



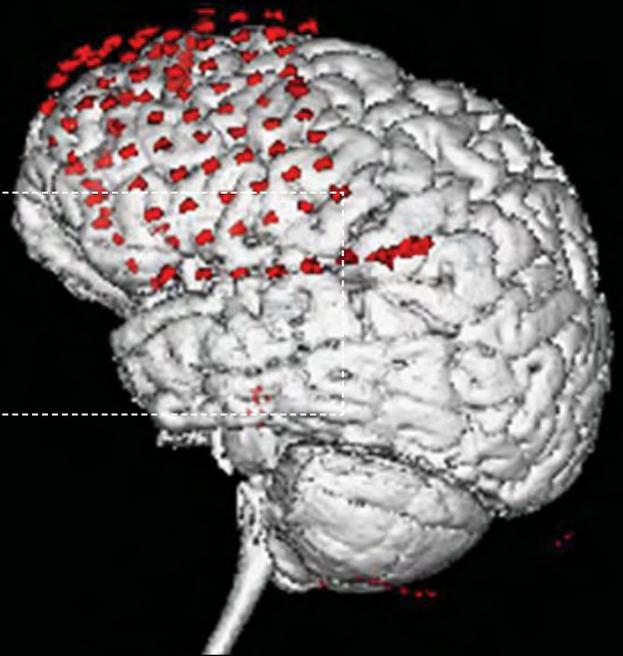
# EPILEPSY. UPDATE.

# A CASE SERIES

*A CME Activity*

## *Selecting Candidates for Epilepsy Surgery*

*Gregory D. Cascino, M.D., F.A.A.N.  
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Three-dimensional MRI  
with implanted subdural electrodes.

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Release Date: April 1, 2009

Expiration Date: April 1, 2010

# Selecting Candidates for Epilepsy Surgery

Although the great majority of epilepsy patients have their seizures controlled by medications, about a third continue to experience seizures and the resulting negative effects on their quality of life. For many of these patients, as illustrated below, surgical removal of the seizure focus brings the seizures under control and allows patients to lead normal and productive lives.



## Case 1

A 33-year-old right-handed man presented because of uncontrolled seizures. The patient had had a prolonged febrile seizure at age 2 but no further seizures until adolescence. The habitual clinical events surrounding his current seizures involved a “rising sensation in my stomach” followed by confusion and difficulty speaking. While awake his EEG was normal, but during light sleep there were left temporal sharp waves. Over 5 years, the patient had at least 1 complex partial seizure each month in spite of trying 10 different antiepileptic drugs (AEDs). The patient was unable to operate a motor vehicle, and work was restricted. The patient’s MRI showed left hippocampal atrophy (Figures 1 and 2). Video EEG monitoring during his characteristic seizures

showed a left fronto-temporal discharge. The patient had significant postictal aphasia. Neuropsychological studies indicated normal intelligence and a verbal memory deficit. The patient underwent a left anterior temporal lobectomy (Tables 1-3). Pathology revealed severe hippocampal neuronal loss with gliosis. The patient has been seizure-free 10 years following surgery and is off medications. He is legally operating a motor vehicle and is employed full-time.

**Table 1. Factors supporting use of surgery for partial epilepsy**

- Seizures are intractable and medically and socially disabling
- Seizure control will improve quality of life
  - Localized region of seizure onset
- Medial temporal lobe seizure onset
- MRI-identified structural abnormality co-existent with the area of seizure onset
  - Presence of mesial temporal sclerosis (MTS), low grade neoplasm, or cavernous hemangioma

**Table 2. Preoperative evaluation for surgery for partial epilepsy**

- Routine awake and asleep EEG recording
- MRI head
- Inpatient video-EEG monitoring
- Neuropsychological studies
- Visual field examination
- Sodium amobarbital study for language and cognitive evaluation\*
- Positron emission tomography (PET) scan\*
- Single-photon emission computed tomography (SPECT) scan\*
- Intracranial video-EEG monitoring\*
- Magnetoencephalography\*
- Functional mapping with electrical stimulation\*

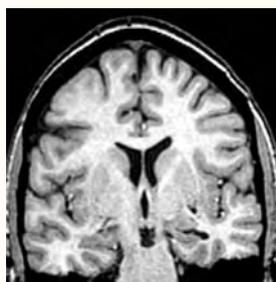
\*Variably performed and not available at all epilepsy centers.

