Editorial

# Evaluating the epilepsy and oncological outcomes of pediatric brain tumors causing seizures

**Shelly Wang[1,2], Aria Fallah[3]**

[1]Division of Neurosurgery, Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [2]Department of Clinical Epidemiology and Biostatistics, Harvard School of Public Health, Boston, Massachusetts, USA; [3]Department of Neurosurgery, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

*Correspondence to:* Aria Fallah, MD, MSc, FRCSC. Department of Neurosurgery, University of California Los Angeles, 300 Stein Plaza, Suite 525, Los Angeles, CA, USA. Email: afallah@mednet.ucla.edu.

Submitted Nov 14, 2015. Accepted for publication Nov 16, 2015.
doi: 10.3978/j.issn.2224-4336.2015.12.04
**View this article at:** http://dx.doi.org/10.3978/j.issn.2224-4336.2015.12.04

We read with great interest a single center retrospective cohort study by Wessling *et al*. titled "Brain tumors in children with refractory seizures—a long-term follow-up study after epilepsy surgery". This is a well-written and concise study of the post-surgical oncological, epileptological, and psychosocial follow-up of children with seizures secondary to brain tumors (1). This single-center cohort study includes 107 patients (aged 1.6–17.7 years), treated between 1988 and 2012, the majority with low-grade tumors (76.6% WHO I, 19.6% WHO II). Tumor localization was temporal in more than half of the patients, and histopathology included gangliogliomas in 57% of the cases, gliomas in 29%, and dysembryoplastic neuroepithelial tumors (DNET) in 14%. In comparison with other studies of post-surgical seizure outcomes in literature, this cohort consisted of disproportionally more ganglioglioma cases—traditionally considered benign tumors with low rates of oncological recurrence and favorable post-surgical seizure outcomes (2). Post-operative complications, including a 5.6% chance of permanent new deficits and a 2.8% chance of surgical complications, were comparable to other studies in literature (3-5).

Epilepsy follow-up was achieved in 103 patients (96.3%) at a mean length of 122.9 months. At last available outcome, 82.2% of patients were seizure free (ILAE class 1), and 54% of patients were not on anti-epileptic medication. This is comparable to other studies of epilepsy outcomes following surgery for pediatric brain tumors (6-9). Seizure outcome was not associated with tumor histopathology, surgical approach, seizure onset, age at surgery, or duration of epilepsy. Oncological and psychological follow-up was achieved in 70 patients (65.4%) at a mean length of 146.5 months. Psychological outcome assessed post-operative intellectual capabilities and education completion; the majority (91.1%) of the children were reported to attend regular kindergarten, school, professional training, and/or university.

While most existing studies in the literature focus on the epilepsy outcome of children following resective epilepsy surgery of brain tumors, this study is unique and further incorporates oncological and psychosocial outcomes in the same cohort of patients. In addition to these strengths, a few methodological and clinical limitations arise which we have outlined below.

It is unclear to us why the authors collected epilepsy outcomes more rigorously than oncology outcomes. The authors used clinical data, ambulant presentations, and telephone questionnaires for the former compared to telephone questionnaires exclusively for the latter. As a result, there are a large proportion of patients with missing oncological follow-up data, thus negatively impacting the internal validity of this study. Additionally, clinical follow-up and radiographic recurrence were not systematically assessed. This study found a 2.9% chance of local recurrence and 1.4% chance of mortality (in a patient with anaplastic astrocytoma WHO III). This low recurrence rate may stem from epidemiologic selection bias due to high attrition rate, or from the limited length of follow-up. As seizure-provoking low-grade pediatric supratentorial tumors are slow growing, future studies should consider

even longer follow-ups beyond 12 years to acquire more extensive data on tumor recurrence and survival.

A second issue involves the extent of surgical resection of the tumor and epileptogenic zone. In this cohort, the majority of patients (61.7%) underwent extended lesionectomy with a rim of surrounding tissue, and further amygdalohippocampectomy if there is pre-operative evidence of temporo-mesial involvement (26.2%). A smaller proportion of patients underwent lobectomy and selective amygdalohippocampectomy. The authors indicated that complete resection of the tumor was attempted in all cases; however, no post-operative magnetic resonance (MR) imaging was available for confirmation. The extent of tumor resection is important; a recent systematic review identified extent of gross-total resection as the strongest predictor of seizure freedom (10), and many authors emphasize complete resection of tumor whenever safe (11,12). It would be insightful to better understand the authors' surgical approach for tumors that involve eloquent cortex, considering the trade-offs between improved epilepsy and oncological outcomes, weighed against post-operative deficits.

