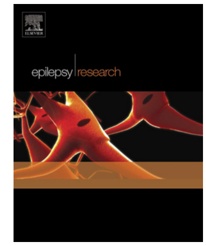
Epilepsy Research (2013) 106, 164—172

journal homepage: www.elsevier.com/locate/epilepsyres



Magnetic source imaging (MSI) in children with neocortical epilepsy: Surgical outcome association with 3D post-resection analysis

Hyunmi Kim [a,*], Pongkiat Kankirawatana [b], Jeff Killen [c], Allan Harrison [b], Ahyuda Oh [d], Curtis Rozzelle [e], Jeffrey Blount [e], Robert Knowlton [f]

[a] *Pediatric Neurology, Emory University School of Medicine, Atlanta, GA, USA*
[b] *Pediatric Neurology, University of Alabama at Birmingham, Birmingham, AL, USA*
[c] *Magnetoecephalogram Laboratory, Neurology, University of Alabama at Birmingham, Birmingham, AL, USA*
[d] *School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA*
[e] *Pediatric Neurosurgery, University of Alabama at Birmingham, Birmingham, AL, USA*
[f] *Neurology, University of Texas, Houston, TX, USA*

Received 2 October 2012 ; received in revised form 27 February 2013; accepted 9 April 2013
Available online 18 May 2013

KEYWORDS
Magnetic source imaging (MSI);
3D post-resection analysis;
Pediatric neocortical epilepsy;
Surgical outcome

Summary
Objective: To investigate the validity of magnetic source imaging (MSI) to localize seizure-onset zone using 3D analysis of pre-operative MSI source imaging coregistered to post-resection MRI following neocortical epilepsy surgery.
Methods: Twenty-two children who had MSI and epilepsy surgery were studied (median age = 11 years, 1 year 2 months—22 years). Only seven (31.8%) had localized lesions on pre-operative conventional brain MRIs. Sixteen (72.7%) underwent intracranial EEG monitoring. Mean post-operative follow-up was 4.7 years (1 year 3 months—8 years 2 months). Fifteen patients (68%) were seizure-free. MEG spike dipole sources were superimposed onto post-operative MRIs. The number and proportion of spike dipoles within resection volume were calculated and compared between seizure free and non-free groups.
Results: Both number of dipole clusters and proportion of dipoles in resection volume were not associated with seizure-free outcome ($p > 0.05$). In seven cases with MRI lesions, six of these with a $\geq$70% dipoles within the resection margin were seizure-free, while one with the proportion <70% was not seizure-free. Further, among the 15 cases with non-localized or normal MRI, five with both the proportion <70% and multiple dipoles clusters were post-operatively seizure free.
Conclusion: Number and density of clustered spike dipole sources within the surgical resection volume is not associated with postoperative seizure-free outcome. MSI successfully localized

* Corresponding author at: Pediatric Neurology, Emory University School of Medicine, 2105 Uppergate Dr NE, Atlanta, GA 30322, USA. Tel.: +1 205 996 7850; fax: +1 205 996 7867.
E-mail addresses: hyunmi.kim@emory.edu (H. Kim), Pkankirawatana@peds.uab.edu (P. Kankirawatana), jkillen@uab.edu (J. Killen), aharrison@uab.edu (A. Harrison), ahyudaoh@uab.edu (A. Oh), Curtis.Rozzelle@childrensal.org (C. Rozzelle), Jeffrey.Blount@childrensal.org (J. Blount), Robert.C.Knowlton@uth.tmc.edu (R. Knowlton).

0920-1211/$ — see front matter
http://dx.doi.org/10.1016/j.eplepsyres.2013.04.004

the perilesional epileptogenic zone in cases with localized MRI lesions, but not in cases with normal MRI in this study. Even if MEG localizes spikes to a single focal region, confirmation of epilepsy localization with intracranial EEG is still recommended in cases with non-lesional MRI.

Introduction

The purpose of pre-surgical evaluation for epilepsy surgery is to localize the seizure-onset zone (i.e., area of cortex that initiates clinical seizures) (Luders et al., 2006). The seizure-onset zone may be indicated by multimodal pre-surgical studies, including clinical seizure semiology, localization of epileptiform abnormalities on scalp electroencephalography (EEG), and structural/functional neuroimaging. Although, intracranial EEG (ICEEG) is considered a ''gold standard'' of localization due to its capability of long-term recording directly from the surface of or within the cortex in real time spontaneous seizure, it has a number of limitations. Amongst many, the most important is limited sampling of a small fraction of cerebral cortex due to practical and safety consideration. To overcome this limitation, accurate preoperative indication what brain region(s) to target with ICEEG is required (Knowlton et al., 2009). A resultant goal of noninvasive epilepsy imaging tests is to improve the hypothesis seizure-onset zone localization that is used to guide ICEEG.