**Table 3. Temporal lobectomy: operative outcome**

Outcome	Patients	(%)
Seizure-free	120	69%
Rare seizures	14	8%
Auras only	12	7%
Nondisabling seizures	2	1%
No significant improvement (<80% seizure reduction)	26	15%
Complications	2	1%

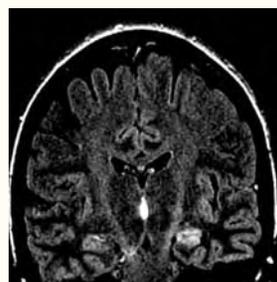
Source: *Neurology*. 1998;51:465-471

**Figure 1.**



MRI head (T1-weighted, oblique-coronal) shows left hippocampal atrophy. (Note the left temporal lobe is on the right side of the figure.)

**Figure 2.**

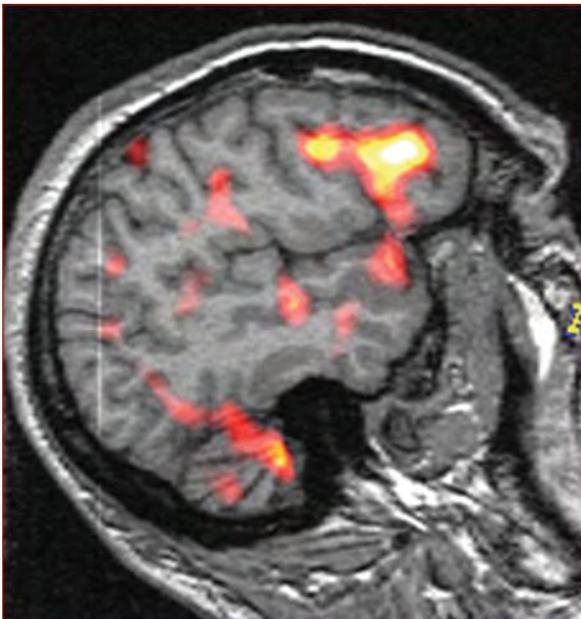


MRI head (FLAIR, oblique-coronal) shows a left hippocampal signal intensity abnormality. (Note the left temporal lobe is on the right side of the figure.)

## Case 2

An 18-year-old right-handed man with no history of symptomatic neurological disease developed seizures at age 18 months. These seizures lasted 1 to 2 minutes, with bicycling movements of the legs, agitation, hypermotor activity of all 4 extremities, and posturing of the right hand. They were not associated with loss of consciousness or aphasia. The patient briefly appeared confused postictally. The seizures occurred during sleep several times per week and were refractory to multiple AEDs. The neurological examination was normal except for a mild reduction in fine finger movements in the right hand and a mild static encephalopathy. Interictal EEGs and MRI of the head were unremarkable. Ictal EEGs had much muscle artifact but also a subtle left frontal discharge. A positron emission tomography (PET) scan was unremarkable. An ictal, single-photon emission computed tomography (SPECT) scan showed left frontal hyperperfusion. A subdural electrode grid revealed a focal seizure discharge concordant with the SPECT abnormality (Figure 3). The patient underwent a left frontal lobe resection of a focal cortical dysplasia (Tables 4 and 5). The patient has been seizure-free 10 years following surgery without operative complications. He is receiving carbamazepine and does not wish to consider AED discontinuation.

**Figure 3.**



A SISCOM (subtraction ictal SPECT coregistered to MRI) study reveals a left frontal abnormality.

**Table 4. Neocortical (non-lesional) surgery: operative outcome**

Outcome	Patients	(%)
Seizure-free	42	47%
Significant improvement ( $\geq 80\%$ seizure reduction)	29	33%
No significant improvement	18	20%

Source: *J Ann Neurol.* 2005;58:814.

**Table 5. Focal cortical dysplasia in adults: operative outcome**

Outcome	Patients	(%)
Seizure-free	11	52%
Rare seizures	4	19%
Significant improvement ( $\geq 80\%$ seizure reduction)	2	10%
No significant improvement	4	19%

Source: *J Ann Acta Neurol Scand.* 2006;113:65-71.

