Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 3/1/13**
(See policy history boxes for previous effective dates)

Title: Magnetoencephalography / Magnetic Source Imaging

Description / Background

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. 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 (MRI) scan, 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 electroencephalogram (EEG) is altered by surrounding brain structures, the magnetic fields are not. Therefore, MSI permits a high-resolution image.

Detection of the weak magnetic fields depends on gradiometer detection coils coupled to a superconducting quantum interference device (SQUID), which 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 1 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, the preservation of which 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

the eloquent functions is variable, even among healthy patients. Therefore, localization of the eloquent cortex often requires such intraoperative invasive functional techniques as cortical stimulation with the patient 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. A preoperative test, which is often used to localize the eloquent hemisphere, is the Wada test. MEG/MSI has been proposed as a substitute for the Wada test.

Another related clinical application 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 malformation, or hippocampal atrophy. If an anatomic abnormality is not detected, patients may undergo a PET scan. In a small subset of patients, extended ECoG or stereotactic electroencephalography EEG (SEEG) with implanted electrodes is considered the gold standard for localizing epileptogenic foci. MEG/MSI has principally been investigated as a supplement to or an alternative to invasive monitoring.

Regulatory Status:

N/A

Medical Policy Statement

The safety and effectiveness of magnetoencephalography and magnetic source imaging have been established. They may be considered useful diagnostic options when indicated for selected patients.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Inclusions:
Magnetoencephalography/magnetic source imaging is considered established in the following situations:

- 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.
- As part of the preoperative evaluation of patients with intractable epilepsy (seizures refractory to at least two first-line anticonvulsants) when standard techniques, such as MRI and EEG, do not provide satisfactory localization of epileptic lesion(s).

Exclusions:
Magnetoencephalography/magnetic source imaging is considered experimental and investigational for all indications not listed under the inclusions.

CPT / HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

S8035 95965 95966 95967

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

Localization of Seizure Focus

This section is based on a 2008 TEC Special Report reviewing the evidence regarding MEG for localization of epileptic lesions. (1) MEG has been proposed as a method for localizing seizure foci for patients with normal or equivocal magnetic resonance imaging (MRI) and negative video-electroencephalogram (EEG) examinations, so-called “nonlesional” epilepsy. Such patients often undergo MEG, positron emission tomography (PET), or ictal-single photon emission computed tomography (SPECT) tests to attempt to localize the seizure focus. They then often undergo invasive intra-cranial 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 thoroughly been evaluated in a comprehensive manner.

Ideally, a randomized trial comparing the outcomes of patients who receive MEG as part of their diagnostic workup compared to patients who do not receive MEG could determine whether MEG improves patient outcomes. However, almost all of the studies evaluating MEG have been retrospective, where MEG, other tests, and surgery have been selectively applied to patients. Since patients often drop out of the diagnostic process before having intracranial EEG (IC-EEG), and many patients ultimately do not undergo surgery, most studies of associations between diagnostic tests and between diagnostic tests and outcomes are biased by selection and ascertainment biases. For example, studies that evaluate the correlation between MEG and IC-EEG invariably do not account for the fact that MEG information was sometimes used to deselect a patient from undergoing IC-EEG. In addition, IC-EEG findings only imperfectly correlate with surgical outcomes, meaning that it is an imperfect reference standard.

Numerous studies have shown associations between MEG findings and other noninvasive and invasive methods diagnostic tests, including IC-EEG, and between MEG findings and surgical outcomes. However, such studies do not allow any conclusions regarding whether MEG added incremental information to aid the management of such patients and whether patients’ outcomes were improved as a result of the additional diagnostic information.

A representative study of MEG by Knowlton and colleagues (2) demonstrates many of the problematic issues of evaluating MEG. 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 are 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.

One study more specifically addresses the concept that MEG may improve the yield of IC-EEG, thus allowing more patients to ultimately receive surgery. In a study by Knowlton et al., (3) out of 77 patients who were recommended to have IC-EEG, MEG results modified the placement of electrodes in 18 of the 77 cases. 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.

Several studies correlate MEG findings to surgical outcomes. Lau et al. (4) performed a meta-analysis of 17 such studies. In this meta-analysis, sensitivity and specificity have unorthodox definitions. Sensitivity is the proportion of patients cured with surgery in whom the MEG-defined epileptic region was resected, and specificity is 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 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 that it is an imperfect predictor of surgical success. However, it does not address the question as to whether MEG contributed original information to improve the probability of cure.

