2023 GW Epilepsy Board Review & Best Practices

Epilepsy Surgery

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THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

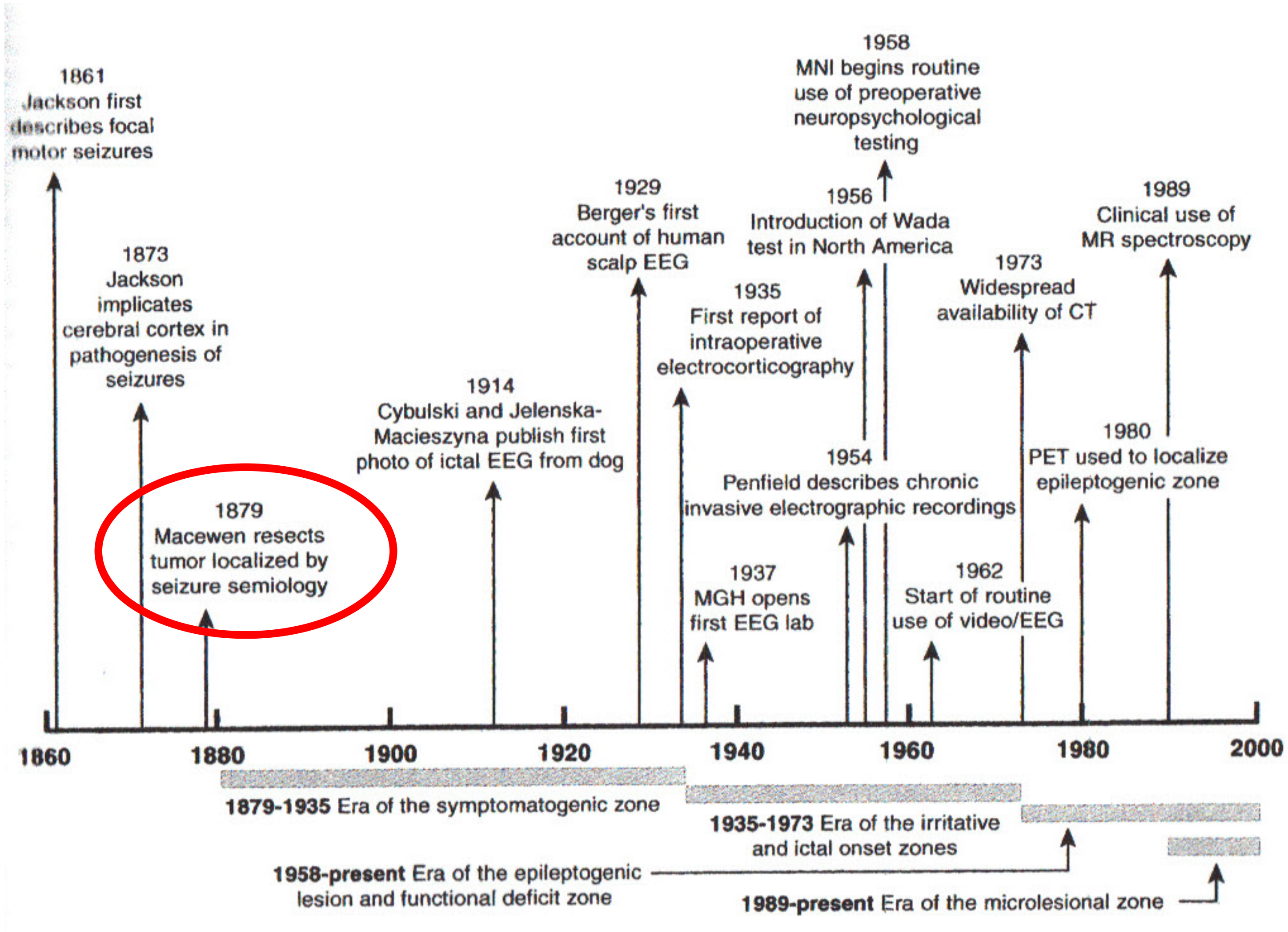
Children's National™ Health System

- No disclosures

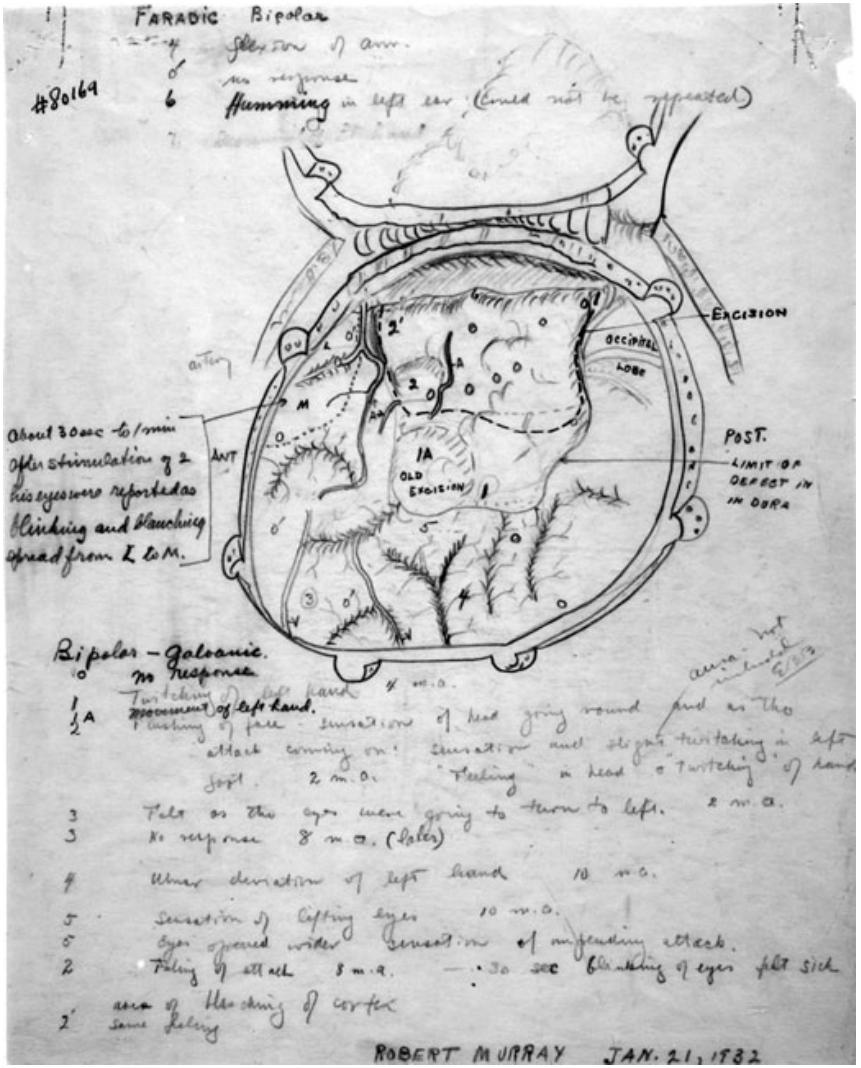
Objectives

- Describe the scope of Epilepsy surgery
- Discuss the recent advances in Epilepsy Surgery
- Discuss the evidence basis for the efficacy of Epilepsy Surgery

Not new: History of Epilepsy Surgery



Not new: History of Epilepsy Surgery



Penfield's drawing of operation in 1932 to show vascular features and double excisions, including his first temporal lobectomy for posttraumatic seizures (Wilder Penfield Archive).
Epilepsia ILAE

Wilder Penfield (sitting) and Herbert Jasper, 1954

Epilepsy Surgery

- Surgery for Epilepsy

– when is it indicated / Timing

- General principles / Evaluation

- Outcome (efficacy)

- When ?
- How ?
- Is it effective ?

When ?

Epilepsy Care

Seizure

Epilepsy diagnosis

Medication trials

Imaging for pathology

Medical intractability

Surgical Consideration

Surgical workup

Surgery

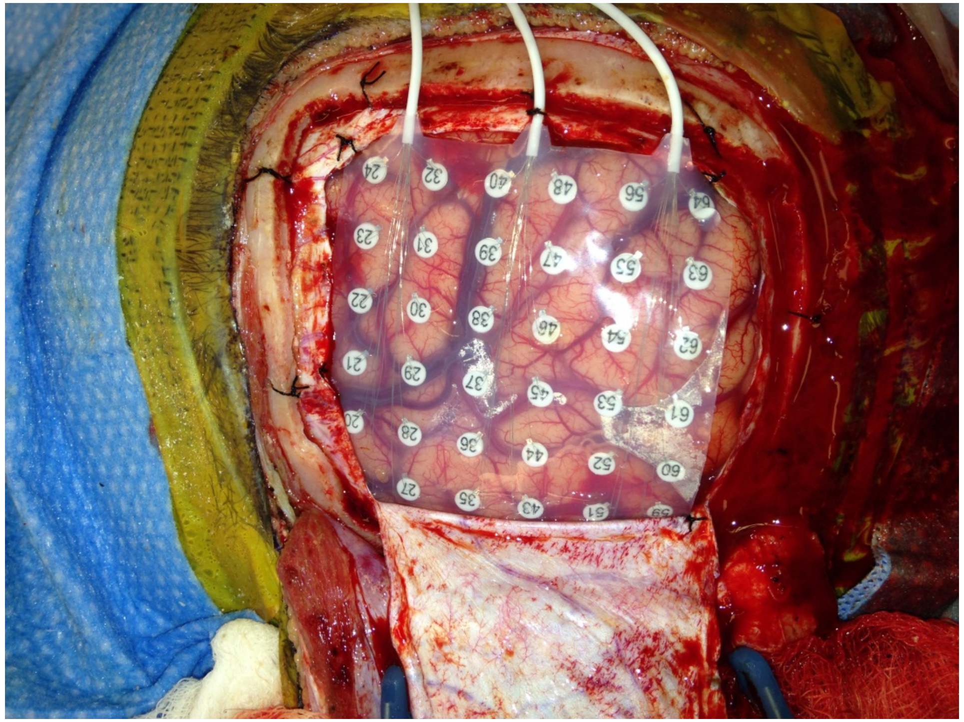
How ?

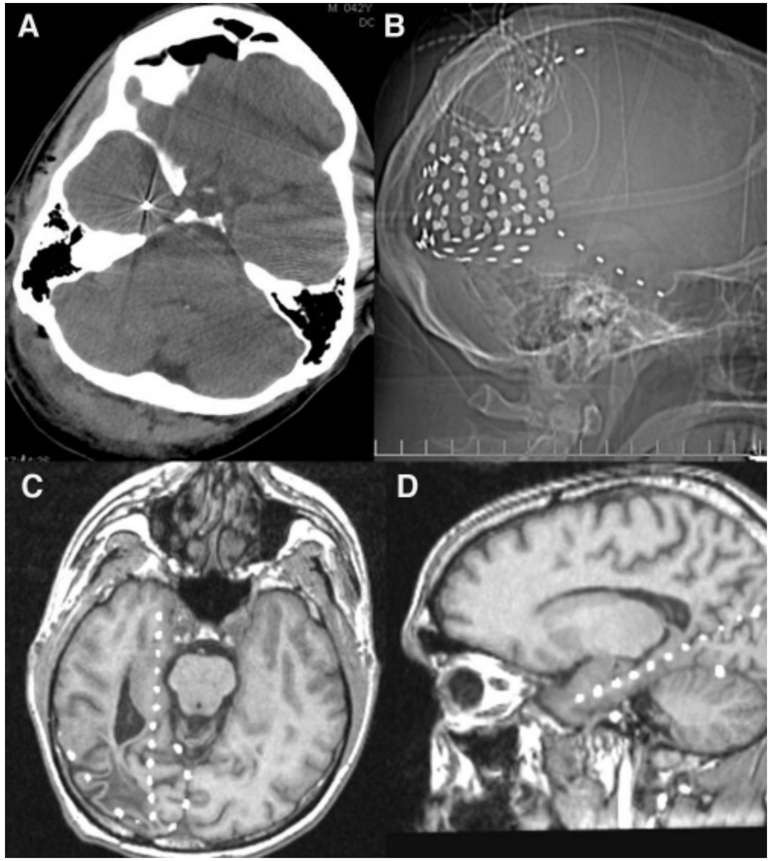
Invasive Intracranial Monitoring

Indications:

- nonlesional localization-related epilepsy, or
- in lesional epilepsy where clinical, neuropsychological, EEG or imaging data are not concordant

Grids and strips, most commonly subdural





Parenchymal "depth" electrodes, especially for recording from hipppocampus

Identification of ictal onset

Brain mapping

cortical stimulation

Phase reversal for mapping the motor cortex

Surgical Treatment of Epilepsy

Figure 2

Curative ⟷ **Palliative**

Pathologies

MTS TLE	**Non-MTS TLE**
Lesional	**Frontal Lobe epilepsy**
- Low Grade Glioma	**SMA/cingulate epilepsy**
- Cav. Malformation	**Malformations of cortical development**

Procedures

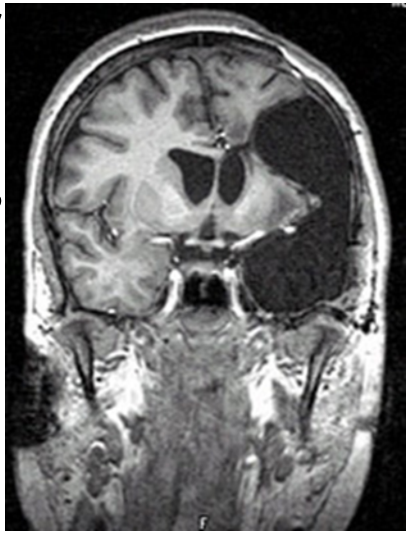
Lesionectomy	**Hemispherectomy**	**Disconnection**
Lobectomy	**Topectomy**	**(Callosotomy)**
	MST's	

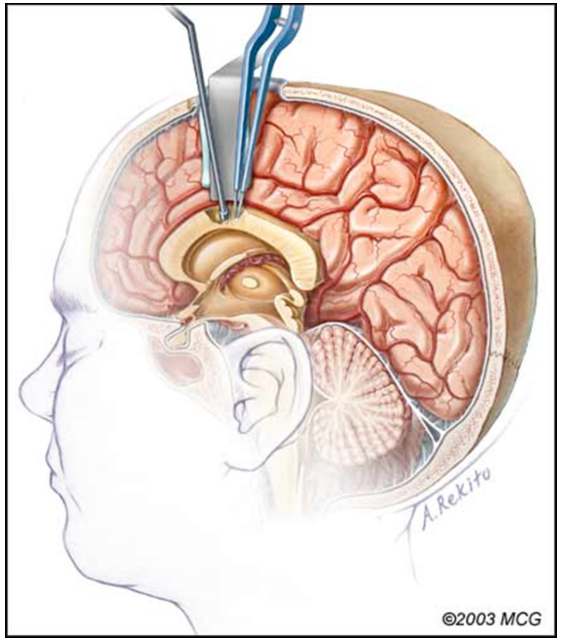
Modified from McKhann G.M. and Howard M.A.: Epilepsy Surgery: Disease Treatment and Investigative Opportunity, in Diseases of the Nervous System: Clinical Neurobiology, 2002.

Established Epilepsy Surgical Procedures

- Resective Surgery:
  - Lesionectomy
  - Selective amygdalohippocampectomy
  - Corticectomy
  - Lobectomy (*e.g.* temporal lobectomy)
  - Multilobar resection
  - Anatomic hemispherectomy

- Disconnective/Palliative Surgery:
  - Functional Hemispherectomy
  - Corpus Callosotomy
  - Multiple Subpial Transections
  - Vagus Nerve Stimulator





Epilepsy Behav. 2018 March ; 80: 68–74. doi:10.1016/j.yebeh.2017.12.041.

A Modern Epilepsy Surgery Treatment Algorithm: Incorporating Traditional and Emerging Technologies

Dario J. Englot, M.D., Ph.D.

"These changes in the new era of epilepsy surgery hinge primarily on:

1. the improvement or development of minimally-invasive diagnostic and ablative procedures
2. the introduction of non-destructive neurostimulation techniques. "

Personal Experience

- Functional and Stereotactic Neurosurgery techniques becomes an integral part of Epilepsy Surgery
- The increasing use of stereotactic techniques (typically minimally invasive) and brain stimulation (neuromodulation) in epilepsy surgery

Novel Epilepsy Surgical Techniques

- Minimally Invasive Epilepsy Surgery (MIES)

  1. Stereoencephalography (SEEG)
  2. Stereotactic MRI-guided laser ablation of epileptogenic foci

- Increasing application of Brain Stimulation (Electrical Neuromodulation) in Epilepsy Surgery

  1. Deep brain Stimulation (DBS)
  2. Responsive Neurostimulation (RNS)

Epilepsy Res. 2015 December ; 118: 68–69. doi:10.1016/j.eplepsyres.2015.09.012.

The persistent under-utilization of epilepsy surgery

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[b]Department of Neurological Surgery, University of California, San Francisco, CA, United States

- Only a small proportion of potential surgical candidates with drug-resistant epilepsy are operated each year.
- Concerns : surgical morbidity, pain, recovery.
- Limitations in surgical options for seizures from eloquent brain areas and generalized epilepsies
- Advances in Epilepsy surgery are driven by advances in surgical technology and these patient concerns and demands

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

Epidemiologist's view: Addressing the epilepsy surgery treatment gap with minimally-invasive techniques

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ARTICLE INFO

Keywords:
Epilepsy surgery
Minimally-invasive surgery
Treatment gap
Epidemiology
Disparities

ABSTRACT

Despite the fact that epilepsy surgery is both safe and effective, a considerable "surgical treatment gap" remains in that most persons who are eligible for surgery do not receive it. It has been argued that epilepsy surgery is one of the most underutilized of all accepted medical treatments in the world. In this article, we review the epidemiology of the epilepsy surgery treatment gap, and consider the role minimally-invasive epilepsy surgery may play in reducing this gap.

- Most patient preferred MIES as initial intervention when offered the option between open or minimally invasive surgery (Willie JT, *Neurosurgery* 2014)

- May increase willingness to access epilepsy surgery

Epilepsy & Behavior 103 (2020) 106533

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

Brief Communication

What can Google Trends and Wikipedia-Pageview analysis tell us about the landscape of epilepsy surgery over time?

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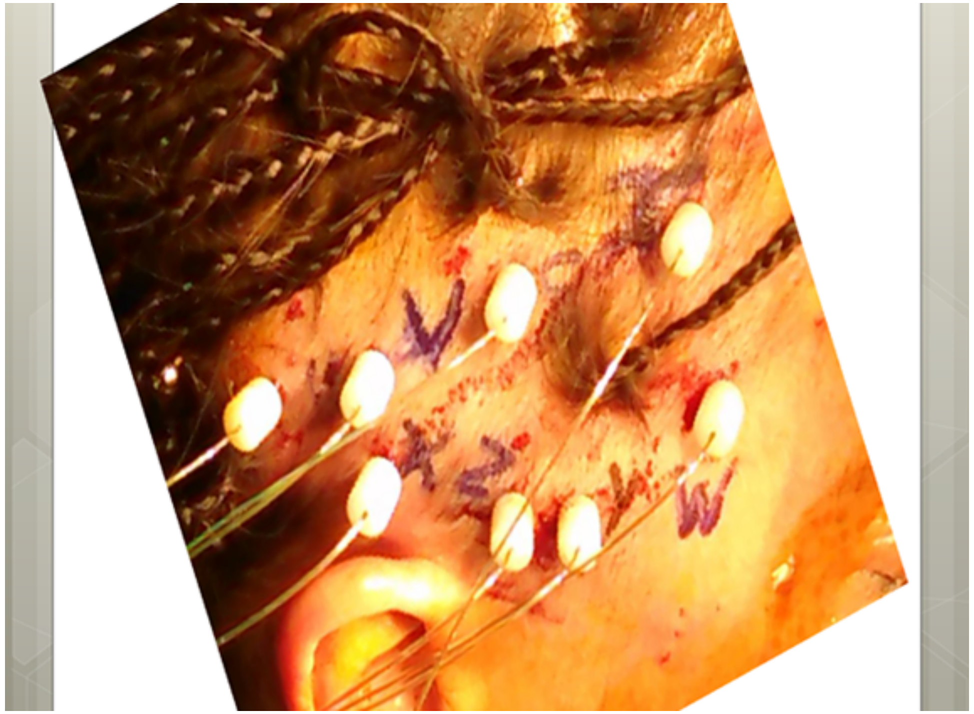
Table 1
Results from Google Trends search between first and final epoch of study.