## DISCUSSION

These cases illustrate 2 common scenarios for patients with focal epilepsy whose seizures are not controlled by medications. The first had mesial temporal lobe epilepsy and the second a focal cortical dysplasia. Although the evaluations were similar, the second required additional information to localize the seizure focus and to assure that surgery would not cause a significant postoperative deficit. Tables 1 and 2 summarize the features of the ideal candidates for epilepsy surgery and the features of the preoperative evaluation.

Mesial temporal lobe epilepsy is often associated with auras (e.g., rising abdominal sensation), complex partial seizures (e.g., altered mentation and behavioral arrest), and rare generalized convulsions. The pathological finding underlying the epileptogenic zone is mesial temporal sclerosis (MTS), which includes hippocampal neuronal loss. The etiology for the loss may have been the febrile seizure in childhood for the patient in Case 1, but often no cause can be identified.

Both patients had intractable partial epilepsy because the seizures were medically refractory. In general, patients are considered intractable if their seizures continue after they have tried a minimum of 2 appropriate AEDs. Because of the significant social and employment consequences of intractable epilepsy, surgery should be considered sooner rather than later. Analyses have consistently shown that

Continued on page 3 (Reverse side)

surgery is much more effective in controlling seizures than trials with new medications for intractable epilepsy (Tables 3 to 5)—for intractable patients, the chances that new AEDs will control seizures are less than 10%. The control of seizures results in a significant improvement in quality of life.

There are a number of concerns about the possible consequences of epilepsy surgery. Surgery may be safely performed in the language-dominant temporal lobe because the site of seizure onset in most individuals involves the amygdala and hippocampus. Although there may be a decline in verbal memory performance after dominant temporal lobe surgery, multiple follow-up studies have not shown significant performance deficits following surgery. Patients with MRI-identified MTS are less likely to experience a postoperative memory decline than those with normal MRI studies. Some patients may experience a transient mood disturbance following surgery, but all studies agree that successful epilepsy surgery leads to a substantial improvement in the quality of life.

The second patient illustrates the challenges associated with non-lesional, neocortical epilepsy. Selected patients with normal MRI head studies and partial epilepsy of extratemporal origin may proceed with surgical treatment. In most of these individuals the seizures emanate from the frontal lobe. Inspection of the excised brain tissue may reveal focal cortical gliosis, nonspecific pathological changes, or normal cerebral cortex. Importantly, individuals with focal cortical dysplasia may have unremarkable MRI head studies. Localization of seizure onset may be difficult and require chronic intracranial EEG monitoring for surgical localization. The operative outcome in these patients is less favorable than in temporal lobe epilepsy or in patients with MRI-identified extratemporal lesional pathology (Tables 4 and 5). Less than 50% of patients with normal MRI studies and extratemporal seizures are rendered seizure-free following focal cortical resection. However, approximately two-thirds of all patients experience a significant reduction in seizure tendency.

The operative morbidity may depend on the localization of seizure onset and the need for chronic intracranial EEG monitoring. The decision regarding a presurgical evaluation and operative procedure in these patients must be individualized. Even for patients with intractable neocortical epilepsy, the chances for seizure control are better with surgery than with medications.

## FAQs Frequently Asked Questions

### *When should I consider sending a patient to surgery?*

Patients with seizures that are socially or physically disabling and that cannot be controlled on 2 or more antiepileptic medications should be considered for evaluation. Patients who are unable to operate a motor vehicle, complete their education, or become employed because of their seizure disorder should be investigated. The diagnostic investigation can be used to classify seizure-type, determine the etiology or cause of the seizure disorder, and localize the site of seizure onset. Patients should understand the rationale for the evaluation is not simply “to have epilepsy surgery,” but rather to identify treatment strategies that will allow the individual to be seizure-free.

