A Reappraisal of the University of Kansas Comprehensive Epilepsy Center

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University of Kansas Medical Center
Surgical volume:
2016: 41 epilepsy surgeries
2015: 14 epilepsy surgeries
Our role as specialists

- Diagnosis and counseling
  - History, history, history
- Etiology
  - Imaging expertise
- QOL
  - Cognitive, psychological, social
- Seizure freedom
- Decrease mortality
- Evaluate for epilepsy surgery
- Educate community and peers
- Cultivate a successful teaching environment
- Provide outstanding EEG and epilepsy services
Epilepsy Surgery Team

- Epileptologists
  - Nancy Hammond
  - Utku Uysal
  - Patrick Landazuri
  - Carol Ulloa
  - Mohamed Hegazy

- Neurosurgeons
  - Paul Camarata
  - Jules Nazzaro
  - Michael Kinsman

- Neuroradiology
  - John Leever

- Neuropsychology
  - Caleb Pearson

- Neurodiagnostics
  - Jamie Kennison

- Program Coordinator
  - Cathy Lauridsen
    - Howard Willyard
    - Max Hardenbrook

- Epilepsy NP
  - Mary Ann Kavalir

- Epilepsy nurses
  - Daisy Guela
  - Mary Komosa

- Nurse manager
  - Adam Meier
19 y/o ambidextrous male with spells of disorientation, j’amais vu, ictal speech=> oral automatisms => head version right => GTC

Apgars 0, 1, 5. NICU x one week
Musical genius
Second opinion to get “more answers”

Left temporal lobe epilepsy, right language dominance, suspect due to hypoxia at birth

Diagnosis of “seizure disorder” is not enough
After experiencing seizures nearly daily since the age of 3, Jessica had surgery 10/2015. A year later, the 35-year-old nursing student is still seizure-free.

Sensitivity:
39% Non-expert standard MRI
50% Expert standard MRI
91% Expert epilepsy protocol MRI
Seizure freedom

- Common sense
- QOL
  - Emotional, cognitive development
  - Disability
  - School, Work
  - Driving
- Morbidity
  - Fractures
  - Dislocated shoulders
  - Burns
  - ICH
  - Broken teeth
  - Memory loss
  - Status epilepticus
- Mortality


Refactory epilepsy is a life-threatening disease
Lest we forget
60/245 (24%) were dead at follow-up
- 55% directly related to epilepsy
- 30% had SUDEP (7% of entire cohort)
- 3% suicide
- Risk factor most predictive of death was absence of 5 year seizure remission

Epilepsy increases risk of premature death
Surgery reduces risk

- Death decreased by 66% in surgical group
- Death decreased by 80% if seizure free after surgery

- Surgical
  - 8.6 deaths/1,000 person yrs
  - 5.2 if seizure free

- Non-surgical
  - 25.3 deaths/1,000 person yrs

Figure 1: Mortality in patients treated with focal resection or transections compared to nonsurgical patients

Neurology. 2016 May 24;86(21):1938-44
Seizure freedom

- 25 y.o. RH male
- Epilepsy since age 19
- GTCs 1-2 times per week x 5 yrs
  - Myoclonic jerks
  - Staring spells
- On lamotrigine 700 mg/d
- Failed levetiracetam, phenytoin
- Quit college after seizures began
- Works part time at McDonalds
- Mayo Clinic video EEG 2012--generalized seizures, absence and myoclonic seizure
Seizure freedom

- What is the diagnosis?
  - JME

- What is the most appropriate next step?
  - Valproate
    - Week 1: LMT 200-200 and VPA 250
    - Week 2: LMT 150-200 and VPA 500
    - Week 3: LMT 100-200 and VPA 250-500
    - Week 4: LMT 100-100 and VPA 500-500
Seizure freedom, JME f/u

- LMT 2, VPA 86
- EEG normal
- SEIZURE FREE
- Started driving again
- Got new and better job
- Thinking about going back to school
- “Back to his old self”
Seizure freedom

- 68 y.o. LH female referred by Dr. Pasnoor
- Epilepsy since age 8 after TBI
- Painful sensation in RUE then RLE => right tonic activity => fall
- Todd’s paresis for 2-3 days
- 1-2 seizures/month
- On levetiracetam 3g/d and topiramate 250/d
- Failed phenytoin, primidone
- Started lacosamide 50 mg BID
Seizure freedom, f/u

