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DOI:  
[10.3389/fneur.2022.1056301](https://doi.org/10.3389/fneur.2022.1056301)

Published: 24/11/2022

*Document Version*  
Publisher's PDF, also known as Version of record

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*Please cite the original version:*  
Alkawadri, R., Enatsu, R., Hämäläinen, M., & Bagi, A. (2022). Editorial: Magnetoencephalography: Methodological innovation paves the way for scientific discoveries and new clinical applications. *Frontiers in Neurology*, 13, 1-4. [1056301]. <https://doi.org/10.3389/fneur.2022.1056301>

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SPECIALTY SECTION  
This article was submitted to  
Applied Neuroimaging,  
a section of the journal  
Frontiers in Neurology

RECEIVED 28 September 2022  
ACCEPTED 13 October 2022  
PUBLISHED 24 November 2022

CITATION  
Alkawadri R, Enatsu R, Hämäläinen M  
and Bagić A (2022) Editorial:  
Magnetoencephalography:  
Methodological innovation paves the  
way for scientific discoveries and new  
clinical applications.  
*Front. Neurol.* 13:1056301.  
doi: 10.3389/fneur.2022.1056301

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# Editorial: Magnetoencephalography: Methodological innovation paves the way for scientific discoveries and new clinical applications

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## KEYWORDS

magnetoencephalography, epilepsy, source localization, epilepsy surgery, source estimate, functional mapping, electromagnetism

## Editorial on the Research Topic

[Magnetoencephalography: Methodological innovation paves the way for scientific discoveries and new clinical applications](#)

In 1971, less than five decades after the inception of electroencephalography (EEG), the first real-time magnetoencephalogram was obtained at MIT using a SQUID magnetometer, propelling magnetoencephalography (MEG) as a feasible approach for studying the human brain (1, 2). Then, in 1992, a multidisciplinary research group at the Low-Temperature Laboratory (LTL) of the Helsinki University of Technology (now part of Aalto University) produced the first whole-head MEG system with more than 100 channels (3). The key to this success was the fruitful interactions between the neuroscientists, physicists, mathematicians, engineers, and clinicians who worked together on the instrumentation, analysis methods, and actual neuroscience and clinical applications. Their success reverberated into several research laboratories worldwide, paving the way for MEG to become a recognized method for studying the brain.

During the 21st century, both basic neuroscience and clinical MEG studies have benefited from the use of high-quality open-source academic software packages, which have enhanced the rigor and reproducibility of scientific investigations using MEG. In addition, Optically Pumped Magnetometers (OPMs), novel room-temperature magnetic field sensors, hold promise for significantly improving the spatial resolution and sensitivity of MEG (4). These new devices will also enable the adaptation of the MEG array to the size of the head so that a high signal-to-noise ratio can be achieved, even in

studies of early brain development (5). To fully capitalize on these advances, one needs improvements to forward and inverse modeling techniques, as well as to the biophysical models of assemblies of neurons. The latter make it possible to suggest mechanisms underlying the observed macroscopic neural currents, lead to new testable hypotheses, and provide links between recordings in animal models and human MEG (6). Portable and real-time brain-computer MEG-based interfaces will likely become more integrated in the future (2, 7, 8).

The only established clinical applications of MEG, however, are the localization and characterization of epileptic activity (9) and presurgical mapping of the eloquent cortex (10). New studies give hope that MEG, used in combination with EEG and other non-invasive brain imaging methods, will in the future be harnessed for better diagnosis and for monitoring treatment efficacy in several neurological and psychiatric diseases (11, 12).

