Curing complicated epilepsy: epilepsy surgery in dual pathology

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Goals of presurgical workup for epilepsy

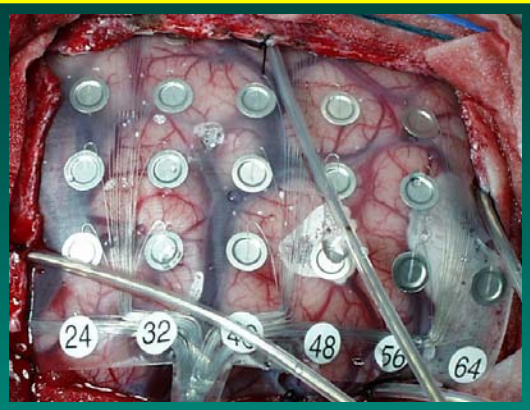
1. Establish the presence of antiepileptic drug (AED) resistance

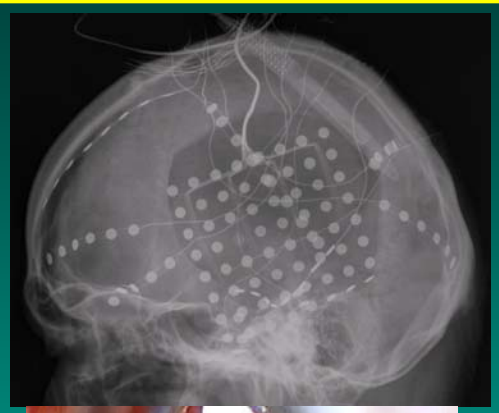
2. Delineate the epileptogenic zone within the brain

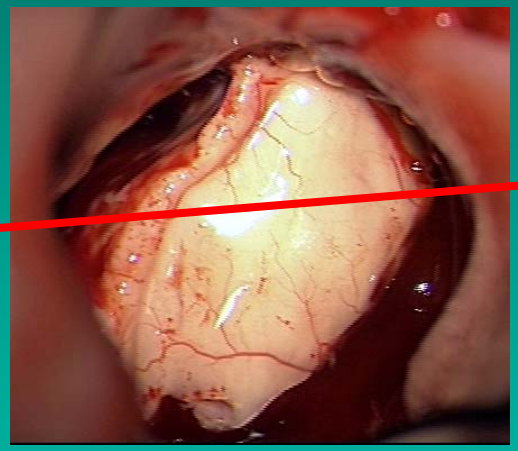
3. Estimate the risk which might occur for postoperative neurologic or cognitive deficits

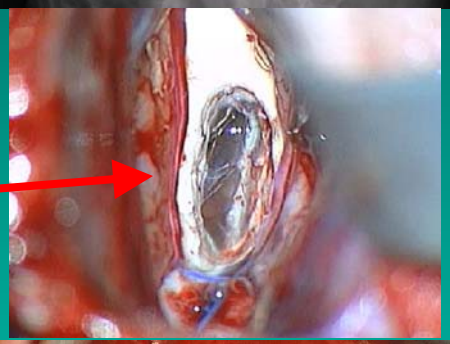
Some types of epilepsy surgery

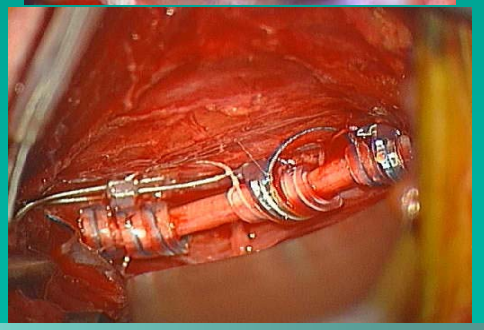
- Intracranial video-EEG monitoring (Phase 2)
- Resective surgery (*e.g.* temporal lobectomy)
- Disconnective surgery (*e.g.* multiple subpial transection, corpus callosotomy)
- Palliative surgery (*e.g.* vagus nerve stimulator implantation)









