Clinical Policy Title: Magnetoencephalography (MEG) and Magnetic Source Imaging (MSI)

Clinical Policy Number: 09.01.07

Effective Date: January 1, 2015
Initial Review Date: July 16, 2014
Most Recent Review Date: August 19, 2015
Next Review Date: August, 2016

ABOUT THIS POLICY: Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

Coverage policy

Select Health of South Carolina considers the use of magnetoencephalography (MEG) and magnetic source imaging (MSI) to be clinically proven and, therefore, medically necessary for pre-surgical evaluation in persons with intractable focal epilepsy to identify and localize areas of epileptiform activity when the following criteria are met:

<table>
<thead>
<tr>
<th>Medically necessary criteria (ALL criteria must be met)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results of surface electroencephalogram (EEG) and anatomic imaging (e.g., MRI) are discordant, or multifocal lesions exist.</td>
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<tr>
<td>Member is a candidate for invasive monitoring (iEEG).</td>
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</table>

Limitations:

All other uses of MEG and MSI are not medically necessary.
**Alternative covered services**

- Electroencephalogram.
- Head computed tomography (CT) with contrast.
- Magnetic resonance imaging (MRI) with or without contrast.
- Functional MRI head without contrast.
- Positron emission tomography (PET) with F-18 fluorodeoxyglucose (FDG)/head CT.
- Ictal single photon emission computed tomography (SPECT).
- Intracarotid amobarbital anesthesia test (Wada test).

**Background**

MEG involves external monitoring of the weak magnetic fields associated with electrical activity within the brain; changes in this neuromagnetic field provide information about brain function. MSI is MEG co-registered with magnetic resonance imaging (MRI). MSI has been investigated as a noninvasive technique for evaluating brain function and for preoperative planning in patients with a variety of neurological disorders, such as tumors, arteriovenous malformations (AVMs), epilepsy, trauma, stroke and neuropsychiatric conditions (Hayes 2008).

Advantages of MEG have been reported as high spatiotemporal resolution, insensitivity to conductivity differences (including skull defects and lesions), high signal-to-noise ratio in superficial areas, focus localization and functional mapping. Disadvantages have been stated as metal implant artefact, cost, insensitivity to radial sources, less sensitivity to deep sources (gradiometers) and limited long-term monitoring feasibility (i.e., low likelihood of ictal recordings) (Stephan 2011).

Purported clinical uses of MEG and MSI include diagnosis of seizure disorders and mass lesions not definable by standard methods; accurate and precise localization of epileptic foci to allow consideration of ablative therapy for refractory seizure disorders; preoperative mapping for mass lesions and vascular malformations prior to neurosurgical intervention to aid in designing surgical approach and surgical limitations; determination of cerebral characteristics in patients with psychiatric disorders; and assessment of normal and abnormal language development (Hayes 2008).

**Searches**

Select Health of South Carolina searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- Centers for Medicare & Medicaid Services (CMS).

We conducted searches on July 6, 2014, using the term “magnetoencephalography” [MeSH]. We included:
• **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use pre-determined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and thus are rated highest in evidence-grading hierarchies.

• **Guidelines based on systematic reviews.**

• **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Select Health of South Carolina identified one comprehensive review by Hayes (2008) along with two systematic reviews (Birch 2012a, Lau 2008), one cost-effectiveness analysis (Burch 2012a) and one decision analysis (Widjaja 2013) published subsequent to the Hayes review which serve as the basis for this policy. The preponderance of studies of MEG and MSI has been conducted in adults for the noninvasive, presurgical evaluation of localization-related refractory epilepsy. Conditions with less definitive evidence examined in the systematic reviews were pretreatment assessment and operative planning in patients with brain lesions (tumors and AVMs) and assessment of neuropsychiatric and learning disorders.

