



Magnetoencephalography—Established but not yet Essential

Epilepsy Currents
2020, Vol. 20(2) 75-77
© The Author(s) 2020
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/1535759720906480
journals.sagepub.com/home/epi



Magnetoencephalography for Epileptic Focus Localization in a Series of 1000 Cases

Rampp S, Stefan H, Wu X, et al. *Brain*. 2019;142(10):3059-3071. doi:10.1093/brain/awz231.

The aim of epilepsy surgery in patients with focal, pharmacoresistant epilepsies is to remove the complete epileptogenic zone to achieve long-term seizure freedom. In addition to a spectrum of diagnostic methods, magnetoencephalography (MEG) focus localization is used for planning of epilepsy surgery. We present results from a retrospective observational cohort study of 1000 patients, evaluated using MEG at the University Hospital Erlangen over the time span of 28 years. One thousand consecutive cases were included in the study, evaluated at the University Hospital Erlangen between 1990 and 2018. All patients underwent MEG as part of clinical workup for epilepsy surgery. Of these, 405 patients underwent epilepsy surgery after MEG, with postsurgical follow-ups of up to 20 years. Sensitivity for interictal epileptic activity was evaluated, in addition to concordance of localization with the consensus of presurgical workup on a lobar level. We evaluate MEG characteristics of patients who underwent epilepsy surgery versus patients who did not proceed to surgery. In operated patients, resection of MEG localizations was related to postsurgical seizure outcomes, including long-term results after several years. In comparison, the association of lesionectomy with seizure outcomes was analyzed. Measures of diagnostic accuracy were calculated for MEG resection and lesionectomy. Sensitivity for interictal epileptic activity was 72% with significant differences between temporal and extra-temporal lobe epilepsy. MEG was concordant with the presurgical consensus in 51% and showed additional or more focal involvement in an additional 32%. Patients who proceeded to surgery showed a significantly higher percentage of monofocal MEG results. Complete MEG resection was associated with significantly higher chances to achieve seizure freedom in the short term and long term. Diagnostic accuracy was significant in temporal and extra-temporal lobe cases but was significantly higher in extra-temporal lobe epilepsy (diagnostic odds ratios of 4.4 and 41.6). Odds ratios were also higher in non-lesional versus lesional cases (42.0 vs 6.2). The results show that MEG provides nonredundant information, which significantly contributes to patient selection, focus localization, and ultimately long-term seizure freedom after epilepsy surgery. Specifically in extra-temporal lobe epilepsy and non-lesional cases, MEG provides excellent accuracy.

Commentary

Magnetoencephalography (MEG) for the localization of the epileptogenic zone entered clinical practice in the late 1990s and was routinely used by the mid-2000s.¹ Since that time, the adoption of this technology by the epilepsy community has been steady but slow. Although there are currently over 25 clinical MEG centers in the United States performing epilepsy studies, many academic centers and large epilepsy practices do not have on-site MEG access in the same manner as say, the now ubiquitous 3T MRI scanner which became commercially available in 1998.² The fact that the MEG scanner needs to be housed in a special magnetically shielded room and the entire system costs over US \$2M (personal communication) may factor into the slow adoption rate. However, the statement that MEG provides added value to the presurgical workup of select patients with epilepsy should not be a controversial one and not

likely to be the reason for the slow adoption. From a scientific perspective, there have been numerous prospective studies^{3,4} and retrospective large series⁵ which have *established* the efficacy and safety of MEG in localizing the epileptogenic zone.

The work of Rampp et al⁶ adds to the existing literature by presenting the largest case series of MEG studied for the localization of epileptogenic foci. This is a single-center retrospective observational cohort study spanning almost 30 years and reviewing 1274 MEG tests. The hypothesis was that MEG supports patient selection, contributes to the identification of the epileptogenic zone in presurgical evaluation, and impacts long-term seizure outcomes after epilepsy surgery. All recordings, source imaging, and interpretation were performed prospectively before surgery. Over the span of the study, 3 different MEG systems were used: a 37-channel radiometer system; a 2 × 37 channel axial gradiometer system or a 148-



Creative Commons Non Commercial No Derivs CC BY-NC-ND: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>) which permits non-commercial use, reproduction and distribution of the work as published without adaptation or alteration, without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).



channel axial gradiometer system; and a 248-channel whole-head magnetometer. Multiple source localization methods with multiple volume conductor models (single sphere, multiple spheres, and boundary element method) and multiple inverse solutions algorithms (LORETTA/sLORETTA, minimum norms, and CLARA) were used with Curry (Compumedics; Charlotte, NC) or BESA (BESA GmbH; Grafelfing, Germany) software. Association of seizure outcome after surgery with MEG/focus hypothesis concordance, as well as MEG resection, was evaluated. Magnetoencephalography detected pathologic spikes/sharp waves in 72% of the recordings, which is similar to other observational studies. Magnetoencephalography findings were “concordant” with the presurgical consensus (derived from video-electroencephalogram, structural and functional testing) in 50% of the patients, “consistent” in 32% and “discordant” in 18%. The percentage was higher in temporal lobe epilepsy cases compared to extra-temporal lobe epilepsy cases, which is not surprising and in line with what is seen in clinical practice. Approximately 40% of the cohort went on to epilepsy surgery. Follow-up data were available at the 1- and 5-year mark for many patients, with a few even up to 20 years. Complete resections of focal MEG localizations were significantly related to Engel 1 outcome. Complete resection of an epileptogenic lesion was also related to a better outcome, compared to cases with partial or no resection. Interestingly, the association of Engel 1 outcomes with complete MEG resections was stronger in non-lesional versus lesional cases.