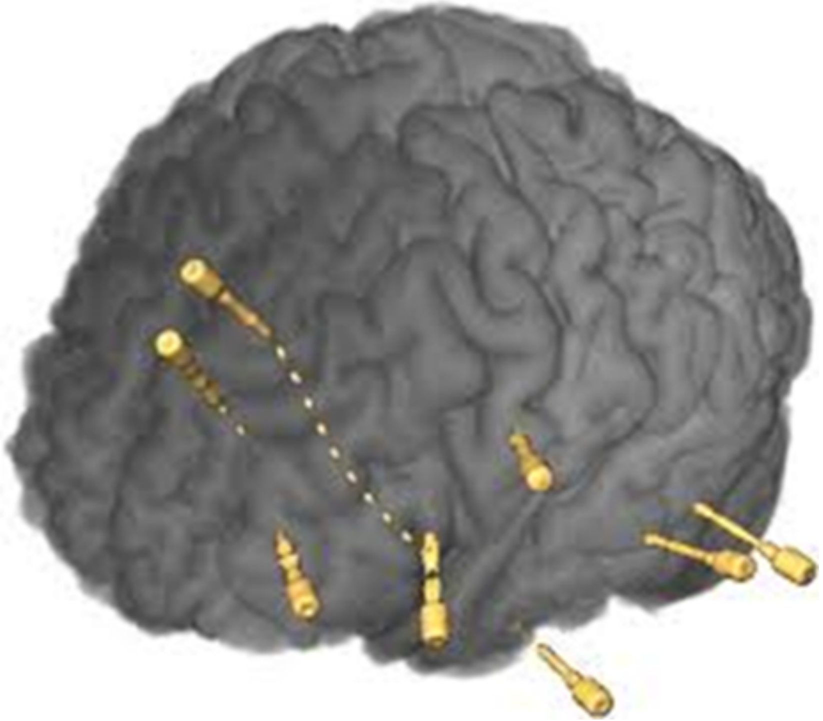
Google Trends search term	First [3 years] epoch Average relative search volume (RSV)	Final [3 years] epoch Average relative search volume (RSV)	Percentage change in relative search volume (RSV) between the epochs
"Epilepsy surgery"	26.9	11.8	−56.1
"Temporal lobe epilepsy"	57.3	27.5	−52.0
"Frontal lobe epilepsy"	26.4	12.8	−51.5
"Occipital lobe epilepsy"	10.2	9.2	−9.8
"Hippocampal sclerosis"	36.9	12.8	−65.3
"Focal cortical dysplasia"	30.2	20.9	−30.8
"Hypothalamic hamartoma"	30.0	16.5	−45.0
"Anterior temporal lobectomy"	14.3	4.6	−67.8
"Frontal lobectomy"	31.9	6.6	−79.3
"Vagal nerve stimulation epilepsy"	2.8	10.8	+285.7
"Laser ablation epilepsy"	0	30.3	+30.3
"Intracranial EEG"	17.8	6.6	−62.9
"Long-term video-EEG monitoring"	39.4	25.5	−35.3
"Insular epilepsy", "extratemporal epilepsy", "posterior quadrant epilepsy", "epilepsy surgery center", "epilepsy surgeon", "frontal lobe epilepsy surgery", "parietal epilepsy surgery", "parietal lobectomy", "occipital epilepsy surgery", "occipital lobectomy"	Returned no results.		

STEREOencephalography (Stereo-EEG, SEEG)

Stereoencephalography (SEEG)

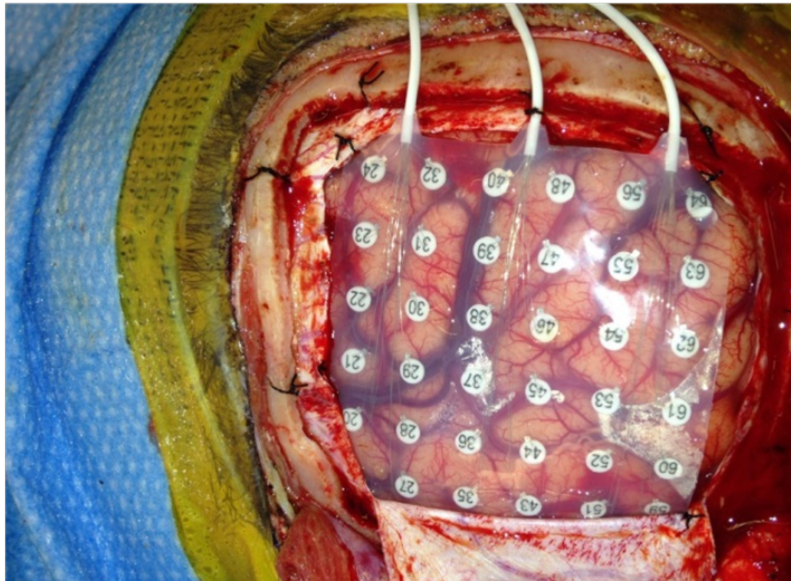
- Stereoelectroencephalography involves the strategic placement of multiple depth electrodes for invasive localization of focal epilepsy





Indications for invasive intracranial monitoring for localization of epileptic focus

- MRI-negative epilepsy
- Electroclinical and imaging data discordance
- Multiple lesions, discordance
- Overlap with functional cortex



Subdural grid

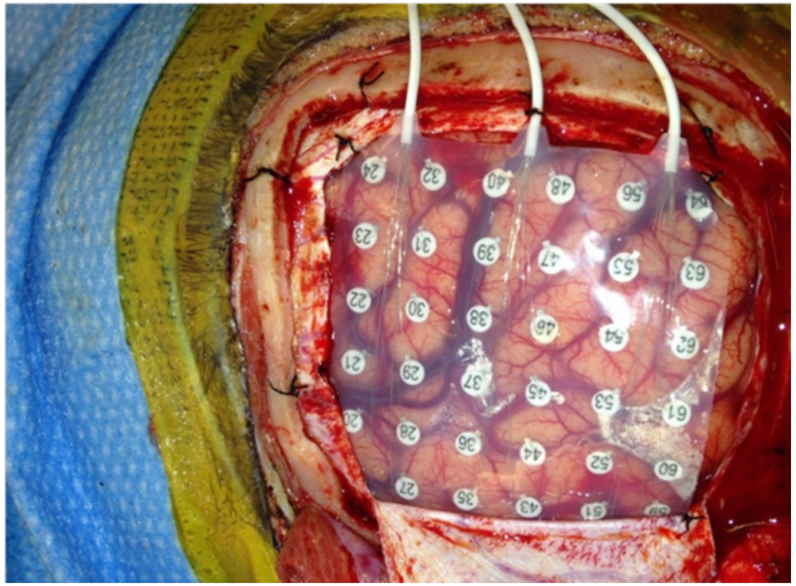
Stereoencephalography (SEEG)

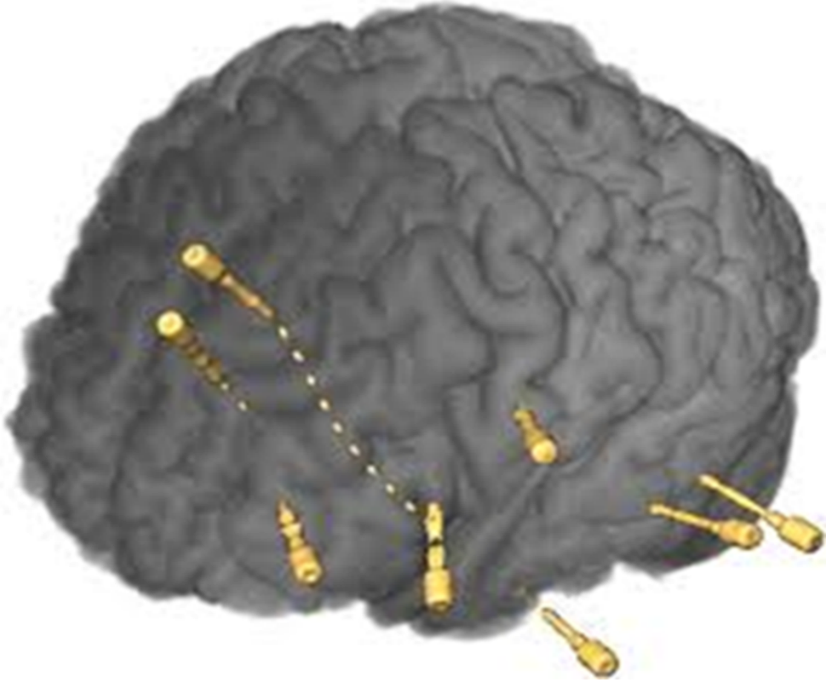
Stereoencephalography

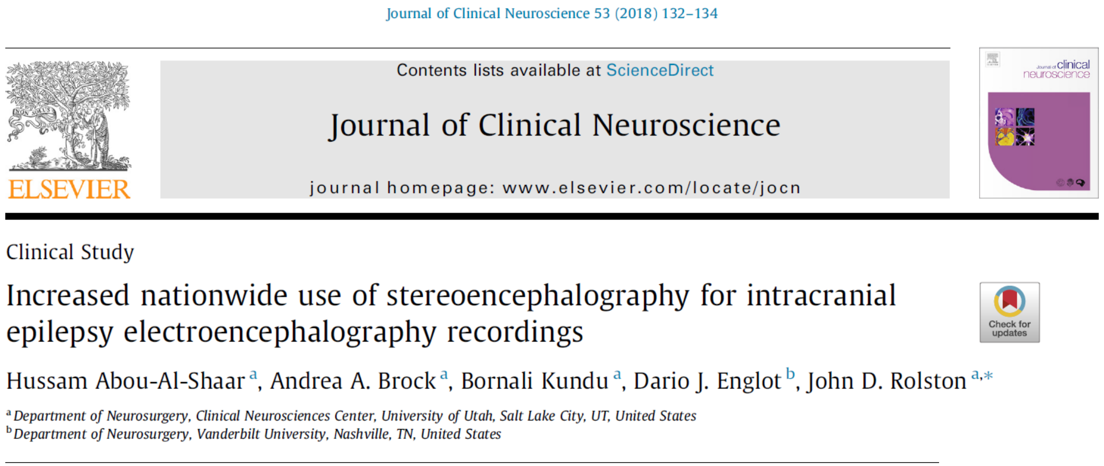
- Differs significantly from the alternative subdural grid approach in 2 major ways:

1. Conceptualization of epileptic zone (EZ) as a 3-D distributed network, rather than as focal pathology with contiguous spread

2. The method of sampling used which is sparse and directed rather than continuous over adjacent brain areas






Journal of Clinical Neuroscience 53 (2018) 132–134

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Journal of Clinical Neuroscience

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

Clinical Study

Increased nationwide use of stereoencephalography for intracranial epilepsy electroencephalography recordings

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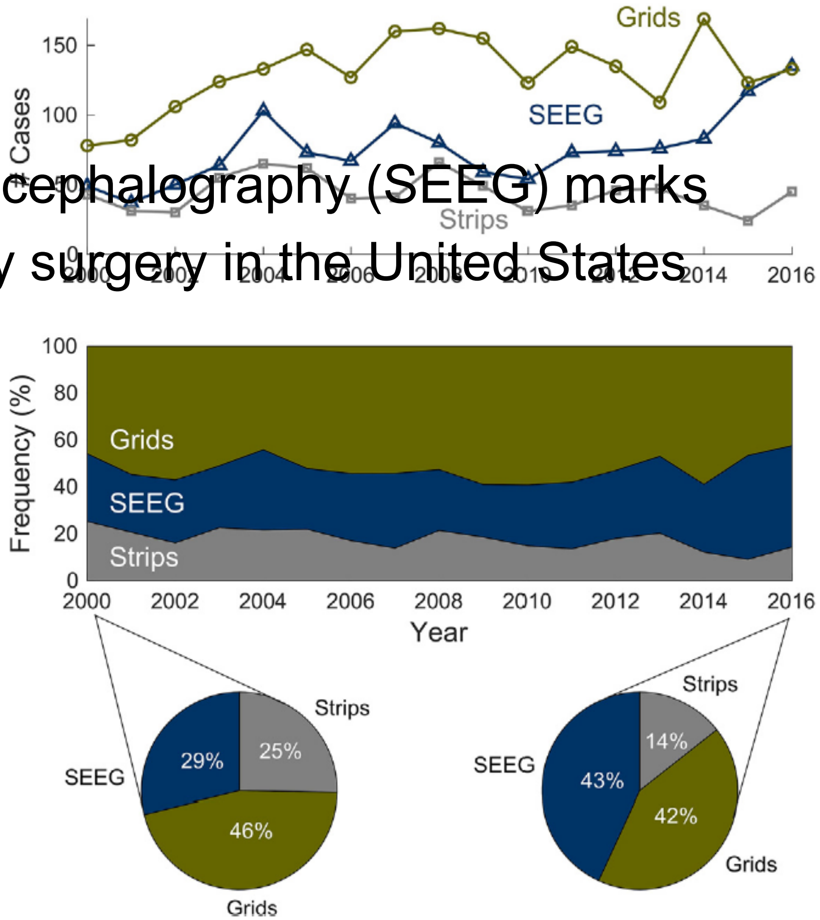
[b] Department of Neurosurgery, Vanderbilt University, Nashville, TN, United States

- The increasing adoption of stereoelectroencephalography (SEEG) marks
- a significant shift in the practice of epilepsy surgery in the United States



SEEG versus SDG

Table 1
A schematic for understanding technique advantages, limitations, and the best surgical candidates for both SDE and SEEG

	SDE	SEEG
Advantages	Accurate anatomic electrical/functional mapping of covered brain surfaces. Monitoring and resection within one hospital stay.	Enhanced targeting capability for deeper targets. Improved bihemispheric monitoring as well as mapping of functional networks. More facile placement in the reoperated patient. Given smaller access to implant leads, lessened wound healing morbidity.
Limitations	Difficulty in coverage of intrasulcal, deep brain and interhemispheric targets. Multilobar or bilateral sampling challenges. Morbidity associated with surgery: infectious consequences, hemorrhage, cerebral edema, if following previous surgery potential for adhesions and difficult dissection. Inaccuracy encountered when SDG used with additional depth electrodes.	Functional mapping restricted. If hemorrhage associated with placement of leads, can be large scale with significant consequences.
Ideal surgical candidates	The patient with a possible cortical target/lesion within eloquent cortex, a virgin surgical resection and/or goal of surgery to perform cortical mapping.	The patient with nonlesional MRI, deep lesions or EZ; and/or the previously operated patient. Also, the patient in whom bilateral exploration is required.

SEEG versus SDG

Table 1
Selection criteria for different methods of invasive monitoring in medically refractory focal epilepsy

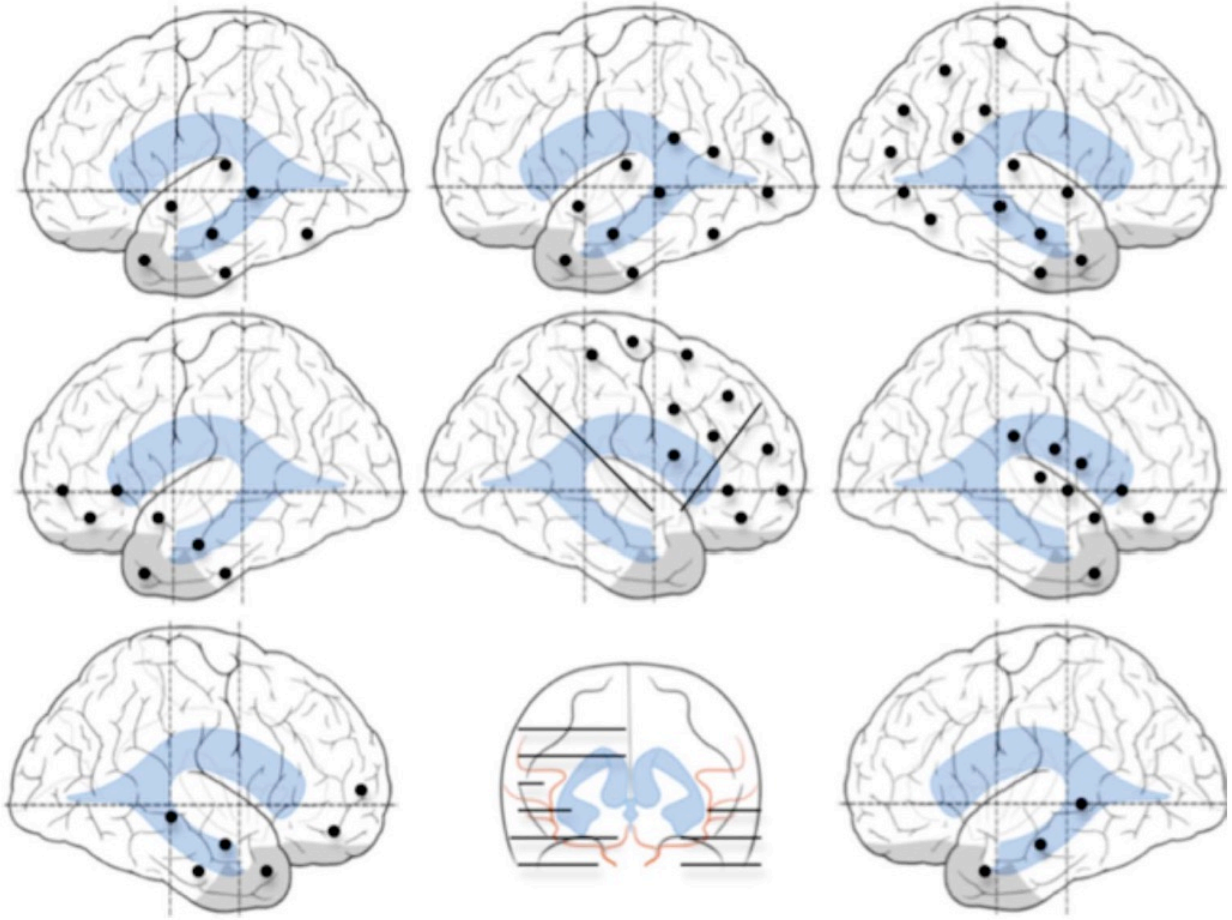
Clinical Scenario	Method of Choice	Second Option
Lesional MRI: Potential epileptogenic lesion is superficially located, near or in the proximity of eloquent cortex. Nonlesional MRI: Hypothetical EZ located in the proximity of eloquent cortex.	SDG	SEEG
Lesional MRI: Potential epileptogenic lesion is located in deep cortical and subcortical areas. Nonlesional MRI: hypothetical EZ is deeply located or located in noneloquent areas.	SEEG	SDG with depths
Need for bilateral explorations and or reoperations.	SEEG	SDG with depths
After subdural grids failure	SEEG	SDG with depths
When the AEC hypothesis suggest the involvement of a more extensive, multilobar epileptic network.	SEEG	SDG with depths
Suspected frontal lobe epilepsy in nonlesional MRI scenario	SEEG	SEEG

