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# Update on Surgical Options for Pediatric Epilepsy

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1

## Speaker Disclosure

- No disclosures



2

## Learning Objectives

1. Understand the role of surgery for pediatric epilepsy patients
2. Define the criteria for considering epilepsy surgery
3. Identify the advantages of newer surgical options for epilepsy patients
4. Recognize the different postoperative outcomes for various types of epilepsy surgeries



3

## Epilepsy

- Prevalence of 1 in 200 people
- Incidence of pediatric epilepsy is 45 per 100,000 children per year

**Table 2. Operational (practical) clinical definition of epilepsy**

Epilepsy is a disease of the brain defined by any of the following conditions

1. At least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years.



4

## Medically Intractable Epilepsy

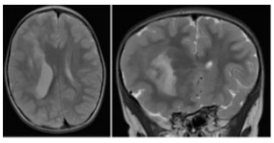
- Persistent seizures despite optimal medical management (2 or more AEDs)
- 20-30% of pediatric epilepsy cases
- Side effects from ongoing seizures and AEDs
  - Medical side effects
  - Damage to developing brain
  - Halted progression of developmental milestones
  - Difficulties in social adaptation
  - Lower quality of life



5

## Why consider surgery?

- After 2-4 AEDs, additional meds offer <5% chance of ending seizures
- Even lower chance of ending seizures if there is a lesion
- Ongoing neurologic morbidity from ongoing seizures AND side effects of AEDs
- Goals of surgery
  - Remove the epileptic focus
  - Reduce or eliminate seizures
  - Preserve healthy brain tissue & function





6

## 2019 Cochrane Review

Cochrane Library

Cochrane Database of Systematic Reviews

**Surgery for epilepsy (Review)**

West S, Nevitt SJ, Cotton J, Gandhi S, Weston J, Sudan A, Ramirez R, Newton R

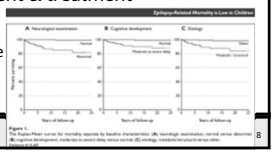
- 182 studies, included 16,855 participants
- Mostly retrospective reviews
- Of 2 RTCs that compared surgery to medications, surgery had better outcomes
- Of 16,756 surgical patients, 64% achieved a "good" outcome (= freedom from seizures)
- Prognostic factors for a better post-surgical outcome
  - Abnormal preop MRI
  - No use of intracranial monitoring
  - Complete surgical resection
  - Presence of mesial temporal sclerosis
  - Presence of a tumor
  - Concordance of preop MRI with EEG



7

## Why consider surgery EARLY?

- Intractable seizures during early childhood
  - Increased risk for intellectual delay
  - Risk of delay in all developmental milestones
- Poor seizure control in adolescence & adulthood
  - Lower rates of high school graduation, marriage, and employment
- Overall lifetime cost of seizure management & treatment
- Mortality risk
  - 0.5% per year and accumulates over a lifetime
  - Related to aspiration events, seizure-related trauma, status epilepticus, SUDEP



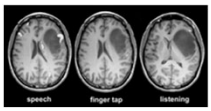



8

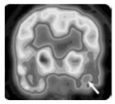
## Pre-op work up

- Video EEG (phase 1)

- Functional MRI




- PET scan



- Neuropsychological testing



9

## Phase 2 monitoring

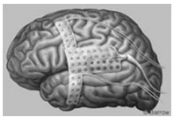
- Invasive monitoring to better characterize seizure origin
- Data is collected during seizures
- "Mapping" may be performed to identify areas to avoid during surgical resection and/or predict postop deficits
  1. Subdural grids/strips
  2. Stereoelectroencephalography (sEEG)

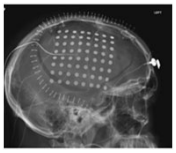


10

## Grids & Strips

- Subdural grid & strip electrodes are placed intraoperatively
- Electrodes are placed directly on the brain
  - Grids of electrodes placed on the surface of the brain
  - Depth electrodes can be placed within the brain parenchyma



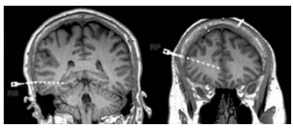




11

## Stereoelectroencephalography (sEEG)

- Ages 2+
  - Consider tolerance of phase 2 mapping
  - Skull thickness not amenable to intra-op anchors used
- Planning with pre-op contrast-enhanced high-resolution MRI
  - Plan electrode trajectories
  - Optimize epileptogenic zones
  - Avoid eloquent brain tissue & vascular areas

