Recent Advances in Epilepsy Surgery

Teeradej Srikijvilaikul, M.D.

Epilepsy Surgery

- Diagnostic (Invasive EEG)
  - Subdural Electrode
  - Stereo-EEG
- Therapeutic Surgery
  - Resection
  - Disconnection
  - Ablation (Minimal Invasive)
    - Thermocoagulation
    - Laser interstitial therapy
    - Focus ultrasound
    - Radiosurgery
  - Neuromodulation
    - Vagal nerve stimulation
    - Deep brain stimulation
    - Responsive neurostimulation

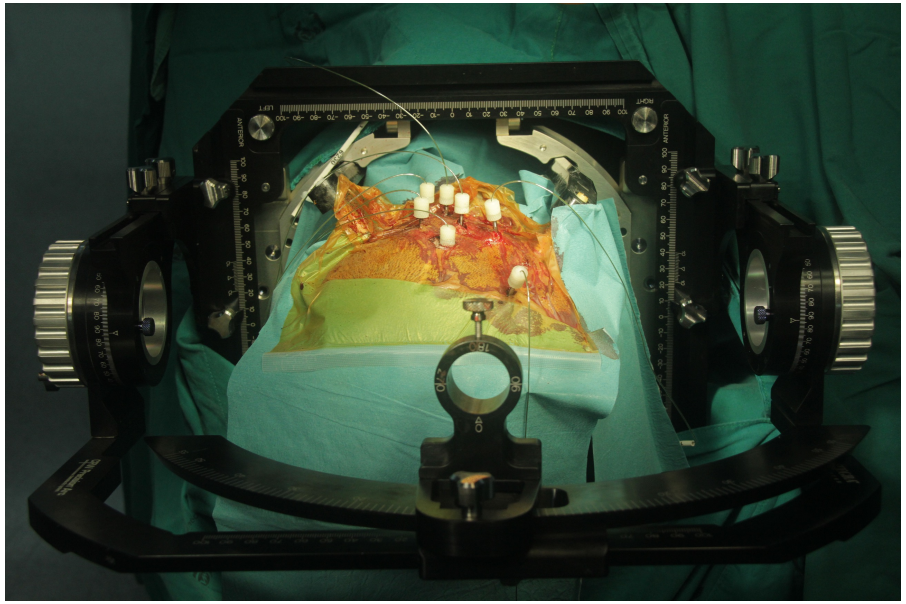
Invasive monitoring in epilepsy surgery: A systematic review

	SEEG	SDE
Seizure freedom after resection	61%	56.4%
Morbidity*	4.8%	15.5%
Mortality	0.2%	0.4%

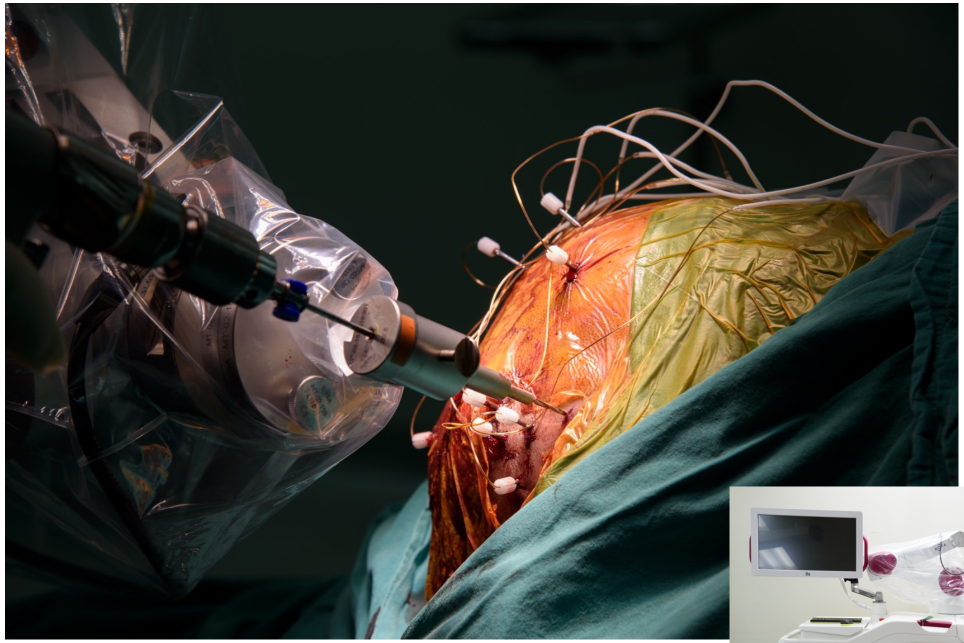
Yan H. Epilepsia 2019

Stereo-EEG

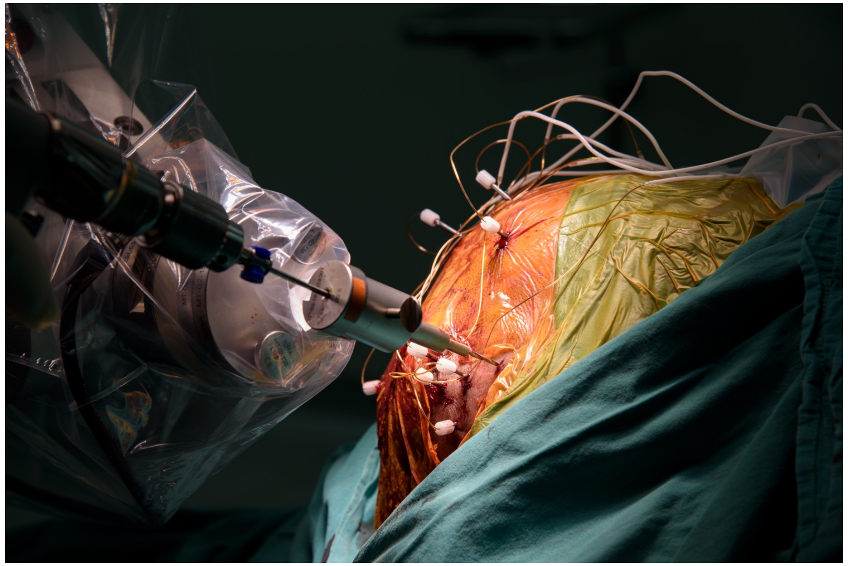
- Frame-based stereotacic SEEG



- Robotic-assisted SEEG



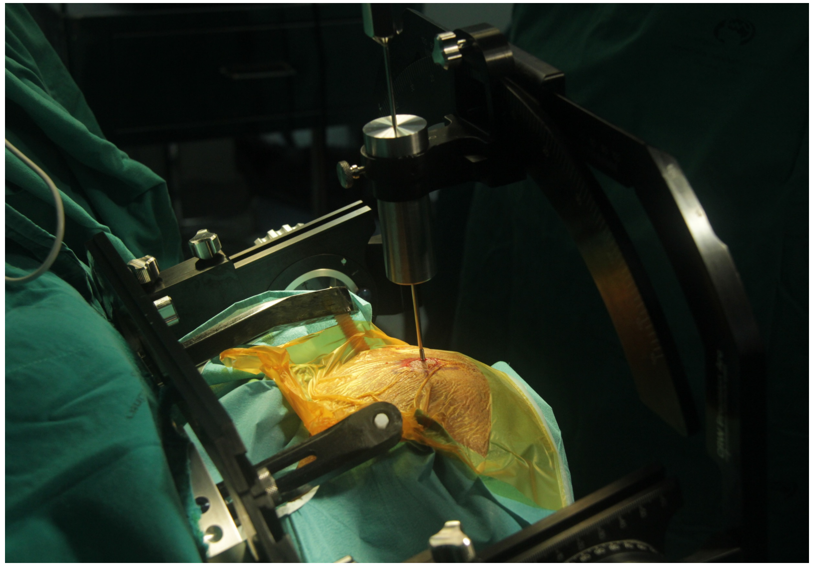
Accuracy of intracranial electrode placement for SEEG: A systematic review and meta-analysis. Epilepsia 2017; 58:921-932



ROBOT

EP error 1.17 mm (0.80-1.53)

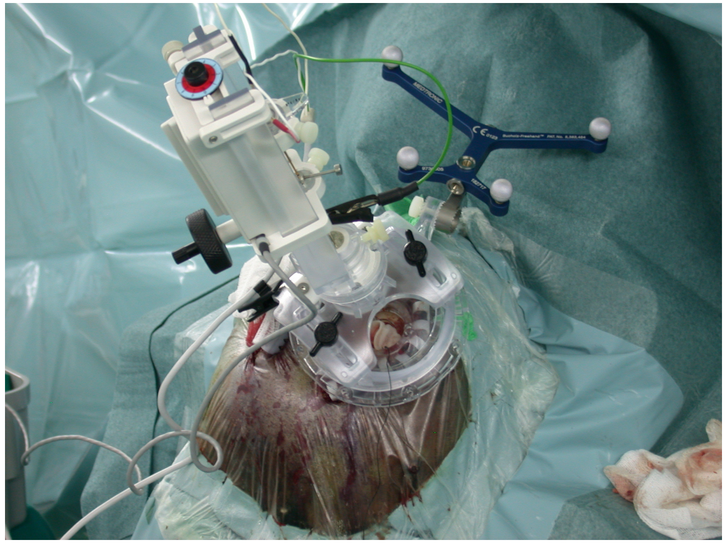
TP error 1.71 mm (1.66-1.75)



Frame-based

EP error 1.43 mm (1.35-1.51)

TP error 1.93 mm (1.05-2.81)



Frameless

EP error 2.45 mm (0.39-4.51)

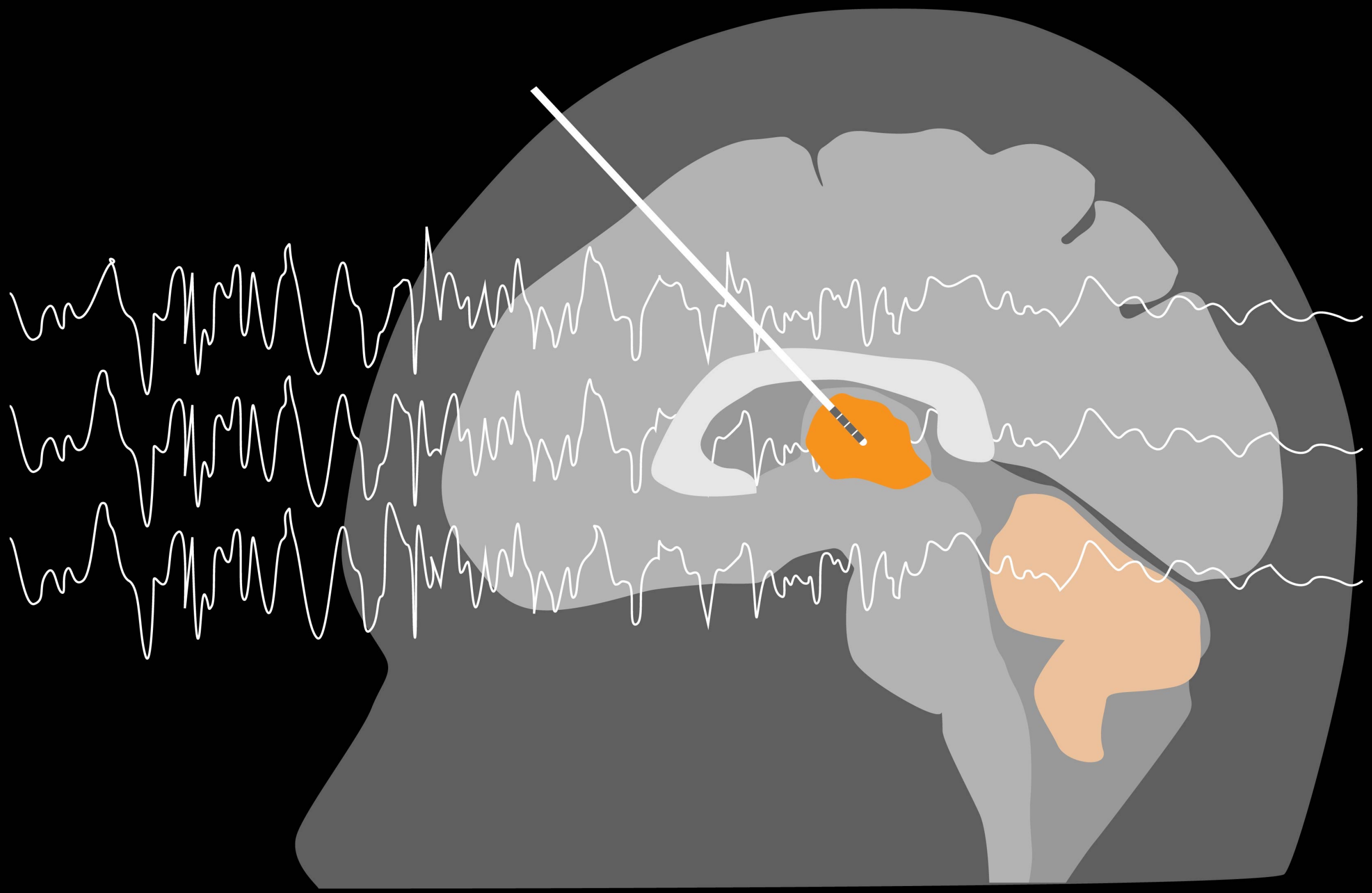
TP error 2.89 mm (2.34-3.44)

Class III evidence

NIT experiences

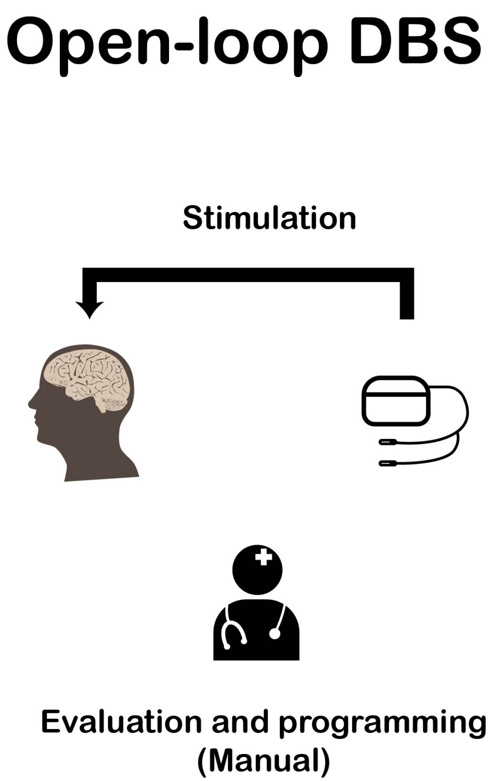
- N=23 (May 2019-June 2022)
- Age 11-50
- SEEG 208 electrodes (mean 8.3; range 5-13)
- Surgical time-Mean 82.9 mins
- Cost (SEEG surgery) 525,652.19 baht/pt

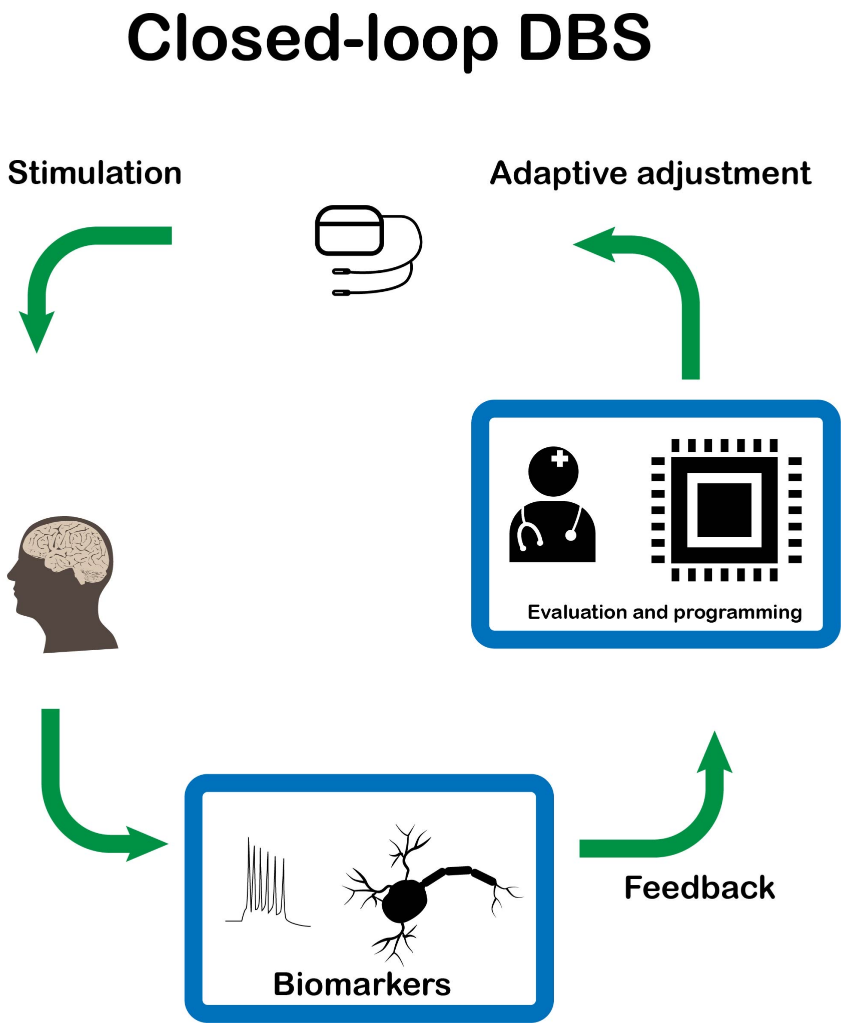
Deep brain stimulation



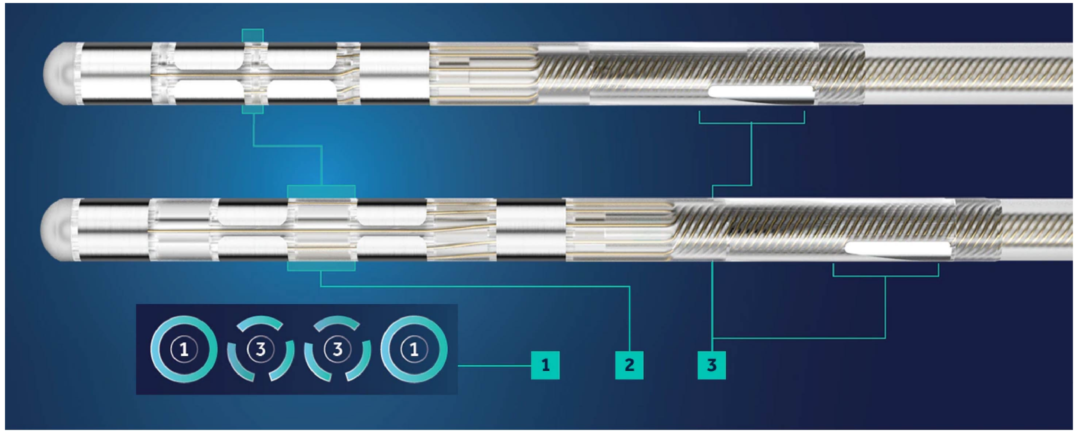
Technological advancement

- Improved materials
- MRI compatibility (1.5-3T)
- Directional
- Sensing of LFPs
- Remote programming


