Medical Policy Manual

Topic: Magnetoencephalography/Magnetic Source Imaging (MSI)

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Section: Radiology

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Magnetoencephalography (MEG) is a noninvasive functional imaging technique in which the weak magnetic forces associated with the electrical activity of the brain are recorded externally on the scalp. Using mathematical modeling, the recorded data are then analyzed to provide an estimated location of the electrical activity. This information can be superimposed on an anatomic image of the brain, typically a magnetic resonance imaging scan (MRI), to produce a functional/anatomic image of the brain, referred to as magnetic source imaging or MSI. The primary advantage of MSI is that while the conductivity and thus the measurement of electrical activity as recorded by the electro-encephalogram (EEG) is altered by surrounding brain structures, the magnetic fields are not. This results, for instance, in better spatial localization of epileptic foci detected by MEG as compared with surface EEG, which can produce distorted signals. However, MEG has some limitations as well, since magnetic fields generated deep within brain tissues decay rapidly over distance and may be less likely to be detected at the surface compared with electrical fields. Therefore, surface EEG and MEG are often considered complimentary technologies.

The technique itself is extremely sophisticated. Detection of the weak magnetic fields depends on gradiometer detection coils coupled to a superconducting quantum interference device (SQUID), which in turn requires a specialized room, shielded from other magnetic sources. Mathematical modeling programs based on idealized assumptions are then used to translate the detected signals into functional images. In its early evolution, clinical applications were limited by the use of only one detection coil requiring lengthy imaging times, which, because of body movement, were also difficult to coordinate with the MRI. However, more recently the technique has evolved to multiple detection coils arranged in an array that can provide data more efficiently over a wide extracranial region.

One clinical application is localization of the pre- and postcentral gyri as a guide to surgical planning in patients scheduled to undergo neurosurgery for epilepsy, brain neoplasms, arteriovenous malformations, or other brain disorders. These gyri contain the “eloquent” sensorimotor areas of the brain involved in sensory, motor or language function. The preservation of these areas is considered critical during any type of brain surgery. In normal situations, these areas can be identified anatomically by MRI, but frequently the anatomy is distorted by underlying disease processes. In addition, the location of eloquent functions is variable even among healthy patients. Therefore, localization of eloquent cortex often requires such intraoperative invasive functional techniques as cortical stimulation under local anesthesia or somatosensory-evoked responses on electrocorticography (ECoG). While these techniques can be done at the same time as the planned resection, they are cumbersome and can add up to 45 minutes of anesthesia time. Furthermore, sometimes these techniques can be limited by the small surgical field. An additional presurgical test that is often used to localize the eloquent hemisphere is the intracarotid amobarbital test (Wada test). MEG/MSI has been proposed as a substitute for the invasive Wada test.

Another related clinical application of MEG/MSI is localization of epileptic foci, particularly for screening of surgical candidates and surgical planning. Alternative techniques include MRI, positron emission tomography (PET), or single photon emission computed tomography (SPECT) scanning. Anatomic imaging (i.e., MRI) is effective when epilepsy is associated with a mass lesion, such as a tumor, vascular malformations, or hippocampal atrophy. If an anatomic abnormality is not detected, patients may undergo a PET scan. In a small subset of patients, extended electrocorticography (ECoG) or stereotactic electroencephalography (SEEG) with implanted electrodes are considered the gold standards for localizing epileptogenic foci. MEG/MSI was principally investigated as an alternative to invasive monitoring.

MSI has also been used as a research tool in the investigation of dyslexia, psychiatric disorders, functional evaluation of the gastrointestinal tract, diagnosis of mesenteric ischemia, and evaluation of uterine contractions in pregnancy.

MEDICAL POLICY CRITERIA

I. Magnetoencephalography and magnetic source imaging may be **medically necessary** for the following indications:

   A. For the purpose of determining the laterality of language function, as a substitute for the Wada test, in patients being prepared for surgery for epilepsy, brain tumors, and other indications requiring brain resection

   B. As part of the preoperative evaluation of patients with intractable epilepsy (seizures refractory to medical therapy) when standard techniques, such as MRI and EEG, do not provide satisfactory localization of epileptic lesion(s).

