Review

The role of FDG-PET, ictal SPECT, and MEG in the epilepsy surgery evaluation

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Abstract

2-\[^{18}\text{F}\]Fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET), ictal single-photon-emission computed tomography (ictal SPECT), and magnetoencephalography (MEG) represent three established functional imaging tests that offer unique information toward the localization of epilepsy for surgery evaluation and treatment. When these tests are combined with high-resolution magnetic resonance imaging (MRI), epilepsy related structure and function disturbances may be localized with a degree of confidence and understanding not possible with electroencephalography (EEG), even ictal recordings with intracranial electrodes, the mainstay of tools for seizure localization. Use of these alternative tests allows an increased percentage of patients to be considered for surgical treatment. In particular, the additional information provided by these techniques has been demonstrated to help those patients with nonlocalizing MRI or extratemporal lobe epilepsy. Studies that address optimal use of these tests (alone and in combination) will build toward the next major advancement in the surgical treatment of epilepsy by allowing better patient selection, less risk, and better surgical outcomes. Ultimately, appropriate use of these tests, combined with more comprehensive functional brain mapping (e.g., with MEG or functional MRI), may lead to completely noninvasive epilepsy surgery evaluation.

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1. Introduction

Twenty percent of the two million Americans with a diagnosis of epilepsy have medically uncontrolled (intractable) seizures [1]. This group accounts for over 75 percent of the cost of epilepsy care in the United States [2]. For many of these patients epilepsy surgery offers the only opportunity to become free of seizures. Advances in technology to localize focal epileptogenic tissue, especially high-resolution structural imaging with magnetic resonance imaging (MRI), have substantially improved the cost effectiveness and success of surgical treatment [3,4].

The large problem that remains is in the group of intractable partial epilepsy patients who do not have an unequivocal, single, focal epileptogenic lesion on MRI. For purposes of resective surgery, long-term electroencephalographic monitoring with scalp-recorded electroencephalography (EEG) without supportive image localization information cannot be relied on to adequately delineate the epileptogenic zone—the tissue necessary and sufficient for the generation of seizures. Conversely, even in patients with visible abnormalities or lesions on MRI, the location and extent of the epileptogenic zone may not be assumed or confirmed if EEG is nonlocalizing. At most epilepsy surgery centers, the majority of these patients undergo long-term intracranial electroencephalography (IC-EEG) with surgically implanted electrodes in an attempt to localize the tissue responsible for seizures. Although IC-EEG procedures add tens of thousands of dollars to the presurgical evaluation [4,5], the value of successful surgery in any patient with intractable epilepsy cannot be underestimated, and it remains unacceptable not to provide the chance for successful treatment, even if IC-EEG is required. However,
what is needed before this step is reliable knowledge from other tests as to whether further evaluation will be of reasonable yield for ultimately finding an epileptogenic zone that is amenable to surgical resection.

Even when invasive tests such as IC-EEG appear clinically necessary, an important problem arises as to where to place electrodes on or in the brain. Critical to the success of IC-EEG recordings is optimal electrode coverage such that limited sampling of the brain—all that is generally allowed for patient safety reasons—does not yield false-negative or incorrect localization of the epileptogenic zone. Another question to be addressed in some cases is whether IC-EEG can provide a solution: Could an accurate clinical decision be made based on noninvasive imaging tests that predict no use in proceeding further in the presurgical evaluation? Conversely, denial of surgery because of misleading presurgical localization, including unsuccessful localization with IC-EEG, is a “reverse risk” that needs to be avoided.

The problems encountered with IC-EEG in localizing epilepsy in difficult surgery cases may be affected favorably by noninvasive alternative functional imaging tests [6]. Ideally, some cases could benefit from functional imaging to the point that IC-EEG could be entirely avoided; or if this is not possible, the functional imaging test could effect better placement of electrodes such that the procedure could yield more reliable results for surgical decision making. At this time many centers use various functional imaging procedures just for these purposes. Unfortunately, no evidence from well-designed trials exists to guide clinicians in the most appropriate or efficient use of available functional imaging modalities.

