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Epilepsy Surgery in Young Children With Tuberous Sclerosis Complex: A Novel Hybrid Multimodal Surgical Approach

BACKGROUND: Surgery has become integral in treating children with tuberous sclerosis complex (TSC)–related drug-resistant epilepsy (DRE).

OBJECTIVE: To describe outcomes of a multimodal diagnostic and therapeutic approach comprising invasive intracranial monitoring and surgical treatment and compare the complementary techniques of open resection and magnetic resonance–guided laser interstitial thermal therapy.

METHODS: Clinical and radiographic data were prospectively collected for pediatric patients undergoing surgical evaluation for TSC-related DRE at our tertiary academic hospital. Seizure freedom, developmental improvement, and Engel class were compared.

RESULTS: Thirty-eight patients (20 females) underwent treatment in January 2016 to April 2019. Thirty-five underwent phase II invasive monitoring with intracranial electrodes: 24 stereoencephalography, 9 craniotomy for grid/electrode placement, and 2 grids + stereoencephalography. With the multimodal approach, 33/38 patients (87%) achieved >50% seizure freedom of the targeted seizure type after initial treatment; 6/9 requiring secondary treatment and 2/2 requiring a third treatment achieved >50% freedom. The median Engel class was II at last follow-up (1.65 years), and 55% of patients were Engel class I/II. The mean age was lower for children undergoing open resection (2.4 vs 4.9 years, $P = .04$). Rates of >50% reduction in seizures (86% open resection vs 88% laser interstitial thermal therapy) and developmental improvement (86% open resection vs 83% magnetic resonance–guided laser interstitial thermal therapy) were similar.

CONCLUSION: This hybrid approach of using both open surgical and minimally invasive techniques is safe and effective in treating DRE secondary to TSC. Clinical trials focused on treatment method with longer follow-up are needed to determine the optimal candidates for each approach and compare the treatment modalities more effectively.

KEY WORDS: Craniotomy, Electrocorticography, Laser ablation, Medically refractory epilepsy, Pediatric epilepsy, Stereoelectroencephalography, Tuberous sclerosis

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Fifty-five percent of children with tuberous sclerosis complex (TSC) are burdened with drug-resistant epilepsy (DRE),[1-12] often significantly affecting their neurologic and cognitive development.[1-12] In fact, 80% of children with TSC may experience intellectual disability, and 30% have autism.[13]

ABBREVIATIONS: AED, antiepileptic drug; **DRE,** drug-resistant epilepsy; **EEG,** electroencephalography; **MRgLITT,** magnetic resonance–guided laser interstitial thermal therapy; **SEEG,** stereoelectroencephalography; **SOZ,** seizure onset zone; **TSC,** tuberous sclerosis complex.

Weiner et al[14] proposed that the multiple seizure foci seen in TSC are not contraindicative to surgery because a 3-stage surgical approach offers an alternative. Evidence is growing that early surgical management maximizes long-term seizure control and facilitates cognitive development in toddlers with DRE due to TSC.[15] Thus, surgery has become integral to treating children with TSC-related DRE.[16-19]

Most surgical series of DRE report traditional open craniotomy aimed at resecting the offending cortical tuber and/or the immediate perituber seizure onset zone (SOZ). In recent years, magnetic

resonance–guided laser interstitial thermal therapy (MRgLITT) has been used for ablating epileptogenic foci and disconnecting seizure networks.[20] However, because precise diagnostic efforts are needed to confirm the epileptogenicity of the offending tuber, the use of MRgLITT in TSC has only been recently described.[15,21,22]

We describe our multimodal surgical approach to treating DRE secondary to TSC that incorporates open and stereotactic techniques on a case-by-case basis. We retrospectively report the outcomes of a series of children treated with this uniform multimodal surgical strategy, in which either resection or laser ablation was potentially available to every patient. This is an emerging indication for the systematic use of stereo electroencephalography (SEEG) as a phase II invasive electroencephalography strategy.[23] In a subgroup comparison of the surgical modalities, we hypothesized that minimally invasive and traditional open approaches both achieve good epilepsy control outcomes in selected patients and serve as complimentary techniques in the comprehensive care of DRE in TSC.

METHODS

This retrospective cohort was treated at a tertiary academic referral center from January 2016 through April 2019 by 2 pediatric epilepsy surgeons through the epilepsy center. Institutional review board approval with a waiver of informed consent was obtained. The report was prepared using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

A multidisciplinary epilepsy committee discussed all patients. Phase I factors including neurophysiology, neuroradiology, and anatomic location informed the selection of the modality of invasive electrode placement. Patients had presurgical evaluation with video electroencephalography, neuropsychological testing (when capable), computed tomography, and MRI studies. Positron emission tomography (PET), magnetoencephalography, and additional ictal/interictal single-photon emission tomography were used as needed by committee consensus. Treatment decisions were also made by committee consensus.