Alomar s. et al, 2016

Specific Criteria for SEEG

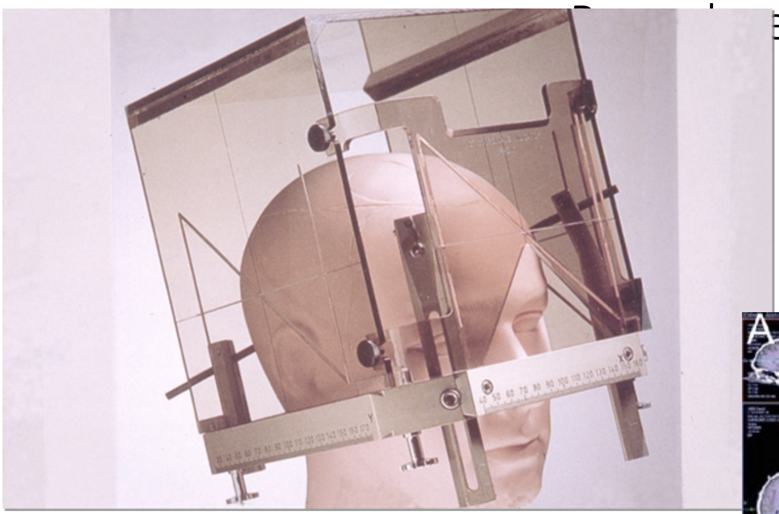
- Deep-seated or difficult-to-cover location of the epilptogeniczone (mesial structures of the temporal lobe, opercular areas, cingulate gyrus, interhemispheric regions, posterior orbitofrontal areas, insula, and depth of sulci)
- Failure of a previous subdural invasive study
- Extensive bihemispheric explorations
- Normal MRI

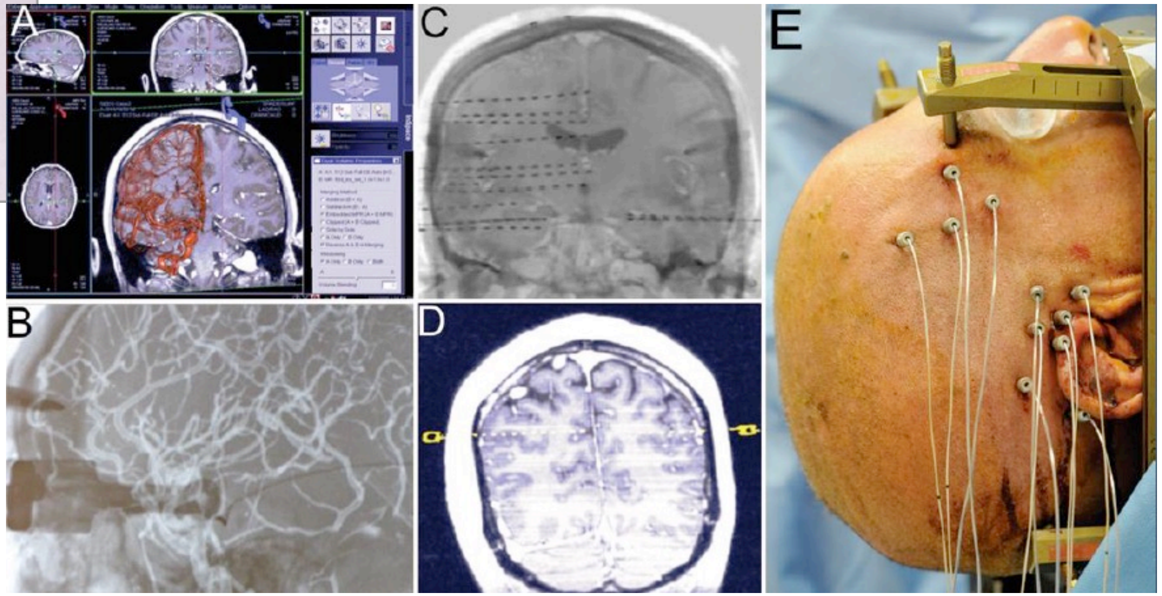
Patterns of SEEG Implantation



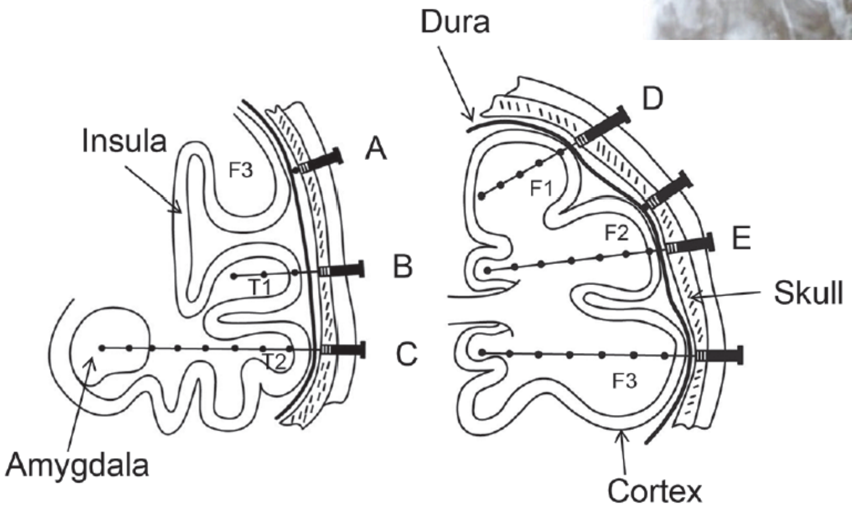
Gonzalez-Martinez et al

e /Technique

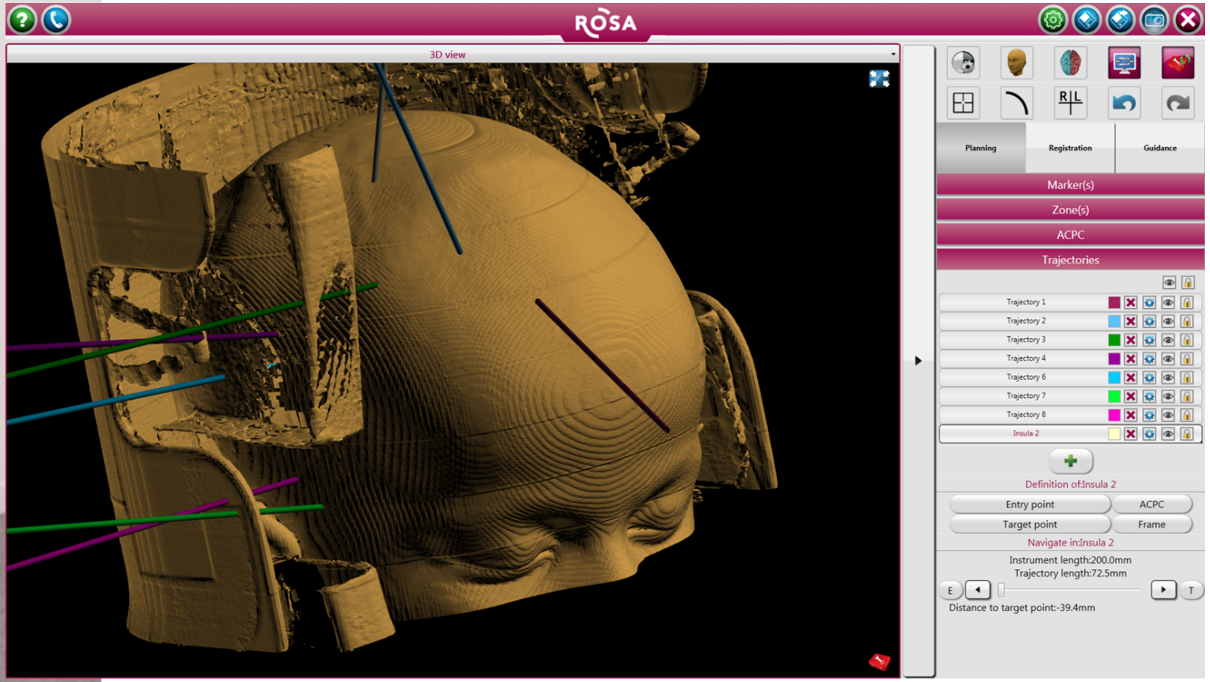


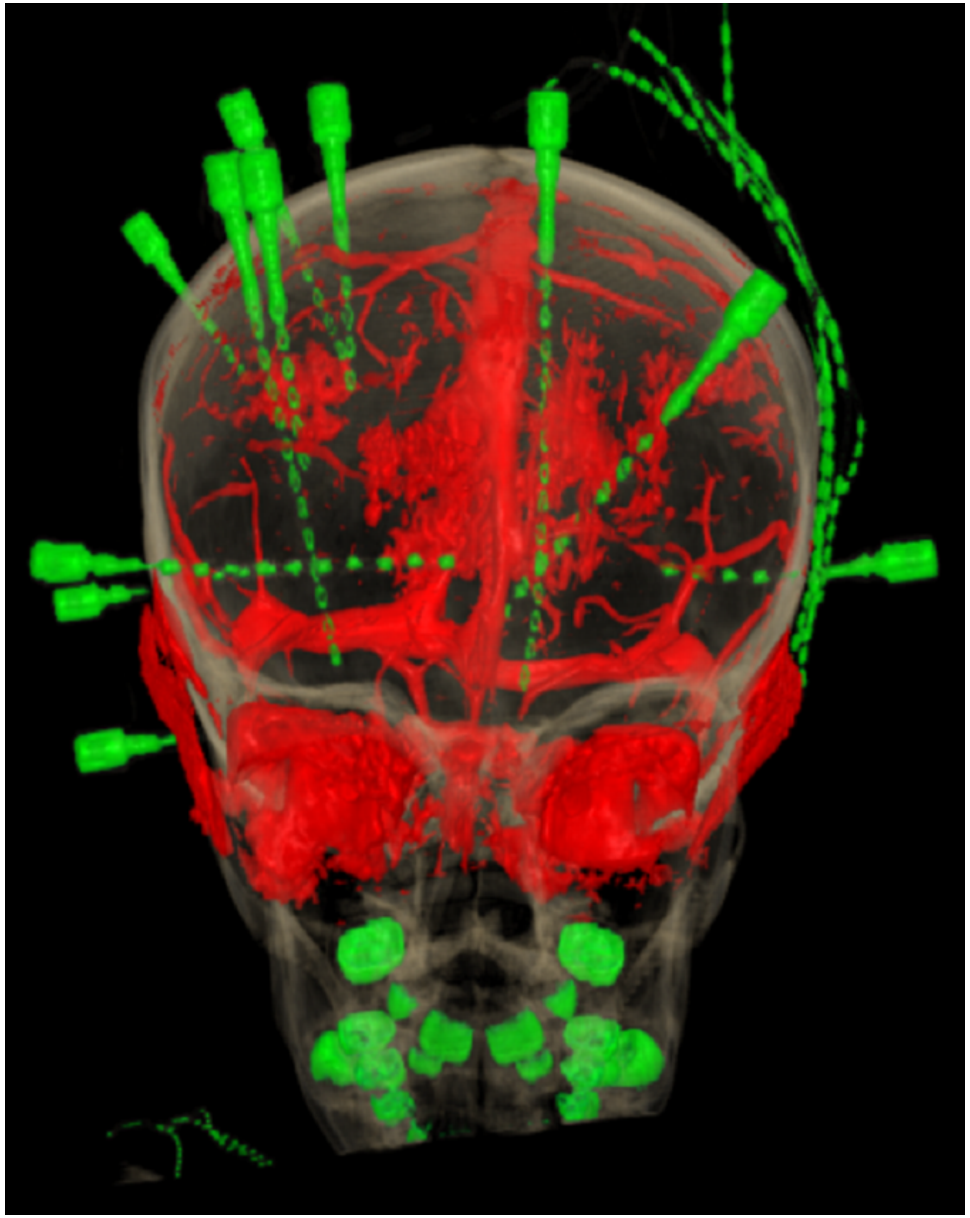


Gonzalez-Martinez, et al. J Neurosurg 2014; 120:639-644.



Neurorobotics (Stereotactic Robots)