The list of noninvasive functional imaging tests assessed as important in the role of epilepsy localization is constantly changing due to rapid technological advances. Those that are to be included in this review include 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET), single-photon-emission computed tomography (SPECT) acquired after injection of radioactive tracer during a seizure (“ictal SPECT”), and magnetoencephalography (MEG) based source localization, which is routinely combined with structural imaging and called magnetic source imaging (MSI). Technical validity and, to some degree, clinical validity are established for all three of these modalities. Functional MRI (fMRI) localization of epileptiform spike-related blood flow changes is a promising technology that is still being developed. Magnetic resonance spectroscopy (MRS) and MRS imaging (MRSI)—MRI-based tools for investigating in vivo metabolic disturbances of numerous biochemical compounds—have not been developed into an accepted clinical tool for epilepsy.

2. FDG-PET

FDG-PET is the most established functional imaging modality in the evaluation of patients with epilepsy. Imaging the topographic distribution of glucose uptake in the brain with FDG-PET is equated to imaging cerebral metabolism. Ictal scans can be useful; however, the long duration for steady-state uptake of glucose (on the order of many minutes compared with partial seizures, which are typically less than a couple of minutes) often leads to scans that contain a difficult-to-interpret mixture of interictal, ictal, and postictal states. Thus, presurgical epilepsy FDG-PET scans are typically performed in the interictal state with the goal of detecting focal areas of decreased metabolism, relative hypometabolism, that are presumed to reflect focal functional disturbances of cerebral activity associated with epileptogenic tissue. What is still remarkable about FDG-PET is that the cause of hypometabolism in and near epileptogenic regions of brain remains unclear.

From a purely imaging standpoint, FDG-PET provides a remarkable depiction of in vivo glucose metabolism. It offers relatively high resolution due to the fact that positron-emitting isotopes emit two photons after a positron is annihilated with an electron. The distance of travel between positron and electron annihilation is very small (on the order of a millimeter or less). This fact, combined with the relatively good intrinsic signal to noise of FDG, allows for images that can now be obtained with an in-plane resolution of 2–3 mm [7].

It is in the evaluation of medically refractory epilepsy surgery candidates with clinically suspected temporal lobe epilepsy that FDG-PET has been best proven to be valuable. Because PET became available before high-resolution structural imaging, it was for years the only modality that might show an abnormality of brain imaging in surgical epilepsy candidates. Sensitivity for detecting relative temporal lobe hypometabolism with FDG-PET in mesial temporal lobe epilepsy (MTLE) ranges between 80 and 90% [7–12]. Much of the variability in sensitivity reflects the heterogeneity of the epilepsy more than the differences in quality or specifications of the PET camera [13]. Only a few studies have addressed the sensitivity and specificity of FDG-PET in MTLE in patients with and without evidence of hippocampal sclerosis on MRI [9,14], with FDG-PET demonstrated to still be reliable in lateralizing the epileptogenic temporal lobe even in “MRI-negative” cases (no evidence of hippocampal sclerosis).

The specificity of FDG-PET for delineating the exact location and extent of the epileptogenic zone is considered significantly less than its sensitivity. This is due in part to the fact that more diffuse or regional relative hypometabolism is seen in the temporal lobe, even additional involvement of extratemporal, basal ganglia, and thalamic regions [15]. The classic pattern for FDG-PET in MTLE (without lesions other than mesial temporal sclerosis) reveals relative hypometabolism in mesial temporal, temporal polar, and anterolateral temporal neocortical regions [15,16].

When structural lesions are present, the presence of hypometabolism approaches 100%, although it too is commonly distributed over an area larger than the lesion itself [11,17]. The question arises as to whether the distribution of hypometabolism beyond the lesion reflects a functional
disturbance directly related to the epileptogenic zone. If not, then FDG-PET would have no clinical utility for patients with focal epileptogenic lesions including hippocampal sclerosis. The latter is the most common epileptogenic pathology in epilepsy surgery candidates, and it can be very reliably detected with MRI [18].