II. Magnetoencephalography and magnetic source imaging are considered **investigational** for all other indications.

SCIENTIFIC EVIDENCE[1]

Literature Appraisal

Ideally, randomized trials comparing the outcomes of patients who received magnetoencephalography (MEG) as part of their diagnostic workup compared with patients who did not receive MEG could determine whether MEG improves patient outcomes. However, it is unlikely that randomized trials will ever be available due to the small number of patients who require this testing. Consequently, almost all of the studies evaluating MEG have been retrospective studies, where MEG, other tests, and surgery have been selectively applied to patients. Since patients often drop out of the diagnostic process before having intra-cranial electroencephalogram (IC-EEG), and many patients ultimately do not undergo surgery, most studies of associations between diagnostic tests and between diagnostic tests and outcomes are irreparably biased by selection and ascertainment biases. For example, studies evaluating the correlation between MEG and IC-EEG invariably did not account for the fact that MEG information was used to deselect a patient from undergoing IC-EEG. In addition, IC-EEG findings only imperfectly correlated with surgical outcomes, meaning that it was an imperfect reference standard.

In light of these obstacles to high quality evidence, the focus of this literature review was on whether there are consistent findings in nonrandomized studies to suggest associations between MEG findings and other noninvasive and invasive diagnostic tests and between MEG findings and surgical outcomes.

<u>Localization of Seizure Focus</u>

Systematic Review

This section was initially based on a 2008 BlueCross BlueShield Association Technology Evaluation Center (TEC) Special Report reviewing the evidence regarding MEG for localization of epileptic lesions.[2] MEG has been proposed as a method for localizing seizure foci for patients with normal or equivocal MRI and negative video-EEG examinations, so-called “nonlesional” epilepsy. Such patients often undergo MEG, positron emission tomography (PET), or ictal-SPECT (single photon emission computed tomography) tests to attempt to localize the seizure focus. They then often undergo invasive IC-EEG, a surgical procedure in which electrodes are inserted next to the brain. MEG would be considered useful if, when compared to not using MEG, it improved patient outcomes. Such improvement in outcomes would include more patients being rendered seizure-free, use of a less invasive and morbid diagnostic workup, and increased surgical success rates. This is a complicated array of outcomes that has not been thoroughly evaluated in a comprehensive manner.

Meta-Analysis

Lau and colleagues performed a meta-analysis of 17 studies that correlated MEG findings to surgical outcomes. In this meta-analysis, sensitivity and specificity had unorthodox definitions.[3] Sensitivity was defined as the proportion of patients cured with surgery, in whom the MEG-defined epileptic region was resected, and specificity was the proportion of patients not cured with surgery in whom the MEG-defined epileptic region was not resected. The pooled sensitivity was 0.84, meaning that among the total number of cured patients, 14% occurred despite the MEG-defined region not being resected. Pooled specificity was 0.52, meaning that among the 48% of patients not cured the MEG-localized region was resected. These results are consistent with an association between resection of the MEG-defined region and surgical cure, but it is an imperfect predictor of surgical success. The analysis did not address the question of whether MEG contributed original information to improve the probability of cure.

Nonrandomized Studies

- A representative study of MEG by Knowlton and colleagues demonstrated many of the problematic issues of evaluating MEG.[4] In this study of 160 patients with nonlesional epilepsy, all had MEG, but only 72 proceeded to IC-EEG. The calculations of diagnostic characteristics of MEG were biased by incomplete ascertainment of the reference standard. However, even examining the diagnostic characteristics of MEG using the 72 patients who underwent IC-EEG, sensitivities and specificities were well below 90%, indicating the likelihood of both false-positive and false-negative studies. Predictive values based on these sensitivities and specificities mean that MEG can neither rule in nor rule out a positive IC-EEG, meaning that MEG cannot be used as a triage test before IC-EEG to avoid the potential morbidity in a subset of patients.

