Aetna considers magnetic source imaging (MSI) or magnetoencephalography (MEG) medically necessary for pre-surgical evaluation in persons with intractable focal epilepsy to identify and localize areas of epileptiform activity, when discordance or continuing questions arise from among other techniques designed to localize a focus.

Aetna considers MSI or MEG experimental and investigational when used as a stand-alone test or as the first order of test after clinical and routine electroencephalographic (EEG) diagnosis of epilepsy because its effectiveness for these indications has not been established.

Aetna considers MSI or MEG experimental and investigational for the following indications (not an all-inclusive list) because its effectiveness for these indications has not been established:
Diagnosis, quantification, and monitoring of neurocognitive problems following aneurysmal subarachnoid hemorrhage
- Differentiation of post-traumatic stress disorder and traumatic brain injury
- Evaluation of alcohol dependence
- Evaluation of Alzheimer's disease
- Evaluation of attention-deficit hyperactivity disorder
- Evaluation of autism
- Evaluation of bipolar disorder
- Evaluation of brain tumors
- Evaluation of bulimia nervosa
- Evaluation of cognitive and mental disorders
- Evaluation of developmental dyslexia
- Evaluation of fibromyalgia
- Evaluation of Huntington's disease
- Evaluation of learning disorders
- Evaluation of major depressive disorder
- Evaluation of migraines
- Evaluation of multiple sclerosis
- Evaluation of Parkinson's disease
- Evaluation of prosopagnosia
- Evaluation of schizophrenia
- Evaluation of social phobia
- Evaluation of stroke rehabilitation
- Evaluation of traumatic brain injury
- Fetal neurological assessment.

See also CPB 0648 - Autism Spectrum Disorders (../600_699/0648.html)

Background
Magnetic source imaging (MSI) or magnetoencephalography (MEG) is a non-invasive functional imaging technique in which the weak magnetic forces associated with the electrical activity of the brain are monitored externally on the scalp, i.e., MSI differs from a standard electroencephalography (EEG) in that it records the magnetic fields instead of the electrical activity. The principal advantage of MSI is that while the measurement of electrical activities is affected by surrounding brain structures, the magnetic fields are not. Thus, when coupled to a MRI, MSI allows a high-resolution functional/anatomical image.
(Smirniotopolous, et al., 2011) concluded that MEG may be appropriate (appropriateness rating of 6 out of 10) for evaluating surgical candidates with medically refractory epilepsy. The Appropriateness Criteria state that MEG is complementary to EEG and may provide confirmatory information for the ictal onset zone (IOZ) localization for potential lesions seen on MRI. MEG provides better spatial resolution (2-3 mm) as compared to EEG (7-10 mm). MEG can also guide the placement of iEEG grids; and in certain patients, it may help distinguish among multiple potential seizure foci. The ACR criteria judged MEG/MSI as usually not appropriate for evaluating new onset seizures.

An assessment conducted by the BlueCross BlueShield Technology Evaluation Center (2003) concluded that there is insufficient evidence to render conclusions regarding the effect of MSI/MEG on health outcomes for either pre-surgical localization of seizure origin or pre-surgical functional mapping. An assessment of MEG from the Ontario Ministry of Health and Long Term Care Medical Advisory Secretariat (2006) found that studies are generally of poor quality, and were graded of low or very-low quality of evidence. Specifically with regard to the use of MEG in epilepsy, the assessment stated that it is unclear whether MEG has similar accuracy in localizing seizure foci as intracranial EEG.

Pataria et al (2005) studied the functional organization of the inter-ictal spike complex in 30 patients with mesial temporal lobe epilepsy (MTLE) using combined MEG/EEG recordings. Spikes could be recorded in 14 patients (47 %) during the 2- to 3-hr MEG/EEG recording session. The MEG and EEG spikes were subjected to separate dipole analyses; the MEG spike dipole localizations were superimposed on MRI scans. All spike dipoles could be localized to the temporal lobe with a clear preponderance in the medial region. Based on dipole orientations in MEG, patients could be classified into 2 groups: (i) patients with anterior medial vertical (AMV) dipoles, suggesting epileptic activity in the mediobasal temporal lobe, and (ii) patients with anterior medial horizontal (AMH) dipoles, indicating involvement of the temporal pole and the anterior parts of the lateral temporal lobe. Whereas patients with AMV dipoles had strictly unitemporal inter-ictal and ictal EEG changes during prolonged video-EEG monitoring, 50 % of patients with AMH...
dipoles showed evidence of bitemporal affection on inter-ictal and ictal EEG. Nine patients underwent epilepsy surgery so far. While all 5 patients with AMV dipoles became completely seizure-free post-operatively (Class Ia), 2 out of 4 patients with AMH dipoles experienced persistent auras (Class Ib). However, this difference was not statistically significant. These researchers concluded that combined MEG/EEG dipole modeling can identify subcompartments of the temporal lobe involved in epileptic activity and may be helpful to differentiate between subtypes of mesial temporal lobe epilepsy non-invasively. The results need to be confirmed in well-designed studies with larger sample sizes.