Initially, the more extensive anterior temporal hypometabolism seen in patients with hippocampal sclerosis was believed to be a secondary functional disturbance, a finding leading to the conclusion that FDG-PET is nonspecific with respect to precise localization of the epileptogenic zone, and therefore, should not guide distribution and extent of surgical resection without other supportive evidence for localization. In temporal lobe epilepsy, this long-held belief has, however, been brought into question by investigators who have pointed out that seizure onsets as defined by intracranial EEG recordings in patients with classic evidence of hippocampal sclerosis frequently involves the temporal polar region as much as the hippocampus [19]. Thus arises the question of whether the extent of temporal lobe hypometabolism should influence the surgical decision between standard anterior temporal lobectomy and selective amygdalohippocampectomy. This question remains to be answered.

The clinical value of FDG-PET in neocortical epilepsy is less clear. Larger reported series have been observational retrospective studies [8,20,21], and only a few have been performed in the era of advanced MRI techniques [8,16,22–25]. Most important, the FDG-PET findings in cases of nonlesional neocortical epilepsy are limited to a few patients scattered among the heterogeneous patients and patient groups.

The limited usefulness of FDG-PET in the neocortex partly reflects the poorer resolution of earlier generation cameras. A greater problem, however, may be the difficulty in interpreting small or subtle focal abnormalities. Coregistered multimodality imaging may provide other supportive localizing information that a questionable PET metabolic abnormality is indeed a true disturbance reflective of the epileptogenic zone. Because of such cases, it should be emphasized that focal defects in metabolism can be found in patients with medically intractable partial epilepsy who have cryptogenic lesions [25]. That is, specifically, some focal cortical dysplasias that cannot be detected with MRI can be detected with FDG-PET [26]. Fig. 1 shows a typical example of FDG-PET detection of a focal metabolic defect associated with cryptogenic localization-related epilepsy of the posterior lateral neocortex of the right temporal lobe. Both EEG and MRI were nonlocalizing in this case.

To address some of the interpretation difficulties inherent in clinical PET scan interpretation, an attempt has been made to use statistical parametric mapping (SPM) analysis. Application of SPM analysis for such a clinical utility is an exciting prospect for improving the accuracy of diagnostic imaging by, at least, eliminating some of the subjectivity and expertise required with visual analysis. In one report on 29 frontal lobe epilepsy patients (normal MRI in 15 patients), SPM analysis was compared with visual interpretation [27]. SPM analysis resulted in a sensitivity of 66% for detecting a localized FDG uptake deficit (36% sensitivity in patients without a structural lesion). This result was not statistically different than the sensitivity of visual analysis, but the comparability to experienced nuclear medicine
specialists in epilepsy imaging is encouraging in the application of SPM to improve the diagnostic accuracy by eliminating some of the subjectivity and expertise required by visual analysis.

But even with improvement in technically valid reading, further complicating the interpretation of FDG-PET abnormalities for guiding surgical treatment are findings from a study correlating neocortical focal hypometabolism with intracranial subdural grid EEG recordings. It was determined that not only is the distribution of hypometabolism often greater in extent, but it also is more likely to be greatest on the margin of the region of seizure onset [28]. Work with [11C]flumazenil (FMZ)-PET, 3-(11C)methyl-l-tryptophan (3-MTrp)-PET, and opioid-based ligands has shown some promise with respect to improved specificity compared with FDG, but these compounds are not widely available and clinical validity is still not established.

3. Ictal SPECT

Single-photon-emission computed tomography (SPECT) is the only modality practically suited for imaging brain activity changes during an actual seizure. Although there may be exceptions occasionally, in the clinical setting all other functional imaging modalities remain confined to detecting metabolic or blood flow derangements, as they may be present in the interictal state. Two technetium-based isotopes have made ictal blood flow imaging possible. Technetium-99m-hexamethylpropyleneamine-oxime (99mTc-HMPAO) has been the radiopharmaceutical used in most ictal or peri-ictal SPECT studies in epilepsy. A more recently available (more convenient) radiotracer is technetium-99m-ethyl cysteinate diethyl ester (99mTc-ECD), which may be nearly as good as HMPAO [29]. Both compounds possess intravascular binding properties such that most of the labeled isotope is trapped in the distribution of brain flow within the first pass following intravenous injection. This unique feature of these isotopes allows what can be conceptually considered a snapshot of cerebral blood flow at a given time of interest, in this case at the earliest time possible an injection can be performed following the signs or symptoms of a seizure.

