**6.01.47 Functional Magnetic Resonance Imaging of the Brain**

**Original Policy Date:** November 1, 2016  
**Effective Date:** November 1, 2017  
**Section:** 6.0 Radiology  
**Page:** Page 1 of 10

### Policy Statement

Functional magnetic resonance imaging may be considered *medically necessary* as a complementary test in the preoperative evaluation of patients with refractory epilepsy or brain tumors who are candidates for neurosurgery when the lesion is in close proximity to an eloquent area of the brain (e.g., controlling verbal or motor function and testing is expected to have an important role in assessing the spatial relationship between the lesion and eloquent brain area.

Functional magnetic resonance imaging is considered *investigational* for all other applications.

### Policy Guidelines

CPT coding specific to functional magnetic resonance imaging differentiates between circumstances when a physician or psychologist does all of the functional testing and when the testing is done by other professionals:

- **70554:** Magnetic resonance imaging, 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

The physician or psychologist who administers the testing would use the following CPT code:

- **96020:** Neurofunctional testing selection and administration during noninvasive imaging functional brain mapping, with test administered entirely by a physician or other qualified health care professional (i.e., psychologist), with review of test results and report

### Description

Functional magnetic resonance imaging (fMRI) is a noninvasive method for localizing areas of brain function and has been used for the presurgical evaluation of eloquent brain areas. Using this method, images are collected while specific activities are performed to assist in the localization of critical cortical areas, as well as the evaluation of language lateralization. Functional magnetic resonance imaging is also being investigated in combination with diffusion tensor imaging and electroencephalography to identify seizure focus.

### Related Policies

- Magnetoencephalography/Magnetic Source Imaging

### Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.
Regulatory Status

Several fMRI hardware (e.g., fMRI Hardware System; Nordic NeuroLab AS) and fMRI software packages (e.g., Brain AcquireRx™/Brain ProcessRx™ Data Suite; Kyron Clinical Imaging) have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process for use with an MRI scanner to perform fMRI. Food and Drug Administration product code: LNH.

Rationale

Background

Presurgical Brain Mapping

Localization of certain areas of the brain (e.g., speech centers) before neurologic surgery for seizure disorders or resection of brain tumors is important because failure to do so can result in damage to language and motor centers; e.g., 25% to 60% of patients who undergo left anterior temporal lobectomy develop dysnomia (language/naming difficulties).

Finding these certain areas of the brain, often called “eloquent” areas, involves the use of the Wada test and direct electrical stimulation. Both the test and the stimulation are fairly invasive and require the expertise of various specialists. Direct intracortical electrical stimulation involves functional mapping of the exposed cortex with electrodes, which may elicit a motor or verbal response including arrest of speech, random answering, or perseveration to stimulation. The Wada test is an inactivating method that blocks the function of 1 hemisphere by injecting amobarbital into the carotid artery, allowing functional testing of the reserve capacity of the nonanesthetized hemisphere.

Functional magnetic resonance imaging (fMRI) is an activation method that uses sequences based on T2-weighted blood oxygen level-dependent response. These studies are often done on magnetic resonance scanners with field strengths of 1.5 tesla or greater. The interhemispheric difference between activated volumes in the left and right hemispheric regions of interest is calculated as the laterality index, which ranges from -1 to 1. A positive laterality index is considered left-dominant, while a negative laterality index is right-dominant. Laterality indexes determined by fMRI may be derived for several different functional areas (regions of interest) that include either the Broca area (language production) or the Wernicke area (language comprehension). Various thresholds (e.g., -0.1 to +0.1, or -0.5 to +0.5) have been proposed to differentiate laterality from bilaterality. Bilateral activation patterns can result from the detection of language-associated, but not the language-essential cortex. Therefore, bilateral activation is not necessarily indicative of a bilateral distribution of language-essential cortex and may be task-dependent. In addition, sensitivity and specificity may change with the application of different statistical thresholds.

