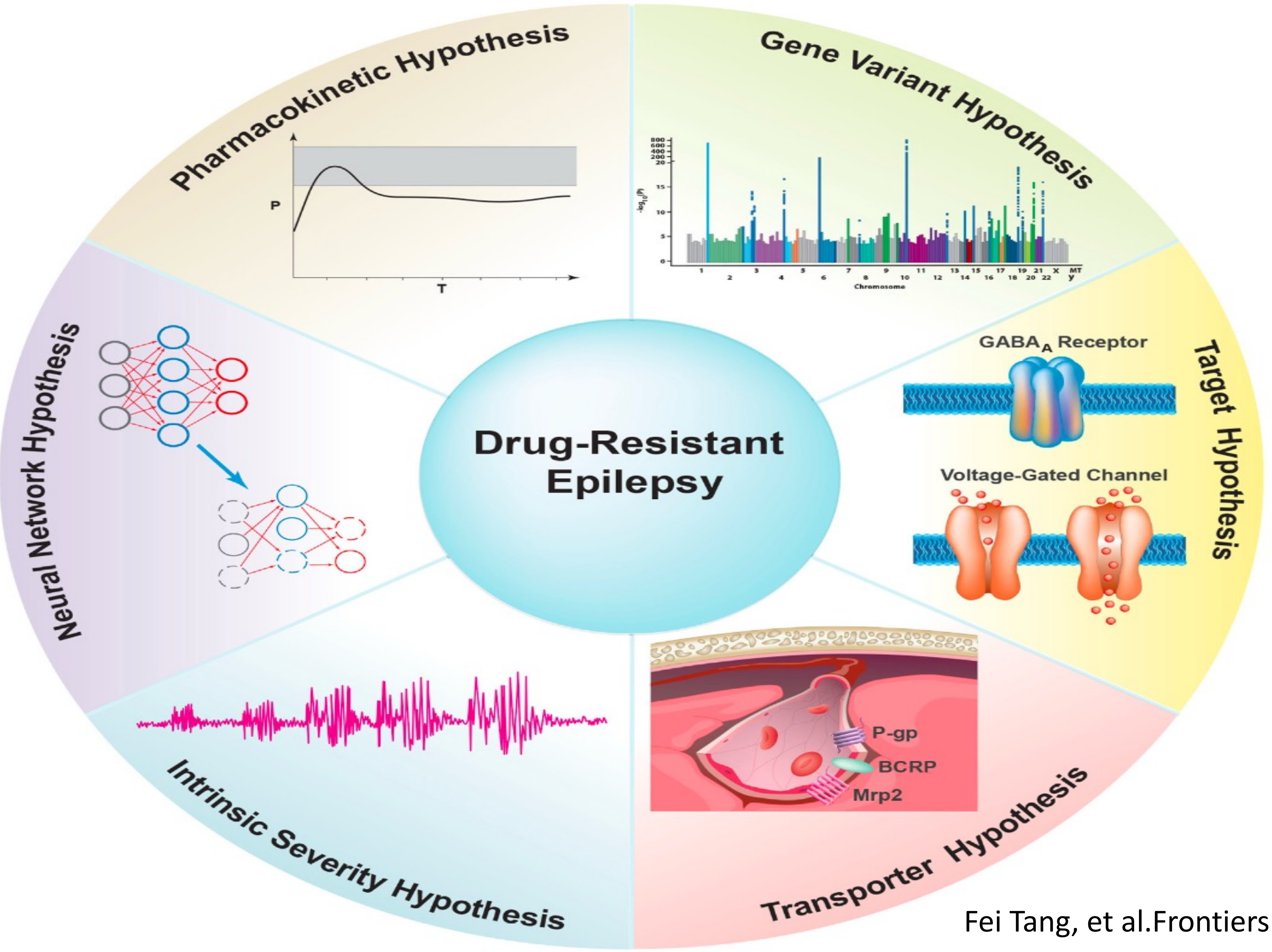
Patients admitted with a diagnosis of drug-resistant focal epilepsy

Using the National Inpatient Sample (NIS) database

Abdul K Ghaith, et al. Neurosurgery 2024

Number of ASDs	Seizure-free patients (% of total cohort)
1	49.5
2	13.3
3	3.7
4	1.0
5	0.4
6	0.2
7	0.2
8	0
9	0

Modified from Bodie, et al. Neurology 2012



Fei Tang, et al.Frontiers in Neurology 2017


DECISION MAKING in Epilepsy Surgery
in 2020s

What is your opinion ?

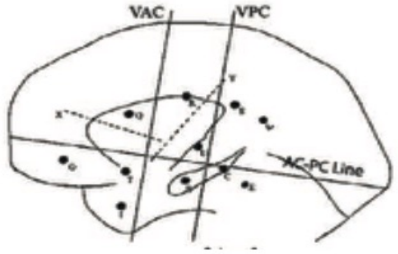
- a — 18 Y Female
- b — 13 Y Girl
- c — 08 Y Girl
- d — 37 Y Male
- e — 33 Y Female

Evolution of the epileptogenic zone (EZ)

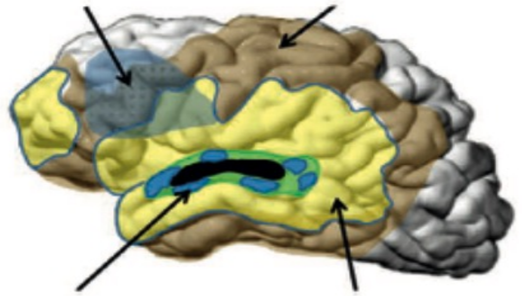
ECoG 1950's | SEEG 1960's | SDE 1990's | 2015

Primary Localization
Secondary Localization
Tertiary Localization

Ictal onset
Zone of primary organization



Spatiotemporal zones of ictal dynamics



Epileptogenic Lesion: 1950s
Herbert Jasper, et al

Jasper HH, et al. Epilepsia 1961

Epileptogenic Zone: 1960s
Talairach & Bancaud

Talairach J,et al. Confin Neurol 1966

Five Cortical Zone: 1990s
Luders et al

Luders HO, et al.Surgical Treatment of the Epilepsy (2nd.ed) 1993

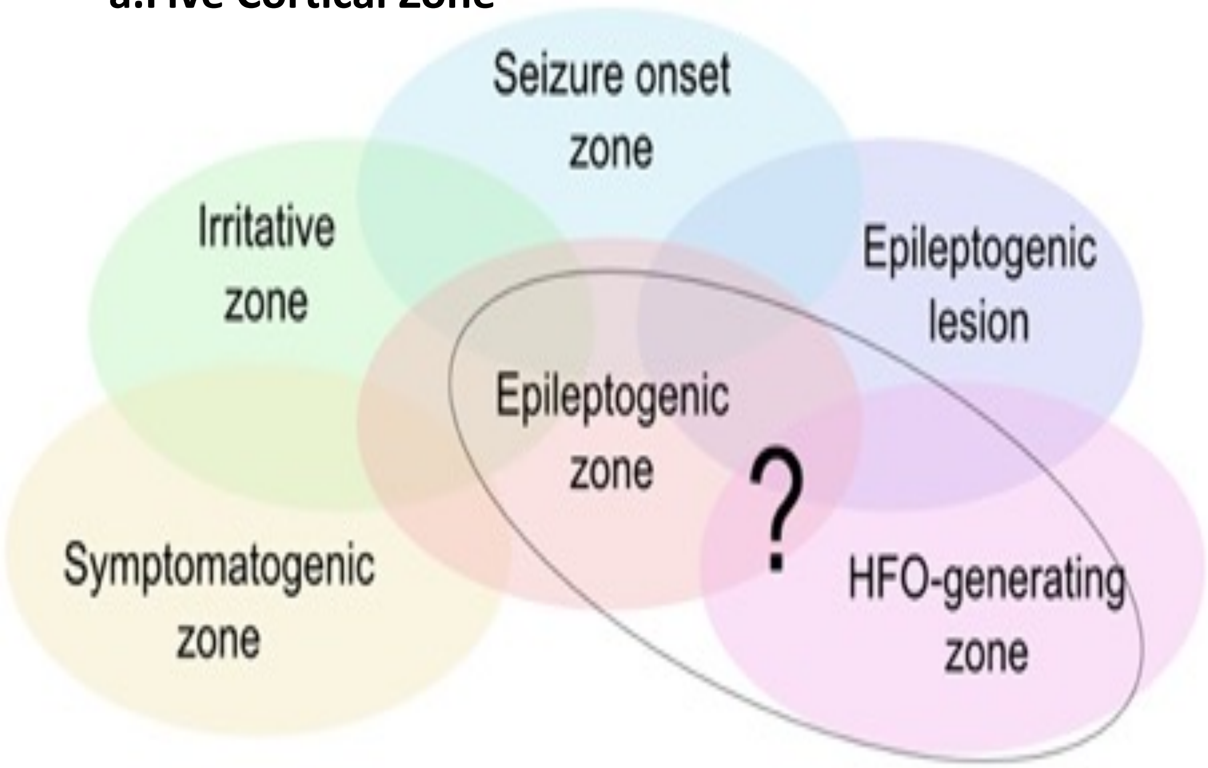
Network Epilepsy: 2000s to Present
Spencer SS.

Spencer SS. Epilepsia 2002

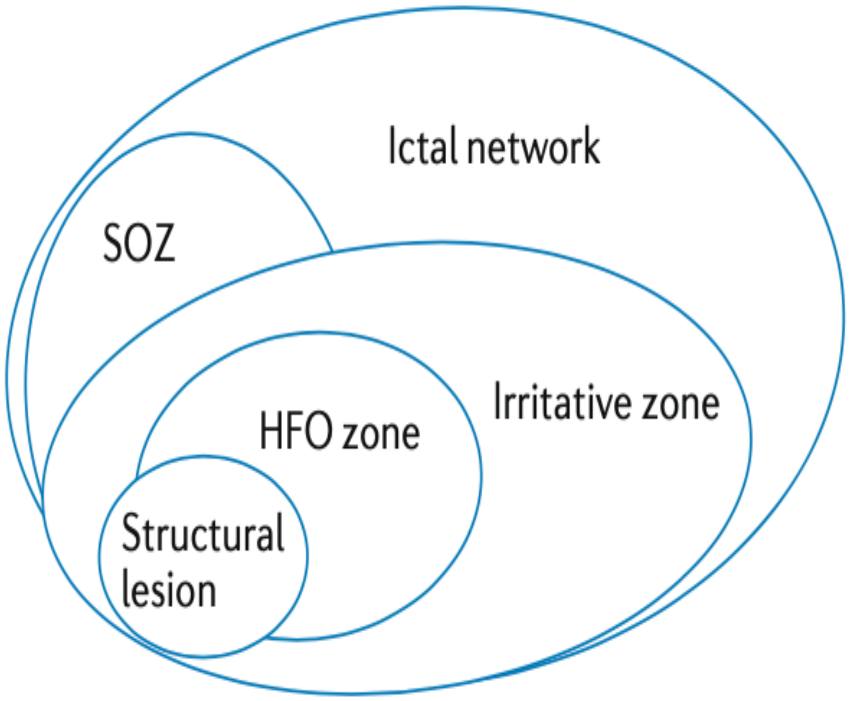
Modified from Lara Jehi. Epilepsy Currents 2028