Open-loop DBS
Stimulation
Evaluation and programming
(Manual)


Closed-loop DBS
Stimulation
Adaptive adjustment
Evaluation and programming
Biomarkers
Feedback

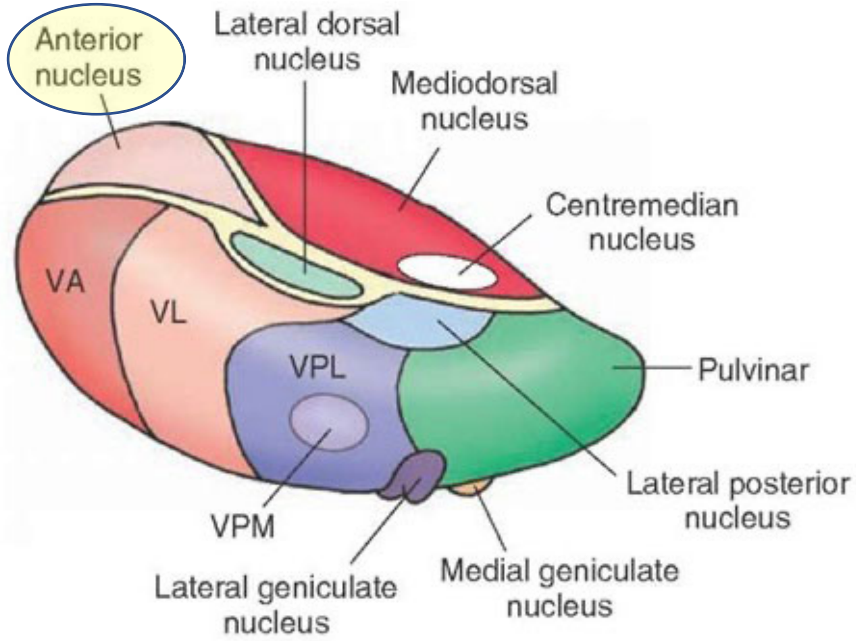
Directional lead

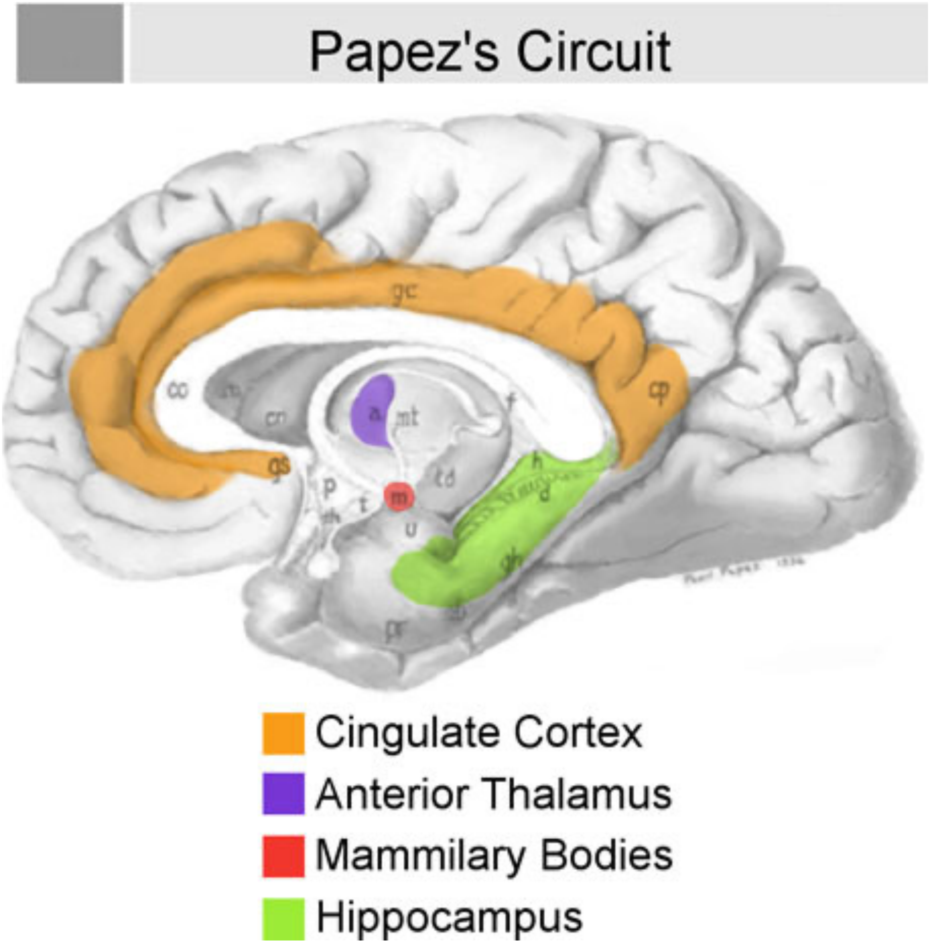


www.medtronic.com

www.bostonscientific.com

Anterior thalamic stimulation





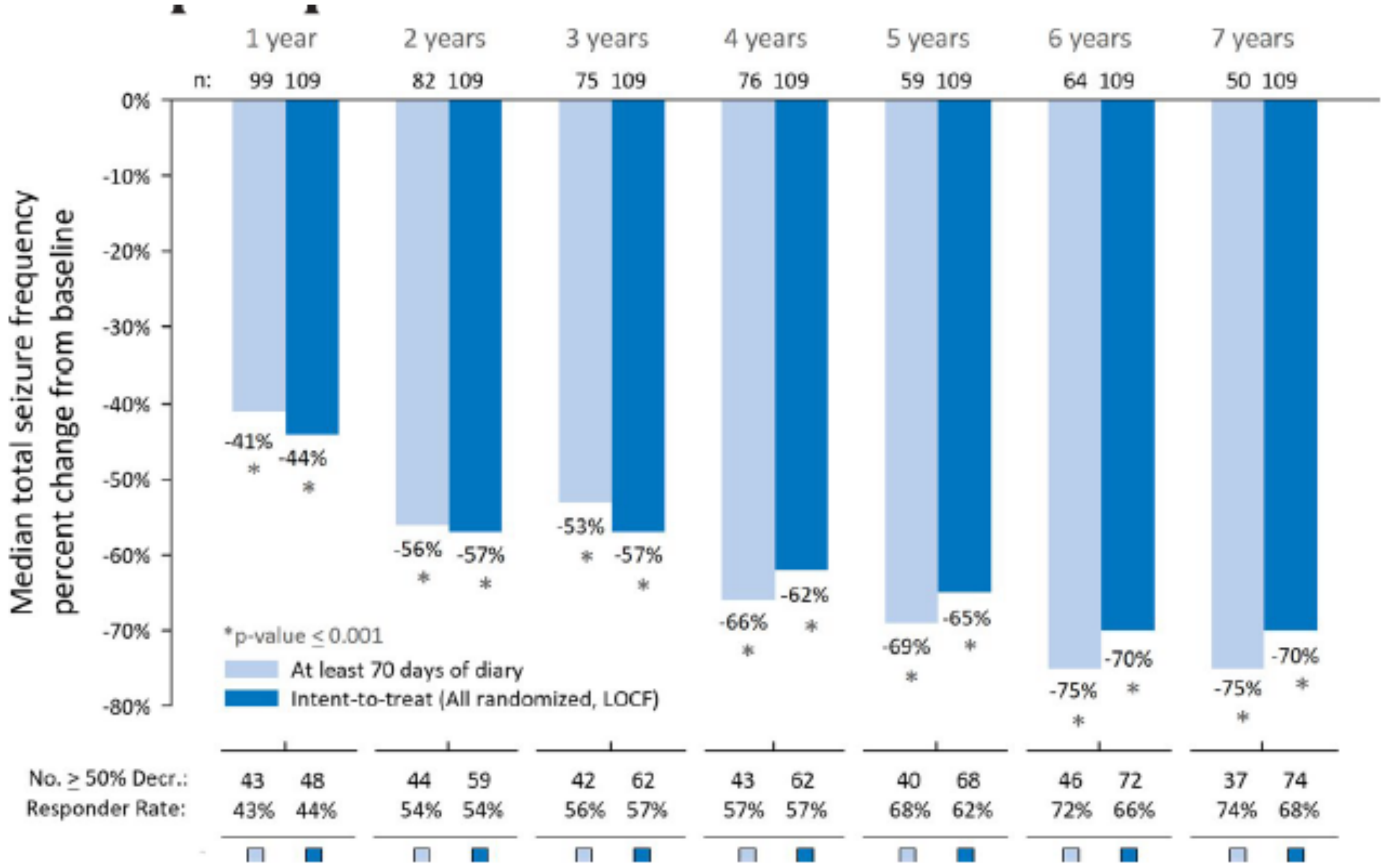
Epilepsia, 51(5):899–908, 2010
doi: 10.1111/j.1528-1167.2010.02536.x

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]

Long-term efficacy of ANT-DBS (SANTE study)



75%

median seizure reduction

18%

Seizure freedom >6 months

Salanova V, et al. Epilepsia 2021

ANT DBS (Single center experiences)

- 29 patients (continuous stimulation 1.5-3.1 V)
- Seizure reduction 71.3%, 73.9% (1,2 years)
- Median seizure reduction 70% (11 years)
- 13.8% seizure free

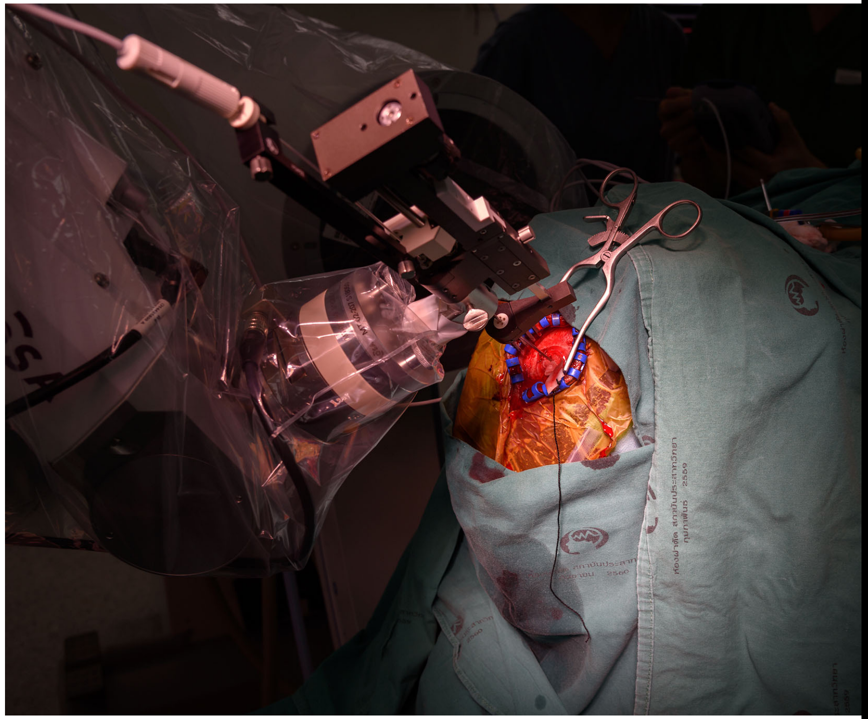
Kim SH, Seizure 2017

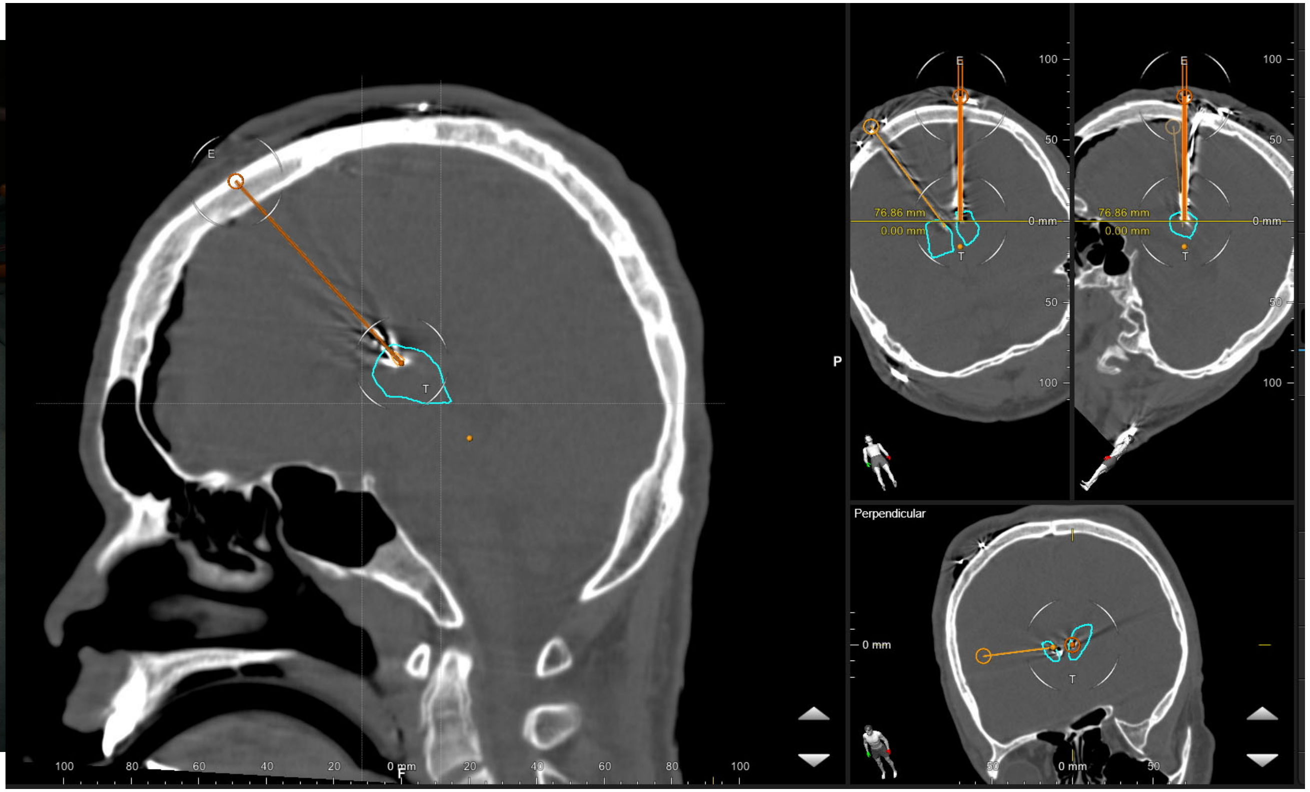
ANT DBS

- Gradual and sustained improvement in seizure reduction overtime
- Median seizure reduction 75% at 7 years
- No trends in worsening of adverse events >10 years
- SUDEP 2.0 deaths per 1000 person-years consistent with VNS, RNS