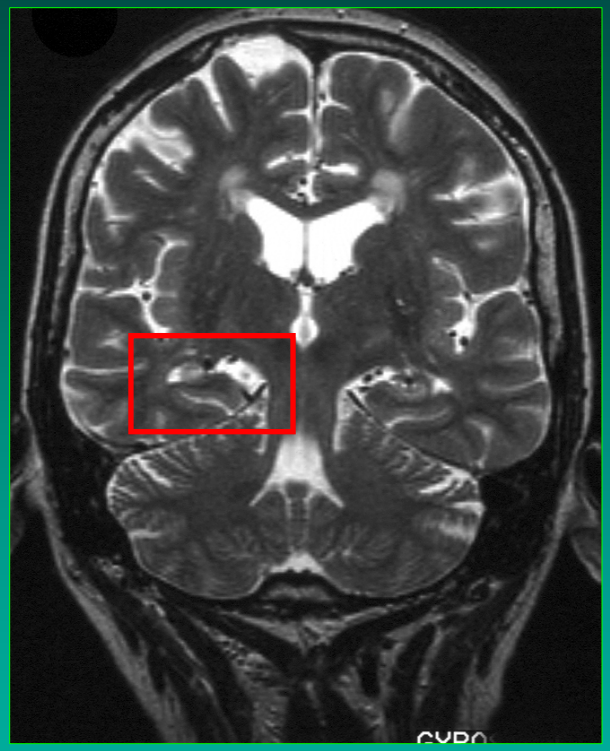


Best candidates for resective epilepsy surgery

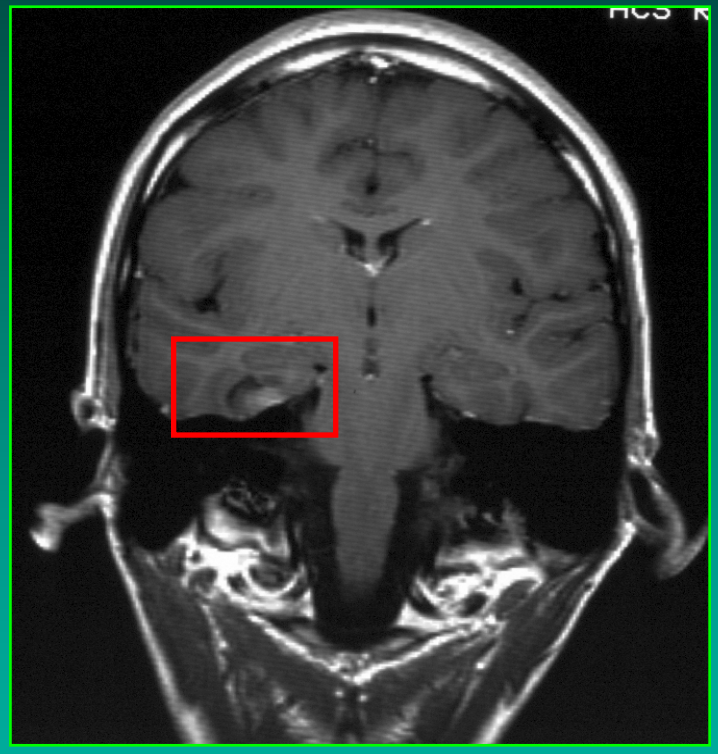
- EEG seizure onset from a focal area
- MRI abnormality in the same region
- Likelihood of being able to remove that region without significant neurologic or cognitive deficits