Minimally Invasive Laser Ablation of Epileptogenic Foci

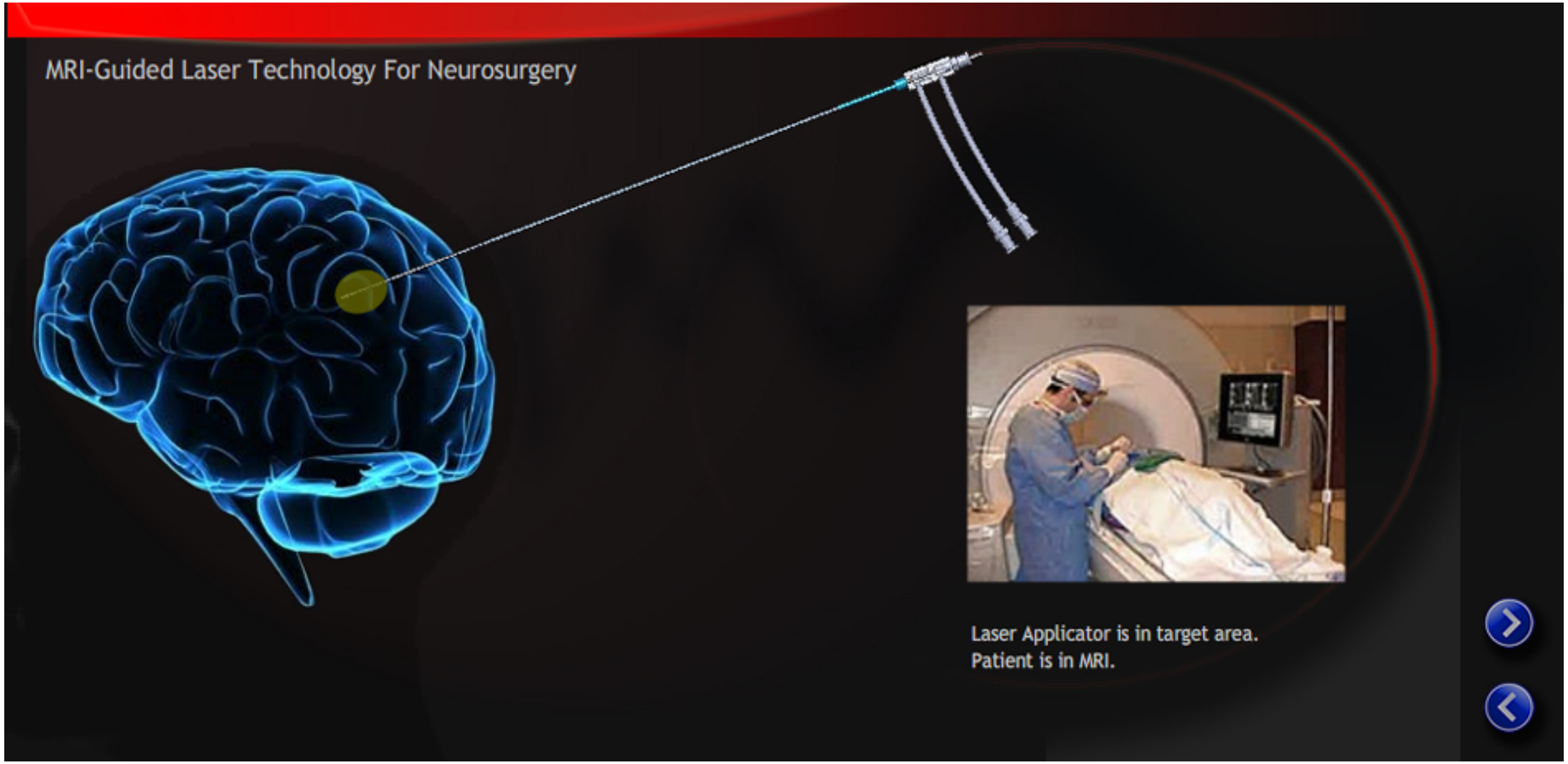
Small 980nm diode laser

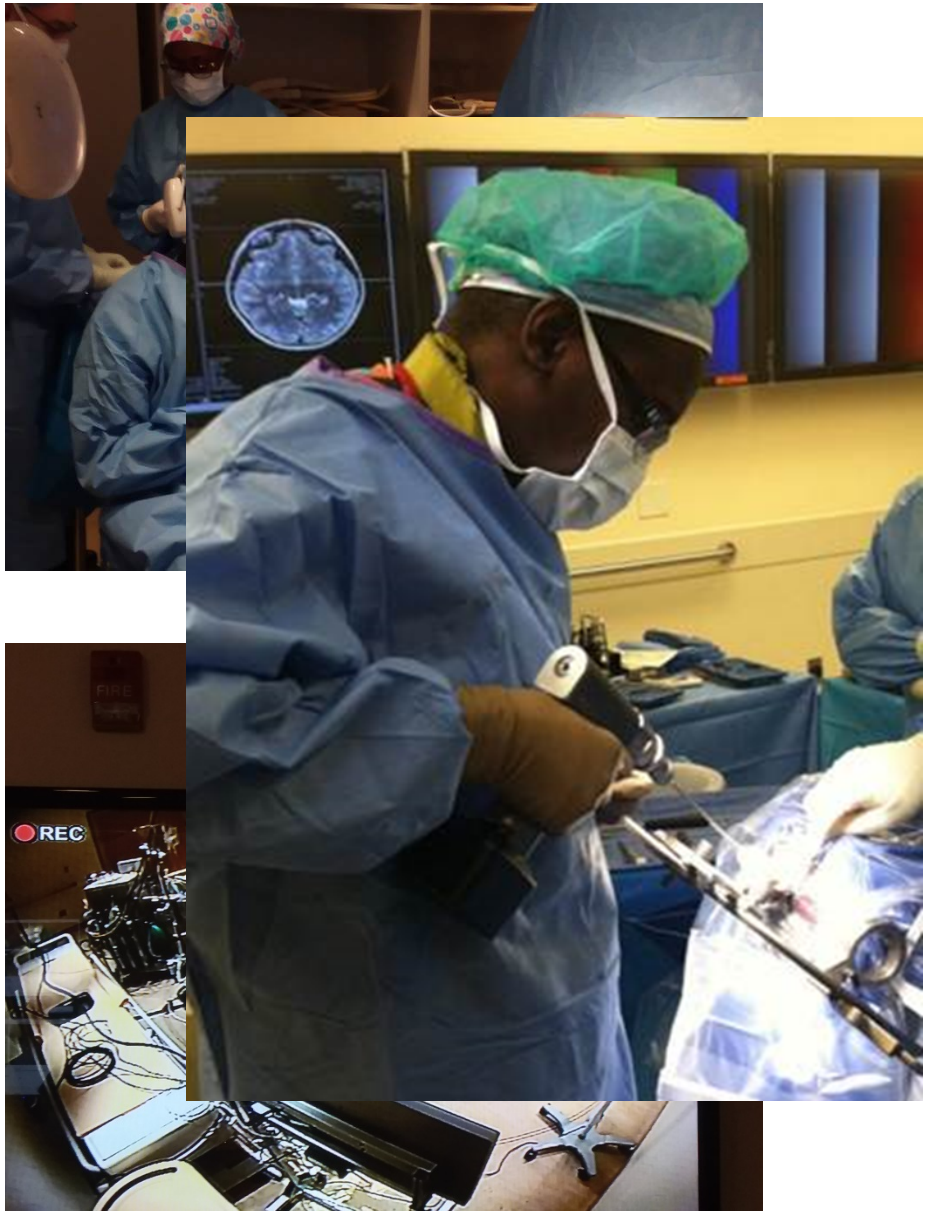
Readily interfaces with MRI

Software: real-time prediction model control features

1.65mm in diameter and includes a

Cooling Catheter and Laser Diffusing Fiber


MRI-Guided Laser Technology For Neurosurgery
Laser Applicator is in target area.
Patient is in MRI.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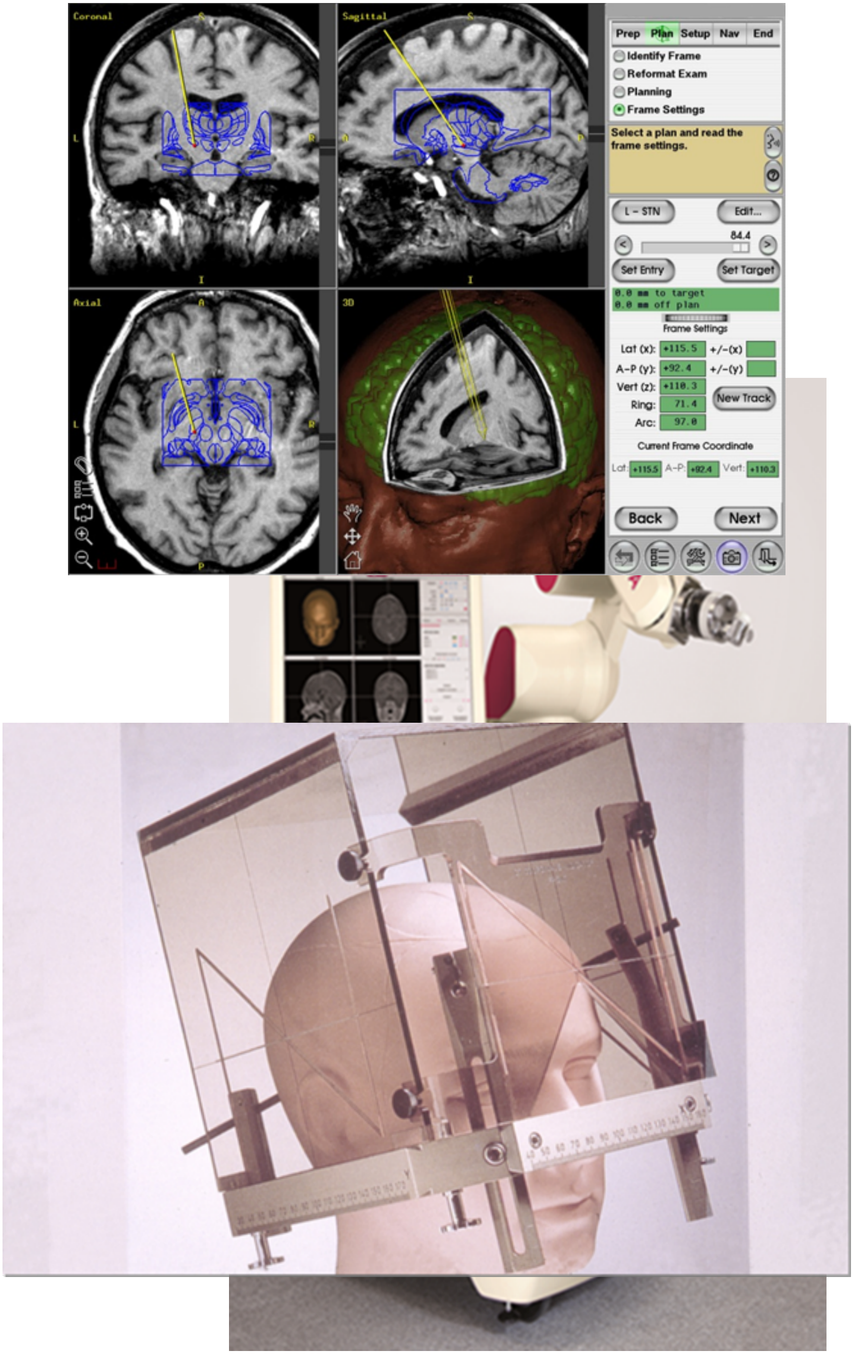
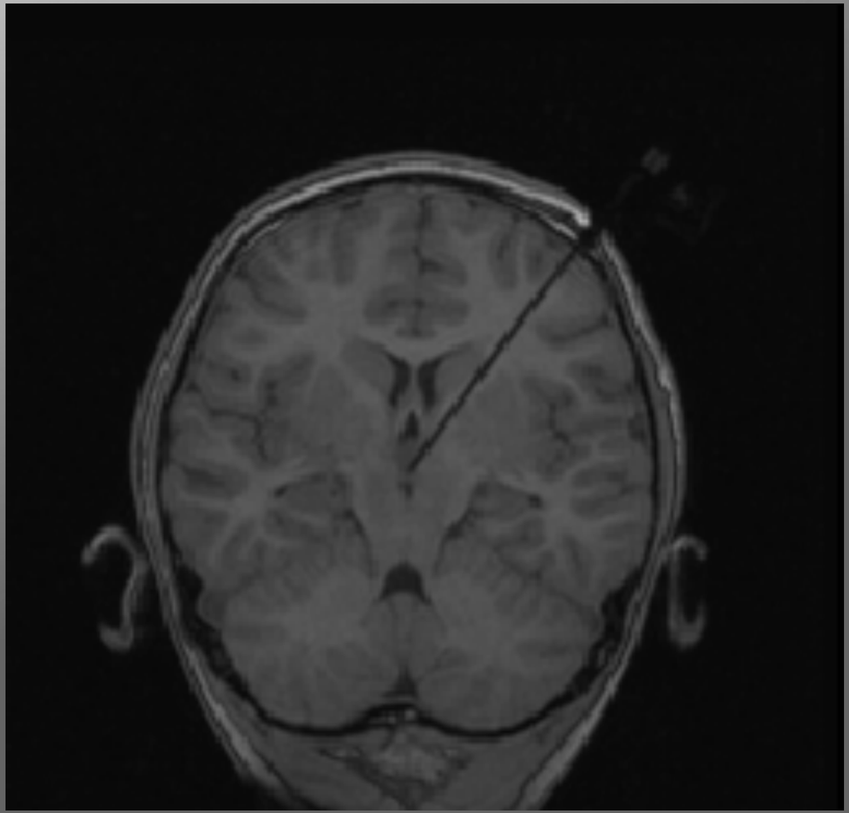

Coronal
Sagittal
Axial
3D
Prep
Plan
Setup
Nav
End
Identify Frame
Reformat Exam
Planning
Frame Settings
Select a plan and read the frame settings.
L - STN
Edit...
84.4
Set Entry
Set Target
Frame Settings
Lat (x):
+115.5
+/-(x)
A-P (y):
+92.4
+/-(y)
Vert (z):
+110.3
Ring:
71.4
Arc:
97.0
New Track
Current Frame Coordinate
Back
Next

Laser Ablation in Pediatric Epilepsy Surgery

- Hypothalamic hamartoma
- Insula
- Periventricular nodular heterotopia
- Tuberous sclerosis
- Mesial temporal sclerosis

- 6 year old girl
- Intractable epilepsy, gelastic seizures since age 3 months

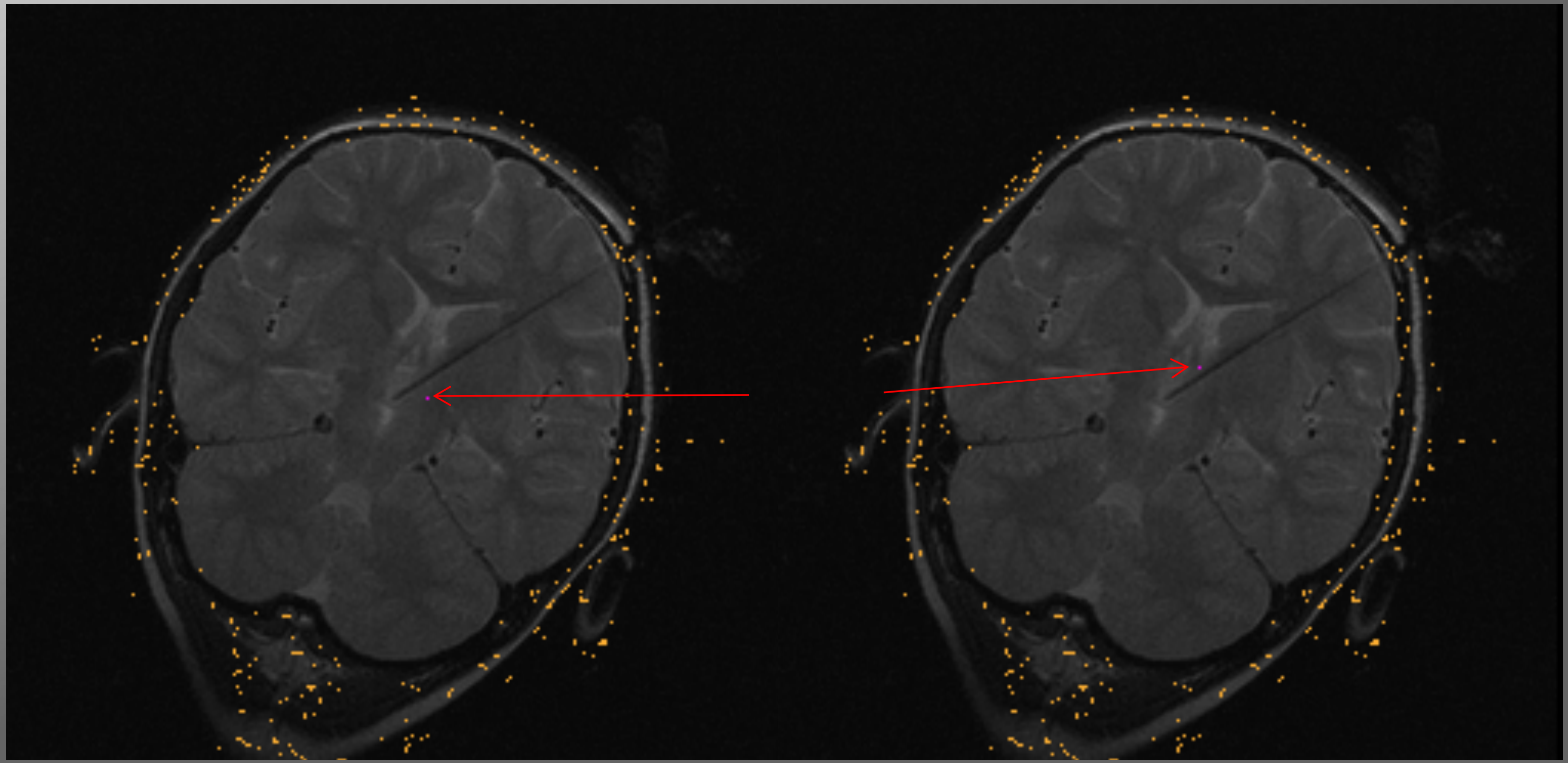
Placement Verification



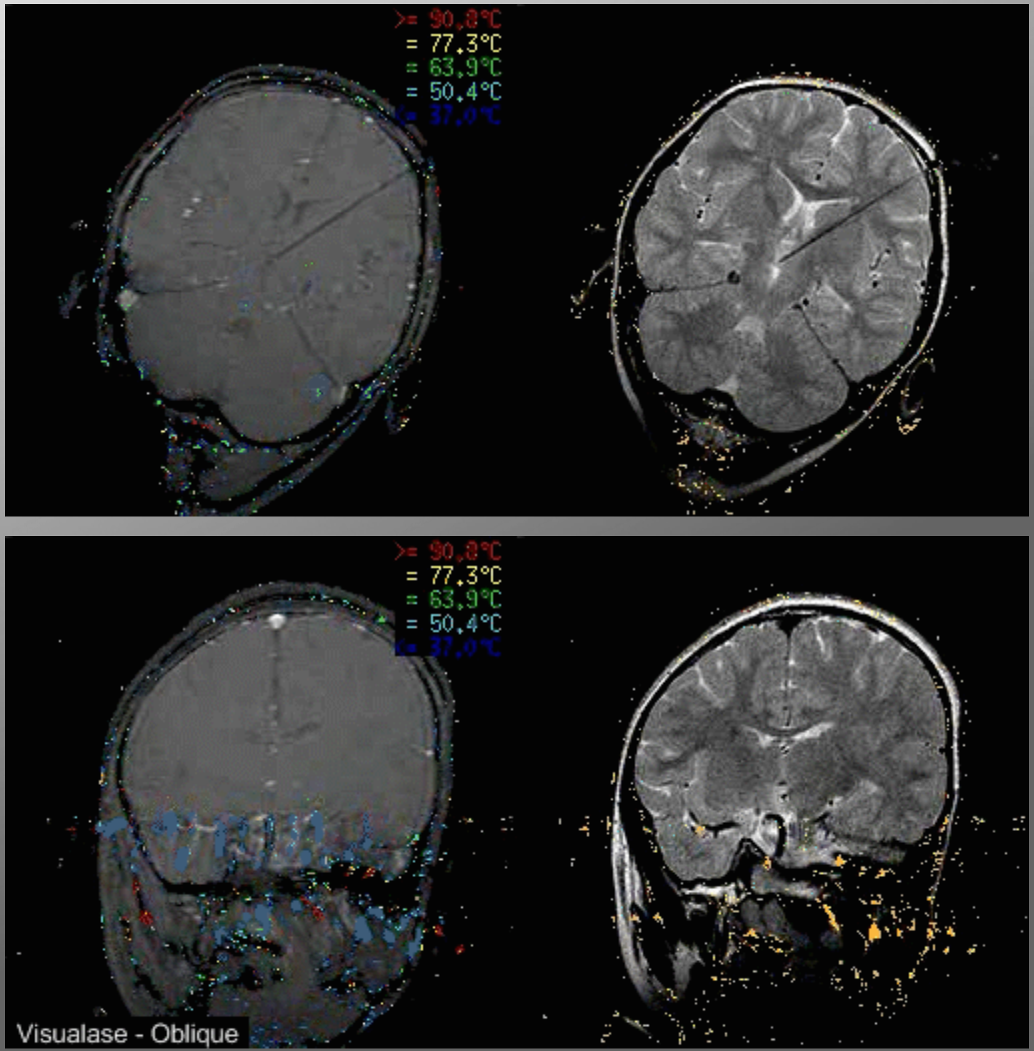
Coronal Oblique 3D Reconstruction
3mm Laser Diffusing Fiber
Stereotactic Placement using Leksell G Frame and Stealth Planning Software

Temperature Safety Markers

Safety markers prevent damage of non-target tissues. The laser is stopped automatically when a selected tissue reaches 47º C.



