Low-grade gliomas associated with intractable epilepsy: seizure outcome utilizing electrocorticography during tumor resection

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✓ Adults and children with low-grade gliomas often present with medically refractory epilepsy. Currently, controversy exists regarding the need for intraoperative electrocorticography (ECoG) to identify and, separately, resect seizure foci versus tumor removal alone to yield maximum seizure control in this patient population. Forty-five patients with low-grade gliomas and intractable epilepsy were retrospectively analyzed with respect to preoperative seizure frequency and duration, number of antiepileptic drugs, intraoperative ECoG data (single versus multiple foci), histology of resected seizure foci, and postoperative control of seizures with or without antiepileptic drugs.

Multiple versus single seizure foci were more likely to be associated with a longer preoperative duration of epilepsy. Of the 45 patients studied, 24 were no longer taking antiepileptic drugs and were seizure-free (mean follow-up interval 54 months). Seventeen patients, who all had complete control of their seizures, remained on antiepileptic drugs at lower doses (mean follow-up interval 44 months); seven of these patients were seizure-free postoperatively, yet the referring physician was reluctant to taper the antiepileptic drugs. Four patients continued to have seizures while receiving antiepileptic drugs, although at a reduced frequency and severity. In this series 41% of the adults versus 85% of the children were seizure-free while no longer receiving antiepileptic drugs, with mean postoperative follow-up periods of 50 and 56 months, respectively. This difference was statistically significant (p = 0.016). Therefore, based on this experience and in comparison with numerous retrospective studies involving similar patients, ECoG is advocated, especially in children and in any patient with a long-standing seizure disorder, to maximize seizure control while minimizing or abolishing the need for postoperative antiepileptic drugs.

KEY WORDS • low-grade glioma • seizure • electrocorticography • anticonvulsant drug

PATIENTS harboring cerebral neoplasms often have a history of seizure activity. The incidence of supratentorial tumors associated with epilepsy varies considerably among reported series. Slow-growing intrinsic tumors such as low-grade astrocytomas, oligodendrogliomas, and gangliogliomas are more likely to give rise to a seizure disorder.[2,25,32–35,47] The critical factors responsible for the development of epilepsy in this context appear to be associated with the indolent growth kinetics and the location of the tumor.[17,32,35] Chronicity of the lesion may account for an adverse effect of the tumor on surrounding cortical neurons,[32] both morphologically and biochemically in the form of neurotransmitter alterations.[11,24,27,37] It has recently been demonstrated that the hyperexcitable cortex surrounding the tumor nidus in low-grade gliomas has a significantly decreased population of gamma-aminobu-tyric acid and somatostatin-containing neurons, when compared to adjacent nontumor nonepileptogenic cortex from the same patient.[23]

Although evidence exists to support the concept of separate seizure foci surrounding a tumor[15,22,30,32] or other structural lesions such as arteriovenous malformations,[8,35,49] controversy remains regarding the inclusion of these peripheral epileptogenic zones in the surgical strategy. Certainly, resection of the tumor alone may result in good postoperative control of the patient's epilepsy.[9,15–17,21,25] However, in patients with intractable epilepsy and low-grade gliomas, resection of the tumor without the aid of intraoperative electrocorticography (ECoG) to define epileptogenic regions may often result in only a slightly reduced or unchanged seizure frequency.[3,9,10,17,21,25,39,40,47] In patients achieving good seizure control with lesion removal alone, dependence

upon antiepileptic drugs to maintain a seizure-free status appears to be essential in some studies,[9,10,17,25] yet such reliance is unclear in other investigations.[21]

In an attempt to clarify this controversy, we reviewed adult and pediatric patients treated at the University of Washington for intractable epilepsy and histologically verified low-grade gliomas, who underwent intraoperative ECoG to resect seizure foci at the time of tumor removal. The goal of our study was to compare this group of patients with historical studies to assess seizure outcome, with or without continuation of antiepileptic drugs following surgery, and to determine the influence of ECoG in effecting seizure control.

Clinical Material and Methods

During the period from 1980 to 1990, all adult and pediatric patients with the diagnosis of a low-grade glioma were retrospectively evaluated to determine seizure frequency prior to surgery and postoperative seizure control. All patients with seizures refractory to medical therapy underwent ECoG during tumor removal at our institution, and these formed the basis for this study. Patients with low-grade gliomas who had occasional seizures or were seizure-free while receiving antiepileptic drugs did not undergo ECoG during tumor removal and were excluded from this study.

The study population included 45 patients, ranging in age between 4 and 73 years (mean 30 years); there were nearly equal numbers of male and female patients. The most common presenting symptom was intractable seizure activity; very few patients had focal motor or sensory signs, which, when present, were subtle. No patient had a fixed language deficit, although several individuals demonstrated occasional interictal or temporary postictal expressive aphasia. Virtually all patients had generalized (tonic-clonic) or partial (complex) seizures, or a combination of both (Table 1).

