MAGNETIC SOURCE IMAGING (MSI) CAN ASSIST IN THE IDENTIFICATION OF EPILEPTOGENIC TUBERS IN CHILDREN WITH TUBEROUS SCLEROSIS COMPLEX (TSC) AND INTRACTABLE EPILEPSY

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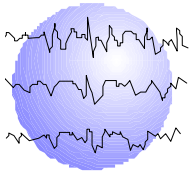

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REVISED ABSTRACT

RATIONALE: Tuberous sclerosis complex (TSC) is a genetic disorder that often presents in childhood with seizures. Many of these patients have intractable epilepsy, but since TSC patients have multiple cortical tubers, identifying the specific tubers that are epileptogenic can be difficult. Magnetic Source Imaging (MSI) may help identify the tuber/s responsible for seizure onset, making epilepsy surgery more feasible for this multifocal disease. This study reports our early experience with MSI in children with TSC and intractable epilepsy.

METHODS: Four children with TSC and intractable seizures (ages 23-months to 18-years) were evaluated at the Minnesota Epilepsy Group, PA for epilepsy surgery. These evaluations included long-term video-EEG monitoring to establish the dominant seizure type/s and their potential site of onset. Following the inpatient evaluation, an outpatient interictal MSI was performed with a 148-channel Magnes 2500 WH System (4-D Neuroimaging, San Diego, CA) at Minnesota Epilepsy Group, PA and United Hospital, St. Paul, MN. Functional MSI was also done for motor, sensory and language when possible if potentially responsible tuber/s.

RESULTS: All patients had at least one potential focus identified that correlated with specific cortical tubers identified by MSI and MRI co-registration. This combined with ictal scalp EEG recordings were used to place indwelling electrodes in order to confirm seizure onset and functional mapping. Post-operative follow-up with regard to areas/tubers resected and seizure outcome will be discussed.

CONCLUSION: Our preliminary results in a small number of children with TSC and intractable epilepsy support the use of MSI to assist in localization of the epileptogenic tubers. If these results are confirmed in a larger number of patients, it may be possible to perform successful epilepsy surgery on TSC patients with as good or better outcomes using less invasive studies than those currently in use.

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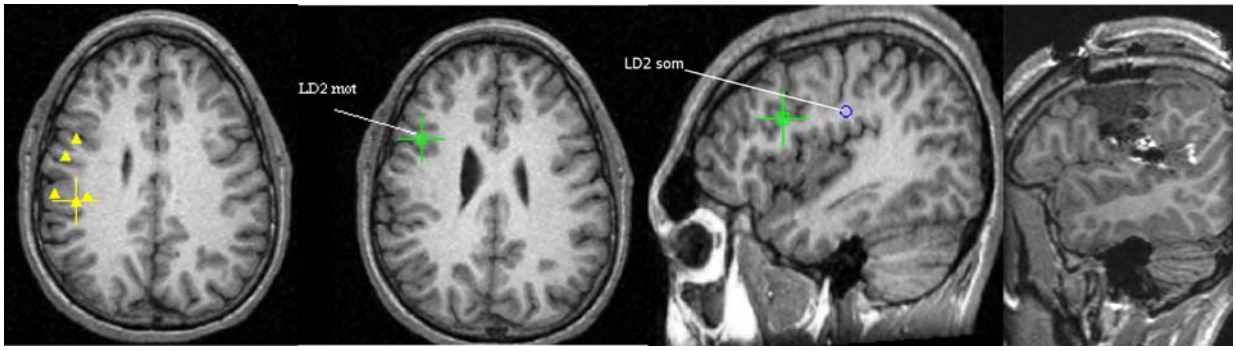
Introduction:

Tuberous Sclerosis Complex (TSC) is a multifocal disease in the central nervous system. Patients often have medically intractable partial onset seizures. It has been difficult to identify the epileptogenic tuber and surrounding epileptogenic zone in these patients with multiple cortical tubers and therefore many patients with a single seizure type, or dominant seizure, have not been considered potential surgical candidates. Early seizure control (with medication or with resective surgery) have overall better outcomes. With its advantage showing intrinsic epileptiform activity, Magnetic Source Imaging (MSI) was applied to help identify the epileptogenic tuber(s) in four children with intractable seizures and multiple cortical tubers. Subdural electrode arrays were placed under the guidance of MSI.