Papanicolaou et al (2005) predicted the replacement of the more invasive procedure with MEG in the near future for temporal lobe epilepsy cases, subsequent to the optimization of the conditions under which pre-operative MEG is performed. Furthermore, in a review on management of intractable epilepsy in infancy and childhood, Wirrell et al (2006) stated that “MEG has proven to be useful in mapping sensory cortex and may also be useful to define eloquent cortex. The author stated that in a recent study (Stefan et al, 2003), magnetic source imaging proved most useful in the localization of extra-temporal foci. The usefulness of MEG in pediatric epilepsy surgery planning remains to be determined”.

Available evidence lacks systematic comparisons to other diagnostic techniques. Furthermore, there are no data specifically documenting how MSI/MEG might alter surgical management (i.e., changing the surgical approach or reducing the time needed for intra-operative mapping).

Knowlton et al (2006) stated that non-invasive brain imaging tests can potentially supplement or even replace the use of intra-cranial EEG (ICEEG) in pre-surgical epilepsy evaluation. These investigators prospectively examined the agreement between MSI and ICEEG localization in epilepsy surgery candidates. Patients completing video monitoring with scalp EEG who had intractable partial epilepsy based on ictal electro-clinico-anatomical features were screened. A total of 49 enrolled patients (mean age of 27 years; ranging from 1 to 61 years) completed MSI and ICEEG studies. Decisions about ICEEG and surgery were made at a consensus conference where MSI could
only influence ICEEG coverage by indicating supplemental coverage to that already planned by an original hypothesis. The positive predictive value of MSI for seizure localization was 82 to 90 %, depending on whether computed against ICEEG alone or in combination with surgical outcome. The kappa score of agreement for MSI with ICEEG was 0.2744 (p < 0.01). These researchers found that MSI yields localizing information with a high positive predictive value in epilepsy surgery candidates who typically require ICEEG. This finding suggested that enough clinical validity exists for MSI to potentially replace ICEEG for seizure localization. Moreover, the authors stated that future studies must ascertain if certain MSI results are more predictive of accurate epilepsy localization, and if so, what other criteria are sufficient to preclude the need for further confirmation by ICEEG. This type of weighting will have to be measured in the context of all other epilepsy localization test. Furthermore, how discordant results from multiple non-invasive tests should be handled in a single surgical decision-making score, either toward or away from surgical resection, will have to be determined from greater outcome evidence.

Sutherling et al (2008) reported on preliminary results of an ongoing, long-term clinical study in epilepsy, where MSI changed surgical decisions. The investigators determined whether MSI changed the surgical decision in a prospective, blinded, crossover-controlled, single-treatment, observational case series. Sixty-nine sequential patients diagnosed with partial epilepsy of suspected neocortical origin had video-EEG and imaging. All met criteria for intracranial EEG (ICEEG). At a surgical conference, a decision was made before and after presentation of MSI. Cases where MSI altered the decision were noted. The investigators found that MSI gave non-redundant information in 23 patients (33 %). Magnetic source imaging added ICEEG electrodes in 9 (13 %) and changed the surgical decision in another 14 (20 %). Based on MSI, 16 patients (23 %) were scheduled for different ICEEG coverage. Twenty-eight have gone to ICEEG, 29 to resection, and 14 to vagal nerve stimulation, including 17 where MSI changed the decision. Additional electrodes in 4 patients covered the correct: hemisphere in 3, lobe in 3, and sublobar ictal onset zone in 1. Magnetic source imaging avoided contralateral electrodes in
2, who both localized on ICEEG; it added information to ICEEG in 1. The investigators concluded that MSI provided non-redundant information in 33% of patients. In those who have undergone surgery to date, MSI added useful information that changed treatment in 6 (9%), without increasing complications. The investigators stated that MSI had benefited 21% who have gone to surgery.

In a cohort study of epilepsy surgery candidates not sufficiently localized with non-invasive studies, Knowlton et al (2008) evaluated the predictive and prognostic value of MSI, PET, and ictal SPECT as compared with intracranial electroencephalography (ICEEG) localization in epilepsy surgery. Of 160 patients enrolled over 4 years, 77 completed ICEEG seizure monitoring. Sensitivity, specificity, and predictive values relative to ICEEG were computed for each modality. Seizures were not captured in 5 patients. Of the 72 diagnostic ICEEG studies, seizure localization results were 74% localized, 10% multi-focal, and 17% non-localized. Sixty-one percent were localized to neocortical regions. Depending on patient subgroup pairs, sensitivity ranged from 58 to 64% (MSI), 22 to 40% (PET), and 39 to 48% (SPECT); specificity ranges were 79 to 88% (MSI), 53 to 63% (PET), and 44 to 50% (SPECT). Gains in diagnostic yield were seen only with the combination of MSI and PET or MSI and ictal SPECT. Localization concordance with ICEEG was greatest with MSI, but a significant difference was demonstrated only between MSI and PET. The investigators found that conclusively positive MSI has a high predictive value for seizures localized with ICEEG, and that diagnostic gain may be achieved with addition of either PET or ictal SPECT to MSI. The investigators noted that diagnostic values for imaging tests are lower than "true values" because of the limitations of ICEEG as a gold standard.