Concepts of the epileptogenic brain

a.Five Cortical Zone



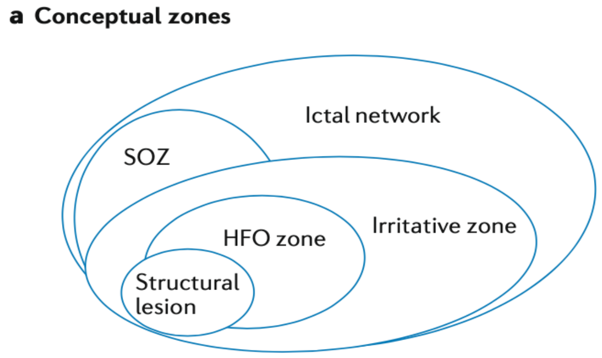
b.Network Epilepsy

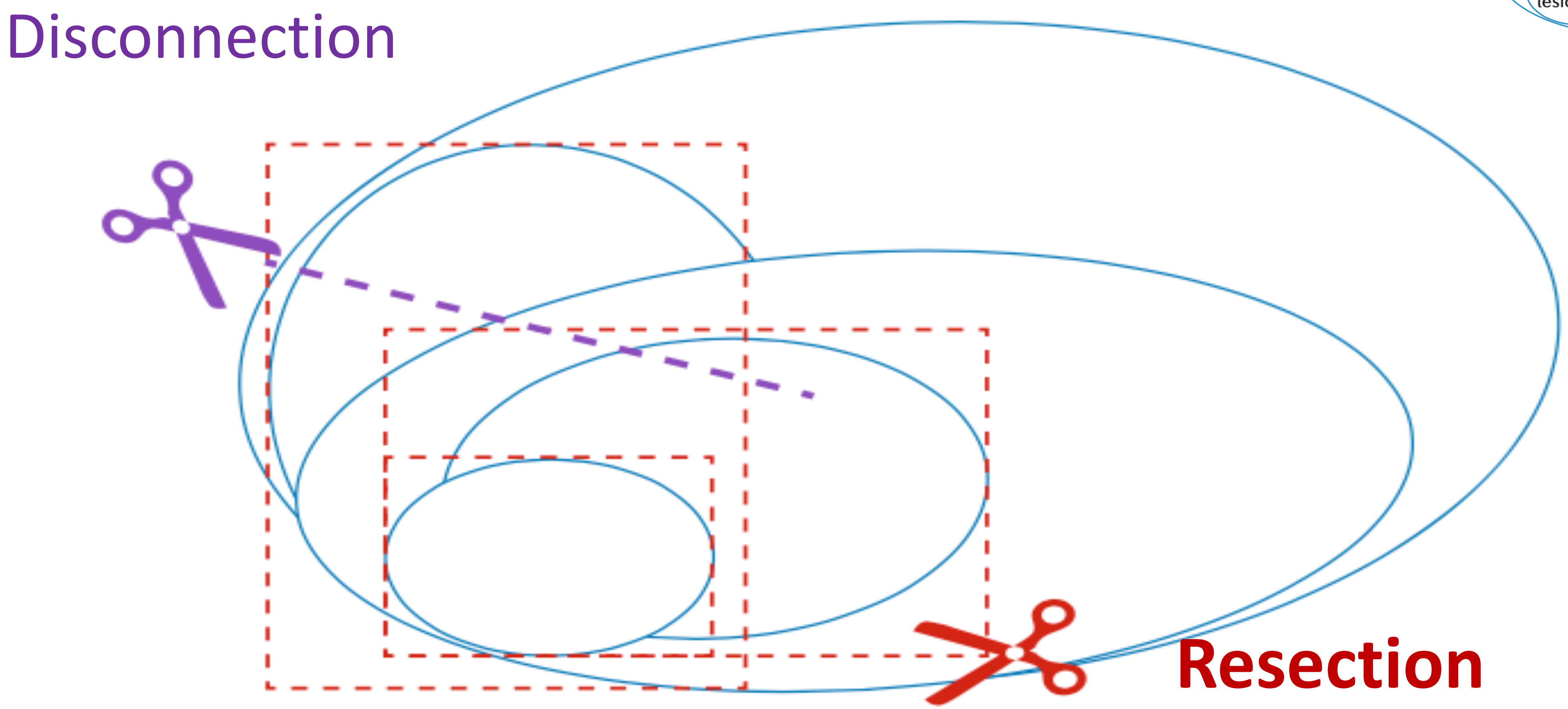


Rosenow F, Luders H. Brain 2001

Zijlmans Maeike, et al. 2019

Surgical strategies





Zijlmans Maeike, et al. 2019

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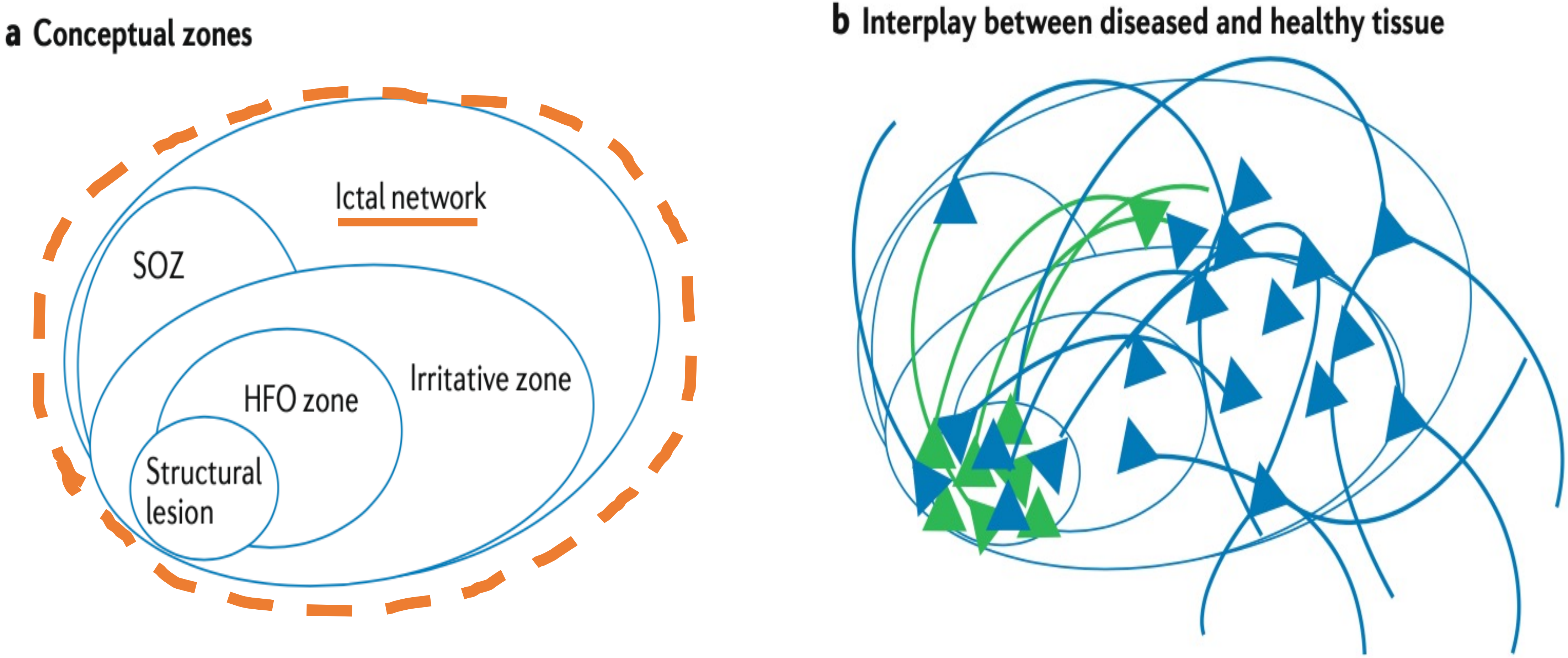
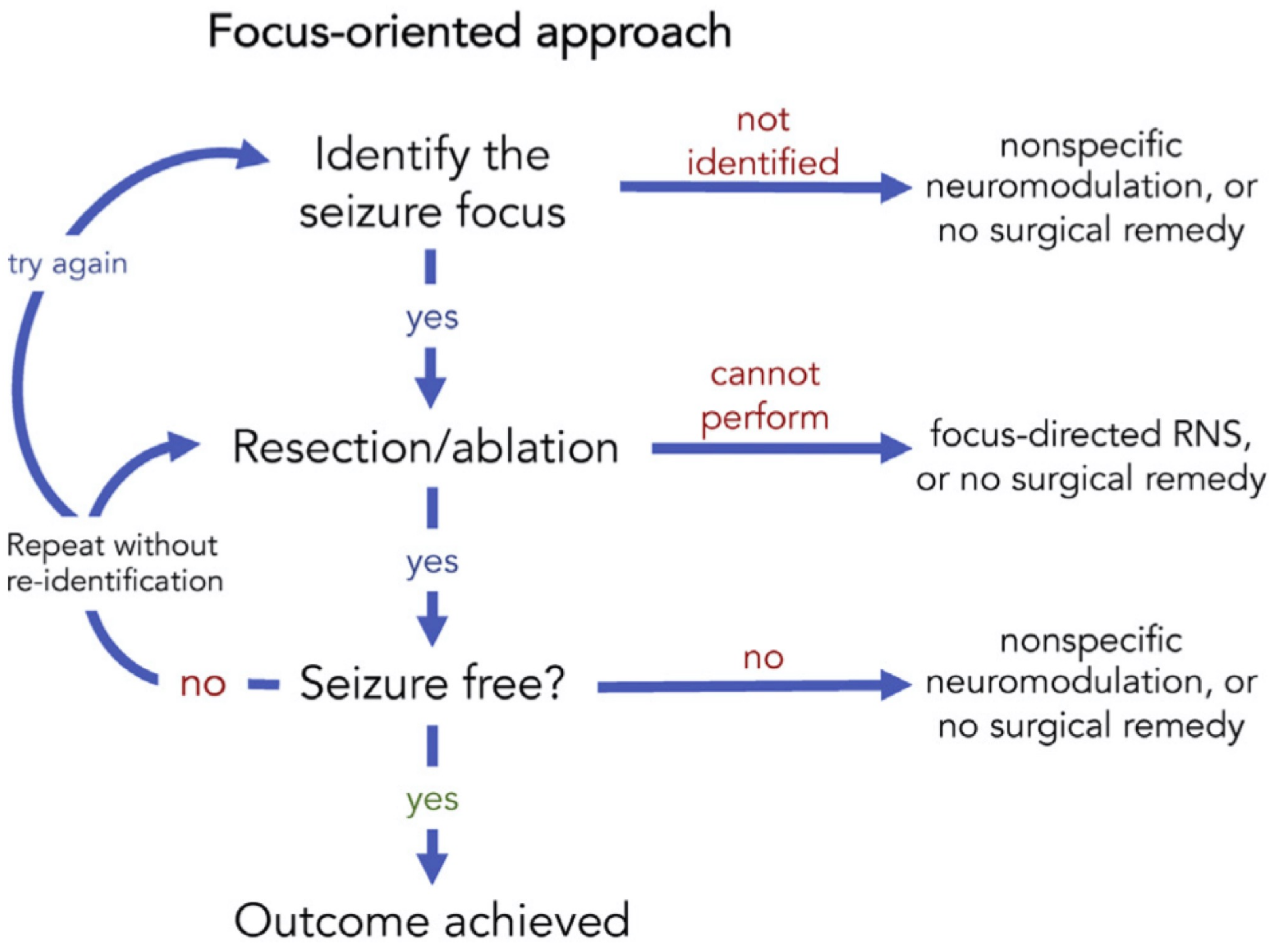