**Presurgical evaluation in patients with intractable focal epilepsy:**

Evidence from systematic reviews is overall of low quality with a high degree of bias. Studies focus on diagnostic accuracy and lack sufficient information to inform clinical practice with reasonable certainty. That said, Burch et al. and a Blue Cross Blue Shield Technology Evaluation Center (BCBSA TEC) Special Report (2009) noted the difficulties in assessing diagnostic technologies used for the purpose of localizing surgical sites that may relieve seizures. The factors that result in surgical cure are not fully understood. Intracranial EEG (IC-EEG) is an imperfect reference standard, and, consequently, correlations to IC-EEG are imperfect. IC-EEG is an invasive procedure that carries risks of complications, and many patients apparently drop out of the diagnostic workup before having this test. IC-EEG is not an “independent” reference standard, because the results of prior diagnostic tests are taken into account in the decision as to where and how to place the electrodes. IC-EEG does not always provide sufficient diagnostic information, and surgical cure can be achieved in the context of a positive or negative noninvasive test of any kind (Burch 2012b, BCBSA TEC 2009).

All patients generally undergo MRI and V-EEG. Patients with lesional epilepsy, sufficiently localized on these studies, proceed to surgery. Patients who have unclear or discordant test results may proceed to other noninvasive tests, such as FDG-PET, ictal SPECT or MEG to provide additional information known to correlate with seizure focus. At this point, a decision is made whether to proceed to IC-EEG. Existing studies of diagnostic accuracy suggest that the sensitivity or specificity of MEG alone is not sufficiently high to bypass IC-EEG in patients proceeding to surgery or to stop the workup. MEG may help guide placement of IC-EEG and, given the gravity of the situation and the uncertainty in determining who should receive
surgery, MEG may provide information that might influence a patient’s decision to undergo the risks of further testing or surgery if the outcome can be slightly better estimated. The decision to proceed to surgery appears to be based not on strict decision rules, but on the strength and consistency of findings that indicate the possibility of removing the part of the brain causing seizures (Burch 2012b, BCBSA TEC 2009).

- The evidence is sufficient to support the medical necessity of MEG and MSI for presurgical evaluation in persons with intractable focal epilepsy to identify and localize areas of epileptiform activity, when standard techniques, such as V-EEG and MRI, are inconclusive. The American College of Radiology (Smirniotopoulos 2011) and the American Academy of Neurology acknowledge the uncertainty in the information and recommend using MEG or MSI as one of several neuroimaging options available when surface EEG and anatomical imaging studies are inconclusive. To realize its optimum clinical potential, a comprehensive evaluation performed in epilepsy referral centers is necessary.

Other indications and populations:

There is a paucity of evidence evaluating the clinical utility of MEG/MSI for other indications and, specifically, in pediatric populations. A critique of the state of knowledge of neuroimaging for language impairment in children identified similar methodological limitations in the literature to those cited by Burch et al. and BCBSA TEC (2009): lack of an adequate control group, inadequate power, incomplete reporting of data, no correction for multiple comparisons, and data dredging and failure to analyze treatment effects appropriately (Bishop 2013).

- The evidence is insufficient to support the medical necessity of MEG/MSI for any other indication.

Policy updates:

We identified no new information that would change the findings in the original policy.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
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<tbody>
<tr>
<td>Hayes, Inc. (2008)</td>
<td>Key points:</td>
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<tr>
<td></td>
<td>• Nineteen case series; sample sizes ranged from 40 to 455 patients using MEG/MSI for epilepsy, structural brain lesions, and psychiatric and learning disorders; low quality with high risk of bias.</td>
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<tr>
<td></td>
<td>• Lack of large, well-designed, randomized studies, lack of postsurgical outcomes, heterogeneity of study populations and the diversity among both interventions and outcome measures.</td>
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<tr>
<td></td>
<td>• Mostly adult patients, very little evidence regarding the use of MEG/MSI in children.</td>
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</tbody>
</table>
• Most of the available studies failed to report any follow-up, although five studies reported follow-up of ≥ 1 year.
• No evidence MEG/MSI reduces the morbidity or mortality associated with epilepsy, brain lesions, or neuropsychiatric or learning disorders.
• Insufficient evidence.

