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: July 20, 2016
Next Review Date: July 2017

Policy contains:
- Refractory epilepsy
- Glioma.
- Magnetoencephalography.
- Magnetic source imaging.

Related policies:
None.

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’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 Prestige Health Choice 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. Prestige Health Choice’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. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage policy

Prestige Health Choice considers the use of magnetoencephalography (MEG) and magnetic source imaging (MSI) to be clinically proven and, therefore, medically necessary for

1. Pre-surgical evaluation in persons with intractable focal epilepsy to identify and localize areas of epileptic form activity when other imaging studies (electroencephalogram/EEG and anatomic imaging/MRI) are discordant, or multifocal lesions exist, and member is a candidate for invasive electroencephalogram (EEG) monitoring

   OR

2. Pre-surgical mapping of the eloquent cortex prior to surgical resection of brain tumor or surgery to correct vascular malformations
Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website can be accessed at http://ahca.myflorida.com/Medicaid/.

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 and recording of the weak magnetic fields associated with naturally-occurring electrical currents within the brain. Changes in this neuromagnetic field detected by MEG provide information about brain function. The most commonly-used type of MEG device is the superconducting quantum interference device, or SQUID.

MSI is a procedure in which the MEG is co-registered with magnetic resonance imaging (MRI). MEG/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, neuropsychiatric conditions (Hayes, 2008). Other disorders that MEG/MSI can help identify include Multiple Sclerosis, Alzheimer’s disease, Sjogren’s syndrome, chronic alcoholism, and facial pain; little conclusive information exists for the test’s ability to diagnose these conditions. MEG/MSI is also used to study vision, audition, and language processing in the fetus and infant – also with no conclusive information on efficacy.

Advantages of MEG/MSI 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**

Prestige Health Choice 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 5, 2014. Search terms were “magnetoencephalography”, “MEG” “Magnetic Source Imaging” and “MSI.”.

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**

We identified one comprehensive review by Hayes (2008), along with two systematic reviews (Birch, 2012a and 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, pre-surgical evaluation of localization-related refractory epilepsy, along with pre-surgical evaluation of brain tumors. Conditions with less definitive evidence examined in the systematic reviews were assessment of neuropsychiatric and learning disorders.

**Pre-surgical 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. Burch et al. 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).

All pre-surgical patients with epilepsy 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).

Some studies have documented positive post-surgical outcomes in epilepsy patients who had undergone MEG/MSI prior to surgery. One found that 85% of patients with specific MEG findings were seizure free, for mean period of 3.6 years (Englot, 2015). Another found that non-redundant (from an EEG) information was found by MSI in 33% of epileptic patients, and that findings changed the surgical decision in 20% (Sutherling, 2008).

The evidence is sufficient to support the medical necessity of MEG/MSI for pre-surgical 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 (Dory, 2012) 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.

**Pre-Surgical evaluation in patients with brain tumors:**
Other than epilepsy, the disorder with the most documentation of MEG/MSI efficacy is brain cancer. One report concluded that MEG gives valuable pre-surgical information of tissue functionality, and thus optimizes pre-operative patient counseling and surgical strategy, after all 79 patients with brain gliomas reported no new neurological deficits six months after surgery (Tarapore, 2012). Another found that MEG testing resulted in 46.2% of 119 glioma patients not considered for surgery, due to tumor invasion to the functional cortex (Ganslandt, 2004). A third concluded that MEG can offer valuable information to plan surgeries as well as structural-functional relationships in healthy controls (Guggisberg, 2008). MEG/MSI is generally considered clinically proven for use in brain cancer patients, prior to surgery.

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: 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:

The July 2016 review of the literature provided the basis for adding the coverage of MEG/MSI for brain tumors and vascular malformations. Nine (9) new references were added, including two (2) in the Summary of Clinical Evidence.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Englot (2015)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td></td>
<td>• 132 subject with focal epilepsy who had surgery after MEG, followed mean 3.6 years</td>
</tr>
<tr>
<td></td>
<td>• 86% with specific MEG findings were seizure-free</td>
</tr>
<tr>
<td></td>
<td>• 37% with non-specific MEG findings were seizure free</td>
</tr>
<tr>
<td>Widjaja (2013)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td></td>
<td>• Markov-based decision model: patients with suspected focal intractable epilepsy on video scalp EEG with normal MR imaging findings</td>
</tr>
<tr>
<td></td>
<td>• Sensitivity and specificity based on Lau 2008</td>
</tr>
<tr>
<td></td>
<td>• 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</td>
</tr>
<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Burch (2012a)          | Key points:                                                                                               ~ 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  |
| Tarapore (2012)        | Key points:                                                                                               ~ 79 subjects with focal brain gliomas, all had pre-surgical MEG  
~ 0% had new neurological deficits six months post-operatively  
~ Conclusion: MEG provides valuable pre-surgical information on tissue functionality, optimizing pre-surgical patient counseling and surgical strategy in subjects with glioma.  |
| Hayes, Inc. (2008)     | Key points:                                                                                               ~ Nineteen case series; sample sizes ranged from 40 to 455 patients  
~ Low quality with high risk of bias  
~ Lack of large, well-designed, randomized studies, lack of postsurgical outcomes, heterogeneity of study populations and the diversity among both interventions and outcome measures  
~ Mostly adult patients, very little evidence regarding the use of MEG/MSI in children.  
~ 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:                                                                                               ~ 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  |
| Ganslandt (2004)       | Key points:                                                                                               ~                                                                      |
Ability of MSI to support clinical decisions pre-surgical in subjects with glioma.

- 119 patients with glioma given MEG to determine further treatment
- 46.2% not considered for surgery due to tumor invasion of functional cortex
- MSI is valuable in clinical decision making process of lesions near important brain areas

Glossary

**Eloquent cortex** — a name used by neurologists for areas of cortex that—if removed—will result in loss of sensory processing or linguistic ability, minor paralysis, or paralysis

**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.

**Glioma** — A type of tumor arising from the supportive “gluey” tissue of the brain.

**Ictal** — An episode of seizure activity.

**Magnetoencephalography (MEG)** — A functional neuroimaging technique for mapping brain activity by recording naturally-occurring magnetic fields produced by electrical currents.

**Magnetic Source Imaging (MSI)** — A technique obtained by combining MEG results with Magnetic Resource Imaging (MRI) results, to create a functional map of brain activity.

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

References

Professional society guidelines/other:


Bagic A, Funke ME, Ebersole J. American Clinical MEG Society (ACMEGS) position statement: the value of magnetoencephalography (MEG)/magnetic source imaging (MSI) in non-invasive pre-surgical...


Peer-reviewed references:


Burch J Hinde S, 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:**

Searched clinicaltrials.gov on July 6, 2016 using terms “MEG” and “MSI.” | Open Studies. 220 studies found for MEG, 153 found for MSI. Two (2) relevant:


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>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comment</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Level II</th>
<th>Description</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>