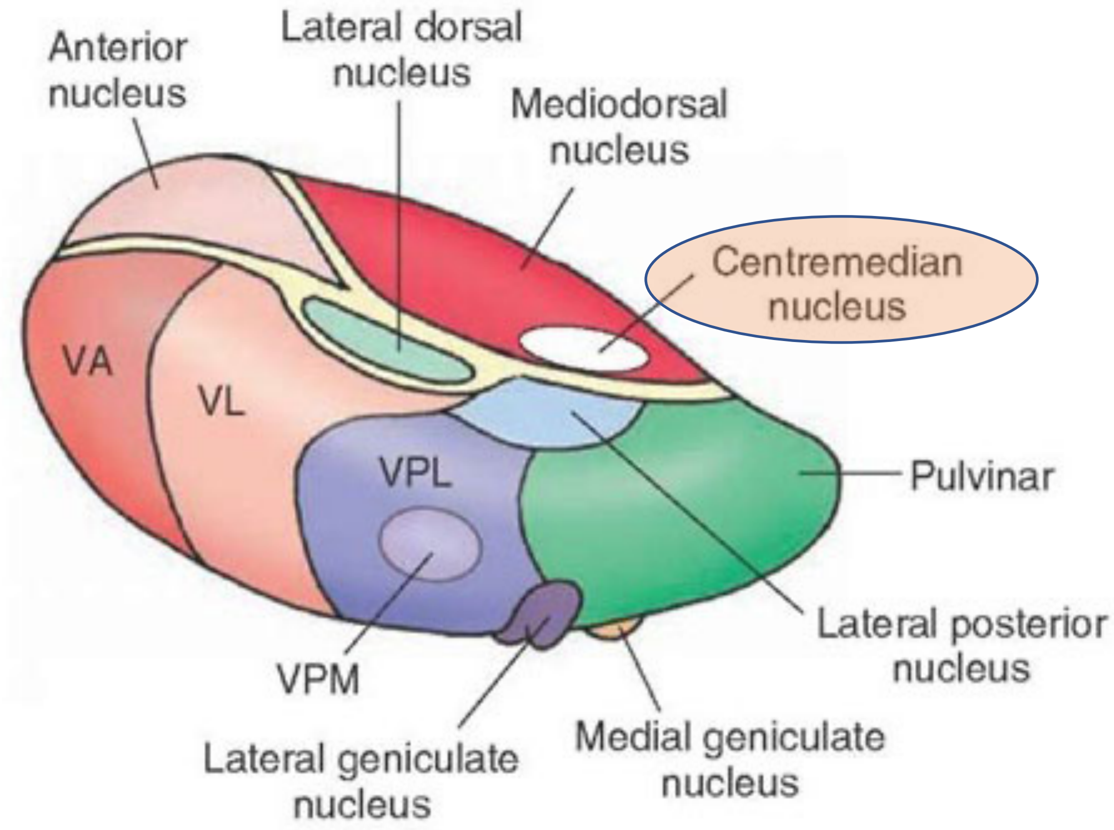
ANT-DBS

Seizure free 3 months at 3 years



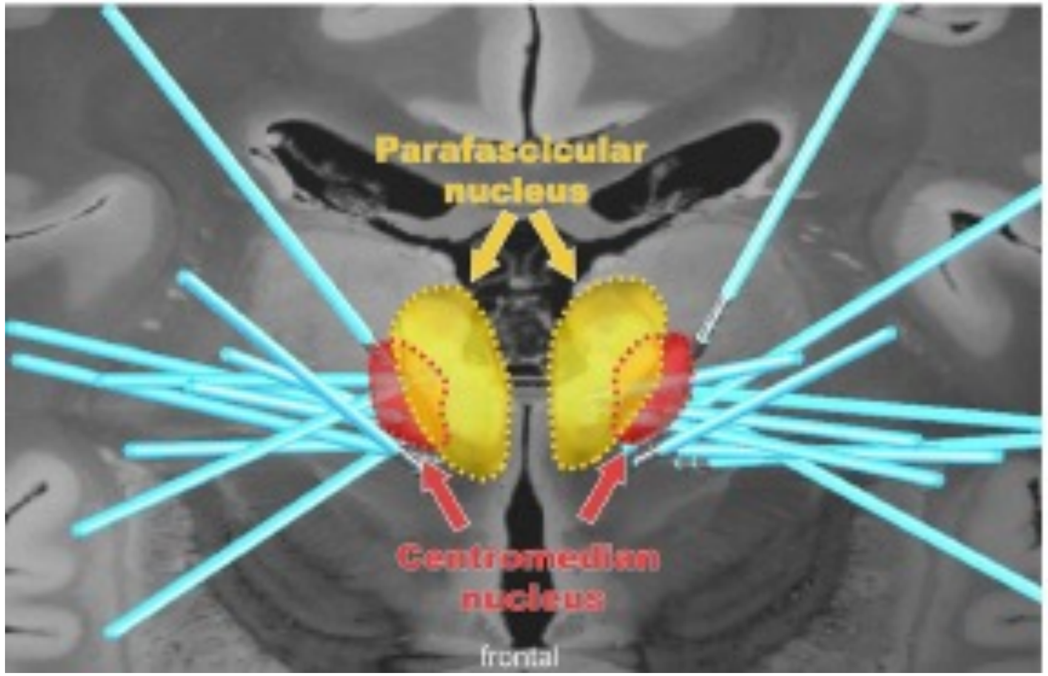


Centromedian neucleus



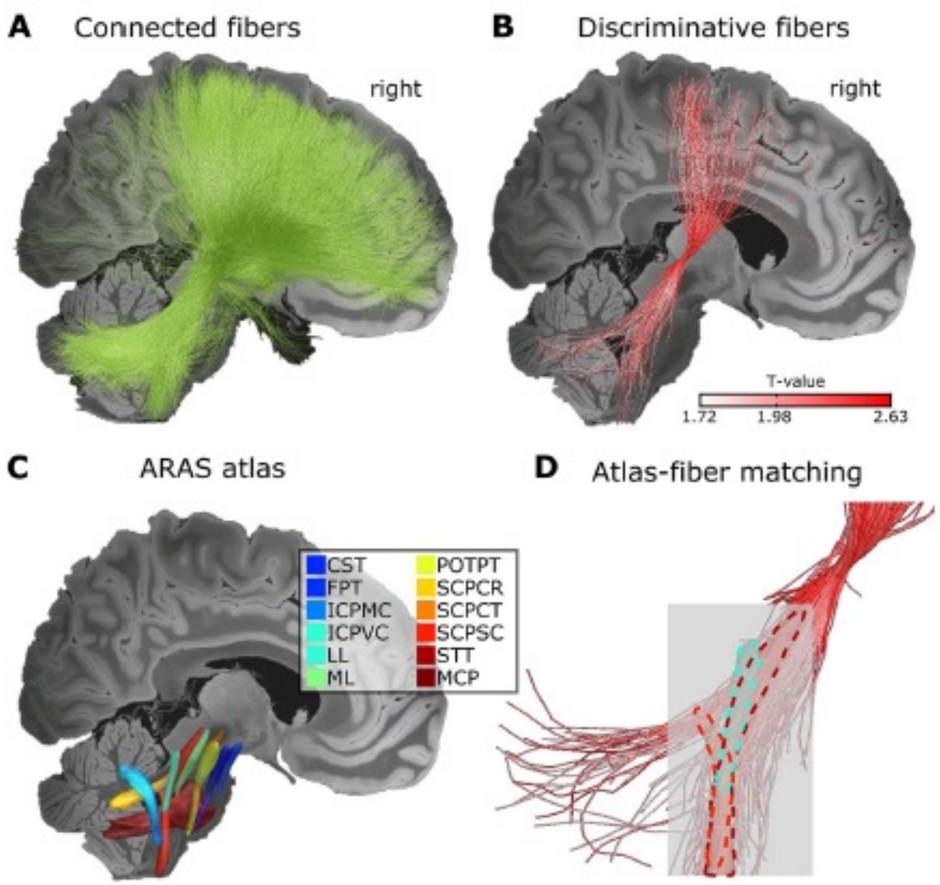
CM-DBS

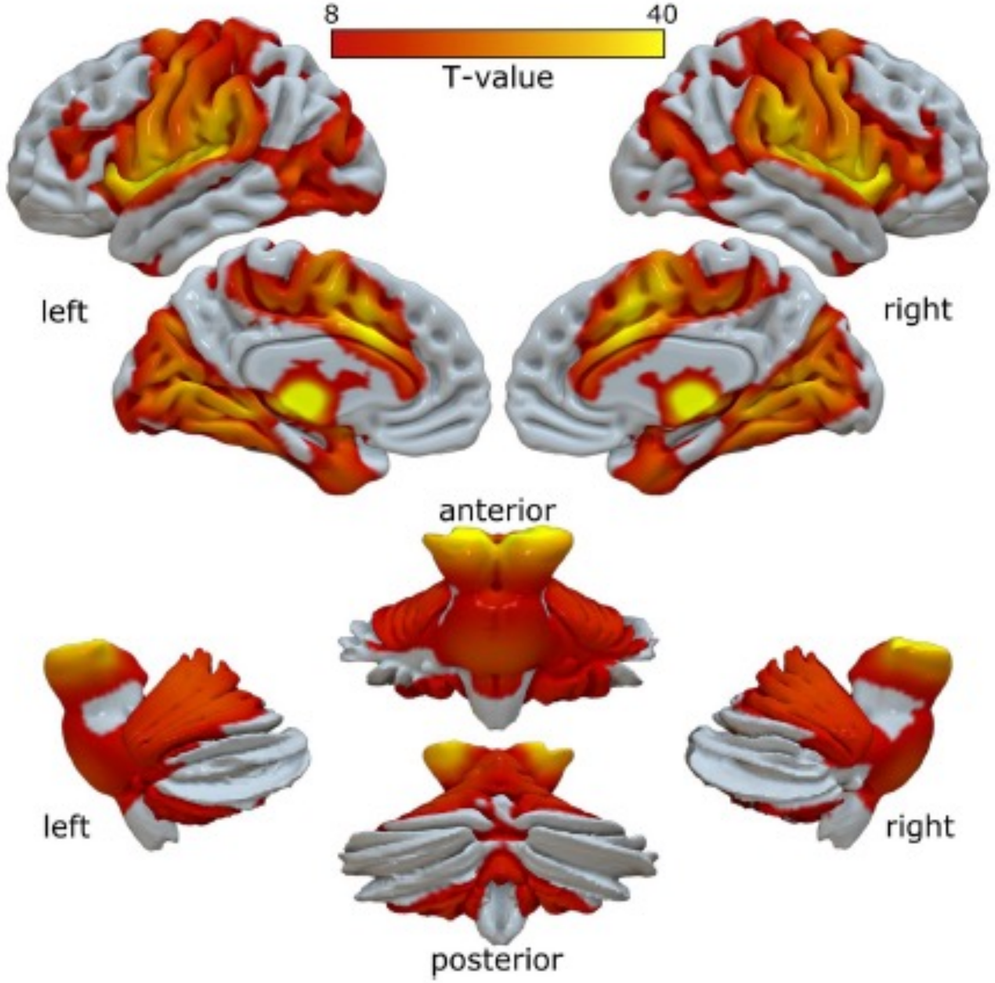
Seizure reduction>50% in 80% (3 months 25%,12 months 52%, 24 months 56%)



Torres CV, et al. Neurotherapeutics 2021; 18:1665-167?.

Network substrates of CM-DBS in generalized epilepsy





Torres CV, et al. Neurotherapeutics 2021; 18:1665-1677.

Seizure: European Journal of Epilepsy 84 (2021) 101–107

Centromedian thalamic nucleus with or without anterior thalamic nucleus deep brain stimulation for epilepsy in children and adults: A retrospective case series

Juan Luis Alcala-Zermeno [a], Nicholas M. Gregg [a], Elaine C. Wirrell [b], Matt Stead [c], Gregory A. Worrell [a], Jamie J. Van Gompel [d], Brian Nils Lundstrom [a,*]

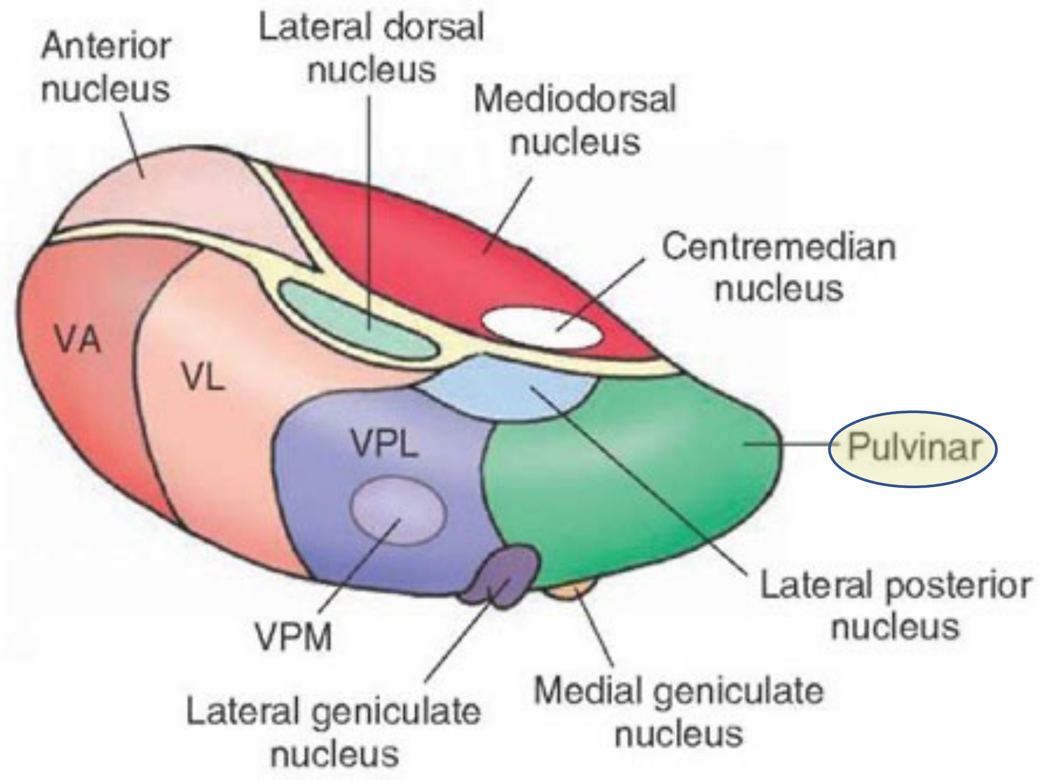
- 16 patients with DRE
- Median seizure frequency reduction 58%, 63% of patients >50% seizure frequency reduction.
- CM and CM+ ANT DBS reduces seizure frequency in patients with generalized, multifocal, posterior origin and poorly localized epilepsy.

DBS targets in epilepsy: systematic review and meta-analysis

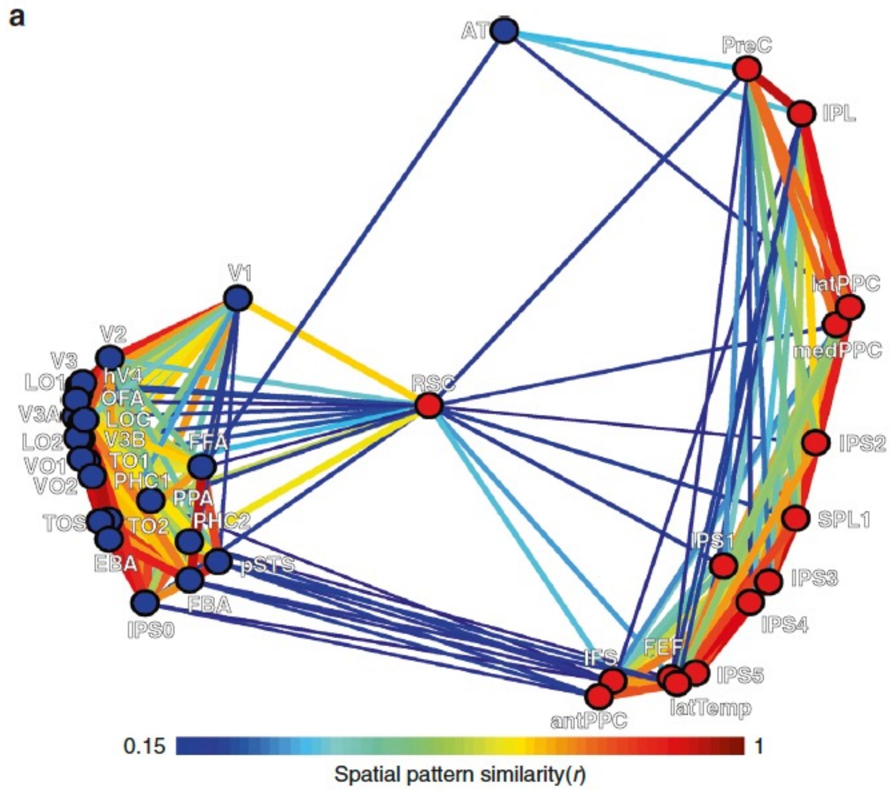
- Mean seizure reduction after ANT, CMT and hippocampal DBS is 60.8%, 73.4% and 67.8%
- ANT-DBS for focal and focal to bilateral tonic-clonic seizures (best evidence)
- CMT-DBS for generalized epilepsy
- Hippocampal DBS for temporal lobe seizures

