Review of the 20-year UCLA experience with surgery for epilepsy[1]

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During the past 20 years, a series of 175 patients with medically intractable complex partial epilepsy has been treated surgically or evaluated with depth electrodes at the UCLA Center for the Health Sciences. Lately, emphasis has been placed on the value of performing the operation on only those patients who have undergone independent evaluations to determine a focal cerebral dysfunction which would confirm electroencephalographic localization. Depth-electrode implantation and telemetric recording of seizures remain an important part of the UCLA evaluation protocol for many of these patients; however, recent experiences have shown that other tests may supersede depth recordings for selected persons.

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Of all patients with epilepsy, the complex partial seizure afflicts 40%.[1] Drug therapy, although widely used, is of limited value for some of these persons. Rodin[2] estimated that as many as 60% of all patients with complex partial seizures do not respond to medical management. Schomer[3] has recently estimated that in the United States as many as 360,000 patients may experience medically refractory partial seizures; 60,000 to 120,000 of these persons may be good candidates for surgery. More than 30 years ago, the safety and efficacy of surgery for selected patients experiencing partial seizures refractory to medical therapy were demonstrated.[4,5] The method used for the selection of patients most likely to benefit from surgery, however, *must* be reliable and minimally invasive.

Twenty years ago, Crandall et al[6] reported their dissat-

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isfaction with total reliance on interictal electroencephalographic techniques for the precise analysis of the complex subcortical epileptogenic activity in patients with partial complex epilepsy. Their report of investigations with depth electrodes surgically implanted into the medial structures of the temporal lobes marked the beginning of the surgery-for-epilepsy program at UCLA. Our report presents an overview of the experiences gained at this hospital during the past two decades and describes our current evaluation protocol.

Clinical evaluation

Criteria for inclusion in study: All patients who underwent depth-electrode implantation for complex partial epilepsy and all patients who had undergone an anterior temporal lobectomy without prior depth-electrode implantation, according to criteria developed in 1979, were included in this study. Patients who were accepted for a preoperative evaluation (*a*) experienced partial seizures, preferably with automatisms, as documented by clinical evidence or electroencephalographic (EEG) findings; (*b*) experienced frequent seizures resistant to documented adequate medical therapy; (*c*) experienced seizures that interfered seriously with daily life; (*d*) did not have a progressive brain disease (e.g., a tumor); and (*e*) did not have severe health problems, psychosis, or marked mental retardation.

Preoperative evaluation: Prior to 1977, patient evaluation was done by scalp interictal EEG recordings and stereotactic depth-electrode (SEEG) telemetry recordings of mesial temporal structures.[6] In 1977, the UCLA protocol for evaluating these patients was expanded to include routine tests of local cerebral dysfunction, as well as electrographic monitoring.[7,8] *Table 1* outlines the current preoperative evaluation. Following the phase I evaluation, most patients who are considered surgical candidates were evaluated according to the phase II protocol which includes SEEG telemetry. For some patients, however, SEEG telemetry was omitted and a lobectomy followed the phase I evaluation. This occurred if (*a*) definite scalp EEG findings showed that seizure origin was localized in the mesial structures of the temporal lobe and revealed frequent interictal spikes in the same area; (*b*) focal hypometabolism of that temporal lobe was demonstrated on positron emission tomography scans; and (*c*) two additional tests confirmed local cerebral dysfunction (e.g., neuropsychologic deficit, Wada memory deficit, or thiopental suppression of fast activity as recorded by the sphenoidal electrodes).[8] During the past four years, approximately one third of all patients have undergone resection without prior SEEG telemetry.

Table 1. Current clinical evaluation scheme

Phase I	Phase II
Scalp/sphenoidal interictal EEG	Video and SEEG telemetry
Video, scalp/sphenoidal telemetry	After-discharge thresholds evaluated
Visual field examination	Micro-electrode studies
Neuropsychologic testing	Intracarotid amytal administered (Wada test)*
Neuroradiologic testing	Thiopental study*
Positron emission tomography	

* If the initial phase I studies suggest that the patient may meet the criteria for a lobectomy without electrode implantation, the Wada test and thiopental study are done with scalp and sphenoidal leads in place rather than with depth electrodes.

