

# CORTICAL DYPLASIA: COMPLETE RESECTION CORRELATES WITH OUTCOME . . . BUT, COMPLETE RESECTION OF WHAT?

**Incomplete Resection of Focal Cortical Dysplasia Is the Main Predictor of Poor Postsurgical Outcome.** Krsek P, Maton B, Jayakar P, Dean P, Korman B, Rey G, Dunoyer C, Pacheco-Jacome E, Morrison G, Ragheb J, Vinters HV, Resnick T, Duchowny M. *Neurology* 2009;72(3):217–223. **BACKGROUND:** Focal cortical dysplasia (FCD) is recognized as the major cause of focal intractable epilepsy in childhood. Various factors influencing postsurgical seizure outcome in pediatric patients with FCD have been reported. **OBJECTIVE:** To analyze different variables in relation to seizure outcome in order to identify prognostic factors for selection of pediatric patients with FCD for epilepsy surgery. **METHODS:** A cohort of 149 patients with histologically confirmed mild malformations of cortical development or FCD with at least 2 years of postoperative follow-up was retrospectively studied; 113 subjects had at least 5 years of postoperative follow-up. Twenty-eight clinical, EEG, MRI, neuropsychological, surgical, and histopathologic parameters were evaluated. **RESULTS:** The only significant predictor of surgical success was completeness of surgical resection, defined as complete removal of the structural MRI lesion (if present) and the cortical region exhibiting prominent ictal and interictal abnormalities on intracranial EEG. Unfavorable surgical outcomes are mostly caused by overlap of dysplastic and eloquent cortical regions. There were nonsignificant trends toward better outcomes in patients with normal intelligence, after hemispherectomy and with FCD type II. Other factors such as age at seizure onset, duration of epilepsy, seizure frequency, associated pathologies including hippocampal sclerosis, extent of EEG and MRI abnormalities, as well as extent and localization of resections did not influence outcome. Twenty-five percent of patients changed Engel's class of seizure outcome after the second postoperative year. **CONCLUSIONS:** The ability to define and fully excise the entire region of dysplastic cortex is the most powerful variable influencing outcome in pediatric patients with focal cortical dysplasia.

**FDG-PET/MRI Coregistration Improves Detection of Cortical Dysplasia in Patients with Epilepsy.** Salamon N, Kung J, Shaw SJ, Koo J, Koh S, Wu JY, Lerner JT, Sankar R, Shields WD, Engel J Jr, Fried I, Miyata H, Yong WH, Vinters HV, Mathern GW. *Neurology* 2008;71(20):1594–1601. **OBJECTIVE:** Patients with cortical dysplasia (CD) are difficult to treat because the MRI abnormality may be undetectable. This study determined whether fluorodeoxyglucose (FDG)-PET/MRI coregistration enhanced the recognition of CD in epilepsy surgery patients. **METHODS:** Patients from 2004–2007 in whom FDG-PET/MRI coregistration was a component of the presurgical evaluation were compared with patients from 2000–2003 without this technique. For the 2004–2007 cohort, neuroimaging and clinical variables were compared between patients with mild Palmini type I and severe Palmini type II CD. **RESULTS:** Compared with the 2000–2003 cohort, from 2004–2007 more CD patients were detected, most had type I CD, and fewer cases required intracranial electrodes. From 2004–2007, 85% of type I CD cases had normal non-University of California, Los Angeles (UCLA) MRI scans. UCLA MRI identified CD in 78% of patients, and 37% of type I CD cases had normal UCLA scans. EEG and neuroimaging findings were concordant in 52% of type I CD patients, compared with 89% of type II CD patients. FDG-PET scans were positive in 71% of CD cases, and type I CD patients had less hypometabolism compared with type II CD patients. Postoperative seizure freedom occurred in 82% of patients, without differences between type I and type II CD cases. **CONCLUSIONS:** Incorporating fluorodeoxyglucose-PET/MRI coregistration into the multimodality presurgical evaluation enhanced the noninvasive identification and successful surgical treatment of patients with cortical dysplasia (CD), especially for the 33% of patients with nonconcordant findings and those with normal MRI scans from mild type I CD.

