Subject: Functional Brain MRI		Original Effective Date: 6/26/13
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PREFACE

This Medical Guidance is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the following website: http://www.cms.hhs.gov/center/coverage.asp.

FDA INDICATIONS

Magnetic resonance imaging is a procedure and, therefore, not subject to FDA regulation. However, any medical devices, drugs, biologics, or tests used as a part of this procedure may be subject to FDA regulation.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina medical coverage guidance (MCG) document and provide the directive for all Medicare members. The directives from this MCG document may be followed if there are no available NCD or LCD documents available and outlined below.

CMS does not have a National Coverage Decision (NCD) or Local Coverage Decision (LCD) specifically for functional magnetic resonance imaging (fMRI). The national coverage decision on magnetic resonance imaging (220.2) provides general guidelines or examples of what may be considered covered rather than as a restrictive list of specific covered indications. Imaging of cortical bone and calcifications, and procedures involving spatial resolution of bone and calcifications, are the only indications specifically listed as not covered. [1]

Please access the Medicare Local Coverage Determination (LCD) for coverage criteria that may be available in you specific region at: http://www.cms.gov/mcd/search.asp?clickon=search

INITIAL COVERAGE CRITERIA

Functional MRI (fMRI) may be considered medically necessary when all of the following criteria are met: [2 6] [ALL]

- For preoperative evaluation of patients who are > 7 years of age with one of the following conditions: [ONE]
  - Medically refractory epilepsy [5 10 11] or
  - Brain tumors; [4 7 12] and
- A candidate for neurosurgery; and
- Lesion is in close proximity to an eloquent area of the brain (e.g., controlling verbal or motor function); and
- Testing is ordered by a neurologist or neurosurgeon and the results are expected to have a role in assessing the spatial relationship between the lesion and eloquent brain area

CONTINUATION OF THERAPY

N/A

COVERAGE EXCLUSIONS

Functional MRI (fMRI) is considered investigational for all other applications because there is insufficient evidence in the published literature evaluating the clinical utility of functional magnetic resonance imaging to improve health care decisions or to predict or improve health outcomes for other conditions/diseases.

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL

Functional MRI (fMRI) is a noninvasive imaging procedure where an MRI is preformed while a part of the body is in use. It is used for the evaluation of eloquent brain areas (areas of the brain cortex responsible for control of speech, language, sensation, motion, visual and other complex functions). fMRI can detect focal changes in blood flow and oxygenation levels that occur when an area of the brain is activated. Images are collected while specific activities are performed to evaluate the proximity of a brain lesion to brain tissue responsible for specific functions such as speech, vision, sensation and movement. Knowledge of the potentially impacted functional areas is primarily used in preoperative planning for neurosurgery. [13]

GENERAL INFORMATION

Summary of Medical Evidence

Functional MRI compared to Wada Testing:

Janecek and colleagues (2013) sought to more definitively characterize Wada/functional magnetic resonance imaging (fMRI) language dominance discordance rates with the largest sample of patients with epilepsy to date, and to examine demographic, clinical, and methodologic predictors of discordance. Two hundred twenty-nine patients with epilepsy underwent both a standardized Wada test and a semantic decision fMRI language protocol in a prospective research study. Language laterality indices were computed for each test using automated and double-blind methods, and Wada/fMRI discordance rates were calculated using objective criteria for discordance. Regression analyses were used to explore a range of variables that might predict discordance, including subject variables, Wada quality indices, and fMRI quality indices. Discordant results were observed in 14% of patients. Discordance was highest among those categorized by either test as having bilateral language. In a multivariate model, the only factor that predicted discordance was the degree of atypical language dominance on fMRI. The authors found that fMRI language lateralization is generally concordant with Wada testing. The degree of rightward shift of language dominance on fMRI testing is strongly correlated with Wada/fMRI discordance, suggesting that fMRI may be more sensitive than Wada to right hemisphere language processing, although the clinical significance of this increased sensitivity is unknown. The relative accuracy of fMRI versus Wada testing for predicting postsurgical language outcome in discordant cases remains a topic for future research. [9]

