# Surgical management of medically refractory epilepsy due to early childhood stroke

## Clinical article

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*Object.* The risk of developing epilepsy after perinatal stroke, hypoxic/ischemic injury, and intracerebral hemorrhage is significant, and seizures may become medically refractory in approximately 25% of these patients. Surgical management can be difficult due to multilobar or bilateral cortical injury, nonfocal or poorly lateralizing video electroencephalography (EEG) findings, and limited functional reserve. In this study the authors describe the surgical approaches, seizure outcomes, and complications in patients with epilepsy due to vascular etiologies in the perinatal period and early infancy.

*Methods*. The records were analyzed of 19 consecutive children and adults with medically refractory epilepsy and evidence of perinatal arterial branch occlusions, hypoxic/ischemic insult, or hemorrhagic strokes, who underwent surgery at the Comprehensive Epilepsy Center of Beth Israel Medical Center and St. Luke's-Roosevelt Hospital Center. Preoperative findings including MRI, video EEG, functional MRI, and neuropsychological testing were analyzed. The majority of patients underwent staged operations with invasive mapping, and all patients had either extra- or intraoperative functional mapping.

*Results*. In 7 patients with large porencephalic cysts due to major arterial branch occlusions, periinsular functional hemispherotomy was performed in 4 children, and in 3 patients, multilobar resections/disconnections were performed, with 1 patient undergoing additional resections 3 years after initial surgery due to recurrence of seizures. All of these patients have been seizure free (Engel Class IA) after a mean 4.5-year follow-up (range 15–77 months). Another 8 patients had intervascular border-zone ischemic infarcts and encephalomalacia, and in this cohort 2 hemispherotomies, 5 multilobar resections/disconnections, and 1 focal cortical resection were performed. Seven of these patients remain seizure free (Engel Class IA) after a mean 4.5-year follow-up (range 9–94 months), and 1 patient suffered a single seizure after 2.5 years of seizure freedom (Engel Class IB, 33-month follow-up). In the final 4 patients with vascular malformation-associated hemorrhagic or ischemic infarction in the perinatal period, a hemispherotomy was performed in 1 case, multilobar resections in 2 cases, and in 1 patient a partial temporal lobectomy was performed, followed 6 months later by a complete temporal and occipital lobectomy due to ongoing seizures. All of these patients have had seizure freedom (Engel Class IA) with a mean follow-up of 4.5 years (range 10–80 months). Complications included transient monoparesis or hemiparesis in 3 patients, transient mutism in 1 patient, infection in 1 patient, and a single case of permanent distal lower-extremity weakness. Transient mood disorders (depression and anxiety) were observed in 2 patients and required medical/therapeutic intervention.

*Conclusions*. Epilepsy surgery is effective in controlling medically intractable seizures after perinatal vascular insults. Seizure foci tend to be widespread and rarely limited to the area of injury identified through neuroimaging, with invasive monitoring directing multilobar resections in many cases. Long-term functional outcomes have been good in these patients, with significant improvements in independence, quality of life, cognitive development, and motor skills, despite transient postoperative monoparesis or hemiparesis and occasional mood disorders. (*http://thejns.org/doi/abs/10.3171/2014.3.PEDS13440*)

KEY WORDS • perinatal • stroke • porencephalic • electrocorticography • epilepsy • vascular disorders

**S** TROKE is the most common cause of acquired disability worldwide,<sup>8</sup> and vascular disease is the most common documentable cause of seizures.<sup>32</sup> Strokeassociated symptomatic seizures carry a much higher risk

Abbreviations used in this paper: AED = antiepileptic drug; EEG = electroencephalography; fMRI = functional MRI; MCA = middle cerebral artery; mRS = modified Rankin Scale; MTS = mesial temporal sclerosis; PCA = posterior cerebral artery.

of subsequent epilepsy and correlate with higher mortality rates than do seizures due to nonvascular insults such as traumatic brain injury or CNS infection.<sup>21</sup> While children are rarely affected by ischemic, embolic, or hemorrhagic stroke, up to two-thirds of patients who experience perinatal infarction will eventually develop epilepsy, and in 25% of these cases, the seizures will be medically intractable.<sup>13,16,25</sup>

Epilepsy surgery in children is safe and effective and can provide substantive gains in quality of life and developmental milestones,<sup>15,36</sup> but in general, it remains an underutilized treatment modality for multiple reasons, including but not limited to historical prejudice, practitioner bias, and parental concern over loss of functional capability.<sup>9,12,19,29</sup> While significant experience has been gained in the surgical treatment of childhood epilepsy secondary to malformations of cortical development and benign tumors, very little has been reported focused on stroke or other vasculogenic causes in children.<sup>7,11,28</sup> In this paper, to demonstrate the safety and efficacy of epilepsy surgery in this population, we describe our series of patients who experienced medically refractory epilepsy due to perinatal infarction and/or hemorrhage, and underwent surgery.

