An update on pediatric surgical epilepsy: Part I

Nisha Gadgil1, Melissa A. LoPresti1, Matthew Muir4, Jeffrey M. Treiber1, Marc Prablek1, Patrick J. Karas1, Sandi K. Lam2

1Department of Neurosurgery, Division of Pediatric Neurosurgery, Baylor College of Medicine/Texas Children's Hospital, Houston, Texas, 2Department of Neurosurgery, Division of Pediatric Neurosurgery, Northwestern University Feinberg School of Medicine/Ann and Robert H. Lurie Children's Hospital, Chicago, IL, USA.

E-mail: Nisha Gadgil - ngadgil@bcm.edu; Melissa A. LoPresti - melissa.lopresti@bcm.edu; Matthew Muir - matthew.muir@bcm.edu; Jeffrey M. Treiber - jeffrey.treiber@bcm.edu; Marc Prablek - marc.prablek@bcm.edu; Patrick J. Karas - patrick.karas@bcm.edu; *Sandi K. Lam - slam@luriechildrens.org

ABSTRACT
Epilepsy affects many children worldwide, with drug-resistant epilepsy affecting 20–40% of all children with epilepsy. This carries a significant burden for patients and their families and is strongly correlated with poor cognitive outcomes, depression, anxiety, developmental delay, and impaired activities of daily living. For this reason, we sought to explore the role of pediatric epilepsy surgery and provide an overview of the factors contributing to epilepsy surgery planning and execution. We review the necessary preoperative evaluations, surgical indications, planning considerations, and surgical options to provide a clear pathway in the evaluation and planning of pediatric epilepsy surgery.

Keywords: Drug-resistant epilepsy, Epilepsy surgery, Pediatric

INTRODUCTION
Epilepsy is estimated to affect 10.5 million children worldwide.[12] In the early pediatric population, achieving seizure freedom is critical to prevent developmental arrest or regression.[1,13] Nevertheless, these patients often require multiple antiepileptic medications, leading to additive side effects, without adequate seizure control. About 20–40% of children have drug-resistant epilepsy (DRE), persistent seizures refractory to two antiepileptic medications,[3,8] presenting significant social, economic, health, and developmental implications.[14]

Surgical treatment of DRE has been shown to be safer and more efficacious compared to medical management.[11] It is aimed to remove or disconnect the epileptogenic zone (EZ), the minimal amount of cortex to produce seizure freedom,[17] from surrounding normal brain while minimizing morbidity. Conventionally, epilepsy surgery focused on resections or disconnections: lobectomy, hemispherectomy, cortical excision, and corpus callosotomy. Overtime, the armamentarium has grown to include newer, less invasive approaches including neuromodulation and ablative techniques.

With advances in technology, there are now multiple indications for the different types of surgery to address pediatric epilepsy. We describe, in Part I, practices and advances in diagnostic workup and surgical strategies.
SURGICAL INDICATIONS

Surgical indications have evolved over time to encompass a wider variety of epilepsy types, applying epilepsy surgery to more patients. Table 1 describes the evolution of indications for surgical evaluation in recent years.

Table 1: Timeline of indications for epilepsy surgery.

| Historically Drug-resistant focal epilepsy impacting quality of life |
| Absence of progressive neurological disease |
| Presence of localizable focal epileptogenic zone |
| American Academy of Neurology, 2003 Disabling complex partial seizures |
| With or without secondarily generalized seizures |
| Failed appropriate trials of first-line antiepileptic drugs |
| International League Against Epilepsy, 2006 Presence of cortical dysplasia, tuberous sclerosis complex, polimicrogyria, hypothalamic hamartoma, hemispheric syndromes, Sturge-Weber syndrome, Rasmussen syndrome, Landau-Kleffner syndrome, and other pathologies with evidence of cortical injury |

SURGICAL PLANNING

Presurgical evaluation identifies the EZ, correlating it with function. Stepwise evaluation should include a detailed clinical history, interictal scalp electroencephalography (EEG), long-term video EEG, high-resolution structural imaging, and other tests as indicated.