- In a more recent study by Knowlton et al. of 77 patients who were recommended to have IC-EEG, MEG results modified the placement of electrodes in 18 cases.[5] Seven cases out of the 18 had positive intracranial seizure recordings involving the additional electrodes placed because of the MEG results. It was concluded that 4 patients are presumed to have had surgery modified as a result of the effect of MEG on altering the placement of electrodes. Surgical outcomes for these 4 patients are not reported. In this type of study, it is difficult to know how the patients would have been treated in the absence of the MEG results. It is stated that there was no additional morbidity resulting from the additional electrode placement. The study is not conclusive regarding the improvement in health outcomes due to use of MEG to alter electrode placement.

<u>Localization of Eloquent and Sensorimotor Areas</u>

Laterality of Language Function

The determination of the laterality of the language function is important to know to determine the suitability of a patient for surgery and what types of additional functional testing might be needed prior to or during surgery. The Wada test is a standard method of determining hemispheric dominance for language. However, it is an invasive test that requires catheterization of the internal carotid arteries, which carries the risk of complications. If MEG provided concordant information with the Wada test, then MEG could be a noninvasive substitute for the Wada test.

Several studies have shown high concordance between the Wada test and MEG. For example, in the largest study by Papanicolaou and co-workers among 85 patients, there was concordance between the MEG and Wada tests in 74 (87%).[6] In no cases were the tests discordant in a way that the findings were completely opposite. The discordant cases occurred mostly where the Wada test indicated left dominance and the MEG indicated bilateral language function. In an alternative type of analysis where the test was being used to evaluate the absence or presence of language function in the side in which surgical treatment was being planned, using the Wada procedure as the gold standard, MEG was 98% sensitive and 83% specific. Thus, if the presence of language function in the surgical site required intraoperative mapping and/or a tailored surgical approach, use of MEG rather than Wada would have “missed” one case where such an approach would be needed, and resulted in five cases in which such an approach was unnecessary (false-positive MEG). It should be noted, however, that the Wada test is not a perfect reference standard, and some discordance may reflect inaccuracy of the reference standard.

Mapping Sensorimotor Areas

The other potential use of MEG would be for the purpose of mapping the sensorimotor area of the brain, again to avoid such areas in the surgical resection area. Intraoperative mapping just before resection is generally done as the reference standard. Preoperative mapping as potentially done by MEG might aid in determining the suitability of the patient for surgery, or for assisting in the planning of other invasive testing.

Similar to the situation for localization of epilepsy focus, the literature is problematic in terms of evaluating the comprehensive outcomes of patients due to ascertainment and selection biases. Recent literature on the use of MEG in localizing the sensorimotor area provided only indirect evidence of utility. Studies tended to be limited to correlations between MEG and intraoperative mapping. The intraoperative mapping would be performed anyway in most resection patients.

A technology assessment on functional brain imaging performed by the Ontario Ministry of Health reviewed ten studies of MEG and invasive functional mapping and showed good to high correspondence between the two tests.[7] However, these studies did not demonstrate that MEG would replace intraoperative mapping or reduce the morbidity of such mapping by allowing a more focused procedure.

A study by Niranjan et al. reviewed the results of 45 patients in whom MEG was used for localizing somatosensory function.[8] In 32 patients who underwent surgery, surgical access routes were planned to avoid regions identified as somatosensory by MEG. All patients retained somatosensory function. It is unknown to what extent MEG provided unique information not provided by other tests. In a study by Tarapore et al., (15) 24 patients underwent MEG, transcranial magnetic stimulation, and intraoperative direct cortical stimulation to identify the motor cortex. MEG and navigated transcranial magnetic stimulation were both able to identify several areas of motor function, and the median distance between corresponding motor areas was 4.71 mm. When comparing MEG to direct cortical stimulation the median distance between corresponding motor sites (12.1 mm) was greater than the distance between navigated transcranial magnetic stimulation and direct cortical stimulation (2.13 mm). This study cannot determine whether MEG provided unique information that contributed to better patient outcomes.