#### **Methods**

#### Record Review

A confidential database of more than 1500 patients with epilepsy treated at the Comprehensive Epilepsy Center of Beth Israel Medical Center and St. Luke's-Roosevelt Hospital Center was searched for cases of medically refractory epilepsy related to early childhood vascular insult. Departmental procedure logs and neurology clinic records were also subsequently reviewed. This retrospective record review received exempt status from the joint Institutional Review Board of St. Luke's-Roosevelt Hospital Center and Beth Israel Medical Center, with waiver of patient consent, because only nonidentifiable data that could not be linked to the patients were collected.

#### Study Population

Nineteen consecutive patients with medically refractory epilepsy and perinatal vasculogenic etiology were identified through a combination of database and departmental surgery log searches. All 19 patients had been referred for surgical evaluation and underwent epilepsy surgery between 2005 and 2012. Although the number of patients identified is consistent with previously reported rates of perinatal stroke and the prevalence of epilepsy in that population,<sup>16,33</sup> it is possible that our search failed to identify all cases of neonatal vascular insult among nonsurgical patients with medically refractory epilepsy. This may be partially due to the requirement to correctly classify seizure disorders in the clinical coding system, with less emphasis on comorbidities. Others have reported similar limitations of searches based on ICD-9 (International Classification of Diseases, Ninth Edition) codes in identifying childhood stroke patients.<sup>17</sup> Our sample did not include any patients with germinal matrix hemorrhage and/or intraventricular hemorrhage associated with prematurity or patients with diffuse anoxic injury,

consistent with prior categorizations of children affected by neurovascular insults<sup>13</sup> not associated with traumatic brain injury.<sup>13,14,16</sup> Of note, vascular insult was the single identifiable pathology in all patients in this study and family history was noncontributory in all cases.

#### Data Collection

Patient demographics, including age, sex, seizure semiology, duration of epilepsy, and disability status at presentation were documented and are detailed in Table 1. The degree of disability or dependence in daily activities was assessed using the modified Rankin Scale (mRS) for stroke patients, adapted to evaluate children as well as adults, and scored as follows: no symptoms at all (0); able to carry out all usual activities despite symptoms, normal development (1); unable to carry out all activities but has age-appropriate independence and no reduction in gross motor skills (2); requiring some help but able to walk without assistance, reduction of 1 level in gross motor skills in younger children (3); unable to walk without assistance but able to attend to own bodily needs, or reduction of at least 2 levels in motor skill development (4); and bedridden, incontinent, requiring constant care (5).<sup>5,37</sup> Seizure category was assigned based on the updated International League Against Epilepsy classification,<sup>4</sup> or for patients evaluated prior to the revision of guidelines, retrospectively classified using current terminology. Medically refractory epilepsy has been defined as epilepsy resistant to two separate singleagent antiepileptic drugs (AEDs),<sup>30,31</sup> but in all cases in our series, multiple single and multiple polytherapy drug trials had been attempted prior to surgery.

All patients underwent preoperative evaluation using high-resolution MRI, including fine-cut sequences through the temporal lobes and other regions of interest. Functional MRI (fMRI) was performed in some patients, as was age-appropriate neuropsychological testing. Functional MRI was conducted using Boston naming and passive word listening tests for delineation of putative Broca's and Wernicke's areas, as well as tactile stimulation for assessments of rolandic areas. On occasion, tractography was performed (Case 7). Sodium amytal (Wada) testing was occasionally but not routinely performed. Video electroencephalography (EEG) monitoring was conducted in all cases, and in 16 of the 19 patients, intracranial grid and strip electrodes were surgically implanted<sup>15</sup> for more comprehensive seizure mapping with electrocorticography and the advantage of extraoperative functional mapping with stimulation.