Surgical Treatment

All patients were deemed surgical candidates for phase II invasive monitoring by the multidisciplinary committee (Figure 1). Phase II monitoring to decipher whether the epilepsy is network or focus predominant consisted of either open surgical treatment including craniotomy with placement of a combination of subdural grids, strip electrodes, and/or depth electrodes or robot-assisted SEEG lead placement. Generally, if a focus-predominant source was suspected, open craniotomy for electrode placement was chosen as a precursor to likely surgical resection. Similarly, if network predominance was suspected, SEEG was considered a better option as a precursor to ablation. Typically, the tubers themselves are targeted with SEEG electrodes, but if peri-tuberal tissue is highly suggestive,[24] electrodes can also be placed there.

After review of the phase II intracranial electrophysiology among the surgeons and epileptologists, the choice was made to proceed with resection of the epileptogenic zone or seizure focus (tuberectomy and lobectomy) (see Figure 2 for case example) or MRgLITT ablation of the epileptogenic zone (see Figure 3 for case example).

Clinical Variables

Data were collected using a prospectively implemented treatment algorithm, and medical records were examined for preoperative evaluation, perioperative treatment strategy, perioperative and postoperative surgical complications, and outcomes. Clinical variables included age, sex, race, age at first seizure, seizure frequency, initial seizure type, number of preoperative antiepileptic drugs (AEDs), presence of TSC genetic mutation or family history, and presence of global developmental or language delay (delayed milestone achievement reported by family members/pediatric epileptologist assessment).

Surgical variables included method of phase II monitoring and surgical treatment strategy at initial surgery and on each follow-up surgical event.

Outcomes

The primary outcomes were Engel classification and >50% reduction in seizure frequency for the targeted seizure type.[25] Engel[26] class I patients were seizure free or had only nondisabling simple partial seizures; those in class II had a >90% reduction of seizure frequency but still had rare focal-onset impaired awareness seizures; those in class III had a 50% to 90% reduction in seizure frequency; and those in class IV had a <50% reduction in seizure frequency. Seizure frequency was reported by family/pediatric epileptologist before and after surgery.

Secondary outcomes included developmental improvement reported by parents and documented by clinical evaluation, major complication (ie, significant motor deficit or infection requiring reoperation), minor complications (eg, wound complications not requiring reoperation or dermoid cyst), time to secondary or tertiary treatment (if needed), and overall follow-up duration.

Statistical Analysis

Data were descriptively reported as means (±SDs) for continuous variables and counts and frequencies for categorical data. A χ^2 test was performed for all comparisons of categorical variables. A Mann-Whitney U test was performed for ordinal variables (Engel classification). An independent t test was used for mean comparisons. Kaplan-Meier analysis was performed to compare time with retreatment. Statistical analysis was performed using SPSS (IBM).

RESULTS

Baseline Demographics and Phase II Monitoring

Thirty-eight patients (20 female and 18 male; mean age 3.9 years) were included in the cohort (Table 1). The mean age differed between open resection (2.4 years) and MRgLITT (4.9 years) ($P = .04$), and children undergoing resection were younger at first seizure (3.3 vs 6.9 months). Patients undergoing open resection had more frequent daily preoperative seizures (46 vs 19) but were taking a similar number of AEDs (3.2 vs 3.1).