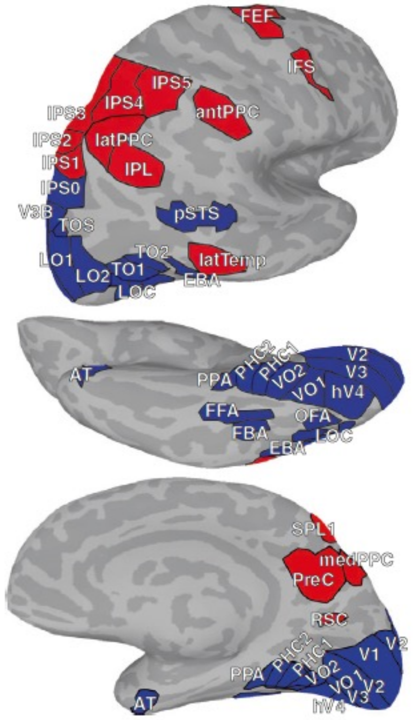
Vetkas A, et al. Epilepsia 2022

Pulvinar DBS -Posterior quadrant epilepsy



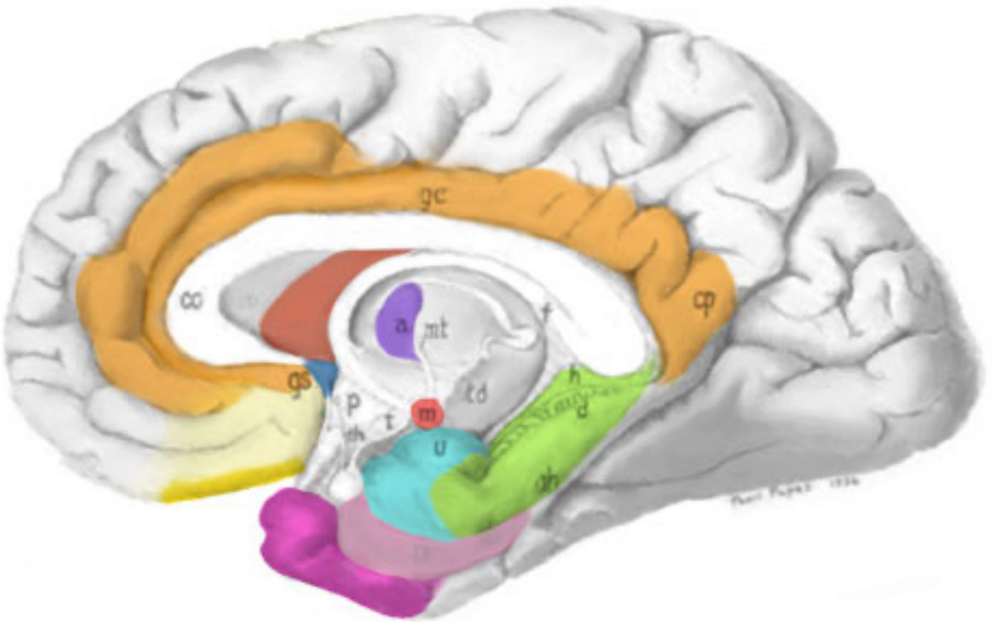
Pulvino-cortical connectivity





Arcaro M, Nat commun 2018

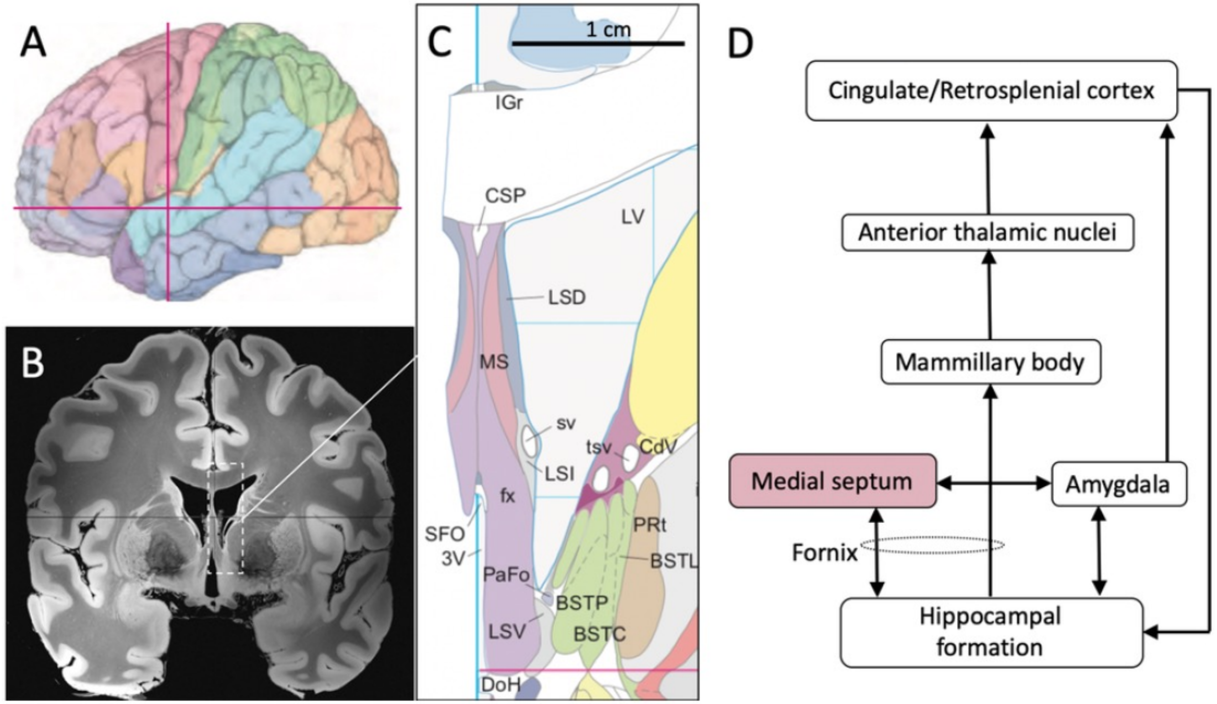
Limbic Structures



- Ventromedial Frontal Cortex
- Caudal Orbital Frontal Cortex
- Temporal Polar Cortex
- Pyriform and Entorhinal Cortex
- Striatum
- Septal Nuclei
- Amygdala

Medial septum deep brain stimulation

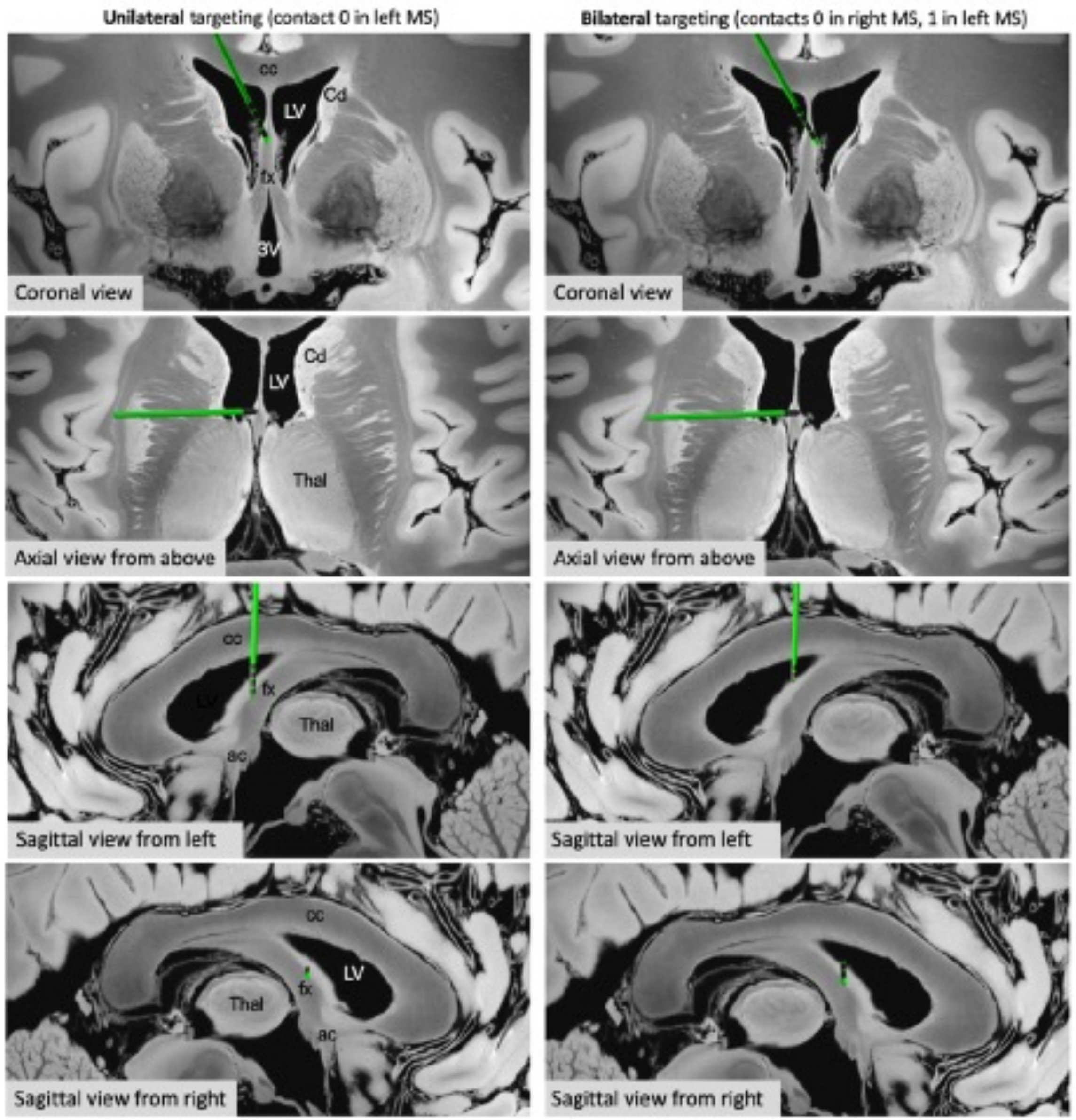
- Small nucleus located in the basal, posterior frontal in the midline, below rostrum of corpus callosum, medial to lateral septum nuclei with diffuse projection to hippocampus



Cole ER, et al. Epilepsia 2022

Medial septum deep brain stimulation

- Primary pacemaker of the hippocampal theta rhythm involving in regulating memory function
- Elevated theta oscillations are thought to represent a seizure-resistant network activity
- DBS of medial septum can reduce seizures and restoring cognitive function
- Treament of schizophrenia,traumatic brain injury, alzheimer's disease



MRI 7 T , Medial septum DBS

Deep brain stimulation in Epilepsy

- RNS and ANT-DBS 75% seizure reduction at 9 and 7 years
- 18% ANT-DBS, 21% RNS had a seizure free period of 6 months or greater
- Modest cognitive improvements and no significant decline is mood
- No significant improvement in verbal memory, visual memory and language tests with ANT-DBS
- Modest improvement in auditory but not visual memory in RNS

Salanova V, et al. Neurology 2015

Geller EB, et al. Epilepsia 2017

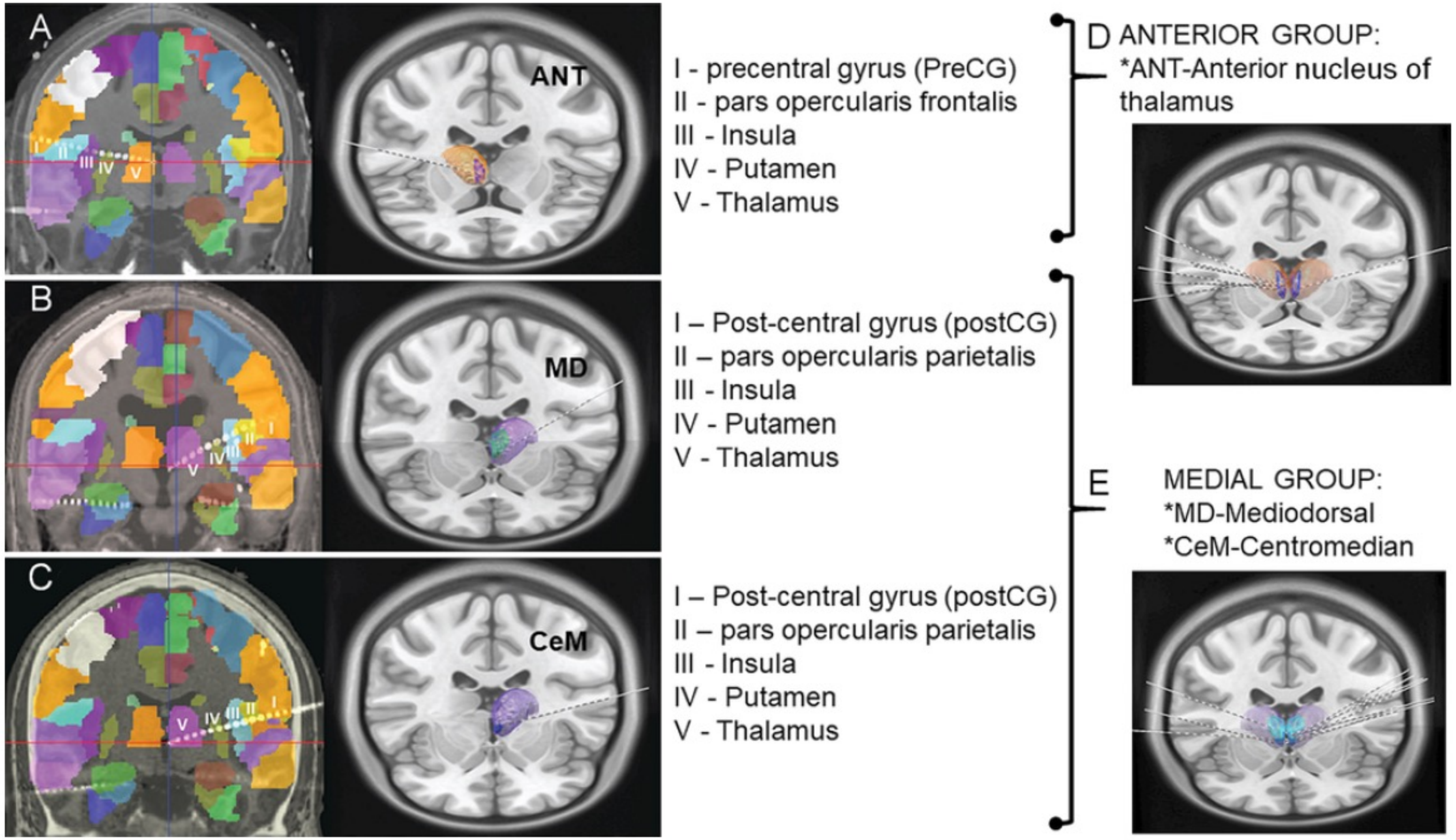
SEEG-Guided Neuromodulation (Thalamic SEEG)

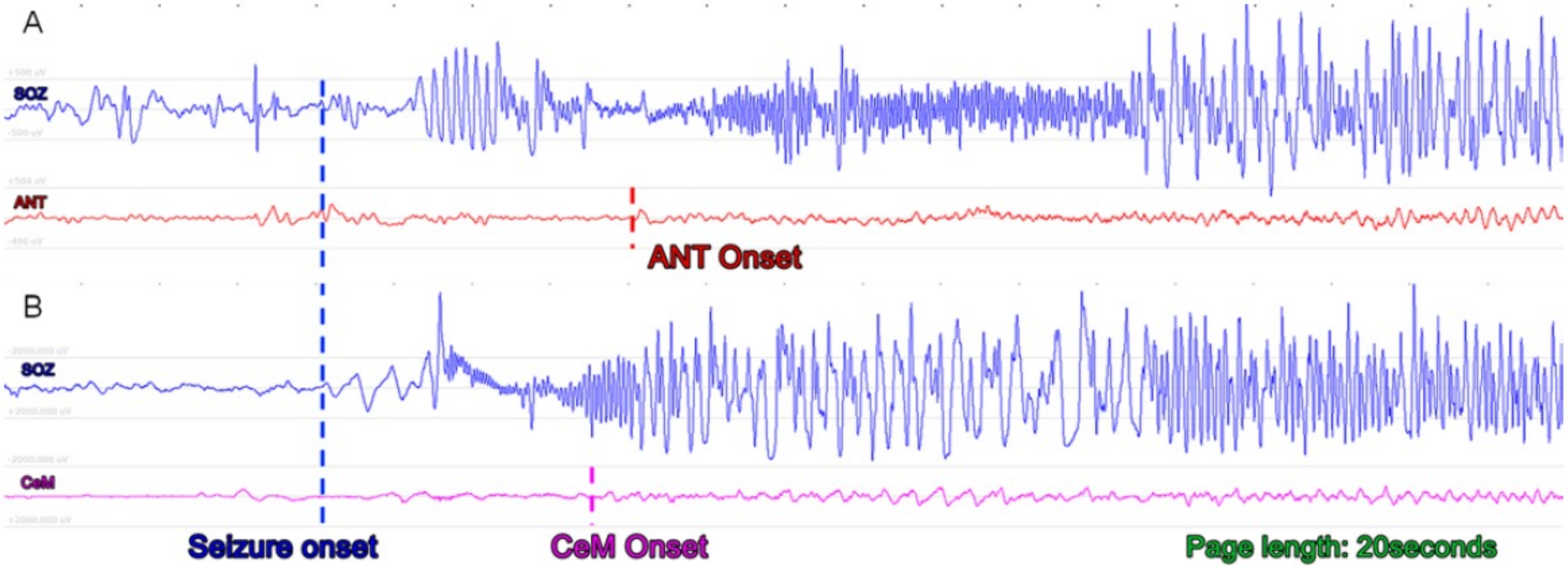
- SEEG-guided resection and SEEG-guided RNS
- Possible to perform patient tailor neuromodulation guided by SEEG