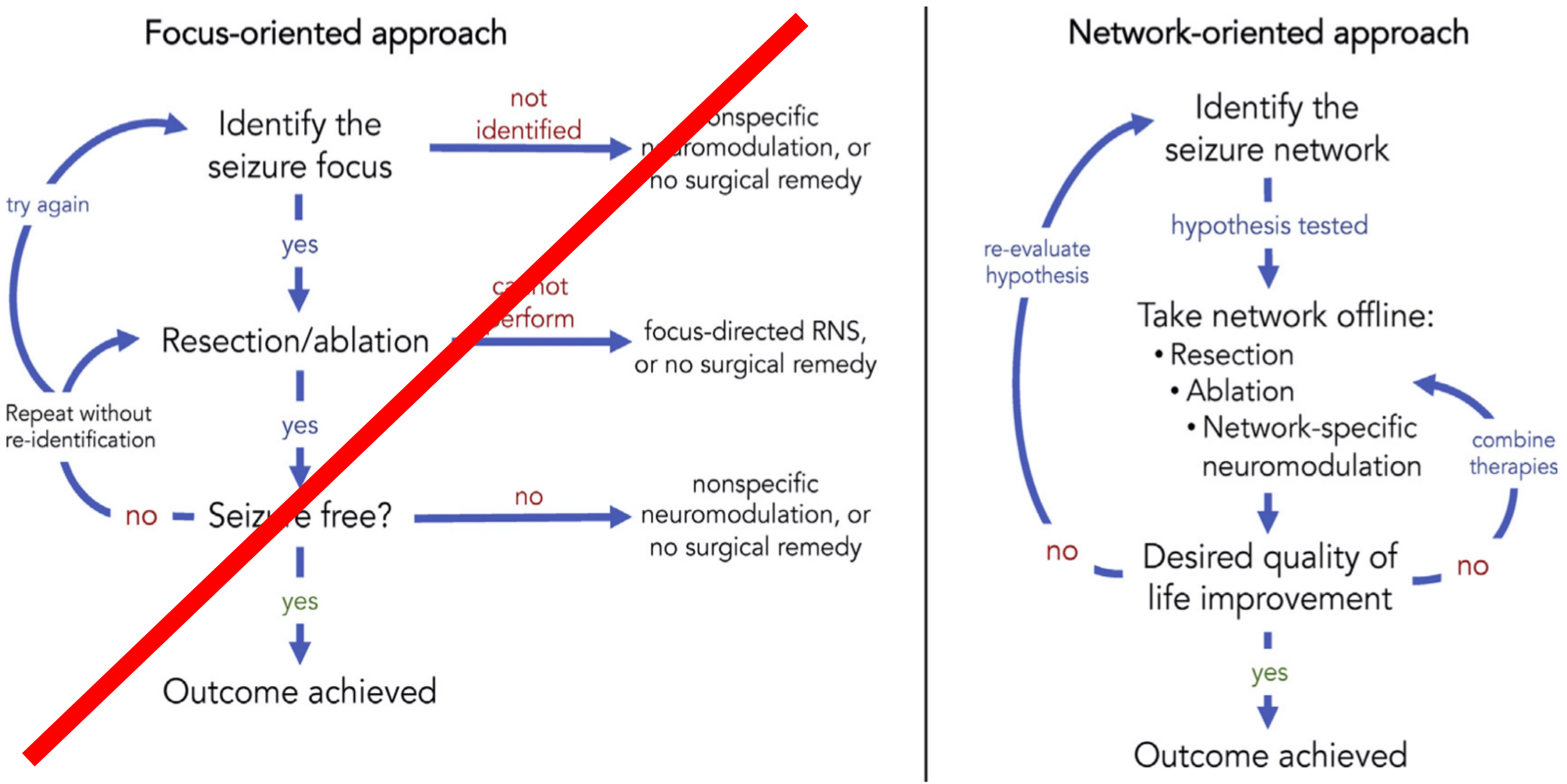
Zijlmans Maeike, et al. 2019

Decision Making in Epilepsy Surgery

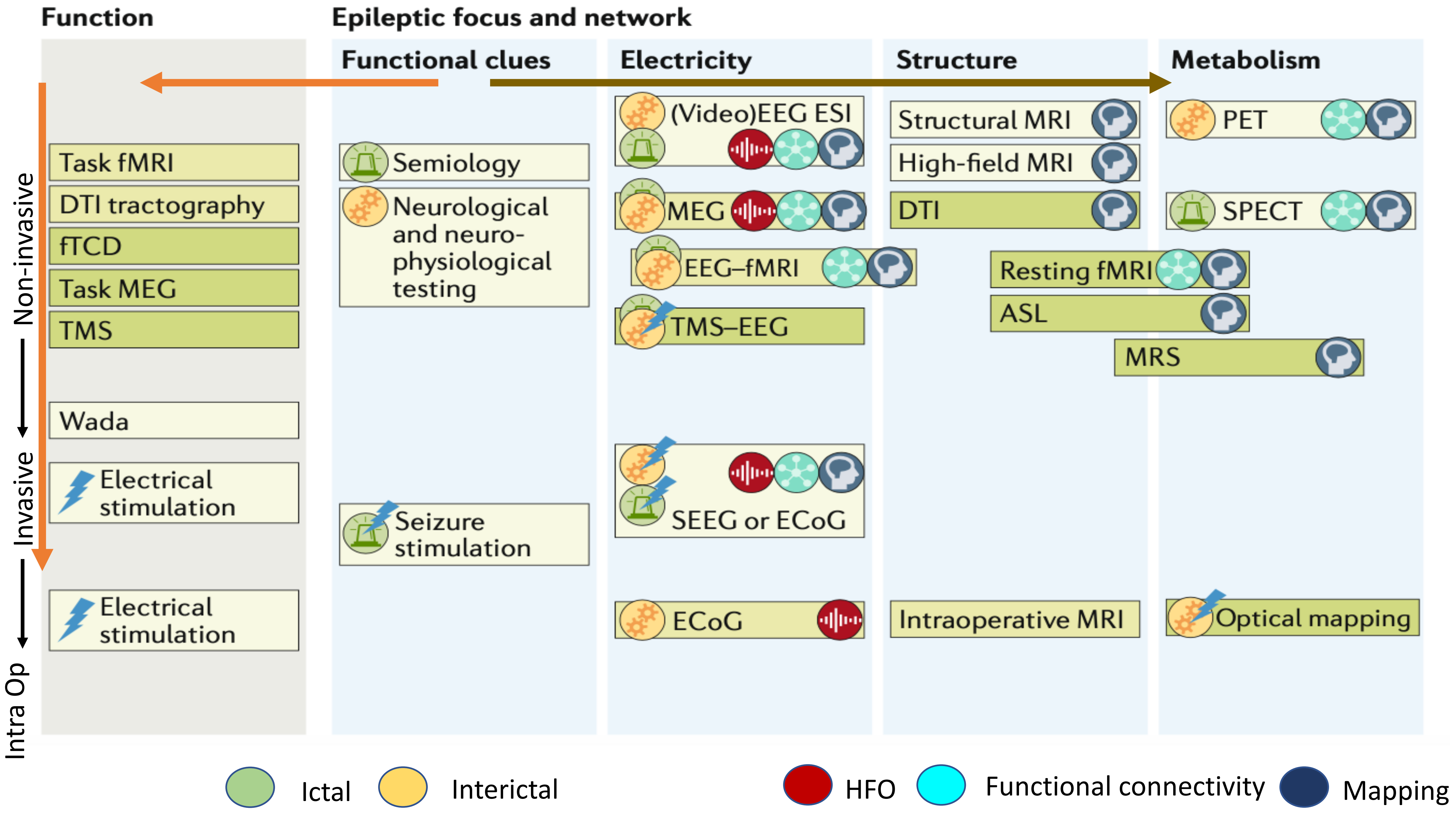


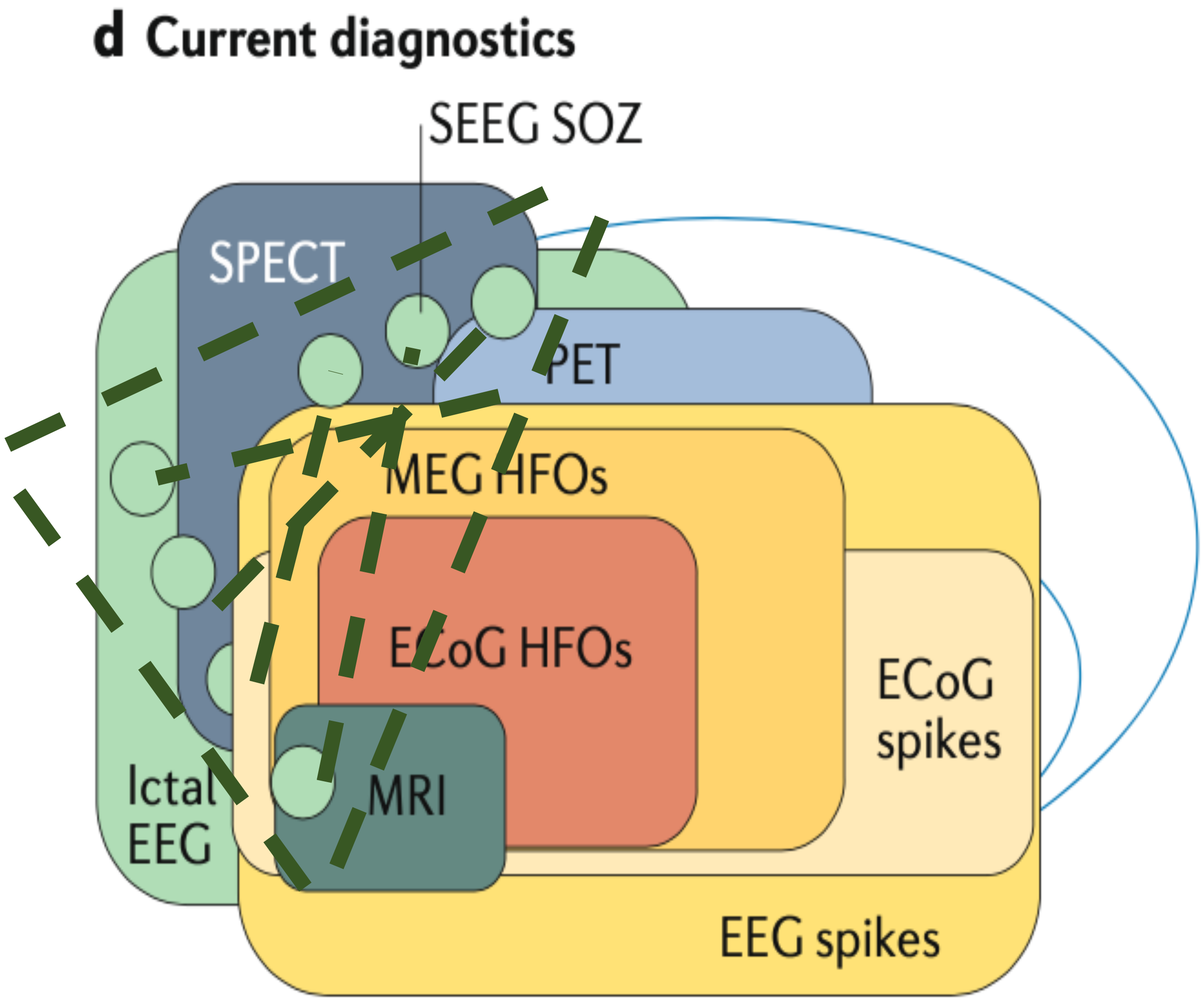
Richardson R Mark. 2020

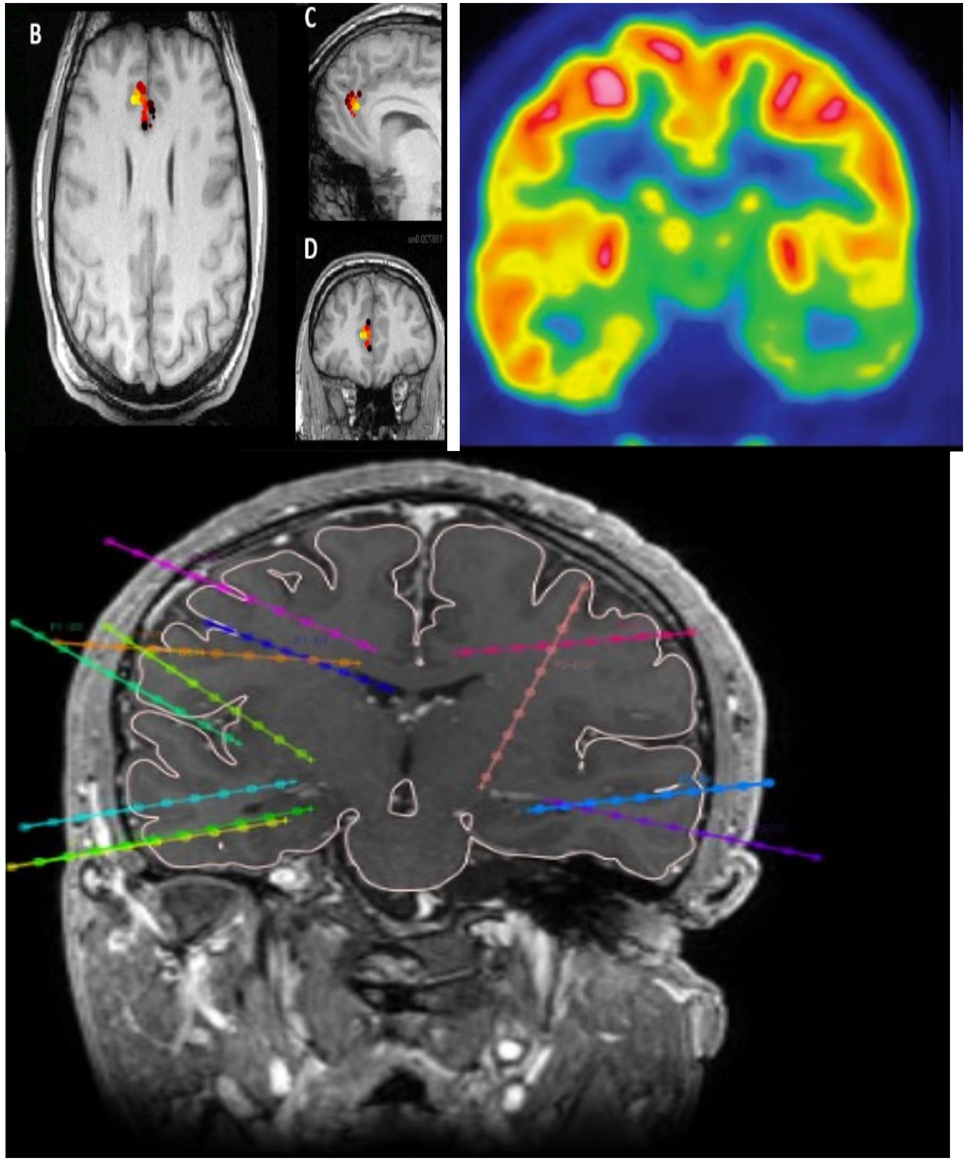
Decision Making in Epilepsy Surgery in 2020s Richardson R Mark.2020