The frequency of seizure activity varied between one per month and more than 10 per day (mean 541 seizures/yr). The preoperative duration of seizures varied from 1 to 324 months (mean 86 months). The majority of patients were treated with multiple drug combinations prior to the operative procedure. At the time of surgery, 40 patients were being treated with two or more anticonvulsant drugs and had therapeutic serum drug levels. The remaining five patients were being treated with only one anticonvulsant agent which was also maintained in the therapeutic range. Preoperative scalp electroencephalographic (EEG) recordings were obtained in 31 patients to determine lateralization and proximity of the seizure focus to the tumor.

All patients underwent preoperative computerized tomography (CT) and 42 had magnetic resonance (MR) imaging. Intravenous contrast agents were used in both or either of the studies in each case. Subtle contrast enhancement was documented in only two of the 45 patients. The CT scans showed the typical appearance of a homogeneously hypodense lesion in every instance, whereas the MR image demonstrated a hypointense signal on T_1-weighted images in all except five patients with lesions appearing iso- or hyperintense.

There were 12 right-sided tumors, and in most cases

TABLE 1
Seizure characteristics in 45 patients in this series

Type of Seizure	No. of Cases
complex partial	15
generalized tonic-clonic/complex partial	15
generalized tonic-clonic	7
generalized tonic-clonic/simple partial	3
simple partial	3
generalized tonic-clonic/absence	1
complex partial/simple partial	1

(33 patients) the mass was located in the dominant (left) hemisphere. Cerebral dominance was determined preoperatively by a history of consistent right-handedness when a left hemisphere lesion was detected. Speech lateralization to the left hemisphere was confirmed in every case using language mapping while the patient was awake during surgery. Right-handed patients with tumors in the right hemisphere were operated on while asleep. Patients who were ambidextrous or who had left-hemisphere tumors with left hand preference or right-hemisphere tumors with left hand preference underwent language localization using the Wada test[45] to confirm cerebral dominance preoperatively.

Subdural electrode arrays were utilized in patients who could not tolerate surgery while awake or for those who needed additional ECoG to further localize and characterize seizure foci prior to the definitive tumor resection. The subdural electrode arrays were inserted 5 to 7 days prior to tumor removal while the patient was under general anesthesia. Extraoperative ECoG, language testing, and localization of the sensorimotor (rolandic) cortex was achieved via stimulation mapping through the electrode array in a telemetry room on the hospital ward.

A seizure focus in this study is defined as an area of epileptic discharges located under an electrode contact or within the confines of several electrodes overlying a contiguous cortical region. Noncontiguous epileptogenic zones are referred to as multiple seizure foci. For example, epileptic discharges originating from the mesial temporal lobe (amygdala, hippocampus, and parahippocampal gyrus) without lateral temporal or frontal discharges represent a single seizure focus. In contrast, epileptiform spike activity emanating from mesial temporal structures and lateral temporal cortical sites associated with a temporal lobe tumor would constitute two (multiple) seizure foci.

The techniques of brain mapping, including ECoG, have been detailed previously.[4,5,31] Briefly, patients operated on while awake are mildly sedated with Innovar fentanyl citrate, 0.5 to 1.0 cc), if needed, and the scalp is anesthetized with a 0.25% lidocaine-bupivacaine mixture. An alternative approach is to use a propofol (Diprivan) infusion during bone flap removal, which provides a deep sedative state that is reversible in 10 minutes. Wide exposure of the cortical surface is essential to map several areas adjacent to and beyond the tumor nidus in order to detect the seizure focus (foci) and identify speech and rolandic cortex. A bipolar

electrode (with 5 mm separation) is used to stimulate the brain utilizing a train of biphasic, square wave pulses (60 Hz, 1 msec, single phase duration). The current varies (2 to 16 mA) depending upon the anesthetic condition of the patient and the afterdischarge threshold. Subcortical motor pathways may also be identified using the bipolar electrode when resecting tumor near the internal capsule or cerebral peduncle.[5]

Electrocorticography is performed using an array of carbon-tipped electrodes held in place with a horseshoe apparatus attached to the skull. Subdural strip electrodes are used to record from the inferior and mesial temporal lobe and the inferior and interhemispheric frontal lobe. Recordings usually extend over a 10- to 20-minute period. An intravenous injection of Brevital (methohexital, 1 mg/kg) may be used to induce epileptiform activity if the interictal record is not informative, but this is rarely necessary. Following pre-resection ECoG, a small electrical current (2 to 8 mA) is applied to the cortex to elicit one or a few afterdischarge potentials, thus establishing the optimum current (just before evoking afterdischarges) for blocking language tasks without provoking seizure activity. Following resection, ECoG is again performed to ensure that all areas of documented epileptiform activity have been resected prior to terminating the procedure. Epileptic activity that is distant from the resection cavity and occasional or that is located in functional cortex is not resected.

Delineation of the tumor and its borders was enhanced with the aid of intraoperative ultrasound.[28] The extent of tumor resection, based upon operative reports and a comparison between preoperative and postoperative imaging studies, was graded as: gross total resection, 100% removal; near-total resection, 90% to 99% removal; subtotal resection, 50% to 90% removal; and partial resection, less than 50% removal. Resected seizure foci were submitted for histological analysis in addition to representative specimens from the tumor and resection cavity margins.