## COMMENTARY

Cortical dysplasia comprises 14% of all published epilepsy surgeries and as many as 75% of epilepsy surgeries in

children under 2 years of age (1). Originally described by Taylor in 1971 (2), the modern classification scheme, updated by Palmieri (3), has as its cardinal feature, cortical disorganization, and dyslamination. These features are further divided into either focal cortical dysplasia (FCD) type 1 (mild) or type 2 (severe), based on the presence of abnormal dysmorphic neurons or balloon cells in type 2. Each type is then further divided into subtypes A and B, based on the presence of either 1) hypertrophic, but not dysmorphic neurons (type 1B) or 2) balloon cells (type 2B). In addition, the abbreviation mMCD is used to describe a mild malformation of cortical development in which ectopic neurons are found in layer 1 or white matter, with the absence of any dyslamination (1).

The surgical treatment of patients with FCD has evolved over time. Since scalp EEG interictal and ictal events tend to be more widespread in FCD than in patients with temporal lobe epilepsy (4) and MRI scans are often normal or reveal only subtle abnormalities (5), clinicians were initially reluctant to consider patients for surgery since outcomes were presumed to be poor. More recently, it was shown that the interictal ECoG had a unique focal signature in human FCD (6) and that the MRI may be focally abnormal in approximately 50% of patients with type 1 FCD and approximately 90% with type 2 FCD (1). Moreover, FDG-PET regions of hypometabolism appear to colocalize with the FCD lesion in 70 to 98 percent of patients (1,7). As a result, more recent surgical series report rates of seizure-freedom ranging from 50 to 80 percent (5,8). However, there is still considerable debate regarding the goals of surgery and how to define the epileptogenic zone that must be removed to achieve the highest rate of seizure freedom.

The epileptogenic zone in FCD has been defined in several different ways for the purpose of surgical excision. Although there is not a comprehensive list, most series describe an imaging abnormality, either defined by MRI or FDG-PET hypometabolism. Likewise, electrographic abnormalities can be recorded acutely with surface ECoG or from chronically implanted electrodes (6). Histologic margins of the FCD lesion can also be defined. A controversy arises from the fact that there is little agreement regarding which of these various modalities best defines the epileptogenic zone and what *exactly* needs to be removed during surgery to increase the likelihood of an Engel I outcome.

For example, in the study by Krsek et al. involving 149 patients, 49 had their epileptogenic zone defined with acute intraoperative ECoG, without implantation of electrodes, while 100 patients underwent implantation of electrodes. Completeness of resection was defined as complete removal of the MRI abnormality and of "significant" ECoG abnormalities. In the group that underwent implantation of electrodes, the ECoG was the most critical factor in determining the epileptogenic zone, including areas of ictal onset as well as rapid spread. Although completeness of resection had the most significant impact on

outcome, curiously the use of chronically implanted electrodes and the presence of an abnormality on MRI scan did not.

In contrast, Salamon et al. report a subgroup of 45 patients in whom FDG-PET was coregistered to stereotactic MRI for navigation in the operating room. In this group, the extent of resection was based on the FDG-PET abnormality that concurred with the ECoG abnormality, but ECoG abnormalities were not chased beyond the FDG-PET defined borders. Only one patient underwent implantation of electrodes in this group and seizure-free rates were extremely high (82%).

The report by Salamon et al. implies that implanted electrodes and ictal onsets may not be necessary to define the epileptogenic zone in patients with FDG-PET abnormalities. However, other recent reports emphasize the importance of MRI and implanted electrodes. For instance, Kim et al. describe a large series of 166 patients with FCD in whom all had MRI, 151 had FDG-PET, and 143 had implanted electrodes (5). Complete resection, based on removal of the MRI abnormality and the ECoG abnormality, was the greatest predictor of seizure-free outcome. Concordance of FDG-PET was not associated with better outcome—neither was a focal ictal onset zone or a focal lesion on MRI. Seizure-free rates were not as high as in the pediatric series presented by Salamon et al., guided primarily by FDG-PET.