Presurgical assessment in 2020s



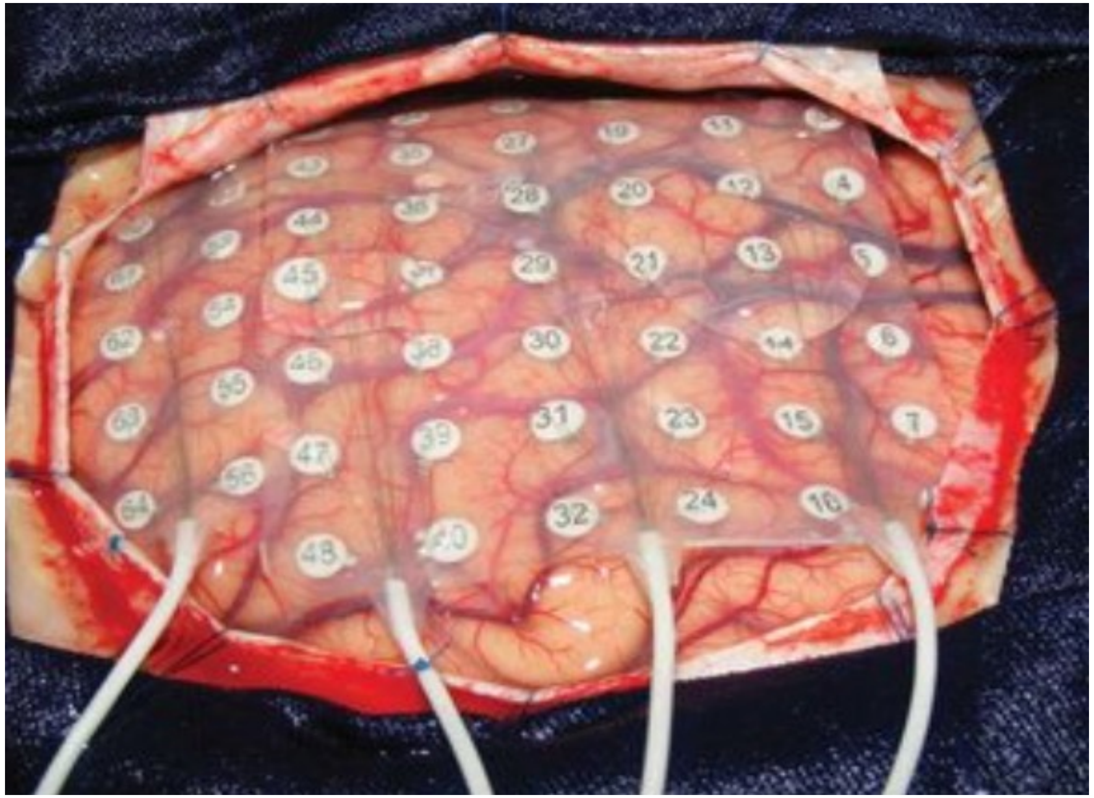


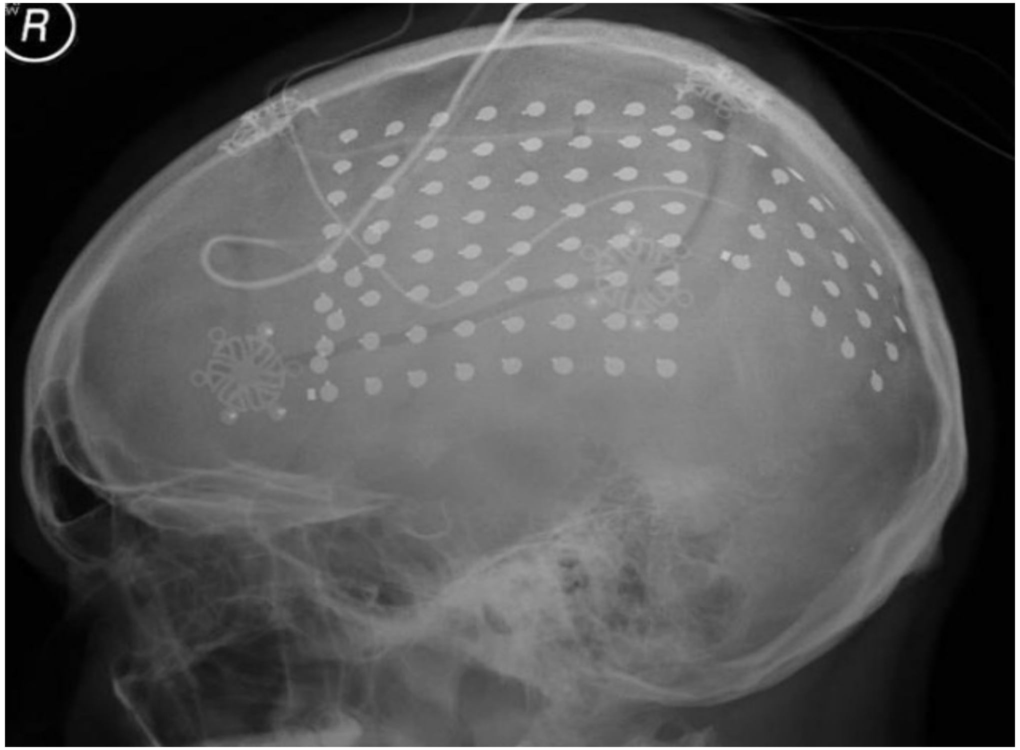


Zijlmans Maeike, et al. 2019

Invasive investigation

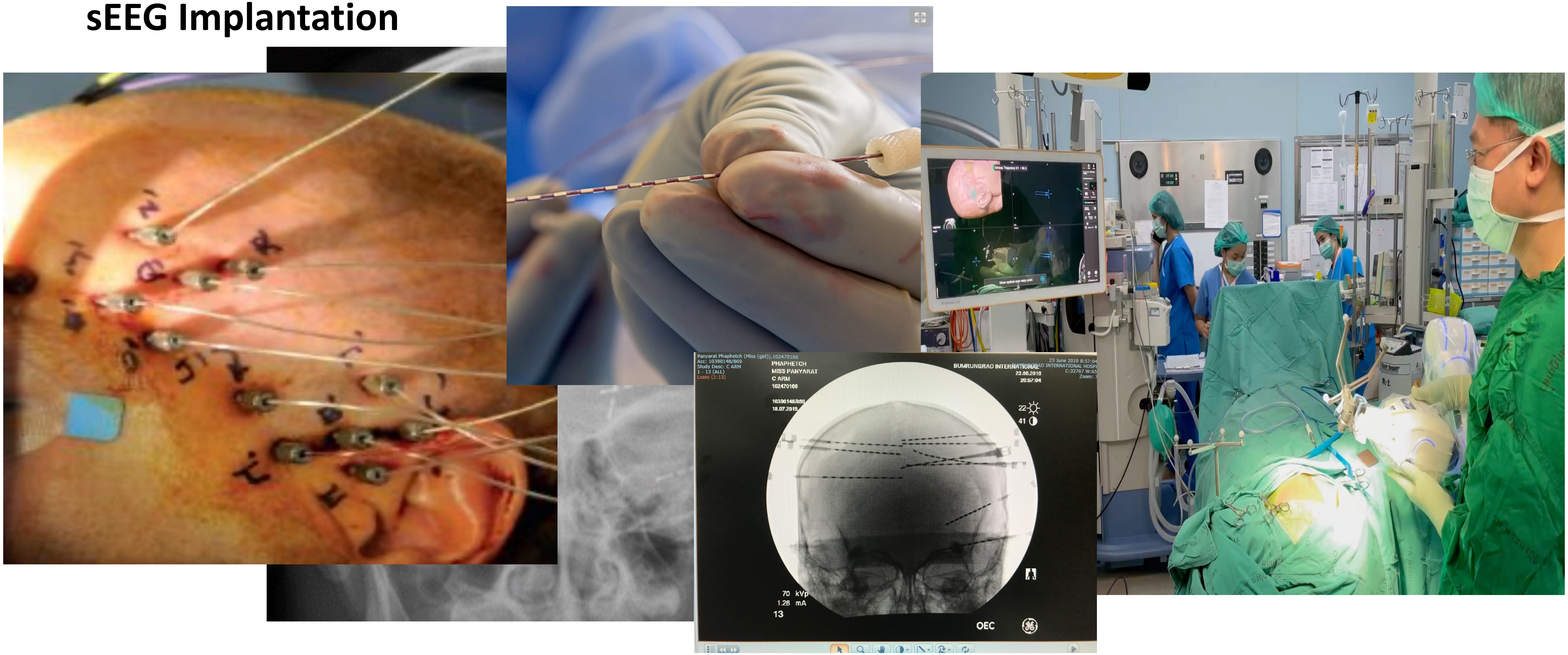
Subdural Grid Implantation



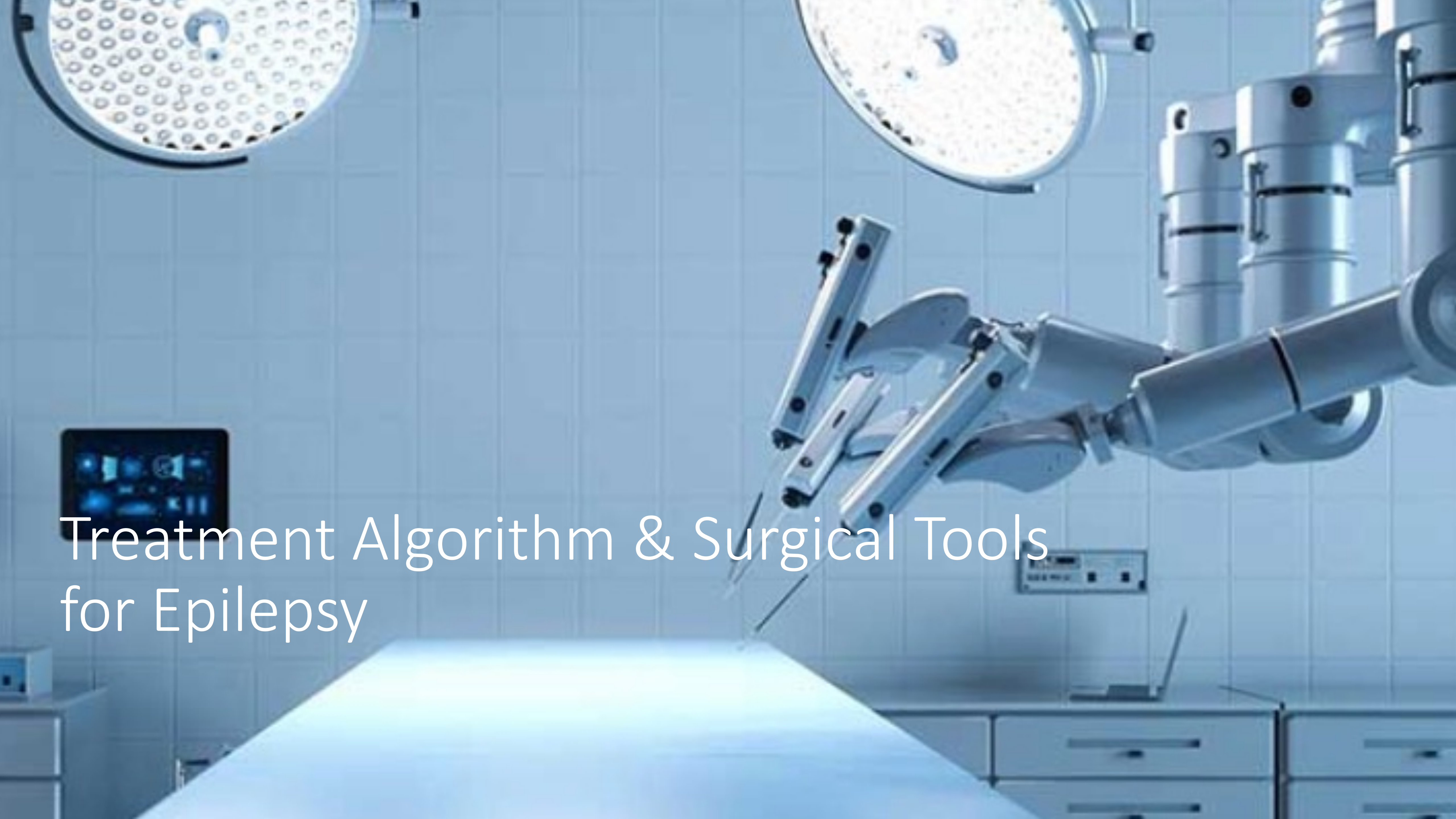


Less Invasive Investigation

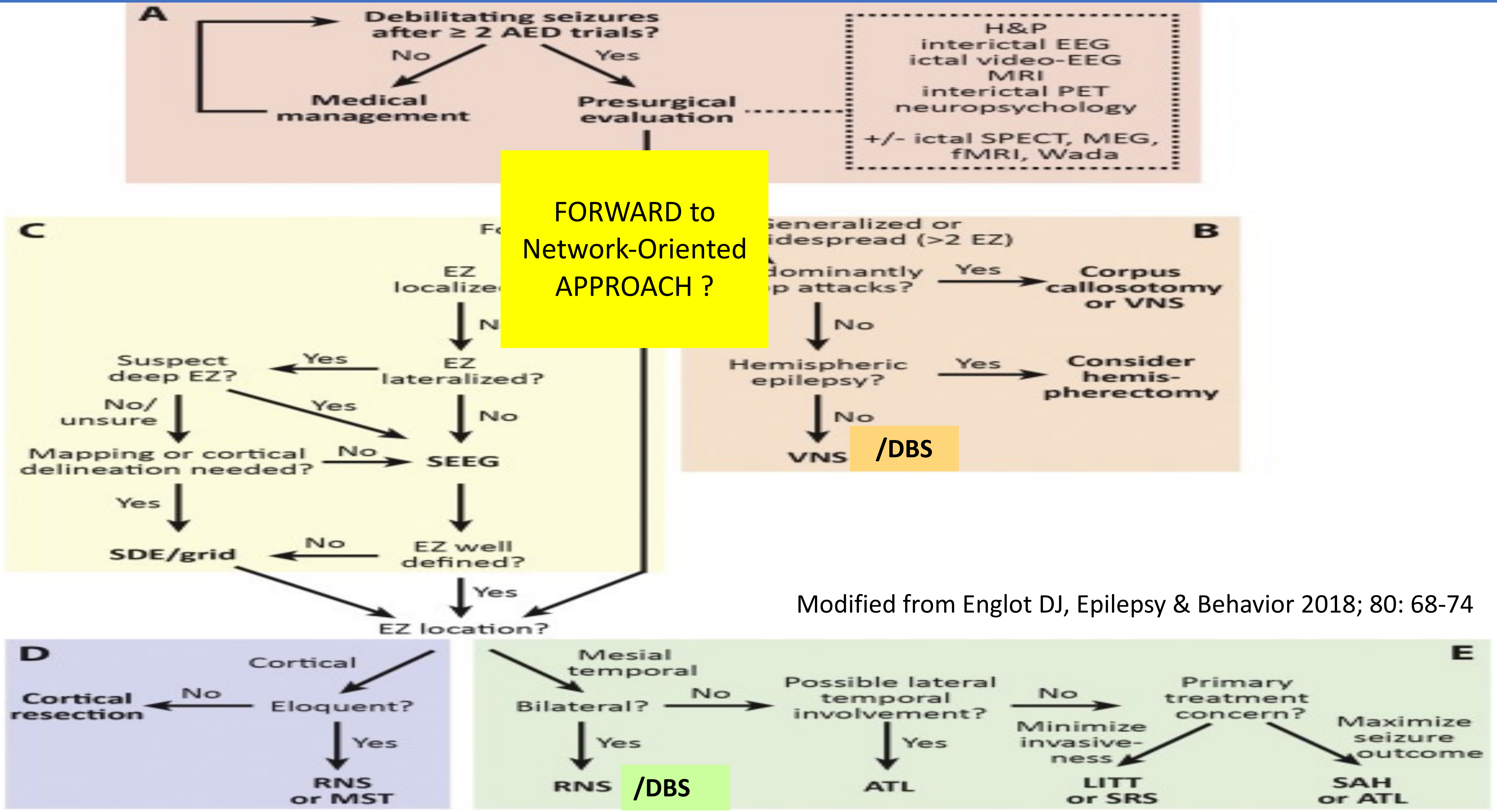
sEEG Implantation



Treatment Algorithm & Surgical Tools for Epilepsy



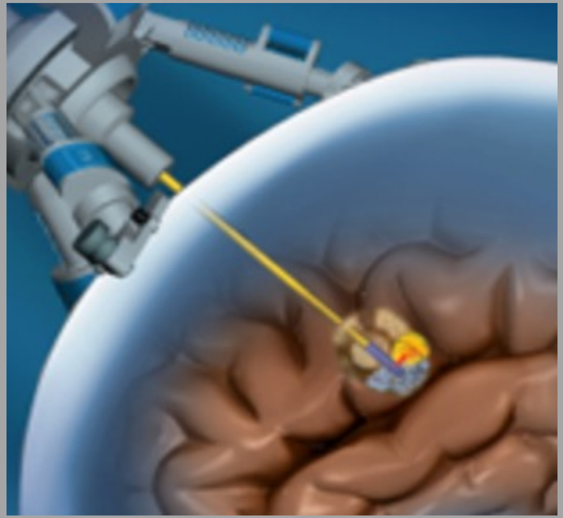
Epilepsy surgery treatment algorithm before 2020s



Modified from Englot DJ, Epilepsy & Behavior 2018; 80: 68-74

Surgical tools for epilepsy surgery 2020s

Resection



Ablation

Modulation

SURGERY

Surgical Resection for Epilepsy Surgery

Mechanism	Surgical removal of epileptogenic zone
Candidate	• Focal epilepsy with well-localized seizure onset zone • MRI-visible lesion or congruent EEG-MRI-SPECT/PET
Efficacy	TLE: 60-80% seizure free at 1-2 Years 50% remain seizure free at 10 Years Extra-TLE: 40-60% seizure free.
Risks	Permanent neurological deficits depending on locations Surgical morbidity about 3-5%. Not suitable for multifocal or generalized epilepsy Requires highly specialized team and facilities.