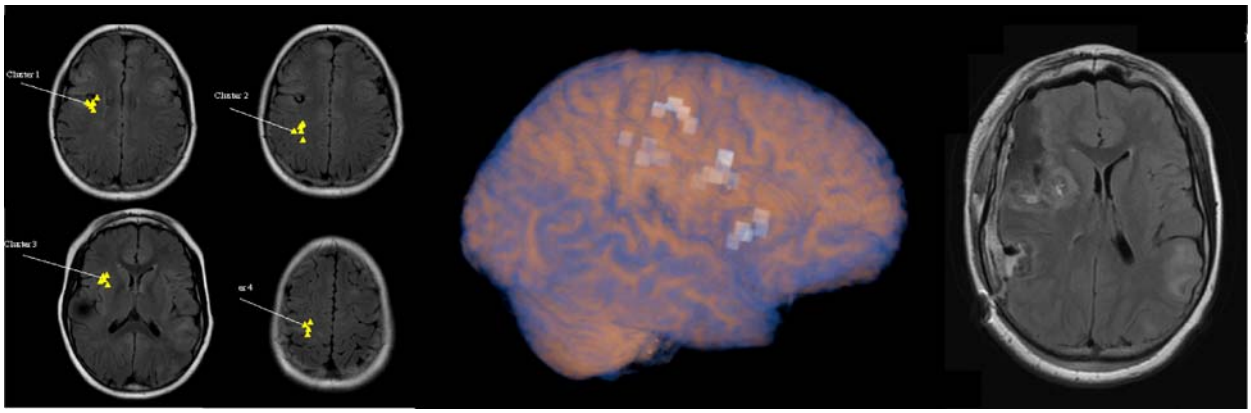
CASE 1

An eighteen-year, two-month old at the time of surgery had onset of complex partial and simple partial seizures at two years of age. These remained refractory to multiple medication trials and the Vagus Nerve Stimulator. Pre-operatively, he was having two to three clusters of simple partial seizures on a weekly basis, requiring Phenobarbital loads a couple of times per month. MSI was acquired for Epileptogenic localization and functional mapping for somatosensory, motor and language functions. The language mapping was failed because of the noise from VNS. Interictal epileptiform activity (yellow triangles), primary motor (green square) and primary somatosensory (blue circle) were mapped by MSI as showed below. Intracranial EEG was recorded and confirmed the MSI findings. On 07/22/2005, a right frontoparietal resection was performed to remove three tubers. He has been seizure free since surgery. He does have some weakness of his left hand as a residual from surgery, which was predicted by MSI.



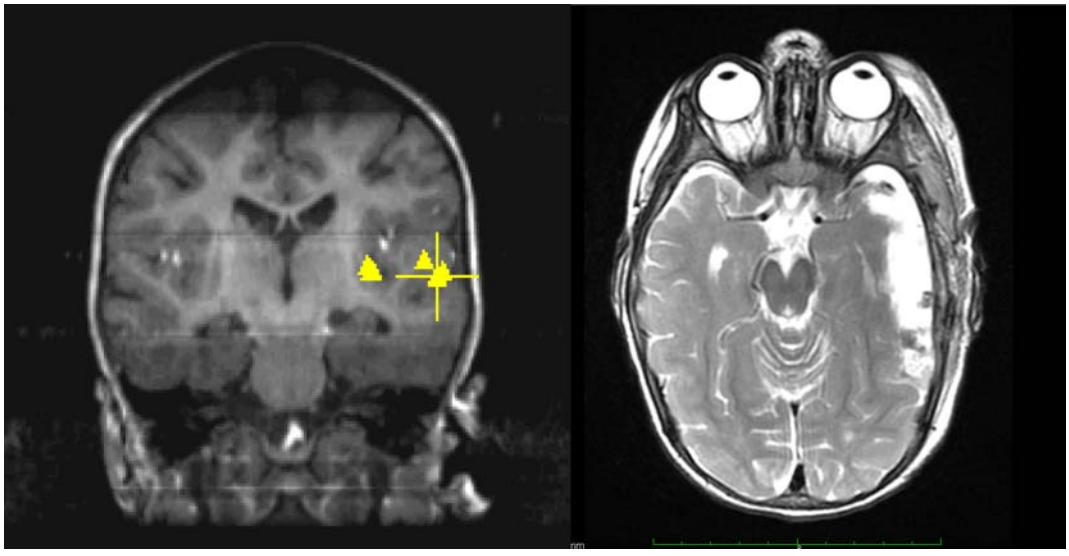
CASE 2

A ten-year, eight-month old girl had onset of seizures at two months of age that remained refractory to multiple medication trials. Preoperatively, she was having one to three seizures per day. MSI was performed under sedation, 4 responsible tubers were identified (yellow triangles on the 4 FLAIR images on the left and white squares on the 3D image). A right frontal topectomy and right temporal parietal topectomy was performed on 05/19/2005. The post-operative FLAIR MR image on the right demonstrates the epileptogenic tubers were removed. She has been seizure free since surgery.