Laser Ablation – Dual Plane Monitoring Videos



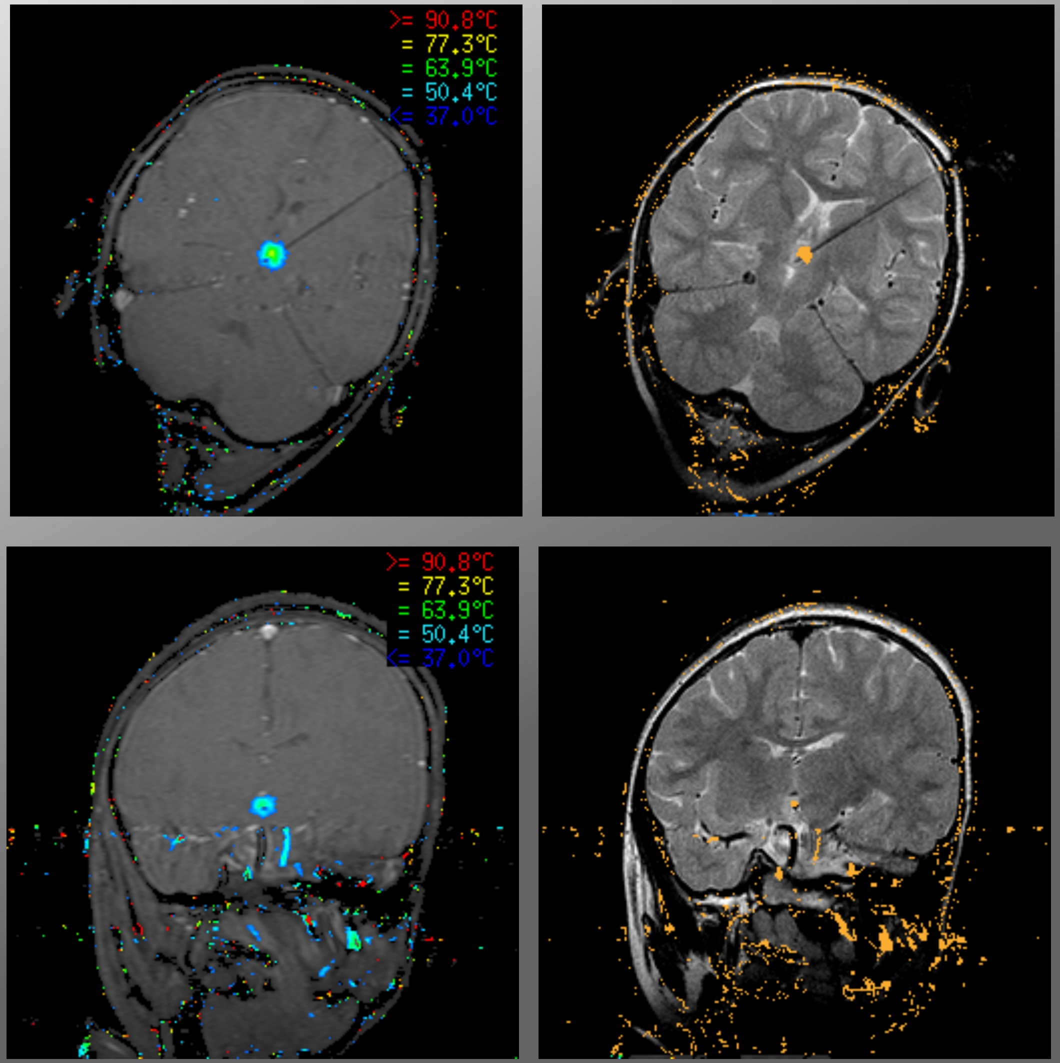
Visualase Treatment Monitoring Videos

Test Dose

2 Watts for 31 seconds
3 Watts for 18 seconds

Treatment Dose

5 Watts for 44 seconds

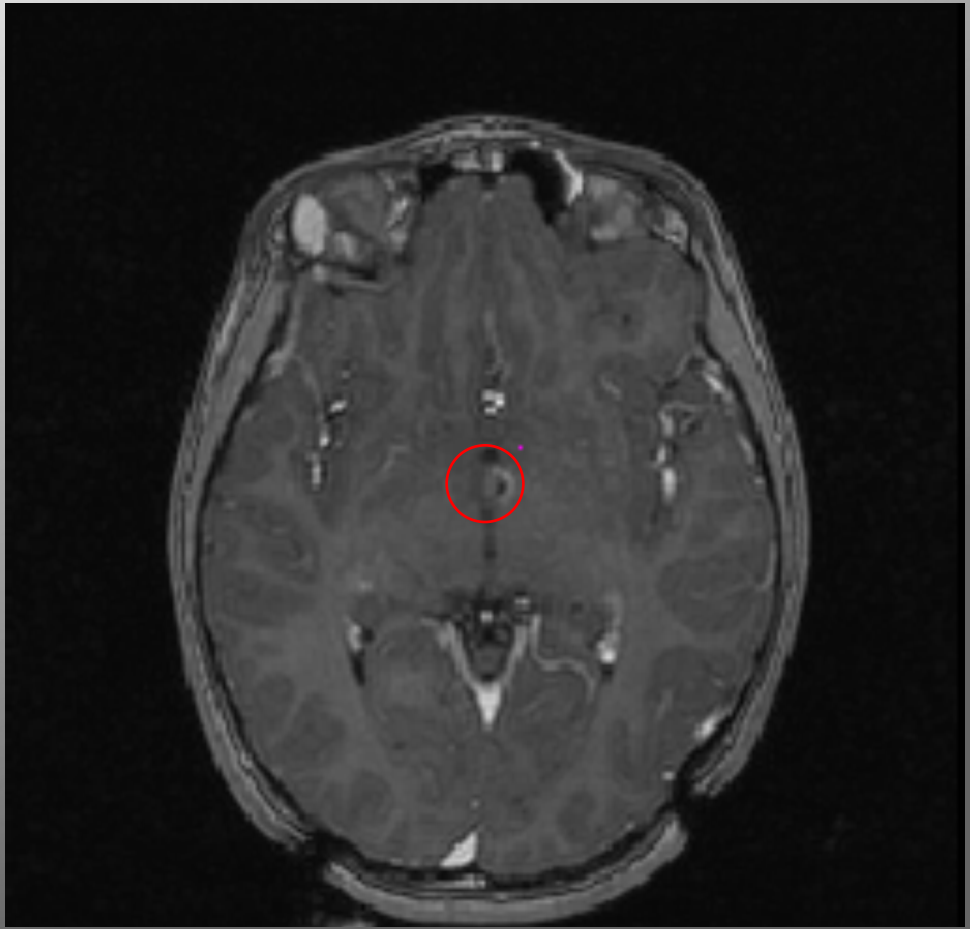


Test Dose

2 Watts for 31 seconds
3 Watts for 18 seconds

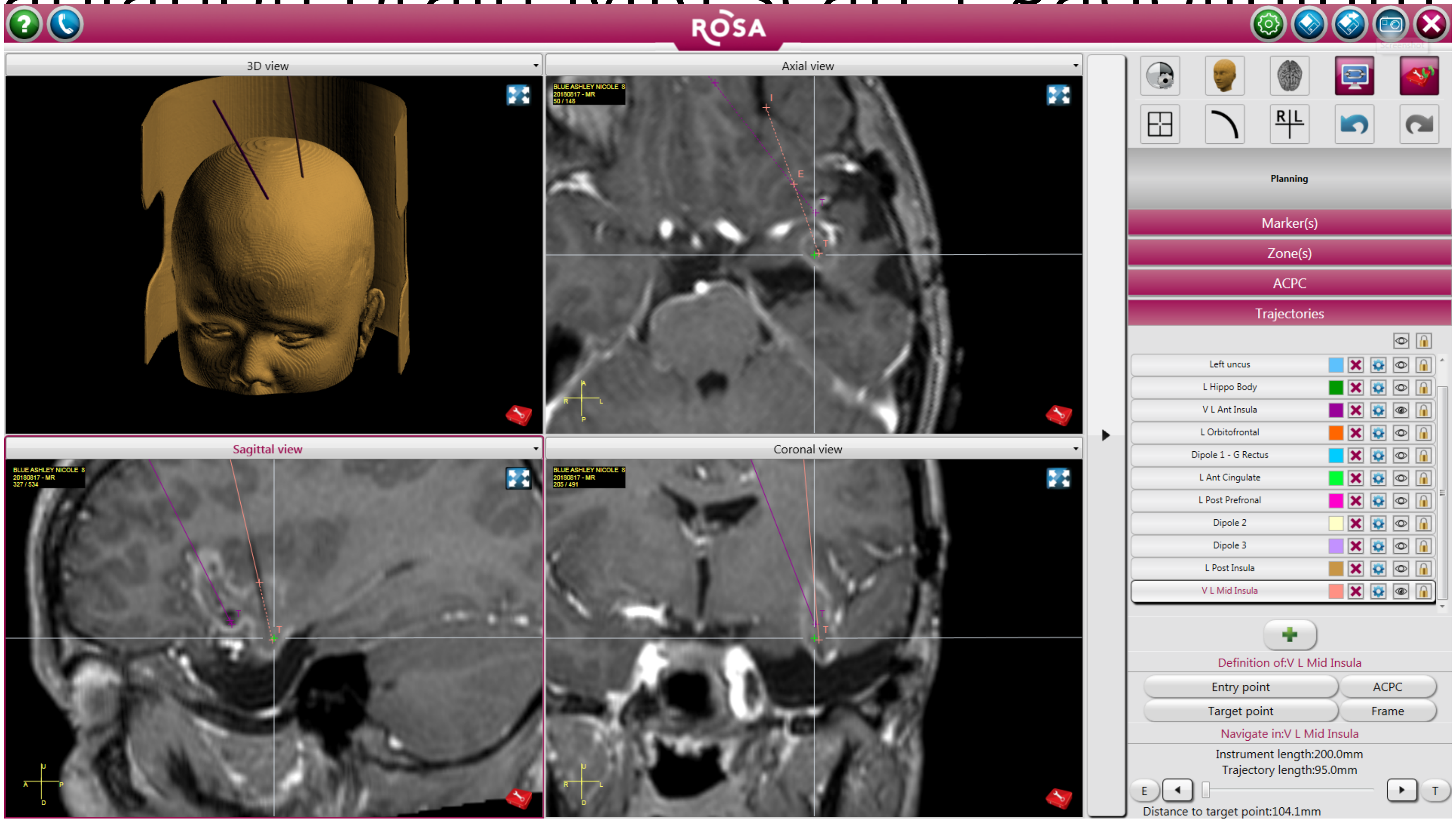
Treatment Dose
5 Watts for 44 seconds

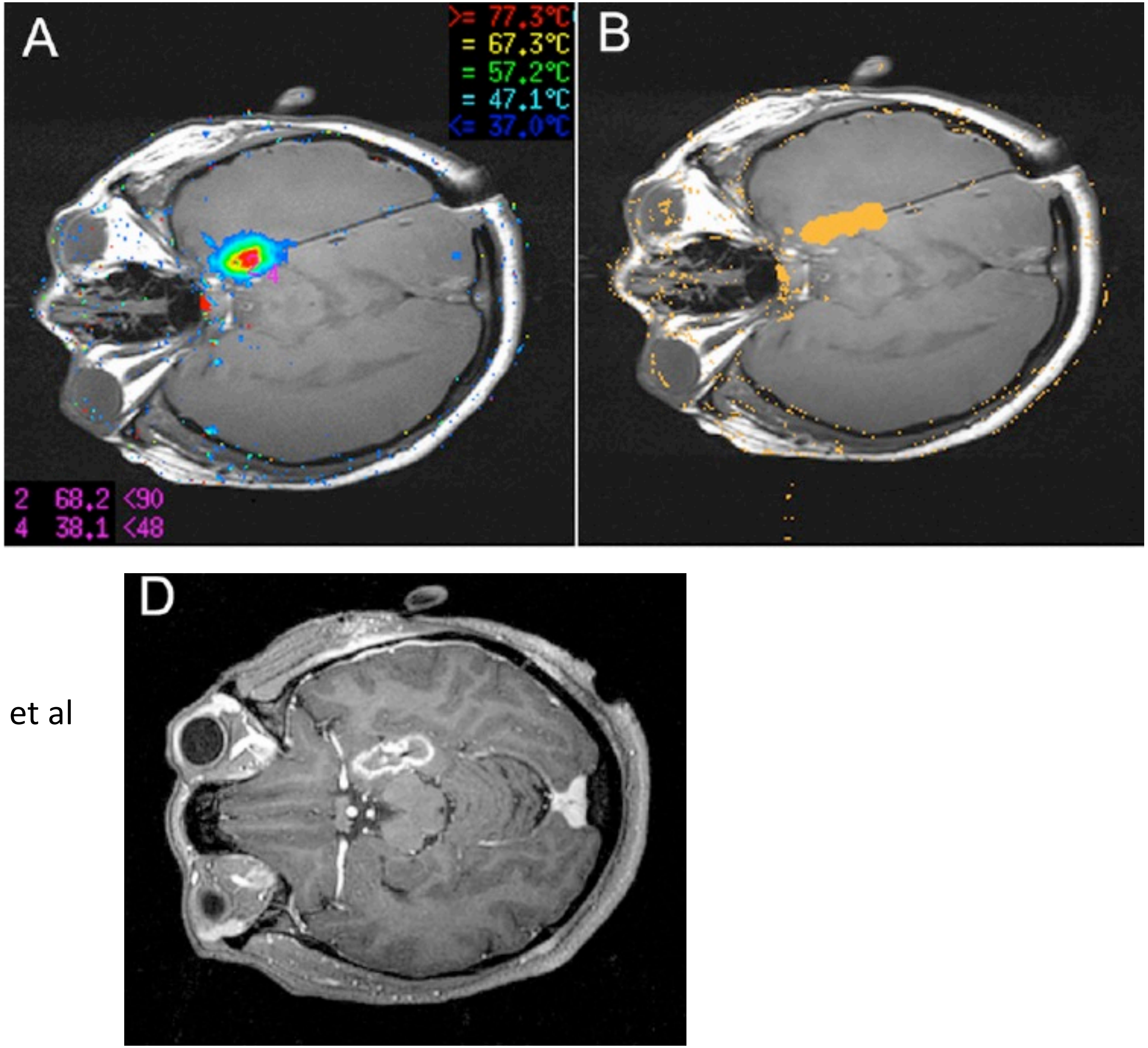
Post-Ablation Imaging



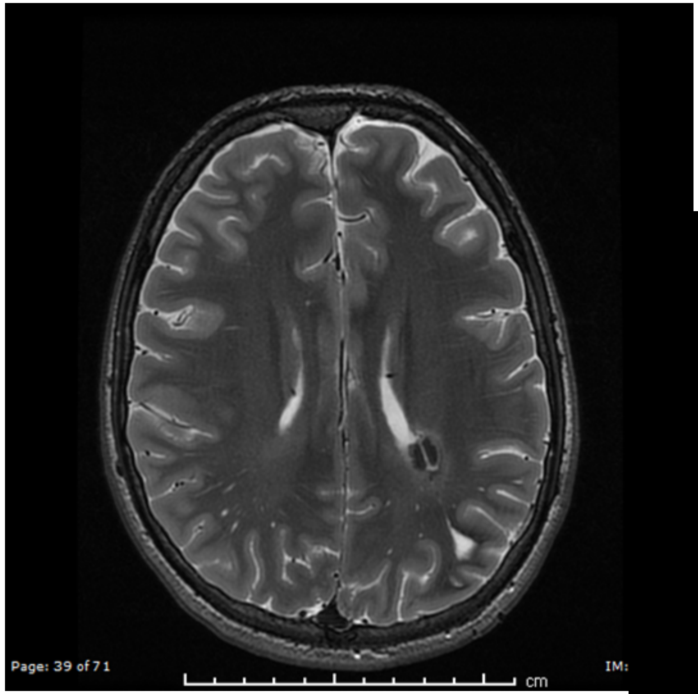
Insula Ablation

Post ablation brain MRI scan + gadolinium



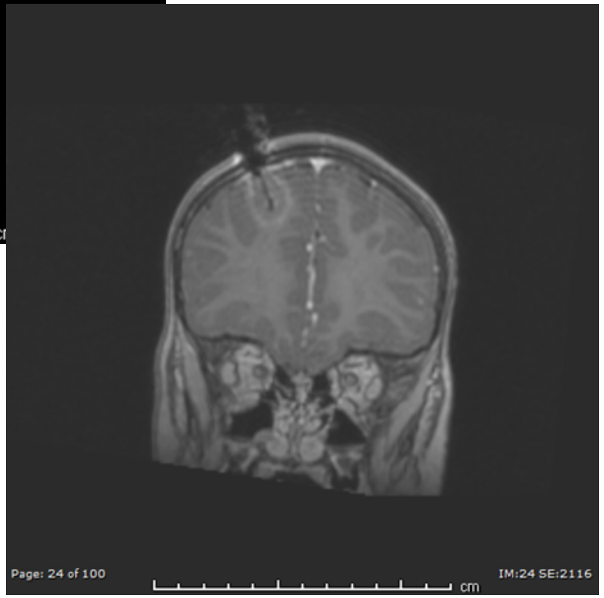


Tao et al



Periventricular nodular heterotopia

Mesial Temporal Sclerosis



Cortical tuber

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MR-guided laser ablation for the treatment of hypothalamic hamartomas

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[c] Section of Neurology, Texas Children's Hospital, Houston, TX, United States
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ARTICLE INFO

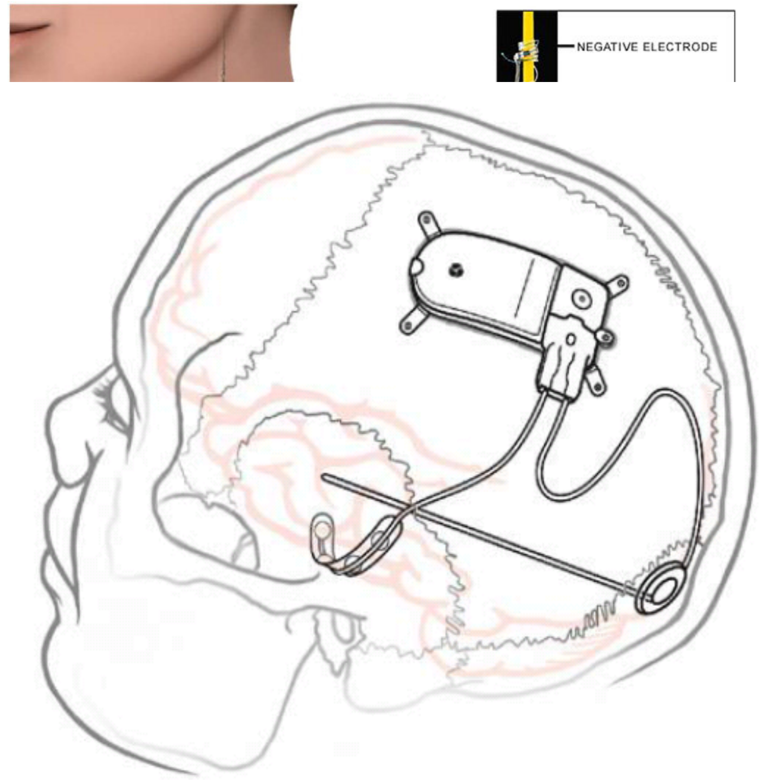
Keywords:
Hypothalamic hamartoma
Stereotactic laser ablation
MRgLITT
Gelastic epilepsy

ABSTRACT

Hypothalamic hamartoma is an archetypal example of subcortical epilepsy that can be associated with intractable gelastic epilepsy, secondary epilepsy, and epileptic encephalopathy. The history of its surgical treatment is fraught with mislocalization of the seizure focus, modest efficacy and a high complication rate. Many minimally invasive techniques have been described to mitigate this high complication profile of which MR-guided laser ablation is one. The technology combines instant effect of thermal coagulation with stereotactic precision and guidance with real time MR thermography. This article presents a series of 71 hypothalamic hamartoma patients operated with laser ablation. Ninety-three percent (93%) were free of gelastic seizures at one year with 23% of the patients requiring more than one ablation. One patient experienced a significant memory deficit and one patient experienced worsening diabetes insipidus. Stereotactic laser ablation appears to be a safe and effective surgical option in the treatment of hypothalamic hamartoma.

Brain Stimulation (Electrical Neuromodulation) in Epilepsy Surgery

Neuromodulation

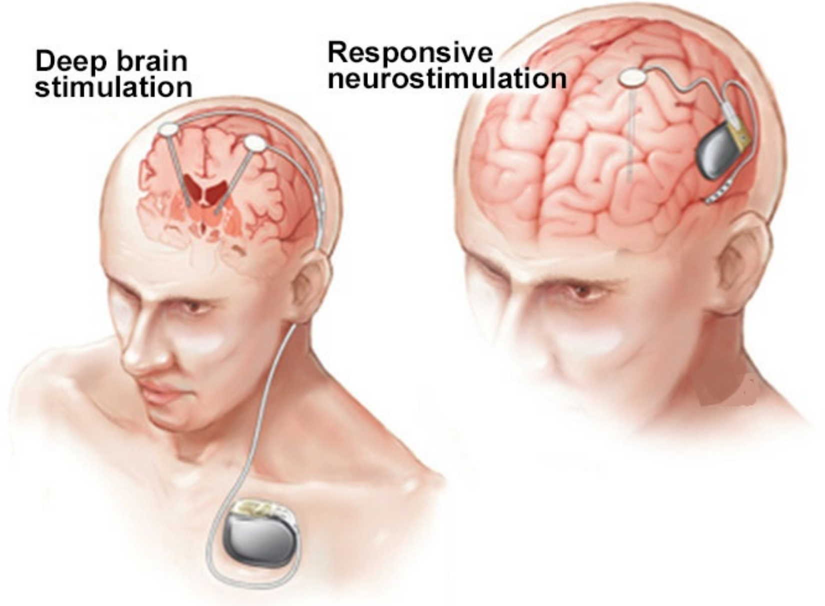


Responsive Neurostimulator (RNS)
FDA: 2013

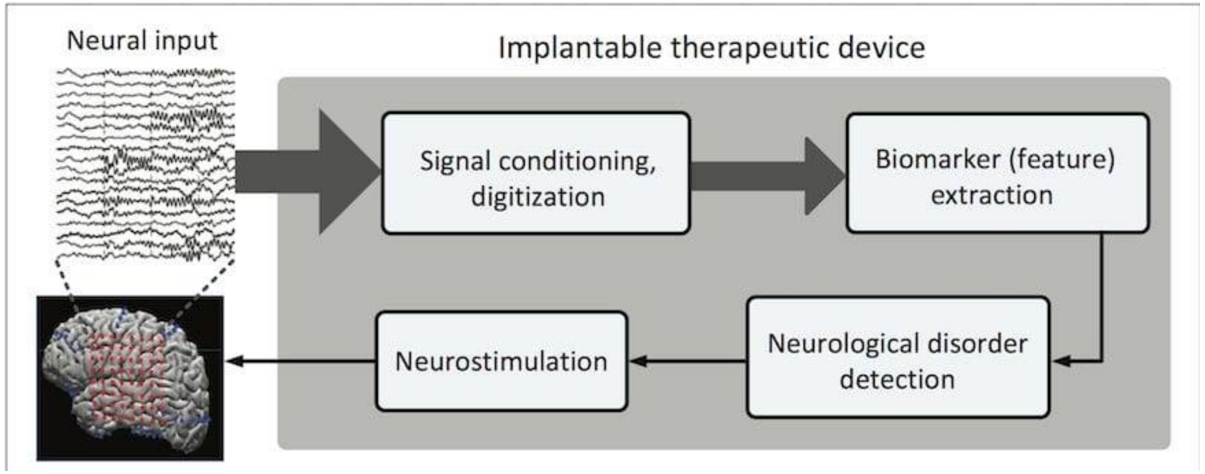
Anterior Thalamic Deep Brain Stimulation
FDA: 2018