➢ **Most commonly patients with medically intractable temporal lobe epilepsy**

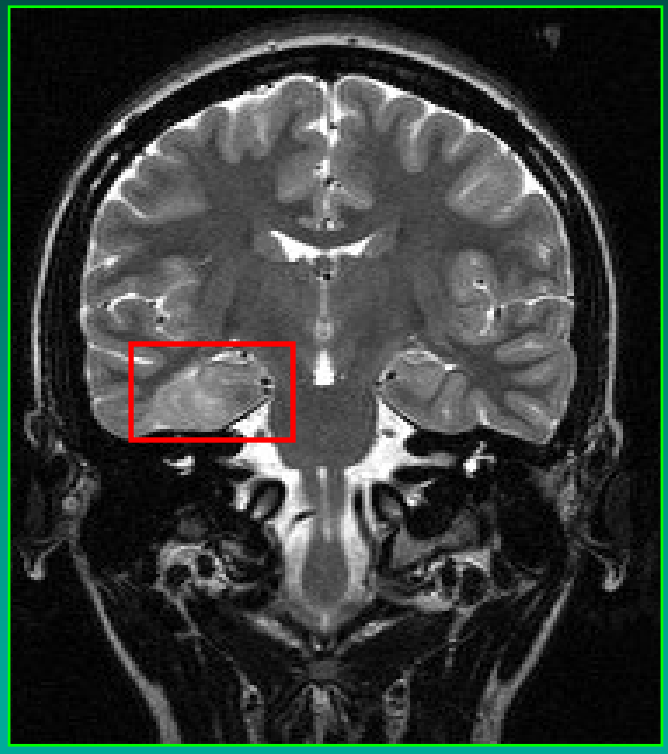
Some causes of temporal lobe epilepsy



Mesial temporal sclerosis



Low-grade glioma