In 2011, Dym et al. reported a meta-analysis of fMRI determined lateralization of language function compared to the Wada test. Inclusion criteria were examination of the same patients with both fMRI and the Wada test; preoperative examination of at least 4 patients; and reporting of the concordance in individual patients. Twenty-three studies with a total of 442 patients were included in the meta-analysis. Language dominance for each patient was classified as typical (left hemispheric language dominance) or atypical (right hemispheric language dominance or bilateral language representation), with most studies using a lateralization index threshold of 0.2. Sensitivity was defined as the ability of functional MRI (fMRI) to depict atypical language representation, and specificity was the ability of fMRI to depict typical language representation. Most of the studies did not specify whether the evaluators were blinded to the results of the other test. With the Wada test as the reference standard, fMRI had a sensitivity of 83.5% and specificity of 88.1%. Specificity was significantly higher with use of a word generation task (95.6%) than with a semantic decision task (69.5%). This analysis may oversimplify the role of fMRI, which in addition to providing information on hemispheric dominance, provides information on the localization of language and motor areas in relation to the tumor or lesion. It is also unlikely that current fMRI protocols utilize a single task (e.g., word generation) to evaluate the eloquent cortex. [3]

Arora et al. (2009) examined the efficacy of functional magnetic resonance imaging (fMRI) for language lateralization using a comprehensive three-task language-mapping approach. Two localization methods and four different metrics for quantifying activation within hemisphere are compared and validated with Wada testing. Sources of discordance between fMRI and Wada lateralization are discussed with respect to specific patient examples. fMRI language mapping was performed in patients with epilepsy (N = 40) using reading sentence comprehension, auditory sentence comprehension, and a verbal fluency task. This was compared with the Wada procedure using both whole-brain and midline exclusion-based analyses. Different laterality scores were examined as a function of statistical threshold to investigate the sensitivity to threshold effects. For the lateralized patients categorized by Wada, fMRI laterality indices (LIs) were concordant with the Wada procedure results in 83.87% patients for the reading task, 83.33% patients for the auditory task, 76.92% patients for the verbal fluency task, and in 91.3% patients for the conjunction analysis. The patients categorized as bilateral via the Wada procedure showed some hemispheric dominance in fMRI, and discrepancies between the Wada test findings and the functional laterality scores arose for a range of reasons. The authors reported that discordance was dependent upon whether whole-brain or midline exclusion method-based lateralization was calculated, and in the former case the inclusion of the occipital and other midline regions often negatively influenced the lateralization scores. Overall fMRI was in agreement with the Wada test in 91.3% of patients, suggesting its utility for clinical use with the proper consideration given to the confounds discussed in this work. [15]

In 2007 Medina et al. performed a meta-analysis of 13 studies involving a total of 240 participants to compare and calculate the sensitivity and specificity of fMRI compared to the Wada test. When using the pooled Wada test data as the reference, fMRI was found to have a high correlation, reflected by both a sensitivity and specificity of 92.5%. The authors reported that fMRI had the highest accuracy in individuals without epilepsy regardless of hand dominance. The lowest accuracy was found in individuals without epilepsy with left hand dominancy. However, this probability of concordance at 81-83% was still considered high by the authors. [16]

Woermann and colleagues (2003) conducted a large comparative study that reviewed the results of fMRI versus the Wada test in the determination of language dominance in 100 subjects with different localization-related epilepsies. The authors found 91% concordance between tests. The overall rate of incorrect results from fMRI was found to be 9% with a range of 3% in left-sided temporal lobe epilepsy (TLE) to 25% in left-sided extratemporal epilepsy. The authors concluded that language fMRI might reduce the necessity of the Wada test for language lateralization, especially in temporal lobe epilepsy. [8]

