American Clinical MEG Society (ACMEGS) Position Statement: The Value of Magnetoencephalography (MEG)/Magnetic Source Imaging (MSI) in Noninvasive Presurgical Evaluation of Patients With Medically Intractable Localization-related Epilepsy

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The American Clinical Magnetoencephalography Society (ACMEGS) is a professional society of physicians and other professionals with doctoral degrees "involved in clinical use of magnetoencephalography (MEG), electroencephalography (EEG), magnetic resonance imaging, or computerized axial tomography" (ACMEGS, Inc, Bylaws, 2006). The ACMEGS is primarily focused on advancing clinical applications of MEG, while representing all American MEG centers and individual professionals concerned with clinical MEG. Currently, our membership is composed of more than 50 individuals and/or collective members, including the most prominent investigators who have made cardinal contributions to the development of the clinical MEG. A significant proportion of 4,000+, peer-reviewed, MEDLINE publications on "MEG" has been authored by members of the American MEG community, including the most sophisticated clinical MEG studies designed and published internationally (Knowlton et al., 2008a,b; Sutherling et al., 2008).

MEG/magnetic source imaging (MSI) is a modern and powerful technology for studying brain function directly and noninvasively by analyzing magnetic fields induced by synchronized neuronal activity that are recorded outside of the skull (Cohen, 1968, 1972; reviewed in Hamalainen et al., 1993; Okada et al., 1984, 1999; Williamson et al., 1991). Routinely, MEG can attain a temporal resolution of less than a millisecond and, under optimal circumstances, spatial resolution of several millimeters (Brenner et al., 1975; Hamalainen et al., 1993; Hari et al., 1988; Okada et al., 1984, 1999; Romani et al., 1982). During the last 40 years, MEG instruments have evolved from a single-channel portable system to the modern whole head systems with more than 300 channels that are housed in multilayered shielded rooms (reviewed in Barkley and Baumgartner, 2003; reviewed in Hamalainen et al., 1993). It is now accepted that MEG/MSI can provide clinicians with accurate and critical information regarding the location of important cerebral sources, such as epileptic foci (Baumgartner, 2000; Ebersole, 1997; Fischer et al., 2005; Iwasaki et al., 2002; Kirsch et al., 2007a; Knake et al., 2006; Knowlton, 2006, 2008; Knowlton et al., 2006; Knowlton et al., 2008a,b; Lin et al., 2003; Mamelak et al., 2002; Mohamed et al., 2007; Oishi et al., 2006; Papanicolaou et al., 2005; Pataraia et al., 2004; RamachandranNair et al., 2007; Rodin et al., 2004; Smith et al., 2000; Stefan et al., 2003; Sutherling et al., 2008; Verrotti et al., 2003), sensory-motor cortex (Alberstone et al., 2000; Brenner et al., 1975; Castillo et al., 2004; Ganslandt et al., 2004; Kirsch et al., 2007b; Korvenoja et al., 2006; Nakasato and Yoshimoto, 2000; Oishi et al., 2003; Okada et al., 1984; Pang et al., 2008), visual (Alberstone et al., 2000; Brenner et al., 1975; Ganslandt et al., 2004; Grover et al., 2006; Nakasato and Yoshimoto, 2000; Nakasato et al., 1996), auditory (Alberstone et al., 2000; Godey et al., 2001; Nakasato and Yoshimoto, 2000; Romani et al., 1982), and language cortex (Bowyer et al., 2004, 2005; Flagg et al., 2005; Ganslandt et al., 2004; Grummich et al., 2006; Hirata et al., 2004; Kamada et al., 2003; Lee et al., 2006; Merrifield et al., 2007; Papanicolaou et al., 2004, 2006; Salmelin, 2007) MEG/MSI findings may be displayed on a patient's magnetic resonance imaging or combined with other imaging modalities to form multimodal neuronavigational maps that can be used directly in stereotactic neuronavigation systems during surgery (Duffner et al., 2003; Firsching et al., 2002; Ganslandt et al., 1999; Kamada et al., 2003, 2007; Nimsky et al., 1999; Ochi and Otsubo, 2008; Rezai et al., 1995, 1996, 1997).