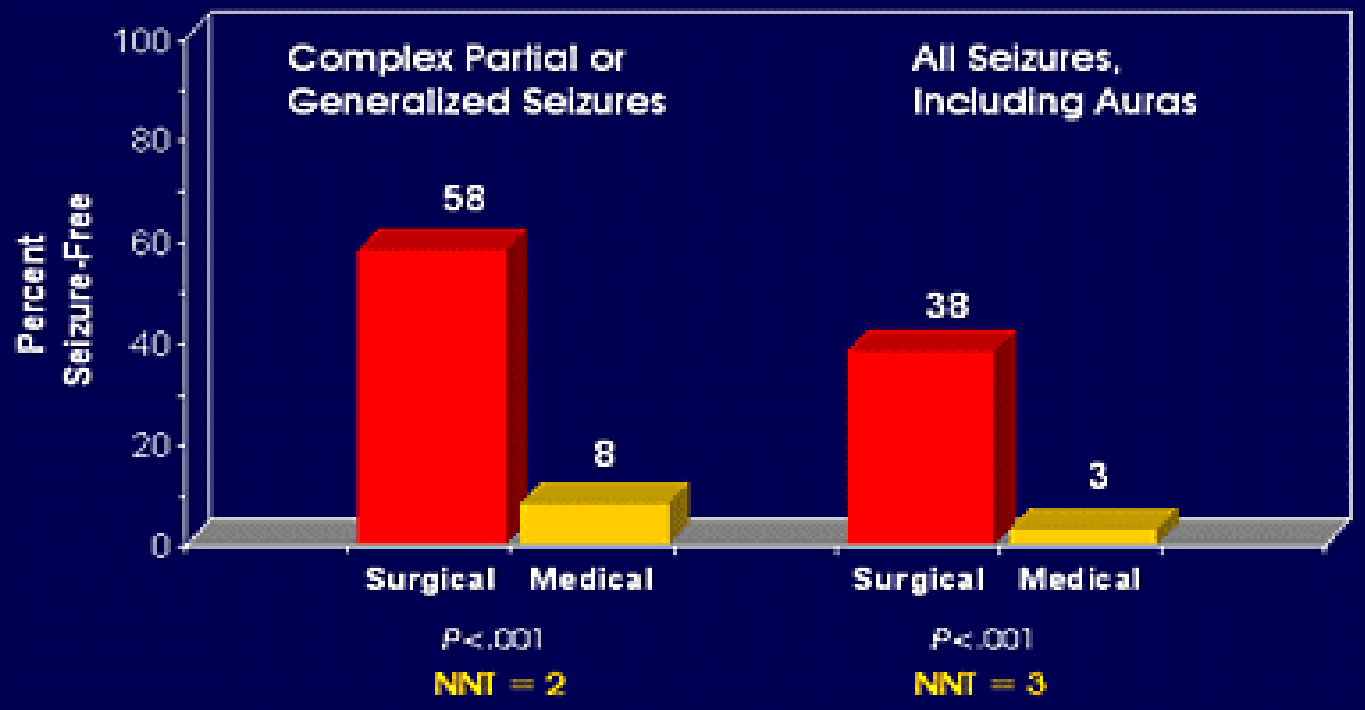


Focal cortical dysplasia

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*

Seizure-Free At 12 Months

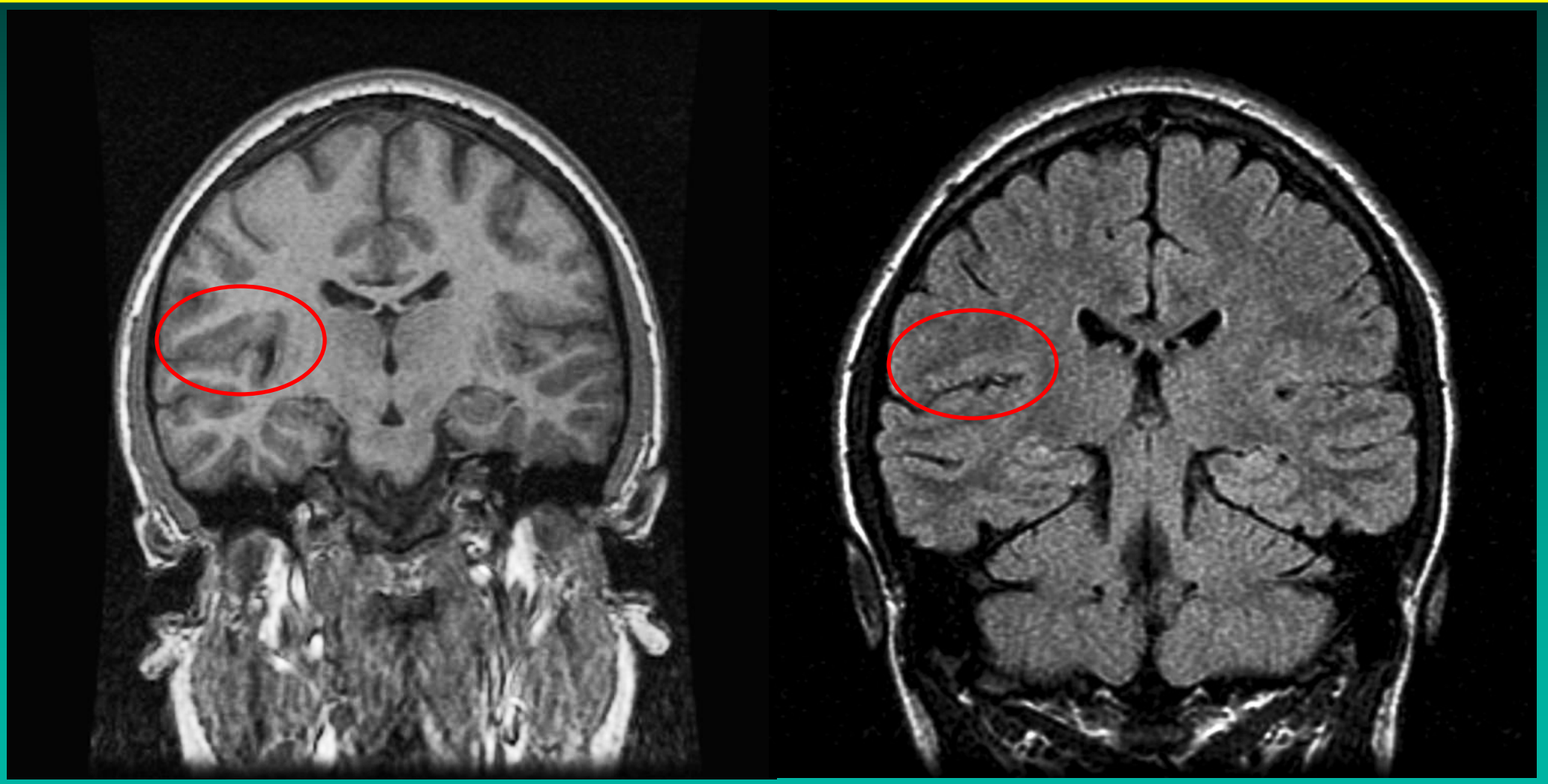


Wiebe S, et al. *N Engl J Med*. 2001.