Magnetic source imaging (MSI) based on magnetoencephalography (MEG) source localization can be used to three-dimensionally localize sources of epileptiform abnormality with high temporal and spatial resolution (Bagic et al., 2009; Hari et al., 1988; Okada et al., 1984; Romani et al., 1982). In contrast to scalp EEG, magnetic fields are not attenuated or distorted by intervening brain, dura, cerebrospinal fluid, bone, or skin (Cohen et al., 1990; Cohen and Cuffin, 1983; Cohen, 1972). MEG is sensitive to tangential sources, which measures predominantly activities in the sulci of superficial cortex and has greater sensitivity to detection of medial and dorsal lateral convexity sources, while EEG is sensitive to both tangential and radial sources. Hence, combined EEG/MEG studies would provide crucial information on the irritative zone (i.e., area of cortex which generates interictal spikes) (Luders et al., 2006) and then improve the hypothesis seizure-onset zone localization.

MSI may effect clinical practice in three ways: (1) screening of epilepsy surgery candidates especially in cases with non-localizable scalp EEG results; (2) improving ICEEG localization yield and accuracy by tailoring ICEEG placement; and (3) aiding noninvasive localization information such that an increased proportion of patients may avoid ICEEG (Knowlton et al., 2009). The additional diagnostic yield from MSI has been reported both in patients with the scalp video-EEG results of partial indication of epilepsy localization and in patients with non-localizing scalp video-EEG results (Pataraia et al., 2004). Including two prospective observational studies (Knowlton et al., 2009; Sutherling et al., 2008), previous studies reported that MSI was highly correlated with the seizure-onset zone identified by intracranial EEG and shown to be useful in guiding placement of intracranial electrodes in neocortical epilepsy (Mamelak et al., 2002; Oishi et al., 2006; Sutherling et al., 2008; Knowlton et al., 2009; Medvedovsky et al., 2012; Schneider et al., 2012). Sutherling et al. found that MSI changed the surgical decision in 23 out of 69 patients (33.3%) and 6 of them had clearly benefited form MSI, while it gave information similar to standard noninvasive video-EEG and imaging in the remaining 46 patients (Sutherling et al., 2008). Another prospective study found that MSI indicated additional electrode coverage in 18 out of 77 (23.4%). In 7 patients with ICEEG affected by MSI, seizure onset involved the additional electrodes and, as a consequence, affected surgical resection (Knowlton et al., 2009).

There are only limited studies using the quantitative spatial correlation to evaluate MSI diagnostic yield (Fischer et al., 2005; Genow et al., 2004; Iwasaki et al., 2002). This study aimed to examine the congruency between MSI localization and resection volume by 3D analysis using co-registration of pre-operative MSI source onto post-operative MRI and to evaluate the MSI localization on post-operative seizure outcome in children with medically intractable neocortical epilepsy. We hypothesized that the proportion of MSI spike dipoles included in the surgical resection volume would be associated with surgical outcome.

Methods

Subjects

Patients completing the pre-surgical workup at the Children's Hospital of Alabama between 2002 and 2009 were retrospectively reviewed. Inclusion criteria were: (1) diagnosis of medically intractable focal epilepsy, (2) pre-operative MSI study, (3) epilepsy surgery, and (4) the postoperative follow-up duration ≥1 year. Forty-eight consecutive patients were identified. Twenty-six patients were excluded due to: (1) less than or equal to three spike dipole source estimates were captured during the MSI test session ($n = 7$), (2) lack of available raw data ($n = 9$), or (3) lack of post-operative brain MRI ($n = 10$). Twenty-two cases were finally included. Surgical candidacy for patients with medically intractable focal epilepsy is decided at epilepsy surgery conference based on the data from multimodal pre-surgical studies, including clinical seizure semiology, localization of epileptiform abnormalities on the long-term scalp EEGs, both structural and functional neuroimaging such as brain MRI (1.5 T) with epilepsy protocol, FDG PET scan, Ictal-SPECT with Subtraction Interictal SPECT Coregistered with MRI (SISCOM) and Ictal-interictal SPECT Analysis by SPM (ISAS), and magnetoencephalography (MEG).