### *Shouldn't I exhaust all medical options before thinking about epilepsy surgery for my patient?*

There is no evidence that multiple trials of medical therapy are likely to be more effective than the initial medications. Combinations of medication have been associated with increased adverse effects, pharmacokinetic interactions, and increased expense. The most effective antiepileptic drugs for partial epilepsy are probably the initial 2 or 3 medications. Perhaps less than 5% of patients with intractable partial epilepsy will be seizure-free with subsequent medication trials. The prolonged duration of intractable epilepsy may also increase psychosocial debilitation. Importantly, patients with intractable epilepsy are at increased risk for morbidity and mortality.

### *Can my patients stop taking antiepileptic drugs after a successful surgery?*

Selected patients who are rendered seizure-free may be candidates for antiepileptic drug taper and withdrawal. However, the risk of seizure recurrence is higher with discontinuance of medication. Patients with compelling reasons to consider drug withdrawal (e.g., pregnancy) may be candidates for antiepileptic taper. Usually patients are followed 1 to 2 years following surgery on medication before considering a drug taper. There are conflicting opinions regarding the duration of antiepileptic drug therapy in seizure-free individuals prior to considering medication taper and withdrawal. Reductions in medical therapy may be appropriate sooner if there is drug toxicity.

### *Isn't brain surgery risky for patients with epilepsy?*

The operative morbidity associated with the most common operative procedure performed for intractable partial epilepsy (i.e., an anterior temporal lobectomy) is approximately 1%. The risks associated with epilepsy surgery depend on several factors including the area of seizure onset, the need for pre-resection intracranial EEG monitoring, the extent of surgical excision, and the patient's other medical issues. Importantly, the morbidity and mortality associated with medically refractory seizures should be evaluated prior to surgery. Patients with intractable epilepsy have a higher risk of sudden death in epilepsy and complications related to seizure activity (e.g., status epilepticus). Ultimately, the risks versus benefits of surgery must be considered for an individual patient.



#### **ABOUT THE AUTHOR**

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## EPILEPSY UPDATE: A CASE SERIES Issue #5

### KNOWLEDGE GAP ADDRESSED

Current practice recommendations in the general neurology community are limited and need to be supported. This activity will make the general neurologist more aware of the complex issues involved in treating patients with epilepsy and be able to apply the appropriate resources.

### LEARNING OBJECTIVES

- Evaluate surgery as an option in order to manage the patient with epilepsy more appropriately and to enhance his/her quality of life.
- Recognize that inadequate seizure control may have consequences that impact a patient's ability to work and participate in society, and surgery may best address these consequences.
- Given that patients with epilepsy can have a number of medical and psychological issues that may make them reluctant to consider surgery, determine the best ways to address these issues.
- Recognize the barriers that patients with epilepsy may encounter in an effort to sustain an optimal quality of life.

### TARGET AUDIENCE

General neurologists, nurses, and other healthcare professionals involved in the care of patients with epilepsy.

### ACCREDITATION STATEMENT

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### FACULTY DISCLOSURES

**Drs. Austin, Bertram, Donner, Gilliam, and Goodkin** – have indicated they have nothing to disclose.

**Dr. Cascino** – Honoraria: AAN, AES; Contracted Research: NeuroPace; Grants: Epilepsy Phenome Genome Project.

**Dr. Sperling** – Speakers' Bureau: Pfizer, Inc., Ortho-McNeil, UCB Pharma; Intellectual Property/Patent Holder: Daeyang; Consulting/Advisory Board: Valeant, Dainippon Pharmaceuticals; Contracted Research: UCB Pharma, Schwarz Pharma, GlaxoSmithKline, Medtronic, NeuroPace, Johnson & Johnson.

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**Fred Lado, M.D., Ph.D.** – has indicated he has nothing to disclose.

### EDITORIAL REVIEWERS

**Paul Shea and Kay Sloves** – have indicated they have nothing to disclose.

## SELF-ASSESSMENT QUIZ

To obtain credit you must read the newsletter and answer the Self-Assessment Quiz and CME Evaluation Survey. Mail them to:

American Epilepsy Society  
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342 North Main Street  
West Hartford, CT 06117-2507  
or Fax to: (860) 586-7550

A CME certificate will be sent to you within 3 weeks should you obtain a grade of 75% (3 of 4 answers correct) or more.