Postoperative management included focal radiotherapy without chemotherapy, and serial CT or MR imaging every 3 to 4 months. Patients were closely followed with regard to their seizure status and antiepileptic drug requirements. It was recommended that antiepileptic drugs be tapered beginning within 12 to 18 months following surgery; this was usually instituted by the referring physician.

Results

Thirty-one patients underwent preoperative surface EEG recording. The EEG tracings correctly localized epileptiform activity to the hemisphere with the tumor in 22 (71%) of these patients. In eight cases the EEG tracings showed no epileptiform discharges, and in the remaining patient seizure activity was generalized over both hemispheres.

Seizure Focus Characteristics

In the entire study group of 45 patients, 56 seizure foci were detected by ECoG. In six patients no seizure focus could be detected. Nine seizure foci occupied functional cortex and were not removed. All of the

remaining epileptic foci were resected and 40 of these were submitted for histological analysis. The location of all seizure foci is listed in Table 2. In patients harboring predominantly temporal lobe tumors, the vast majority of the epileptiform discharges originated from mesial temporal lobe structures, such as the amygdala, uncus, anterior hippocampus, and parahippocampal gyrus. Of those patients with a lateral temporal seizure focus, all but two patients had evidence of additional epileptiform discharges emanating from mesial structures. In 40 patients (89%), ECoG was performed after resection and 24 persistent seizure foci were identified and, except for nine foci located in functional cortex, were resected.

Eighteen patients (40%) had two separate (multiple) seizure foci in the following lobes: mesial and lateral temporal (78%), mesial temporal and frontal (6%), and parietal and frontal (17%). Seventeen (94%) of these 18 patients had a seizure frequency of greater than one per week, and the epilepsy had persisted for longer than 3 years in 14 (78%). There were 21 patients with a single epileptic focus, and of those patients only 12 (57%) had a duration of symptoms longer than 3 years. The difference between these two groups (those with single vs. multiple seizure foci) in terms of seizure duration was

TABLE 2
Location of seizure focus in 45 cases

Location	No. of Cases
temporal lobe tumors	29
mesial temporal focus	26
lateral temporal focus	15
frontal lobe tumors	8
focus adjacent to tumor*	8
parietal lobe tumors	8
focus adjacent to tumor	7†

* The focus was within the same lobe as the tumor.
† No focus was found in one patient with a tumor in the facial motor cortex.

TABLE 3
Duration and frequency of seizures in single vs. multiple-focus cases

Seizure Occurrence	Single Focus	Multiple Focus
frequency > 1/wk	95%	94%
duration > 3/yr*	54%	78%

* Significance: p = 0.307, Fisher's exact test.

TABLE 4
Tumor pathology in 45 patients

Tumor Type	No. of Cases
astrocytoma	13
oligodendroglioma	14
ganglioglioma	9
oligoastrocytoma	9

not statistically significant. Five of the remaining nine patients with a single seizure focus had suffered seizures for only 6 months or less preoperatively. However, the seizure frequency was similar in both groups of patients regardless of whether they had single or multiple seizure foci (Table 3).

Pathology of Tumor and Seizure Foci

The extent of tumor resection was as follows: gross total resection was performed in 29 cases (64%); near-total resection in 10 (22%); and subtotal resection in six (13%). The tumor pathology is listed in Table 4. Of the 40 seizure foci submitted for histology, 36 foci (90%) did not contain tumor infiltration. The majority of these 36 foci were characterized as having mild gliosis, especially in the subpial region as demonstrated with Holzer preparation; yet most of these foci were completely normal on sections with hematoxylin and eosin staining.

Seizure Outcome

For the entire study group of 45 patients, 41 (91%) are seizure-free at the present time (mean follow-up period 50 months). Currently, 24 patients who have not had any seizure activity are not taking antiepileptic drugs (mean follow-up period 54 months, mean time off antiepileptic drugs 40 months). Another 17 patients are seizure-free but continue to take antiepileptic drugs at lower doses than preoperatively (mean follow-up 44 months). Ten of these patients have had one or two

seizures at some time in the postoperative period, usually after having their antiepileptic drugs discontinued (mean time to first postoperative seizure 38 months; mean time off antiepileptic drugs until the first seizure occurred 14 months); these cases are summarized in Table 5. The remaining seven patients (all adults) are still receiving antiepileptic drugs without an explanation at the time of this retrospective analysis. In each case, the patient lives away from our institution and was primarily under the care of the referring physician who preferred not to taper their medications, although none had seizure activity postoperatively.