In a separate paper, Knowlton et al (2008) examined the outcomes of cohort subjects with epilepsy who subsequently underwent surgical resection. Of 160 patients enrolled, 62 completed ICEEG and subsequent surgical resection; 61% resulted in an Engel I seizure-free outcome at a minimum of 1-year follow-up (mean = 3.4 years). Sensitivity, specificity, and predictive values were computed for each modality. Multi-variate
logistical regression was used to identify prediction of surgical outcome by imaging test. The investigators reported that MSI sensitivity for a conclusively localized study was 55% with a positive predictive value of 78%. Eliminating non-diagnostic MSI cases (no spikes captured during recording) yielded a corrected negative predictive value of 64%. With available comparison subgroups FDG-PET and ictal SPECT values were similar to MSI. The odds ratio (adjusted for epilepsy and MRI classification) for MSI prediction of seizure-free outcome was 4.4 (p = 0.01). In cases with both PET and MSI, the adjusted odds ratio for PET was 7.1 (p <0.01) and for MSI was 6.4 (p = 0.01). In the cases with all 3 tests (n = 27), ictal SPECT had the highest OR of 9.1 (p = 0.05). The investigators concluded that MSI, FDG-PET, and ictal SPECT each have clinical value in predicting seizure-free surgical outcome in epilepsy surgery candidates who typically require ICEEG.

Rampp and Stefan (2007) stated that while MEG systems are still expensive and complex, the technique’s characteristics offer promising possibilities for the investigation of epilepsy patients (e.g., for focus localization and pre-surgical functional mapping).

Lam et al (2008) conducted a systematic evidence review of evidence of the effectiveness of MEG in the pre-surgical evaluation of localization-related epilepsies. The investigators identified studies correlating surgical outcome (seizure freedom) with MEG source localization and resection area. The investigators found these studies of MEG reported wide ranging sensitivities (range of 0.20 to 1.0), specificities (0.06 to 1.00), positive likelihood ratios (0.67 to 2.0), and negative likelihood ratios (0.40 to 2.13). Based upon the results of their systematic review of the literature, the investigators concluded that "there is insufficient evidence in the current literature to support the relationship between the use of MEG in surgical planning and seizure-free outcome after epilepsy surgery." The investigators stated that additional studies are needed.

In a review on interictal electromagnetic source imaging in focal epilepsy, Leijten and Huiskamp (2008) noted that whether MEG is superior to EEG is still unresolved, because fair comparisons are
lacking. Clinical studies have not yet adopted all technical possibilities. Localization accuracy seems high, but studies lack uniformity regarding methods, goals and outcome parameters. Therefore, the final place of electromagnetic source imaging in the pre-surgical work-up is still to be determined. The diagnostic potential is probably highest in extra-temporal epilepsies, and lowest in mesial temporal lobe epilepsy. The authors concluded that electromagnetic source imaging has evolved technically and can provide valuable localization information in the pre-surgical evaluation of patients with epilepsy. However, standardization of the technique is required before further clinical studies can better establish its role in pre-surgical evaluation of focal epilepsy.

A BlueCross BlueShield Association's technology assessment on MEG and MSI for the purpose of pre-surgical localization of epileptic lesions (2009) that "[t]he argument that MEG improves the diagnostic yield of IC-EEG is often made, but it is difficult to identify studies that can support this argument. Studies that compare IC-EEG to MEG do not inform this particular question. On the other hand, given the gravity of this particular situation, there are some possible arguments to be made on behalf of MEG. Given that current decision-making regarding who should receive surgery and what type of surgery is done with some uncertainty and lack of a true reference standard, an additional piece of information that is known to correlate with seizure focus could be arguably of some value in making difficult decisions. The diagnostic test is easy to perform and non-invasive. Also, IC-EEG and surgery are extremely invasive procedures that do not always provide diagnostic information. Information from MEG might influence a patient’s decision to undergo the risks of further testing or surgery if the outcome can be slightly better estimated. However, given that one possible outcome of use of MEG may result in avoidance of tests and procedures that may benefit the patient, it is not possible to rule out harm from use of the test. The net effect of the use of MEG on patient outcomes for this indication remains to be determined".