Table 2: Presurgical epilepsy evaluation.

| Test | Purpose | Strengths/weaknesses |
|------|---------|---------------------|
| Interictal scalp EEG | Identification of interictal electrical abnormalities (e.g., spike and sharp wave or focal rhythmic slow-wave activity). | Inexpensive; sensitive to cortical currents in all orientations. Low spatial resolution; low diagnostic yield; attenuated by skull/scalp. |
| Long-term video EEG | Analysis of ictal semiology and correlation with ictal EEG. | Rules out nonepileptic seizures; allows better classification of seizure type and localization. Low spatial resolution; attenuated by skull/scalp. |
| High-resolution MRI | Detection of structural epileptogenic lesion. | Protocolled to detect hippocampal sclerosis and focal cortical dysplasia. Nonexpert reading fails to detect subtle lesions. May detect subtle deficits as well as cognitive reserve. |
| Neuropsychological/Neuropsychiatric assessment | Evaluation of cognitive capabilities and functional deficits. | Dependent on skill of administering clinician and cooperation of subject. |
| Magnetoencephalography | Identification of magnetic fields produced by interictal epileptic discharges. | Sensitive to smaller cortical sources than EEG; lack of attenuation by skull/scalp. More sensitive to superficial cortical activity; sensitive only to currents tangential to scalp surface. |
| Functional MRI | Identification of eloquent cortex by mapping language, motor, and memory tasks. | Acceptable concordance with Wada testing in language localization. For sensorimotor tasks, electrocortical stimulation more reliable; dependent on patient cooperation and education. |
| Interictal positron emission tomography | Detection of interictal glucose hypometabolism within epileptic foci. | Can detect MRI-negative focal epilepsies (e.g., cortical dysplasia, temporal lobe epilepsy). Distribution of hypometabolism is wider than the seizure focus; less reliable in extratemporal epilepsy. |
| Ictal single-photon emission computed tomography | Detection of region of increased cerebral blood flow induced by a seizure. | Well correlated with ictal focus. Yield depends on timing of tracer injection; not feasible if seizures infrequent. |

EEG: Electroencephalography, MRI: Magnetic resonance imaging
| Surgery                  | Clinical application                                                                 | Outcomes                                                                                                                                                                                                 | Considerations                                                                                                                                                                                                 |
|-------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Resection of lesion     | DRE originating from cortical-based lesions                                           | Over half of pediatric patients obtain seizure freedom following lesionectomy of cortical lesions. Cure can occur if seizure originates from single lesion. Multifocal epilepsy may necessitate multiple EZ resections or disconnections. Favorable seizure outcomes correlate with MRI confirmation of resection. Cortical mapping may allow for maximal resection while minimizing neurological impairment. Intraoperative electrocorticography may guide extended lesionectomy of tissue adjacent to the primary pathology if necessary. |                                                                                                                                                                                                 |
| Lobectomy               | Temporal lobe epilepsy is the most common surgically amenable cause of DRE in children (e.g., 20% of cases)                                         | Anterior temporal lobectomy, with selective amygdalohippocampectomy, provide improved seizure outcomes in 60–80% of pediatric patients. Associated risks of homonymous superior quadrantanopsia, language deficits, and rarely contralateral hemiparesis. Early temporal lobectomy in children with DRE of temporal lobe origin may improve neurocognitive outcomes without impacting cognitive functions. |                                                                                                                                                                                                 |
| Hemispherectomy         | Disorders are characterized by severe unilateral hemispheric damage: porencephaly, Sturge-Weber syndrome, and Rasmussen encephalitis                             | Hemispherectomy provides excellent seizure freedom with anywhere from 54% to 90% of Engel 1 seizure freedom. Functional over anatomic hemispherectomy may avoid complications such as superficial hemosiderosis and hydrocephalus. Various techniques and endoscopic approaches allow functional disconnection with minimal cortical removal. |                                                                                                                                                                                                 |
| Corpus callosotomy      | Palliative procedure for patients with generalized seizures or rapid secondary generalization, particularly for drop attacks (atonic, tonic, or myoclonic seizures) | Improvement in seizure frequency has been noted in 65–85% of pediatric patients. Anterior callosotomy with preservation of the splenium may avoid disconnection syndrome with improved seizure control and lower relapse after complete callosotomy. Endoscopic techniques have been recently introduced to more focally reduce seizure burden. |                                                                                                                                                                                                 |

DRE: Drug-resistant epilepsy
magnetic resonance imaging (MRI), and neuropsychological/neuropsychiatric assessment\cite{22} and also included magnetoencephalography (MEG), functional MRI (fMRI), interictal positron emission tomography, and ictal single-photon emission computed tomography [Table 2]. Conventionally, the Wada test had been used for cortical stimulation mapping; this may be supplemented or supplanted with MRI\cite{19} as well as MEG or resting state fMRI\cite{6}.