Four patients in the study group continue to have seizures while receiving antiepileptic drugs, although at a markedly reduced frequency and severity (Table 6). In one patient (Case 11), a single seizure focus was identified and found to be unresectable due to involvement of functional cortex. In Cases 12 and 13, diffuse tumor infiltration throughout areas of the rolandic cortex resulted in subtotal tumor resection. In both of these circumstances, the residual tumor undercuts functional cortex, which may explain why the seizure pattern has changed from complex to simple partial seizures. Case 14 was considered a surgical failure because post-resection ECoG was not performed, thus leaving behind potentially resectable seizure foci.

A comparison between seizure control without anticonvulsant drugs in adults and children demonstrated that 13 (41%) of the 32 adults were seizure-free and no longer taking antiepileptic drugs (mean follow-up

TABLE 5

Characteristics of patients with postoperative seizures who are seizure-free on antiepileptic drugs*

Case No.	Time of First Seizure Postop	Time Off AED's Prior to Seizure	Postop Follow-Up Period	Seizure Type	Current Status
1	60 mos	6 mos	65 mos	SP	seizure-free on AED's
2	42 mos	23 mos	48 mos	SP	infrequent sensory seizures on AED's
3	55 mos	52 mos	58 mos	CP	seizure-free on AED's
4	30 mos	18 mos	33 mos	ill-defined	seizure-free on AED's
5	34 mos	24 mos	41 mos	GTC	seizure-free on AED's
6	23 mos	12 mos	51 mos	GTC	seizure-free on AED's
7	82 mos	NA	87 mos	GTC	seizure-free on AED's
8	14 mos	NA	50 mos	status epilepticus	seizure-free on AED's
9	18 mos	NA	31 mos	GTC	seizure-free on AED's
10	36 mos	NA	58 mos	GTC	seizure-free on AED's

* AED = antiepileptic drug; NA = AED's never discontinued; SP = simple partial; CP = complex partial; GTC = generalized tonic-clonic.

TABLE 6

Characteristics of four patients who continue to have seizures while receiving antiepileptic drugs*

Case No.	Preop Seizures			Postop Seizures		Comment
	Type	Frequency	Duration	Type	Frequency	
11	CP	1/day	18 yrs	SP	3/mo	unresectable seizure focus in language cortex; GTR of tumor
12	CP, GTC	4/day	3 yrs	SP	2/mo	no seizure focus detected; STR of tumor in facial motor cortex
13	CP, GTC	10/mo	4 yrs	SP	1/wk	seizure focus resected, STR of tumor in rolandic cortex
14	CP, GTC	2/wk	6 yrs	SP	3/mo	no post-resection ECoG

* CP = complex partial seizures; SP = simple partial seizures; GTC = generalized tonic-clonic seizures; GTR = gross total resection; STR = subtotal resection; ECoG = electrocorticography.

period 50 months; mean time off antiepileptic drugs 36 months). If the seven additional adults receiving drugs without explanation are added to this group, assuming they would now be successfully tapered off their medications, then a maximum of 20 (71%) of 28 adults who are seizure-free would be off antiepileptic drugs. The remaining four adults have had seizures while still receiving antiepileptic drugs (Table 6). In contrast, all 13 pediatric patients (< 19 years of age at surgery) no longer have seizures (mean follow-up period 56 months). Eleven (85%) of these 13 children are off antiepileptic drugs (mean follow-up period 58 months; mean time off antiepileptic drugs 44 months). The difference between seizure control in adults and children who no longer take antiepileptic drugs is statistically significant (p = 0.016, Fisher's exact test).

Discussion

Tumor Resection With Electrocorticography

Our approach to the management of patients with intractable seizures associated with low-grade gliomas has been to identify and resect, when possible, a seizure focus or multiple epileptogenic foci in addition to performing a radical tumor removal. In our study, pediatric patients fared much better than adults with regard to long-term seizure control without antiepileptic drugs. In the former group, all patients are seizure-free while no longer receiving antiepileptic drugs except for two children who had one or more seizures late in the postoperative period and are now receiving one anticonvulsant drug. The majority (88%) of adults are seizure-free (41% off antiepileptic drugs, 47% on antiepileptic drugs), although seven patients in the group taking anticonvulsant drugs have, for unexplained reasons, not had them tapered by the primary-care (referring) physician. Four adult patients (12%), while receiving antiepileptic drugs, continue to have seizures but at a greatly reduced frequency and severity compared with their preoperative condition. In considering the entire group of adult and pediatric patients, excluding the three patients with unresectable seizure foci and tumors within functional cortex and the one without post-resection ECoG, 41 patients (91%) are seizure-free.

The concept of using ECoG to facilitate control of seizures in this particular patient population is not novel. However, when analyzing the literature as to the efficacy of ECoG, it is essential to consider patients who were similar to our study population, namely, individuals with seizures refractory to medical therapy associated with low-grade gliomas. We do not advocate the routine use of ECoG during tumor resection if the patient has achieved complete seizure control preoperatively or has only an occasional seizure while receiving medication. In this situation, radical tumor resection alone often controls the epilepsy with or without the need for postoperative antiepileptic drugs.