Magnetoecephalography can not replace, but may guide the placement of intracranial EEG and, in some patients, avoid an unnecessary intracranial EEG (AAN, 2009).
Magnetoencephalography is not the first order of test after clinical and routine EEG diagnosis of epilepsy. It is one of several advanced pre-surgical investigative technologies. The need for MEG is much lower than surface EEG and anatomical imaging studies (AAN, 2009). Magnetoencephalography is not a stand-alone test. To realize its optimum clinical potential a comprehensive team evaluation, such as that available in comprehensive epilepsy centers, is necessary. The team usually comprises a neurologist with expertise in epilepsy, a neurosurgeon, MEG-physicists, psychologists, nurses and staff experienced in treatment of seizure disorders.

Although the literature contains some information regarding the clinical use of MSI in the pre-surgical mapping of eloquent cortex in patients with intra-cranial tumors or arterio-venous malformations, there is insufficient scientific evidence regarding its effectiveness for this indication. Critical outcomes are lacking, such as comparison of MSI with intra-operative methods and whether the use of MSI would change the management of patients such that clinical outcomes are improved.

Language and memory functions may reside in both or one hemisphere in patients with epilepsy. Determination of laterality is important to preserve as much language and memory functions as feasible during resective surgery. The intracarotid amobarbital test (Wada test) has long been used for language and memory localization. It has both merits and shortcomings when compared with newer tests. It is invasive, uncomfortable and carries certain morbidity. Several alternatives such as neuropsychological testing, functional MRI (fMRI), MEG, behavioral testing and SPECT-PET are available. Each has certain advantages and disadvantages.

There is limited evidence for the use of MEG as a substitute or supplement to the Wada test to identify the eloquent cortex for removal of brain tumors or arterio-venous malformations. Pelletier et al (2007) compared all the Wada alternatives in a comprehensive review. Magnetoencephalography, while requiring patient co-operation, had the advantage of being a non-invasive direct measure with excellent temporal resolution.
Pelletier et al (2007) reported that the high concordance between the findings of the Wada test and neuroimaging techniques, especially fMRI, MEG, functional transcranial Doppler and possibly near infrared spectroscopy, is encouraging and holds promise that the Wada procedure will be eventually replaced by these non-invasive techniques. Pelletier et al (2007) concluded, however, that these methods still need to be refined, and certain incongruities between the Wada procedure and these techniques have to be addressed. For instance, fMRI provides little information regarding right hemisphere participation in language processing in patients with bilateral speech representation. Magnetoencephalography has the disadvantage that it is limited to the evaluation of receptive language. Furthermore, to obtain conclusive and reliable activation patterns, both fMRI and MEG require that the patient remain motionless in the scanner and comply with the test instructions. This restricts the application of these imaging techniques in young children and special populations. Pelletier et al (2007) stated that these neuroimaging techniques vary with regard to their spatial and temporal resolution. Functional MRI has good spatial resolution and relatively poor temporal resolution. The reverse is true for MEG. Furthermore, different techniques target different functions. The authors suggested that a multi-modal approach, combining several techniques, is therefore the safest way to provide the surgeon with reliable information.

There is additional evidence for the use of MEG to localize the eloquent cortex in resections for nonepilepsy lesions. Grover et al (2007) reported on a retrospective study where visual evoked cortical magnetic field (VEF) waveforms were recorded from both hemifields in 21 patients with temporo-parieto-occipital mass lesions to identify preserved visual pathways. Fifteen patients had visual symptoms pre-operatively. Magnetoencephalography VEF responses were detected, using single equivalent current dipole, in 17 of 21 patients studied. Displaced or abnormal responses were seen in 15 patients with disruption of pathway in 1 patient. Three of 21 patients had alterations in the surgical approach or the planned resection based on the MEG findings. The investigators concluded that the surgical outcome for these 3 patients suggested that the MEG
study may have played a useful role in pre-surgical planning.

Korjenova et al (2006) prospectively evaluated MEG and fMRI imaging, as compared with intra-operative cortical mapping, to localize the central sulcus. Fifteen patients (6 men, 9 women; age range of 25 to 58 years) with a lesion near the primary sensorimotor cortex (13 gliomas, 1 cavernous hemangioma, and 1 meningioma) were examined. Magnetoencephalography and fMRI localizations were compared with intra-operative cortical mappings. Magnetoencephalography depicted the central sulcus correctly in all 15 patients, as verified at intra-operative mapping. The fMRI localization results agreed with the intra-operative mappings in 11 patients. The investigators concluded that, although both MEG and fMRI can provide useful information for neurosurgical planning, in the present study, MEG proved to be superior for locating the central sulcus.