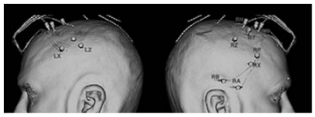


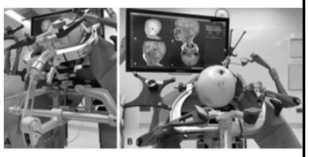


12

## Stereoelectroencephalography (sEEG)

- Robot assisted lead placement
  - Allows for precision placement
  - Decreases operative time
- Operation
  - Patient placed in a frame
  - Face is "registered" using laser-based facial recognition from pre-op studies
  - Robot creates twist drill holes
  - Guide bolts screwed into place to create the trajectories
  - Electrodes are placed using a stylet into each trajectory
  - Electrodes are connected externally to electrocorticography recording setup







13

## sEEG Risks

- Intraparenchymal hemorrhage
- Subdural hematoma
- Infection
- Failure to capture seizures during monitoring



14

## Management during phase 2 monitoring

- AEDs weaned
- Strict bedrest
- 1:1 supervision at all times
  - Within arms reach
- Monitor until seizure activity
- sEEG leads removal
  - Sedation or general anesthesia
- Discharge & plan for next surgery



15

## Surgical Options

**Curative**

1. Laser Ablation
2. Lesionectomy
3. Lobectomy
4. Hemispherectomy

**Palliative**

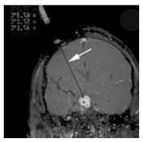
1. VNS
2. RNS
3. DBS



16

## Laser interstitial thermal therapy (LITT)

- Uses thermal energy to target tissue to induce cell death
- MRI-guided
- Advantages
  - Can be used for foci in deep and/or eloquent regions
  - Less invasive
  - Shorter hospital stay (average 24 hours)
- Best for epilepsy caused by
  - Hypothalamic hamartoma
  - Low-grade glioma
  - Cortical dysplasia

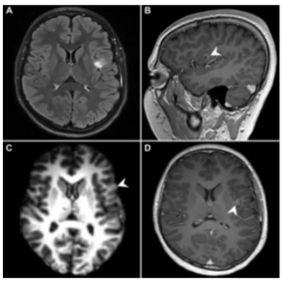




17

## LITT surgery

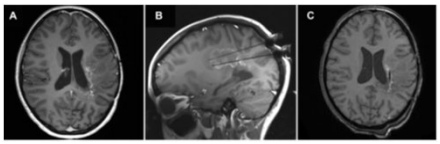
- Needle biopsy performed in OR
- Laser catheter placed
- Thermometry performed in MRI






18

## LITT Risks



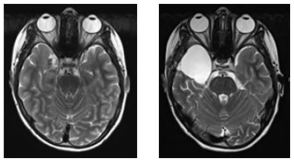

- Hematoma or injury caused by catheter placement
- Thermal ablation beyond boundaries of lesion
- Ongoing seizures related to insufficient resection



19

## Lesionectomy

- Removal of a lesion/seizure focus
- Low-grade tumors, cortical dysplasia, vascular lesions
- Extent of resection predicts seizure freedom
- 72-92% success rates





20

## Lobectomy

- Removal of an area of the brain
- Temporal lobectomy is the most common
  - Highest risk is a decline in verbal memory
- Using functional MRI
  - Helped to predict post-op deficits
  - Pre-operatively identified areas responsible for motor, language & memory
  - Helped to determine surgical approach & extent of resection
  - Neuropsychological testing needed to determine if patients could participate in fMRI, tailor tasks, and coach patients during fMRI



21

## Lesionectomy/Lobectomy Risks

- Damage to eloquent brain tissue
- Deficits depend on the area that is resected
  - Temporal lobe important for language & memory
  - Hemispherectomy will cause hemiparesis & homonymous hemianopia
- Risk of incomplete resection
- Risk of ongoing seizures
- Younger patients are more likely to make more complete recoveries



22

## Hemispherectomy

- Removal or disconnection of a cerebral hemisphere
  - For children with diffuse seizure onset
  - Common causes: perinatal ischemia, Sturge-Weber, hemimegalencephaly, Rasmussen encephalitis
- Functional hemispherectomy
  - Now gold standard
  - 80% + rates of seizure freedom
  - Increased preservation of function



23

## Hemispherectomy Risks

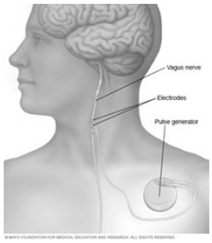
- Almost 50% of patients already have lateralized deficits pre-operatively
- Brain has already started to re-wire
- Post-op deficits
  - Hemiparesis
  - Hemianopia
  - Hydrocephalus