In previous studies, little was known regarding the outcome of seizures and the need for continuation of antiepileptic drugs following surgery. Gonzalez and Elvidge[22] demonstrated a greater control of seizures when tumor resection was combined with ECoG-guided removal of the seizure focus, yet the status of antiepileptic drug requirement was not documented. In two studies completed by Van Buren and colleagues,[43,44] in which ECoG was used, details regarding seizure control in those particular patients with temporal lobe tumors was not provided. Although Rasmussen[35] reported that, of 91 patients with low-grade gliomas and intractable epilepsy who survived long enough to be evaluated, as many as 79% had either no seizures or a marked reduction with a median follow-up period of 7 years; however, no information was given regarding the use of antiepileptic drugs to achieve that outcome.

Ribarić[36] reported two patients with excellent seizure control following resection of multiple ECoG-verified seizure foci, yet no description of antiepileptic drug usage to attain a seizure-free condition was provided. However, this work emphasized another issue that became apparent in our study, namely, that multiple seizure foci associated with low-grade gliomas commonly occur in patients with a longer seizure history. This may further support the need to use ECoG during tumor resection in patients with a long-standing seizure disorder to facilitate localization of multiple epileptogenic foci that might have been missed without intraoperative mapping.

In a series of children with structural lesions of the temporal lobe, Drake, *et al.*,[13] described their experience with ECoG-directed resection of seizure foci and emphasized the concept that seizure activity often originates from the brain adjacent to the tumor. Six of their 11 patients were rendered seizure-free with or without antiepileptic drugs, while the remaining patients required antiepileptic drugs to reduce their seizure frequency by 50%. Although post-resection ECoG was used to maximize seizure control, it is unclear if both mesial structures (exposed hippocampus) and lateral temporal lobe cortex were remapped in the Drake study as we did in our patients.

In an earlier report from the Cleveland Clinic Epilepsy Program, Wyllie, *et al.*,[48] using subdural recordings to map areas of seizure activity, documented superior seizure control in patients with "structural" lesions when the extent of the epileptogenic focus resection was complete. Their excellent results were accomplished even when a less than total resection of the mass was completed. The implication from this work is that multiple foci are often present, thus necessitating extraoperative ECoG to augment the tumor resection. Awad, *et al.*,[3] subsequently reviewed many of the same patients, correlating seizure control with the proximity of the epileptogenic focus to the structural lesion, as well as the extent of lesion and focus resection. In essence, the amount of the lesion removed significantly affected postoperative seizure control. Even when the seizure focus was less than completely resected, seizure control was good if the lesion was completely resected. However, if "lesionectomy" was subtotal, seizure control was better when a more aggressive focus resection was carried out. All of the patients in that series continue to require antiepileptic drugs to maintain their level of postoperative seizure control, which is distinctly different from our patient popula-

tion. It may be that our results were positively affected by our reliance on post-resection ECoG, since persistent epileptiform activity following tumor resection has previously been shown to be associated with recurrence of seizures.[19] Other investigators have also utilized a surgical approach that does not include, as part of the resection, multiple recordings following initial tumor and seizure focus removal.[1,18,46] Nonetheless, because low-grade gliomas are often diffuse and difficult to delineate, subtotal tumor resection further supports the need to map independently and fully resect single or multiple epileptogenic areas for optimum seizure control.

Tumor and Adjacent Parenchymal Resection Without Electrocorticography

Whereas some investigators advocate the use of ECoG during tumor resection, there are several published studies that have not utilized this technique as a necessary adjunct to achieve maximum seizure control. In each of these latter series, in addition to removal of the tumor, brain adjacent to the lesion was included in the resection strategy. In an earlier study with this approach by Falconer and Cavanagh,[14] nine of 13 patients harboring tumors with intractable epilepsy became seizure-free, although no mention was made of antiepileptic drugs. The authors stated that their good results were influenced by removal of brain surrounding the lesion, which "interrupted neuronal circuits which were involved in the seizure mechanism." Similarly, Lindsay, et al.,[29] reported two children with low-grade temporal lobe gliomas who became seizure-free following a radical temporal lobectomy including the tumor.

Spencer and colleagues[40] compared the status of 19 patients with gliomas who underwent surgery to remove the mass only with that of patients who had "seizure surgery," defined by the authors as removal of adjacent mesial temporal or frontal lobe brain tissue. All except four patients had follow-up periods longer than 6 months. Every patient who underwent the more extensive procedure had greater than 95% reduction in seizure frequency, compared with approximately 50% of patients with mass resection or biopsy alone who achieved the same results. Although the authors demonstrated better results with seizure surgery, they did not encourage the routine use of monitoring to improve the seizure outcome. Nonetheless, their patients did not have complete relief of seizure activity and no mention was made regarding the need for postoperative antiepileptic drugs. Sperling, et al.,[41] reported an example of minimal tumor resection in the posterior temporal lobe that achieved complete seizure control because anterior, nontumor-involved temporal lobe structures were resected. Nonetheless, that patient required continued antiepileptic drugs to maintain a seizure-free condition.