Description of tests to determine regional dysfunction: If the results of the interictal EEG and phase I telemetry studies suggested that a patient could avoid depth-electrode implantation, the thiopental study was performed with the scalp and sphenoidal electrodes in place. Otherwise, the study was done with the depth electrodes in place. During continuous EEG monitoring, thiopental (25 mg) was injected intravenously every 30 seconds until the corneal reflex was eradicated.[9,10] The EEG was then analyzed for activation of focal spike activity and for focal attenuation in barbiturate-induced fast activity as recorded by one sphenoidal lead. The protocol for recording from surface and depth leads was similar. Decreased fast activity usually occurred in most or all derivatives of the mesial temporal structures on one side.

As with the thiopental study, if the interictal and ictal EEG records suggested that the patient could undergo a lobectomy without electrode implantation, the Wada test was done with the scalp electrodes in place.[11] Otherwise, the test was carried out with the depth electrodes in place. After transfemoral catheterization, a four- to six-second intracarotid injection of sodium amobarbital (125 mg) was administered to lateralize language dominance and study short-term memory.[12] Fifteen minutes after the injection, the patients were asked to recognize pictures of common objects, written words, and unfamiliar forms.[13] The EEG was recorded simultaneously to aid in determination of spread and duration of drug action.

Positron emission tomography was performed as described previously.[14] F-18-fluorodeoxyglucose (FDG) and N-13-ammonia have been used to indicate local cerebral glucose use and cerebral perfusion. Currently, the image results used at UCLA are based on the FDG scans.

Neuropsychologic studies were designed to evaluate a broad range of brain functions with an emphasis on tests that could show temporal lobe dysfunction. Lateralization of this dysfunction was based on comparisons of a patient's verbal vs. non-verbal short-term memory. The immediate and delayed recall by the patient of prose and associative learning was compared with the visual-reproduction subtests of the Wechsler Memory Scale[15] and the Rey-Osterrieth draw-and-recall tests.[16] In the absence of other cognitive deficiencies, a verbal memory loss has been correlated with a dominant temporal lobe lesion, while difficulties in recalling visual non-verbal material has been associated with a lesion in the nondominant temporal lobe.

Description of surgical procedures: The selection of depth-recording sites requires careful consideration since only a limited number of locations can be used. We have implanted the medial temporal limbic structures anteriorly to posteriorly, bilaterally, and symmetrically. Fine bipolar and multicontact electrodes have been inserted in a transverse direction through the middle and inferior temporal gyri into the basolateral amygdala; through the anterior, middle, and posterior pes hippocampi; and then through the anterior, middle, and posterior parahippocampal gyri. This route was selected because it involves the shortest distance, traverses a nearly avascular region, and encompasses the sites of most common microscopic pathology. Additional fine wire electrodes or epidural electrodes were placed in those patients in whom clinical, radiologic, or EEG findings suggested extratemporal pathology.

Stereotactic operations were performed with the patient under general anesthesia and the head positioned in the Todd-Wells apparatus. Teleradiography (14-ft. source-to-skin distance) was used to reduce magnification errors. The stereotactic coordinates were obtained from the Talairach atlas in which the temporal lobe structures are referenced to an axis along the temporal horn and neocortical areas are identified in relationship to the anterior commissure-posterior commissure axis and the midline.[17] Insulated nail calvarial electrodes in the International 10–20 system were used for scalp recordings.

Two days after the operation, the patients underwent SEEG telemetry studies and video monitoring. Frequently, administration of anticonvulsant medication was slowly decreased. Chain-linkage, common-reference, and concentric bipolar recordings were evaluated continuously using at least 13 channels and registered on 1-in magnetic tape before subsequent printing on EEG paper. In special circumstances, two telemetry transmitters were linked for 26-channel recording.

An anterior temporal lobectomy was carried out as previously described[8] based on the en bloc resection as introduced by Falconer.[18] For most patients, general anesthesia was used. At the speech-dominant hemisphere, 4.5 cm of anterior temporal lobe (as measured along the middle temporal gyrus) was the usual limit of resection. At the nondominant hemisphere, the excision was usually 6.0 cm long. The posterior resection line was angled at 45° so that more of the inferior temporal gyrus was removed than the superior gyrus.