Postoperative seizure outcomes were evaluated using the Engel classification system.<sup>10,39</sup> Functional outcomes were assessed based on a combination of neuropsychological evaluations (7 patients), Quality of Life in Epilepsy questionnaires completed by families (7 patients), and reports of patient/parent-perceived postsurgical improvements collected during follow-up evaluations (all patients). Documented improvements in cognition, child's behavior, and quality of life were scored as "++," while a score of "+++" was used to indicate a life-changing functional outcome, such as the ability to walk without support in a teenager who was wheelchair bound prior to surgery, or the ability to live independently in an adult

	Age at Op	Duration of	Disability					- - -
5	s), sex	Epilepsy	Status	sz semiology	MIKI FINAINGS	VIGEO EEG	Invasive Monitoring	surgical Ireatment
	9, F	5 yrs	ო	focal motor, rapidly evolving to bilat convulsive Sz	It MCA distribution; porence- phalic cyst sparing tem- poral lobe	lt frontal, temporal, & parasagittal spikes	ictal & interictal multifocal It spikes	It functional hemispherotomy
÷.	25 (15 mos), M	14 mos	4	focal motor, rapidly evolving to bilat convulsive Sz	rt MCA occlusion, rt central porencephalic cyst	near continuous rt hemi- spheric spiking	involvement of entire rt hemi- sphere w/ electrodecre- ment; no focal onset	rt functional hemispherotomy
	11, M	4 yrs	<b>с</b>	focal motor, rapidly evolving to bilat convulsive Sz	It MCA occlusion, It parieto- occipital porencephalic cyst, It MTS	It posterior parietooccipi- totemporal onset	It occipital ictal onset w/ temporal & parietal pro- gression	It temporal & partial occipital Iobectomy
	35, F	34 yrs	ო	focal motor, rapidly evolving to bilat convulsive Sz	rt MCA branch occlusion, rt frontoparietal porence- phalic cyst, rt MTS	rt frontotemporal onset	ictal onset & interictal spikes (rt mesial temporal) w/ rapid frontal spread	rt temporal & partial frontal Iobectomy
	16, M	6 yrs	<del></del>	focal motor, rapidly evolving to bilat convulsive Sz	It PCA CVA, It parietooccipi- tal porencephalic cyst	It parietal & occipital onset; It temporal onset	It occipital & lat temporal ictal onset; It mesial temporal	It lat occipital & temporal resec- tion, It temporal lobectomy
	12, M	12 yrs	4	focal motor, evolving to bilat convulsive Sz	large porencephaly, It MCA territory	diffuse It-sided onsets	none	It functional hemispherotomy
	7, F	4 yrs	ო	focal motor, rapidly evolving to bilat convulsive Sz	rt MCA branch, rt porence- phalic cyst	rt parietooccipital; rt frontal	none	rt hemispherotomy
	15, M	6 yrs	7	focal motor, rapidly evolving to bilat convulsive Sz	It parietooccipital infarct, It parietooccipital encepha- lomalacia, rt superior parietal encephalomalacia	It parietooccipital spikes	ictal onset in It mesial pari- etooccipital region; inter- ictal: lat temporooccipital spikes	It parietooccipital & inferior tem- poral resection
	12, M	12 yrs	7	focal motor, rapidly evolving to bilat convulsive Sz	bilat parietooccipital infarcts, bilat parietooccipital encephalomalacia (rt > lt)	rt temporoparietooccipital spike/wave, most pro- nounced at occipital pole	lat temporal, suboccipital & posterior parietooccipi- tal ictal onsets; no mesial epileptiform discharges	rt lat temporal resection, pari- etooccipital disconnection
	11, M	2 yrs	~	focal motor, rapidly evolving to bilat convulsive Sz	bilat parietal infarcts, bilat parietal encephalomalacia	rt occipital onset	ictal onset in superior pari- etal lobule	rt focal resection superior pari- etal lobule
	17, F	17 yrs	4	focal motor, rapidly evolving to bilat convulsive Sz	It temporoparietal infarct, bilat encephalomalacia	It temporoparietal onset	It frontotemporal ictal onset	It temporal lobectomy, It frontal disconnection
	12, M	11 yrs	ი	focal motor, rapidly evolving to bilat convulsive Sz	rt frontoparietal operculum stroke	rt frontoparietal onsets	rt hemisphere	rt hemispherotomy
	12, M	12 yrs	4	focal motor w/ dyscognitive features, evolving to bilat convulsive Sz	It frontotemporoparietal in- farcts	It frontotemporal onsets	It temporal, parietooccipital ictal onsets	It temporal lobectomy, It poste- rior quadrantectomy
	19, M	17 yrs	-	focal motor, rapidly evolving to bilat convulsive Sz	It occipital infarct	It temporooccipital onsets	It temporal, occipital ictal onsets	It temporooccipital disconnec- tion
								(continued)