Lau (2008)  
Key points:  
Presurgical evaluation of localization-related epilepsies  
• Systematic review of 17 studies of MEG/MSI.  
• Sensitivity 0.84 (range: 0.20 – 1.0) values for all articles, specificity 0.52 (0.06 – 1.00) values, positive likelihood ratios (0.67 – 2.0) and negative likelihood ratios (0.40 – 2.13) for some studies compared with the reference standard of intracranial EEG and surgical outcome.
• Insufficient evidence to support the relationship between the use of MEG in surgical planning and seizure-free outcome after epilepsy surgery.

Burch 2012a  
Key points:  
Presurgical evaluation of localization-related epilepsies  
• Systematic review of diagnostic accuracy, clinical utility and cost-effectiveness of non-invasive technologies used to define the seizure focus in surgical candidates with refractory partial epilepsy not caused by tumors, vascular malformations or trauma; five diagnostic accuracy studies and one study of outcome prediction using MEG/MSI.
• Overall quality of the available evidence was poor.
• There is no acceptable reference standard; reporting of clinical outcomes tends to be only following surgery; and decision level and clinical effectiveness studies are lacking. The additional value of diagnostic technologies for the localization of epileptic foci is related to the impact on treatment decisions and the value of the treatments themselves; this needs to be considered fully in informing cost-effectiveness.
• Available evidence is unreliable to inform clinical practice on the use of MEG.

Widjaja 2013  
Key points:  
Presurgical evaluation of localization-related epilepsies  
• Markov-based decision model: patients with suspected focal intractable epilepsy on video scalp EEG with normal MR imaging findings.
• Sensitivity and specificity based on Lau 2008.
• PET + MEG and SPECT were the preferred strategies in the base case. The choice of test was dependent on the sensitivity and specificity of test strategies and willingness to pay. High degree of uncertainty.

Glossary

Arteriovenous malformation (AVM) — An abnormal connection between arteries and veins in the brain. An AVM is usually congenital.

Epilepsy — Any of a group of syndromes characterized by paroxysmal transient disturbances of brain function that may be manifested as episodic impairment or loss of consciousness, abnormal motor phenomena, psychic or sensory disturbances, or perturbation of the autonomic nervous system; symptoms are due to disturbance of the electrical activity of the brain.
Ictal — An episode of seizure activity.

Refractory seizure disorder — Epilepsy inadequately controlled with anti-epileptic drug therapy.

References

Professional society guidelines/other:


Peer-reviewed references:


Burch J HS, Palmer S, Beyer F, et al. The clinical effectiveness and cost effectiveness of technologies used to visualise the seizure focus in people with refractory epilepsy being considered for surgery: a systematic review and decision-analytical model. Health Technol Asses. 2012;16(34).(a).


**Clinical trials:**


**CMS National Coverage Determinations (NCDs):**

No NCDs identified as of the writing of this policy.

**Local Coverage Determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**Commonly submitted codes:**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comment</th>
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<tbody>
<tr>
<td>95965</td>
<td>Magnetoencephalography (MEG), recording and analysis; for spontaneous brain magnetic activity (e.g., epileptic cerebral cortex localization).</td>
<td></td>
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<tr>
<td>ICD-9 Code</td>
<td>Description</td>
<td>Comment</td>
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<tr>
<td>345.51</td>
<td>Intractable, focal epilepsy.</td>
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<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comment</th>
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<tbody>
<tr>
<td>G40.011</td>
<td>Focal epilepsy, intractable, with status epilepticus</td>
<td></td>
</tr>
<tr>
<td>G40.019</td>
<td>Focal epilepsy, intractable, without status epilepticus</td>
<td></td>
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