The localizing information available from successful ictal SPECT scans (injections within 45 seconds of seizure onset) can be extremely valuable in all localization-related partial epilepsies [30–36]. However, because of the complexity of physiology in rapidly evolving seizures, reliable interpretation of regional cerebral blood flow (rCBF) changes depicted in SPECT scans is often difficult. Perceived changes can appear to be complex or subtle and may be subject to reviewer bias.

A recent advance that has dramatically improved ictal SPECT is image digital subtraction of an interictal scan from an ictal scan, and then coregistration to MRI anatomical images [37–40]. Subtraction techniques allow comparison with the patient’s individual baseline pattern of rCBF variability, and subsequently, detection of changes in blood flow that may be reflective of not an absolute increase but of a relative one from an interictal state of focal relative hypoperfusion. Further, with coregistration to MRI, anatomical detail is provided for precise localization that is not possible with relatively low-resolution SPECT.

Limitations that remain with ictal SPECT center mainly around the logistics of successfully infusing the isotope as early as possible after onset of a seizure. The very patients who are likely to benefit from ictal SPECT most are those with seizures that arise in the neocortex (outside of the mesial temporal structures), the type of seizures that frequently are brief and may spread very rapidly, leading to the possibility of ambiguous ictal blood flow changes [25]. In fact, the changes may be misleading if an area of brain remote from the seizure onset zone takes over as the main generator of seizure activity. Another consequence of the difficult logistics associated with ictal SPECT is the high cost of resources necessary to have health care staff sitting at the patient’s bedside waiting for the onset of a seizure. Some centers, with the help of basic engineering groups, have devised and implemented automated or semiautomated injection systems. These operational issues remain an area that needs to be improved to reduce cost, improve accuracy, and ultimately bring this true advance in presurgical evaluation to more patients. For when successful ictal injections (within at least 45 seconds) can be made in stereotypical focal onset seizures, ictal SPECT can be the only tool to localize seizures. Repeatedly, studies show that true ictal SPECT is accurate in predicting surgical localization, even when ictal EEG and MRI have been nonlocalizing [40–44]. Further, ictal SPECT concordance with site of surgical resection has been shown to be an independent predictor of seizure-free outcome for both temporal and extratemporal lobe epilepsies [45].

Although subtraction techniques have improved the sensitivity, specificity, and interrater reliability of ictal SPECT, further improvement in accurate interpretation may involve the use of SPM analysis techniques. In this context an ictal SPECT from a patient can be compared with a normal brain SPECT atlas using SPM to identify regions of statistically significant alterations in rCBF related to seizure activity.

A few studies support SPM analysis of ictal SPECT scans [45–47]. Further refinement of SPM-ictal SPECT methodology has been shown in a methodological pilot study to identify ictal increases in rCBF from subtraction images [45]. This work included the use of pairs of sequential interictal images from epilepsy patients and controls to define a standard deviation image so that scan–scan regional variance could be taken into account to improve sensitivity. More recent work that included pairs of scans for the controls, thus allowing assessment of interscan variability, demonstrated that SPM analysis of ictal–interictal differences was concordant with conventional subtraction analysis [46]. Most importantly, this work took advantage of subtraction analysis and combined it with the inherent objectivity of SPM analysis. Fig. 2 shows an example of
SPM analysis of ictal SPECT difference imaging in the same patient with cryptogenic right lateral temporal lobe epilepsy depicted with FDG-PET in Fig. 1. In this case, ictal SPECT was uncertain on conventional reading of both ictal and interictal side-by-side visualization and subtraction with coregistration to MRI. The SPM analysis is much clearer, although two discrete regions show ictal rCBF changes.

4. MSI/MEG

Magnetic source imaging (MSI) is a combination of magnetoencephalography (MEG) and coregistered anatomical imaging (MRI in most cases) [48]. In the evaluation of epilepsy, MEG is mostly used in an attempt to localize the source of interictal epileptiform discharges (spikes or sharp waves as described on EEG). MEG is similar to
EEG; however, unlike electrical currents measured with EEG, which are attenuated in strength and spatially blurred by tissues between brain and scalp surface, magnetic fields are not significantly affected by intervening tissue layers [49]. The most important aspect of MEG’s potential advantage over EEG is that it allows cerebral sources to be modeled more simply; and this, in turn, may allow for more clinically reliable localization of brain activity [50].