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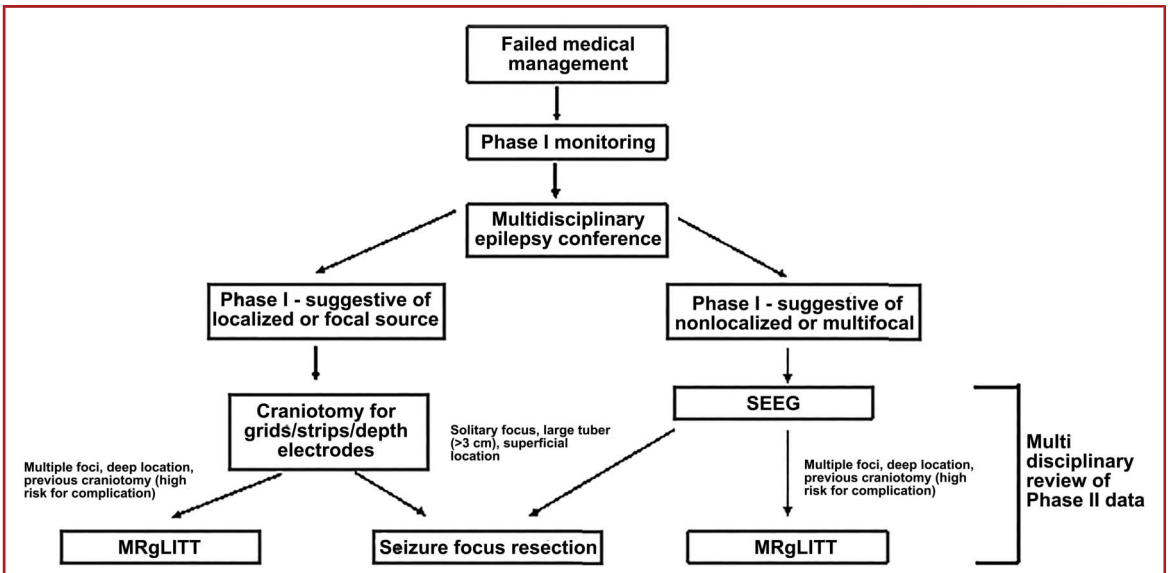

FIGURE 1. *Treatment algorithm based on phase I and II data at our institution. MRgLITT magnetic resonance–guided laser interstitial thermal therapy; SEEG, stereoelectroencephalography.*

Thirty-five (92%) patients underwent phase II invasive monitoring, 2 underwent tuber resection, and 1 underwent MRgLITT without phase II monitoring. Of the 35 patients who underwent phase II monitoring, 9 (26%) underwent craniotomy for grid/electrode placement, 24 (69%) underwent robot-guided SEEG placement, and 2 (6%) had both SEEG and craniotomy for grids/electrodes.

All patients who had craniotomy for phase II monitoring underwent subsequent open resection. All but 1 patient who had SEEG phase II monitoring underwent MRgLITT as a first treatment. The 2 patients who had both SEEG and craniotomy underwent open resection.

Treatment Patterns

Fourteen children underwent open resection and 24 underwent MRgLITT as primary surgical treatment (Table 2). The median number of targets for MRgLITT was 3 (range 2-6). Nine patients underwent a second surgery, and 2 underwent a third surgery (Table 3). Five patients initially treated with MRgLITT required additional treatment: 3 open resection, 1 MRgLITT, and 1 MRgLITT, followed by resection. Four children who underwent open resection required further treatment: 2 MRgLITT, 1 resection, and 1 MRgLITT, followed by resection. There was no significant difference between treatment methods with respect to time to second surgery (410 vs 657 days).

Thirteen patients had prior resective treatment (including 12 craniotomies) at other institutions. Two of the patients had undergone at least 2 previous resections. Ten of the 13 who were treated elsewhere underwent MRgLITT at our institution.

Seizure Outcomes and Complications by Cohort

With the combined multimodal approach including open resection and MRgLITT, 33 patients (87%) achieved >50% seizure freedom of the targeted seizure type after initial treatment, with 6/9 (66%) doing so after secondary treatment and 2/2 (100%) achieving >50% seizure freedom after third treatment. The median Engel class was II, and 55% of patients were Engel class I or II at last follow-up (1.6 years; 57% open resection vs 54% MRgLITT). Rates of >50% reduction in seizures (86% open resection vs 88% MRgLITT), developmental improvement (86% vs 83%, respectively), and reduction in seizure medications (29% vs 38%, respectively) were comparable, with similar rates of minor and major complications (Table 2). Length of stay was significantly lower in the MRgLITT cohort (5.5 vs 3.2 days).

Complications occurred in 12 patients (6 open resection and 6 MRgLITT). Three major complications (all transient hemiparesis that resolved within 1 month) and 3 minor complications (delayed wound healing, superficial fluid collection, and transient hyponatremia) occurred in the open resection cohort. Four major complications occurred in the MRgLITT group: 1 transient hemiparesis that resolved within 1 month; 1 transient hemiparesis that resolved followed by catheter entry-site brain abscess requiring surgical aspiration; 1 asymptomatic intracranial hemorrhage; and 1 seizure that led to death, presumably sudden unexpected death in epilepsy, in a patient who had MRgLITT, followed by open resection. Two minor complications occurred in the MRgLITT cohort: 1 entry-site dermoid cyst not requiring surgery and 1 aseptic meningitis requiring lumbar puncture and steroid therapy.