- “Doctor, you cured me after just one visit!”
- 8 months seizure free
36 y/o man with progressive myoclonic epilepsy since age 16
Frequent myoclonus
Past GTCs
Wheelchair bound
On levetiracetam 4g/d, lamotrigine 600 mg/d, clonazepam 4 mg/d
Past AEDs: zonisamide, topiramate, valproate
Has been evaluated at St Lukes, Mayo

What can we offer?
QOL, PME

- Provided info on PME
- EMG (same day)
- PT
- Pain management
- SW
- Insomnia
- Muscle/skin biopsy (d/w Dr. Dimachkie)
  - No lafora bodies or ragged red fibers
- Genetic testing
  - CLN8 gene p.R54H variant (G to A substitution at nucleotide position 161)
  - Unknown clinical significance
- Contacted researchers regarding brivaracetam in Unverricht-Lundborg disease
- Reviewed data on VNS and PME
  - Since he only has myoclonus at this time, less likely to have efficacy
Pre-surgical evaluation

- Epilepsy Clinic
- Video EEG monitoring unit
- Advanced imaging
  - 3T MRI
  - Functional MRI
  - PET
  - SPECT
  - DTI
- Neuropsychological testing
- Wada
- Epilepsy surgery conference
- Neurosurgery clinic
- OR
Procedures

- Subdural grid and strip electrodes
- Stereo EEG (depth electrodes)
- Cortical mapping (bedside and awake)
- Resection
- Laser thermal ablation
- Responsive neurostimulation
- Vagus nerve stimulation
- Corpus callosotomy
Advanced neuroimaging
FDG-PET
Cerebral glucose metabolism

Surgical outcome in PET-positive, MRI-negative patients with temporal lobe epilepsy

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†James Evans, †Ashwini Sharan, and *Scott Mintzer

Departments of *Neurology and †Neurosurgery, Thomas Jefferson University, Philadelphia, Pennsylvania, U.S.A.
Advanced neuroimaging

fMRI

DTI
Case 1, Mr. K

- 72 y.o. RH male
- Epilepsy since age 12
- Son with febrile seizure
- Epigastric sensation => feels disconnected => oral automatisms
  - Left head version => GTC
- CPS 1-2 times per month
- Failed 9 AEDs and VNS
- Came specifically to seek surgical options
Right temporal sharp wave
Right temporal seizure
Right hippocampal sclerosis
MRI-guided laser interstitial thermal therapy for treatment of medically refractory non-lesional mesial temporal lobe epilepsy: Outcomes, complications, and current limitations: A review

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- 38 pts (80 pts)
  - 3/4 MTS
- 53% seizure free
- 60% with MTS seizure free
  - vs 75% with standard ATL
- Complications at 30 days (68 pts)
  - Laser fiber misplacement or heat spread along ventricular surface affecting Meyer’s loop
  - Limit heat in posterior hippocampus

**Benefits**
- Minimally invasive
- Faster recovery
- Can have open resection later
- Neuropsych outcomes
- For UKH, cost effective
  - Average direct costs 30% less than open procedure

**Limitations**
- Research lacking for use in epilepsy
- New, less established procedure
- Lower seizure freedom rate
Laser thermal ablation
Laser thermal ablation

Real time MR thermal imaging
• Thermal necrosis zone
• Temperature of surrounding tissue

Frame

Laser Delivery Probe

Laser

©Monteris Medical
Laser Thermal Ablation
Mr. K
Case 2, Ms. K

- 46 y.o. RH female
- Epilepsy since age 31
- 2.5 mos premie; emergency C section
- MVA two months prior to seizure onset
- Cephalic sensation => derealization => rising epigastric sensation => unresponsive stare with oral automatisms
- 1-2 seizures per month
- Failed 7 AEDs
- Invasive evaluation 2004:
  - Left temporal lobe epilepsy
  - No surgery due to risk of verbal memory loss >50%
2016 video EEG

- Left > right anterior temporal spikes
- 3/6 seizures left temporal
- 1/6 seizures right temporal
- 2/6 seizures not well localized
Left anterior/basal temporal encephalocele (sphenoid wing)
Normal hippocampi
FDG PET—bitemporal hypometabolism
fMRI—Left hemisphere language
Neuropsych