For most source localization methodologies, the goal is to solve what is called the “inverse problem.” This theoretical problem involves calculating what electrical or magnetic field topography (over the scalp) would result from a given current source(s). Calculating the configuration of the source(s) that generates an observed magnetic field may have more than one solution. To address this problem, numerous major constraining assumptions about the sources are required. By comparison of the calculated with the measured field strength, it is possible to determine if the estimated source, called a “model source,” actually reflects the measurement. Although some centers may use a realistic head shape model (based on MRI), the most popular form of modeling MEG for clinical application uses the single equivalent current dipole (ECD) model. For review of source modeling with MEG, see Gallen et al. [48].

The most accurate source localizations occur when sources are near the scalp and the convexities of the neocortex due to the fact that the field strength of a dipolar source decreases by the square of the distance from the source. Interestingly, this relative insensitivity to deep sources can actually facilitate the task of source localization. In contrast, EEG signal contains a convolution of both distant and nearby sources, which create a more complex and difficult source to analyze for localization. Thus, in addition to the advantage that magnetic fields are not distorted and as attenuated by tissues between the scalp and brain source, MEG may have a particular advantage for accurate localization of neocortical epileptiform sources.

Confirmation of the accuracy and clinical validity of MEG localization of epilepsy has been attempted from numerous direct and indirect approaches. The direct methods reflect mainly work done with either implanted dipoles using special intracranial (IC) electrodes or simultaneous IC-EEG and MEG recordings. Indirect confirmation comes from studies demonstrating colocalization with known epileptogenic substrates either visible on functional or structural imaging or confirmed with subsequent IC-EEG and successful surgical outcomes with supportive histopathology [9,51–64].

Recordings with implanted dipoles (created by a pair of special electrodes included with IC-EEG electrode implantation) provide a control of variables and parameters nearly equal to that in rigorous phantom studies but truly in vivo in human brain and skull. Results from dipoles placed in mesial, basal, and inferior lateral temporal regions showed that MEG-predicted localizations were within 1, 2, and 4 mm, respectively, of the actual locations [65,66]. These findings provided fundamental support for the validity of the entire system (from hardware to localization model to brain coregistration) to accurately localize sources in the human head. This type of testing, however, may not account for the type of variable complex spontaneous paroxysmal discharges typical of most human partial epilepsies.

Simultaneous IC-EEG–MEG studies elucidate details on the true capabilities and limitations of MEG to estimate various types and locations of spontaneous epileptiform paroxysms. With respect to depth of interictal spike sources in temporal lobe epilepsy, it is clear that MEG detects few, if any, mesial- or “hippocampal-only” spikes recorded with subdural strip electrodes [62,67–70]. Basal temporal sources appear to require at least 6 cm², and lateral neocortical sources, 3–4 cm², of contiguous cortical activity. Similar to lateral temporal lobe sources, for MEG to detect the majority of spikes recorded from the dorsal lateral frontal lobe, activation of at least three subdural electrodes (1 cm apart) is required [69,70]. In the one reported case of mesial frontal-only spikes, MEG failed to record any epileptiform paroxysms. Thus, it should be understood that MEG does not necessarily provide a clear advantage to EEG with respect to sensitivity of detection of deep epileptiform sources. This parallel sensitivity excludes any patient-specific skull or brain anatomy abnormalities that would affect electrical potentials and magnetic fields differentially, e.g., surgical skull defects, where MEG would be at an advantage. Furthermore, given the classic estimate of 6 cm² required for EEG to detect spikes, MEG may be more sensitive for convexity neocortical sources. Finally, MEG is intrinsically better at recording and detecting signals from sources that are oriented primarily tangentially to the convexity such as intrasylvian cortex [71].