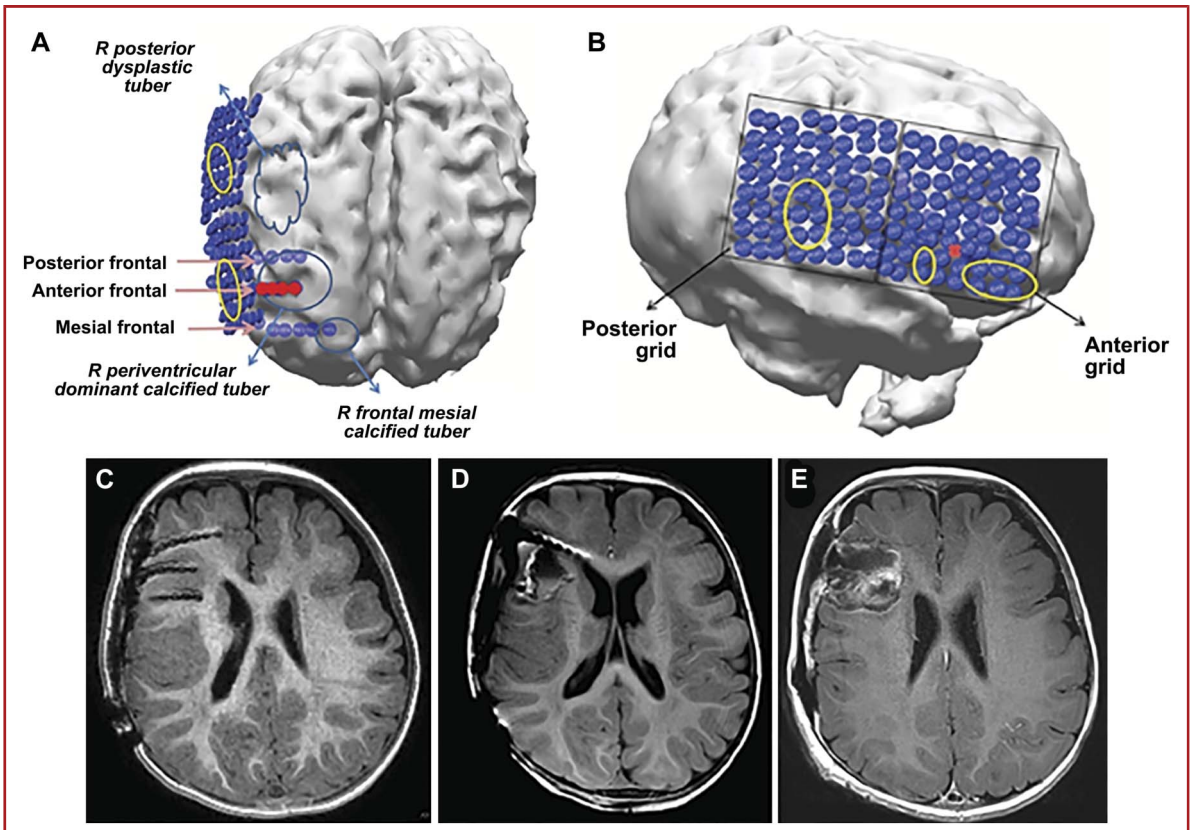

FIGURE 2. *This case illustrates the use of open resection after craniotomy for cortical grid placement in a patient with medically and surgically refractory epilepsy related to TSC. A 10-month-old girl, first diagnosed with TSC 4 months after presenting with seizures and found to have the TSC1 mutation, underwent surgical epilepsy evaluation. Her initial seizures were characterized by eyes rolling up and to the right; these were successfully treated with levetiracetam then vigabatrin for a 3-month period. Atonic seizures then surfaced at a frequency of over 100 per day and proved refractory to 9 medications. The patient had poor seizure control on vigabatrin and topiramate. She had developmental delay, with army crawling at 6 months but no standing by 10 months, and nonspecific "mama" and "dada" speech at 8 months. Her Bayley developmental scale composite score was 85 (low average). A brain MRI showed bilateral multifocal tubers with dominant right frontal periventricular and right frontal dysplastic tubers and tubers in the left occipital lobe, right anterior frontal lobe, right periatrial region, and periventricular white matter of frontal horns. Her phase 1 video EEG monitoring showed seizures arising from right central and right frontocentral regions. Positron emission tomography-computed tomography showed decreased metabolic uptake throughout bilateral cerebral hemispheres, most prominent within the bilateral anterior frontal paramedian lobes and right posterior frontal lobe. Magnetoencephalography showed spikes tightly clustered to the right precentral and central sulci, with rare left temporal spikes localized to the left posterior temporal region and sylvian fissure. Given the concordance between the phase 1 workup and the dominant right frontal tubers, we proceeded with a craniotomy for placement of right frontal cortical grids with depth electrodes in and around the frontal tubers. Phase 2 intracranial electrode monitoring localized seizure onset to the right frontal dominant tuber, with subsequent spread anteriorly and posteriorly. She underwent resection of the right frontal tuber/epileptogenic zone, with reimplantation of the right