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Surgical Treatment	hemispherotomy	mpletion of It temporal lo- bectomy & occipital lobec- tomy (following initial lat temporal resection)	temporal lobectomy, partial frontal & occipital resection	lobectomy	functional hemispherotomy	srebrovascular accident; Sz =
Invasive Monitoring	diffuse rt-sided onsets rt	It mesial temporal & oc- cc cipital ictal onsets	rt frontal, temporal, & basal rt occipital ictal onsets	It mesial temporal onsets It I	none (preceded by bilat It i strips as separate procedure)	surgery are given. CVA = CVA o
Video EEG	bilat spikes w/ probable rt- sided onsets	occipital spiking; postictal It central slowing, status post It anterior temporal lobectomy	rt frontotemporal spikes/ sharps	bilat temporal onsets	It frontotemporal onsets	II details of the most recent s
MRI Findings	rt hemispheric atrophy	It temporal hemorrhagic CVA, It temporal porence- phalic cyst	rt temporal hemorrhagic CVA, rt temporal poren- cephalic cyst, rt occipital atrophy	It MTS, occipital atrophy	It temporoparietooccipital encephalomalacia	res are in parentheses, and fu
Sz Semiology	focal motor, evolving to bilat convulsive Sz	focal motor, rapidly evolving to bilat convulsive Sz	focal motor, rapidly evolving to bilat convulsive Sz	focal motor, occasionally evolving to bilat convulsions	focal motor, occasionally evolving to bilat convulsions	rations (see text), prior procedu
Disability Status†	4	ი	7	-	б	ultiple oper
Duration of Epilepsy	10.5 yrs	1 yr	7 yrs	12 yrs	4 yrs	underwent m
Age at Op (yrs), Sex	11, M	Ч Т	8, M	16, M	8, Э	atients who
Case No.	15	16	1	18	19	* For p

TABLE 1: Patient demographics, preoperative findings, and surgical approaches\* (*continued*)

Childhood stroke and epilepsy surgery

seizure. † Disability status was scored from 0 (no symptoms) to 5 (bedridden), following the mRS scale (see *Methods*).

who had been dependent on his or her parents while suffering from medically refractory epilepsy (Table 2).

#### Results

#### Cases 1-7

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Of the 19 patients identified with vasculogenic epilepsy, 7 had large middle cerebral artery (MCA) occlusions resulting in porencephalic cysts without any evidence of intracranial hypertension (Table 1, Cases 1-7; Fig. 1A). In these patients, ages at the time of surgery ranged from 15 months to 35 years (median age 11 years), with equal distribution between the sexes. Duration of epilepsy represented the majority of the patient's life in most cases; one exception was a teenager (Case 5) with a previously unrecognized porencephalic temporoparietooccipital cyst, who developed seizures after puberty and came to surgery after 3 years of medically refractory epilepsy. Seizure semiology predominantly consisted of focal motor seizures, with good video EEG correlates in all 7 cases. Functional MRI results proved useful in providing expected functional information in all cases except one (Case 7), in which tractography suggested robust corticospinal projections from the stroke-affected side and created concern over functional loss that did not materialize after hemispherotomy.

Staged epilepsy surgery was performed in most of these patients, with implantation of grid and strip electrodes in 4 patients, and 2 operations without chronic recordings separated by 3 years in the fifth patient. Onestage hemispherotomy was performed in the other 2 patients. Stage II operations, with removal of grid/strip electrodes, involved functional hemispherotomies in 2 patients. In the remaining 3 patients, multilobar resections, including temporal lobectomy and amygdalohippocampectomy, were combined with frontal or occipital neocortical resections; in each of these cases, preoperative function and age precluded hemispherotomy. All patients in this subgroup are seizure free with Engel Class IA outcomes at a mean follow-up of 53 months (range 15-77 months; Table 2). One patient (Case 5) underwent 2 separate staged surgeries, 3 years apart (see Illustrative Case below). Two patients in this subgroup experienced postoperative mood disorders (depression in Case 4 and anxiety in Case 5) that resolved with outpatient therapy. There were no long-term complications in these patients. An illustrative case from these cases is presented below.

#### Illustrative Case (Case 5)

This 13-year-old boy presented with 3 years of seizures that involved staring spells and automatisms ending in tonic movements of the right upper extremity, coupled

Case No.	Engel Class*	Follow-Up Duration (mos)	AEDs	Functional Improvement†	Disability Status‡
1	IA	72	none	+++	3
2	IA	75	none	+++	3
3	IA	74	monotherapy	+++	2
4	IA	77	none	+++	3
5	IC	34	polytherapy	+++	0
	IA	36			
6	IA	15	polytherapy	+++	3
7	IA	22	monotherapy	+++	2
8	IA	66	monotherapy	+++	3
9	IA	67	monotherapy	+++	1
10	IA	94	none	+++	1
11	IB	33	polytherapy	++	4
12	IA	32	monotherapy	+++	3
13	IA	50	monotherapy	++	4
14	IA	9	monotherapy	+++	0
15	IA	70	none	+++	3
16	IVA	6	monotherapy	++	3
	IA	80			
17	IA	68	monotherapy	+++	2
18	IA	57	monotherapy	+++	0
19	IA	10	polytherapy	++	3