Epilepsy:

de Ribaupierre et al. (2012) compared the contributions of language fMRI and depth electrode stimulations to optimize language mapping in eight children (7.5-15.5 years) with left frontal or temporal epilepsy who underwent language fMRI and language stimulation with depth electrodes as part of their comprehensive presurgical workup. fMRI data collected during sentence generation were analyzed using statistical parametric mapping (SPM2) (false discovery rate [FDR] $p < 0.05$). Bipolar stimulations were performed during language production tasks. By coregistering fMRI and postimplantation computed tomography (CT) images, we were able to directly compare the cortical areas identified by both investigations. fMRI during sentence generation robustly showed activation in the whole perisylvian regions with little reorganization (left hemisphere dominant in 7). Of the 184 electrode contacts tested for language, only 8 were positive (language disruption) in three of the seven patients with periictal language impairment and left language dominance. All of the positive contacts colocalized with an fMRI activated cluster, that is, fMRI did not miss any region critical to language (sensitivity = 100%). However, 54 of the 176 negative contacts were within activated clusters (low specificity). The authors reported that in children with epilepsy, the sensitivity of fMRI during sentence generation allows for the detection of all critical regions displayed by cortical stimulation within the large perisylvian language network, but with a low specificity. It is, therefore, useful to optimize the placement of intracranial electrodes when language mapping is necessary. Systematic planning of the electrode placement according to language fMRI maps should increase the yield of extraoperative cortical stimulation, which appears rather low in children when compared to adults.

Thorton and associates reported on a 2011 multicenter study that compared presurgical interictal discharge-related BOLD signal changes with intracranial EEG and postoperative outcome in 23 patients with refractory epilepsy. The 23 patients were selected for analysis based on a diagnosis of focal cortical dysplasia from structural MRI or histology out of 65 patients who were undergoing presurgical evaluation for refractory focal epilepsy. The EEG-fMRI results were not used in the planning of intracranial EEG or surgical resections. Twelve of the 23 patients (52%) had interictal discharges during EEG-fMRI recording, and 11 of the 12 (92%) had significant interictal discharge-related hemodynamic changes. In the 11 patients with a BOLD response, fMRI results were concordant with the intracranial EEG-determined seizure onset zone in 5 patients (45%), and the majority (4 of the 5) had a 50% or greater reduction in seizure frequency following resective surgery. The other 6 of 11 patients had widespread or discordant regions of fMRI signal change, and the majority (n=5) had either a poor surgical outcome or a widespread seizure onset zone that precluded surgery. This study is described as the first prospective systematic evaluation of the potential role of EEG-fMRI in the presurgical evaluation of patients with focal cortical dysplasia. It should be considered exploratory. Another 2011 paper from many of the same investigators describes a recently developed method to evaluate EEG-fMRI results in the absence of visually identifiable interictal epileptiform spikes. [5]

Medina et al. (2006) prospectively evaluated the effect of functional magnetic resonance (MR) imaging on diagnostic work-up and treatment planning in patients with seizure disorders who are candidates for surgical treatment. Sixty consecutively enrolled patients (33 males, 27 females; mean age, 15.8 years +/- 8.7 [standard deviation]; range, 6.8-44.2 years) were prospectively examined. Forty-five (75%) patients were right handed, nine (15%) were left handed, and six (10%) had indeterminate hand dominance. Prospective questionnaires were used to evaluate diagnostic work-up, counseling, and treatment plans of the seizure team before and after functional MR imaging. Confidence level scales were used to determine effect of functional MR imaging on diagnostic and therapeutic thinking. Paired t test and 95% confidence interval analyses were performed. In 53 patients, language mapping was performed; in 33, motor mapping; and in seven, visual mapping. The study revealed change in anatomic location or lateralization of language-receptive (Wernicke) (28% of patients) and language-expressive (Broca) (21% of patients) areas. Statistically significant increases were found in confidence levels after functional MR imaging in regard to motor and visual cortical function evaluation. In 35 (58%) of 60 patients, the seizure team thought that functional MR imaging results altered patient and family counseling. In 38 (63%) of 60 patients, functional MR imaging results helped to avoid further studies, including Wada test. In 31 (52%) and 25 (42%) of 60 patients, intraoperative mapping and surgical plans, respectively, were altered because of functional MR imaging results. In five (8%) patients, two-stage surgery with extra-operative direct electrical stimulation mapping was averted, and resection was accomplished in one stage. In four (7%) patients, extent of surgical resection was altered because eloquent areas were identified close to seizure focus. The authors concluded that functional MR imaging results influenced diagnostic and therapeutic decision making of the seizure team; results indicated language dominance changed, confidence level in identification of critical brain function areas increased, patient and family counseling were altered, and intraoperative mapping and surgical approach were altered. [11]