frontal grid and depth electrodes. She was continued in the hospital for postresection phase 2b monitoring, and additional subclinical seizures were noted. The subclinical seizures were arising from the anterior resection cavity, so she was taken to surgery for resection of the seizure focus around the margin of the first resection cavity, in addition to removal of the intracranial electrodes. She recovered uneventfully and was discharged from the hospital 4 days after her final surgery. After surgery, she was seizure free and was eventually weaned off her seizure medications. She began walking at 18 to 20 months and has good receptive language skill development but significantly delayed expressive language. Overall, she has made significant developmental progress over the 2 years since surgery. At 2-year follow-up, she has remained seizure free off medications. Of note, a recent routine EEG showed frequent spiking activity in the left temporal region, which may be suggestive of a newly developing epileptogenic focus.* **A**, *Superior and* **B**, *lateral views of the intracranial grid and depth electrode placement (blue dots). The ictal onset zone is shown in red, arising from within the right periventricular dominant calcified tuber. The epileptic activity then quickly spreads anteriorly and posteriorly through the right frontal lobe (yellow circles).* **C**, *The pre-resection, postintracranial electrode implantation axial T1-weighted MRI shows the location of the depth electrodes in and around the dominant right frontal periventricular calcified tuber.* **D**, *The phase 2b recording phase after resection of the right frontal periventricular dominant tuber demonstrates the depth electrode passing just anterior to the resection cavity. This electrode recorded multiple subclinical seizures during phase 2b recording and prompted additional resection of epileptogenic tissue.* **E**, *The final postoperative scan, after the additional resection and removal of intracranial electrodes, shows that both the right frontal periventricular tuber and the surrounding epileptogenic tissue were removed to achieve seizure freedom. EEG, electroencephalography; TSC, tuberous sclerosis complex.*

