



Combining Electrical and Magnetic Fields for Source Analysis: A(n) Attractive or Repelling Thought

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Electromagnetic Source Imaging in Presurgical Workup of Patients With Epilepsy: A Prospective Study.

Duez L, Tankisi H, Hansen PO, et al. *Neurology*. 2019;92(6):e576-e586. doi:10.1212/WNL.0000000000006877. Epub 2019 Jan 4. PMID: 30610090

Objective: To determine the diagnostic accuracy and clinical utility of electromagnetic source imaging (EMSI) in presurgical evaluation of patients with epilepsy. **Methods:** We prospectively recorded magnetoencephalography (MEG) simultaneously with electroencephalogram (EEG) and performed EMSI, comprising electric source imaging, magnetic source imaging, and analysis of combined MEG-EEG data sets, using 2 different software packages. As reference standard for irritative zone (IZ) and seizure onset zone (SOZ), we used intracranial recordings and for localization accuracy outcome 1 year after operation. **Results:** We included 141 consecutive patients. Electromagnetic source imaging showed localized epileptiform discharges in 94 (67%) patients. Most (72%) of the epileptiform discharge clusters were identified by both modalities, 15% only by EEG, and 14% only by MEG. Agreement was substantial between inverse solutions and moderate between software packages. Electromagnetic source imaging provided new information that changed the management plan in 34% of the patients, and these changes were useful in 80%. Depending on the method, EMSI had a concordance of 53% to 89% with IZ and 35% to 73% with SOZ. Localization accuracy of EMSI was between 44% and 57% which was not significantly different from magnetic resonance imaging (49%-76%) and PET (54%-85%). Combined EMSI achieved significantly higher odds ratio compared to electric source imaging and magnetic source imaging. **Conclusion:** Electromagnetic source imaging has accuracy similar to established imaging methods and provides clinically useful, new information in 34% of the patients. **Classification of evidence:** This study provides class IV evidence that EMSI had a concordance of 53% to 89% and 35% to 73% (depending on analysis) for the localization of epileptic focus when compared to intracranial recordings (IZ and SOZ), respectively.

Commentary

Electrical currents of neuronal activity produce both electrical potentials and magnetic fields. The electrical potentials are generated by extracellular currents and are recorded at the scalp with electroencephalogram (EEG). Magnetic fields, in contrast, are created by intracellular currents of apical dendrites, which are recorded at the scalp with MEG.¹ Two intrinsic characteristics of MEG recording that differ from EEG recording are (1) magnetic fields are minimally affected by conductivities of intervening structures and tissue between brain and scalp and (2) MEG measures only a subset of neuronal activity that is tangential to the scalp. Magnetic source imaging (MSI) for the localization of the epileptogenic zone entered clinical practice in the late 1990s and was routinely used by the mid 2000s. Electric source imaging (ESI) with an expanded electrode array for epilepsy evaluation entered clinical use in a small number of centers in the early 2000s² and became increasingly more utilized over the next decade.

For a period of 5 to 10 years, the 2 source imaging/localization techniques were studied mostly in parallel by 2 camps of investigators who for the most part set out to prove the superiority of their technique. The MEG camp touted the ability of MEG signals to not be attenuated by skull and scalp tissue and thus better “see” the underlying neuronal activity. The EEG camp noted that EEG recordings could detect radial sources in addition to tangential sources and thus provided a “more complete” representation of the underlying neuronal activity. The EEG camp also noted that magnetic field strength decreases exponentially over distance and thus MEG may not sample deep structures well.³ In response to claims that MSI provided better source localization, ESI investigators countered that early EEG source imaging studies were hampered by low-density International 10-20 System electrode arrays that cannot be reasonably compared to MEG systems, which then routinely contained over 122 sensors.