Preparation of data: Clinical studies of this type have generated a great deal of information that has been difficult to store, retrieve, and analyze. Therefore, an interactive data base management system was developed on a microcomputer. The dBase II assembly language relational database management system was used.[19] As currently implemented, information regarding medical history, seizure etiology and frequency, description of aura, anticonvulsant use, results of neuroradiologic and neuropsychologic tests, scalp and depth EEG findings, and follow-up examinations are stored. As many as 2,000 characters can be divided into 64 separate categories.

Results

Patient population: The data in *Table 2* review the number of patients evaluated with depth implants and treated surgically during the years

Table 2. Patients included in this study

Description	Number of patients	
	Before 1977	After 1977
Patients with depth-electrode implantation	106	57
Patients undergoing lobectomy with SEEG telemetry	59	35
Patients undergoing lobectomy without SEEG telemetry	0	12
Patients undergoing extratemporal resections	10	4

of this study. The typical patient was approximately 25 years old and had had epilepsy for more than 10 years. Seizure onset was usually during adolescence and was rarely less than three years previous to the study. One quarter of the patients reported a family history of epilepsy. Nineteen per cent of the patients gave a history of febrile convulsion. Thirteen per cent gave a history of status epilepticus at some point during the course of the disorder. Forty per cent experienced generalized seizures (usually about 1–3/yr). We suspect that many of these seizures were actually secondary rather than primary generalized attacks. Of the 157 patients seen, only 28 had abnormal neurologic findings (mild reflex assymetries or cognitive deficits). The average full-scale intelligence quotient recorded in 139 patients was 102 (range, 63–132).

Complications of SEEG telemetry: Depth-electrode implantation is not a minor operation. In our series, two patients died due to an intracranial hemorrhage within 24 hours after implantation. Modifications in the electrode design and implant procedure have been undertaken in an effort to prevent a recurrence. In two other patients, intracranial hemorrhage also occurred, but the electrodes were removed and the subdural hematoma was evaluated without any subsequent detectable residual neurologic deficits. In one instance, cerebritis was shown on the postoperative computed-tomographic scan, but was treated successfully. Minor scalp infections disappeared after electrode removal.

In addition, during the past six years, 5 patients awaiting admission to the hospital for an evaluation have died as a direct result of seizure complications.

Positron emission tomography: The results of FDG scanning in an initial series of 25 patients showed that regional cerebral hypometabolism correlated with the presence of a pathologic lesion.[20] In 22 of the patients, hypometabolic zones were observed on the images; in 19, a corresponding focal pathologic abnormality (temporal sclerosis of the mesial structures [15], small neoplasms [2], angioma [1], and heterotopia [1]) was found. Scans of 3 patients with no microscopically identified abnormality of the temporal lobectomy specimen were normal. Interictal studies using N-13-ammonia as a marker of regional cerebral blood flow have shown that, in most patients, an area of hypoperfusion corresponds to the zone of hypometabolism.[14] Nevertheless, the blood-flow changes are less marked than the metabolic suppression, therefore, these studies have not been pursued.

Thiopental studies: In a preliminary evaluation of the first 25 patients undergoing thiopental studies, assymetric attenuation of fast activity was on the same side as the deep seizure focus in 15 (60%) of the patients. In 9 patients (36%), no significant assymetry was found, and in 1 patient, the slowing of fast activity was noted on the side opposite the deep seizure focus.

Neuropsychologic studies: Our analysis revealed that patients with evidence of focal temporal lobe dysfunction on the neuropsychology tests were more likely to benefit from a temporary lobectomy than those patients with evidence of extratemporal damage. This conclusion was reflected in a recent study that described patients with the highest preoperative intellectual level and the best ability to function psychosocially as having the best control of seizures postoperatively.[21] Similarly, patients with no neuropsychologic evidence of dysfunction contralateral to the epileptic focus had the best prognosis.

Postoperative results: Approximately 70% of all patients undergoing depth-electrode implantation have subsequently undergone a lobectomy. Those patients in whom the depth-electrode recordings showed a bilateral, multifocal, or diffuse seizure origin did not undergo subsequent surgery. Since 1979, an additional 12 patients have undergone a lobectomy without undergoing electrode implantation.