\* At a mean of 53 months of follow-up, all patients have had excellent seizure control with associated behavioral improvement.
† Functional outcomes were measured with parental/patient report and neuropsychological assessments. Mild to moderate improvements in cognition, behavior, and quality of life were considered "significant" (++); "marked" improvement (+++) reflected life-changing gains in degree of independence, in addition to improvements in cognition, behavior, and/or quality of life (see *Methods*).
‡ Disability status at indicated follow-up times was scored from 0 (no symptoms) to 5 (bedridden), following the mRS scale (see *Methods*).



Fig. 1. Images demonstrating a surgical target remote from the area of vascular insult in Case 5. A: Preoperative coronal MR image showing a porencephalic cyst. B: Exposure of porencephaly and surrounding cortex. C: Placement of electrodes with complete coverage of the area of vascular insult. D: Partial left temporal and lateral occipital lobectomy.

with behavioral problems that were characterized as being consistent with anger outbursts. Ictal events were occurring on average two times per week, and were refractory to therapeutic doses of levetiracetam, carbamazepine, and valproic acid. Magnetic resonance imaging at presentation revealed a previously unrecognized porencephalic cyst in the left occipital lobe consistent with a perinatal posterior cerebral artery (PCA) stroke (Fig. 1A). Visual field testing confirmed a right superior quadrantanopsia, and neuropsychological testing showed normal intelligence and fluctuations in attention and working memory. Video EEG suggested parietooccipital onsets in the region of the porencephaly. The patient presented for staged surgery with implantation of grid and strip electrodes, and invasive monitoring disclosed lateral posterotemporal and occipital interictal discharges and ictal onsets. Of note, there were no interictal or ictal electrographic signatures in the area immediately adjacent to the porencephalic cyst. The patient underwent a lateral temporooccipital neocortical resection, and enjoyed an improvement in seizure control and behavior without further visual field compromise. Seizures recurred after 18 months, and the patient underwent a staged reoperation (Fig. 1B and C), which now demonstrated mesial temporal onsets that had not been observed at the initial intervention despite mesial temporal electrode coverage. After further left anterior temporal lobectomy and amygdalohippocampectomy (Fig. 1D), the patient has been seizure free (after 36 months of follow-up) on a reduced AED regimen, and has completed 3 years of college.

## Cases 8–15

Another 8 patients had ischemic infarction affecting the border zone of two arterial territories or encephalomalacia presumed to be from a known early vascular in-

sult. Seven males and 1 female were included, ranging in age from 11–19 years (Table 1, Cases 8–15; Fig. 2). The duration of epilepsy involved most of each patient's life in all except 1 case, in which a 2-year duration of seizures was observed in an adolescent, and a workup disclosed previously unrecognized bilateral infarcts. Three of the 8 patients in this group had MRI evidence of bilateral infarcts in interarterial border-zone regions, and in all patients more than 1 lobe was involved in the vascular injury. All 8 patients underwent invasive monitoring, and in 5 of the 8, video EEG failed to pinpoint the epileptogenic zone when compared with intracranial recordings. Multilobar resections were performed in 4 patients, and hemispherotomies were performed in 2 patients (Cases 12 and 15). The patient in Case 12 had a small infarction of the right opercular region with widespread multilobar seizure onsets (Fig. 2). Only 1 patient underwent a resection limited to the region of the infarct area. All 8 patients have had Engel Class I outcomes (7 with Class IA, 1 with Class IB) at a mean follow-up of 53 months (range 9-94 months; Table 2). Immediate postoperative outcomes in this group included transient monoplegia of the right lower extremity, leading to a permanent distal lower extremity weakness in a patient whose epileptogenic zone included the medial bank of the primary sensory cortex in the setting of a contralateral, mirror-image, watershed infarct. At 6 months postoperatively, the patient was able to walk with a brace, and at 5 years postoperatively he ambulates with the assistance of an ankle-foot orthosis and a cane. Three other patients with hemispherotomy or multilobar resections/disconnections had transient weakness (Cases 11 and 12) and Gerstmann syndrome (Case 14) that fully resolved between 3 and 6 months after surgery. Another patient in this group had a positive culture (Staphylococ-



Fig. 2. Coronal MR image in Case 12, who suffered a perinatal ischemic infarct in the right parietal operculum. Despite the limited regional injury, invasive monitoring demonstrated widespread seizure onsets, and given the patient's preoperative functional capabilities, a right periinsular functional hemispherotomy was performed.