Robot-assisted stereoelectroencephalography exploration of the limbic thalamus in human focal epilepsy: implantation technique and complications in the first 24 patients

*Ganne Chaitanya, MBBS, PhD,[1,2] Andrew K. Romeo, MD,[3] Adeel Ilyas, MD,[2,3] Auriana Irannejad,[1,2] Emilia Toth, PhD,[1,2] Galal Elsayed, MD,[3] J. Nicole Bentley, MD,[3] Kristen O. Riley, MD,[3] and Sandipan Pati, MD[1,2]

[1]Department of Neurology, [2]Epilepsy and Cognitive Neurophysiology Laboratory, and [3]Department of Neurosurgery, University of Alabama at Birmingham, Alabama



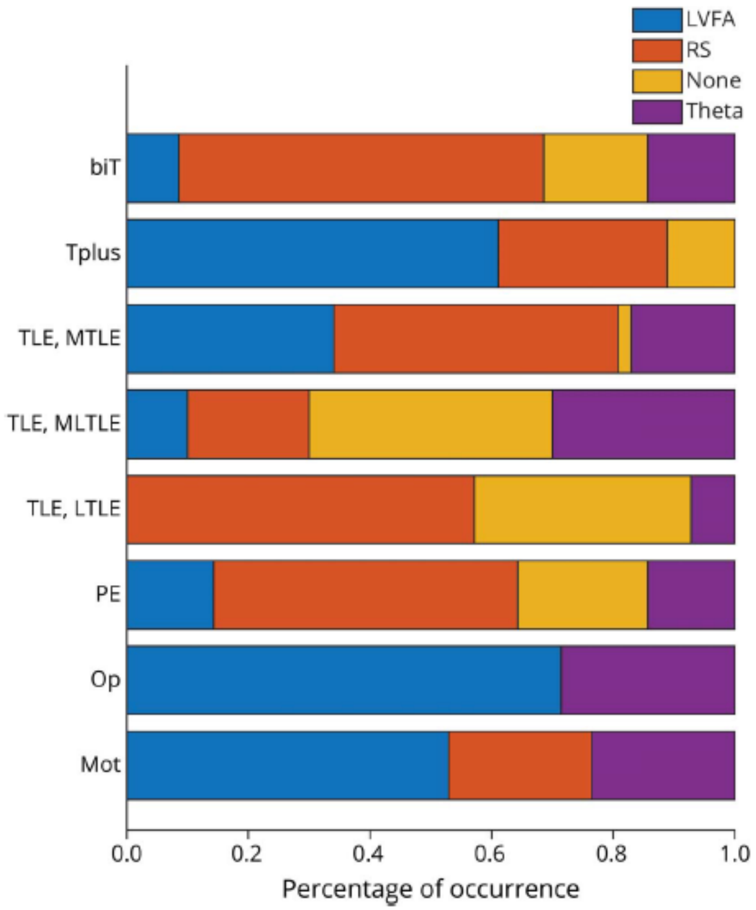

A
SOZ
ANT
ANT Onset
B
SOZ
CeM
Seizure onset
CeM Onset
Page length: 20seconds

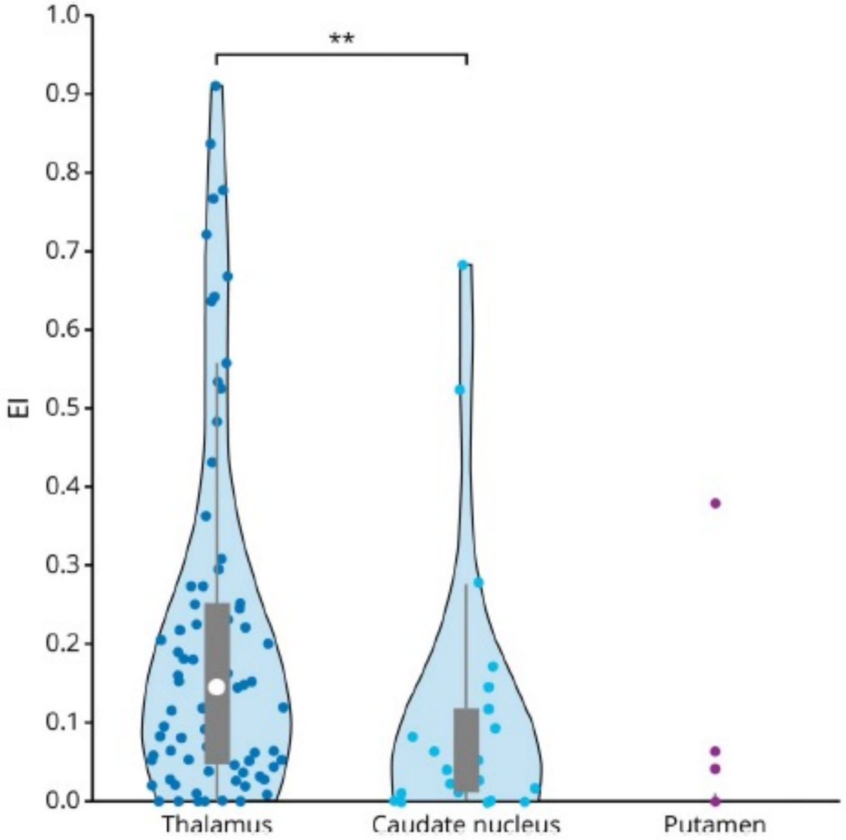
Ictal Signature of thalamus and basal ganglia

- Epilepsies are cortical-subcortical disease in which epileptogenicity can affect subcotical structures, particularly the thalamus.
  - 86% of patients, thalamus involved during seizures
  - 20% showed high epileptogenicity
- Thalamic epileptogenicity was correlated with the extension of epileptogenic network.
- High thalamic epileptogenicity was found in bitemporal, insulo-opercular, and motor system epilepsies.
- Thalamic epileptogenicity correlated with postsurgical outcome.

Pizzo F. Neurology 2021

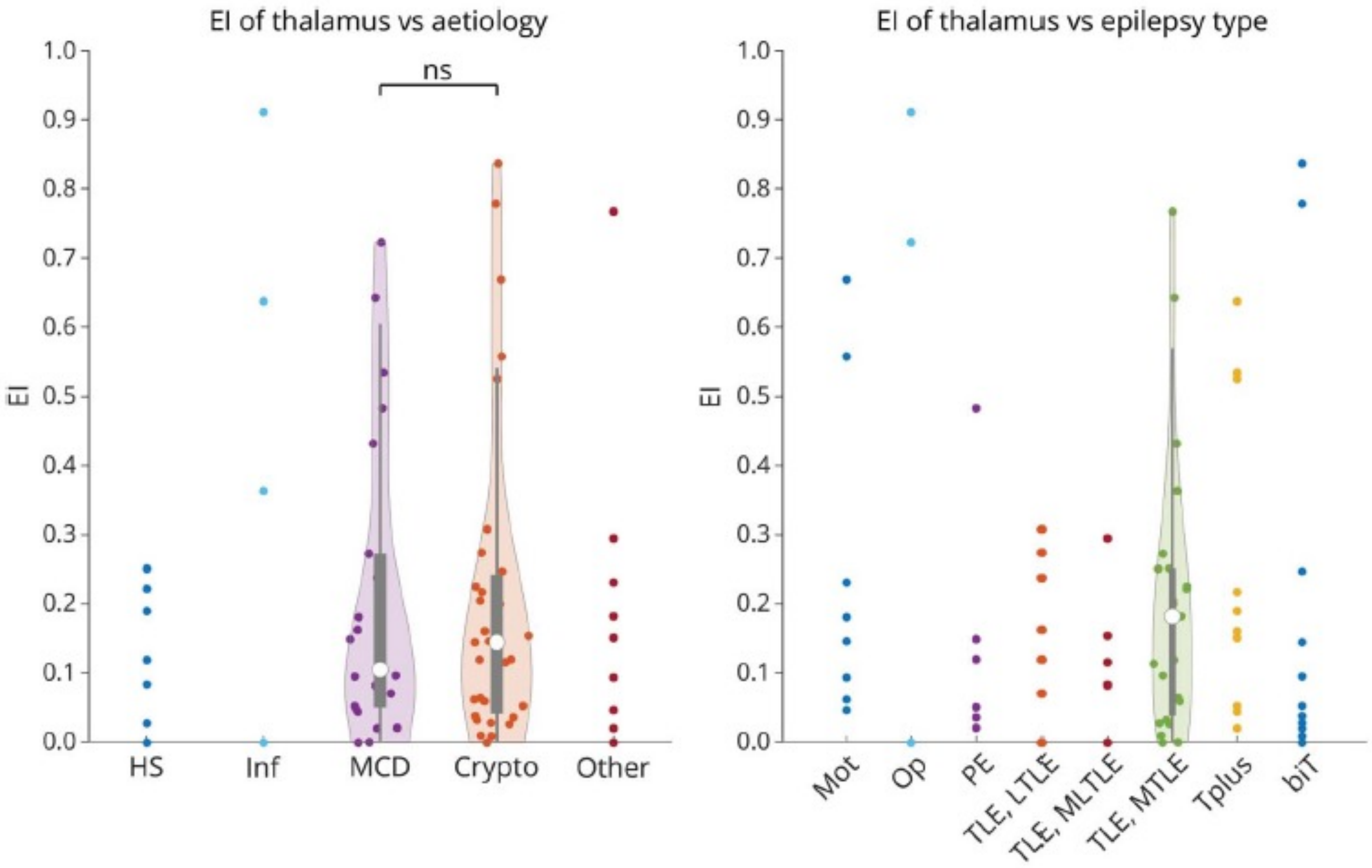
Ictal Signature of thalamus and basal ganglia





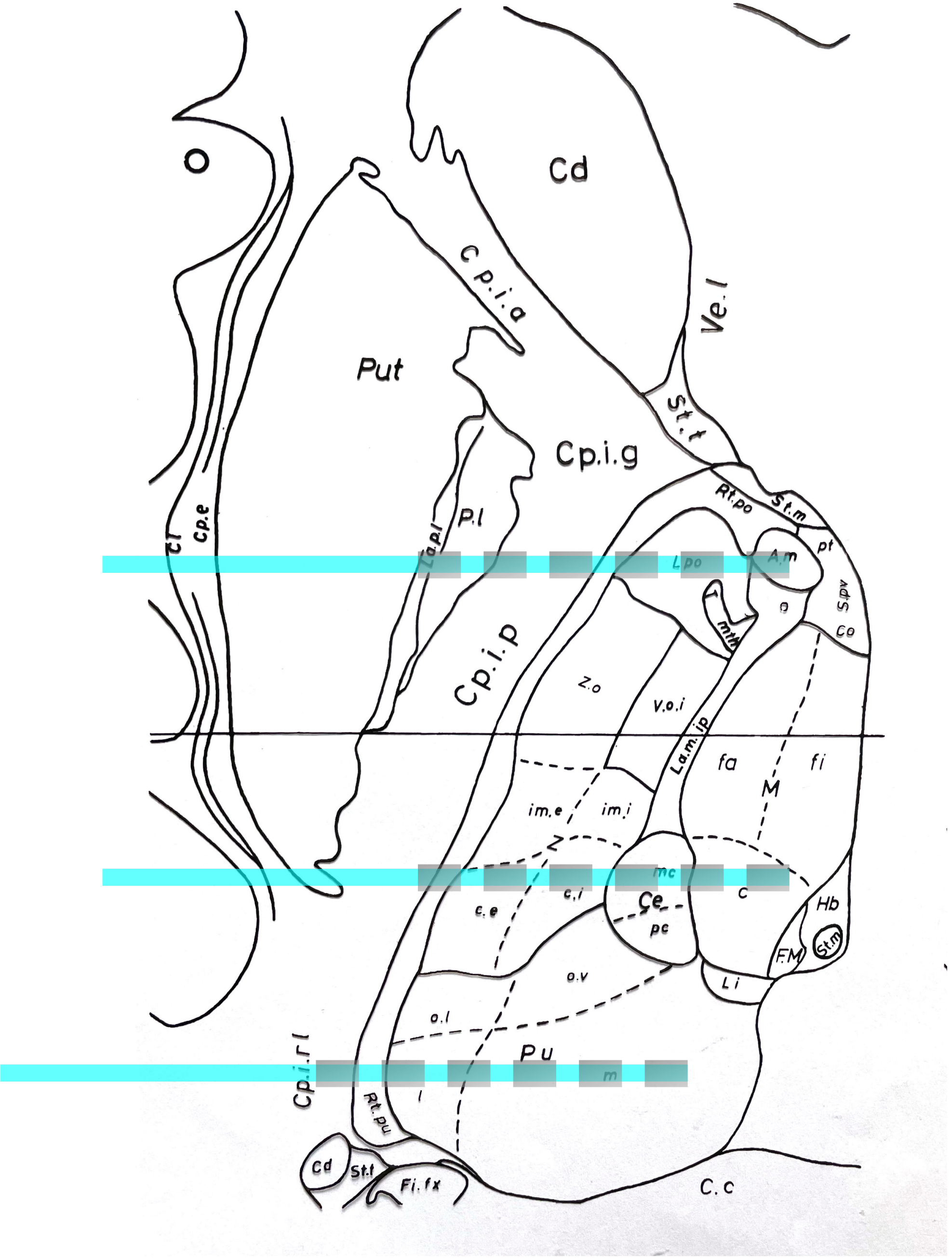
Thalamus vs caudate nucleus Wilcoxon rank sum test $p < 0.01$.

Pizzo F. Neurology 2021



Pizzo F. Neurology 2021

Thalamic SEEG



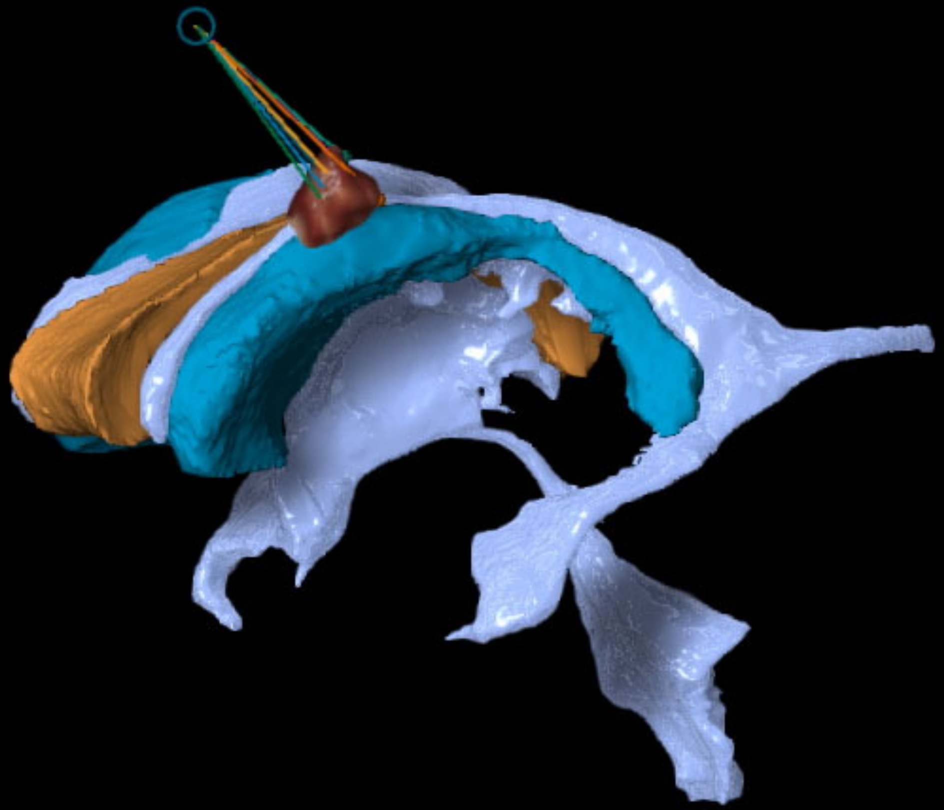
Neuromodulation in epilepsy

- DBS (LFP), RNS
- Target
- Seizure type
- Electrode location
- Stimulation parameter

Ablation (Minimally invasive)

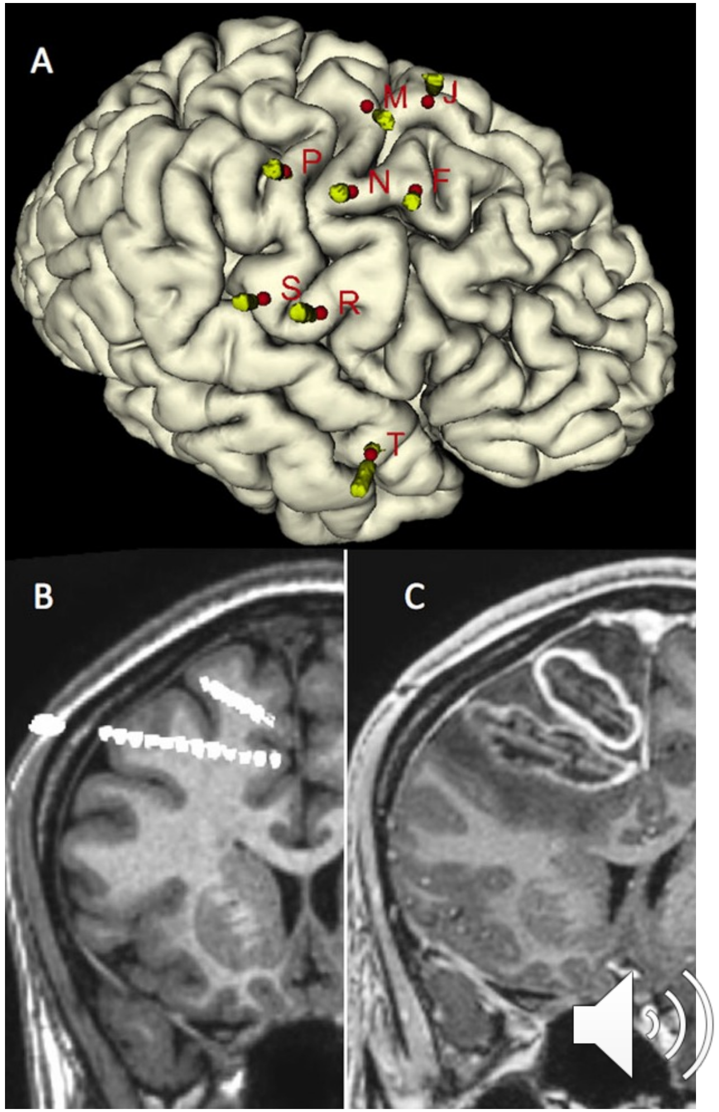
- Conventional Surgery
  - Perception that patient has "one good surgery"
- Ablative Procedures
  - Opportunity to ablate several and segmented approaches
  - Goal: Ablate the best known target/trajectopries, and observation for a period of time, and re-explore/re-ablate if needed.