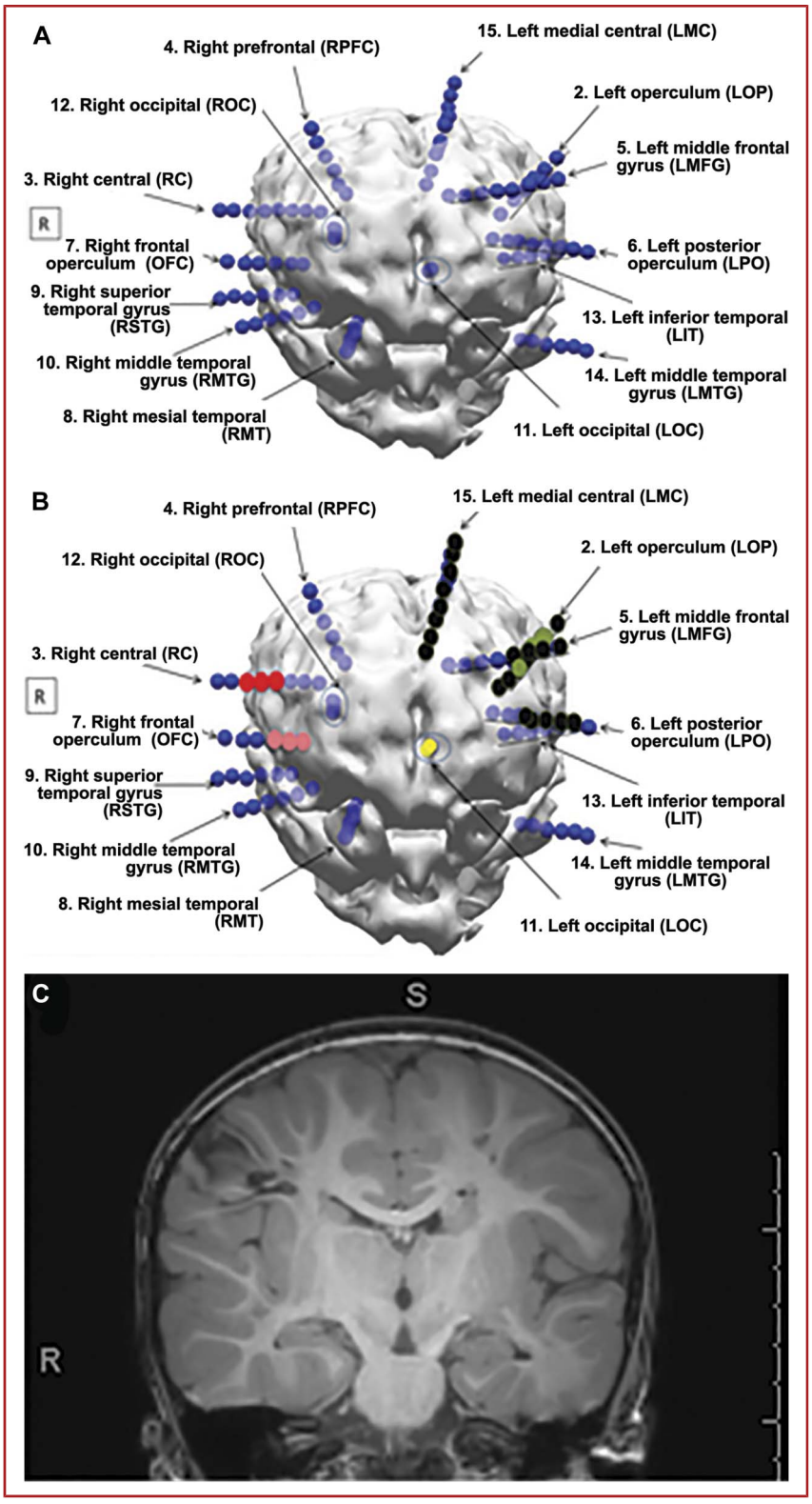

FIGURE 3. *This case illustrates the use of magnetic resonance–guided laser interstitial thermal therapy after SEEG of a patient with medically and surgically refractory epilepsy related to TSC. The patient was a 2-year-old girl with TSC and epilepsy with a history of 2 prior craniotomies for tuberectomy at an outside institution. She had generalized seizures often more than 15 times per day despite her past treatments. After initial evaluation and phase I monitoring, the child was recommended for phase II monitoring. Preoperative EEG, electromyography, MRI, and positron emission tomography were assessed. The initial consensus based on these data supported a right temporal onset of her seizures; however, given the presence of multiple bilateral tubers, the patient was recommended for phase II monitoring with SEEG. Targets for electrode placement were decided by a multidisciplinary team consisting of an epileptologist and neurosurgeon, based on the phase I data.* **A** *and* **B**, *Illustrations showing electrode placements (frontal view).* **A**, *Fifteen depth electrodes were placed, and the patient was monitored for 5 days before a consensus on seizure focus localization.* **B**, *Ultimately, 2 target corridors were identified (in red) based on ictal onset and spread during typical seizure events, 1 in the right central area and 1 in the right frontal operculum.* **C**, *Coronal T1 MRI demonstrating the 2 ablative corridors; there were no perioperative complications, with an adequate ablation of the targets. The patient did well clinically and had complete resolution of her typical seizure, albeit with continued minor seizures. EEG, electroencephalography; SEEG, stereoelectroencephalography; TSC, tuberous sclerosis complex.*

DISCUSSION

Children with TSC-related epilepsy are often neurologically and developmentally devastated by early-onset seizures. Historically, most of these children were not considered surgical candidates because of the multifocality of their disease and difficulty in seizure localization,[1-12,14,16] but Weiner et al[14] demonstrated that many children in this riskier group could have good outcome after epilepsy surgery. Here, we present results from our multimodal surgical approach to treating DRE secondary to TSC. Our approach is personalized to each patient, based on the phase I epilepsy evaluation, and uses either or both open and stereotactic techniques. We believe that this is one of the first and largest series describing this hybrid approach in pediatric patients with TSC. Using these data, we have also compared the use of open resection vs MRgLITT in TSC-related epilepsy in patients selected for each approach. We select patients for either open or minimally invasive strategies based on factors unique to each patient. Hence, the treatment groups are different, with the open resection cohort being younger and having a higher epilepsy burden.