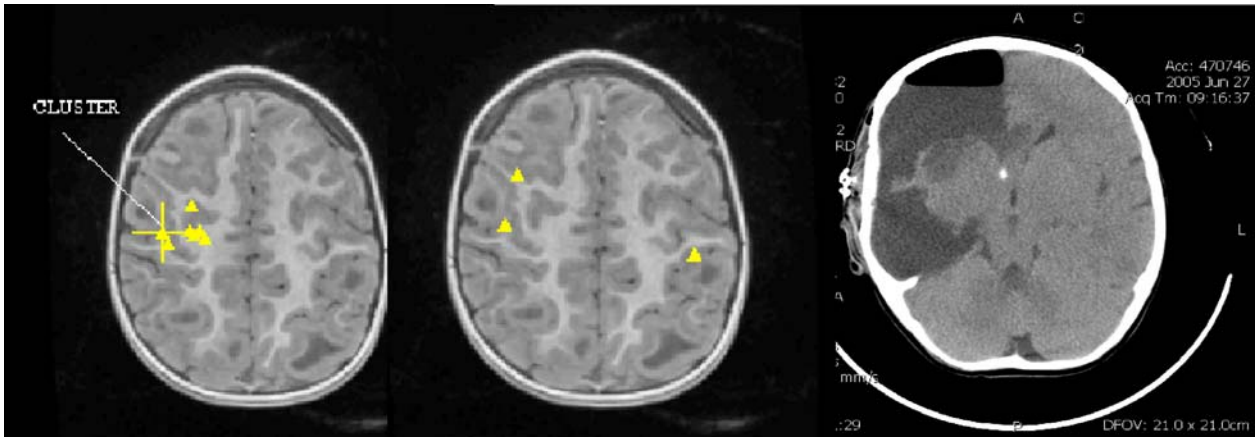
CASE 3

A 24-month-old at the time of surgery, presented with infantile spasms at five months of age which responded to Vigabatrin. Multiple complex partial seizures then developed that were unresponsive to multiple medication trials. Pre-operatively, she was having one to four complex partial seizures per day and was being loaded with Valium several times per week. MSI was performed under sedation to find epileptogenic tubers. The interictal spikes were found bilaterally, Intracranial electrodes were placed guided by MSI. A left temporal tuber resection at left lateral temporal topectomy with an anterior 2/3 corpus callosotomy was performed 04/21/2005. She had several break through seizures in the first couple of months postoperatively (a different seizure type) but has been seizure free since then.



CASE 4

A two-year, two month old boy presented at two months of age with infantile spasms that responded to Vigabatrin. He was diagnosed at that time with TSC. Following a brief seizure free period, complex partial seizures recurred and were refractory to multiple medication trials. Preoperatively, he was having multiple CPS daily. Most of the interictal spikes are located at right frontal lobe defined by MSI as shown on the MR images below (yellow triangles). A right frontal topectomy, right temporal lobectomy and resection of a tuber in the right parieto-occipital junction was performed on 06/24/2005 following recording from subdural electrodes, which placement was guided by the MSI. Invasive EEG confirmed the findings from MSI. He has remained seizure free since surgery.



SUMMARY AND CONCLUSION

Patients with TSC and intractable epilepsy can have successful resective epilepsy surgery. In the past it has been difficult to identify the epileptogenic tuber and surrounding epileptogenic zone. We employed magnetic source imaging to tentatively identify the area as well as functional cortex. MSI guided the placement of intracranial electrodes placement. Ictal invasive monitoring with subdural electrode arrays confirmed the MSI findings. Specific seizures were targeted in each of the four patients presented. All four patients have been seizure free since surgery (follow-up ranging from five months to eight months). MSI could define the responsible tuber and eloquent regions. It appears to be a promising tool for identification of a seizure focus (or foci) in a multifocal disease such as TSC.