Thermocoagulation



Stereoelectroencephalography-guided radiofrequency thermocoagulation (SEEG-guided RF-TC)

- 89 patients underwent SEEG evaluation and RF-TC of presumed epileptogenic zone
- Seizure free 16 patients (18%), worthwhile improvement 9 (10.1%)
- Favorable results in patients with heterotopy (p=0.0001389), MRI +ve, HS



Cossu M. J Neurosurg 2015

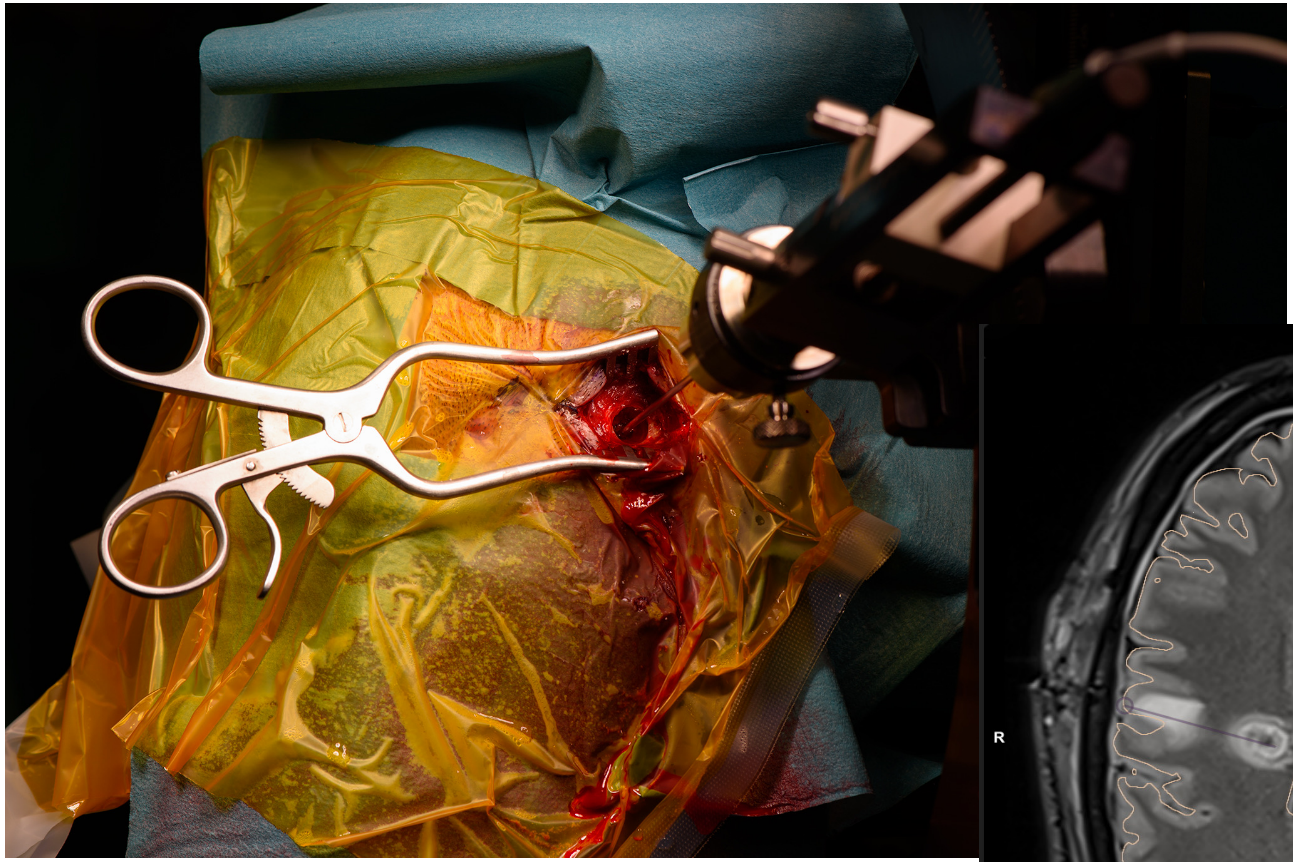
Cossu M. Epilepsia 2017

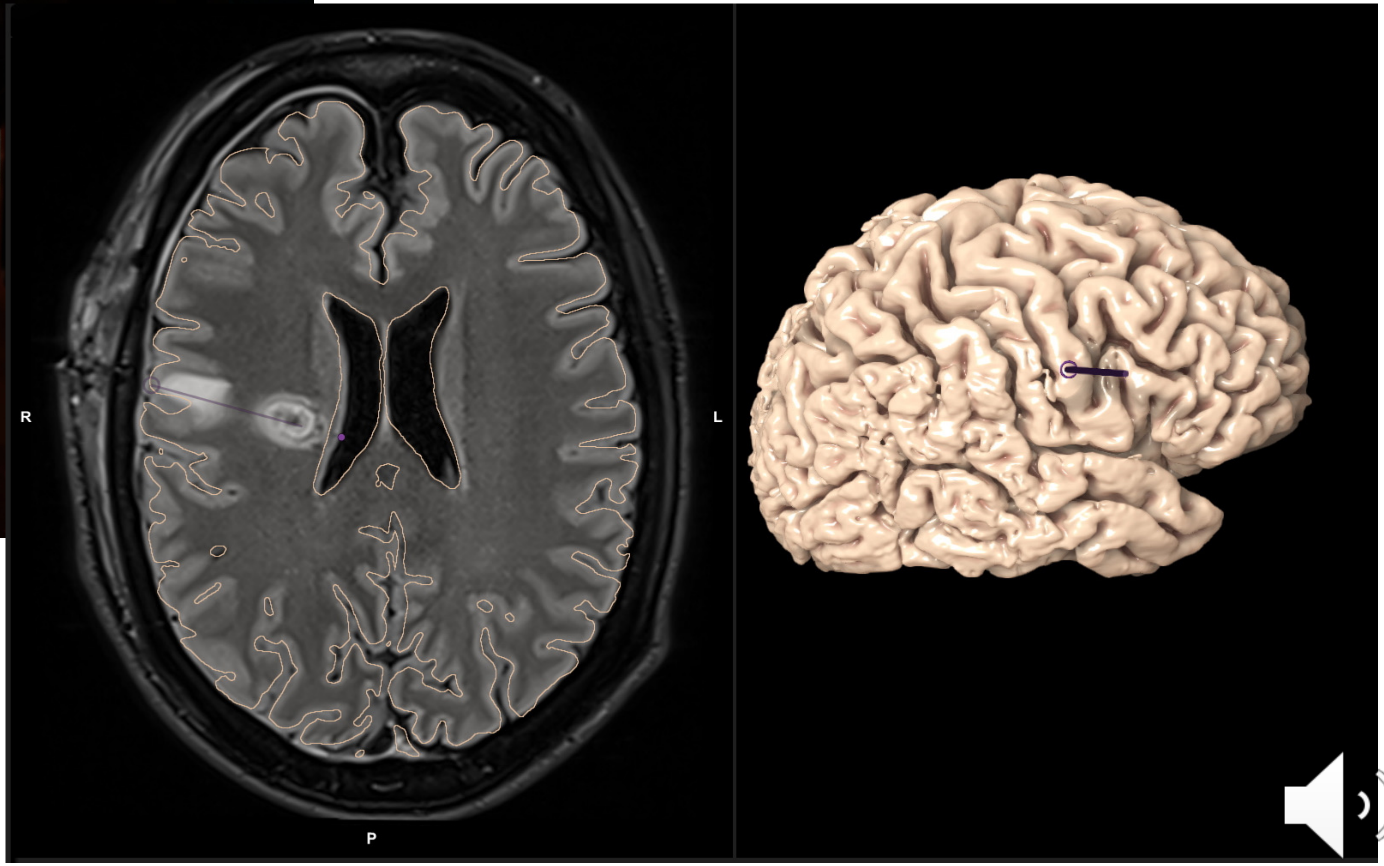
SEEG-TC in malformation of cortical development poorly accessible to surgical resection

- 14 patients
- 9 patients (64%) experienced long-term decrease in seizure frequency >50%
- 4 (28.5%) patients were seizure free
- Responders: focal low-volatge fast activity, electrical stimulation induced spontaneous seizures