It is thus heartening and of interest to see the work of Duez et al who used simultaneously acquired MEG and high-density



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EEG data sets individually and in combination for source localization of the epileptogenic focus. The authors studied 141 consecutive patients with medically refractory focal epilepsy undergoing presurgical evaluation. All patients had MEG studies acquired with a gradiometer/magnetometer system with 306 sensors, and 115 patients also had simultaneous high-density EEG with at least 64 electrodes. Magnetoencephalography and EEG data were analyzed with 2 software packages (BESA-Research 6 and CURRY 7 Neuroimaging Suite) using 2 different inverse solutions (equivalent dipole model [ECD] and distributed source model [DSM]). A separate data set of combined MEG and EEG spikes were signal averaged and analyzed with CURRY. Electroencephalogram data analyzed with BESA and using the equivalent current dipole model produced the highest concordance with the seizure onset zone, as defined by intracranial ictal EEG data. Magnetoencephalography data analyzed with CURRY and using the equivalent current dipole model produced the highest positive predictive value for achieving 1-year seizure-free outcome after epilepsy surgery. Combined EEG–MEG source modeling (cEMSI) produced the highest odds ratio for achieving 1-year seizure-free outcomes but was not superior to MSI or ESI in determining the seizure onset zone or predicting 1-year seizure-free outcome. The effect of EMSI on patient management planning was assessed in a subgroup of 85 patients in who EMSI was part of the decision-making process. In 34% (29/85), EMSI changed the management plan, and the authors report that an overall 18% (16/85) benefited from the changes related to EMSI data.


Perhaps not surprisingly, no analysis method was consistently superior to another. This was an ambitious study that looked at 3 data sets using 2 different source analysis software packages constrained by 2 different inverse solutions, resulting in 10 different source analysis methods. The source analysis method with the highest concordance with the seizure onset zone was BESA ECD EEG, but the method with the highest concordance with the irritative zone was BESA ECD MEG. The source method with the highest positive predictive value for 1-year seizure freedom was CURRY ECD MEG and the method with the highest odds ratio for 1-year seizure freedom was CURRY DSM cEMSI. A quick look at the 95% confidence intervals for these results confirms that the ranges overlap with almost all methods. And yet, there were clear trends. The use of CURRY DSM achieved a higher concordance with both irritative and seizure onset zones than CURRY ECD. When using BESA, the opposite is true with ECD outperforming DSM. It may be that a specific source analysis software is best paired with a specific inverse solution when testing for a specific condition (ie, the seizure onset zone). However, the data from this study do not allow us to draw any conclusions.

One of the strengths of this study is that the data are prospectively gathered and incorporated into the surgical planning process in a subgroup of patients. Previous studies relied on retrospective analysis of MEG data⁴ to determine the likelihood of MSI to impact clinical outcomes or prospectively performed ESI analysis⁵ which was not considered for surgical planning purposes. Duez et al have implicitly acknowledged


that MSI and ESI are appropriate clinical tools for presurgical evaluation and have used these tests in a prospective real-world setting. While the authors are to be commended for the prospective determination of the utility of electromagnetic source imaging to surgical outcome, a weakness of this well-designed study and well-written article is the lack of detail as to which source imaging analysis method was used. Given the multitude of analysis methods used in this study, it is important to clearly define for the reader which EMSI (ESI or MSI or cEMSI or all) contributed to the decision-making process. Not having this clarity makes it difficult to fully understand the utility of specific source imaging techniques to achieving an excellent surgical outcome.

Despite the prior comment, this study highlights the progress made in the field of source localization imaging. In a landmark paper for its time, Stefan et al⁶ in 2003 quantified the contribution of MSI to the general result of presurgical evaluation in 104 patients with drug-resistant epilepsy. They found that MSI “supplied . . . information crucial to decision making in 10%.” Their criterion to achieve this threshold was when MSI had an impact on the final decision for treatment or if the treatment decision would likely have been different without the MSI data. In the present article, 34% of the analyzed group had a change in management based on consideration of EMSI data. The treatment changes included implantation of intracranial electrodes in patients previously deemed poor surgical candidates, a change in the location of implanted electrodes, or skipping implantation and proceeding directly to operation. This improvement in clinical utility over the past 15 years is noteworthy and should be celebrated.

Recent literature^{7,8} suggest a changing landscape in the types of epilepsy we see, with a decreasing incidence of patients with mesial temporal sclerosis and a higher proportion of patients with normal magnetic resonance imaging and complex seizure semiologies. While electromagnetic source imaging may not be necessary in working up patients with hippocampal atrophy and concordant EEG and PET data, Duez et al supply new evidence that EMSI provides added value in the presurgical evaluation of complex cases of drug-resistant focal epilepsy.

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