Furthermore, surgical resection of the surrounding peritumoral epileptogenic zone correlates to seizure freedom. Traditionally, oncological cytoreduction of brain tumors associated with epilepsy was the main goal. However, there is increasing evidence advocating for resection of surrounding epileptogenic foci, oftentimes with intra-operative electrocorticography (ECoG), for improved epilepsy outcomes. A recent prospective study explored the distinction between the goals of lesionectomy and more extensive epilepsy operations, and reported a lower rate of post-operative seizure and redo surgery in patients who underwent extended epileptogenic surgeries (9). Other studies have advocated for epileptogenic resections in children to minimize or abolish the need for postoperative antiepileptic drugs (13). Specifically, routine ECoG-guided resections for non-eloquent areas have been advocated for optimal seizure management (7,14). Although the authors used ECoG in only eight cases, the technique nearly reached statistical significance for better seizure outcome. It would be useful to better understand the authors' criteria for utilizing intraoperative ECoG, and whether its use changed the extent of resection. In the future, case-control cohort studies comparing the added value of ECoG-guided resections to lesionectomy-only procedures can be considered.

Lastly, as this is a single center series, poor external validity of this study limits its generalizability to other centers with possibly different surgical approaches to the management of seizures related to pediatric brain tumors. Other methodological constraints include the lack of a control, or comparison group.

However, we thank the authors for providing an insightful paper regarding their experience in a relatively large patient cohort. They illustrate the complex surgical goals of epilepsy surgery associated with pediatric brain tumors: recurrence-free survival, seizure control, and appropriate psychosocial outcomes. Proceeding forward, future studies should involve multi-center collaborations, routine postoperative MR imaging and transparent decision-making regarding the use or disuse of ECoG-guided resections. This will allow us to draw more definitive conclusions in the surgical management of these children.

## Acknowledgements

None.

## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

## References

1. Wessling C, Bartels S, Sassen R, et al. Brain tumors in children with refractory seizures—a long-term follow-up study after epilepsy surgery. Childs Nerv Syst 2015;31:1471-7.
2. Ogiwara H, Nordli DR, DiPatri AJ, et al. Pediatric epileptogenic gangliogliomas: seizure outcome and surgical results. J Neurosurg Pediatr 2010;5:271-6.
3. Rydenhag B, Silander HC. Complications of epilepsy surgery after 654 procedures in Sweden, September 1990-1995: a multicenter study based on the Swedish National Epilepsy Surgery Register. Neurosurgery 2001;49:51-6; discussion 56-7.
4. Kim SK, Wang KC, Hwang YS, et al. Epilepsy surgery in children: outcomes and complications. J Neurosurg Pediatr 2008;1:277-83.
5. Lee JH, Hwang YS, Shin JJ, et al. Surgical complications of epilepsy surgery procedures : experience of 179 procedures in a single institute. J Korean Neurosurg Soc 2008;44:234-9.
6. Uliel-Sibony S, Kramer U, Fried I, et al. Pediatric

 

temporal low-grade glial tumors: epilepsy outcome following resection in 48 children. Childs Nerv Syst 2011;27:1413-8.
7. Fallah A, Weil AG, Sur S, et al. Epilepsy surgery related to pediatric brain tumors: Miami Children's Hospital experience. J Neurosurg Pediatr 2015;16:675-80.
8. Alsemari A, Al-Otaibi F, Baz S, et al. Epilepsy surgery series: a study of 502 consecutive patients from a developing country. Epilepsy Res Treat 2014;2014:286801.
9. Tandon N, Esquenazi Y. Resection strategies in tumoral epilepsy: is a lesionectomy enough? Epilepsia 2013;54 Suppl 9:72-8.
10. Englot DJ, Berger MS, Barbaro NM, et al. Predictors of seizure freedom after resection of supratentorial low-grade gliomas. A review. J Neurosurg 2011;115:240-4.
11. Chang EF, Christie C, Sullivan JE, et al. Seizure control outcomes after resection of dysembryoplastic neuroepithelial tumor in 50 patients. J Neurosurg Pediatr 2010;5:123-30.
12. Southwell DG, Garcia PA, Berger MS, et al. Long-term seizure control outcomes after resection of gangliogliomas. Neurosurgery 2012;70:1406-13; discussion 1413-4.
13. Berger MS, Ghatan S, Haglund MM, et al. Low-grade gliomas associated with intractable epilepsy: seizure outcome utilizing electrocorticography during tumor resection. J Neurosurg 1993;79:62-9.
14. Brahimaj B, Greiner HM, Leach JL, et al. The surgical management of pediatric brain tumors causing epilepsy: consideration of the epileptogenic zone. Childs Nerv Syst 2014;30:1383-91.

**Cite this article as:** Wang S, Fallah A. Evaluating the epilepsy and oncological outcomes of pediatric brain tumors causing seizures. Transl Pediatr 2016;5(1):9-11. doi: 10.3978/j.issn.2224-4336.2015.12.04

 