To that end, MEG has already changed clinical approaches and improved surgical outcomes in epilepsy (13–19), but, paradoxically, it has not yet secured its place in clinical practice (20–23). Furthermore, among the over 20 million patients with drug-resistant epilepsy (DRE) worldwide (2, 24), millions of potential surgical candidates continue to suffer unnecessarily because of the vast underutilization of surgery for epilepsy (2, 15, 25, 26). It appears that the epilepsy community does not have an efficient solution for this cardinal challenge (15, 25–27). Perhaps the blatant lack of synergies between MEG practitioners and the epilepsy community represents an opportunity to change this unfavorable clinical reality; i.e., these two groups could come together to promote non-pharmacologic DRE treatment options and thereby considerably increase the number of comprehensively evaluated patients, including many who could unquestionably benefit from an MEG (9, 23, 28). Yet it seems that previously initiated (i.e., currently stagnant and challenging) efforts to harmonize clinical MEG practice must materialize before we can expect MEG to take its proper place and be used at proper volume in clinical practice (29, 30). Considering that epilepsy surgery is an underutilized tool at large, this possibly applies even more to the underuse of MEG in the context of non-invasive presurgical mapping of the eloquent cortices as part of preparation for surgical interventions (9, 10, 23), where variability in clinical practice may be even greater and the concerted efforts of clinical magnetoencephalographers and neurosurgeons are necessary. In addition to the promise of possible new uses, such as ictal MEG (31, 32), real-world advances have been complicated by logistical concerns, e.g., the duration of recording; monetary, regulatory, or simply practice styles (e.g., handling referrals in less well-established indications such as non-surgical EEG-negative epilepsies); or attitudes toward research (33). However, this has opened doors that allow a more thoughtful approach to applying forward and inverse solutions between old, well-known, and practical ones, like single-point (i.e., single equivalent current dipole) solutions, and perhaps theoretically better and more realistic ones that are already gaining momentum after a slight lag taking advantage

of computational and hardware exponential advances. Another ongoing challenge is the lack of a good platform for worldwide data repositories, as well as of consortia that would allow real-time collaboration in an area still practiced in the form of medical art and expert consensus. This is not just a problem with MEG, but with epilepsy surgery in general.

In this collection, we aimed to provide a comprehensive update on the most recent advances in MEG utilization in clinical pre-surgical evaluation, functional mapping, cognitive neuroscience, source localization techniques, and the most recent technological advances. We also highlight network analysis as a newly emerged technique that has approached the pathophysiology of epilepsy from different perspectives. In no particular order: [Laohathai et al.](#) discussed fundamental proficiency in the practice of MEG in clinical epilepsy care. [Cao et al.](#) presented a perspective on using quantitative network analysis methods for assessing the epileptogenic zone. [Sun et al.](#) used magnetoencephalography and graph theory analysis to reveal the dynamics of functional connectivity networks during seizure termination in patients with childhood absence epilepsy. [Aung et al.](#) discussed how MEG's excellent temporal and spatial resolutions contribute to the understanding of a subject with both clinical and surgical importance: i.e., what constitutes the boundary between focal, frontal, and generalized epilepsies. [Khan et al.](#) reported on different frequency-specific hubs accounting for age-specific maturation. [Matsubara et al.](#) discovered that specific functional connectivity was bolstered in patients with benign adult familial myoclonus epilepsy, implying that ipsilateral sensorimotor responses may be a pathologically enhanced motor response homologous to the giant component. [Jousmäki](#) offered a unique set of skills and tools that enhance or complement existing commercial solutions with practical mapping applications both in clinical research and in practice. Similarly, [Anastasopoulou et al.](#) presented an innovative system that derived kinematic profiles of oro-facial movements during speech, with multiple potential cross-disciplinary applications. [Clarke et al.](#) presented a practical approach to addressing noise in data *via* pre-processing and demonstrated it with infant MEG data. Lastly, [Mylonas et al.](#) presented a multimodal, non-invasive neurophysiological approach for sleep spindle source localization and discussed its potential clinical applications.

Since its early clinical studies, MEG has provided a non-invasive tool with almost unparalleled temporal and spatial resolutions for various clinical and investigative situations. It has not yet settled in the clinical mainstream, mainly due to the lack of awareness about its indications and potential among practicing physicians, along with its suboptimal representation in the clinical training curricula. This is in addition to the known practical challenges in clinical settings, with their complex and expensive technical prerequisites and environments that are hardly ideal for investigating the true breadth of potential clinical applications. Furthermore, practical implementation of theoretical advances in the software and hardware solutions

could potentially replace current, more invasive clinical approaches—for instance, by accurately assessing deep sources and subcortical structures. We believe this journal issue provides a stepping-stone in the right direction to future scientific discoveries and new clinical applications.

## Author contributions

RA, RE, MH, and AB: draft of the manuscript, conceptualization, and revision of the manuscript. All authors contributed to the article and approved the submitted version.

## Acknowledgments

The guest editors acknowledge all authors and reviewers of the included manuscripts.