2001, 2012 RCT studies: Wiebe et al, Engel et al

AAN, AES and ILAE Guidelines strongly recommend early surgical evaluation for appropriate candidates.

Neuromodulation

- Neuromodulation is technology that acts directly upon neurological system.

- It is the alternation of nervous system activities by delivering electrical or pharmaceutical agents directlly to a target area.
- It works by actively stimulating nervous areas to produce a natural biological response.

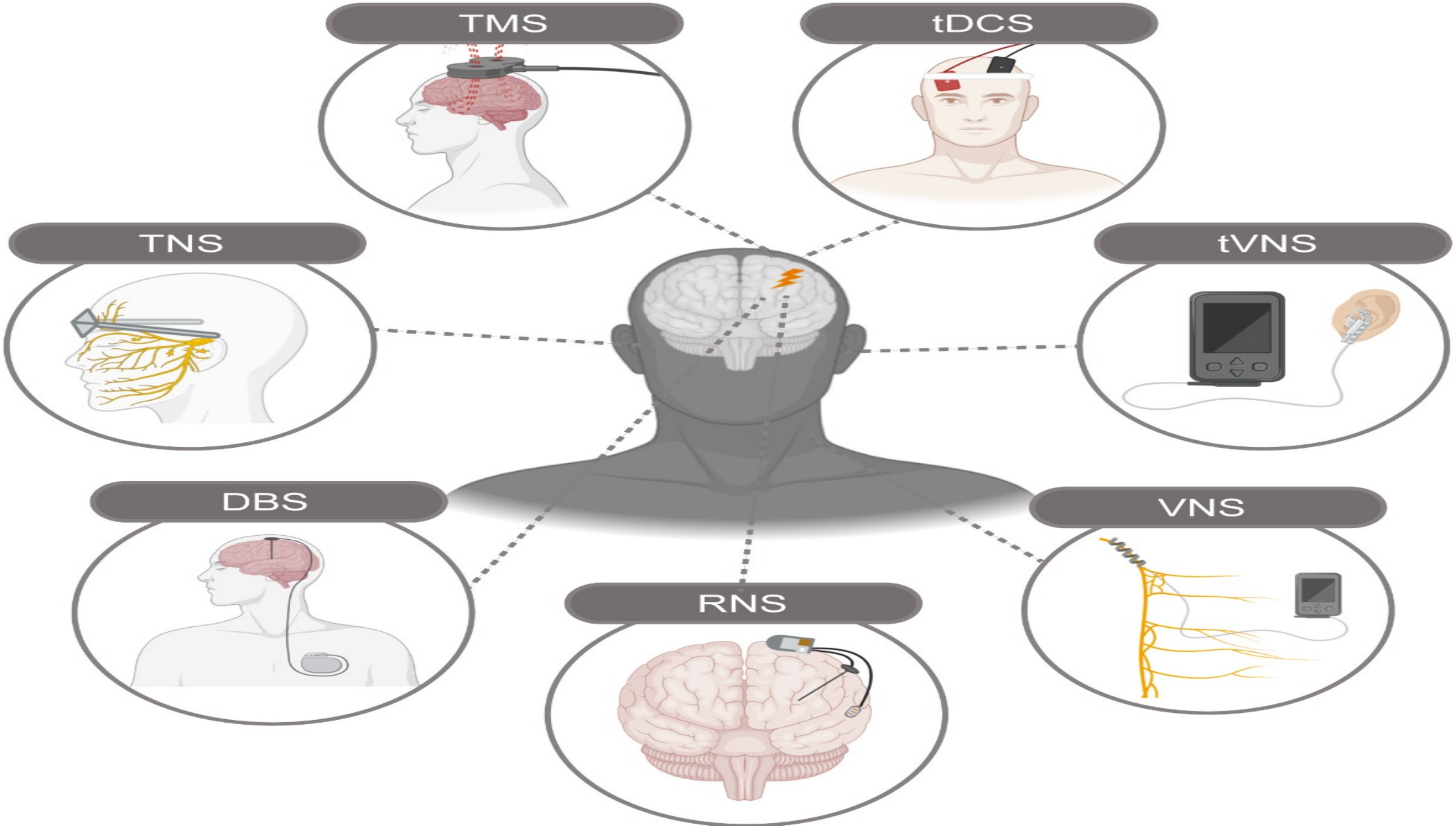
Krames, et al. (eds.) Neuromodulation V.1-2 2009

Neuromodulation

Neuromodulatory approaches	
Invasive	**Non-invasive**
• Brain-computer interface • Cochlear implant • Deep brain stimulation • Dorsal root ganglion stimulation • Gastric/Intestinal electrical stimulation • Motor cortex stimulation • Peripheral nerve stimulation* • Peripheral subcutaneous field stimulation • Retinal stimulation • Responsive neurostimulation • Spinal cord stimulation • Vagus nerve stimulation	• Electroconvulsive therapy • Functional electrical stimulation • Low-intensity focused ultrasound stimulation** • Non-invasive vagus nerve stimulation (auricular, cervical) • Peripheral nerve stimulation* • Transcranial alternating current stimulation • Transcranial direct current stimulation • Transcutaneous electrical nerve stimulation • Temporal interference stimulation • Transcranial magnetic stimulation • Transcranial ultrasound stimulation**
Possibly neuromodulatory and/or offered within the same program	
• Intrathecal drug delivery (e.g. ITB) • Intraventricular drug delivery (e.g. ITB) • Lumboperitoneal shunt** • Ventriculoperitoneal shunt** • Intestinal pump-based infusion (e.g. LICG)	• Drug infusion (e.g. ketamine) • Subcutaneous pump-based infusion (e.g. CSAI)

Alfonso Fasano, et al. (eds) Neurotherapeutics 2024

Neuromodulation for Epilepsy



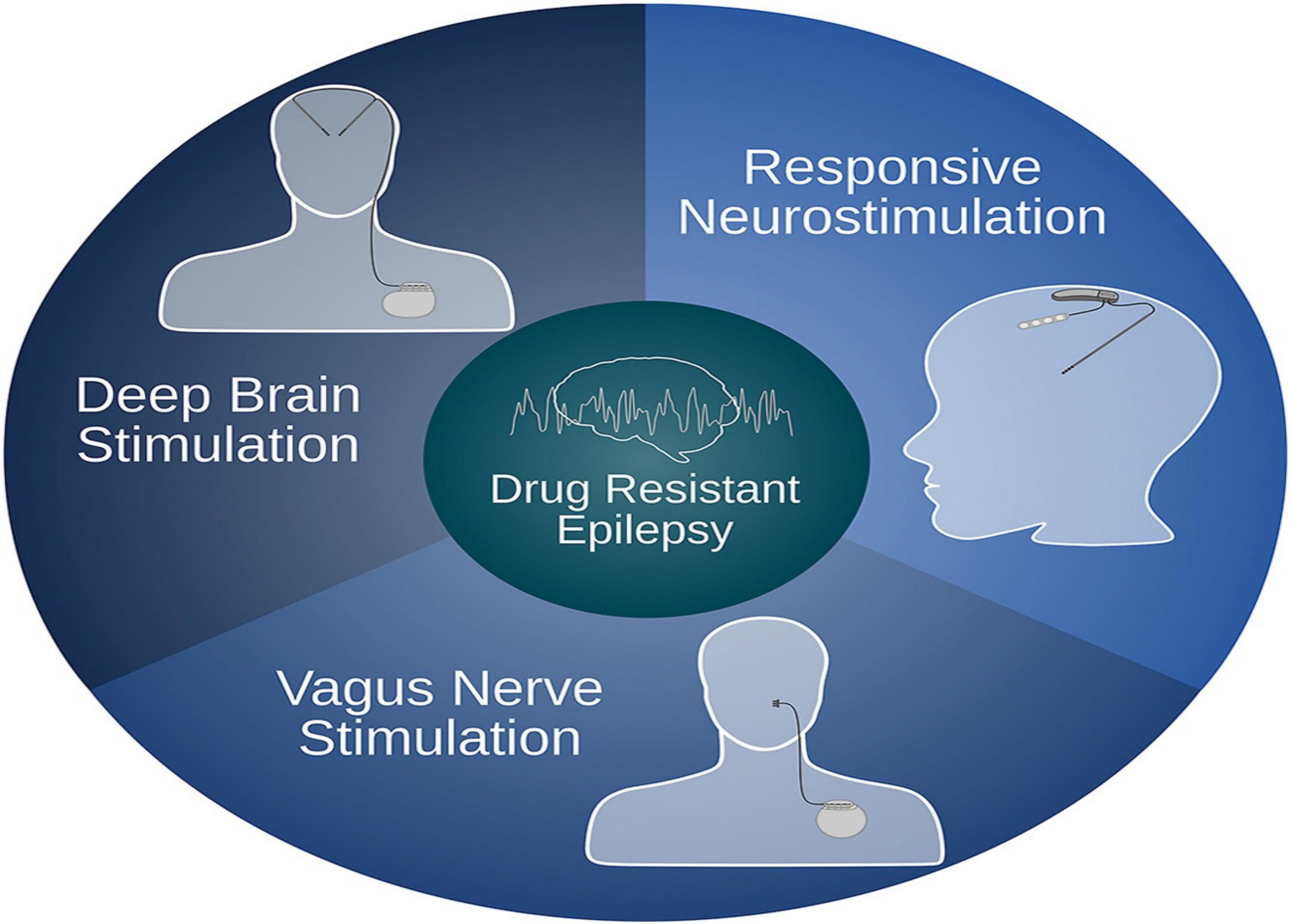
Tao Xue, et al. Acta Neurologica Scand 2022

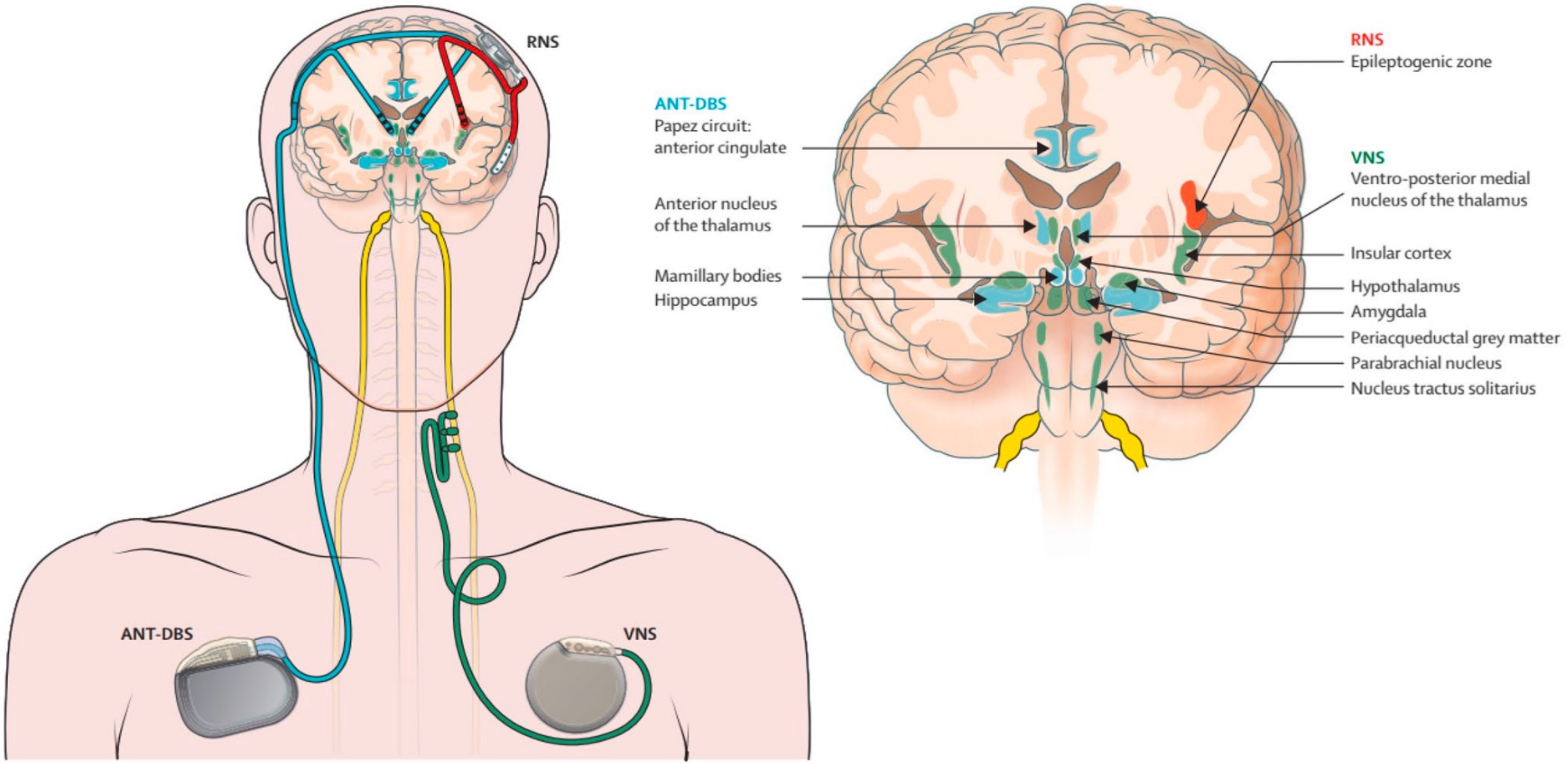
Neuromodulation for Epilepsy Surgery

Mechanism	Interrupt the abnormal electrical foci of SOZ Moderate thalamic activitiy & Disrupt epileptic network Generate Neuroplasticity
Candidate	• Multifocal,Generalized or Unresectable • EZ at eloquent areas • MRI-invisible lesion or in-congruent EEG-MRI-SPECT/PET
Efficacy	VNS:seizure reduction 35% at 1 Y, Long- term f/u 43% at3 Y, Sz free* 8% at 5Y DBS:seizure reduction 54% at 2 Y, Long-term f/u 73% at 9 Y, Sz free* 13%at 2Y & 18% at 7Y RNS:seizure reducation 55% at 2Y, Long-term f/u 84% at 3 Y. SZ free* 9% at 2Y & 28% at 9Y
Risks	Implant side effects (pain, infection, mood/sleep disturbance) Stimulation issue