Where the EZ cannot be characterized with noninvasive testing, or noninvasive testing yields contradictory results, Phase 2 assessment utilizing intracranial EEG monitoring may be pursued. Implantation of subdural grids and depth electrodes allows more accurate localization of the EZ than scalp EEG. Functional zones may be identified through cortical stimulation mapping. However, invasive electrocorticography may carry a complication rate of up to 20% (e.g., intracranial hematoma).\cite{30}

For those who are not candidates or have failed surgery, vagus nerve stimulation may palliatively reduce seizures by 50–75%.\cite{2,28} Targeted, responsive neuromodulation is also an option, discussed in Part 2.

SURGICAL OPTIONS

Several surgical options exist based on the seizure type, lesion type, size and location, and EZ characteristics. Lesionectomy is favored for singular cortical-based lesions and can be curative. Lobectomy is used for more focal lesions and proven superior in cases of temporal lobe epilepsy over medical management (Class I evidence).\cite{31} Hemispherectomy, reserved for lesions affecting an entire cerebral hemisphere, has evolved to focus on tissue disconnection rather than resection. Corpus callosotomy palliatively prevents synchronization of epileptic activity between hemispheres and is reserved for those most affected by generalized DRE. The clinical application, outcomes, and considerations for each approach are detailed in Table 3.

SURGICAL CONSIDERATIONS IN PEDIATRICS

Pediatric epilepsy is more diverse in etiology and semiology with migrational disorders, congenital epileptic syndromes, and extratemporal epileptogenic foci more common in children. Therefore, cortical excisions and hemispherectomies are perhaps more common than temporal lobectomies in the pediatric population versus adults. In addition, DRE impacts neurodevelopment in children. Early surgical intervention limits the time on intolerable medications, minimizes cognitive delays and learning disabilities, and improves psychomotor development.\cite{27} Children brains exhibit greater plasticity versus adults, increasing the potential for rehabilitation following even extensive resective or disconnective procedures.\cite{27}

Figure 1: Flowchart demonstrating strategies in the surgical management of drug-resistant epilepsy. The goal of epilepsy surgery can range from curative to palliative, with various available techniques to achieve a range of seizure outcome.

IDENTIFICATION OF CANDIDATES FOR EPILEPSY SURGERY

It is critical to identify the best candidates for epilepsy surgery. The goals include cure or palliation and may warrant a variety of open versus stereotactic techniques [Figure 1]. With growing technology, there is enhanced ability tailor treatment to individual patients.

Despite the growing appreciation for the deleterious developmental and psychosocial effects of pediatric DRE, there are too few surgical referrals,\cite{23} with <1% of patients with DRE referred to epilepsy centers. This may be explained by limited access, cost, and misconceptions regarding who may benefit from evaluation.\cite{25} With continuing innovation in the field of pediatric epilepsy surgery, it is imperative that continued strides be made in patient recruitment and referral to enhance clinical outcomes.

CONCLUSION

Here, we reviewed, summarized, and synthesized important practices and advances in diagnostic workup and surgical strategies of epilepsy surgery. Future increased awareness of the role of epilepsy surgery in children with DRE is critical to increase the breadth of impact.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Asarnow RF, LoPresti C, Guthrie D, Elliott T, Cynn V, Shields WD, et al. Developmental outcomes in children receiving resection surgery for medically intractable infantile spasms. Dev Med Child Neurol 1997;39:430-40.
2. Benbadis SR, Geller E, Ryvlin P, Schachter S, Wheless J,
Introduction

Pediatric surgical epilepsy is a complex field that requires a multidisciplinary approach. Advances in surgical techniques and monitoring methods have led to improved outcomes in children with intractable epilepsy. This article will provide an overview of the latest developments in surgical epilepsy, focusing on the role of functional hemispherectomy and lesionectomy.

Functional Hemispherectomy

Functional hemispherectomy is a surgical procedure that involves the removal of half of the brain to control seizures. It is particularly useful in children with intractable seizures that cannot be controlled with medication.