Nearly 3 million Americans are afflicted with epilepsy (Hauser and Hesdorffer, 1990). Approximately 30% suffer from seizures that are refractory to medications despite the 20 antiepileptic drugs that are currently available (Brodie, 2005; Kwan and Brodie, 2000). These patients are responsible for 80% of the $12.5 billon annual cost of epilepsy to society (Begley et al., 2000). A significant minority of these patients with epilepsy have localization-related or focal epilepsy that may be amenable to surgical therapy (Engel, 2003, 2008). Thus, competent estimates indicate that 100,000 to 200,000 patients with uncontrolled epilepsy may be surgical candidates (Engel, 2003; Engel and Shewmon, 1993). Epilepsy surgery has been proven to be superior to medical treatment in patients with temporal lobe epilepsy in a randomized controlled trial (Engel, 2008; Engel et al., 2003; Wiebe et al., 2001), and a recent analysis revealed that "the combination of surgery with medical treatment is four times as likely as medical treatment alone to achieve freedom from seizures" (Schmidt and Stavem, In press). Furthermore, long-term follow-up studies showed that many patients who underwent resective brain surgery remain seizure free (Spencer and Huh, 2008; Téllez-Zenteno et al., 2005, 2007, 2008) and that "in carefully selected patients, epilepsy surgery can control seizures, improve quality of life, and reduce costs of medical care" (Kuzniecky and Devinsky, 2007). However, for multiple reasons, epilepsy surgery, the only potential cure for epilepsy (Engel, 2003, 2008; Spencer and Huh, 2008; Wiebe et al., 2001), is offered to only 2% to 3% of potential surgical candidates (Engel, 2003).

The critical and often rate-limiting factor in epilepsy surgery is functional localization of the epileptic focus that may not be adequately supplied by traditional diagnostic investigations, including EEG, video-EEG monitoring, magnetic resonance imaging, and in some cases positron emission tomography (PET) and single-photon emission computed tomography (SPECT) scans (Barkley

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and Baumgartner, 2003; Engel, 2003, 2008; Knowlton et al., 2006; Kuzniecky and Devinsky, 2007; Langfitt and Wiebe, 2008; Papanicolaou et al., 2005; Stefan et al., 2003; Wheless et al., 1999). Too frequently these studies fail to identify clearly the seizure focus (Barkley and Baumgartner, 2003; Knowlton, 2008; Knowlton et al., 2006; Knowlton et al., 2008a,b; Papanicolaou et al., 2005; Rodin et al., 2004; Stefan et al., 2003; Sutherling et al., 2008). Alternatively, the identified focus is complex, ambiguous, or closely positioned to the eloquent cortices, making surgery dangerous (Barkley and Baumgartner, 2003; Knowlton, 2008; Knowlton et al., 2006; Knowlton et al., 2008a,b; Rodin et al., 2004; Stefan et al., 2003; Sutherling et al., 2008). Clinicians uniformly agree that additional and nonredundant localizing information, preferably acquired noninvasively, are necessary for making clinical decisions in these situations (Barkley and Baumgartner, 2003; Knowlton, 2008; Knowlton et al., 2006; Knowlton et al., 2008a,b; Stefan et al., 2003; Sutherling et al., 2008).

The ability of MEG/MSI to fill this diagnostic gap has been demonstrated in numerous published studies (Assaf et al., 2004; Fischer et al., 2005; Iwasaki et al., 2002; Kirsch et al., 2007a,b; Knake et al., 2006; Knowlton et al., 2006; Knowlton, 2008; Knowlton et al., 2008a,b; Lin et al., 2003; Mamelak et al., 2002; Mohamed et al., 2007; Oishi et al., 2006; Papanicolaou et al., 2005; Pataraia et al., 2004; RamachandranNair et al., 2007; Rodin et al., 2004; Smith et al., 2000; Stefan et al., 2003; Sutherling et al., 2008; Verrotti et al., 2003). In fact, almost 700 peer-reviewed, MEDLINE publications on "MEG" are devoted to "epilepsy." These have established that MEG/MSI may locate epileptogenic foci, not otherwise identifiable or localizable, in up to 30% of patients (Stefan et al., 2003; Sutherling et al., 2008) and clarify the spatial relationships of these foci to eloquent cortices noninvasively (Castillo et al., 2004; Papanicolaou et al., 2004 2005; Pataraia et al., 2004). Two recent and meticulously designed studies have proven the usefulness and predictive value of MEG (Knowlton et al., 2008ab). In addition, the first prospective and blinded study of MEG/MSI demonstrated that nonredundant information that positively affected clinical decision making and proved to be beneficial for the outcome was obtained in 33% of patients (Sutherling et al., 2008).