Benke et al. (2006) sought to establish the power of language fMRI to detect language lateralization during presurgical assessment, we compared the findings of a semantic decision paradigm with the results of a standard intracarotid amobarbital test (IAT) in 68 patients with chronic intractable right and left temporal lobe epilepsy (rTLE, n=28; lTLE, n=40) who consecutively underwent a presurgical evaluation program. The patient group also included 14 (20.6%) subjects with atypical (bilateral or right hemisphere) speech. Four raters used a visual analysis procedure to determine the laterality of speech-related activation individually for each patient. Overall congruence between fMRI-based laterality and the laterality quotient of the IAT was 89.3% in rTLE and 72.5% in lTLE patients. Concordance was best in rTLE patients with left speech. In lTLE patients, language fMRI identified atypical, right hemisphere speech dominance in every case, but missed left hemisphere speech dominance in 17.2%. Frontal activations had higher concordance with the IAT than did activations in temporoparietal or combined regions of interest (ROIs). Because of methodologic problems, recognition of bilateral speech was difficult. The authours found that this data provides evidence that language fMRI as used in the present study has limited correlation with the IAT, especially in patients with lTLE and with mixed speech dominance. Further refinements regarding the paradigms and analysis procedures will be needed to improve the contribution of language fMRI for presurgical assessment. [10]

Brain Tumors:

Wengenroth et al. (2011) compared localization of eloquent tumor-adjacent brain areas by fMRI versus structural MRI imaging in 77 consecutive patients with brain tumors of the central region. During fMRI, the patients performed self-paced tongue up and down movements with closed lips, complex finger tapping with sequential finger-to-thumb opposition, as well as repetitive toe flexion-extension of the side contralateral to the respective lesion. The motor hand area was localized in 76/77 patients (99%) by fMRI and in 66/77 patients (86%) by structural MRI. Motor areas of the foot and tongue were investigated in 70 patients and could be identified by fMRI in 96% (tongue representation) and 97% (foot representation) of patients. Morphologic landmarks for the motor hand area were found to be reliable in the unaffected hemisphere (97% success rate) but not in the tumor-affected hemisphere (86% success rate). In 14% of patients, it was not possible to identify the motor hand area at all according to anatomic criteria. There are no reliable morphological landmarks for motor foot and tongue areas, and these representations could only be located by fMRI. After consideration of the clinical condition, tumor etiology, and fMRI results, the decision for neurosurgical operation was made in 52 patients (67.5%). In 16 patients, the decision against surgery was based mainly on fMRI results, which provided evidence that major neurologic impairments would be expected after surgery. fMRI-based risk assessment before surgery had a high correlation with the clinical outcome and corresponded in 46 of 52 operative patients (88%) who had only minimal deficits or functional improvement postoperatively. [7]

In 2010 Talacchi and associates described a five-year experience in the surgical management of malignant gliomas around motor areas with an evaluation of the impact of functional magnetic resonance imaging (fMRI) plus navigator and intraoperative neurophysiology (IN). End-points were extent of removal, morbidity, and survival. Variables describing patient and tumor characteristics and treatment modalities were statistically weighted in relation to treatment outcome. Tumor depth ($P = 0.01$), midline shift ≥1 cm. ($P = 0.05$), and insular location (P = 0.001) negatively affected extent of removal, whereas IN (P < 0.001) and fMRI plus navigator (P = 0.02) contributed to increasing the rate of total removal (73%, 71% vs. 40%). Postoperative motor impairment was mild and transient in a minority of cases (20%). General complications, as defined by the Glioma Outcome Project, occurred in 23% of cases. IN was the only factor associated with acute postoperative motor deterioration (P < 0.001). IN and age >65 years (P = 0.01) were associated with the occurrence of complications. Overall survival was significantly higher in patients operated with IN or fMRI plus navigator (P < 0.01). Comparing different surgical strategies used in the same period, the authors observed that supportive technologies in glioma surgery have their primary impact on the quality of resection and survival. IN led to transient motor impairment and some additional complications which did not affect functional outcome. [18]