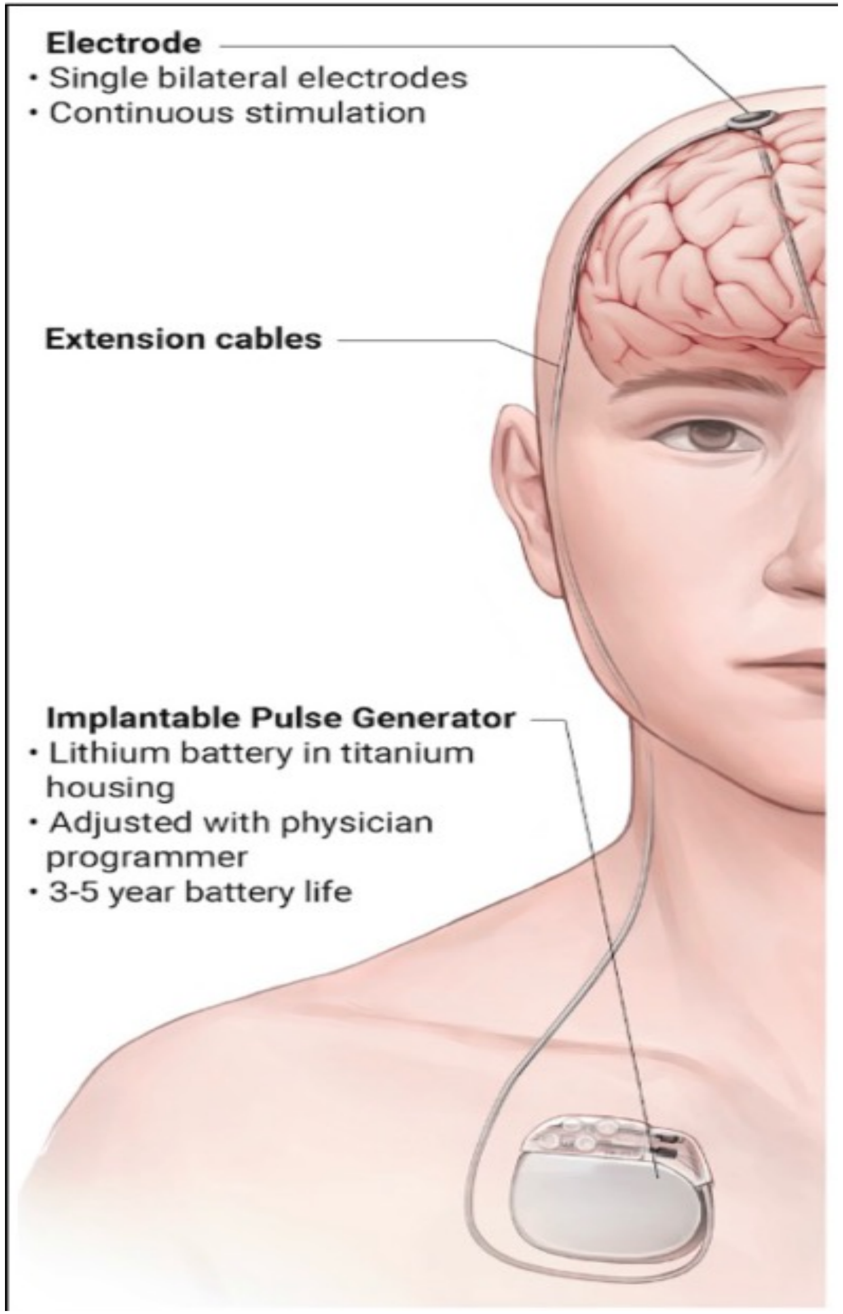
2001, 2012 RCT studies: Wiebe et al, Engel et al

AAN, AES and ILAE Guidelines strongly recommend early surgical evaluation for appropriate candidates.

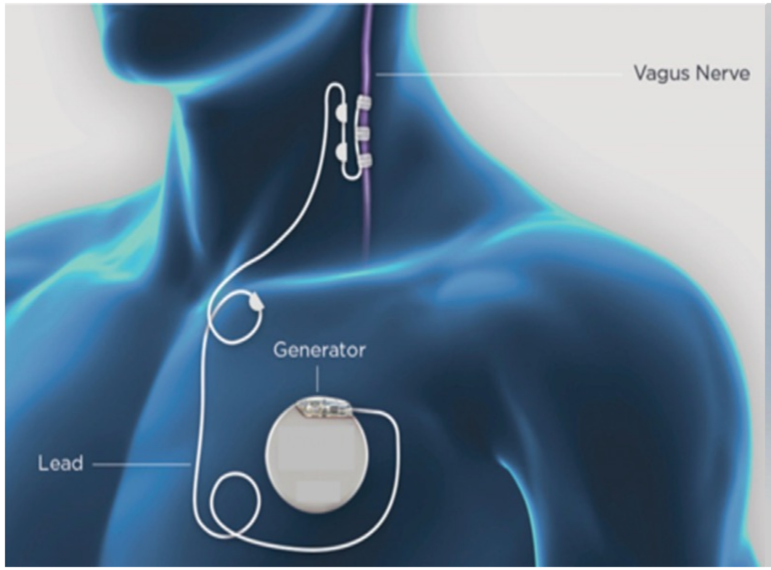

Responsive
Neurostimulation
Deep Brain
Stimulation
Drug Resistant
Epilepsy
Vagus Nerve
Stimulation

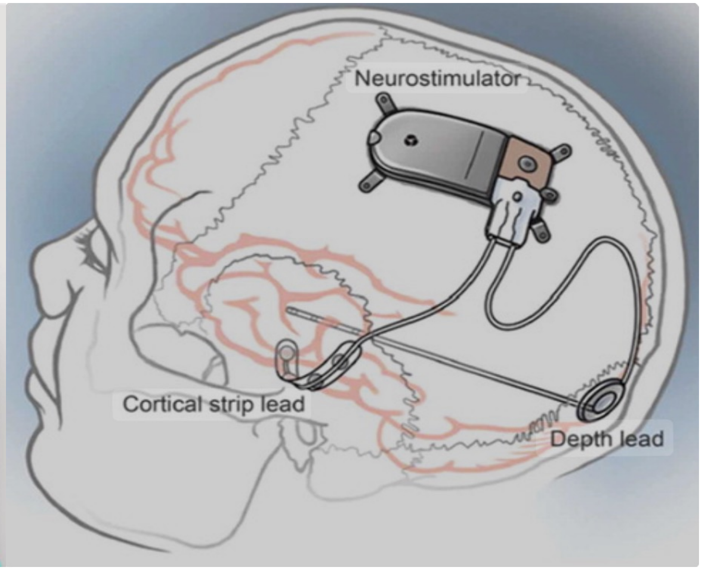


HusamEddin Salama, et al. Neurological Sciences 2024



	Vagus Nerve Stimulation	Deep Brain Stimulation	Responsive Neurostimulation
Indication	Partial-onset seizures (Adults and children >4y, off-label in younger children)	Focal and secondary generalized seizures (ANT) or generalized epilepsy (CM) (Adults, off-label in children)	Focal epilepsy arising from 1 to 2 foci (Adults, off-label in children)
Advantages	Approved for pediatric use. MRI-compatible	Multiple targets allow for better patient selection. MRI-compatible	Can be applied to up to 2 eloquent foci. MRI-compatible
Limitations	Up to 50 % of patients remain refractory to treatment	Lack of significant pediatric data	Limited data on pediatric populations





Flavia Venetucci Gouveia, et al. Neurotherapeutics 2024

TABLE 2. Perioperative and Postc... ...fractor...

Variable	I...	...	Total (N = 3343)	P value
Ischemic stroke			[illegible]	**.049**
Postoperative SAH			12 (0.4%)	.330
Neurological complications			91 (2.7%)	**<.001**
Pulmonary complications			41 (1.2%)	.185
DVT/PE complications			19 (0.6%)	.922
Cardiac complications			7 (0.2%)	.585
Urinary complications			21 (0.6%)	.695
Hematoma			39 (1.2%)	**.002**
Wound dehiscence			10 (0.3%)	.868
Wound infection			8 (0.2%)	.516
Mean LOS in days (95% CI)	2...		6.9 (6.6-7.2)	**<.001**
Nonhome discharge			525 (15.7%)	**<.001**
Death			11 (0.3%)	.616
Mean total charges in USD (95% CI)	140 6...	...0)	183 892 (178 000-191 000)	**<.001**

DVT/PE, deep vein thrombosis/pulmonary e... ...noid hemorrhage; VNS, vagus nerve stimulation.
Bold entries indicate $P < 0.05$.

Trends in the Utilization of Surgical Modalities for the Treatment of Drug-Resistant Epilepsy: A Comprehensive 10-Year Analysis Using the National Inpatient Sample

Abdul Karim Ghaith, MD[‡§*], **Victor Gabriel El-Hajj, BS**[‡§||*], **Jesus E. Sanchez-Garavito, MD**[¶], **Cameron Zamanian, BS**[‡§], **Marc Ghanem, MD**[‡§], **Antonio Bon-Nieves, BS**[‡§], **Baibing Chen, MD, MPH**[#**], **Cornelia N. Drees, MD**[††], **David Miller, MD**[§§], **Jonathon J. Parker, MD, PhD**[|||], **Joao Paulo Almeida, MD**[¶], **Adrian Elmi-Terander, MD, PhD**[||], **William Tatum, DO**[#], **Erik H. Middlebrooks, MD**[§§], **Mohamad Bydon, MD**[‡§], **Jamie J. Van-Gompel, MD**[§], **Brian N. Lundstrom, MD, PhD**[¶¶], **Sanjeet S. Grewal, MD**[¶]

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*Abdul Karim Ghaith and Victor Gabriel El-Hajj contributed equally to this work.

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BACKGROUND AND OBJECTIVES: Epilepsy is considered one of the most prevalent and severe chronic neurological disorders worldwide. Our study aims to analyze the national trends in different treatment modalities for individuals with drug-resistant epilepsy and investigate the outcomes associated with these procedural trends in the United States.
METHODS: Using the National Inpatient Sample database from 2010 to 2020, patients with drug-resistant focal epilepsy who underwent laser interstitial thermal therapy (LITT), open surgical resection, vagus nerve stimulation (VNS), or responsive neurostimulation (RNS) were identified. Trend analysis was performed using piecewise joinpoint regression. Propensity score matching was used to compare outcomes between 10 years prepandemic before 2020 and the first peak of the COVID-19 pandemic.
RESULTS: This study analyzed a total of 33 969 patients with a diagnosis of drug-resistant epilepsy, with 3343 patients receiving surgical resection (78%), VNS (8.21%), RNS (8%), and LITT (6%). Between 2010 and 2020, there was an increase in the use of invasive electroencephalography monitoring for seizure zone localization ($P = .003$). There was an increase in the use of LITT and RNS ($P < .001$), while the use of surgical resection and VNS decreased over time ($P < .001$). Most of these patients (89%) were treated during the pre-COVID pandemic era (2010-2019), while a minority (11%) underwent treatment during the COVID pandemic (2020). After propensity score matching, the rate of pulmonary complications, postprocedural hematoma formation, and mortality were slightly higher during the pandemic compared with the prepandemic period ($P = .045$, $P = .033$, and $P = .026$, respectively).
CONCLUSION: This study indicates a relative decrease in the use of surgical resections, as a treatment for drug-resistant focal epilepsy. By contrast, newer, minimally invasive surgical approaches including LITT and RNS showed gradual increases in usage.

KEY WORDS: DBS, LIIT, Refractory epilepsy, RNS, VNS, Drug resistant, Epilepsy

Neurosurgery 94:1191–1200, 2024 https://doi.org/10.1227/neu.0000000000002811

ABBREVIATIONS: DRE, drug-resistant epilepsy; **EEG,** electroencephalography; ***ICD,*** *International Classification of Diseases*; **LOS,** length of stay; **LITT,** laser interstitial thermal therapy; **NIS,** National Inpatient Sample; **PE,** pulmonary embolism; **RNS,** responsive neurostimulation; **VNS,** vagal nerve stimulation.