(Electrical) Neuromodulation for Epilepsy – Brain Stimulation for Epilepsy

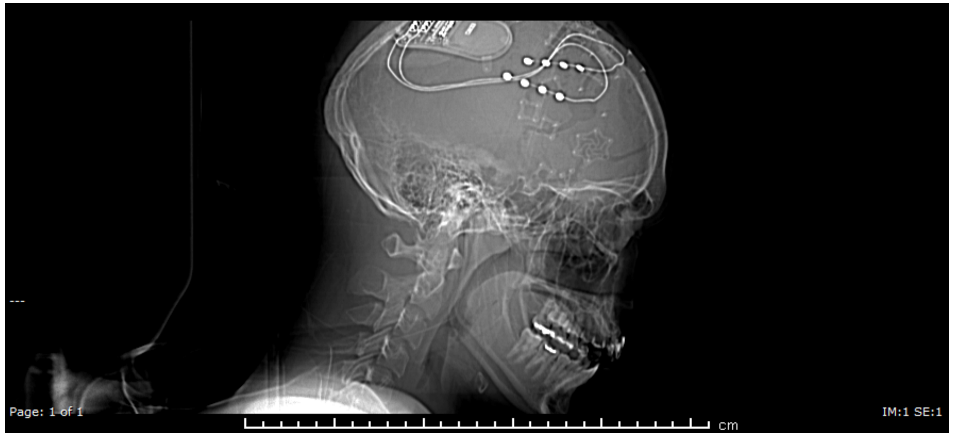
- Two therapeutic strategies
- 1. Deep brain Simulation – electrical stimulation of remote "pacemaker" structures of an epileptogenic network. Usually "Open loop" Stimulation

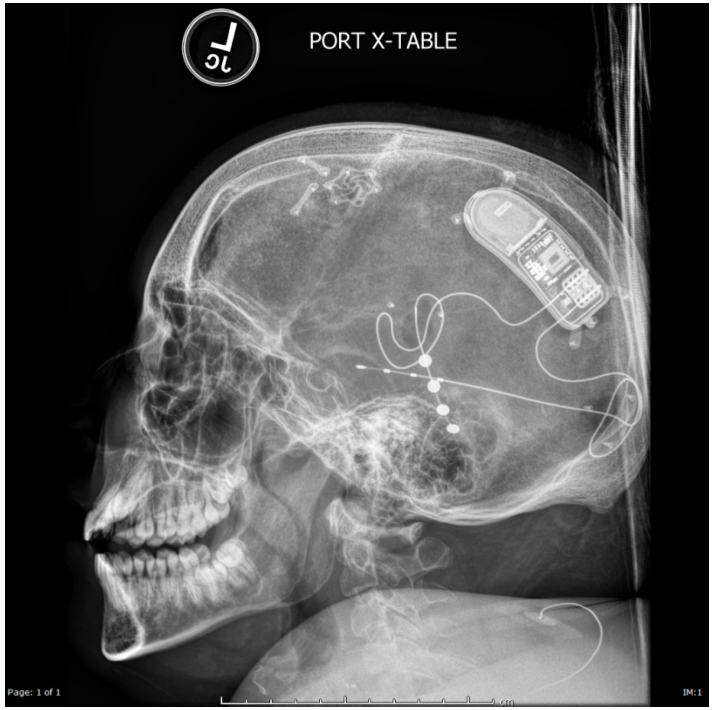


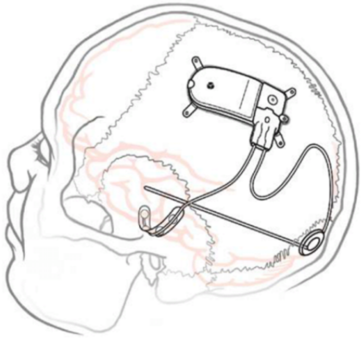
- 2. Responsive Neurostimulation (RNS); direct stimulation of the ictal onset zone (neocortex, hippocampus in medial temporal lobe epilepsy). Usually "Closed loop" Stimulation



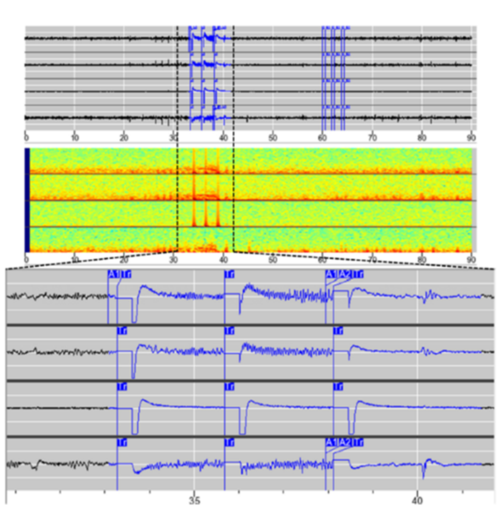
Responsive Neurostimulation (RNS)





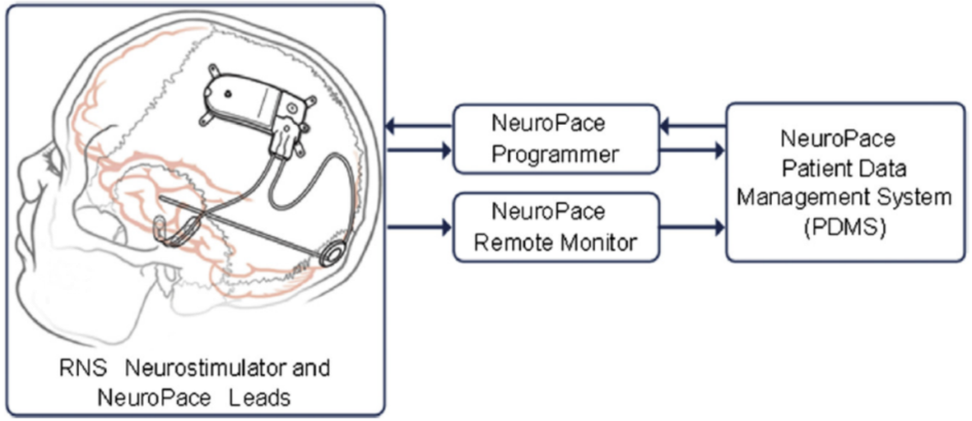


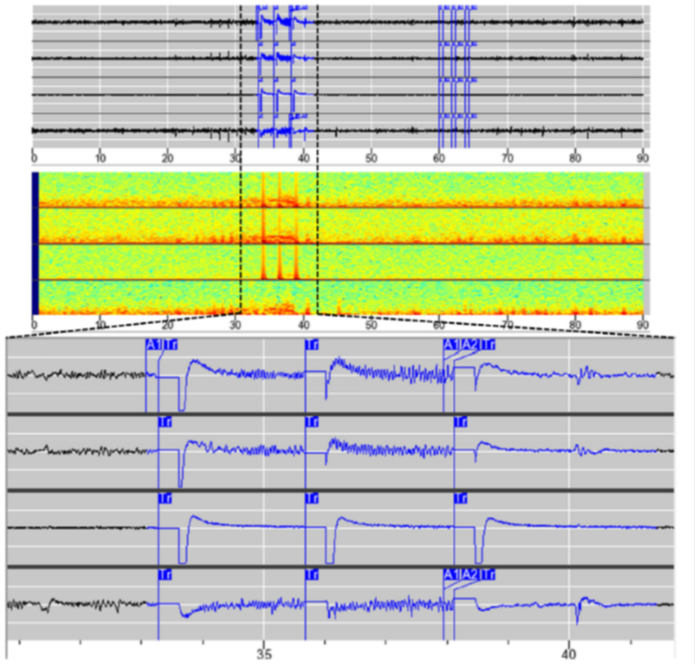
- Components: Cranially seated neurostimulator connected to 1 or 2 depth or cortical strip leads
- Each lead can be used for both sensing and stimulating.
- The physician programs detection and stimulation settings and retrieves and reviews data provided by the neurostimulator



RNS

- Closed-loop responsive direct brain stimulation
- Components: The cranially seated neurostimulator connected to 1 or 2 depth or cortical strip leads that are surgically placed in the brain at 1 or 2 seizure foci.
- Each lead can be used for both sensing and stimulating.
- The physician programs detection and stimulation settings and retrieves and reviews data provided by the neurostimulator





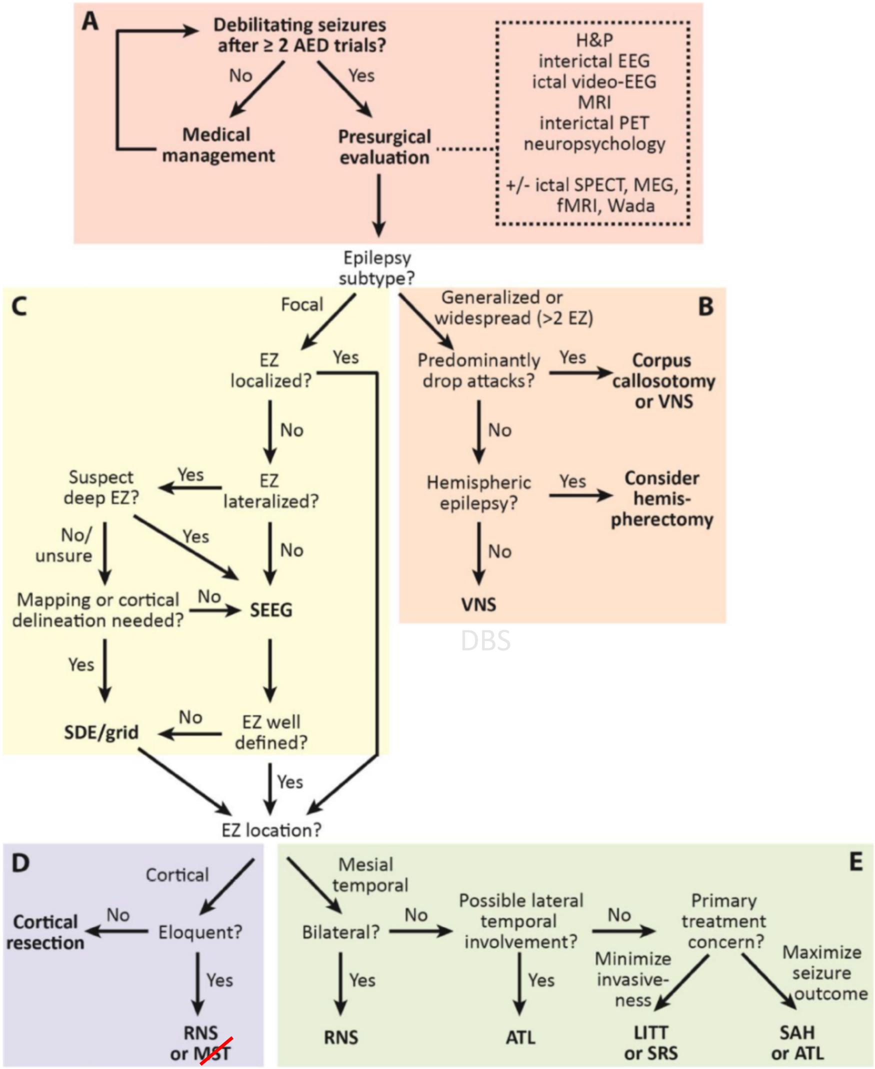
Electrical Neuromodulation

- In general, neuromodulation therapies have excellent safety profiles
- Not expected to provide freedom from seizures or antiepileptic medications.
- Aim is palliative: reduce seizure frequency or prevent secondary generalization.

Epilepsy Behav. 2018 March ; 80: 68–74. doi:10.1016/j.yebeh.2017.12.041.

A Modern Epilepsy Surgery Treatment Algorithm: Incorporating Traditional and Emerging Technologies

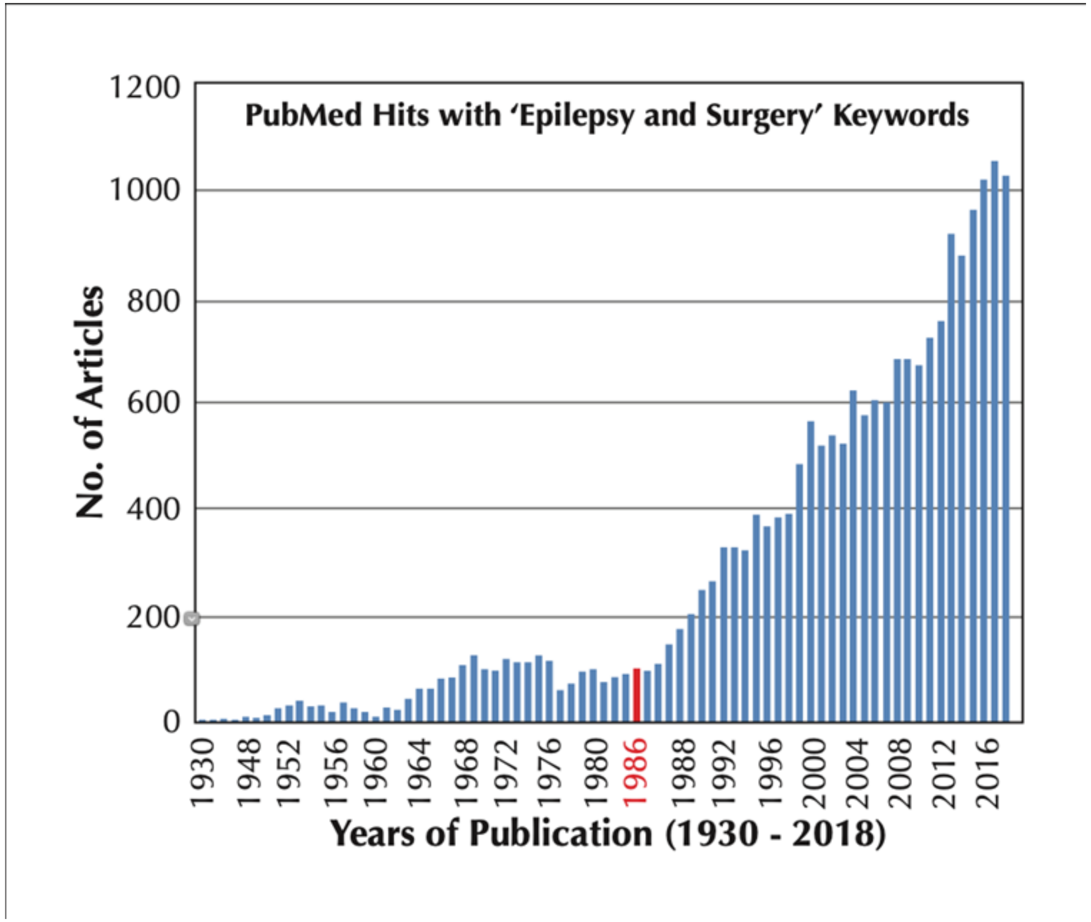
Dario J. Englot, M.D., Ph.D.



Does it work ?

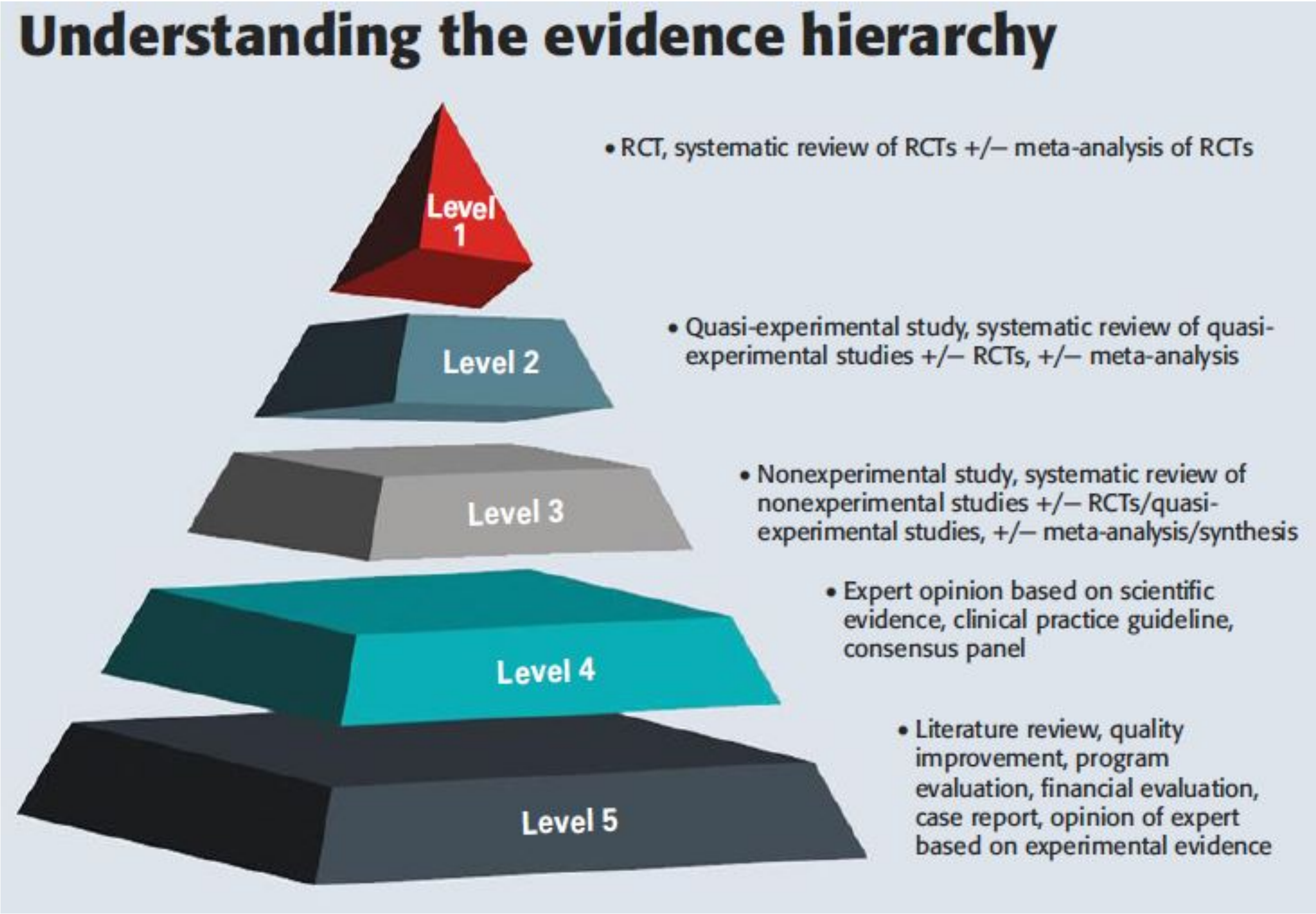
Yes

Explosion in publications related to Epilepsy surgery



Engel J, Epileptic Disord 2019

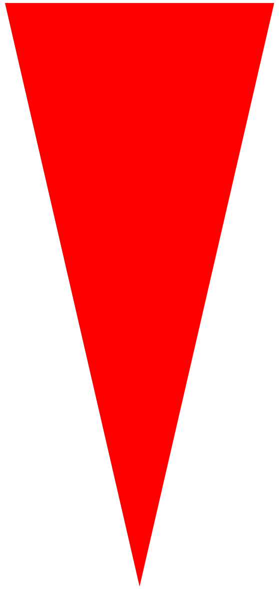
- Challenging to stay current in the field of expertise
- Foundation for clinical practice and future research.