Well-delineated lesion colocalization represents strong validation of MEG spike source localization, particularly with low-grade tumors or tumorlike lesions (e.g., hamartomas) that clearly are the single focal cause of a given patient’s epilepsy. Even in many cases when the lesion itself is not “intrinsically” epileptogenic, immediately adjacent tissue is usually the source of spikes and seizure onset. This may not always be the case with developmental or tumorlike lesions (e.g., focal cortical dysplasias), where epileptiform discharges may extend up to several centimeters away from the MRI-visible lesion. Still, in nearly all cases, a topographical relationship of spikes to the lesion can be delineated in detailed fashion with IC-EEG and then compared with MEG localizations. Such studies have consistently shown the MEG findings to be remarkably concordant with the IC-EEG findings, including those for various tumors and malformations of cortical development [9,63,72]. The confidence evoked by colocalization with intrinsically epileptogenic lesions emphasizes that regardless of all issues involved with MEG methods, including the limits and assumptions associated with source modeling, epilepsy MEG spike source localization can be remarkably accurate.
In contrast to the preceding example, other lesions are associated with perilesional epileptogenic tissue. One of the main challenges is to determine the eccentric location and extent of neighboring tissue that should be included in the resection, in addition to the lesion removal. This issue was addressed specifically in an MEG study of 12 children with lesional neocortical epilepsy [63] and similar work with cavernous angiomata [73]. The spatial relationship of spike sources with respect to the lesion correlated with electrocorticographic (ECoG) findings in all cases. Preliminary work examining the extent of resection in lesional cases showed that favorable seizure outcome was associated with inclusion of the majority of spike sources in the resection volume (not just the lesion) [74]. Thus, even with lesions that often suggest the obvious location of seizure sources, MEG spike source localization not only can confirm whether the lesion is epileptogenic, but also can delineate what neighboring tissue is epileptogenic and important to remove. In ambiguously localizing malformations such as polymicrogyria, the same applies, and MEG spike source localization may equally have a role in localizing the epileptogenic subregions [75].

Cryptogenic lesions, those that are not visible on high-quality MRI, are true challenges in the “needle-in-the-haystack” concept of epilepsy localization. Detection of these lesions is one of the main focuses of clinically applied functional epilepsy imaging. MEG can play a similar, but even more important role by directly revealing the source of epileptiform disturbance in relation to the cryptic pathology, tying together the epileptogenic significance of focal functional abnormalities on imaging. This typically applies to cryptic cortical dysplasia that may or may not be associated with changes on PET or ictal SPECT [9,58]. The best support for confirming localization in these cases has come from studies with IC-EEG. Two studies have shown very good concordance between interictal MEG and seizure localization with subdural grid electrodes [59,64]. Fig. 3 illustrates an example of MEG spike localization in the same patient shown in Figs. 1 and 2 who had cryptogenic right lateral temporal lobe epilepsy. MEG spike source estimates were completely colocalized with the focal metabolic defect seen on FDG-PET and also one of the two regions of increased rCBF revealed with SPM analysis of ictal SPECT difference imaging. Taken together, the three imaging tests provided the only confident data localizing epilep- sy to this completely normal-appearing brain tissue on MRI that was associated with nonlocalizing ictal scalp EEG recordings. Intracranial EEG recordings with a subdural grid confirmed the image-based localization, and the patient was rendered seizure-free with a focal resection confined to the posterior lateral temporal neocortex.

MEG localization of epilepsy in the temporal lobe depends greatly on whether the patient has true MTLE or lateral temporal lobe epilepsy (LTLE). For MTLE, it is necessary to identify and characterize entorhinal, amygdala, and hippocampal spike sources as the predominant epileptiform disturbance of cerebral activity. However, the depth of mesial sources (3–4 cm) is such that their detection sensitivity is very low, and in most cases, detection should not be considered possible [76].

Analysis of dipole orientations has provided some degree of solution to this problem [62,77,78]. Correlation with subsequent IC-EEG recordings showed that anterior temporal dipole sources with a vertical orientation were associated with mesial onset seizures and imaging defined hippocampal atrophy, whereas those anterior spike sources with predominantly horizontal orientation reflected basal and temporal polar sources more often. Of even further importance is the clinical distinction, posterior vertical sources strongly correlated with LTLE, a crucial distinction to be made in the context of surgical treatment. Thus, it has been proposed that dipole orientations are more important than absolute dipole localization in TLE [77]. Further prospective testing of this observation is needed before the clinical role of MEG spike source localization in TLE can be established.