## References

- Cohen D. Magnetoencephalography: detection of the brain's electrical activity with a superconducting magnetometer. *Science*. (1972) 175:664–6. doi: 10.1126/science.175.4022.664
- Alkawadri R. Brain-computer interface (BCI) applications in mapping of epileptic brain networks based on intracranial-EEG: An update. *Front Neurosci*. (2019) 13:191. doi: 10.3389/fnins.2019.00191
- Hämäläinen MS. Magnetoencephalography: a tool for functional brain imaging. *Brain Topogr*. (1992) 5:95–102. doi: 10.1007/BF01129036
- Boto E, Meyer SS, Shah V, Alem O, Knappe S, Kruger P, et al. A new generation of magnetoencephalography: room temperature measurements using optically-pumped magnetometers. *Neuroimage*. (2017) 149:404–14. doi: 10.1016/j.neuroimage.2017.01.034
- Jas M, Jones SR, Hämäläinen MS. Whole-head OPM-MEG enables noninvasive assessment of functional connectivity. *Trends Neurosci*. (2021) 44:510–2. doi: 10.1016/j.tins.2021.04.006
- Hämäläinen M, Lundqvist D. MEG as an enabling tool in neuroscience: transcending boundaries with new analysis methods and devices. *Magnetoencephalogr Signals Dyn Cortical Networks*. (2019) 2019:3–39. doi: 10.1007/978-3-030-00087-5\_81
- Mcclay WA, Yadav N, Ozbek Y, Haas A, Attias HT, Nagarajan SS. A real-time magnetoencephalography brain-computer interface using interactive 3D visualization and the Hadoop ecosystem. *Brain Sci*. (2015) 5:419–40. doi: 10.3390/brainsci5040419
- Paek AY, Kilicarslan A, Korenko B, Gerginov V, Knappe S, Contreras-Vidal JL. Towards a portable magnetoencephalography based brain computer interface with optically-pumped magnetometers. In: *2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC): IEEE*. (2020). p. 3420–3.
- Bagić A, Funke ME, Ebersole J, Committee APS. ACMEGS Position Statement Committee: American Clinical MEG Society (ACMEGS) position statement: the value of magnetoencephalography (MEG)/magnetic source imaging (MSI) in noninvasive presurgical evaluation of patients with medically intractable localization-related epilepsy. *J Clin Neurophysiol*. (2009) 26:290–3. doi: 10.1097/WNP.0b013e3181b49d50
- Bagić A, Bowyer S, Kirsch H, Funke M, Burgess R. ACMEGS Position Statement Committee American Clinical MEG Society (ACMEGS) Position Statement# 2: the value of magnetoencephalography (MEG)/magnetic source imaging (MSI) in noninvasive presurgical mapping of eloquent cortices of patients preparing for surgical interventions. *J Clin Neurophysiol*. (2017) 34:189–95. doi: 10.1097/WNP.0000000000000366