24

## VNS

- Generator implanted at left chest
- Leads thread up to the vagus nerve
- Vagus nerve is stimulated via electrical current
- Designed to prevent seizures and respond to tachycardia to shorten a seizure
- Magnet will stimulate the VNS generator to stop a seizure in progress
- Indicated for age 4+






25

## VNS Management

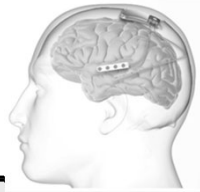
- Generators are turned on at 2 weeks postop
- Device is ramped up every 1-2 weeks to increase the impulse output
- Battery lasts 6 years on average
- Battery changes require repeat operation
- VNS Risks
  - Skin infection
  - Temporary bradycardia
  - Changes in voice quality or hoarseness
  - Increased coughing & drooling
- Outcomes vary: 50-90% reduction in seizure frequency



26

## Responsive NeuroStimulation (RNS)

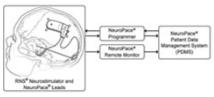
- FDA approved in 2013 for 18+ years
- Neurostimulator device is implanted in the skull
- 2 implantable leads, each with 4 contacts
  - Either surface or depth electrodes
- Battery life ~ 8 years
- Risks
  - Intracranial hemorrhage at time of implantation
  - Infection



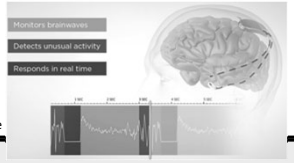


27

## RNS Management




- Only closed loop system
- RNS records ECoG AND delivers stimulation
- First month operates in “detection” only
- RNS is programmed with triggers and parameters for stimulation
- MRI “safety mode” during MRI




Images from NeuroPace



28

## RNS Outcomes

- Efficacy improves over time
  - 44% median reduction in seizure frequency at 1 year
  - 53% median reduction at 2 years
  - 60-66% median reduction at 3-6 years
  - 75% median reduction at 9 years
- No cognitive adverse effects
- Improvements in quality of life
- Statically significant reductions in risk of SUDEP



29

## Deep Brain Stimulation (DBS)

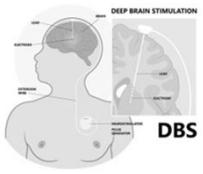
- Initially used for movement disorders in adults
- FDA approved for epilepsy patients 18+ years of age
- Pulse generator implanted in chest (or abdomen)
- Depth electrode implanted into the thalamus
  - Placement of electrode can vary
- Delivers electrical stimulation to modulate cortical excitability
- Trialed after a failed ablation and/or inadequate response from VNS



30

## DBS Management & Risks & Outcomes

- Pulse generator is programmed
- Risks
  - Infection
  - Skin erosion
  - Electrode lead breakage
- 50-85% reduction in seizure frequency
- Statistically significant improvements in quality of life






31

## Questions/Limitations

- Long-term consequences of placing electrodes into a developing brain
- No studies comparing VNS vs RNS vs DBS



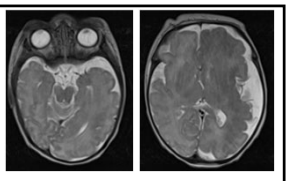
32

# Case Studies

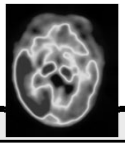


33

## NS



- Born at 37 weeks
- MRI on day 1 of life due to prenatally diagnosed ventriculomegaly
- L hemimegalencephaly
- Seizures started at 14 days of life
- Evaluated in multi-disciplinary Epilepsy clinic at 2 months of life
  - Already on 4 AEDs
  - NG-tube feeds
- Admitted at 2.5 months of age
  - Video EEG
  - PET scan



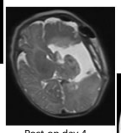


34

## NS Epilepsy Surgery

- L craniotomy for functional hemispherectomy July 2020 (3 months old)
  - EVD placement (removed POD 4)
  - PICU postop (1 day only)
  - R-sided weakness
  - Discharged POD 6
  - Continued on NG-tube feeds
  - No seizures post-op

Day of OR



Post-op day 4

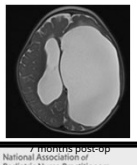
1 month post-op



35

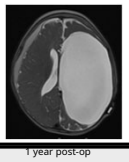
## NS Recovery

- Began weaning off AEDs at 2 months post-op
- 7 months postop developed hydrocephalus
- VP shunt placed March 2021
- 1 AED only at 1 year post-op