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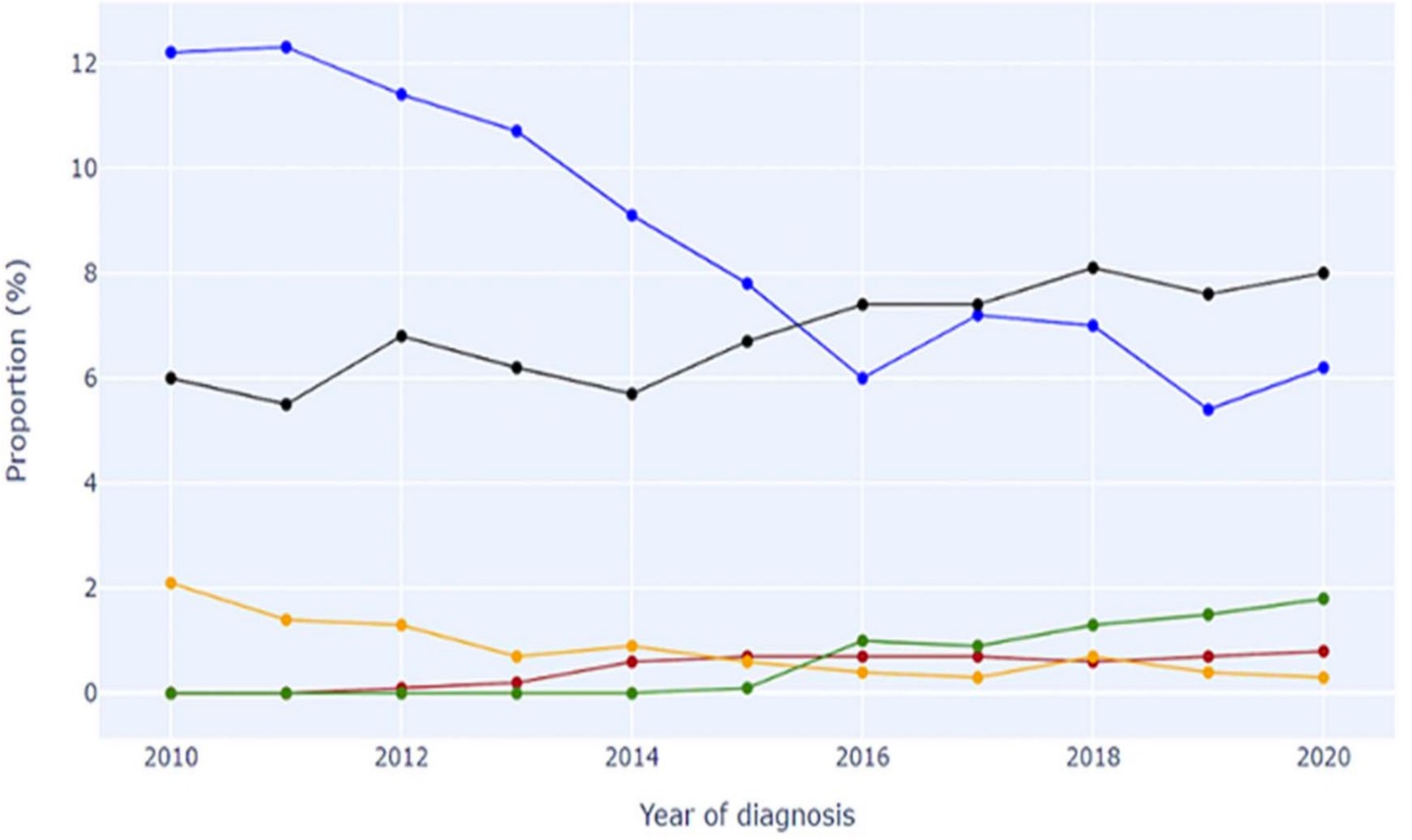

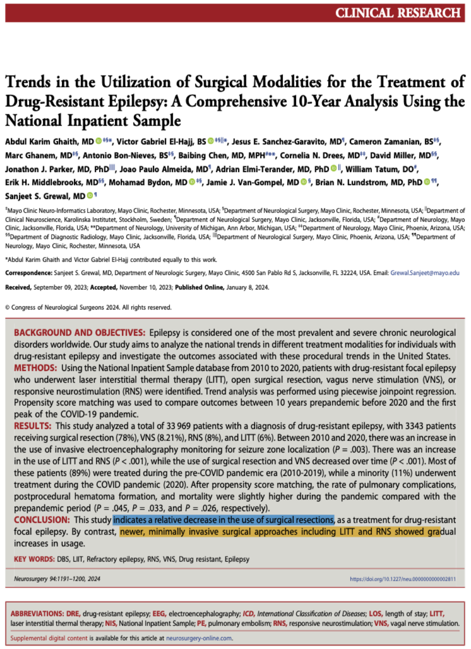

CLINICAL RESEARCH

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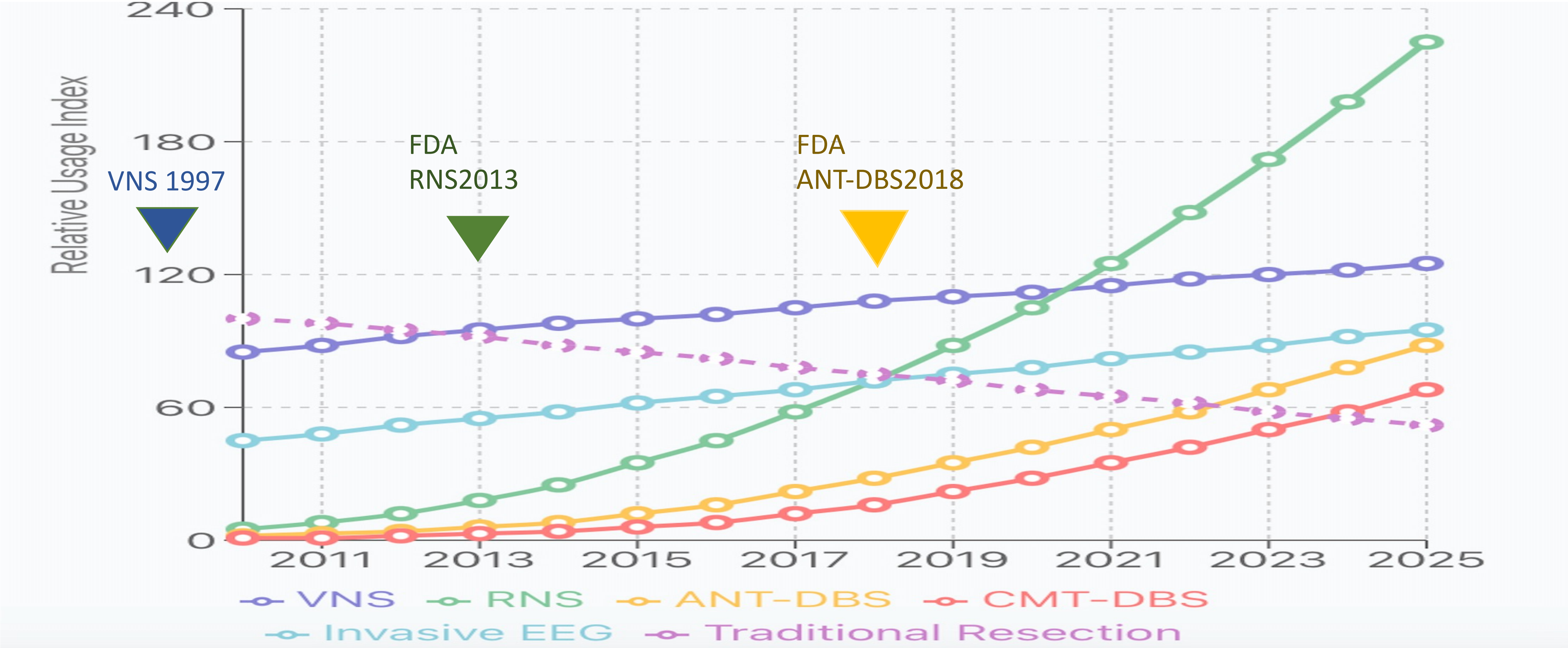
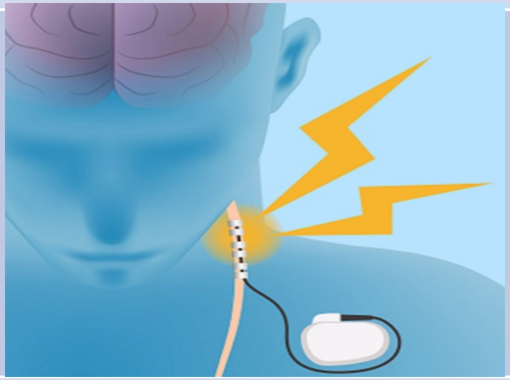
Trends of patients with DRE receiving the different surgical treatment

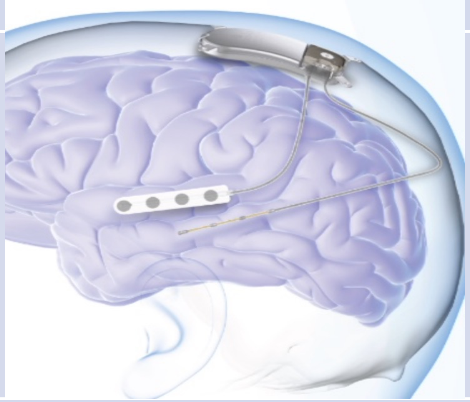
Surgical Treatmets Trends for DRE (2020-2025)

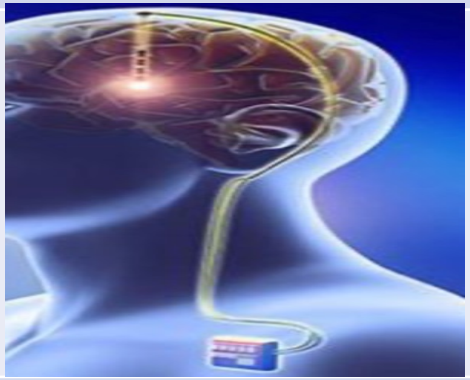


Abdul K Ghaith, et al. Neurosurgery 2024
Qinghua Li, et al. Front Hum Neurosci 2024

Neuromodulation for DRE







VNS

RNS

DBS

Table 1 Summary of surgical therapies for DRE

Techniques	Strengths	Limitations	Indications
Resective surgery	Achieves substantial seizure reduction or even complete seizure freedom	Risk of neurological deficits and surgical complications	Suitable for patients with a localized, well-defined epilepsy focus that is unresponsive to medical therapy
MRgFUS	Non-invasive with precise targeting; real-time MRI guidance; shorter hospital stays and faster recovery	Limited to well-localized seizure foci; less effective for complex epilepsies	Suitable for DRE and patients ineligible for traditional surgery
RF-TC	High precision with a lower risk of neurological deficits	Risks include hemorrhage, infection, and potential injury to adjacent brain structures	Focal epilepsy, particularly when the epileptogenic focus is located in deep-seated or functionally critical areas
LITT	Minimally invasive; highly targeted tissue destruction; reduced recovery time	Limited to specific types of epilepsy; potential for incomplete ablation	Localized epilepsy, particularly in cases where conventional surgery is not an option
VNS	Significantly reduces seizure frequency and addresses comorbid conditions like depression and anxiety	May cause side effects such as hoarseness, cough, or throat discomfort	DRE, especially in patients unsuitable for resective surgery
TA-VNS	Non-invasive, portable, and flexible; improves seizure control, mood, and cognition	Limited evidence for long-term effectiveness; mild discomfort at the stimulation site	DRE, especially in patients unsuitable for resective surgery
DBS	Reversible and adjustable; effective for multifocal or generalized epilepsy; modulates neural activity without destroying tissue	Risks of infection, hemorrhage, and device malfunction; potential cognitive or mood disturbances	DRE, particularly in patients with multifocal or generalized epilepsy
RNS	Real-time response to seizure activity; minimally invasive with reduced surgical risks and faster recovery	Requires long-term monitoring and follow-up	Focal epilepsy that is difficult to localize and multifocal epilepsy

DBS deep brain stimulation, *DRE* drug-resistant epilepsy, *LITT* laser interstitial thermal therapy, *MRgFUS* magnetic resonance-guided focused ultrasound, *RF-TC* radiofrequency thermocoagulation, *RNS* responsive neurostimulation, *TA-VNS* transcutaneous auricular vagus nerve stimulation, *VNS* vagus nerve stimulation

Chen Zhong, et al. Neurol Ther 2025

Table 6 Summary of the different neuromodulation techniques

	VNS	ATN-DBS	RNS
FDA approval	VNS therapy was approved for epilepsy in 1997	ATN-DBS was approved for epilepsy in 2018	RNS was approved in 2013
Indications	It is used for generalized epilepsy, and it was approved in 2007 by the FDA to treat depression. It is worth to know that 13–37% of patients with epilepsy have depression	It is more effective in treating focal epilepsy	It is used for the management of highly localized focal seizures with one or two foci, especially where surgery is not an option either due to patient denial or medical issues
Open/closed loop	It is generally an open-loop system, but the new AspireSR® model detects the changes in the heart rate, usually more than 20% of the baseline heart rate	Open loop	RNS is a closed-loop system that consists of three steps: (1) brain electrical activity monitoring, (2) detection of abnormal electrical activity, (3) neurostimulators send an electrical signal in a try to interrupt or cease the upcoming seizure
Efficacy	Two large randomized clinical trials, E03 (multinational), showed a median seizure reduction of 24.5% after the 1.3 mA stimulation. E05 (US centers) reported a median seizure reduction of 27.9% after the 1.3 mA stimulation, and long-term follow-up studies showed improvement in the efficacy over time	DBS was approved after the SANTE trial in 2018. There was a reduction in seizure in 40.4% of patients after 3 months, 56% after 25 months, and up to 75% after 7 years	RNS was highly effective for the management of DRE. In the 7-year open-label long-time follow-up trial, the median percent reduction in adult patients with focal epilepsy was 58% after 3 years and 75% after 9 years. Another study showed that the median seizure frequency reductions in RNS-treated adult patients with refractory epilepsy was up to 67% after 1 year, 75% after 2 years, and 82% after 3 years
Use in pediatric seizures	It is approved for children > 4 years. A retrospective study on 86 patients under the age of 6 years reported a median seizure reduction of more than 50% after 1 year and 60% after 2 years	Clinical trials are needed to determine the exact results of using ATN-DBS in children	RNS is not FDA-approved for the management of DRE in pediatrics. However, it has been used off-label for the management of patients with DRE with no other alternative options. The studies showed comparable results when compared to RNS use in adults
Adverse effects	Cough and laryngeal paresthesia, surgical site infection, and worsening of OSA	Surgery-related: surgical site pain, infection, and paresthesia Stimulation-related: headache and dizziness	Post-surgical infections, hemorrhage, lead damage and revision