Clinical Practice Guidelines and Position Statements

American Academy of Neurology (AAN)[9]

In 2009, the Medical Economics and Management Committee (MEM) of the AAN published a model medical policy for MEG. The model policy reported the results of a number of clinical trials but did not provide a critical analysis of the quality of the studies. Nor did the model policy describe the process by which the evidence was used to reach conclusions. For example, the AAN concluded that the Knowlton and colleagues article[4] demonstrated the value of MEG for localization of seizure foci despite the low sensitivity, specificity, positive- and negative-predictive values (72%, 70%, 78% and 64%, respectively). In addressing the lack of rigorous clinical trials for localization of seizure foci using MEG, the model policy noted more scrutiny for MEG than some earlier diagnostic technologies such as intracranial EEG and the Wada test which have “become the reference standard by virtue of [their] longevity” rather than based on clinical trial evidence. “The value of MEG lies in its ability to provide either new and non-duplicative or supplemental information to existing localizing technologies.”

The listed indications were for presurgical evaluation of the following:

- To identify and localize area(s) of epileptiform activity in patients with intractable focal epilepsy when other diagnostic techniques are inconclusive
- To identify, localize, and preserve eloquent cortex during resection surgery for brain tumors and vascular malformations

The limitations for MEG were that it is not a stand-alone test or the first order of test, but is one of several presurgical investigative technologies. In addition, MEG cannot replace but may guide placement of intracranial EEG.

American College of Radiology (ACR)[10]

A 2014 update of the ACR consensus-based practice guideline for seizures and epilepsy stated that only EEG using either scalp or intracranial electrodes and MEG "directly measure the brain's electrical activity. As such, they could or should be the gold standard for localization." In addition, the guideline stated that both EEG and MEG offer significantly higher temporal resolution than PET, ictal SPECT, and functional magnetic resonance imaging (fMRI). Below are the guideline conclusions for the role of MEG/MSI for preoperative diagnostic workup in surgical candidates with medically refractory epilepsy and/or for other surgical planning. In this patient population, MEG/MSI:

- May identify the ictal onset zone (IOZ) in nonlesional patients (normal MRI)
- Can provide confirmatory localization information for IOZ localization for potential lesions seen on MRI
- May help distinguish among multiple potential seizure foci in certain patients
- May guide placement of iEEG
- May substitute for invasive testing
- May be useful when other tests are discordant
- Is not a frontline or stand-alone tool
- Has the most value in the hands of experienced users in epilepsy referral centers

The American Clinical Magnetoencephalography Society (ACMEGS)[11]

In a 2011 consensus-based practice guideline on preoperative functional brain mapping using magnetic evoked fields, the ACMEGS listed the following indications for MEG evoked fields:

- Localization of somatosensory cortex, and primary motor, auditory, and visual cortexes
- Localization of the central sulcus in conjunction with motor evoked fields
- Biologic quality check of coordinate transformation (spatial biocalibration)
- Determining the language-dominant hemisphere in patients with either organic or functional brain diseases before surgical interventions
- Objective functional evaluation of language processing (i.e., identification of location and latencies)

Summary

Though the evidence is limited, magnetoencephalography/magnetic source imaging (MEG/MSI) has evolved to a standard of care as a noninvasive substitute for the Wada test in preoperative brain mapping in selected surgical candidates. In addition, clinical practice guidelines that address MEG/MSI consistently consider this imaging to add valuable information to conventional MRI and EEG. It is reasonable to conclude that preoperative MEG/MSI may provide additional diagnostic accuracy when standard techniques for localization of epileptic foci are inconclusive or discordant. Therefore, these indications for preoperative MEG/MSI are considered medically necessary in carefully selected patients.

There is currently insufficient evidence that on how magnetoencephalography/magnetic source imaging (MEG/MSI) may be used to improve patient health outcomes other than for preoperative evaluation of selected brain surgery candidates. Therefore, MEG/MSI is considered investigational for all other indications.

REFERENCES

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	95965	Magnetoencephalography (MEG), recording and analysis; for spontaneous brain magnetic activity (eg, epileptic cerebral cortex localization)
	95966	for evoked magnetic fields, single modality (eg, sensory, motor, language, or visual cortex localization)
	95967	for evoked magnetic fields, each additional modality (eg, sensory, motor, language, or visual cortex localization) (List separately in addition to code for primary procedure)
HCPCS	S8035	Magnetic source imaging