In 2008 Bizzi and colleagues assessed the sensitivity and specificity of fMRI for mapping language and motor functions using intraoperative intracortical mapping as the reference standard. Thirty-four consecutive patients with a focal mass adjacent to eloquent cortex were included in the study. A site-by-site comparison between fMRI and intracortical mapping was performed with verb generation or finger tapping of the contralateral hand. A total of 251 sites were tested; 141 in patients evaluated with verb generation and 110 in patients evaluated with finger tapping. For hand motor function alone, sensitivity and specificity were 88% and 87%, respectively. For language, sensitivity and specificity were 80% and 78%, respectively. The fMRI for Broca's area showed 100% sensitivity and 68% specificity, while the fMRI for Wernicke's area showed 64% sensitivity and 85% specificity. Sensitivity of fMRI decreased from 93% for World Health Organization Grade II gliomas to 65% for Grade IV gliomas. In another study, fMRI was concordant with direct electrical stimulation in 23 of 26 (88%) cases. [4]

Amiez et al. (2008) sought to develop new pre- and intraoperative tools to specifically assess the function of the rostral part of the dorsal premotor cortex (PMdr) in 4 patients with brain tumors close to this region. Using functional magnetic resonance (fMR) imaging and a task developed to assess accurate selection between competing responses based on conditional rules, the authors preoperatively assessed the function of the PMdr in 4 patients with brain tumors close to this region. In 1 patient, the authors developed an intraoperative procedure to assess performance on the task during the tumor resection. Preoperative fMR imaging data showed specific activity increases in the vicinity of the tumors, that is, in the PMdr. As confirmed by postoperative structural MR imaging, the extent of the tumor resection was optimal and the functional region within the PMdr was preserved. Furthermore, patients exhibited no postoperative deficits during task performance, demonstrating that the function was preserved. Intraoperative behavioral results demonstrated that the cognitive processes underlying performance on the task remained intact throughout the tumor resection. The authors reported that these findings suggest that preoperative fMR imaging, together with intraoperative behavioral evaluation, may be a useful paradigm to assist neurosurgeons in preserving cognitive function in patients with brain tumors. [17]

Petrella and colleagues (2006) prospectively evaluated the effect of pre-operative fMRI localization of language and motor areas on therapeutic decision making in patients with potentially resectable brain tumors. A total of

39 consecutive patients (19 men, 20 women; mean age of 42.2 years) referred for fMRI for possible tumor resection were evaluated. A pre-operative diagnosis of brain tumor was made in all patients. Sentence completion and bilateral hand squeeze tasks were used to map language and sensorimotor areas. Neurosurgeons completed questionnaires regarding the proposed treatment plan before and after fMRI and after surgery. They also gave confidence ratings for fMRI results and estimated the effect on surgical time, extent of resection, and surgical approach. The effect of fMRI on changes in treatment plan was assessed with the Wilcoxon signed rank test. Differences in confidence ratings between altered and un-altered treatment plans were assessed with the Mann-Whitney U test. The estimated influence of fMRI on surgical time, extent of resection, and surgical approach was denoted with summary statistics. Treatment plans before and after fMRI differed in 19 patients ($p < 0.05$), with a more aggressive approach recommended after imaging in 18 patients. There were no significant differences in confidence ratings for fMRI between altered and un-altered plans. Functional MRI resulted in reduced surgical time (estimated reduction, 15 to 60 minutes) in 22 patients who underwent surgery, a more aggressive resection in 6, and a smaller craniotomy in 2. The authors concluded that fMRI enables the selection of a more aggressive therapeutic approach than might otherwise be considered because of functional risk. In certain patients, surgical time may be shortened, the extent of resection increased, and craniotomy size decreased. [12]

Hayes, Cochrane, UpToDate, MD Consult etc.