Catenoix H. Neurosurgery 2015

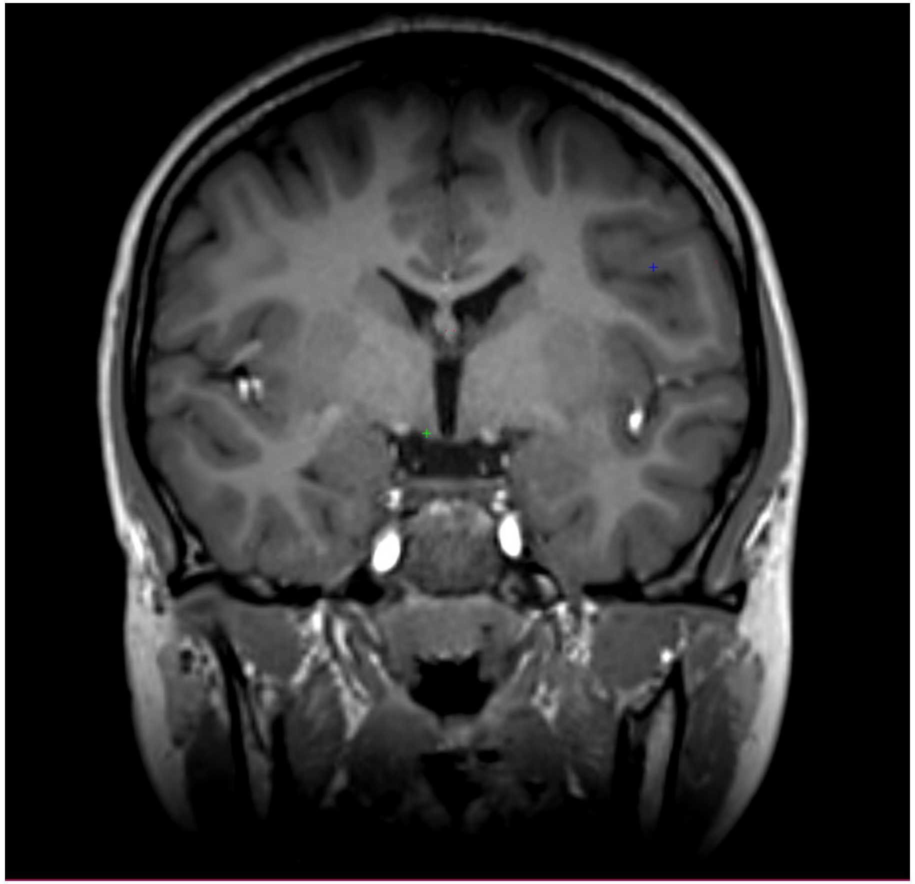
Nonlesional

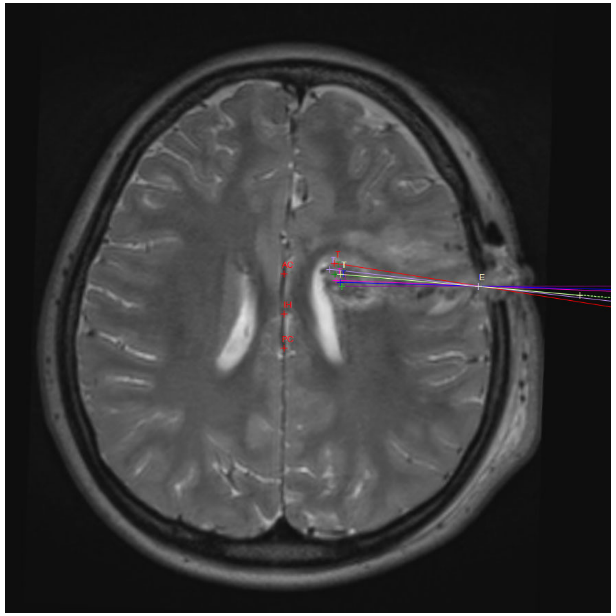


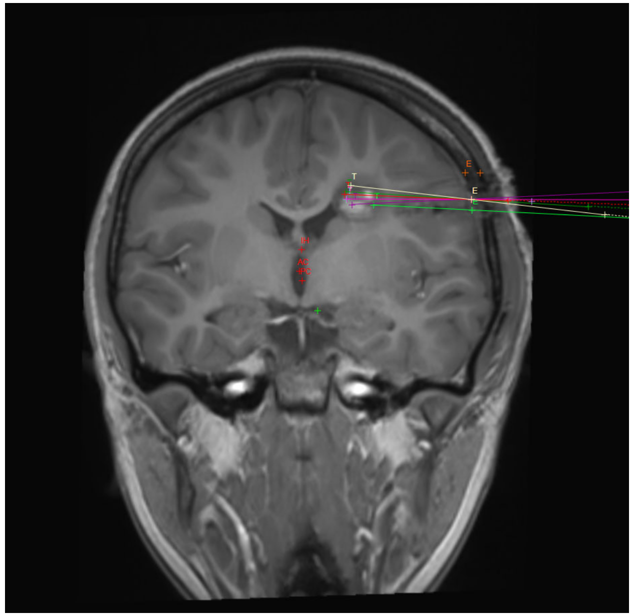


Seizure free @ 1 year

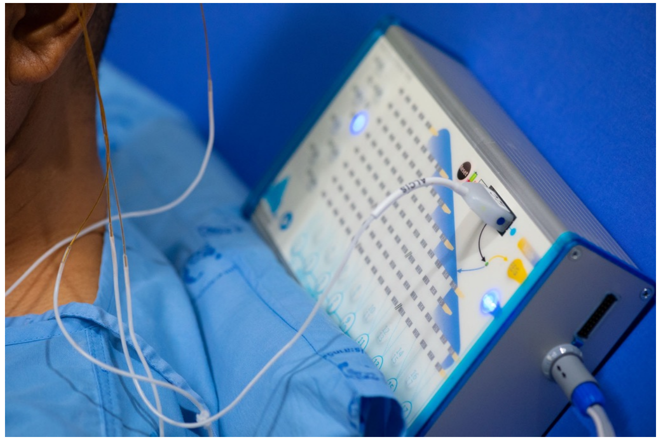
Periventricular heterotopia

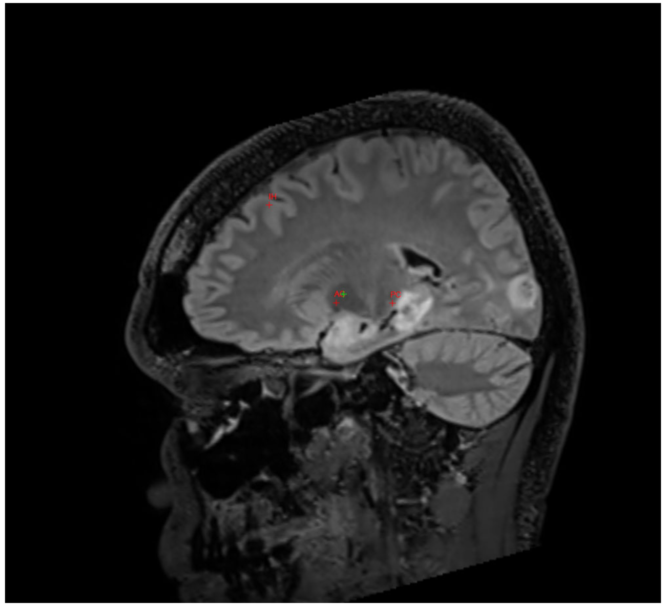


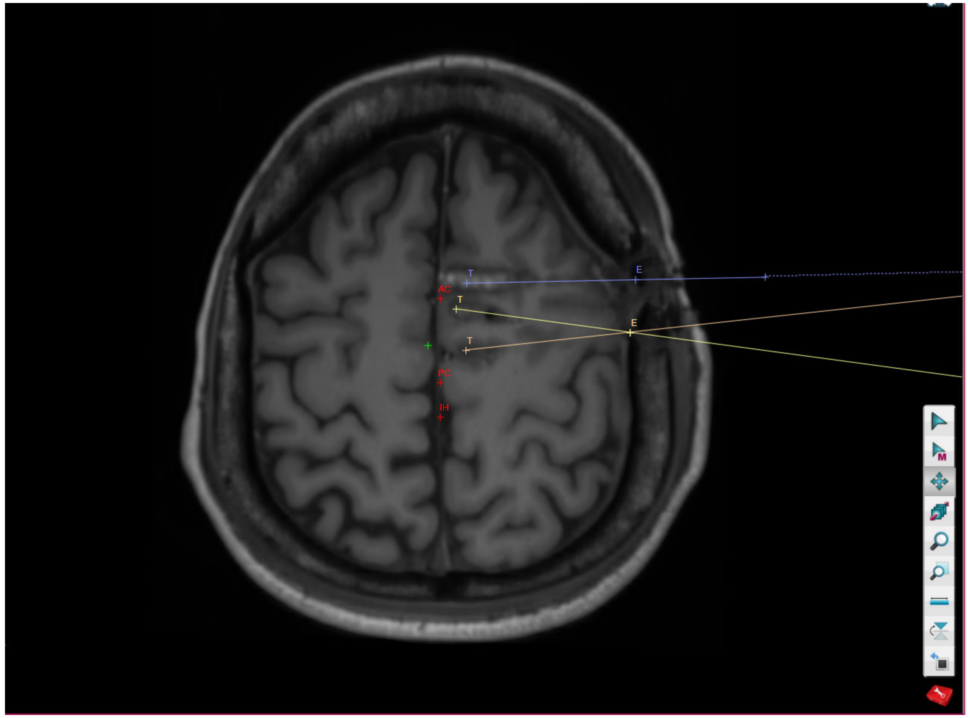




SEEG-guided RF-TC (nonlesional)



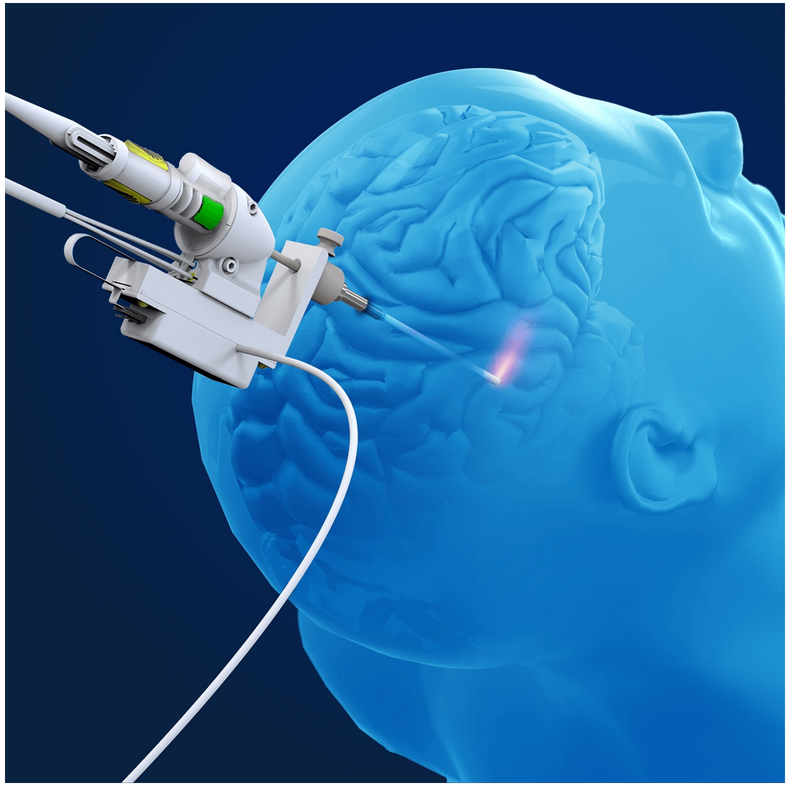




Nonlesional, seizure onset at central region

MRI guided Laser Interstitial thermal therapy

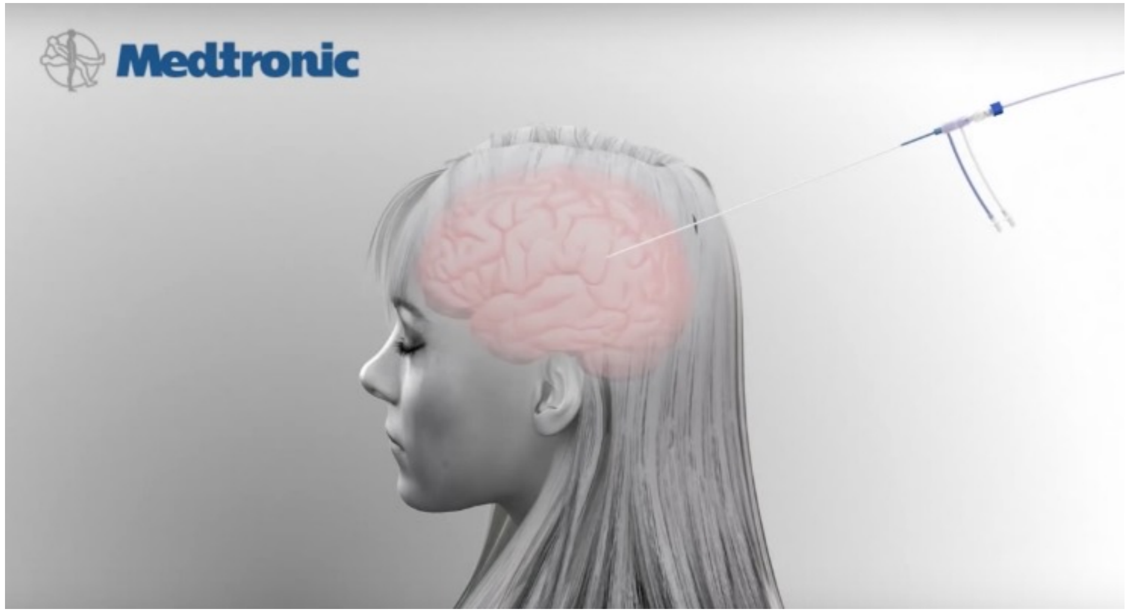
(MRgLITT)



NeuroBlade (Monteris)

6 mm cylindrical tip, or side fire tip

CO_2 coolant

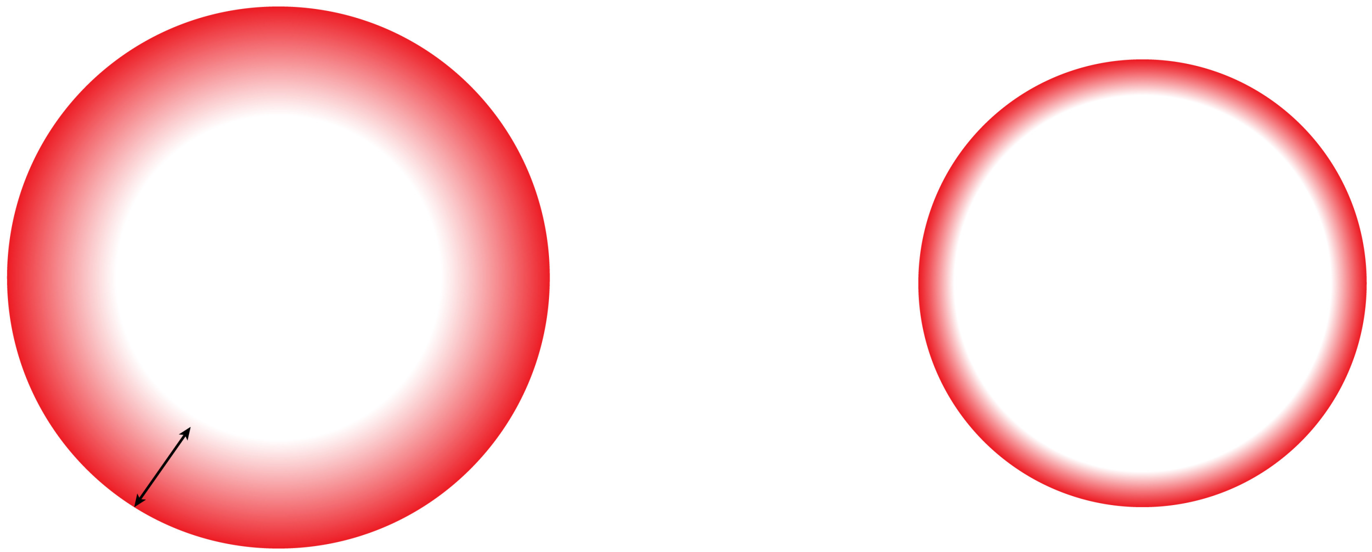


Visualase (Medtronic)

3- or 10 mm cylindrical tip

Saline coolant

Transition zone between dead and viable tissue



Radiofrequency (5-10 mm)

Laser (<1 mm)

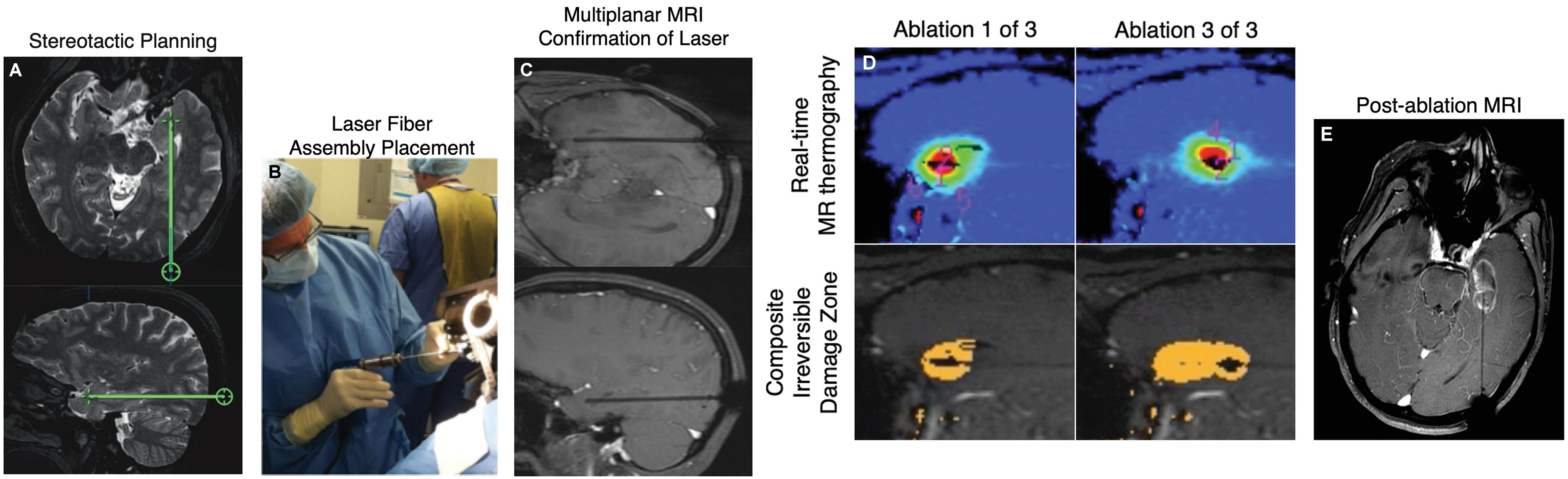
Advantage

- Low morbidity
- Small incision
- Confirmation of targeting before ablation
- Immediate effect, minimal hospital stay

Applications

- MTS/MTLE
- Hypothalamic hamrtoma
- FCD, Bottom of sulcus FCD
- Nonlesional extratemporal epilepsy
- Tuberous sclerosis
- Periventricular nodular heterotopia
- Cavernomas
- Temporal encephalocele
- Corpus callosotomy

Youngerman BE. Neurosurgery 86:E366-E382, 2020



Youngerman BE. Neurosurgery 86:E366-E382, 2020

MRgLITT

- Minimal disruption of tissues
  - Decreased collateral damage
- Less surgical morbidity
  - Pain
  - Length of stay
- Easily coupled to stereoEEG
- Increased acceptance/referrals
  - Patient refusing open surgery
  - Referring neurologists refusing open surgery
- Less suited to large onset zone

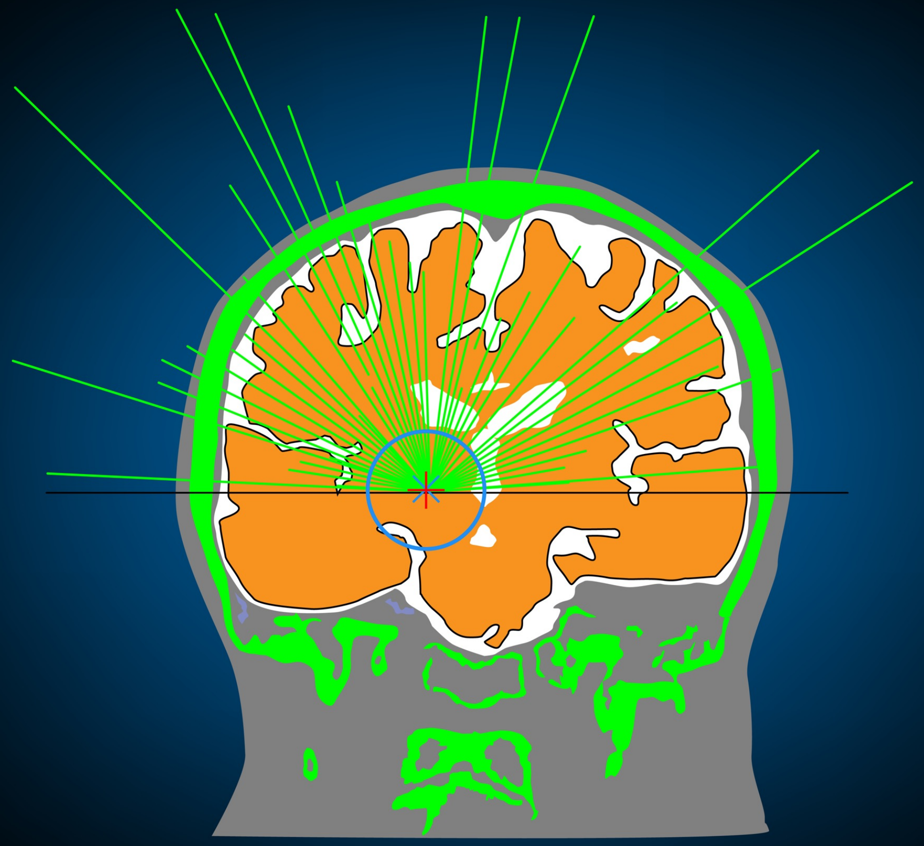
Comparison of minimally invasive and traditional surgical approaches for MTLE: A systematic review and meta-analysis of outcome

	Engel Class I	Major complications
MRgLITT	57%	3.8%
Radiofrequency ablation	44%	3.47%
ATL	69%	10.9%
aAHE	66%	7.4%

Cognitive outcome might be more favorable after MRgLITT compared to ATL and sAHE

Kohlhase K. Epilepsia 2020

Transcranial Focused Ultrasound



Transcranial focused ultrasound

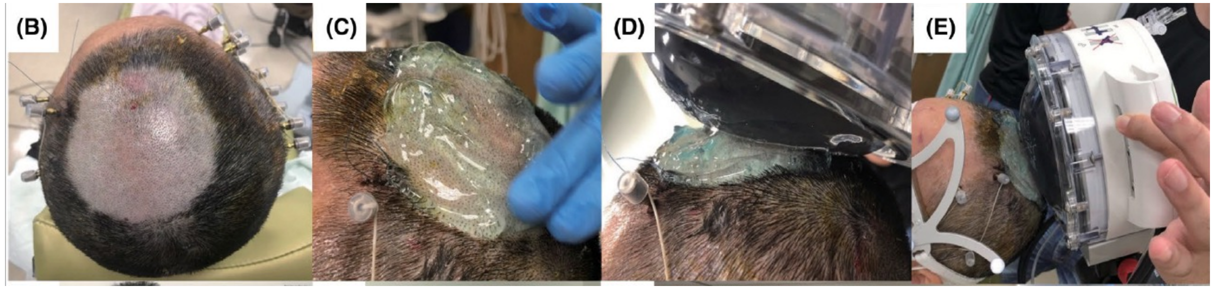
- Low-intensity FUS- modulatory effects
- High-intensity FUS –Lesioning effects

Low Intensity FUS (LIFUS)

- Employing a low acoustic energy far below the level that induces temperature changes in the brain tisuue (HIFUS 1000 W/cm^3 vs LIFUS 3 W/cm^3)
- Energy delivered are so low as to not result in any ablative effect, tissue damge, or permanent structural changes.
- Safely modulate neural tissue transcranially (noninvasive) and painless.
- Waves can be transmitted through the skull and modulate deep structures with a sharply focused beam without causing tisuue destruction.
- Modulation of auditory, visual, sensory and motor functions by positioning the beam focus over correlating cortex.
- Mechanism: mechanical/vibrating disruption of tissue.