Dearholt SL et al

Bibliometrics and Citation Frequency

- Resective Epilepsy Surgery
- Stereotactic Radiosurgery (SRS)
- Deep Brain Stimulation for Epilepsy
- Responsive Neurostimulation (RNS)
- Stereoencephalography (SEEG)
- Laser Interstitial thermal therapy (LITT)



Resective Epilepsy Surgery

Resective Epilepsy Surgery

The New England
Journal of Medicine

VOLUME 345 AUGUST 2, 2001 NUMBER 5

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

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

Google Scholar Citation: 3173

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Surgery for Drug-Resistant Epilepsy in Children

Rekha Dwivedi, Ph.D., Bhargavi Ramanujam, M.D., D.M.,
P. Sarat Chandra, M.Ch., Savita Sapra, Ph.D., Sheffali Gulati, M.D., D.M.,
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Chitra Sarkar, M.D., and Manjari Tripathi, M.D., D.M.

Google Scholar Citations: 253

Early Surgical Therapy for Drug-Resistant Temporal Lobe Epilepsy

A Randomized Trial

Google Scholar Citations: 850

The New England
Journal of Medicine

VOLUME 345 AUGUST 2, 2001 NUMBER 5

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

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

- 80 patients randomized: 40 to surgery, 40 to AED
- Primary outcome : freedom from seizures

- Results:
- At one year, 58% in surgical group versus 8% in medical group ($p<0.001$)
- One patient in the medical group died.

Epilepsia, 53(5):765–770, 2012
doi: 10.1111/j.1528-1167.2012.03455.x

CRITICAL REVIEW AND INVITED COMMENTARY

The most cited works in epilepsy: Trends in the "Citation Classics"

*George M. Ibrahim, †O. Carter Snead III, *James T. Rutka, and *Andres M. Lozano

*Division of Neurosurgery, Toronto Western Hospital and The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada; and †Division of Neurology, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

Article is termed a "Citation Classic" once it has accumulated more than 400 citations.

Table 1. Top 10 epilepsy-specific Citation Classics

Rank	Article	Citations
1	Racine RJ. (1972) Modification of seizure activity by electrical stimulation: II. Motor seizure. *Electroencephalogr Clin Neurophysiol* 32:281–294	3,749
2	Kwan P, Brodie MJ. (2000) Early identification of refractory epilepsy. *N Engl J Med* 342:314–319	1,419
3	Ben-Ari Y. (1985) Limbic seizure and brain damage produced by kainic acid: mechanisms and relevance to human temporal lobe epilepsy. *Neuroscience* 14:375–403	1,351
4	Morgan JI, Cohen DR, Hempstead JL, Curran T. (1987) Mapping patterns of c-fos expression in the central nervous system after seizure. *Science* 237:192–197	1,303
5	Nibuya M, Morinobu S, Duman RS. (1995) Regulation of BDNF and trkB mRNA in rat brain by chronic electroconvulsive seizure and antidepressant drug treatment. *J Neurosci* 15:7539–7547	1,193
6	Parent JM, Yu TW, Leibowitz RT, Geschwind DH, Sloviter RS, Lowenstein DH. (1997) Dentate granule cell neurogenesis is increased by seizures and contributes to aberrant network reorganization in the adult rat hippocampus. *J Neurosci* 17:3727–3738	1,162
7	Engel J. (2001) A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 42:796–803	1,123
8	Hauser WA, Annegers JF, Kurland LT. (1993) Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935–1984. *Epilepsia* 34:453–468	996
9	Shoffner JM, Lott MT, Lezza AM, Seibel P, Ballinger SW, Wallace DC. (1990) Myoclonic epilepsy and ragged-red fiber disease (MERRF) is associated with a mitochondrial DNA tRNALys mutation. *Cell* 61:931–937	961
10	Wiebe S, Blume WT, Girvin JP, Eliasziw M. (2001) A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Eng J Med* 345:311–318	911

TABLE 1. *Top 18 Epilepsy-Specific Citation Classics (All Articles With >1,000 Citations)*

Current Rank	2011 Rank	Article	Current # Scopus citations	2011 # Publish or Perish Citations	Current # Google Scholar Citations
1	n/a	Proposal for revised classification of epilepsies and epileptic syndromes: Commission on classification and terminology of the international league against epilepsy. *Epilepsia* [Internet]. 1989;30:389–399.	4592	n/a	n/a
2	1	Racine RJ. Modification of seizure activity by electrical stimulation: II. Motor seizure. *Electroencephalogr Clin Neurophysiol* [Internet]. 1972;32:281–294.	4248	3749	5607
3	n/a	Proposal for revised clinical and electroencephalographic classification of epileptic seizures: From the commission on classification and terminology of the international league against epilepsy. *Epilepsia* [Internet]. 1981;22:489–501.	2805	n/a	n/a
4	n/a	Goddard GV, McIntyre DC, Leech CK. A permanent change in brain function resulting from daily electrical stimulation. *Exp Neurol* [Internet]. 1969;25:295–330.	2269	n/a	n/a
5	2	Kwan P, Brodie MJ. Early identification of refractory epilepsy. *New Engl J Med* [Internet]. 2000;342:314–319.	2217	1419	3262
6	n/a	Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, Van Emde Boas W, Engel J, French J, Glauser TA, Mathern GW, Moshé SL, Nordli D, Plouin P, Scheffer IE. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE commission on classification and terminology, 2005–2009. *Epilepsia* [Internet]. 2010;51:676–685.	1772	n/a	2671
7	10	Wiebe S, Blume WT, Girvin JP, Eliasziw M. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *New Engl J Med* [Internet]. 2001;345:311–318.	1516	911	2091
8	5	Nibuya M, Morinobu S, Duman RS. Regulation of BDNF and trkB mRNA in rat brain by chronic electroconvulsive seizure and antidepressant drug treatments. *J Neurosci* [Internet]. 1995;15:7539–7547.	1464	1193	1945
9	7	Engel J Jr.. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: Report of the ILAE task force on classification and terminology. *Epilepsia* [Internet]. 2001;42:796–803.	1449	1123	2074
10	3	Ben-Ari Y. Limbic seizure and brain damage produced by kainic acid: Mechanisms and relevance to human temporal lobe epilepsy. *Neuroscience* [Internet]. 1985;14:375–403.	1379	1351	1702
11	6	Parent JM, Yu TW, Leibowitz RT, Geschwind DH, Sloviter RS, Lowenstein DH. Dentate granule cell neurogenesis is increased by seizures and contributes to aberrant network reorganization in the adult rat hippocampus. *J Neurosci* [Internet]. 1997;17:3727–3738.	1322	1162	1702
12	4	Morgan JI, Cohen DR, Hempstead JL, Curran T. Mapping patterns of c-fos expression in the central nervous system after seizure. *Science* [Internet]. 1987;237:192–196.	**1265**	**1303**	1657
13	8	Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935–1984. *Epilepsia* [Internet]. 1993;34:453–458.	1210	996	1754
14	42	Fisher RS, Van Emde Boas W, Blume W, Elger C, Genton P, Lee P, Engel J Jr. Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau For Epilepsy (IBE). *Epilepsia* [Internet]. 2005;46:470–472.	1162	525	2292
15	n/a	Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, Dessain SK, Rosenfeld MR, Balice-Gordon R, Lynch DR. Anti-NMDA-receptor encephalitis: Case series and analysis of the effects of antibodies. *Lancet Neurol* [Internet]. 2008;7:1091–1098.	1128	n/a	n/a
16	12	Tanaka K, Watase K, Manabe T, Yamada K, Watanabe M, Takahashi K, Iwama H, Nishikawa T, Ichihara N, Kikuchi T, Okuyama S, Kawashima N, Hori S, Takimoto M, Wada K. Epilepsy and exacerbation of brain injury in mice lacking the glutamate transporter GLT-1. *Science* [Internet]. 1997;276:1699–1702.	1108	848	1381
17	n/a	Commission on Epidemiology and Prognosis, International League Against Epilepsy. Guidelines for epidemiologic studies on epilepsy. [Internet]. 1993;34:592–596.	1087	n/a	n/a
18	9	Shoffner JM, Lott MT, Lezza AMS, Seibel P, Ballinger SW, Wallace DC. Myoclonic epilepsy and ragged-red fiber disease (MERRF) is associated with a mitochondrial DNA tRNALys mutation. *Cell* [Internet]. 1990;61:931–937.	1022	961	1345

Kellogg et al. Epilepsy Currents 2018

Early Surgical Therapy for Drug-Resistant Temporal Lobe Epilepsy

A Randomized Trial

Engel et al, JAMA 2012

Design:

- Multicenter, controlled, parallel-group clinical trial
- 16 US epilepsy surgery
- 38 participants with mesial temporal lobe epilepsy (MTLE) for no more than 2 consecutive years following adequate trials of 2 brand-name AEDs
- Participants were randomized to continued AED treatment or AMTR and observed for 2 years.

Main Outcome Measures

- Primary outcome variable was freedom from disabling seizures during year 2 of follow-up.

Results

- 0 of 23 participants in the medical group and 11 of 15 in the surgical group were seizure free during year 2 of follow-up (odds ratio=; 95% CI, 11.8 to ; *P*.001).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Surgery for Drug-Resistant Epilepsy in Children

Rekha Dwivedi, Ph.D., Bhargavi Ramanujam, M.D., D.M.,
P. Sarat Chandra, M.Ch., Savita Sapra, Ph.D., Sheffali Gulati, M.D., D.M.,
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Chitra Sarkar, M.D., and Manjari Tripathi, M.D., D.M.

Google Scholar Citations: 253

N Engl J Med 2017;377:1639-47

DESIGN:

- Single-center trial
- Random assignment of 116 pediatric patients (18 years of age or younger) with drug-resistant epilepsy
- 57 assigned to brain surgery versus 59 patients to receive medical therapy alone.
- Primary outcome: freedom from seizures at 12 months.

RESULTS

- At 12 months, freedom from seizures occurred in 44 patients (77%) in the surgery group and in 4 (7%) in the medical-therapy group (P<0.001).

Stereotactic Radiosurgery (SRS)

Stereotactic Radiosurgery (SRS)

Accepted: 14 February 2018
DOI: 10.1111/epi.14045

FULL-LENGTH ORIGINAL RESEARCH

Epilepsia

Radiosurgery versus open surgery for mesial temporal lobe epilepsy: The randomized, controlled ROSE trial

Nicholas M. Barbaro[1] | Mark Quigg[2] | Mariann M. Ward[3] | Edward F. Chang[3] | Donna K. Broshek[4] | John T. Langfitt[5] | Guofen Yan[6] | Kenneth D. Laxer[7] | Andrew J. Cole[8] | Penny K. Sneed[9] | Christopher P. Hess[10] | Wei Yu[6] | Manjari Tripathi[11] | Christianne N. Heck[12] | John W. Miller[13] | Paul A. Garcia[14] | Andrew McEvoy[15] | Nathan B. Fountain[2] | Vincenta Salanova[16] | Robert C. Knowlton[14] | Anto Bagić[17] | Thomas Henry[18] | Siddharth Kapoor[19] | Guy McKhann[20] | Adriana E. Palade[21] | Markus Reuber[22] | Evelyn Tecoma[23]

Google citation: 55

Design:

- 58 patients randomized (31 in SRS, 27 in ATL).
- Sixteen (52%) SRS and 21 (78%) ATL patients achieved seizure remission (difference = 26%, P value at the 15% noninferiority margin = .82).

Significance: These data suggest that ATL has an advantage over SRS in terms of proportion of seizure remission

Deep Brain Stimulation

Evidence for Anterior Thalamic Nucleus Stimulation in Epilepsy (SANTE Trial)

Epilepsia, 51(5):899–908, 2010
doi: 10.1111/j.1528-1167.2010.02536.x

FULL-LENGTH ORIGINAL RESEARCH

Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy

*Robert Fisher, †Vicenta Salanova, †Thomas Witt, †Robert Worth, ‡Thomas Henry, ‡Robert Gross, §Kalarickal Oommen, ¶Ivan Osorio, ¶Jules Nazzaro, #Douglas Labar, #Michael Kaplitt, **Michael Sperling, ††Evan Sandok, ††John Neal, ‡‡Adrian Handforth, §§John Stern, ‡‡Antonio DeSalles, ¶¶Steve Chung, ¶¶Andrew Shetter, ##Donna Bergen, ##Roy Bakay, *Jaimie Henderson, ***Jacqueline French, ***Gordon Baltuch, †††William Rosenfeld, †††Andrew Youkilis, ‡‡‡William Marks, ‡‡‡Paul Garcia, ‡‡‡Nicolas Barbaro, §§§Nathan Fountain, ¶¶¶Carl Bazil, ¶¶¶Robert Goodman, ¶¶¶Guy McKhann, ###K. Babu Krishnamurthy, ###Steven Papavassiliou, ‡Charles Epstein, ***John Pollard, ****Lisa Tonder, ****Joan Grebin, ****Robert Coffey, ****Nina Graves, and the SANTE Study Group[1]

*Stanford University, Stanford, California, U.S.A.; †Indiana University, Indianapolis, Indiana, U.S.A.; ‡Emory University, Atlanta, Georgia, U.S.A.; §University of Oklahoma, Oklahoma City, Oklahoma, U.S.A.; ¶University of Kansas, Kansas City, Kansas, U.S.A.; #Weill-Cornell, New York, New York, U.S.A.; **Thomas Jefferson University, Philadelphia, Pennsylvania, U.S.A.; ††Marshfield Clinic, Marshfield, Wisconsin, U.S.A.; ‡‡Veterans Affairs Greater Los Angeles Healthcare System, Los Angeles, California, U.S.A.; §§Geffen School of Medicine at UCLA, Los Angeles, California, U.S.A.; ¶¶Barrow Neurological Institute, Phoenix, Arizona, U.S.A.; ##Rush Presbyterian St. Luke's Medical Center, Chicago, Illinois, U.S.A.; ***University of Pennsylvania, Philadelphia, Pennsylvania, U.S.A.; †††St. Luke's N. Medical Building, St. Louis, Missouri, U.S.A.; ‡‡‡University of California San Francisco, California, U.S.A.; §§§University of Virginia School of Medicine, Charlottesville, Virginia, U.S.A.; ¶¶¶Columbia University College of Physicians and Surgeons, New York, New York, U.S.A.; ###Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, U.S.A.; and ****Medtronic, Minneapolis, Minnesota, U.S.A.

Google Scholar Citation: 1309

- Multicenter, double-blind, randomized trial - bilateral AN of thalamus DBS
- 110 participants randomized
- 3 month blinded phase, then unblinded stimulation
- In the blinded phase, patients with active AN stimulation reported a 40% decrease in seizure frequency, versus a 15% decrease in the stimulation OFF group, a significant difference (P = .002).
- In long-term (5 year) follow-up, the mean reduction in seizure frequency was 69%, and 68% of patients reported 50% or better reduction in seizure frequency.

Responsive Neurostimulation

Evidence for Efficacy of Responsive Neurostimulation

FULL-LENGTH ORIGINAL RESEARCH

Two-year seizure reduction in adults with medically intractable partial onset epilepsy treated with responsive neurostimulation: Final results of the RNS System Pivotal trial

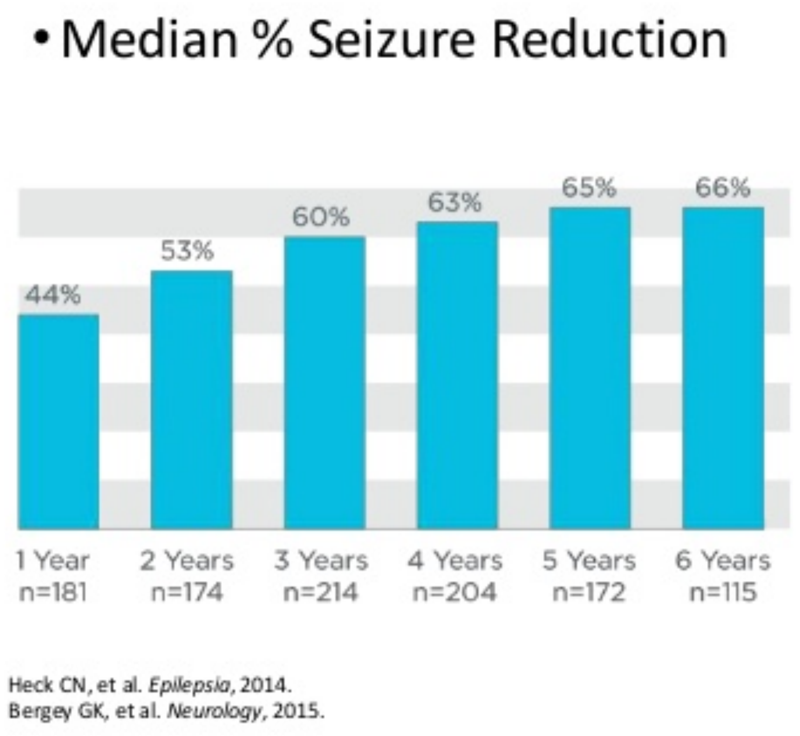
[1]Christianne N. Heck, [2]David King-Stephens, [3]Andrew D. Massey, [4]Dileep R. Nair, [5]Barbara C. Jobst, [6]Gregory L. Barkley, [7]Vicenta Salanova, [8]Andrew J. Cole, [9]Michael C. Smith, [10]Ryder P. Gwinn, [11]Christopher Skidmore, [12]Paul C. Van Ness, [13]Gregory K. Bergey, [14]Yong D. Park, [15]Ian Miller, [16]Eric Geller, [17]Paul A. Rutecki, [18]Richard Zimmerman, [19]David C. Spencer, [20]Alica Goldman, [21]Jonathan C. Edwards, [22]James W. Leiphart, [23]Robert E. Wharen, [24]James Fessler, [25]Nathan B. Fountain, [26]Gregory A. Worrell, [27]Robert E. Gross, [28]Stephan Eisenschenk, [29]Robert B. Duckrow, [29]Lawrence J. Hirsch, [30]Carl Bazil, [31]Cormac A. O'Donovan, [32]Felice T. Sun, [32]Tracy A. Courtney, [32]Cairn G. Seale, and [32,33]Martha J. Morrell

Epilepsia, 55(3):432–441, 2014
doi: 10.1111/epi.12534

Google Scholar Citations: 440

Results: All 191 subjects were randomized. The percent change in seizures at the end of the blinded period was −37.9% in the active and −17.3% in the sham stimulation group ($p = 0.012$, Generalized Estimating Equations). The median percent reduction in seizures in the OLP was 44% at 1 year and 53% at 2 years, which represents a progressive and significant improvement with time ($p < 0.0001$). The serious adverse event rate was not different between subjects receiving active and sham stimulation. Adverse events were consistent with the known risks of an implanted medical device, seizures, and of other epilepsy treatments. There were no adverse effects on neuropsychological function or mood.