*cus aureus)* that was treated with intravenous antibiotics for 8 weeks, without subsequent osteomyelitis. An illustrative case from these cases is presented below.

## Illustrative Case (Case 9)

This 12-year-old boy presented with bilateral infarcts of the parietal lobes, more extensive on the right side. Video EEG suggested right temporal onsets, but because of bilateral vascular injury, the patient underwent placement of a strip electrode covering the left parietal encephalomalacia, in addition to a grid and strip electrode montage over the right hemisphere, to determine if independent epileptiform discharges arose from the contralateral area of injury. Invasive monitoring demonstrated right parietooccipital onsets with rapid spread to the lateral temporal lobe, and thus a right temporoparietooccipital resection/ disconnection was performed with resultant seizure freedom (after 67 months of follow-up), independence, and behavioral, cognitive, and psychosocial improvement.

## Cases 16-19

Four other patients had epilepsy associated with hemorrhage resulting from vascular malformations, including 2 males and 2 females, ranging in age from 6 months to 16 years (Table 1, Cases 16-19). Etiologies included a vein of Galen malformation in a patient who experienced a treatment-related subarachnoid and intraventricular hemorrhage in the neonatal period. In this patient, MRI revealed diffuse brain atrophy and left hippocampal atrophy. Another patient had a giant PCA aneurysm that ruptured and was treated with endovascular intervention in the neonatal period, with subsequent right temporal encephalomalacia, right mesial temporal sclerosis (MTS), and right occipital cortical atrophy. The third patient in this group had a left temporal arteriovenous malformation that ruptured and was removed at another center at 3 months of age, and MRI revealed left anterior temporal encephalomalacia. In the fourth patient, an arteriovenous malformation encompassing the left parietal and occipital lobes ruptured at 4 months of age and was treated with serial embolization and surgery, with resultant extensive parietooccipital encephalomalacia. Invasive monitoring results were not in full agreement with video EEG findings in all 3 patients who had intracranial recordings. In the patient with the vein of Galen malformation, EEG showed bitemporal interictal signatures and ictal onsets, and therefore bilateral strip electrodes were placed initially. Left temporal onsets were disclosed and the patient underwent a dominant temporal lobectomy with amygdalohippocampectomy. The patient with the previously ruptured PCA aneurysm had a normal sensorimotor examination, and while invasive monitoring disclosed multilobar involvement, he was not a candidate for hemispherotomy. Therefore, a frontal, temporal, and occipital resection was performed. In the patient with a history of left temporal cavernous malformation rupture (Case 16), an initial limited resection of the temporal lobe resulted in only short-term seizure freedom, despite invasive mapping that pointed to lateral temporal onsets. She returned to surgery with subdural electrodes 6 months later, where

a more extensive temporal lobectomy and occipital resection were performed. In the final patient with extensive left hemispheric change due to the large arteriovenous malformation and prior surgery, a hemispherotomy was performed by frontal disconnection and residual callosal section in a single stage. All patients are seizure free after a mean follow-up of 54 months (range 10–80 months, Table 2). A single adverse outcome in this group occurred in Case 19, involving transient mutism that resolved within 3 months. An illustrative case from these cases is presented below.

## Illustrative Case (Case 17)

This 8-year-old boy presented with medically refractory seizures of 7 years' duration, with intact sensorimotor function. He had a history of a large perimesencephalic arteriovenous fistula that had bled early in the neonatal period, and treatment with endovascular coils. Magnetic resonance imaging showed anterior temporal encephalomalacia, mesial temporal atrophy, and occipital lobe atrophy, consistent with right PCA stroke. Video EEG showed diffuse right-sided onsets. Upon implantation, multilobar involvement, including frontal, temporal, and occipital epileptiform abnormalities, were observed. A multilobar resection was performed, including an orbitofrontal topectomy, a formal temporal lobectomy that included a hippocampectomy, and a basal occipital resection. A hemispherotomy was precluded due to normal rolandic function. The patient remains seizure free after 68 months of follow-up and has made significant gains in cognitive functions and learning ability.

## Discussion

In a series of patients with medically refractory epilepsy associated with vascular insults early in life, we provide evidence that surgery can produce successful long-term outcomes. Given the challenges associated with bilateral areas of injury, potentially reduced functional reserve, widespread seizure foci, and frequent lack of direct correlation between extent of lesion and the epileptogenic zone, we believe that invasive evaluation gives the most complete and thorough delineation of the epileptogenic zone, improving the sensitivity and specificity of surgical intervention<sup>2</sup> in this etiology without an increase in morbidity.