TABLE 1. Baseline Comparison of Demographic and Clinical Information for the Treatment Groups

Variable	Full cohort	Resection	LITT therapy
Mean age (y)	3.9	2.4	4.9
Sex			
Female	20 (52.6%)	11 (73%)	9 (39%)
Male	18 (47.4%)	4 (27%)	14 (61%)
Race			
White	34 (89.5%)	15	19
Asian	2 (5.3%)	0	2
Hispanic	2 (5.3%)	0	2
Mean age of first seizure (mo)	5.52	3.34	6.95
Mean seizure frequency (#/d)	30	46	19
Initial seizure type			
Epileptic spasm	21 (55.3%)	9 (60%)	12 (52%)
Focal motor	7 (18.4%)	4 (27%)	3 (13%)
Bilateral tonic-clonic	4 (10.5%)	0	4 (17%)
Focal behavioral arrest	6 (15.8%)	2 (13%)	4 (17%)
Mean no. of AEDs	3.1	3.2	3.1
TSC mutation	26 (81.3%)	11/12 (92%)	15/20 (75%)
Family history of TSC	2 (5.3%)	1 (7%)	1 (4%)
Global developmental delay	33 (86.8%)	14 (93%)	19 (83%)
Language delay	36 (94.7%)	13 (87%)	23 (100%)

AED, antiepileptic drug; TSC, tuberous sclerosis complex.

The use of MRgLITT is well established in neurosurgery, specifically in epilepsy surgery,[20] but its use in multifocal TSC-related epilepsy has only recently been reported.[15,21,27-30] MRgLITT avoids extensive open surgery—which may promote scar formation that makes reoperations more challenging—and allows for focal treatment of epileptogenic lesions while recognizing that additional treatments may be needed in the future.[20] Other potential advantages include decreased length of stay, less perioperative pain, and lower rates of perioperative complications. In this study, length of stay was lower and seizure outcomes and complication rates were similar.

Previous reports of TSC-related epilepsy treated with tuberectomy or lobectomy carried a 55% to 70% rate of Engel I outcomes.[31-34] In this study, similar rates of good outcomes were achieved in 57% of open resection patients and 54% of patients treated with MRgLITT. These data reveal that the emerging and less invasive option can be chosen in select cases of TSC without inferior seizure outcomes. Further detailed analysis of ablation volume/tumor volume ratios may help better predict seizure outcomes for MRgLITT.[15]

Complimentary Treatment Methods

Previous limitations in treating TSC-related epilepsy included extratemporal location, multifocal onset, bilateral involvement,

TABLE 2. Comparison of Surgical and Overall Outcomes for the 2 Treatment Groups

First treatment	Full cohort (n = 38)	Resection (n = 14)	MRgLITT (n = 24)
Phase II monitoring—Grids craniotomy	9 (26%)	9 (64%)	0 (0%)
Phase II monitoring—SEEG	24 (69%)	1 (7%)	23 (96%)
Phase II monitoring—Grids + SEEG	2 (6%)	2 (14%)	0 (0%)
No phase II monitoring	3 (8%)	2 (14%)	1 (4%)
Length of phase II monitoring (d)	6.7	7.1	6.5
Length of postoperative stay (d)	4	5.5	3.2
Developmental improvement	32 (84%)	12 (86%)	20 (83%)
50% reduction in targeted seizures	33 (87%)	12 (86%)	21 (88%)
Second treatment	**Full cohort (n = 9)**	**Resection (n = 4)**	**MRgLITT (n = 5)**
Phase II monitoring—Grids craniotomy	2 (22%)	2 (50%)	0
Phase II monitoring—SEEG[a]	7 (78%)	2[a] (50%)	5 (100%)
Length of phase II monitoring (d)	6.6	8	7.25
Length of postoperative stay	3.5	4.7	3.2
Developmental improvement	6 (66%)	4 (100%)	2 (40%)
50% reduction in targeted seizures	6 (66%)	4 (100%)	2 (40%)
Time to second surgery (d)	538.4	410	657.3
Third treatment	**Full cohort (n = 2)**	**Resection (n = 2)**	**MRgLITT (n = 0)**
Phase II monitoring—Grids craniotomy	1 (50%)	1 (50%)	0
Phase II monitoring—SEEG	1 (50%)	1 (50%)	0
Developmental improvement	2 (100%)	2 (100%)	0
50% reduction in targeted seizures	2 (100%)	2 (100%)	0
Time to third surgery (days)	7	7	—
Overall outcome	**Full cohort (n = 38)**	**Resection (n = 14)**	**MRgLITT (n = 24)**
Reduction in medication	13 (34%)	4 (29%)	9 (38%)
Minor complication	5 (13%)	3 (21%)	2 (8.3%)
Major complication	7 (18%)	3 (21%)	4 (16%)
Median Engel class at last follow-up	2	2	2
Engel class of I or II	21 (55%)	8 (57%)	13 (54%)
Follow-up time (y)	1.65	1.44	1.77

MRgLITT, magnetic resonance–guided laser interstitial thermal therapy; SEEG, stereoelectroencephalography.
[a]One child underwent second SEEG, but was explanted, then underwent a separate episode of phase II monitoring, followed by resection.