The highest standards of clinical care include sound judgment and rational utilization of resources. Therefore, it is inappropriate to use an expensive study, if a more cost effective one provides clinically adequate results. Thus, it is only when traditional EEG studies (routine laboratory, ambulatory, and video-EEG long-term monitoring) fail to deliver sufficient localizing information for planning a direct surgical intervention or invasive monitoring that MEG is indicated (Knake et al., 2006; Knowlton, 2008; Knowlton et al., 2008ab; RamachandranNair et al., 2007; Sutherling et al., 2008). On the basis of the current published evidence (a few selected examples: Knake et al., 2006, Knowlton et al., 2006; Knowlton et al., 2008ab; RamachandranNair et al., 2007; Stefan et al., 2003; Sutherling et al., 2008), the ACMEGS supports the routine use of MEG/MSI in presurgical epilepsy evaluations because it can improve noninvasive evaluation that is ordinarily much cheaper and safer than invasive studies (Barkley and Baumgartner, 2003; Knowlton, 2008), and because it can enhance the yield of invasive studies by directing the placement of grids, strips, and depth electrodes (Knowlton et al., 2008ab; RamachandranNair et al., 2007; Sutherling et al., 2008). Overall, these may reduce costs and improve the accuracy of epilepsy evaluations, thus making surgery a more appealing treatment option (Barkley and Baumgartner, 2003; Knowlton et al., 2006; Knowlton, 2008; Knowlton et al., 2008ab; Papanicolaou et al., 2005; RamachandranNair et al., 2007; Stefan et al., 2003; Sutherling et al., 2008).

On the basis of the all available published evidence, the ACMEGS considers the current state of MEG/MSI technology to be completely mature for routine use in presurgical evaluations of patients with epilepsy. The ACMEGS also supports the widely accepted and scientifically supported position that MEG and EEG are complementary modalities that yield the best results when combined. Consequently, the debate about superiority among these two complementary modalities is clinically irrelevant for the acceptance of MEG as a routine clinical test. The ACMEGS does, however, encourage further comparative studies that may lead to new advancements in electromagnetic neuroimaging.

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Therefore, after considering the entire body of published evidence (MEDLINE search for "epilepsy" and "MEG" gleaned 665 hits; accessed on April 20, 2009) and appreciating the publication of a milestone class I study (Sutherling et al., 2008), the ACMEGS acknowledges that sufficient credible evidence has been published to support a position statement regarding the value of MEG in the presurgical evaluation of patients with medically intractable localization-related epilepsy. Accordingly, the following principles regarding the routine use of MEG/MSI are proposed.

The ACMEGS supports:

1. The routine clinical use of MEG/MSI in obtaining noninvasive, nonredundant localizing information in presurgical evaluation of patients with medically intractable localization-related epilepsy.
2. The determination of MEG/MSI indications for an individual patient by an epileptologist or a clinical team associated with a National Association of Epilepsy Centers-designated epilepsy center.
3. The routine use of MEG/MSI when traditional EEG methods and magnetic resonance imaging are implemented and provide insufficient localizing information.
4. The progressive movement of insurers toward complete coverage for MEG/MSI. It is in the best interest of patients to have appropriate and timely access to the best possible care. This includes MEG/MSI, as well as previously established diagnostic tests.
5. Uses for MEG/MSI indicated by accepted standards of clinical judgment and care and the rational utilization of resources without further restrictions.
6. Further systematic clinical research that seeks to establish other clinical indications for MEG/MSI.

The ACMEGS invites and encourages other medical societies and organizations including but not limited to the American Clinical Neurophysiology Society (ACNS), American Academy of Neurology (AAN), American Epilepsy Society (AES), and the American Society of Neuroradiology (ASNR) to support this statement and/or adopt complementary position statements. The ACMEGS intends to enhance the practice of clinical MEG/MSI further by developing practice parameters.

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