Clinical history: complicated epilepsy

- 16-year-old right-handed young man
- Seizures began at age 18 months
- Multiple medications failed
- In 2000, had VNS placed
- Underwent VNS removal in 6/07 to allow MEG without metallic artifact
- Considered candidate for phase II intracranial video-EEG monitoring

Preoperative MRI



Electrode placement 8/20/07

- Plan: place R temporoparietal grid electrode with multiple subdural strip and depth electrodes for epilepsy monitoring

Electrode placement 8/20/07

1. Right dorsolateral frontal 8-contact strip
2. Right frontopolar 8-contact strip
3. Right orbitofrontal 6-contact strip
4. Right temporoparietal 64-contact grid
5. Right hippocampal 4-contact depth
6. Right anterior subtemporal 6-contact strip
7. Right middle subtemporal 6-contact strip
8. Right posterior subtemporal 6-contact strip

Phase II video-EEG monitoring

- Monitoring of seizures and interictal activity demonstrated ictal onset over the right parietal region underneath the grid
- In addition, he had significant interictal activity in this region and also in the right hippocampus

Extraoperative mapping data

- Region of ictal onset in right parietal lobe under the grid demonstrated no functional sites

What is dual pathology?

- Coexistence of mesial temporal sclerosis (MTS) with an additional potentially epileptogenic lesion
- Found in 5-30% of patients with intractable partial epilepsy
- Greater proportion in children than adults
- Histologically proven dual pathology may consist of MTS +:
  - Cortical dysplasia
  - Vascular malformation
  - Infarct
  - Tumor

Dual pathology: literature survey

- Levesque *et al.* 1991. Surgical treatment of limbic epilepsy associated with extrahippocampal lesions: the problem of dual pathology. *J. Neurosurg.* 75:364-370.
  - 178 patients at UCLA undergoing temporal lobectomies
  - 30% had evidence of extrahippocampal lesions (heterotopia to tumors)
- Nakasato *et al.* 1992. Seizure outcome following standard temporal lobectomy: correlation with hippocampal neuron loss and extrahippocampal pathology.
  - 149 patients undergoing temporal lobectomies
  - Found that patients with dual pathology (extrahippocampal lesion + severe hippocampal cell loss) more often had residual seizure activity

Dual pathology: literature survey

- Cendes *et al.* 1995. Frequency and characteristics of dual pathology in patients with lesional epilepsy. *Neurology* 45:2058-2064.
  - 167 patients at MNI with extrahippocampal lesions
  - 25 patients (15%) had abnormal hippocampus by imaging ("dual pathology")
  - Dual pathology more common in NMDs, gliosis, less common with tumors, vascular lesions
- Li *et al.* 1997. Surgical treatment of patients with single and dual pathology: relevance of lesion and of hippocampal atrophy to seizure outcome. *Neurology* 48:437-444.
  - 64 patients with lesional epilepsy, 13 had dual pathology
  - 2/10 with "single" resection became seizure-free, 3/3 with "dual" resection

Brain (1999), **122,** 799–805

Surgical outcome in patients with epilepsy and dual pathology

L. M. Li,[1] F. Cendes,[1] F. Andermann,[1] C. Watson,[2] D. R. Fish,[3] M. J. Cook,[4] F. Dubeau,[1] J. S. Duncan,[3] S. D. Shorvon,[3] S. F. Berkovic,[5] S. Free,[3] A. Olivier,[1] W. Harkness[3] and D. L. Arnold[1]

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- Reported the outcomes of 41 procedures in 38 patients with dual pathology
- Separated into lesionectomy, hippocampectomy, and lesionectomy + hippocampectomy

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Table 2 *Different surgical approaches and outcome in patients with dual pathology*

	Lesionectomy	Resection of atrophic hippocampus	Lesionectomy plus resection of atrophic hippocampus
Class I	2	2	12*
Class II	3	1	1
Class III–IV	11	7†	2
Seizure-free/total	2/16 (12.5%)	2/10 (20%)	11/15 (73%)‡
Class I–II/total	5/16 (31%)	3/10 (30%)	13/15 (86%)‡

*One patient had rare auras; †six of seven patients had associated periventricular nodular heterotopia; ‡multivariate analysis of variance: $F(1,40) = 9.02$, $P = 0.0009$.