MRI alone is clearly not adequate in guiding surgical resections for FCD, since the histologic abnormality and electrographic abnormality often occur beyond this margin; in fact, the histological margin can also extend beyond the electrographic margin (7). Likewise, the FDG-PET area of hypometabolism is more widespread than the MRI abnormality (1). It would be interesting to compare the extent of the histologic abnormality with the area of FDG-PET hypometabolism. If indeed the two correspond, the finding would validate the use of FDG-PET in guiding surgical resections.

Another possible explanation for the association between completeness of resection of the FDG-PET abnormality and outcome can be drawn from an analogy with mesial temporal lobe epilepsy. FDG-PET clearly shows regions of hypometabolism that extend well beyond the epileptogenic zone. After selective amygdalohippocampectomy, FDG-PET hypometabolism often returns to normal, further demonstrating that these areas of brain are not part of the epileptic focus (9). Along a similar line, the hypometabolic FDG-PET areas identified in FCD may represent regions of early ictal spread surrounding the ictal onset zone. Thus, FDG-PET guided surgery may just increase the overall volume of resected tissue in a non-specific manner. To address this issue, it would be useful to obtain postresection FDG-PET in FCD patients for whom the FDG-PET abnormality was not completely removed, to assess whether or not metabolism normalized.

*by Theodore H. Schwartz, MD, FACS*

## References

1. Lerner JT, Salamon N, Hauptman JS, Velasco TR, Hemb M, Wu JY, Sankar R, Donald Shields W, Engel Jr J, Fried I, Cepeda C, Andre VM, Levine MS, Miyata H, Yong WH, Vinters HV, Mathern GW. Assessment and surgical outcomes for mild type I and severe type II cortical dysplasia: a critical review and the UCLA experience. *Epilepsia* 2009.
2. Taylor DC, Falconer MA, Bruton CJ, Corsellis JA. Focal dysplasia of the cerebral cortex in epilepsy. *J Neurol Neurosurg Psychiatry* 1971;34:369–387.
3. Palmini A, Najm I, Avanzini G, Babb T, Guerrini R, Foldvary-Schaefer N, Jackson G, Lüders HO, Prayson R, Spreafico R, Vinters HV. Terminology and classification of the cortical dysplasias. *Neurology* 2004;62:S2–S8.
4. Raymond AA, Fish DR, Sisodiya SM, Alsanjari N, Stevens JM, Shorvon SD. Abnormalities of gyration, heterotopias, tuberous sclerosis, focal cortical dysplasia, microdysgenesis, dysembryoplastic neuroepithelial tumour and dysgenesis of the archicortex in epilepsy. Clinical, EEG and neuroimaging features in 100 adult patients. *Brain* 1995;118:629–660.
5. Kim DW, Lee SK, Chu K, Park KI, Lee SY, Lee CH, Chung CK, Choe G, Kim JY. Predictors of surgical outcome and pathologic considerations in focal cortical dysplasia. *Neurology* 2009;72:211–216.
6. Palmini A, Gambardella A, Andermann F, Dubeau F, da Costa JC, Olivier A, Tampieri D, Gloor P, Quesney F, Andermann E. Intrinsic epileptogenicity of human dysplastic cortex as suggested by corticography and surgical results. *Ann Neurol* 1995;37:476–487.
7. Cohen-Gadol AA, Ozduman K, Bronen RA, Kim JH, Spencer DD. Long-term outcome after epilepsy surgery for focal cortical dysplasia. *J Neurosurg* 2004;101:55–65.
8. Widdess-Walsh P, Jeha L, Nair D, Kotagal P, Bingaman W, Najm I. Subdural electrode analysis in focal cortical dysplasia: predictors of surgical outcome. *Neurology* 2007;69:660–667.
9. Takaya S, Mikuni N, Mitsueda T, Satow T, Taki J, Kinoshita M, Miyamoto S, Hashimoto N, Ikeda A, Fukuyama H. Improved cerebral function in mesial temporal lobe epilepsy after subtemporal amygdalohippocampectomy. *Brain* 2009;132:185–194.