and overlap of functional cortex.[35,36] Our multimodal approach tackles these challenges. Overall, the use of SEEG as a survey technique for lateralizing/localizing the SOZ in TSC is novel and not an original indication. With further experience with SEEG, there is evidence that multiple tubers may form an epileptic network, but specific tubers or "nodes" are primarily responsible for the initiation of discharges; thus, ablation or disruption of these "nodes" is critical in treatment.[15]

The decision-making at our institution stems from evidence from phase I data, specifically indicating whether the seizure pattern is more focal or more diffuse. The presence of a large dominant cortical tuber in a location concordant with seizure semiology and other phase I studies such as positron emission tomography, single-photon emission tomography, and magnetoencephalography generally prompts an open approach. If there is a suggestion of network or the presence of widely distributed cortical tubers without a clear dominant focus (including suspected bilateral SOZs), SEEG phase II invasive monitoring is chosen. The treatment algorithm is presented in Figure 1. As previously demonstrated, retreatment and reoperation are often needed in the setting of TSC-related epilepsy. Both techniques are used in a complimentary fashion as evidenced by reoperation strategies highlighted above (Table 3).

In this cohort study, the patients who initially underwent open resection had more severe epilepsy. Thus, the question arises: Does open resection have a role in very young children who are in "crisis" who may then go on to MRgLITT to fine tune their seizure control at a later point in time? Although we performed a head-to-head analysis in this study, it is a biased comparison given our selection criteria. We did demonstrate, however, that a tailored approach is appropriate, and there are good candidates for both open resection and MRgLITT. Open resection may not be appropriate for all children, just as MRgLITT may not be appropriate for all children.

TABLE 3. Reoperations Among the 38 Children Treated

First surgery	Second surgery	Third surgery
MRgLITT →	Open resection	
MRgLITT →	Open resection	
MRgLITT →	Open resection	
MRgLITT →	MRgLITT →	Open resection
MRgLITT →	MRgLITT	
Open resection →	MRgLITT →	Open resection
Open resection →	MRgLITT	
Open resection →	Open resection	
Open resection →	MRgLITT	

MRgLITT, magnetic resonance–guided laser interstitial thermal therapy.

We chose to define complications as major and minor to examine them in greater detail. The low number of children with sustained long-term weakness in this series is multifactorial. As part of phase II monitoring, when possible, motor mapping is performed to inform surgical decision-making and reduce the risk of long-term motor deficits after surgical treatment. Intraoperative measures taken include motor mapping with direct cortical stimulation and phase reversal if indicated. In addition, previous evidence has shown that tubers are likely nonfunctional[37]; therefore, local tissue is of more concern than the lesion with respect to complication avoidance.

Limitations

Although this direct comparison of open resection and MRgLITT sheds light on the potential for multimodal treatment and enhances our knowledge about the use of MRgLITT in this population, there are limitations. The open resection cohort was younger than the MRgLITT cohort. Patients undergoing open resection had a higher average rate of daily preoperative seizures but were taking a similar number of AEDs, which might indicate that they were more severely affected preoperatively. The nature of TSC-related epilepsy is atypical when compared with lesional epilepsy; thus, recurrent seizures and the need for retreatment are important metrics. In addition, many children with TSC will have developmental delay despite seizure control. We measured global developmental delay based on milestone achievement; this subjective measure could be improved with formal neuropsychological testing, which was not available in this study. Similarly, the 50% improvement is a subjective measure based on parents' report and neurology evaluation, which are both nonquantitative and subject to bias. The primary outcomes were collected based on the available follow-up and not at uniform time points.

The location of tubers and seizure foci may also determine the treatment decision and potential for seizure freedom and must be considered. We encourage all centers to make decisions based on individual phase I monitoring and surgeon/center experience in a multidisciplinary fashion. Further prospective, randomized investigation of techniques to treat TSC-related epilepsy is warranted. Further details regarding MRgLITT seizure outcomes for TSC and the relationship to size, enhancement pattern, and calcification are also needed. This report is the product of the experience and technical capabilities of the mutlidisciplinary epilepsy team at our center and may not be generalizable to other centers.

CONCLUSION

Surgical intervention is critical in the modern treatment of TSC-related epilepsy. We propose that a hybrid approach of open surgical and stereotactic techniques is effective and safe in treating this disease. Ultimately, surgical treatment of TSC-related epilepsy requires an iterative, systematic schema, given the changes in seizure patterns over time and the high propensity for retreatment. Although we have used MRgLITT and open surgery in a complimentary fashion in this study, more long-term follow-up and clinical trials focused on the treatment method are needed to determine the optimal candidates for either approach and compare the treatment modalities more effectively.

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