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Temporal lobe epilepsy: analysis of patients with dual pathology

Salanova V, Markand O, Worth R. Temporal lobe epilepsy: analysis of patients with dual pathology.
Acta Neurol Scand 2004: 109: 126–131. © Blackwell Munksgaard 2003.

V. Salanova, O. Markand, R. Worth
Departments of Neurology and Neurosurgery, Indiana University School of Medicine, Indianapolis, IN, USA

- Of 240 patients with TLE, 37 (15%) had hippocampal sclerosis or temporal lobe gliosis with another lesion (dual pathology)
  - Lesions included heterotopia, cortical dysplasia, vascular malformations, DNET, trauma, remote infarction
- 70% became seizure-free postoperatively (mean 7.4 years follow-up)

Epilepsy surgery in dual pathology: literature summary

	Age	Follow-up (years)	Number of patients	Patients with MTS+/ patients with MTS	Proportion seizure free after surgery
Benifla et al[73]	<18 years	2	106	7/23	74% all patients, 88% MTS+ (absence of auras, auras only, or rare disabling seizures or nocturnal seizures only)
Cascino et al[90]	Adult	1	15	3/15	100% (MTS+)
Cossu et al[67]	<16 years	2	113	9/11	68%
Duchowny et al[69]	2–11 years	1	16	2/2	69% all patients, 50% MTS+
Li et al[89]	8–73 years	1	64	13/64	100% MTS+ if both hippocampus and lesion resected
Li et al[86]	14–63 years	1	38	11/15	73% MTS+ if both hippocampus and lesion resected
Mittal et al[74]	<19 yrs	5–20	109	27/49	82% all patients, 74% MTS+
Mohamed et al[72]	4–20 years	1–7	34	11/14	78% all patients, 90% MTS+
Salanova et al[87]	8–59 years	1	240	37/130	70% MTS+
Terra-Bustamante et al[70]	<18 years	1	35	5/14	77% all patients, 80% MTS+

MTS=mesial temporal sclerosis alone. MTS+=dual pathology.

Table 2: **Surgical studies reporting dual pathology results**

Lancet Neurology 7:525-537 (2008)

- Dual pathology does not portend a poorer prognosis than MTS alone when and if the hippocampus and the additional lesion or cortical dysplasia are both completely resected

Caveats regarding dual pathology literature

- Nonrandomized, “single-center” reports
- The number of patients with clearly defined dual pathology is often very small within a series
- The extent of resection of the lesion and the MTS is not always well specified
- Definition of dual pathology differs among centers
- Follow-up is often shorter than needed to observe the usual decline over time of seizure-free outcome in patients with dual pathology
- Criteria for seizure freedom are not always uniform between studies
- Dual resection effects on neuropsychological status?

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Review

When should a resection sparing mesial structures be considered for temporal lobe epilepsy?

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ABSTRACT

Anteromesial temporal lobectomy (AMTL) is an effective and safe treatment for refractory temporal lobe epilepsy (TLE) caused by hippocampal sclerosis (HS). It is possible that modifications to this procedure could offer improved seizure control or a reduction in functional consequences in some patients. Reviewed here is the issue of when it might be appropriate to perform a resection for TLE that spares the mesial structures, particularly the hippocampus and parahippocampal gyrus. This issue is particularly important for dominant hemipshere TLE and for patients without obvious HS, as these are the patients at greatest risk for verbal memory decline following AMTL. Current evidence suggests that mesial structure-sparing resections may be worth consideration for two types of patients: those with temporal lobe foreign tissue lesions outside the mesial structures, and those with temporal lobe hypometabolism on fluorodeoxyglucose positron emission tomography but a normal MRI. Patients with dual pathology (i.e., HS plus another epileptogenic lesion) are unlikely to benefit from a resection that spares the mesial temporal lobe. There is little evidence to state whether resections of this kind are worthwhile for cryptogenic TLE, or for mesial TLE with preserved memory function. There is a clear need to move beyond the field's present focus on the hippocampus and investigate new approaches to TLE that may minimize the risks of functional consequences in patients without HS.