Pilot study of focused ultrasound for drug-resistant epilepsy

- Six patients with DRE undergoing SEEG for localization of SOZ.
- 2 patients had decreased seizure frequency within day 3.
- Posttreatment MRI revealed no lesion or brain edema.
- Significant changes in spectral power of SEEG at target electrodes during FUS.



Lee CC. Epilepsia 2021

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Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Safety of focused ultrasound neuromodulation in humans with temporal lobe epilepsy

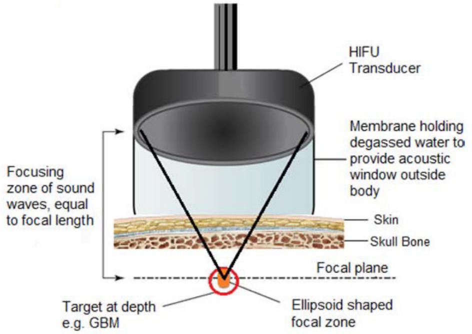
John M. Stern [a], Norman M. Spivak [b, c], Sergio A. Becerra [b], Taylor P. Kuhn [b], Alexander S. Korb [b, d], David Kronemyer [b], Négar Khanlou [e], Samuel D. Reyes [c], Martin M. Monti [b, c, f, n], Caroline Schnakers [c], Patricia Walshaw [b], Inna Keselman [a], Mark S. Cohen [a, b, f, g, h, i, j, n], William Yong [e], Itzhak Fried [c, n], Sheldon E. Jordan [k], Mark E. Schafer [d, l], Jerome Engel Jr. [a, b, m, n], Alexander Bystritsky [b, d, *]

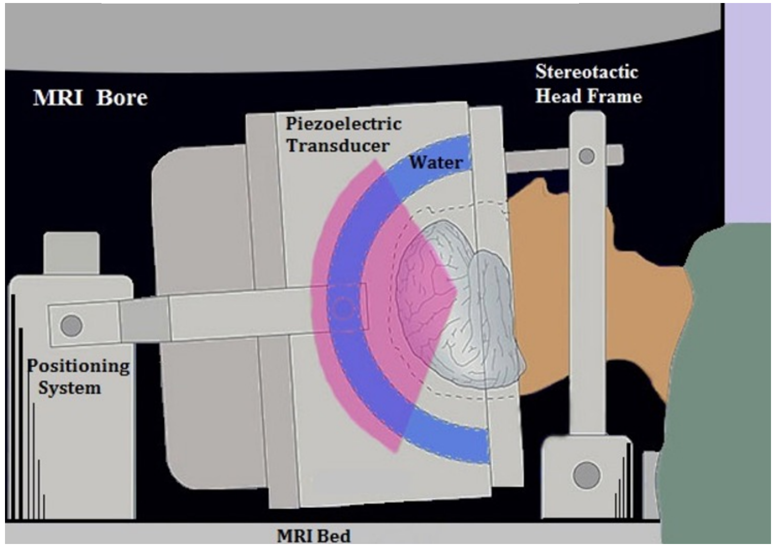
- Safety and efficacy of tFUS in patients with refractory TLE electing to undergoing TL.
- No detectable damage to tissue after resection.
- Neuropsychological testing did not show any significant changes after tFUS.

MRI Guided Focused Ultrasound (MRgFUS)

High Intensity FUS

- 1074 tiny ultrasonic emitters in half sphere
- Ultrasound: sound vibration > 20,000 Hz
- Created by electrically induced vibrations of piezoelectric crystals
- Vibration of molecules in tissue; T>56C , >2 sec =>coagulative necrosis
- FDA approved for thalamotomy for essential tremor in 2017.





Quadi SA,et al. Neurosurg Focus 44:E16,2018


Tools
Overlays
Treatment
3D
LAI
Ex: 2253
Se: 617R
Im: 77
Ax S39.9
L146.9 P112.0 S69.0
AC-PC: -147.9 -118.0 2.0
RPI
RPS
Tx OAx
150mm
bw: 41.7 KHz
TR: 5.4 TE: 2.5
Sonicate
Align
Verify
Treat Low
Treat High
40° - 45°
46° - 50°
51° - 55°
56° - 60°
<40 °C
Limit
46 °C
Estimated Temperature
Spot Coordinates
RAS
RL
R15.8
AP
A9.6
SI
S41.1
AC-PC
ML
15.0
AP
6.6
SI
2.0
Diameter
2.2 mm
Spot Length
3.8 mm
MRI
Ready
Device
Ready [Cooling, Circulating 15 C, Dissolved Oxy 0.58]
Energy
900 J
Power
100 W
Duration
10 Sec
Time Extension
3 Sec
Cooling
27 Sec
Frequency
0.66 MHz
Apodization
None
Advanced
Transducer
Average Power
Element Number
N/A
Element Data
N/A
Enable Elements
Disable Elements
Elements On
995
Skull Area
369 cm 2
Focal Power
12 W
Skull Score
0.41
CT Filter
GE_BONEPLUS
Calculate
DELL


SIGNA
Architect
00:00
INSIGHTEC

MRgFUS

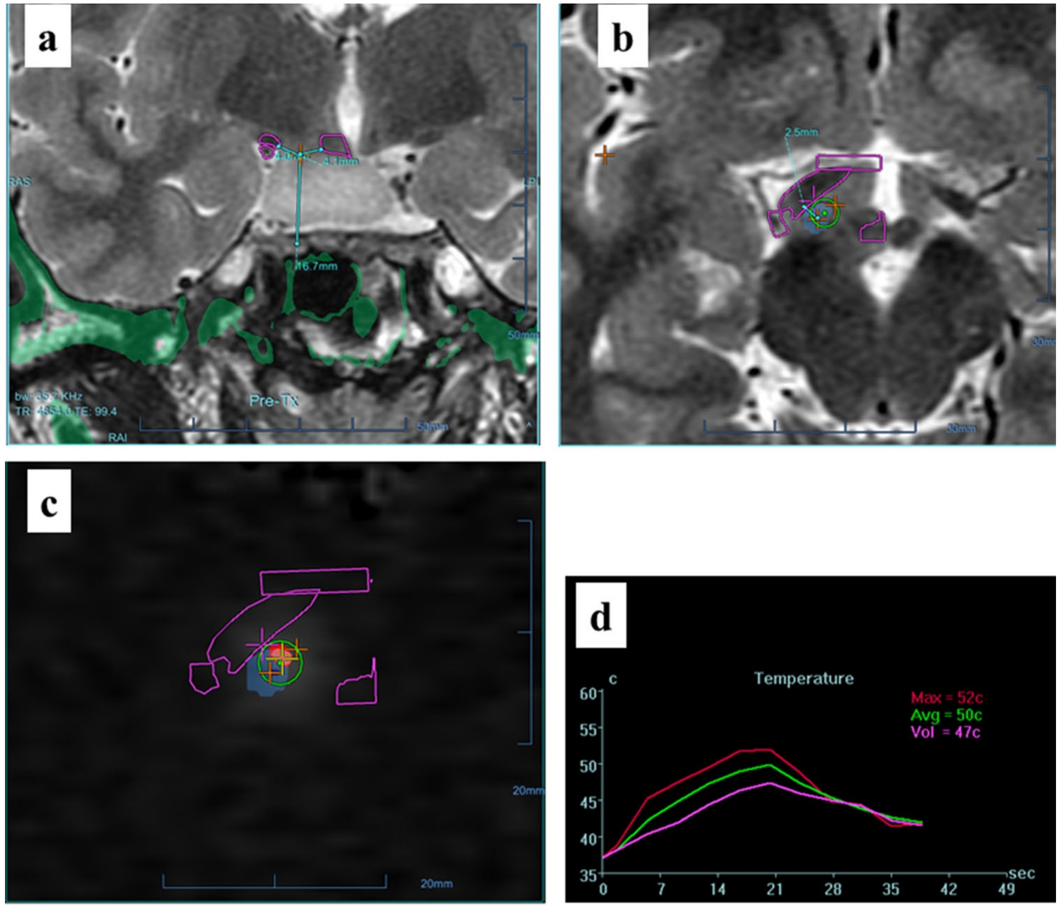
- Advantages
  - Direct anatomic targeting with visualization of the lesion site
  - Immediate effects (indirect confirmation with intra-op testing of patient function)
  - Enlarge lesion in steps
  - Outpatient procedure
- Disadvantages and risks
  - Require shaving of the head
  - Absorption and reflection of ultrasound waves can be problematic (distortion)
  - Skull heating
  - Cavitation (microbubbles)

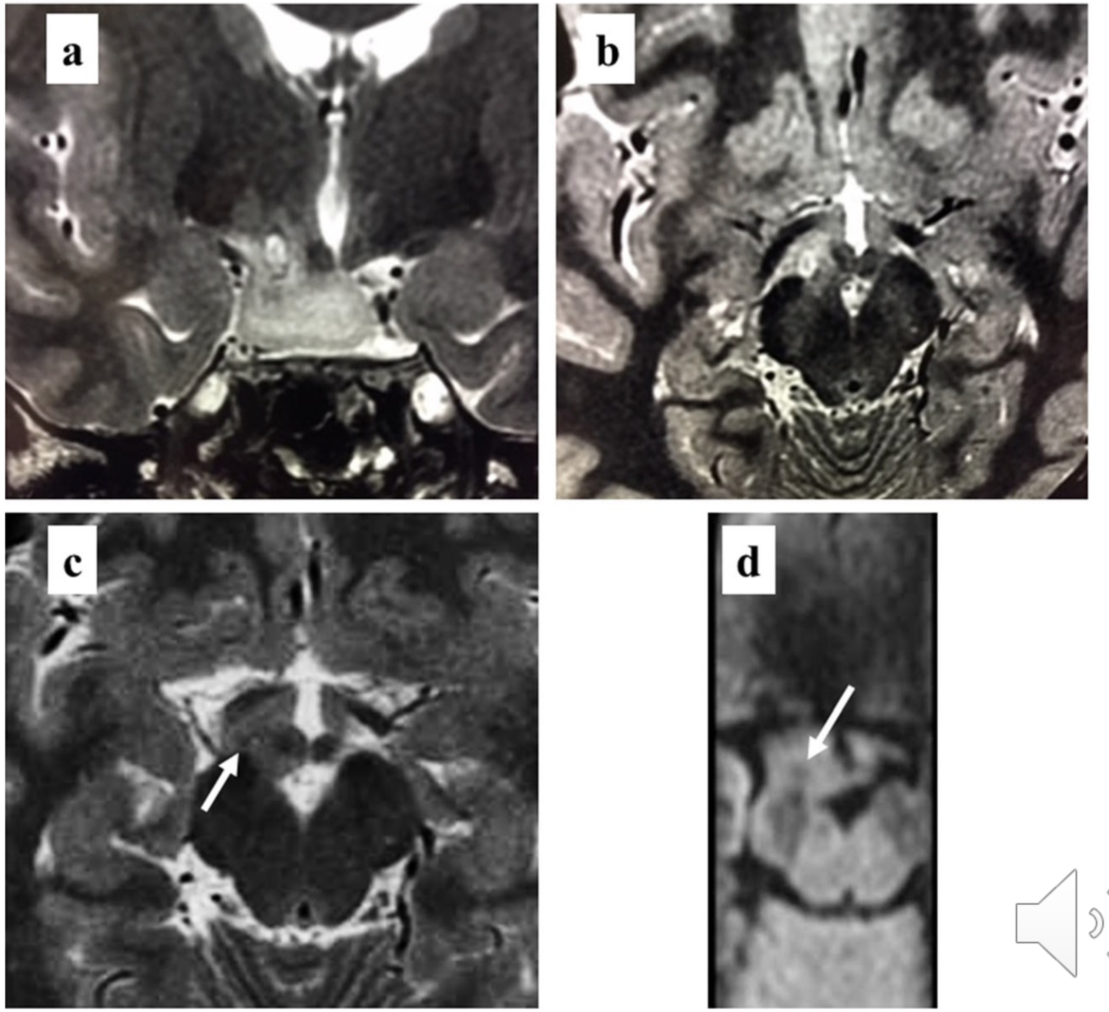
Case Report - Functional Neurosurgery - Epilepsy | Published: 02 July 2020

Magnetic resonance–guided focused ultrasound ablation of hypothalamic hamartoma as a disconnection surgery: a case report

Toshio Yamaguchi, Tomokatu Hori, Hiroki Hori, Masahito Takasaki, Keiichi Abe, Takaomi Taira, Kenji Ishii & Kazuo Watanabe

Acta Neurochirurgica **162**, 2513–2517 (2020) | Cite this article





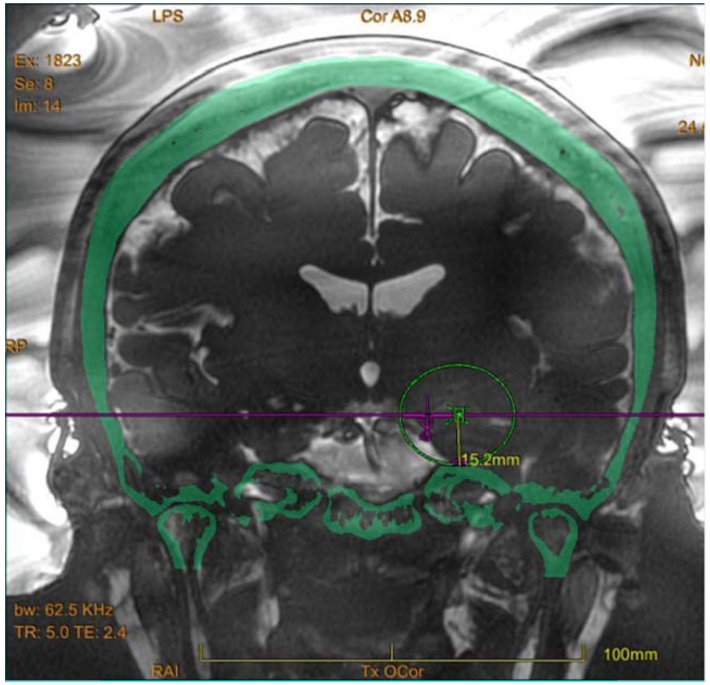
Abe et al. BMC Neurology (2020) 20:160
https://doi.org/10.1186/s12883-020-01744-x

BMC Neurology

CASE REPORT Open Access

Magnetic resonance-guided focused ultrasound for mesial temporal lobe epilepsy: a case report

Keiichi Abe[1*], Toshio Yamaguchi[2], Hiroki Hori[3], Masatake Sumi[1], Shiro Horisawa[1], Takaomi Taira[1] and Tomokatsu Hori[4]

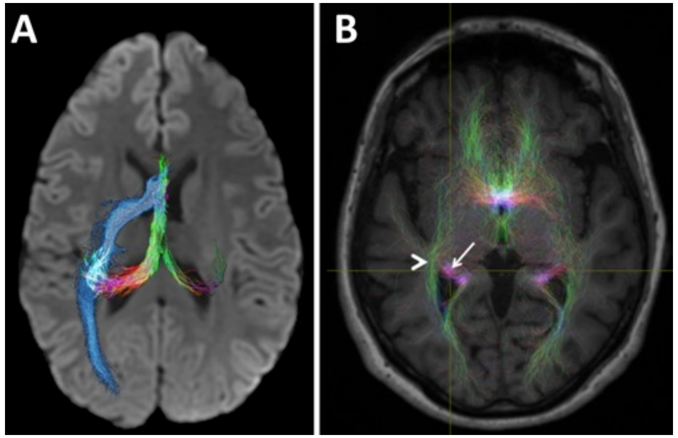


- 36-year-old woman with left MTLE
- Sub-ablations temperatures (48 C)
- Post-op MRI: no lesion
- Post-op PET: Increased metabolism left lateral temporal, bilateral striata, bilateral frontal base, posterior cingulate
- Seizure outcome: Engel III

CLINICAL ARTICLE
J Neurosurg 133:63–70, 2020

Magnetic resonance–guided focused ultrasound for ablation of mesial temporal epilepsy circuits: modeling and theoretical feasibility of a novel noninvasive approach

Whitney E. Parker, MD, PhD,[1] Elizabeth K. Weidman, MD,[2] J. Levi Chazen, MD,[2]
Sumit N. Niogi, MD, PhD,[2] Rafael Uribe-Cardenas, MD, MHS,[1] Michael G. Kaplitt, MD, PhD,[1] and
Caitlin E. Hoffman, MD[1]



Targeting at fornix-fimbria temporal outflow tract

Conculsion

- SEEG
- Neuromodulation- Tailored surgery
- Minimally invasive surgery

Thank you