No deaths have occurred after a temporal lobectomy, but complications have included partial hemiparesis (3 patients), lasting oculomotor paresis (1 patient), and hydrocephalus (1 patient).

Seizure frequency alone does not give a full picture of the results of surgery. The socioeconomic status of some patients has been described.[22] Significant social gains have been experienced by patients free of seizures.[21] The categories of seizure control used in this analysis are shown in *Table 3*. In most cases, both the patient and family members were interviewed during a follow-up examination to estimate seizure frequency. In the evaluation prior to 1977, 44% of the patients were considered class 1; those categorized in classes 1, 2, and 3 (83%) were thought to have benefited from surgery. Of those patients undergoing SEEG telemetry since 1977, 62% were considered class 1; those categorized in classes 1, 2, and 3 (97%) were thought to have benefited from surgery. Since 1977, of the patients who underwent a lobectomy without SEEG telemetry, 75% were subsequently labeled class 1; the condition of all 12 improved significantly. Nonparametric statistical analysis of these results has shown that the differences between the series of patients before and after 1977 were statistically significant ($P < 0.01$).[23]

Comparison of scalp records to depth records: Although we use a variety of preoperative tests, the electrographic depth recording of a spontaneous, typical seizure best indicates the need for a temporal lobectomy. For example, in 16% of our patients, the side of seizure origin was determined with SEEG telemetry to be contralateral to the side of prominent interictal spiking. When disagreement between the interictal surface EEG spike and the deep ictal focus occurred, surgery was based on the latter sign. The outcome of those patients in whom the deep seizure focus was contralateral to the predominant scalp spike was not statistically different from the outcome of those in whom the scalp spike was ipsilateral to the focus.

Because the scalp ictal recording is more difficult to interpret, it is often less informative than the interictal record. In 25% of the patients, the scalp ictal focus cannot be determined with certainty. In some patients, for example, the behavior change may precede the electrographic change or the surface EEG changes may be diffuse or bilateral. When a well-defined focus was suspected for other reasons and patients underwent SEEG telemetry, 65% eventually received a lobectomy. Subsequently, 46% were categorized in class 1. The condition of all patients improved considerably. On the other hand, in 30% of the patients who underwent SEEG telemetry for all reasons, depth-electrode recordings documented bilateral or multifocal seizures and thus a lobectomy was not performed.

Discussion

Progress in defining indications for surgery for epilepsy has been difficult. Reports from various centers cannot be compared easily because so many different variables may be involved. For example, patient selection criteria may vary. While some physicians rely only on interictal scalp recordings, others depend on depth recordings. We use one method of depth-electrode implantation, other physicians use different techniques (epidural recordings, subdural strips, single multi-contact leads). Criteria for interpretation of the electrographic ictal origin are not well defined. The limits of temporal lobe resection and the extent of hippocampal resection have not been standardized. The classification of postoperative findings varies.

Table 3. Postoperative seizure class criteria*

Class	Description
1	Seizure-free with or without auras
2	No more than one complex partial seizure/yr, with or without rare generalized attacks or nocturnal seizures only
3	Worthwhile reduction of seizures (>90% reduction from the preoperative frequency)
4	No worthwhile improvement

* "Neighborhood" seizures (focal motor seizures occurring in relation to a resection) occurring in the first month after the operation and those occurring when medication was withdrawn have not been considered in this classification.

Results of surgery alone do not indicate the efficacy of the preoperative evaluation. Outcome statistics depend largely on the number of chances a surgical team is willing to take. A complete assessment can only be made when the number of patients who do not undergo but may have benefited from surgery is known. This information, unfortunately, is impossible to obtain.

Retrospective studies of this sort do not provide controlled data and, subsequently, firm conclusions. Yet, a preoperative evaluation to identify both epileptic excitability and regional cerebral dysfunction has been the major factor leading to better postoperative results in our series since 1977. Those patients with focal abnormalities, especially when there is documented epileptogenic potential in the same region in which there is evidence of an interictal focal functional deficit, benefit most from a resection. While the FDG scan documentation of focal hypometabolism is correlated with a pathologic lesion, we still use positron emission tomography and the other previously described tests to determine cerebral dysfunction, thus localizing the potential epileptogenic site, and to guide decisions regarding placement of the depth electrodes.

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