The main strength of this paper is the sheer volume of the clinical material—almost 1300 MEG studies in 1000 consecutive patients evaluated as part of the workup for possible epilepsy surgery. A recent meta-analysis⁷ found 23 papers that associated MEG spiking to surgical resection site and then to surgical outcome. The total N was 440 in those 23 studies. When one notes that 405 patients underwent epilepsy surgery in Rampp et al, the contribution to the literature is immediately obvious. Adding to this, the longitudinal duration of this study spanning 28 years and a trial conducted at one of the oldest and most established MEG centers in Europe, and you have an impressive collection of carefully acquired data. If there were any doubts regarding the amount of available scientific data on MEG as a diagnostic tool for epilepsy, this study should dispel those concerns.

And yet, some of the strengths are also reflected in the limitations. During the long duration of the study, technological advancements in MEG hardware and software at the study site changed the study methodology. Over the course of study, 3 different MEG sensors acquired the data, ranging from a 37-channel partial hemisphere system to a 248-channel whole-head system. Multiple localization methods were utilized. While the authors did perform subgroup analyses and report that the results were not significantly different from era to era, one cannot help but wonder whether this unexpected finding is generalizable to all MEG centers or more due to the skill and expertise of the staff at Erlangen. The structure of this study also is designed to highlight the utility of MEG as a technology


rather than as a specific method, as multiple methods were used. Some of the data presented in this paper have been previously described.⁸ In a way, the paper almost acts as a review of the Erlangen experience over 3 separate eras.

The findings in this paper are in line with other studies on the subject and do not break significant new ground. A single-center prospective study of MEG (3) found a positive predictive value of 78% and a corrected negative predictive value of 64% with respect to the surgical outcome (compared to 83% and 65%, respectively, for the current study). A retrospective cohort study of 132 patients⁵ with a similar design to the current study was able to record interictal discharges in 78% of patients (compared to 72%) and found localizing MEG spikes predicted seizure freedom with a diagnostic odds ratio of 5.1 (compared to 8.4).

Rampp et al have contributed to firmly establishing MEG as one of the diagnostic tools in the presurgical evaluation of drug-resistant epilepsy. The next step for the field is to elevate the technology from “it would be nice to have in my backyard” to “I need this at my center”. What is needed to make this jump are new findings that would make MEG *essential* in the diagnostic workup for epilepsy surgery. One potential major advancement is for MEG to identify noninvasive biomarkers of the epileptogenic focus with high positive and negative predictive values. Coincidentally, in the very next issue of *Brain* after Rampp et al is another MEG paper⁹ reporting to be the first noninvasive study to detect high-frequency oscillations, address the efficacy of high-frequency oscillations over the different neural oscillatory frequencies, localize them and clinically validate them with the postsurgical outcome in patients with medically refractory epilepsy. Further studies that replicate and validate the finding that high-frequency oscillations detected by MEG significantly improve the presurgical assessment and can predict the postsurgical outcome would make MEG an indispensable technology in every epilepsy center.

By Jerry J. Shih 

ORCID iD

Jerry J. Shih  <https://orcid.org/0000-0002-0680-0362>

References

1. Knowlton RC, Shih JJ. Magnetoencephalography in epilepsy. *Epilepsia*. 2004;45(Suppl 4):61-71. PMID: 15281961.
2. Edelman R. The history of MR imaging as seen through the pages of radiology. *Radiology*. 2014;273(2 Suppl):S181-S200. doi:10.1148/radiol.14140706.
3. Knowlton RC, Elgavish RA, Bartolucci A, et al. Functional imaging: II. prediction of epilepsy surgery outcome. *Ann Neurol*. 2008; 64(1):35-41. doi:10.1002/ana.21419. PMID: 18570291.
4. Duez L, Tankisi H, Hansen PO, et al. Electromagnetic source imaging in presurgical workup of patients with epilepsy: a prospective study. *Neurology*. 2019;92(6):e576-e586. doi:10.1212/WNL.0000000000006877. PMID: 30610090.



5. Englot DJ, Nagarajan SS, Imber BS, et al. Epileptogenic zone localization using magnetoencephalography predicts seizure freedom in epilepsy surgery. *Epilepsia*. 2015;56(6):949-958. doi:10.1111/epi.13002. PMID: 25921215.
6. Rampp S, Stefan H, Wu X, et al. Magnetoencephalography for epileptic focus localization in a series of 1000 cases. *Brain*. 2019;142(10):3059-3071. doi:10.1093/brain/awz231. PMID: 31373622.
7. Sharma P, Seeck M, Beniczky S. Accuracy of interictal and ictal electric and magnetic source imaging: a systematic review and meta-analysis. *Front Neurol*. 2019;10:1250. doi:10.3389/fneur.2019.01250. eCollection 2019. PMID: 31849817.
8. Stefan H, Hummel C, Scheler G, et al. Magnetic brain source imaging of focal epileptic activity: a synopsis of 455 cases. *Brain*. 2003;126(Pt 11):2396-2405. PMID: 12876149.
9. Velmurugan J, Nagarajan SS, Mariyappa N, et al. Magnetoencephalography imaging of high frequency oscillations strengthens presurgical localization and outcome prediction. *Brain*. 2019;142(11):3514-3529. doi:10.1093/brain/awz284. PMID: 31553044.