HusamEddin Salama, et al. Neurological Sciences 2024

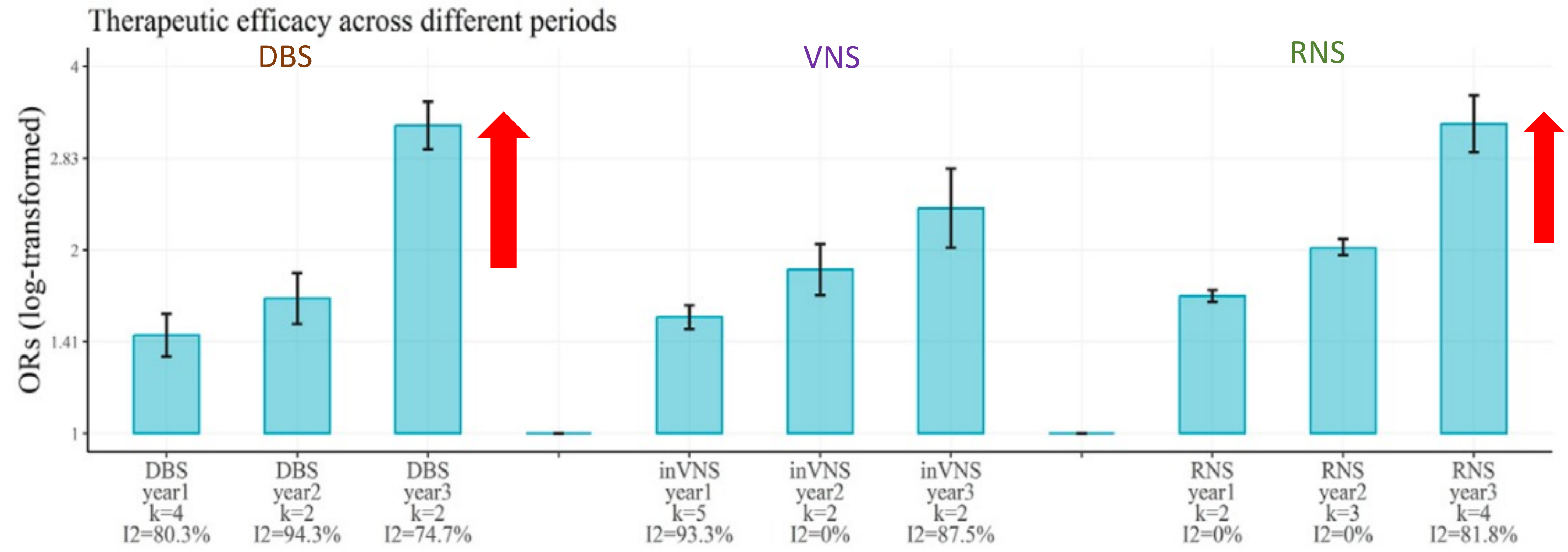


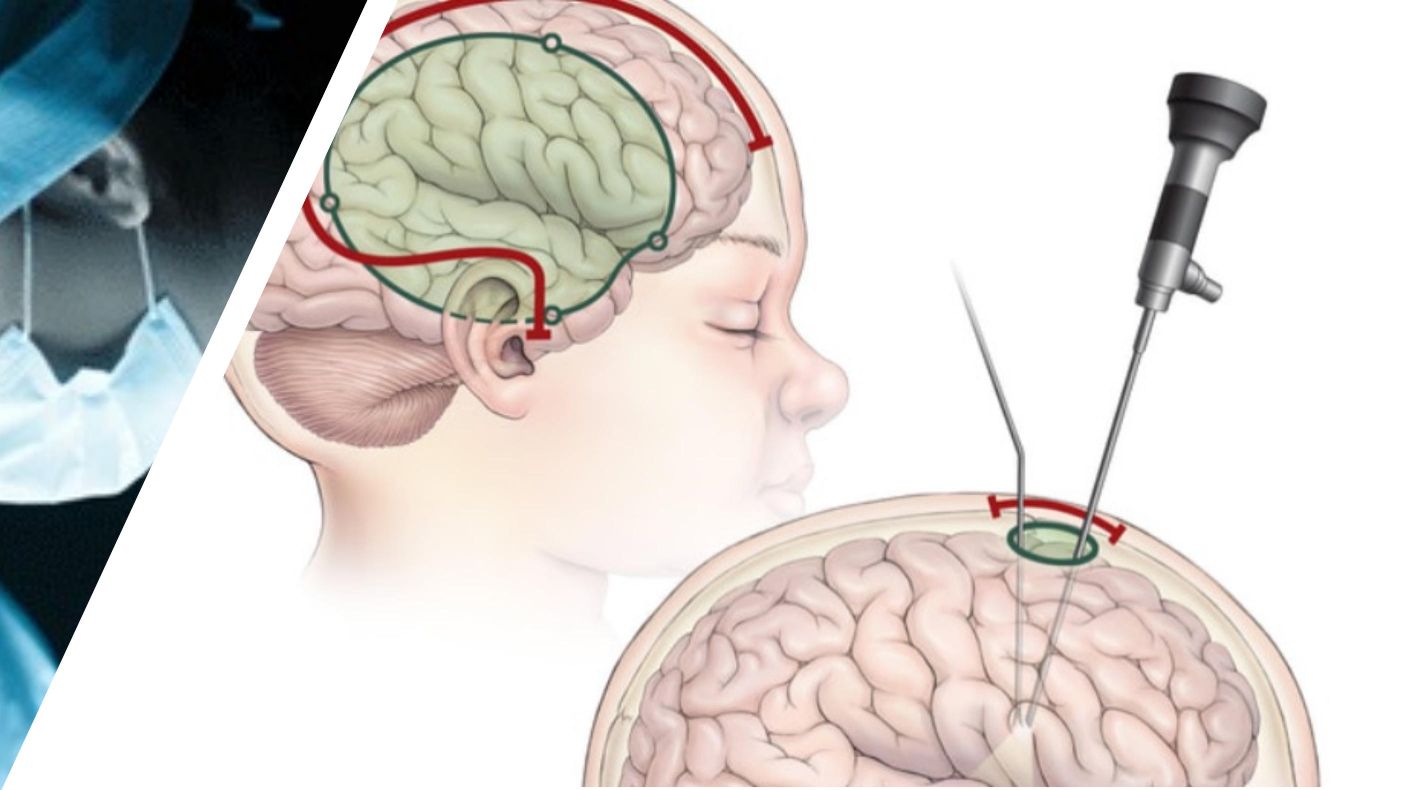
Figure 5. Dynamic changes in the short-term (year 1), medium-term (year 2), and long-term (year 3) efficacy of DBS, inVNS, and RNS. RNS, responsive neurostimulation; DBS, deep brain stimulation; inVNS, invasive vagus nerve stimulation; OR, odds ratio.

Jianwei Shi, et al. World Neurosurg 2025

Clinical approach to **Neuromodulation** selection

	Highly Localized (1-2 foci)		**Poorly Localized or Multifocal (3+ foci)**	**Generalized Onset**
	Temporal Lobe	Eloquent cortex		
Primary	**RNS**	**RNS**	**ANT-DBS**	CM-DBS
Alternative	**ANT DBS** *HC DBS*	**ANT-DBS** **CM-DBS**	RNS (Regional)	

T J Foutz, 2021


What is your opinion ?

- a) 18 Y Female
- b) 13 Y Girl
- c) 08 Y Girl
- d) 37 Y Male
- e) 33 Y Female

Current Guidelines & Trends (2025)

- **Early surgical evaluation** is now strongly recommended within 2-3 years of DRE diagnosis.
- **Surgical resection** remains **the gold standard.**
- **RNS** is increasing used for **bilateral or eloquent cortex epilepsy**.
- **DBS** is growing option for **patient with no other surgical targets**.
- **VNS** remains a good option for **generalized epilepsy in children and adults.**
- **Combination therapies*** (e.g. AEDs + DBS, /+VNS/ +RNS)after failed surgery are increasingly common.

Siraruj S, 2025

SURGICAL TREATMENT FOR DRUG-RESISTANT EPILEPSY

Siraruj S, 2025

Aspect	Surgical Resection	Neuromodulation (VNS, RNS, DBS)
Main Goal	Cure or Seizure freedom	Reduce Seizure frequency/ Severity
Best Candidates	Focal epilepsy with a clearly identified seizure onset zone (SOZ)	Multifocal, bilateral, generalized or eloquent cortex epilepsy (unresectable)
Effectiveness	60-80% seizure freedom esp.in TLE	50-70% seizure reduction (freedom in 5-20%)
Onset of Benefit	immediate or within weeks	Gradual (months to years*)
Reversibility	Irreversible	Reversible
Risks/Side Effect	Neurological deficits, invasive	Implant side effect, Stimulation issues
Age Suitability	Children & adults	Mostly adults: RNS/DBS*, VNS also in children
Long-term Outcome	Strong for sustained seizure free	Good long-term seizure control
Device/Follow-up Need	Routine	High (Programming, battery changes*, monitoring)
When Preferred	Clear SOZ , non-eloquent brain	Non-resectable cases, Unclear focus, Pt preference
Cost-Effectiveness	High (if successful)	Higher initial cost; High to moderate (long-term)

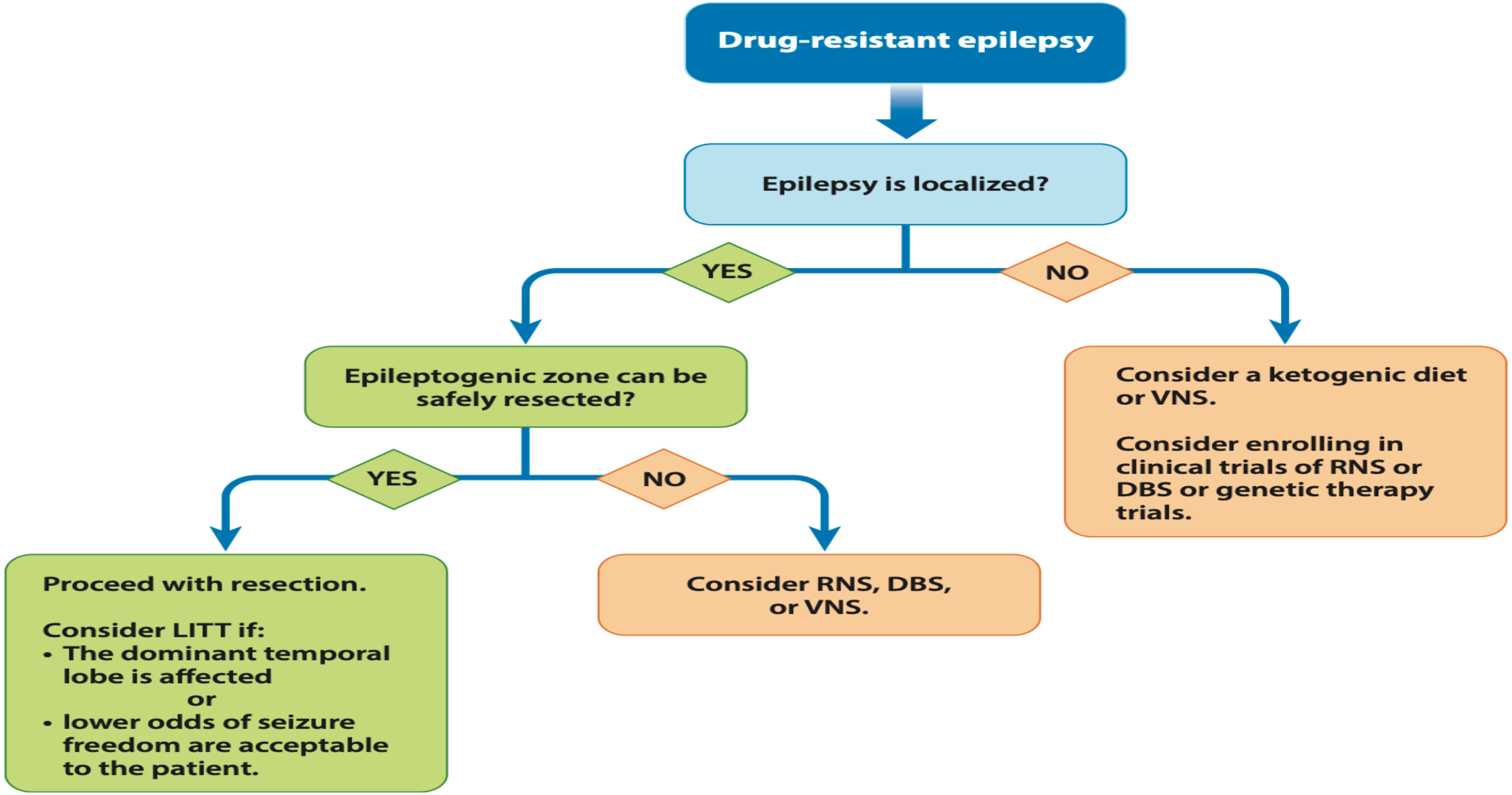
Take Home Message

- In focal epilepsy with clear locations: Surgical resection offers the highest chance for seizure free.

- Non-surgical candidates/ diffuse seizure location / eloquent cortex epilepsy: Neuromodulation is the best.

- The choice of treatment must be depended on CEP’s team expert and based on seizure type, imaging, EEG, risk tolerance and patient’s affordable.

Take Home Message



Lara Jehi. Annu.Rev.Med.2025


That's all Folks!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