Tumor Removal Alone

Penfield, et al.,[32] and White, et al.,[47] reviewed patients with astrocytomas who had seizures preoperatively. It is not known whether these patients had intractable epilepsy but, following tumor removal, 85% and 90% of patients, respectively, continued to suffer

seizures. Falconer, et al.,[15] reported two patients with posterior temporal gliomas who became seizure-free following tumor resection without removing adjacent temporal lobe structures. However, one patient continued to require antiepileptic drugs in order to maintain a seizure-free condition. In 1963, Schisano, et al.,[39] described patients with astrocytomas and epilepsy; after resection of the tumor, seizures persisted in 39% of the patients. There was no mention of antiepileptic drugs.

Adults and children with gangliogliomas are particularly susceptible to the development of seizures due to the chronic nature of this particular type of lesion. Three series have addressed seizure control without the use of ECoG following resection of gangliogliomas.[12,26,42] Collectively, 11 of 25 patients were documented as having intractable seizures and six (55%) of these patients were stated to be seizure-free following tumor resection. Two of the three series fail to mention the use of antiepileptic drugs postoperatively. Sutton, et al.,[42] indicated that all of their patients (50% of whom were seizure-free) remained on antiepileptic therapy. Of the nine patients with ganglioglioma in our study, six patients were seizure-free while not taking antiepileptic drugs, two were seizure-free while receiving antiepileptic drugs, and the remaining patient continues to have seizures at a reduced frequency while receiving anticonvulsant therapy.

In a study conducted by Goldring, et al.,[21] regarding seizure control in 40 patients with glial tumors who had a "chronic seizure disorder," ECoG was utilized during tumor resection in only three cases. Information is not provided with reference to the frequency of seizures and the number of antiepileptic drugs used by each patient. Although 82% of these patients were seizure-free following surgery, seven patients had anterior temporal lobectomies, and ECoG was used in three additional patients. Also, 23 patients had temporal lobe tumors that often involved mesial structures, thus implying that lesion resection in this area may have involved portions of the amygdala, hippocampus, and parahippocampal gyrus. No mention is made regarding postoperative use of antiepileptic drugs to maintain the 82% seizure-free status.

In reports by Cascino and coworkers,[9,10] in which computer-assisted stereotactic surgery resulted in the purest form of tumor resection alone without removing adjacent potentially epileptogenic brain, 86% of the 30 patients had reduction in their seizure frequency; however, 97% remained on antiepileptic therapy. The authors concluded that tumor resection alone in a patient with medically refractory epilepsy is often inadequate, as removal of the seizure focus (foci) adjacent to the lesion cannot be accomplished with their surgical technique. Continued use of antiepileptic drugs is usually necessary and, in some patients, an additional operation may be required for persistent epilepsy. Boon, et al.,[7] described 50 patients with structural lesions (38 of them tumors) and intractable epilepsy in which long-term follow-up was available. In their series, the lesion was removed with a "variable amount of surrounding brain" and the extent of resection was apparently determined by "obtaining tumor free margins;" however, the ex-

tent of tumor and adjacent brain resection was not quantified, and the number of margins submitted for analysis and the percentage of those margins with infiltrating tumor were not delineated. In addition, no information based upon the pathological diagnosis of the primary tumor, as it correlated with seizure outcome, was provided. Nonetheless, in the entire group, 83% of the patients were seizure-free without the use of ECoG, although no data were given regarding the requirement of antiepileptic drugs to maintain the reported outcome.

Tumor Removal Without Electrocorticography in Pediatric Patients

A review of the literature failed to disclose similar series of children and adolescents with intractable epilepsy and low-grade gliomas with results comparable to ours when ECoG was not utilized. Blume, *et al.*,[6] reported the best results in seizure control when a "complete" tumor removal was accomplished. Under these circumstances, 87% of the children in their series were seizure-free, whereas only 33% of patients with a partial tumor resection had no further seizure activity. Although the follow-up period was comparable to ours, most of the patients in Blume's series still required antiepileptic drugs, albeit at a "lesser" amount. Rutledge, *et al.*,[38] reported three infants with gliomas involving the temporal lobe (two of which were low grade), who presented with intractable seizures. Following tumor resection without ECoG, all three children became seizure-free (mean follow-up period 6.3 months) but required continuation of antiepileptic drugs.

Goldring[20] summarized his results utilizing extraoperative EEG recording from an epidurally implanted electrode array in 40 children with gliomas (the majority were low grade). Although the patients had "intractable" seizures, no data were provided on the seizure frequency or location of the epileptiform discharges in relation to the tumor. The author stated that the "presumed epileptogenic cortex adjacent to the lesion" was not resected. Seven patients underwent an anterior temporal lobectomy in addition to tumor resection and, in other cases, excision of cortex to "gain access" to the tumor was undertaken. Goldring stated that over 80% of those patients with gliomas who underwent removal of the lesion as previously described had cessation of their seizures. Therefore, it is difficult to know how many patients underwent tumor removal alone. Again, as in other reports, no mention was made of the need for postoperative antiepileptic drugs.