The American Clinical MEG Society released a position statement that supports the routine clinical use of MEG/MSI for pre-surgical evaluation of patients with medically intractable seizures. (5) In this statement, they specifically cite a study by Sutherling et al. (6) as being a “milestone class I study.” Class I evidence usually refers to randomized comparisons of treatment. However, the study by Sutherling et al. is called by its authors a “prospective, blinded crossover-controlled, single-treatment, observational case series.” The study attempts to determine the proportion of patients in whom the diagnostic or treatment strategy was changed as a consequence of MEG. They concluded that the test provided nonredundant information in 33% of patients, changed treatment in 9% of surgical patients, and benefited 21% of patients who had surgery. There was no control group in this study. Benefit of MEG was inferred by assumptions of what might have occurred in the absence of the MEG result. Less than half of the 69 patients went on to receive IC-EEG; thus, there appears to be incomplete accounting for outcomes of all patients in the study. A similar study by De Tiege et al. (7) also attempted to determine the number of patients in whom management decisions were altered based on MEG results. They concluded that clinical management was altered in 13% of all patients.

Conclusions.

There are no clinical trials demonstrating the utility of MEG in determining location of seizure focus and no high-quality studies of diagnostic accuracy. The available evidence on diagnostic accuracy is limited by ascertainment and selection biases because MEG findings were used to select and deselect patients in the diagnostic pathway thus, making it difficult to determine the role of MEG for the purpose of seizure localization. The evidence supporting the effect of MEG on patient outcomes is indirect and incomplete. Surgical management may be altered in a minority of patients based on MEG, but there is insufficient evidence to conclude that outcomes are improved as a result of these management changes. Trials with a control group are needed to determine whether good outcomes can be attributed to the change in management induced by knowledge of MEG findings.

Localization of Eloquent and Sensorimotor Areas

In a 2003 TEC Assessment of MEG, the evidence for this particular indication concluded that the evidence was insufficient to demonstrate efficacy. (8) At that time, the studies reviewed had relatively weak study methods and very limited numbers of subjects. There are two ways to analyze the potential utility of MEG for this indication. MEG could potentially be a noninvasive substitute for the Wada test, which is a standard method of determining hemispheric dominance for language. The Wada test requires catheterization of the internal carotid arteries, which carries the risk of complications. 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. If MEG provides concordant information with the Wada test, then such information would be obtained in a safe, noninvasive manner.

Several studies have shown high concordance between the Wada test and MEG. In the largest study, by Papanicolaou and co-workers, among 85 patients, there was concordance between the MEG and Wada tests in 74 (87%). (9) In no cases were the tests discordant in a way that the findings were completely opposite. The discordant cases occurred mostly when the Wada test indicated left dominance and the MEG indicated bilateral language function. In an alternative type of analysis, where the test is being used to evaluate the absence or presence of language function in the side in which surgical treatment is 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 requires 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 5 cases where such an approach was unnecessary (false-positive MEG). However, it should be noted that the Wada test is not a perfect reference standard, and some discordance may reflect inaccuracy of the reference standard. In another study by Hirata et al., MEG and the Wada test agreed in 19/20 (95%) of cases. (10)

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. Studies tend to be limited to correlations between MEG and intraoperative mapping. The intraoperative mapping would be performed anyway in most resection patients. Several of the studies evaluated in the 2003

TEC Assessment showed good to high concordance between MEG findings and intraoperative mapping. (8) A technology assessment on functional brain imaging performed by the Ontario Ministry of Health reviewed 10 studies of MEG and invasive functional mapping and showed good to high correspondence between the two tests. (11) However, these studies do not demonstrate that MEG would replace intraoperative mapping or reduce the morbidity of such mapping by allowing a more focused procedure.

Conclusions

There are no clinical trials that demonstrate the utility of using MEG for localization and lateralization of eloquent and sensorimotor regions of the brain. The available evidence consists of studies that correlate results of MEG with the Wada test, which is an alternative method for localization. The evidence generally shows that the concordance between MEG and the Wada test is high. Since MEG is a less invasive alternative to the Wada test, this evidence indicates that it is a reasonable alternative. There is also some evidence that the correlation of MEG with intraoperative mapping of eloquent and sensorimotor regions is high, but the test has not demonstrated sufficient accuracy to replace intraoperative mapping.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

In response to requests, Blue Cross Blue Shield Association received input from 2 physician specialty societies (5 reviewers) and 2 academic medical centers while this policy was under review in 2011. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. There was support for use of MEG/MSI for both localization of language function and as part of the preoperative evaluation of intractable seizures. Those providing clinical input indicated that use of MEG/MSI in the preoperative evaluation leads to identification of additional individuals whose epilepsy may be cured using a surgical approach.

Summary

The published evidence on MEG is suboptimal, with no clinical trials demonstrating utility. The literature on diagnostic accuracy has methodologic limitations, primarily selection bias and ascertainment bias. The available studies report that this test has high concordance with the Wada test, which is currently the main alternative for localizing eloquent functions. Management is changed in some patients based on MEG testing, but it has not been demonstrated that these changes in management lead to improved outcomes. Clinical input obtained in 2011 indicated consensus for use of MEG as a substitute for the Wada test in determining the laterality of language function in patients being considered for surgery to treat epilepsy, brain tumors, and other structural brain lesions. Clinical input also demonstrated consensus on use of MEG as part of the preoperative evaluation of patients with intractable epilepsy when standard techniques, such as MRI, are inconclusive.