Options for treatment in these patients include a limited resection of the scar around the porencephalic cyst. Such "uncapping" was reported in a series of patients from Koch and Krähling, who described a series of 37 patients who underwent fenestration of their porencephalic cysts and communication with the lateral ventricles, which the authors postulated "reduce[s] epileptogenic irritation to the surrounding structures," resulting in seizure freedom in 23 (62%) of their cases.<sup>27</sup> While one might predict that the epileptogenic tissue would be confined to the damaged, penumbral region, patients in our series often showed seizure onsets remote from the penumbra of the porencephaly (Cases 1–5 and 7) or lobe involved in an area of ischemic stroke (Cases 8, 9, and 11–14) or prior vascular injury (Cases 16–19). In Case 12, the area

of damage was small but the distribution of the epileptogenic zone was widespread, suggesting that early injury of integral regions such as the mesial temporal structures or the insular and frontoparietal opercular regions (Fig. 2) results in the disruption of a widespread neural network and the kindling of multiple epileptogenic regions. The understanding that MTS occurs remotely from prior areas of infarction and is involved in the epileptic network contributing to medically intractable epilepsy is well recognized.<sup>5,18,19</sup>

Hemispherotomy certainly circumvents the problem of widespread epileptogenic networks in the setting of early vascular injury and is one of the most effective forms of epilepsy surgery across all etiologies, with seizure freedom rates as high as more than 90%.<sup>1,35,36</sup> Hemispheric disconnection/anatomical resection has been the mainstay of surgical therapy for large perinatal porencephalic cysts after MCA stroke.<sup>18,34,35</sup> In this subgroup, outstanding seizure control rates with Engel Class IA outcomes in almost 90% of patients have been reported.<sup>6,34</sup> We used this technique in 4 patients in this series after invasive mapping and in 3 others in a single stage with equally good outcomes. Two of these patients presented for surgery at an advanced age, so the team was hesitant to recommend a 1-stage hemispherotomy, and in all 4 patients who underwent invasive monitoring, the parents were reluctant to agree to hemispherotomy without electrographic evidence to justify it. Retrospectively, 2 of the 4 patients could have been spared staged surgeries and proceeded directly to a hemispherotomy (Cases 1 and 2), despite parental reluctance. We subsequently modified our practice and recommend 1-stage hemispherotomy in cases of large stroke-related porencephalic cysts associated with hemiparesis/hemiplegia (Cases 6 and 7). However, in the patient with a small ischemic infarct in the right insula, parietal, and frontal operculum (Case 12, Fig. 2), video EEG showed lateralized but poorly defined seizure onsets and the MRI did not predict widespread injury to the hemisphere, revealed by invasive monitoring. Similarly, in Case 15, bilateral electrode coverage allowed us to approach hemispherotomy with greater prognostic confidence of seizure freedom after video EEG demonstrated bilateral epileptic signatures, but invasive monitoring ruled out bihemispheric involvement. In cases in which functional preservation is a contraindication to hemispherotomy, invasive monitoring can be useful in identifying multifocal pathology and distinguishing these areas from sensorimotor and language areas. In the only adult in our series, a 35-year-old with a large frontoparietal porencephalic cyst (Case 4), invasive monitoring led to a frontal and temporal resection, as opposed to a hemispherotomy, sparing residual sensorimotor cortex and the visual field in the nondominant hemisphere.

A tailored approach to similar cases has also been described in 2 prior surgical series. Carreño et al.<sup>6</sup> reported a series of 22 patients with adequate follow-up who had vascular congenital hemiparesis and medically intractable epilepsy. Thirteen of the 22 patients in their series underwent a single-stage hemispherotomy, resulting in an 85% Engel Class I outcome (11 patients). The remaining patients had a variety of operations, including anterior temporal lobec-

tomy, temporal lobectomy with parietooccipital disconnection, anterior two-thirds callosotomy, frontal lobectomy, medial parietal resection, and porencephaly drainage, with good seizure control in approximately half of these cases. In the 6 patients who had a temporal lobectomy, 2 patients had subdural electrodes, 2 had epidural electrodes, and the others underwent resection based on noninvasive monitoring. The authors attested that "invasive studies are often necessary to ensure focal seizure onset and perform functional mapping" when hemispherotomy was not indicated or contraindicated due to loss of a visual field or other functional loss.<sup>6</sup> Iida et al.<sup>23</sup> described a series of 8 patients with perinatal strokes and epilepsy surgery followed for an average of 8 years. All of the patients in their series benefited from surgery, with complete cessation of seizures in 4 patients and very rare generalized tonic-clonic seizures, drop attacks, and focal motor seizures in the remaining patients. Only 1 patient in their series had chronic invasive electrode recordings in the form of stereo-EEG due to two distinct seizure semiologies, but all patients underwent intraoperative electrocorticography that the authors believed was indispensable in achieving a superior seizure-free outcome over "cyst uncapping,"23 due to the nature of separate seizure foci remote from the area of porencephaly.