Finally, in a study conducted by Hirsch, *et al.*,[25] 42 children with low-grade astrocytomas and oligodendrogliomas were assessed regarding seizure control without the use of intraoperative ECoG. Preoperative seizures were documented in only 32 of the patients, and 20 of these (62%) were classified as intractable. Virtually all patients had a "macroscopically complete" tumor resection and surrounding cortex was not removed. One difficulty with interpretation of their results is that patients with intractable seizures were not separately analyzed. Nonetheless, 57% of the entire series of children were seizure-free while no longer

receiving antiepileptic drugs; an additional 24% of patients required antiepileptic drugs to remain seizure-free and the remaining children (19%) continued to have seizures despite antiepileptic drugs.

Conclusions

Based upon the experience presented here, we advocate the use of intraoperative ECoG to maximize seizure control with the least likelihood of requiring postoperative antiepileptic drugs in patients with medically refractory epilepsy associated with a low-grade glioma. This is particularly important in children and in any patient with a long-standing seizure disorder, which is usually associated with the finding of multiple epileptogenic foci.

References

1. Ajmone-Marsan C, Baldwin M: Electrocorticography, in Baldwin M, Bailey P (eds): **Temporal Lobe Epilepsy.** Springfield, Ill: Charles C Thomas, 1958
2. Arseni C, Petrovici IN: Epilepsy of temporal lobe tumours. **Eur Neurol 5:**201–214, 1971
3. Awad IA, Rosenfeld J, Ahl J, et al: Intractable epilepsy and structural lesions of the brain: mapping, resection strategies, and seizure outcome. **Epilepsia 32:**179–186, 1991
4. Berger MS, Kincaid J, Ojemann GA, et al: Brain mapping techniques to maximize resection, safety, and seizure control in children with brain tumors. **Neurosurgery 25:**786–792, 1989
5. Berger MS, Ojemann GA, Lettich E: Neurophysiological monitoring during astrocytoma surgery. **Neurosurg Clin North Am 1:**65–80, 1990
6. Blume WT, Girvin JP, Kaufmann JCE: Childhood brain tumors presenting as chronic uncontrolled focal seizure disorders. **Ann Neurol 12:**538–541, 1982
7. Boon PA, Williamson PD, Fried I, et al: Intracranial, intraaxial, space-occupying lesions in patients with intractable partial seizures: an anatomical, neuropsychological, and surgical correlation. **Epilepsia 32:**467–476, 1991
8. Buckingham MJ, Crone KR, Ball WS, et al: Management of cerebral cavernous angiomas in children presenting with seizures. **Childs Nerv Syst 5:**347–349, 1989
9. Cascino GD: Epilepsy and brain tumors: implications for treatment. **Epilepsia 31 (Suppl 3):**37–44, 1990
10. Cascino GD, Kelly PJ, Hirschorn KA, et al: Stereotactic resection of intra-axial cerebral lesions in partial epilepsy. **Mayo Clin Proc 65:**1053–1060, 1990
11. de Lanerolle NC, Kim JH, Robbins RJ, et al: Hippocampal interneuron loss and plasticity in human temporal lobe epilepsy. **Brain Res 495:**387–395, 1989
12. Demierre B, Stichnoth FA, Hori A, et al: Intracerebral ganglioglioma. **J Neurosurg 65:**177–182, 1986
13. Drake J, Hoffman HJ, Kobayashi J, et al: Surgical management of children with temporal lobe epilepsy and mass lesions. **Neurosurgery 21:**792–797, 1987
14. Falconer MA, Cavanagh JB: Clinico-pathological considerations of temporal lobe epilepsy due to small focal lesions. A study of cases submitted to operation. **Brain 82:**483–504, 1959
15. Falconer MA, Driver MV, Serafetinides EA: Temporal lobe epilepsy due to distant lesions: two cases relieved by operation. **Brain 85:**521–534, 1962
16. Falconer MA, Kennedy WA: Epilepsy due to small focal temporal lesions with bilateral independent spike-discharging foci. A study of seven cases relieved by operation.

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J Neurol Neurosurg Psychiatry 24:205–212, 1961

17. Franceschetti S, Binelli S, Casazza M, et al: Influence of surgery and antiepileptic drugs on seizures symptomatic of cerebral tumours. Acta Neurochir 103:47–51, 1990

18. Gibbs FA, Amador L, Rich C: Electroencephalographic findings and therapeutic results in surgical treatment of psychomotor epilepsy, in Baldwin M, Bailey P (eds): Temporal Lobe Epilepsy. Springfield, Ill: Charles C Thomas, 1958, pp 358–367

19. Gloor P: Contributions of electroencephalography and electrocorticography to the neurosurgical treatment of the epilepsies. Adv Neurol 8:59–105, 1975

20. Goldring S: Pediatric epilepsy surgery. Epilepsia 28: S82–S102, 1987

21. Goldring S, Rich KM, Picker S: Experience with gliomas in patients presenting with a chronic seizure disorder. Clin Neurosurg 33:15–42, 1986