Responsive Neurostimulation



- Median percent reduction in seizures was 66% by year six.
- As with other stimulation approaches, responder rates improved over time (Morrell, M.R. Investigators Nine-year Prospective Safety and Effectiveness Outcomes from the Long-Term Treatment Trial of the RNS® System. *Brain Stimul.* **2019**, *12*, 469)

ARTICLE OPEN ACCESS CLASS OF EVIDENCE

Nine-year prospective efficacy and safety of brain-responsive neurostimulation for focal epilepsy

Dileep R. Nair, MD, Kenneth D. Laxer, MD, Peter B. Weber, MD, Anthony M. Murro, MD, Yong D. Park, MD, Gregory L. Barkley, MD, Brien J. Smith, MD, Ryder P. Gwinn, MD, Michael J. Doherty, MD, Katherine H. Noe, MD, PhD, Richard S. Zimmerman, MD, Gregory K. Bergey, MD, William S. Anderson, MD, PhD, Christianne Heck, MD, Charles Y. Liu, MD, PhD, Ricky W. Lee, MD, Toni Sadler, PA-C, Robert B. Duckrow, MD, Lawrence J. Hirsch, MD, Robert E. Wharen, Jr., MD, William Tatum, DO, Shraddha Srinivasan, MD, Guy M. McKhann, MD, Mark A. Agostini, MD, Andreas V. Alexopoulos, MD, MPH, Barbara C. Jobst, MD, David W. Roberts, MD, Vicenta Salanova, MD, Thomas
Gregory A. Worrell, MD, PhD, Brian N. Lundstrom, MD,
David C. Spencer, MD, Lia Ernst, MD, Christopher T. Sk
Eric B. Geller, MD, Michel J. Berg, MD, A. James Fessler,
Eli M. Mizrahi, MD, Robert E. Gross, MD, PhD, Donald
Douglas R. Labar, MD, PhD, Nathan B. Fountain, MD,
Nicole R. Villemarette-Pittman, PhD, Stephan Eisensch
Tracy A. Courtney, BS, Felice T. Sun, PhD, Cairn G. Seal
Martha J. Morrell, MD, on behalf of the RNS System LT

Correspondence
Dr. Morrell
mmorrell@neuropace.com

Neurology® 2020;95:e1244-e1256. doi:10.1212/WN

Table 3 Seizure frequency reduction and responder rates at 9 years according to region of seizure onset

Region of seizure onset	Median reduction (IQR), %	Responder rate, %
All MTL (n = 66)	73 (58–96)	77
MTL bilateral (n = 48)	71.9 (56–90)	77
MTL unilateral (n = 18)	94 (64–100)	78
All temporal (n = 95) MTL, lateral, MTL + lateral	73 (47–93)	72
All neocortical (n = 70)	81 (34–100)	70
Lateral temporal (n = 19)	81 (33–99)	58
Frontal (n = 21)	93 (31–100)	71
Other (n = 30)	79 (52–93)	77

Abbreviations: IQR = interquartile range; MTL = mesial temporal lobe.

Stereoencephalography

SEEG: Technique & Electrode Placement Accuracy

Accuracy of intracranial electrode placement for stereoelectroencephalography: A systematic review and meta-analysis

*Vejay N. Vakharia, †Rachel Sparks, ‡Aidan G. O'Keeffe, *Roman Rodionov, *Anna Miserocchi, *Andrew McEvoy, *†Sebastien Ourselin, and *John Duncan

Epilepsia, 58(6):921–932, 2017
doi: 10.1111/epi.13713

- No prospective controlled clinical trials
- Robotic trajectory guidance systems
- Supporting evidence is limited to class 3 only.

Robot-Assisted Stereotaxy Reduces Target Error: A Meta-Analysis and Meta-Regression of 6056 Trajectories

Lucas R. Philipp, MD, MPH
Caio M. Matias, MD, PhD
Sara Thalheimer, BA
Shyle H. Mehta, MA
Ashwini Sharan, MD
Chengyuan Wu, MD, MSBmE

Department of Neurological Surgery, Thomas Jefferson University Hospitals, Philadelphia, Pennsylvania

An early iteration of the manuscript abstract was accepted as a digital poster for display at the 2019 CNS Annual Meeting in San Francisco, California, October 19-23, 2019.

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Received, November 7, 2019.
Accepted, July 12, 2020.
Published Online, October 12, 2020.

BACKGROUND: The pursuit of improved accuracy for localization and electrode implantation in deep brain stimulation (DBS) and stereoelectroencephalography (sEEG) has fostered an abundance of disparate surgical/stereotactic practices. Specific practices/technologies directly modify implantation accuracy; however, no study has described their respective influence in multivariable context.

OBJECTIVE: To synthesize the known literature to statistically quantify factors affecting implantation accuracy.

METHODS: A systematic review and meta-analysis was conducted to determine the inverse-variance weighted pooled mean target error (MTE) of implanted electrodes among patients undergoing DBS or sEEG. MTE was defined as Euclidean distance between planned and final electrode tip. Meta-regression identified moderators of MTE in a multivariable-adjusted model.

RESULTS: A total of 37 eligible studies were identified from a search return of 2,901 potential articles (2002-2018) – 27 DBS and 10 sEEG. Random-effects pooled MTE = 1.91 mm (95% CI: 1.7-2.1) for DBS and 2.34 mm (95% CI: 2.1-2.6) for sEEG. Meta-regression identified study year, robot use, frame/frameless technique, and intraoperative electrophysiologic testing (iEPT) as significant multivariable-adjusted moderators of MTE ($P < .0001$, $R^2 = 0.63$). Study year was associated with a 0.92-mm MTE reduction over the 16-yr study period ($P = .0035$), and robot use with a 0.79-mm decrease ($P = .0019$). Frameless technique was associated with a mean 0.50-mm (95% CI: 0.17-0.84) increase, and iEPT use with a 0.45-mm (95% CI: 0.10-0.80) increase in MTE. Registration method, imaging type, intraoperative imaging, target, and demographics were not significantly associated with MTE on multivariable analysis.

CONCLUSION: Robot assistance for stereotactic electrode implantation is independently associated with improved accuracy and reduced target error. This remains true regardless of other procedural factors, including frame-based vs frameless technique.

KEY WORDS: DBS, Electrode implantation, Meta-analysis, sEEG, Stereotactic accuracy, Stereotactic techniques, Target error

Outcomes: SEEG versus Subdural Grids

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Surgical outcomes related to invasive EEG monitoring with subdural grids or depth electrodes in adults: A systematic review and meta-analysis

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Results: 19 articles containing 1025 SDG-interventions and 16 publications comprising 974 SEEG-monitors were researched. The rate of resective surgery deriving from SDG-monitoring hovered at 88.8% (95%CI:83.3–92.6%) (I^2 = 77.0%;p < 0.001); in SEEG-group, 79.0% (95%CI:70.4–85.7%) (I^2 = 72.5%;p < 0.001) was measured. After SDG-interventions, percentage of post-resective follow-up escalated to 96.0% (95%CI:92.0–98.1%) (I^2 = 49.1%;p = 0.010), and in SEEG-group, it reached 94.9% (95%CI:89.3–97.6%) (I^2 = 80.2%;p < 0.001). In SDG-group, ratio of seizure-free outcomes reached 55.9% (95%CI:50.9–60.8%) (I^2 = 54.47%;p = 0.002). Using SEEG-monitor, seizure-freedom occurred in 64.7% (95%CI:59.2–69.8%) (I^2 = 11.9%;p = 0.32). Assessing lesional cases, likelihood of Engel I outcome was found in 57.3% (95%CI:48.7%–65.6%) (I^2 = 69.9%;p < 0.001), using SDG; while in SEEG-group, it was 71.6% (95%CI:61.6%–79.9%) (I^2 = 24.5%;p = 0.225). In temporal subgroup, ratio of seizure-freedom was found to be 56.7% (95%CI:51.5%–61.9%) (I^2 = 3.2%;p = 0.412) in SDG-group; whereas, SEEG-group reached 73.9% (95%CI:64.4%–81.6%); (I^2 = 0.00%;p = 0.45). Significant differences between seizure-free outcomes were found in overall (p = 0.02), lesional (p = 0.031), and also, temporal (p = 0.002) comparisons.

Conclusions: SEEG-interventions were associated, at least, non-inferiorly, with seizure-freedom compared with SDG-monitors in temporal, lesional and overall subgroups.

Is the use of Stereotactic Electroencephalography Safe and Effective in Children? A Meta-Analysis of the use of Stereotactic Electroencephalography in Comparison to Subdural Grids for Invasive Epilepsy Monitoring in Pediatric Subjects

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BACKGROUND: Stereoelectroencephalography (SEEG) is an alternative addition to subdural grids (SDG) in invasive extra-operative monitoring for medically refractory epilepsy. Few studies exist on the clinical efficacy and safety of these techniques in pediatric populations.

OBJECTIVE: To provide a comparative quantitative summary of surgical complications and postoperative seizure freedom associated with invasive extra-operative presurgical techniques in pediatric patients.

METHODS: The systematic review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A literature search was conducted utilizing Ovid Medline, Embase, Pubmed, and the Cochrane database.

RESULTS: Fourteen papers with a total of 697 pediatric patients undergoing invasive SDG monitoring and 9 papers with a total of 277 pediatric patients undergoing SEEG monitoring were utilized in the systemic review. Cerebral spinal fluid (CSF) leaks were the most common adverse event in the SDG studies (pooled prevalence 11.9% 95% confidence interval [CI] 5.7-23.3). There was one case of CSF leak in the SEEG studies. Intracranial hemorrhages (SDG: 10.7%, 95% CI 5.3-20.3; SEEG: 2.9%, 95% CI –0.7 to 10.8) and infection (SDG: 10.8%, 95% CI 6.7-17) were more common in the SDG studies reviewed. At the time of the last postoperative visit, a greater percentage of pediatric patients achieved seizure freedom in the SEEG studies (SEEG: 66.5%, 95% CI 58.8-73.4; SDG: 52.1%, 95% CI 43.0-61.1).

CONCLUSION: SEEG is a safe alternative to SDG and should be considered on an individual basis for selected pediatric patients.

KEY WORDS: SEEG, Pediatric, Epilepsy, Invasive monitoring

Laser Interstitial Thermal Therapy

Magnetic Resonance Imaging-Guided Laser Interstitial Thermal Therapy for Epilepsy: Systematic Review of Technique, Indications, and Outcomes

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BACKGROUND: For patients with focal drug-resistant epilepsy (DRE), surgical resection of the epileptogenic zone (EZ) may offer seizure freedom and benefits for quality of life. Yet, concerns remain regarding invasiveness, morbidity, and neurocognitive side effects. Magnetic resonance-guided laser interstitial thermal therapy (MRgLITT) has emerged as a less invasive option for stereotactic ablation rather than resection of the EZ.

OBJECTIVE: To provide an introduction to MRgLITT for epilepsy, including historical development, surgical technique, and role in therapy.

METHODS: The development of MRgLITT is briefly recounted. A systematic review identified reported techniques and indication-specific outcomes of MRgLITT for DRE in human studies regardless of sample size or follow-up duration. Potential advantages and disadvantages compared to available alternatives for each indication are assessed in an unstructured review.

RESULTS: Techniques and outcomes are reported for mesial temporal lobe epilepsy, hypothalamic hamartoma, focal cortical dysplasia, nonlesional epilepsy, tuberous sclerosis, periventricular nodular heterotopia, cerebral cavernous malformations, poststroke epilepsy, temporal encephalocele, and corpus callosotomy.

CONCLUSION: MRgLITT offers access to foci virtually anywhere in the brain with minimal disruption of the overlying cortex and white matter, promising fewer neurological side effects and less surgical morbidity and pain. Compared to other ablative techniques, MRgLITT offers immediate, discrete lesions with real-time monitoring of temperature beyond the fiber tip for damage estimates and off-target injury prevention. Applications of MRgLITT for epilepsy are growing rapidly and, although more evidence of safety and efficacy is needed, there are potential advantages for some patients.

KEY WORDS: MRI-guided laser interstitial thermal therapy (MRgLITT), Epilepsy, Mesial temporal lobe epilepsy, Mesial temporal sclerosis, Focal cortical dysplasia, Hypothalamic hamartoma, Stereoelectroencephalography (SEEG)

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FULL-LENGTH ORIGINAL RESEARCH

Epilepsia

Effects of surgical targeting in laser interstitial thermal therapy for mesial temporal lobe epilepsy: A multicenter study of 234 patients

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Adverse Events

...) ICH with VFD; 1 (5%) 4th CN palsy ...sient); 2 worsened mood (1 suicide)

...%) VFD; 1 (14%) postop sz

...) VFD (1 transient and 1 permanent

...) VFD (transient); 1 (3%) ICH/IVH (no ...it)

...%) VFD; 1 (10%) hemorrhage

...) VFD (HH); 1 (5%) acute psychiatric ...ode

...) delayed onset optic neuritis

...%) VFD (2 HH)[c]

...) VFD (4 transient, 1 persistent HH); ...(2%) ICH with VFD; 1 (2%) operative ...(no deficit); 4 (7%) transient CN III or ...lsies

...) VFD (SQ); 2 (7%) transient CN palsies

Sprissler 2019[47]	16	V + NR	14.5 (12-32)	7/16 (44)	7/16 (44)	[f]4/11 (36)	[f]2/5 (40)	NR
Wu 2019[48]	[g]234	NR (multi-center)	NR (12-75)	134/234 (58)	134/234 (58)	NR	NR	3 (1.3%) hemorrhage; 12 (5.1%) VFD; 10 (4.3%) worsened affective disorder; 1 (0.4%) death (SUDEP at 12 months postop)

CN – cranial nerve; CRW – Cosman-Robert-Wells head frame; f/u – follow-up; HH – homonymous hemianopsia; ICH – intracerebral hemorrhage; IVH – intraventricular hemorrhage; Leksell – Leksell head frame; MTS – mesial temporal sclerosis; NR – not reported; OR – laser fiber placed in operating room, not otherwise specified; SDH – subdural hematoma; SUDEP – sudden unexpected death in epilepsy; V – Visualase; VFD – visual field deficit; yr – year.

[a]Includes 2 patients with low-grade glioma.

[b]Includes 1 patients with low grade glioma.

[c]A total of 12 patients underwent formal visual field testing: 2 had clinically significant HH, 3 had noticeable superior quadrantanopsia, and 3 had "silent" quadrantanopsia.

[d]Three patients underwent repeat ablation.

[e]One patient underwent repeat ablation.

[f]Note, the number of seizure free patients in the subgroups (4 + 2) does not sum to the total number of seizure free (7).

[g]Multicenter series including patients from Jermakowicz 2017,[34] Youngerman 2018,[35] and Le 2018.[46]

TABLE 2. Hypothalamic Hamartoma

Study	N	Seizure types	LITT technique	F/u, months, median (range)	Seizure freedom: *Last F/u*	Seizure freedom: *≥1-Yr F/u*	Adverse Events
Lewis 2015[49]	1	NR	V + Leksell	4.5	0/1 (0)	-	None
Zubkov 2015[50]	1	CPS	NR	8	NGS: 0/1 (0)	-	Disabling amnestic syndrome from bilateral mammillary body damage (in the context of previous right ATL for FCD)
Burrows 2016[51]	3	GS	V + Leksell	30 (28-32)	GS: 1/2 (50)	GS: 1/2 (50)	1 (33%) hyponatremia, weight gain; 1 (33%) small tract hemorrhage (no deficit)
Brandmeir 2016[52]	1	GS	V + ROSA	6	GS: 1/1 (100)	-	1 (17%) transient hemiparesis; 1 (17%) unintentional weight loss
Rolston 2016[53]	2	GS/TCS/CPS	V + Leksell	6 (5-7)	GS: 1/1 (100) NGS: 1/1 (100)	-	1 (50%) transient hyperphagia and amnesia
Buckley 2016[54]	6	GS ± SPS/CPS/SGS	V + CRW	9.7 (2-18)	GS: 4/6 (67) NGS: 3/5 (60)	GS: 1/3 (33) NGS: 1/3 (33)	3 (50%)transient neurological symptoms (hemiparesis, dysphasia, blurred vision); 1 (17%) intralesional hemorrhage (no deficit)
Du 2017[55]	8	GS/CPS/TC/SPS/RA	V + NR	23.5 (7-30)	GS: 3/3 (100) NGS: 4/5 (80)	GS: 2/2 (100) NGS: 3/3 (100)	1 (13%) operative EDH; 1 (13%) short-term memory loss
Wright 2018[56]	1	GS	NB + AXiiiS	24	GS: 1/1 (100)	GS: 1/1 (100)	None
Southwell 2018[57]	5	GS/TCS/CPS/AS/NS	V + ClearPoint	21 (7-45)	GS: 2/4 (50) NGS: 3/5 (60)	GS: 1/3 (33) NGS: 2/4 (50)	1 (20%) precocious puberty
Xu 2018[58]	18	GS/TCS/CPS	V + HF	18.4 (7.9-28.6)	GS: 12/15 (80) NGS: 5/9 (56)	GS: 9/12 (75) NGS: 5/9 (56)	7 (39%) transient neurological deficits (hemiparesis, facial droop); 4 (22%) persistent (3 leg/foot weakness, 1 Horner's syndrome) 2 (11%) hypothyroidism 4 (22%) short-term memory deficit 4 (22%) weight gain
Curry 2018[59] (incl. Curry 2012,[26] Boerwinkle 2018[60])	71	GS ± NGS	V/NB + CRW/ ROSA/ClearPoint	12 (12)	[a]GS: 66/71 (93) NGS: NR	GS: 66/71 (93) NG: NR	1 (1%) worsened DI; 1 (1%) severe short-term memory loss (in patient with previous right ATL); 3 (4.2%) transient hyponatremia; 4 (5.6%) delayed wound healing; 9 (12.7%) temporary increase in gelastic seizures
Arocho-Quinones 2019[61]	1	GS/NS	NR + Leksell	36	GS: 1/1 (100) NGS: 1/1 (100)	GS: 1/1 (100) NGS: 1/1 (100)	None

AS – absence seizures; ATL – anterior temporal lobectomy; AXiiiS – Monteris AXiiiS skull-mounted mini-frame; ClearPoint – ClearPoint skull-mounted stereotactic system; CPS – complex partial seizure; CRW – Cosman-Robert-Wells stereotactic head frame; DI – diabetes insipidus; EDH – epidural hematoma; FCD – focal cortical dysplasia; f/u – follow-up; GS – gelastic seizures; HF – head frame, unspecified; Leksell – Leksell stereotactic head frame; LITT – laser interstitial thermal therapy; NB – NeuroBlate laser ablation system; NGS – nongelastic seizures; NR – not reported; NS – nocturnal seizures; RA – rage attacks; ROSA – ROSA robotic surgical assistant; SGS – secondary generalized seizures; SPS – simple partial seizures; TCS – tonic-clonic seizures; V – Visualase laser ablation system.

[a]A total of 23% of patients required more than 1 ablation; 25% had failed other surgical or radiosurgical interventions; 12% were seizure free off medication. A total of 21 patients "had secondary seizures that were lessened by ablation and controlled with medicines."

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MR-guided laser ablation for the treatment of hypothalamic hamartomas

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ABSTRACT

Hypothalamic hamartoma is an archetypal example of subcortical epilepsy that can be associated with intractable gelastic epilepsy, secondary epilepsy, and epileptic encephalopathy. The history of its surgical treatment is fraught with mislocalization of the seizure focus, modest efficacy and a high complication rate. Many minimally invasive techniques have been described to mitigate this high complication profile of which MR-guided laser ablation is one. The technology combines instant effect of thermal coagulation with stereotactic precision and guidance with real time MR thermography. This article presents a series of 71 hypothalamic hamartoma patients operated with laser ablation. Ninety-three percent (93%) were free of gelastic seizures at one year with 23% of the patients requiring more than one ablation. One patient experienced a significant memory deficit and one patient experienced worsening diabetes insipidus. Stereotactic laser ablation appears to be a safe and effective surgical option in the treatment of hypothalamic hamartoma.

Conclusions

- Epilepsy Surgery continues to evolve
- Major advances: Minimally Invasive Epilepsy Surgery (Stereoencephalography, Laser ablation) and increasing use of Brain Stimulation (Responsive Neurostimulation, Deep Brain Stimulation)
- Increasing number of cases
- HIFU is a technology to watch out for (FDA approved for functional neurosurgery but still in research for epilepsy)
- Challenge may be in how to integrate the old with the new

Thank you