There is also insufficient evidence to support the use of MSI/MEG for other indications including the diagnosis and treatment of various neurological conditions/diseases such as Alzheimer's disease, autism, cognitive and mental disorders, learning disabilities, developmental dyslexia, multiple sclerosis, Parkinson's disease, schizophrenia, stroke rehabilitation, and traumatic brain injury. Currently, there are reliable data from well-designed clinical studies that report the test performance (sensitivity, specificity, positive and negative predictive values) and clinical utility of MSI/MEG for these indications.

Haddad and colleagues (2011) stated that the fetal brain remains inaccessible to neurophysiological studies. Magnetoencephalography is being assessed to fill this gap. These researchers performed 40 fetal MEG (fMEG) recordings with gestational ages (GA) ranging from 30 to 37 weeks. The data from each recording were divided into 15 second epochs, which in turn were classified as continuous (CO), discontinuous (DC), or artifact. The fetal behavioral state, quiet or active sleep, was determined using previously defined criteria based on fetal movements and heart rate variability. These investigators studied the correlation between the fetal state, the GA and the percentage of CO and DC epochs. They also analyzed the spectral
edge frequency (SEF) and studied its relation with state and GA. They found that the odds of a DC epoch decreased by 6 % per week as the GA increased (p = 0.0036). This decrease was mainly generated by changes during quiet sleep, which showed 52 % DC epochs before a 35-week GA versus 38 % after 35 weeks (p = 0.0006). Active sleep did not show a significant change in DC epochs with GA. When both states were compared for MEG patterns within each GA group (before and after 35 weeks), the early group was found to have more DC epochs in quiet sleep (54 %) compared to active sleep (42 %) (p = 0.036). No significant difference in DC epochs between the 2 states was noted in the late GA group. Analysis of SEF showed a significant difference (p = 0.0014) before and after a 35-week GA, with higher SEF noted at late GA. However, when both quiet and active sleep states were compared within each GA group, the SEF did not show a significant difference. The authors concluded that fMEG shows reproducible variations in gross features and frequency content, depending on GA and behavioral state. They stated that fetal MEG is a promising tool to investigate fetal brain physiology and maturation.

Xiang et al (2013) quantitatively evaluated cortical dysfunction in pediatric migraine; a total of 31 adolescents with acute migraine and age- and gender-matched controls were studied using a MEG system at a sampling rate of 6,000 Hz. Neuro-magnetic brain activation was elicited by a finger-tapping task. The spectral and spatial signatures of MEG data in 5 to 2,884 Hz were analyzed using Morlet wavelet and beam-formers. Compared with controls, 31 migraine subjects during their headache attack phases (ictal) showed significantly prolonged latencies of neuro-magnetic activation in 5 to 30 Hz, increased spectral power in 100 to 200 Hz, and a higher likelihood of neuro-magnetic activation in the supplementary motor area, the occipital and ipsilateral sensorimotor cortices, in 2,200 to 2,800 Hz. Of the 31 migraine subjects, 16 migraine subjects during their headache-free phases (inter-ictal) showed that there were no significant differences between inter-ictal and control MEG data except that inter-ictal spectral power in 100 to 200 Hz was significantly decreased. The results demonstrated that migraine subjects had significantly aberrant ictal brain activation, which can normalize inter-ictally.
The spread of abnormal ictal brain activation in both low- and high-frequency ranges triggered by movements may play a key role in the cascade of migraine attacks. The authors concluded that this was the first study focusing on the spectral and spatial signatures of cortical dysfunction in adolescents with migraine using MEG signals in a frequency range of 5 to 2,884 Hz. Moreover, they stated that this methodology analyzing aberrant brain activation may be important for developing new therapeutic interventions for migraine in the future.

Furthermore, UpToDate reviews on “Pathophysiology, clinical features, and diagnosis of migraine in children” (Cruse, 2014) and “Pathophysiology, clinical manifestations, and diagnosis of migraine in adults” (Cutrer et al, 2014) do not mention the use of magnetic source imaging or magnetoencephalography.