The clinical value of MEG in TLE has also been demonstrated with respect to distribution of spikes and seizure surgery outcome with anterior medial temporal lobectomy. Iwasaki and colleagues classified spike localizations into two groups—anterior temporal (AT) and non-AT localization—based on whether greater than 70% of spike sources were anterior to a boundary line equally dividing the anterior–posterior extent of the temporal lobe [79]. Patients showing AT localization became seizure-free and spike-free following anterior temporal lobectomy. It is yet to be determined, but initial results suggest that patients with non-AT localizations (with or without evidence of MTS on MRI) should undergo IC-EEG evaluations to confirm localization and improve outcome.

Another unique application advantage of MEG over EEG is in patients who have had craniotomies and surgical resections. In these patients, electrical potentials recorded at the scalp are distorted by cranial defects and the biophysical disturbances of brain volume changes. This situation is particularly applicable in patients with recurrent seizures after epilepsy surgeries who are contemplating repeat surgery. It has been confirmed with IC-EEG that MEG can be successful in localizing postsurgical epileptiform disturbances [80]. Aiding or eliminating difficult repeat IC-EEG studies (because of dural adhesions) would be a true contribution of MEG. Further, prognostic studies are anticipated that evaluate more formally the extent of MEG spike sources included in the surgical resection cavities.

Two relatively large observational studies have been published on the potential impact of MEG on surgical evaluation and treatment. The first of these studies was retrospective and included 455 patients [81]. MEG was found to be in lobar concordance with ultimate surgical localization in 54–80% patients (depending on instrument used). More importantly, MEG provided localizing information not available from EEG and other studies in 24% of patients, and further, MEG altered or influenced surgical decision making in 11%. The second study was prospective.
Fig. 3. (A) MEG tracings from each of 148 magnetometers (covering the entire scalp) for a typical spike recorded in the same 17-year-old patient seen in Figs. 1 and 2. The sharp wave has a dipolar magnetic flux pattern that can be visualized over the lateral aspect of the right hemisphere. The intersection between polarity changes for incoming and outgoing magnetic flux is centered near channels 88 and 108 (just posterior to EEG electrode position for T4). (B) Dipole source estimates (black triangles outlined in black) for spikes identical to that show in (A). The surrounding circles represent the 95% confidence volume for the computed source localization. These spike sources remarkably colocalize with the focal metabolic defect seen on FDG-PET and the posterior focal increase in rCBF depicted in Figs. 1 and 2, respectively. Subsequent intracranial EEG with a subdural grid confirmed epilepsy localization precisely to this region, and the patient is seizure-free after focal surgical resection.
and included 82 patients [82]. Comparison was made to degree of overlap with surgical resection site (MEG was not used to influence surgical decision making). Redundancy (perfect agreement) was seen with video/EEG localization and MEG in 32% of patients; however, MEG colocalized with the resected region in nearly 60% of patients who had nonlocalizing video/EEG. One conclusion to be drawn from both of these works is that MEG may be particularly helpful in patients clinically suspected of having focal onset seizures amenable to surgical treatment, but who have ambiguously localizing or nonlocalizing EEG and MRI.

5. Conclusions

The main aim of this review was to address the role of FDG-PET, ictal SPECT, and MEG in presurgical epilepsy localization as studies support to date. As should be expected, different strengths and weaknesses apply to all three, and no single modality appears clearly superior overall to any of the others. As such, the different modalities are, to an important degree, complementary by definition. As demonstrated in the numerous reported series using each of these imaging tools, successful localization (ultimate surgical seizure-free outcomes) can be accomplished that might otherwise not have been possible without the information provided by the tests. Most importantly, it is very likely that in certain subpopulations of patients (both neocortical lesion and cryptogenic partial epilepsies), some combination of localizing tests supporting clinical and volumetric MRI in the evaluation of patients with partial epilepsy: Neurology 1995;45:123–6.


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