### 1. Potential adverse effects of antiepileptic drug polypharmacy in the management of partial epilepsy:

- a. reduced compliance
- b. dose-related side effects
- c. pharmacokinetic interactions
- d. increased cost of medications
- e. all of the above

### 2. True or False: Patients with partial epilepsy should only undergo a presurgical evaluation if they are experiencing generalized tonic-clonic seizures.

### 3. The most common pathology associated with temporal lobe epilepsy in patients undergoing epilepsy surgery is:

- a. primary brain tumor
- b. mesial temporal sclerosis
- c. gliosis
- d. malformation of cortical development

### 4. True or False: A normal MRI head precludes an excellent response to epilepsy surgery.

Please circle the correct answers:

1. a b c d e

2. T F

3. a b c d

4. T F

## CME EVALUATION SURVEY

Complete the Evaluation (please be sure to indicate how long it took to complete this activity). The amount of time you attest to on this evaluation will be reflected on your certificate.

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### 1. Effectiveness in Meeting Identified Learning Objectives

Was the activity effective in meeting the identified learning objectives?

SCALE:  5=Excellent  4=Very Good  3=Satisfactory  2=Fair  1=Poor

Evaluate surgery as an option in order to manage the patient with epilepsy more appropriately and to enhance his/her quality of life.

5  4  3  2  1

Recognize that inadequate seizure control may have consequences that impact a patient's ability to work and participate in society, and surgery may best address these consequences.

5  4  3  2  1

Given that patients with epilepsy can have a number of medical and psychological issues that may make them reluctant to consider surgery, determine the best ways to address these issues.

5  4  3  2  1

Recognize the barriers that patients with epilepsy may encounter in an effort to sustain an optimal quality of life.

5  4  3  2  1

## 2. Questions Relating to Your Intent to Make Practice Changes

Based upon your participation in this CME activity, please answer the following:

Did the information in this activity increase your ability to judge whether your patients who have epilepsy are potentially candidates for surgery?

YES  NO

Did the information in this activity increase your confidence in recommending surgery for your patients?

YES  NO

Will the information in this newsletter alter or influence the discussions that you have with patients about surgery when trying to achieve adequate seizure control?

YES  NO

Can we contact you in a follow-up survey to measure the impact of this educational intervention?

YES  NO

### 3. Based on your participation in this CME activity, which of the following strategies do you now plan to use in your practice that you haven't used before? (Check all that apply)

I will consider surgery for my patients who fail to achieve seizure control after 2 or more medications have been tried.

I will consider recommending surgery for my patients who have temporal lobe epilepsy not adequately controlled on medication.

I will consider recommending surgery for my patients when foci can be located and after combinations of AEDs are unsuccessful in achieving seizure control.

I will evaluate my epilepsy patients as candidates for surgery if they do not achieve adequate seizure control or have unacceptable side effects on multiple medications.

### 4. Are there any barriers to implementing these strategies? (Check all that apply)

Time

Cost

Staffing

Institutional treatment algorithm differences

Formulary

Patient adherence

Other: \_\_\_\_\_

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Gregory D. Cascino, M.D., F.A.A.N.	5 <input type="checkbox"/> 4 <input type="checkbox"/> 3 <input type="checkbox"/> 2 <input type="checkbox"/> 1 <input type="checkbox"/>	5 <input type="checkbox"/> 4 <input type="checkbox"/> 3 <input type="checkbox"/> 2 <input type="checkbox"/> 1 <input type="checkbox"/>	<input type="checkbox"/> Yes <input type="checkbox"/> No

If no, please describe below:

### 6. Please rate the educational value/dinical relevance of the content:

Just Right  Too Advanced  Too Basic

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If you answered "No" to any of the above questions, please provide details:

### 8. Based upon the topic of this case series, "Selecting Candidates for Epilepsy Surgery," please list additional topics that you would like to hear about that will better help you manage your patients.

1.) \_\_\_\_\_

2.) \_\_\_\_\_

### 9. Are you interested in the following modalities of learning?

(Check all that apply)

Podcast/downloadable audio files  Publications  Webcast  Case Studies

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### 10. Would you like to continue receiving this publication?

Yes  No

### 11. Please send me AES membership information.

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Signature \_\_\_\_\_

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