Simultaneous electroencephalography (EEG) and fMRI is being investigated for the localization of seizures. Simultaneous EEG-fMRI combines the temporal resolution of EEG and the spatial resolution of fMRI. Simultaneous EEG-fMRI may allow for the detection of cerebral hemodynamic changes associated with seizures and interictal epileptiform discharges that are identified on scalp EEG. Another potential use of simultaneous EEG-fMRI is to facilitate the implantation strategy of invasive subdural electrodes.

Literature Review

Functional magnetic resonance imaging (fMRI) can be thought of as a type of diagnostic test to determine the location of eloquent cortex or seizure focus. Assessment of a diagnostic technology typically focuses on 3 categories of evidence: technical reliability, diagnostic accuracy, and impact on health outcomes. Technical reliability refers to how well the technology measures and records the parameter(s) that it is purported to evaluate. Evaluation of technical reliability may include various measures of validity (e.g., criterion validity, construct validity) and reliability (e.g., test-retest reliability, agreement among multiple reviewers). Clinical validity is the ability of a test to diagnose accurately a clinical condition in relevant populations.
of patients compared with a reference standard. Measures of clinical validity include sensitivity, specificity, predictive values, likelihood ratios, and area under the curve analysis. To determine the clinical utility of the diagnostic technology, a demonstration that the diagnostic information can be used to improve patient outcomes is essential. In most cases, a chain of evidence needs to be constructed to determine whether there is a tight linkage between the diagnostic technology and improvement in health outcomes.

For fMRI, comparators for language laterality may be the Wada test and intracortical mapping. Health outcomes can be directly assessed by the impact of the test on surgical outcomes.

**Presurgical Mapping of the Eloquent Cortex**

**Technical Reliability**

Some research has focused on establishing and improving standardized protocols and analysis for presurgical evaluation of the eloquent cortex; e.g., Stippich et al (2007) described a routine preoperative fMRI protocol in 81 consecutive patients (70 with tumors on the left side, 11 with tumors on the right side and language deficits). Patients were trained to recall simple sentences (picture cues) or to generate words in a category (word cues). The combination of tasks permitted localization of both the Broca (language expressive) and Wernicke (language receptive) areas and determination of hemispheric language dominance in 79 (98%) patients. Based on fMRI findings, surgical plans were modified in 9 (11%) patients. The authors noted that, although fMRI can localize the center of an area, resection borders cannot be reliably determined by this technique. Ruff et al (2008) found no optimal threshold for reliably determining the language laterality index. In addition to the statistical threshold, the language laterality index varied as a result of presence of tumor, prior surgery, and language task. In another report, Wellmer et al (2008) assessed whether currently recommended thresholds for the fMRI laterality index helped identify atypical dominant patients (i.e., not left-dominant) with sufficient safety for presurgical settings. Depending on the chosen laterality index threshold for unilateral language dominance, between 2 (9%) and 5 (23%) patients in this sample would have been misclassified as typical dominant.

**Clinical Validity**

**Wada Testing as the Reference Standard**

In 2011, Dym et al reported on a meta-analysis of fMRI-determined lateralization of language function compared with the Wada test. Twenty-three studies (total N=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 laterality index threshold of 0.2. Sensitivity was defined as the ability of fMRI to depict atypical language representation, and specificity was the ability of fMRI to depict typical language representation. Most studies did not specify whether evaluators were blinded to results of the other test. With the Wada test as the reference standard, fMRI had a sensitivity of 84% and specificity of 88%. Specificity was significantly higher with the use of a word generation task (96%) than with a semantic decision task (70%). This analysis may have oversimplified 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 use a single task (e.g., word generation) to evaluate the eloquent cortex.

**Intracortical Mapping as the Reference Standard**

Bizzi et al (2008) reported on 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 the eloquent cortex were studied. 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, the sensitivity and specificity were 88% and 87% respectively. For language, the sensitivity and specificity were 80% and 78% respectively. Functional MRI for the
Broca area showed 100% sensitivity and 68% specificity, while fMRI for the Wernicke area showed 64% sensitivity and 85% specificity. The sensitivity of fMRI decreased from 93% for World Health Organization grade II gliomas to 65% for grade IV gliomas. In another study (2005), fMRI was concordant with direct electrical stimulation in 23 (88%) of 26 cases.