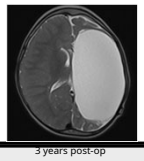


7 months post-op

8 months post-op



1 year post-op



3 years post-op



36

## NS Follow up

- 2023 (age 3)
  - No seizures since surgery
  - R-sided hemiparesis (2/5 strength, no hand opening)
  - Walking in gait trainer
  - Single word vocalizations & signs
  - Comprehensive therapies
  - Developmental preschool 3 days/week
  - Off all AEDs
  - Rectal diastat PRN
- G-tube placed Jan 2024



37

## CL

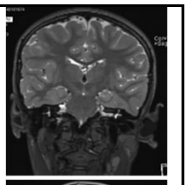
- 12 yo F with hx tuberous sclerosis & intractable epilepsy
  - Infantile spasms at 4 months (vigabactrin)
  - Focal seizures at 18 months (levetiracetam/lamotrigine)
  - SEGA in 2016 (everolimus)
  - AEDs caused "cognitive slowing"
- Video EEG Aug 2020
  - Diffuse onset of seizures with bifrontal generalized discharges

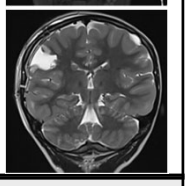


38

## CL's surgeries

- Stereo EEG for phase 2 monitoring Nov 2020
  - Seizure focus in L anterior & R frontal tubers
  - Scheduled for laser ablation of both tumors
- R craniotomy for resection of R frontal tuber March 2021
  - L-sided facial weakness postop
  - Seizure freedom only a few days
  - "smaller" seizures subsided but "bigger" seizures continued







39

## CL surgeries cont'd

- Additional phase 2 monitoring with subdural grid electrodes June 2021
  - L frontal & R hemisphere
  - Included mapping
- 1st stage R tuber resection June 2021
- 2nd stage R tuber resection June 2021
  - No postop deficits
  - Increase in seizures for 1st month, then improvement
  - Increased seizures at 6 months postop
- VNS placement Jan 2024



40

## SS

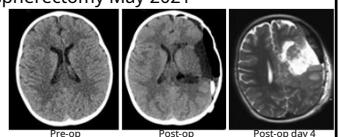
- 6 yo M with hx Rasmussen's encephalitis & intractable epilepsy
  - Seizures began at age 3
  - Developmentally on track
  - Plateau in some milestones around age 3-4
  - Increase in behavioral outbursts, aggression & impulsivity when started on AEDs
- L stereotactic biopsies w/ ROSA April 2021
  - Discharged POD 1
  - Biopsies confirmed Rasmussen's encephalitis



41

## SS Epilepsy surgery

- L craniotomy for functional hemispherectomy May 2021
  - EVD placement (removed POD 4)
  - PICU post-op
- Postoperatively
  - R hemiplegia
  - Expressive aphasia
    - Initial mutism, first words on POD 10
  - Required NG-tube feeds
  - Brief setback with rhinovirus (returned to ICU for respiratory support)
    - Prolonged WOB (related to neuromuscular weakness?)
  - No seizures
- Disposition to Rehab on POD 19



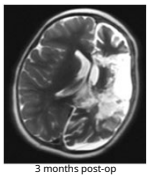
Pre-op Post-op Post-op day 4



42

## SS Recovery

- 3 week admission to inpatient rehab
  - No seizures
  - Tapered off prednisolone
  - Advanced to regular solid diet with ½ nectar thick liquids
    - NG-tube removed
  - Ongoing R-sided weakness
    - Ambulating up to 200 feet with assistance & R AFO
    - Improvements in ADLs
  - Ongoing expressive aphasia
    - Saying single words
    - Frustration related to deficits
- Plan for developmental preschool at discharge



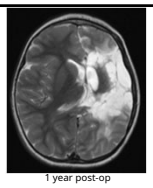
3 months post-op



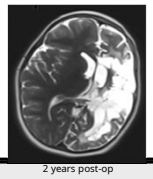
43

## SS Follow up

- Brief hospitalization June 2022
  - Severe headaches when weaning off zonisamide
  - No structural changes on imaging
- Daily headaches ~1 year
- No seizures, weaned off AEDs
- Hypertonia
  - Started on baclofen & received botox
- End of 2023 (age 6)
  - Running, riding a scooter, wears R AFO
  - L-handed, wears R hand splint
  - Difficulties with reading and writing
  - Speaks in full sentences
  - Regular diet and toilet trained
  - R visual field cut
  - School-based therapies



1 year post-op



2 years post-op



44

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45

## Questions?



46