da Costa et al (2015) stated that awareness to neurocognitive issues after mild traumatic brain injury (mTBI) is increasing, but currently no imaging markers are available for mTBI. Advanced structural imaging recently showed microstructural tissue changes and axonal injury, mild but likely sufficient to lead to functional deficits. Magnetoencephalography has high temporal and spatial resolution, combining structural and electrophysiological information, and can be used to examine brain activation patterns of regions involved with specific tasks. In this study, a total of 16 adults with mTBI and 16 matched controls were submitted to neuropsychological testing (Wechsler Abbreviated Scale of Intelligence (WASI); Conners; Alcohol Use Disorders Identification Test (AUDIT); Generalized Anxiety Disorder Seven-item Scale (GAD-7); Patient Health Questionnaire (PHQ-9); Symptom Checklist and Symptom Severity Score (SCAT2)) and MEG while tested for mental flexibility (Intra-Extra Dimensional set-shifting tasks). Three-dimensional maps were generated using synthetic aperture magnetometry beam-forming analyses to identify differences in regional activation and activation times. Reaction times and accuracy between groups were compared using 2 × 2 mixed analysis of variance. While accuracy was similar, patients with mTBI reaction time was delayed and sequence of activation of brain regions disorganized, with involvement of extra regions such as the occipital lobes, not
used by controls. Examination of activation time showed significant delays in the right insula and left posterior parietal cortex in patients with mTBI. The authors concluded that patients with mTBI showed significant delays in the activation of important areas involved in executive function. In addition, more regions of the brain are involved in an apparent compensatory effort. They stated that these findings suggested that MEG can detect subtle neural changes associated with cognitive dysfunction and thus, may eventually be useful for capturing and tracking the onset and course of cognitive symptoms associated with mTBI.

Wang et al (2014a) examined the right and left hemispheric auditory sensory gating of the M50 (pre-attentive processing) and M100 (early attentive processing) in patients diagnosed with bipolar I disorder by using MEG. Whole-head MEG data were acquired during the standard paired-click paradigm in 20 bipolar I disorder patients and 20 healthy controls. The M50 and the M100 responses were investigated, and dipole source localizations were also investigated. Sensory gating was determined by measuring the strength of the M50 and the M100 response to the second click divided by that of the first click (S2/S1). In every subject, M50 and M100 dipolar sources were localized to the left and right posterior portion of superior temporal gyrus (STG). Bipolar I disorder patients showed bilateral gating deficits in M50 and M100. The bilateral M50 S2 source strengths were significantly higher in the bipolar I disorder group compared to the control group. The authors concluded that these findings suggested that bipolar I disorder patients have auditory gating deficits at both pre-attentive and early attentive levels, which might be related to STG structural abnormality. The main drawbacks of this study were (i) small sample size (n = 20 patients) and (ii) patients were taking a wide range of medications that could not be controlled for; more studies with larger sample sizes are needed to ascertain the clinical value of MEG in the management of patients with bipolar disorder.

Wang et al (2014b) investigated the M100 and M200 auditory responses in patients with schizophrenia and bipolar disorder and compared them with healthy controls by means of MEG.
Whole-head MEG data were acquired during an auditory oddball paradigm in 24 schizophrenia patients, 26 bipolar I disorder patients, and 31 healthy controls. The strengths and latencies of M100 and M200 in both hemispheres and the dipole source localizations were investigated from the standard stimuli. The M100 and M200 dipolar sources were localized to the left and right posterior portion of the STG in all the subjects. An asymmetric pattern of M100 and M200 auditory response with more anterior sources in the right STG was observed in the healthy controls. However, both the schizophrenia and bipolar disorder patients showed a symmetric M100 and M200 source pattern. When compared with the healthy control group, both patient groups showed significantly reduced M100 and M200 source strength in both hemispheres. The authors concluded that these findings suggested that early auditory information processing deficits may be similar in schizophrenia and bipolar disorder and may be related to abnormalities of the STG. The main drawback of this study was its small sample size (n = 24 for schizophrenia, and n = 26 for bipolar disorder; and there may be overlapping of bipolar patients in these 2 studies (Wang et al, 2014a and 2014b).

Feuerriegel et al (2015) evaluated evidence for configural and affective face processing abnormalities as measured by the N170 and Vertex Positive Potential (VPP) event-related potential components, and analogous M170 MEG component, in neurological and psychiatric disorders. A total of 1,251 unique articles were identified using PsychINFO and PubMed databases; 67 studies were selected for review, which employed various tasks to measure the N170, M170 or VPP; the 13 neurological/psychiatric conditions were attention-deficit hyperactivity disorder (ADHD), alcohol dependence, Alzheimer's disease, autism spectrum disorders (ASDs), bipolar disorder, bulimia nervosa, fibromyalgia, Huntington's disease, major depressive disorder, Parkinson's disease, prosopagnosia, schizophrenia and social phobia. Smaller N170 and VPP amplitudes to faces compared to healthy controls were consistently reported in schizophrenia but not in ASDs. In schizophrenia, N170 and VPP measures were not correlated with clinical symptoms. Findings from other disorders were highly
inconsistent; however, reported group differences were almost always smaller amplitudes or slower latencies to emotional faces in disordered groups regardless of diagnosis. The authors concluded that these findings suggested that N170/VPP abnormalities index non-specific facial affect processing dysfunction in these neurological and psychiatric conditions, reflecting social impairments being broadly characteristic of these groups. They noted that the N170 and analogous components hold promise as diagnostic and treatment monitoring biomarkers for social dysfunction.