- Normal
- Largely unchanged compared to 2004

Wada

- Left hemisphere language
- 9/16 memory scores bilaterally
Hypothesis/Plan

- Left anterior/basal temporal neocortical epilepsy due to encephalocele
- r/o left hippocampal seizures
- r/o right temporal seizures
- Invasive monitoring with bitemporal depth electrodes
Phase II results

- Independent left and right hippocampal spikes, encephalocele spikes
- 3/8 seizures encephalocele
- 5/8 seizures left hippocampus
- No seizures from the right
Left and right hippocampal spikes
Left encephalocele spikes
Encephalocele seizure
Encephalocele seizure
Left hippocampal seizure
Options:

1) Left anterior/mesial temporal resection
   - Best chance of seizure freedom
   - Teacher; significant memory decline not acceptable

2) Left temporal tip/encephalocele resection plus RNS of left hippocampus

3) Left tip/encephalocele resection only; consider RNS in future
   - Multiple encephaloceles noted in OR
Case 3, Mr. G
Impression/Plan

- Bi-temporal epilepsy
  - Suspect right is primary focus
- Bitemporal RNS
- Longer period of monitoring may lead to a unilateral resection
Status epilepticus
Responsive Neurostimulation (RNS)

- Neuropace
- FDA 2013
  - 18 and older
  - Failed 2 AEDs
  - Partial onset sz at 1-2 foci
- Closed loop stimulation
  - Seizure pattern detection
  - Cortical stimulation
- Settings refined over time

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Common settings in trials</th>
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<tbody>
<tr>
<td>Current</td>
<td>1.5 – 3 mA</td>
</tr>
<tr>
<td>Pulse-width</td>
<td>160 μs</td>
</tr>
<tr>
<td>Burst duration</td>
<td>100 – 200 ms</td>
</tr>
<tr>
<td>Frequency</td>
<td>100 – 200 Hz</td>
</tr>
</tbody>
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RNS seizure detection
RNS clinical trials

Feasibility Trial
65 patients implanted

Pivotal Trial
Double blind RCT
191 patients implanted

Open Label Long-term Treatment Trial
7 year follow on study, 230 enrolled
RNS patient characteristics (n=256)

History
- 32% with prior VNS
- 34% with prior epilepsy surgery
- 65% localized with intracranial monitoring

Mesial temporal:
- 28% unilateral
- 72% bilateral

Neocortical:
- 45% non-mesial temporal
- 38% frontal
- 14% parietal
- 4% occipital
RNS efficacy increases over time

Median % Seizure Reduction

- Seizure-Free Intervals
  - ≥ 1 year: 13%

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RNS adverse events

- 3.5% risk of soft tissue infection per procedure
  - Battery life ~ 4 yrs
- 2.7% ICH
  - Asymptomatic
VNS vs RNS
Multicenter, controlled, prospective studies
Median % seizure reduction (focal onset)

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“The epilepsy team...is a key support for the neurointensivists by providing 24/7 access to both EEG monitoring and the expertise of an epileptologist.”

--Dr. Husmann
Improved resident education and EEG services

- “The updated epilepsy program has provided a healthy and thriving academic environment enhancing my ability to better identify and treat patients with epilepsy.” -- Tekk B.

- “There is more emphasis on teaching the residents overall. One area to improve might be more EEG teaching sessions...” -- Hala S.

- “Provision of inpatient overnight/weekend STAT EEGs has improved significantly in the last two years” -- Matthew M.

- “The open communication and responsiveness to requests for urgent EEG monitoring or simply discussing a complicated case has been refreshing and comforting.” -- Dr. Ford
Community education
Research

- Feasibility Study on Laser Interstitial Thermal Therapy Ablation for the Treatment of Medically Refractory Epilepsy (FLARE)
- Multicenter NIH grant application for neocortical epilepsy surgery trial
Future goals

- Continued growth on all fronts
- National recognition
- Epilepsy fellowship (July 2018)
- Recruitment of epilepsy specific neurosurgeon
- Eradicate the term “seizure disorder”
- **CHANGE the landscape of epilepsy care**
  - 1% of intractable patients are referred to a comprehensive epilepsy center
  - 20 year delay in referral despite AAN practice parameter 2003
  - **Drug resistant epilepsy is a life threatening disease**
  - Early referral