Based on the available scientific literature, the results of clinical input, and a strong indirect chain of evidence that outcomes are improved, MEG/MSI may be considered medically necessary as a substitute for the Wada test for the purpose of determining laterality of language function. MEG may also be considered medically necessary as part of the preoperative evaluation of patients with intractable epilepsy when standard techniques such as MRI are inconclusive.

Government Regulations

National / Local:

There are no national or local Michigan coverage determinations on magnetoencephalography or magnetic source imaging. All codes are payable (except for S8035, as Medicare does not recognize S codes).

Michigan Department of Community Health:

The MDCH Practitioner and Medical Clinic Database indicates procedure codes 95965-95967 require manual review; clinical documentation required. There is no information available for procedure code S8035.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

References

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Special Report: Magnetoencephalography and magnetic source imaging for the purpose of presurgical localization of epileptic lesions—a challenge for technology evaluation. TEC Assessments 2008; Volume 23, Tab 8.
2. Knowlton RC, Elgavish RA, Limdi N et al. Functional imaging: I. Relative predictive value of intracranial electroencephalography. Ann Neurol 2008; 64(1):25-34.
3. Knowlton RC, Razdan SN, Limdi N et al. Effect of epilepsy magnetic source imaging on intracranial electrode placement. Ann Neurol 2009; 65(6):716-23.
4. Lau M, Yam D, Burneo JG. A systematic review on MEG and its use in the presurgical evaluation of localization-related epilepsy. Epilepsy Res 2008; 79(2-3):97-104.
5. Bagic A, Funke ME, Ebersole J. American Clinical MEG Society (ACMEGS) position statement: the value of magnetoencephalography (MEG)/magnetic source imaging in noninvasive presurgical evaluation of patients with medical intractable localization-related epilepsy. J Clin Neurophysiol 2009; 26(4):1-4.
6. Sutherling WW, Mamelak AN, Thyerlei D et al. Influence of magnetic source imaging for planning intracranial EEG in epilepsy. Neurology 2008; 71(13):990-6.
7. De Tiege X, Carrette E, Legros B et al. Clinical added value of magnetic source imaging in the presurgical evaluation of refractory focal epilepsy. J Neurol Neurosurg Psychiatry 2012; 83(4):417-23.
8. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Magnetoencephalography (MEG) and magnetic source imaging (MSI): presurgical localization of epileptic lesions and presurgical function mapping. TEC Assessments 2003; Volume 18, Tab 6.

9. Papanicolaou AC, Simos PG, Castillo EM et al. Magnetocephalography: a noninvasive alternative to the Wada procedure. J Neurosurg 2004; 100(5):867-76.
10. Hirata M, Kato A, Taniguchi M et al. Determination of language dominance with synthetic aperture magnetometry: comparison with the Wada test. Neuroimage 2004; 23(1):46-53.
11. Ontario Ministry of Health, Medical Advisory Secretariat (MAS). Functional brain imaging. Health Technology Policy Assessment. Toronto, ON: MAS; December 2006. Available online at: http://www.health.gov.on.ca/english/providers/program/ohtac/tech/reviews/pdf/rev_fbi_012507.pdf. Last accessed November 2008.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 9/25/12, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/20/04	5/20/04	6/29/04	Joint policy established
6/15/05	6/15/05	5/21/05	Routine maintenance
5/1/07	3/1/07	3/30/07	Routine maintenance
3/1/10	1/4/10	12/8/09	Policy updated with TEC Special Report and literature review. Rationale and references completely revised. Policy statement changed to state that use of magnetoencephalography and magnetic source imaging is considered established when done for the purpose of • Determining the laterality of language function, as an alternative to invasive testing, such as the Wada test, in patients being prepared for surgery for epilepsy, brain tumors and other indications requiring brain resection. • Establishing epileptic focus in patients with seizures when other noninvasive tests are inconclusive or contradictory in localizing site of abnormality, as an alternative to invasive testing. All other uses of MEG considered investigational.
9/1/11	6/21/11	6/21/11	Policy statement changed to, “The safety and effectiveness of magnetoencephalography and magnetic source imaging have been established. They may be considered useful diagnostic options when indicated for selected patients”. References updated.
3/1/13	12/11/12	12/31/12	Policy reformatted to mirror BCBSA.

Next Review Date: 4th Qtr, 2013

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN: N/A	Revised: N/A
BCBSM: N/A	Revised: N/A

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: MAGNETOENCEPHALOGRAPHY/MAGNETIC SOURCE IMAGING

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply.
BCNA (Medicare Advantage)	CPT codes 95965-95967 are payable by Medicare. HCPCS code S8035 is not recognized by Medicare.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.
Blue Cross Complete of Michigan	Covered; criteria apply.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.