Hayes does not have a medical technology directory report for functional MRI.

UpToDate:

In a report on Neuroimaging in the Evaluation of Seizures and Epilepsy [6] the clinical utility of functional MRI was evaluated. The following are some indications and precautions for fMRI:

- fMRI can be used to noninvasively map motor, sensory, and language functions, and is most commonly used as part of surgical planning to predict and limit postoperative neurologic deficits, particularly language function. fMRI may eventually replace the carotid amobarbital (Wada) test, particularly for language lateralization.
- With regard to memory function, early work suggests that fMRI may be able to visualize the functional anatomy of memory tasks, and may eventually assist decision-making and planning of epilepsy surgery. Interpretation of fMRI requires caution; it is an indirect measure of brain function.
- Discrepancies with the Wada test have been described. Its sensitivity and specificity are imperfect (84 and 88 percent compared to the Wada test, in one analysis), particularly in extratemporal epilepsy, and analyses have not been standardized.
- Patients that cannot complete fMRI or have inconclusive fMRI results still require preoperative Wada testing.
- Simultaneous recording of EEG and fMRI can visualize the BOLD response during interictal or ictal epileptic activity.
- This emerging technique could assist in identifying targets for surgical treatment. However, the utility of fMRI for this purpose is not yet established.

DynaMed

In a report called Epilepsy in Children (2012) imaging studies used for diagnostic evaluation may include functional MRI to map functional cortical areas and relationship to epileptogenic cortex in patients as part of preparation for surgery, but is limited to children > 7-8 years old as patient training and cooperation is necessary. [19]

In a report called Epilepsy in Adults (2013) imaging studies used for diagnostic evaluation may include functional MRI when used prior to surgical treatment to lateralize language function areas and visualize functional anatomy of memory tasks. [20]

Professional Organizations

The American College of Radiology (ACR), the American Society of Neuroradiology (ASNR), and the Society for Pediatric Radiology, Practice Guideline for the Performance of Functional Magnetic Resonance Imaging (fMRI) of the Brain [2]: This guideline was revised 2012 and indicates that Functional magnetic resonance imaging (fMRI) using blood oxygenation level dependent imaging (BOLD) technique is a tool for evaluating eloquent cortex in relation to a focal brain lesion, such as a neoplasm or vascular malformation. According to the guidelines the clinical indications for fMRI include the all of the following:

- Assessment of intracranial tumoral disease for:
  - Presurgical planning and operative risk assessment.
  - Assessment of eloquent cortex (e.g., language, sensory motor, visual centers) in relation to a tumor or other focal lesion.
  - Surgical planning (biopsy or resection)
  - Therapeutic follow-up
- Evaluation of preserved eloquent cortex
- Assessment of eloquent cortex for epilepsy surgery

CODING INFORMATION

CPT	Description
70554	Magnetic resonance imagining, brain, functional MRI; including test selection and administration of repetitive body part movement and/or visual stimulation, not requiring physician or psychologist administration
70555	Magnetic resonance imaging, brain, functional MRI; requiring physician or psychologist administration of entire neurofunctional testing
96020	Neurofunctional testing selection and administration during noninvasive imaging functional brain mapping, with test administered entirely by a physician or psychologist, with review of test results and report

HCPCS	Description
N/A	

ICD-9	Description
191.0-191.9	Malignant neoplasm of brain
225.0	Benign neoplasm of brain
345.00-345.91	Epilepsy

ICD-10	Description
C71.0-C71.9	Malignant neoplasm of brain
D33.0-D33.2	Benign neoplasm of brain
G40.00-G40.919	Epilepsy

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