22. Gonzalez D, Elvidge AR: On the occurrence of epilepsy caused by astrocytoma of the cerebral hemispheres. J Neurosurg 19:470–482, 1962

23. Haglund MM, Berger MS, Kunkel DD, et al: Changes in gamma-aminobutyric acid and somatostatin in epileptic cortex associated with low-grade gliomas. J Neurosurg 77:209–216, 1992

24. Hanna GR: Morphological changes in primary and secondary epileptic foci, in Mayersdorf A, Schmidt RP (eds): Secondary Epileptogenesis. New York: Raven Press, 1982, pp 115–130

25. Hirsch JF, Sainte Rose C, Pierre-Khan A, et al: Benign astrocytic and oligodendrocytic tumors of the cerebral hemispheres in children. J Neurosurg 70:568–572, 1989

26. Kalyan-Raman UP, Olivero WC: Ganglioglioma: a correlative clinicopathological and radiological study of ten surgically treated cases with follow-up. Neurosurgery 20: 428–433, 1987

27. Kim JH, Guimaraes PO, Shen MY, et al: Hippocampal neuronal density in temporal lobe epilepsy with and without gliomas. Acta Neuropathol 80:41–45, 1990

28. LeRoux PD, Berger MS, Ojemann GA, et al: Correlation of intraoperative ultrasound tumor volumes and margins with preoperative computerized tomography scans. An intraoperative method to enhance tumor resection. J Neurosurg 71:691–698, 1989

29. Lindsay J, Ounsted C, Richards P: Long-term outcome in children with temporal lobe seizures. V: Indications and contra-indications for neurosurgery. Dev Med Child Neurol 26:25–32, 1984

30. Morrell F: Secondary epileptogenesis in man. Arch Neurol 42:318–335, 1985

31. Ojemann G, Ojemann J, Lettich E, et al: Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. J Neurosurg 71:316–326, 1989

32. Penfield W, Erickson TC, Tarlov I: Relation of intracranial tumors and symptomatic epilepsy. Arch Neurol Psychiatry 44:300–315, 1940

33. Piepmeier JM: Observations on the current treatment of low-grade astrocytic tumors of the cerebral hemispheres. J Neurosurg 67:177–181, 1987

34. Pilcher WH, Silbergeld DL, Berger MS, et al: Intraoperative electrocorticography during tumor resection: impact on seizure outcome in patients with gangliogliomas. J Neurosurg 78:891–902, 1993

35. Rasmussen TB: Surgery of epilepsy associated with brain tumors. Adv Neurol 8:227–239, 1975

36. Ribarić I: Excision of two and three independent and separate ipsilateral potentially epileptogenic cortical areas. Acta Neurochir Suppl 33:145–148, 1984

37. Robbins RJ, Brines ML, Spencer DD: Distribution of the somatostatin gene in the hippocampus of patients with temporal lobe epilepsy. Epilepsia 31:624, 1990 (Abstract)

38. Rutledge SL, Snead OC III, Morawetz R, et al: Brain tumors presenting as a seizure disorder in infants. J Child Neurol 2:214–219, 1987

39. Schisano G, Tovi D, Nordenstam H: Spongioblastoma polare of the cerebral hemisphere. J Neurosurg 20: 241–251, 1963

40. Spencer DD, Spencer SS, Mattson RH, et al: Intracerebral masses in patients with intractable partial epilepsy. Neurology 34:432–436, 1984

41. Sperling MR, Cahan LD, Brown WJ: Relief of seizures from a predominantly posterior temporal tumor with anterior temporal lobectomy. Epilepsia 30:559–563, 1989

42. Sutton LN, Packer RJ, Rorke LB, et al: Cerebral gangliomas during childhood. Neurosurgery 13:124–128, 1983

43. Van Buren JM, Ajmone Marsan C, Mutsuga N: Temporal-lobe seizures with additional foci treated by resection. J Neurosurg 43:596–607, 1975

44. Van Buren JM, Ajmone-Marsan C, Mutsuga N, et al: Surgery of temporal lobe epilepsy. Adv Neurol 8:155–196, 1975

45. Wada J, Rasmussen T: Intracarotid injections of sodium amytal for the lateralization of cerebral speech dominance. Experimental and clinical observations. J Neurosurg 17:266–282, 1960

46. Walker AE, Lichtenstein RS, Marshall C: A critical analysis of electroencephalography in temporal lobe epilepsy. Arch Neurol 2:172–182, 1960

47. White JC, Liu CT, Mixter WJ: Focal epilepsy. A statistical study of its causes and the results of surgical treatment. I. Epilepsy secondary to intracranial tumors. N Engl J Med 238:891–899, 1948

48. Wyllie E, Lüders H, Morris HH III, et al: Clinical outcome after complete or partial cortical resection for intractable epilepsy. Neurology 37:1634–1641, 1987

49. Yeh HS, Kashiwagi S, Tew JM Jr, et al: Surgical management of epilepsy associated with cerebral arteriovenous malformations. J Neurosurg 72:216–223, 1990