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Progression from frontal–parietal to mesial–temporal epilepsy after fluid percussion injury in the rat

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Summary

We recently described an *in vivo* model of post-traumatic epilepsy (PTE) in the rat where chronic spontaneous recurrent seizures appear following a single episode of fluid percussion injury (FPI). PTE, studied during the first 2 months post-injury, was focal and seizures originated predominantly from the frontal–parietal neocortex at or around the injury site. However, rarer bilateral seizures originating from a different and undefined focus were also observed. To shed light on the Posttraumatic Epileptogenic mechanisms and on the generation of bilateral seizures, we studied rats up to 7 months post-injury. *In vivo* paired epidural and depth-electrode recordings indicated that the anterior hippocampus evolves into an epileptic focus which initiates bilateral seizures. The rate of frontal–parietal seizures remained constant over time after 2 weeks post-injury, while the rate of hippocampal seizures greatly increased over time, suggesting that different mechanisms mediate neocortical and hippocampal post-traumatic epileptogenesis. Because of different temporal evolution of these foci, the epileptic syndrome was characterized by predominant frontal–parietal seizures early after injury, but by predominant mesio-temporal seizures at later time points. Pathological analysis demonstrated progressive hippocampal and temporal cortex pathology that paralleled the increase in frequency and duration of bilateral seizures. These results demonstrate that FPI-induced frontal–parietal epilepsy (FPE) progresses to mesial–temporal lobe epilepsy (MTLE) with dual pathology. These observations establish numerous similarities between FPI-induced and human PTE and further validate it as a clinically relevant model of PTE.

Our case: surgical plan

- Removal of electrodes
- Right parietal topectomy
- Right selective amygdalohippocampectomy

My mom took me to Dr. Lin because she was told by another doctor that I did not have epilepsy. I was scared because I did not know what was happening to me. One moment I was fine the next moment I had a sick taste in my mouth and my head would hurt seconds before I would have a seizure. After the seizure I would feel very sleepy and would have to go to sleep.

My mom asked me if I wanted to have brain surgery. I told her yes, I did not want to live like this for the rest of my life. My mom told me that I could die or be worse than I was. I told her I was willing to take the chance and I knew that I would be ok, I trusted the doctors because they listen to me & my mom. All the doctors listen to what was going on with me and I felt like they really cared about me, like I was one of their kids. The doctors did not only talk to my mom & dad but, they also talked to me telling me what was going on. They treated me like I did have a brain and that I was a person.

I was a little scared, I remembered waking up after the first surgery in the ICU with my head bandage. I could feel the wires coming out of my brain. The hardest part was not taking a shower and waiting for me to have a seizure. Everybody that cared for me made sure that I was pain free and made me feel special.

My second surgery I remember waking up in the recovery room and I felt cold and I wanted to go to my room. The nurses were nice to me and put more blankets on me. When I woke up in the ICU my eyes hurt I could not see. My doctors made sure that my eyes were checked quickly. I remember not having any bandages on my head and half of my head was like a balloon. The doctors and the nurses made sure I knew the swelling in my head would go down. I went home I think a couple of days after the surgery.

Since the surgery I haven't had any seizures and have gone off one of my medications. I now can walk home from school. I go out with my friends. I have had to relearn some things, but it is easier and I have learned more than before. My mom no longer scares me in the middle of the night because she no longer checks on me. I am also taking the bus and I am getting work experience. I have passed the Math part of the exit exam and I'm currently studying to pass the English. My goal is to graduate, get my license, and start college this fall. None of this would have been possible without UCI Epilepsy Center and all of the Doctors, Nurses, and the Neuro Techs who took care of me during my journey with epilepsy.