Alhourani and associates (2016) stated that mTBI leads to long-term cognitive sequelae in a significant portion of patients. Disruption of normal neural communication across functional brain networks may explain the deficits in memory and attention observed following mTBI. These investigators used MEG to examine functional connectivity during a resting state in a group of mTBI subjects (n = 9) compared with age-matched control subjects (n = 15). They adopted a data-driven, exploratory analysis in source space using phase locking value across different frequency bands. They observed a significant reduction in functional connectivity in band-specific networks in mTBI compared with control subjects. These networks spanned multiple cortical regions involved in the default mode network (DMN). The DMN is thought to subserve memory and attention during periods when an individual is not engaged in a specific task, and its disruption may lead to cognitive deficits after mTBI. These researchers further applied graph theoretical analysis on the functional connectivity matrices. They stated that these findings suggested reduced local efficiency in different brain regions in mTBI patients. The authors concluded that MEG can be a potential tool to investigate and detect network alterations in patients with mTBI. They stated that the value of MEG to reveal potential neurophysiological biomarkers for mTBI patients warrants further exploration.

*Diagnosis, Quantification, and Monitoring of Neurocognitive Problems Following Aneurysmal Subarachnoid Hemorrhage:*

de Costa and colleagues (2016) stated that among good outcome
survivors of aneurysmal subarachnoid hemorrhage (aSAH), only 23 % have normal neurocognitive performance, despite imaging that is often normal. These researchers examined the use of MEG after endovascular treatment of ruptured aneurysms. Good outcome aSAH patients treated with coiling and matched controls were recruited. Clinical assessments and resting-state MEG and anatomical MRI images were obtained. Brain space was normalized to standard Montreal Neurological Institute (MNI) brain. Areas of interest were identified with Automated Anatomical Labeling (AAL) and "electrodes" reconstructed using vector beamformer. Spectral power density estimates for each location was averaged across the brain to derive mean signal power. Virtual-sensor data closest to the coil was assessed for signal quality. A total of 13 aSAH patients and 13 matched controls were recruited. Mean age was 54.5 years (SD = 9.9) for controls and 56.8 years (SD = 11.8) for aSAH. The majority of aneurysms (62 %) were in the midline. Mean time from aSAH to MEG was 18.8 months (2.4 to 67.5; SD = 19). Data quality was comparable in both groups, including the virtual-sensors close to the coil mass. Mean signal power showed no significant spectral alterations in the aSAH group. The authors concluded that MEG is feasible in aSAH patients after endovascular treatment. They stated that these findings suggested that the signal quality and strength was good, and the presence of coils did not interfere with testing. They stated that considering the common neurocognitive complaints of aSAH survivors, MEG could be developed to diagnose, quantify, and monitor neurocognitive problems after aSAH.

The main drawbacks of this study were: (i) this was a small (n = 13 for aSAH) feasibility study, (ii) the study sample had a high percentage of midline aneurysms, and this may influence neurocognitive sequela, and (iii) MEG signal characteristics were evaluated in the same seed locations for aSAH and matched controls, thus, the only differences were the previous hemorrhage and the presence of the coils.

Differentiation of Post-Traumatic Stress Disorder and Traumatic Brain Injury:
Rowland and colleagues (2017) evaluated alterations in whole-brain resting-state networks associated with post-traumatic stress disorder (PTSD) and mTBI. Networks were constructed from locations of peak statistical power on an individual basis from MEG source series data by applying the weighted phase lag index and surrogate data thresholding procedures. Networks representing activity in the alpha bandwidth as well as wideband activity (DC-80 Hz) were created. Statistical comparisons were adjusted for age and education level. Alpha network results demonstrate reductions in network structure associated with PTSD, but no differences associated with mTBI. Wideband network results demonstrated a shift in connectivity from the alpha to theta bandwidth in both PTSD and mTBI. In addition, contrasting alterations in network structure were noted, with increased randomness associated with PTSD and increased structure associated with mTBI. The authors concluded that these findings demonstrated the potential of the analysis of MEG resting-state networks to differentiate 2 highly co-morbid conditions.

### CPT Codes / HCPCS Codes / ICD-10 Codes

**Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":**

**ICD-10 codes will become effective as of October 1, 2015:**

**CPT codes covered if selection criteria are met:**

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<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>95965</td>
<td>Magnetoencephalography (MEG), recording and analysis; for spontaneous brain magnetic activity (e.g., epileptic cerebral cortex localization)</td>
</tr>
<tr>
<td>95966</td>
<td>for evoked magnetic fields, single modality (e.g., sensory, motor, language, or visual cortex localization)</td>
</tr>
<tr>
<td>+ 95967</td>
<td>for evoked magnetic fields, each additional modality (e.g., sensory, motor, language, or visual cortex localization) (List separately in addition to code for primary procedure)</td>
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**HCPCS codes covered if selection criteria are met:**