In our series, all patients except 3 had chronic intracranial recordings in the form of subdural grid and strip electrodes, which provided us with an improved ability to effectively and comprehensively delineate the epileptogenic zone and tailor resections and disconnections to preserve functional cortical areas. In the patients with porencephalic cysts (Cases 1-7), the extent of resection (Case 3), the sparing of visual cortex in a more mature patient (Case 4), and the successful elimination of seizures after initial failed surgery (Case 5) were aided with invasive monitoring. In the group of patients with other ischemic and hemorrhagic strokes, invasive monitoring was useful in all 11 cases, either in tailoring of the extent of resection (inclusion of mesial temporal structures, multilobar resections in temporal "plus" epilepsy [involving the temporal lobe and 1 or more adjacent structures], and hemispherotomy in the case of a small opercular stroke; Cases 10-18), ruling out the possibility of bihemispheric seizure onsets (Cases 15 and 18), or determining the safety of resection in cases of bilateral injury with the ability to perform extraoperative stimulation mapping in children (Cases 8-10). While we readily acknowledge the limitations of retrospective analysis, including practice patterns at our center, we believe that invasive monitoring led to improved outcomes in this group of patients.

All 19 patients in our series had Engel Class I outcomes at the last follow-up evaluation. Other than 1 wound infection associated with prolonged intracranial recording, there were no adverse events related to staging of surgeries and chronic intracranial electrode recordings. Similar complication rates have been previously described in surgical series involving children who underwent staged epilepsy surgery.<sup>24,38</sup> Although staged resections necessitate more immediate discomfort, expense, and risk, the results in our series suggest that the likelihood of longerterm seizure control and low morbidity may justify this approach, particularly in light of the known association of porencephalic cysts and stroke-related foci to distant epileptogenic zones, and dual and sometimes triple pathologies giving rise to medically intractable seizures.<sup>22</sup>

The temporary deficits incurred in our series, particularly in the setting of multilobar disconnections and hemispherotomies, are well-recognized side effects of major epilepsy operations.<sup>3,26</sup> The benefit of long-lasting seizure freedom in this series of children greatly outweighs the hardships encountered in these patients. In the patient with a permanent lower-extremity weakness requiring the use of an ankle-foot orthosis and cane for ambulation (Case 8), the deficit is believed to have resulted from the contralateral perinatal injury the patient sustained and a lack of functional reserve from the sensorimotor region of the opposite hemisphere. Nevertheless, while great precaution is taken to protect against lifechanging functional deficits from epilepsy surgery, permanent morbidity can occur and must be weighed against the risk of ongoing, medically intractable seizures.<sup>26</sup> The long-term benefits of seizure freedom from medical and social perspectives validate this sentiment.<sup>20</sup>

Our results suggest that patients with medically refractory epilepsy following perinatal vascular insult can become good surgical candidates, and bilateral injury does not necessarily lead to to bilateral seizure onsets and preclude surgical intervention. Excellent seizure-freedom rates are possible, similar to those achievable in cases of cortical malformations or other structural abnormalities. Most patients with early childhood stroke can be treated safely and successfully with resective surgery, because the risk of creating a new functional deficit does not appear to be exacerbated by interrupting epileptogenic zones in stroke-affected regions. We acknowledge the limitations of this study, including a retrospective design lacking a control group, and a small sample size (the incidence of perinatal stroke is low), but hope that the data presented here will be useful to practitioners and caregivers in guiding clinical decision-making and risk assessment in the definitive treatment of stroke-associated epilepsy.

#### Conclusions

Tailored surgical approaches can produce successful outcomes in epilepsy patients with a history of perinatal stroke. In our series, vasculogenic epilepsy was typically associated with widespread seizure onsets, often in areas remote from the region affected by stroke/hemorrhage, and in many cases multilobar resections were necessary to achieve long-term seizure freedom.

#### Disclosure

Patricia McGoldrick is a consultant for Lundbeck, and has ownership in UCB. Dr. Goodman is a consultant for NeuroPace, Inc. Dr. Wolf is a consultant to Glaxo, Lundbeck, Novartis, UCB, Cyberonics, and Eisai. The remaining authors have no conflicts of interest to disclose. This study was supported entirely by the Department of Neurosurgery of St. Luke's-Roosevelt Hospital Center and Beth Israel Medical Center. The authors have not received any external funding for the study from government or private sources.

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