Lesionectomy

Lesionectomy is a surgical procedure that involves the removal of a lesion or tumor to control seizures. It is particularly useful in children with focal lesions that are causing seizures.

Epilepsy Surgery Outcomes

Surgical outcomes in children with epilepsy have improved significantly in recent years. The use of sophisticated presurgical evaluation techniques, such as functional MRI and PET scanning, has helped to identify the epileptogenic zone with greater accuracy.

Predictors of Outcome

Several factors have been identified as predictors of surgical outcome in children with epilepsy. These include the age of the child, the duration of seizures, and the presence of other neurological comorbidities.

Conclusion

Pediatric surgical epilepsy is a rapidly evolving field. Advances in surgical techniques and monitoring methods have led to improved outcomes in children with intractable epilepsy. Continued research is needed to identify new approaches that will further improve surgical outcomes in this population.

References

[1] Gadgil, et al.: Part I update on pediatric surgical epilepsy

[2] Lüders HO, Najm I, Nair D, Widdess-Walsh P, Bingman W. The epileptogenic zone: General principles. Epileptic Disord 2006;8 Suppl 2:S1-9.

[3] Otsuka T, Yoshimoto T. Surgical treatment of intractable epilepsy in children: Indication for resective surgery. Epilepsia 2000;41 Suppl 9:26-7.

[4] Papanicolaou AC, Rezaie R, Narayana S, Choudhari AF, Babajani-Feremi A, Boop FA, et al. On the relative merits of invasive and non-invasive pre-surgical brain mapping: New tools in ablative epilepsy surgery. Epilepsia Res 2018;142:153-5.

[5] Radhakrishnan A, Menon R, Abraham M, VilaniGlam G, Sharma S, Thomas B, et al. Predictors of outcome after surgery in 134 children with drug-resistant TLE. Epilepsia Res 2018;139:150-6.

[6] Ramírez-Molina JL, Di Giacomo R, MariVani V, Deleo F, Cardinafe F, EscáGue-Ge-Daccaret AM, et al. Surgical outcomes in two different age groups with Focal Cortical Dysplasia Type II: Any real difference? Epilepsy Behav 2017;70:45-9.

[7] Rathore C, Radhakrishnan K. Concept of epilepsy surgery and presurgical evaluation. Epileptic Disord 2015;17:19-31.

[8] Ravindra VM, Sweeney MT, Bollo RJ. Recent developments in the surgical management of paediatric epilepsy. Arch Dis Child 2017;102:760-6.

[9] Roth J, Carlson C, Devinsky O, Harter DH, Macalister WS, Weiner HL. Safety of staged epilepsy surgery in children. Neurosurgery 2014;74:154-62.

[10] Shen A, Quaid KT, Porter BE. Delay in pediatric epilepsy surgery: A caregiver’s perspective. Epilepsy Behav 2018;78:175-6.

[11] Smyth MD, Vellmana AK, Asano E, Sood S. Corpus callosotomy-Open and endoscopic surgical techniques. Epilepsia 2017;58 Suppl 1:73-9.

[12] Sugano H, Arai H. Epilepsy surgery for pediatric epilepsy: Optimal timing of surgical intervention. Neurol Med Chir (Tokyo) 2015;55:399-406.

[13] Tanganelli P, Ferrero S, Colotto P, Regesta G. Vagus nerve stimulation for treatment of medically resistant epilepsy. Evaluation of long-term outcome. Clin Neurol Neurosurg 2002;105:9-13.

[14] Taigher B, Richards M. Functional hemispherectomy. Axone 1992;14:29-32.

[15] Vale FL, Pollock G, Dionisio J, Benbadis SR, Tatum WO. Outcome and complications of chronically implanted subdural electrodes for the treatment of medically resistant epilepsy. Clin Neurol Neurosurg 2013;115:985-90.

[16] Wiebe S, Blume WT, Girvin JP, Eliasziw M, Effectiveness and Efficiency of Surgery for Temporal Lobe Epilepsy Study Group. A randomized, controlled trial of surgery for temporal-lobe epilepsy. N Engl J Med 2001;345:311-8.

How to cite this article: Gadgil N, LoPresti MA, Muir M, Treiber JM, Prabhat M, Karas PJ, et al. An update on pediatric surgical epilepsy: Part I. Surg Neurol Int 2019;10:257.