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<td>Magnetic source imaging</td>
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**ICD-10 codes covered if selection criteria are met:**
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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G40.011 - G40.019</td>
<td>Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with and without status epilepticus</td>
</tr>
<tr>
<td>G40.111 - G40.119</td>
<td>Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable with and without status epilepticus</td>
</tr>
<tr>
<td>G40.211 - G40.219</td>
<td>Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable with and without status epilepticus</td>
</tr>
<tr>
<td>G40.311</td>
<td>Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus</td>
</tr>
<tr>
<td>G40.319</td>
<td>Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus</td>
</tr>
<tr>
<td>G40.A11 - G40.A19</td>
<td>Absence epileptic syndrome, intractable</td>
</tr>
<tr>
<td>G40.B11 - G40.B19</td>
<td>Juvenile myoclonic epilepsy, intractable</td>
</tr>
<tr>
<td>G40.411 - G40.419</td>
<td>Other generalized epilepsy and epileptic syndromes, intractable, with and without status epilepticus</td>
</tr>
<tr>
<td>G40.811 - G40.89</td>
<td>Other epilepsy and seizures, intractable, with and without status epilepticus</td>
</tr>
<tr>
<td>G40.911 - G40.919</td>
<td>Epilepsy, unspecified, intractable</td>
</tr>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):**

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C71.0 - C71.9</td>
<td>Malignant neoplasm of brain</td>
</tr>
<tr>
<td>F01 - F99</td>
<td>Mental and behavioral disorders</td>
</tr>
<tr>
<td>G10</td>
<td>Huntington's disease</td>
</tr>
<tr>
<td>G20 - G21.9</td>
<td>Parkinson's disease</td>
</tr>
<tr>
<td>G30.0 - G30.9</td>
<td>Alzheimer’s disease</td>
</tr>
<tr>
<td>G35</td>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>G40.101 - G40.109</td>
<td>Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable with and without status epilepticus</td>
</tr>
<tr>
<td>G40.201 - G40.209</td>
<td>Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, not intractable with and without status epilepticus</td>
</tr>
<tr>
<td>G40.301</td>
<td>Generalized idiopathic epilepsy and epileptic syndromes, not intractable, with status epilepticus</td>
</tr>
<tr>
<td>G40.309</td>
<td>Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus</td>
</tr>
<tr>
<td>G40.A01 - G40.A09</td>
<td>Absence epileptic syndrome, not intractable</td>
</tr>
<tr>
<td>G40.B01 - G40.B09</td>
<td>Juvenile myoclonic epilepsy, not intractable</td>
</tr>
<tr>
<td>G40.401 - G40.409</td>
<td>Other generalized epilepsy and epileptic syndromes, not intractable, with and without status epilepticus</td>
</tr>
<tr>
<td>G40.501 - G40.509</td>
<td>Special epileptic syndromes, not intractable, with and without status epilepticus</td>
</tr>
<tr>
<td>G40.801 - G40.802</td>
<td>Other epilepsy and seizures, not intractable, with and without status epilepticus</td>
</tr>
<tr>
<td>G40.901 - G40.909</td>
<td>Epilepsy, unspecified, not intractable, with and without status epilepticus</td>
</tr>
<tr>
<td>G43.001 - G43.919</td>
<td>Migraine</td>
</tr>
<tr>
<td>H53.16</td>
<td>Psychophysical visual disturbances [prosopagnosia]</td>
</tr>
<tr>
<td>I69.00 - I69.998</td>
<td>Sequelae of cerebrovascular disease</td>
</tr>
<tr>
<td>M79.7</td>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>O28.0 - O28.9</td>
<td>Abnormal findings on antenatal screening of mother</td>
</tr>
<tr>
<td>R56.00 - R56.9</td>
<td>Convulsions</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>S02.0xx+</td>
<td>Other and unspecified skull fractures</td>
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<tr>
<td>S02.19x+</td>
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<tr>
<td>S02.8xx+</td>
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<tr>
<td>S02.92x+</td>
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<tr>
<td>S02.0xS</td>
<td>Fracture of skull and face bones, sequela</td>
</tr>
<tr>
<td>S02.92xS</td>
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<tr>
<td>S06.0x0+</td>
<td>Intracranial injury</td>
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<tr>
<td>S06.9x9+</td>
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<tr>
<td>S06.0xS</td>
<td>Intracranial injury, sequela</td>
</tr>
<tr>
<td>S06.9xS</td>
<td></td>
</tr>
<tr>
<td>Z01.89</td>
<td>Encounter for other specified special examinations</td>
</tr>
<tr>
<td>Z13.858</td>
<td>Encounter for screening for other nervous system disorders</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


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Amendment to
Aetna Clinical Policy Bulletin Number:
0279 - Magnetic Source Imaging/Magnetoencephalography

There are no amendments for Medicaid.