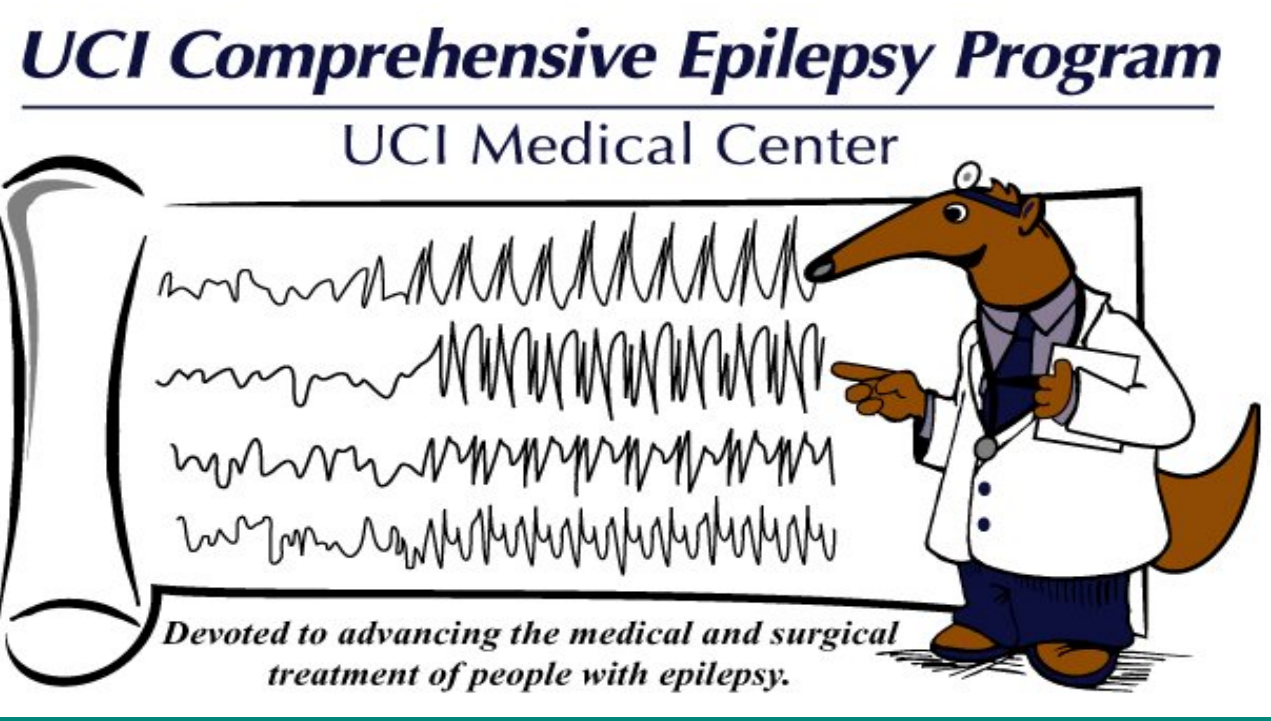
Thomas E. Phelan II, January 2009

Factors influencing success of epilepsy surgery

- Focality
- Presence of obvious lesion on MRI
- Concordance of EEG and MRI localization
- Ability to perform “full” procedure without potential neurologic morbidity
- Quality of surgery (completeness of resection or disconnection)

Summary

- Surgery for complicated epilepsy should be considered in medically intractable patients, even in those with “dual pathology”
- Outcomes of surgery in patients with dual pathology are similar to those of other epilepsy surgeries *if* both pathologies can be safely resected
- The management of complicated epilepsy must:
  - incorporate detailed electrophysiological mapping of the epileptogenic zone(s)
  - incorporate detailed cortical mapping of function
  - identify and successfully treat/resect epileptic tissue with minimal or no side effects on normal brain tissue



Every patient with epilepsy deserves:

- full diagnostic workup
- adequate medication trial
- access to comprehensive epilepsy surgery
- chance at seizure freedom

www.ucihealth.com/epilepsy

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