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- O'Reilly C, Lewis JD, Elsabbagh M. Is functional brain connectivity atypical in autism? A systematic review of EEG and MEG studies. *PLoS ONE*. (2017) 12:e0175870. doi: 10.1371/journal.pone.0175870
- Roberts TP, Kuschner ES, Edgar JC. Biomarkers for autism spectrum disorder: opportunities for magnetoencephalography (MEG). *J Neurodev Disord*. (2021) 13:1–9. doi: 10.1186/s11689-021-09385-y
- Sutherland WW, Mamelak AN, Thyerlei D, Maleeva T, Minazad Y, Philpott L, et al. Influence of magnetic source imaging for planning intracranial EEG in epilepsy. *Neurology*. (2008) 71:990–6. doi: 10.1212/01.wnl.0000326591.29858.1a
- Knowlton RC, Razdan SN, Limdi N, Elgavish RA, Killen J, Blount J, et al. Effect of epilepsy magnetic source imaging on intracranial electrode placement. *Ann Neurol*. (2009) 65:716–23. doi: 10.1002/ana.21660
- Englot DJ, Nagarajan SS, Imber BS, Raygor KP, Honma SM, Mizuiri D, et al. Epileptogenic zone localization using magnetoencephalography predicts seizure freedom in epilepsy surgery. *Epilepsia*. (2015) 56:949–58. doi: 10.1111/epi.13002
- Murakami H, Wang ZI, Marashly A, Krishnan B, Prayson RA, Kakisaka Y, et al. Correlating magnetoencephalography to stereo-electroencephalography in patients undergoing epilepsy surgery. *Brain*. (2016) 139:2935–47. doi: 10.1093/brain/aww215
- Ramp S, Stefan H, Wu X, Kaltenhauser M, Maess B, Schmitt FC, et al. Magnetoencephalography for epileptic focus localization in a series of 1000 cases. *Brain*. (2019) 142:3059–71. doi: 10.1093/brain/awz231
- Burgess RC. MEG for greater sensitivity and more precise localization in epilepsy. *Neuroimaging Clin N Am*. (2020). 30:145–58. doi: 10.1016/j.nic.2020.02.004
- Burgess RC, Alkawadri R. Electromagnetic source imaging for stereo EEG planning. In: *A Practical Approach to Stereo EEG*. *demosMedical*. (2020). p. 35–48.
- Bagić AI. Disparities in clinical magnetoencephalography practice in the United States: a survey-based appraisal. *J Clin Neurophysiol*. (2011) 28:341–7. doi: 10.1097/WNO.0b013e3181c162a
- Shiraishi H, Ozaki I, Iguchi Y, Ishii R, Kamada K, Kameyama S, et al. Questionnaire survey of current status and problems in clinical applications of magnetoencephalography (MEG) in Japan. *Jpn J Clin Neurophysiol*. (2012) 40:119–30. doi: 10.11422/jscn.40.119
- Bagić A. An ignored lighthouse: is there underappreciation and underutilization of electro-magnetic source imaging? *Clin Neurophysiol*. (2014) 125:2322–3. doi: 10.1016/j.clinph.2014.04.017
- Bagić AI, Burgess RC. Utilization of MEG among the US epilepsy centers: a survey-based appraisal. *J Clin*

- Neurophysiol.* (2020) 37:599–605. doi: 10.1097/WNP.0000000000000716
24. Begley C, Wagner RG, Abraham A, Beghi E, Newton C, Kwon CS, et al. The global cost of epilepsy: a systematic review and extrapolation. *Epilepsia.* (2022) 63:892–903. doi: 10.1111/epi.17165
25. Wiebe S. Still an elusive target: guiding practice for epilepsy surgery. *Neurology.* (2010) 75:678–9. doi: 10.1212/WNL.0b013e3181eee510
26. Engel J Jr, Wiebe S. Who is a surgical candidate? *Handb Clin Neurol.* (2012) 108:821–8. doi: 10.1016/B978-0-444-52899-5.00030-7
27. Haneef Z, Stern J, Dewar S, Engel J Jr. Referral pattern for epilepsy surgery after evidence-based recommendations: a retrospective study. *Neurology.* (2010) 75:699–704. doi: 10.1212/WNL.0b013e3181eee457
28. Bagić AI, Burgess RC. Clinical magnetoencephalography practice in the United States ten years later: a survey-based reappraisal. *J Clin Neurophysiol.* (2020) 37:592–8. doi: 10.1097/WNP.0000000000000693
29. Bagić AI, Barkley GL, Chung CK, De Tiege X, Ebersole JS, Funke ME, et al. Clinical practice guidelines or clinical research guidelines? *Clin Neurophysiol.* (2018) 129:2054–5. doi: 10.1016/j.clinph.2018.06.015
30. Bagić AI, Rampp S. It is time to harmonize clinical MEG practice internationally. *Clin Neurophysiol.* (2020) 131:1769–71. doi: 10.1016/j.clinph.2020.04.020
31. Alkawadri R, Krishnan B, Kakisaka Y, Nair D, Mosher JC, Burgess RC, et al. Localization of the ictal onset zone with MEG using minimum norm estimate of a narrow band at seizure onset versus standard single current dipole modeling. *Clin Neurophysiol.* (2013) 124:1915–8. doi: 10.1016/j.clinph.2013.03.016
32. Alkawadri R, Burgess RC, Kakisaka Y, Mosher JC, Alexopoulos AV. Assessment of the utility of ictal magnetoencephalography in the localization of the epileptic seizure onset zone. *JAMA Neurol.* (2018) 75:1264–72. doi: 10.1001/jamaneurol.2018.1430
33. Alkawadri R, Burgess R, Isitan C, Wang IZ, Kakisaka Y, Alexopoulos AV. Yield of repeat routine MEG recordings in clinical practice. *Epilepsy Behav.* (2013) 27:416–9. doi: 10.1016/j.yebeh.2013.02.028