Postoperative Language Changes as the Reference Standard
In 2003, Sabsevitz et al reported on a series of 24 consecutive patients who underwent both fMRI and Wada testing before left anterior temporal lobectomy for seizure disorders. While both tests were predictive of language changes, in this study, fMRI had a sensitivity of 100% and specificity of 57% while results for the Wada test were 100% and 43%, respectively. In 2013, this group of investigators reported that 32 (14%) of 229 epilepsy patients showed discordance between fMRI and Wada testing, and that discordance was highest when either test indicated that language was bilateral. For 10 patients who had discordant results, underwent left temporal lobe surgery, and had preoperative and 6-month postoperative language testing, fMRI was more accurate in predicting naming outcomes in 7 patients; the Wada test was more accurate in 2 patients, and the 2 tests were equally accurate in 1 patient. Results from this small prospective study suggested that fMRI may be more accurate than the Wada test in predicting postsurgical language outcomes.

Clinical Utility
Use of preoperative fMRI in combination with intraoperative MRI has been reported to permit more complete resection of tumors without affecting eloquent neurologic function. In this 2009 case series of 29 patients, preoperative fMRI was performed to identify and coregister areas of brain activation for motor, speech, and short-term memory before brain tumor resection. Areas of brain activation that were identified preoperatively were superimposed on 1.5- or 3-tesla scanners during the operative procedure, allowing the surgeon to avoid brain areas where damage would result in a postoperative neurologic deficit. Postoperative neurologic morbidity was reported to be low in the 27 patients in whom an fMRI-guided tumor resection was possible.

In a 2011 report, Wengenroth et al compared the localization of eloquent tumor-adjacent brain areas using fMRI or structural MRI in 77 consecutive patients with brain tumors of the central region. The motor hand area was localized in 76 (99%) of 77 patients by fMRI and in 66 (86%) of 77 patients 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). After consideration of the clinical condition, tumor etiology, and fMRI results, the decision for neurosurgery was made in 52 (68%) patients. 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. Functional MRI-based risk assessment before surgery had a high correlation with the clinical outcome and corresponded in 46 (88%) of 52 operative patients who had functional improvement or only minimal deficits postoperatively.

Petrella et al reported on the impact of fMRI preoperatively on 39 consecutive patients with brain tumors in 2006. Treatment plans differed in 19 patients after fMRI, with a more aggressive approach recommended after imaging in 18 patients. However, the impact of the altered treatment plans on outcomes was not assessed. Functional MRI resulted in reduced surgical time for 22 patients; it also led to decisions to perform craniotomy in 13 patients in whom less invasive approaches had been initially planned. Medina et al (2005) evaluated 60 consecutive patients preoperatively. Language mapping was performed in 53 patients, motor mapping was done in 33, and visual mapping was in 7. The fMRI study revealed a change in anatomic location or lateralization of language reception (Wernicke) in 28% of patients and in language expression (Broca) in 21%. In 38 (63%) patients, fMRI helped to avoid further studies, including the Wada test. In 31 (52%) and 25 (42%) of the patients, intraoperative mapping and surgical plans, respectively, were altered because of fMRI results. Others have reported that successful preoperative fMRI
decreased intracortical mapping time from about 50 minutes to 30 minutes and total operating
time from an average 8.5 hours to about 7 hours.13

Section Summary: Presurgical Mapping of the Eloquent Cortex
The diagnostic accuracy of fMRI has been compared with the Wada test and with intracortical
mapping to evaluate postoperative language changes. Sensitivity and specificity depend on
the specific task but have been shown to be predictive of hemispheric dominance in a
substantial percentage of patients. In a study that used postoperative language changes as the
reference standard, both fMRI and the Wada test had high sensitivity and moderate specificity.
When results were discordant between tests, fMRI was slightly more accurate. Evidence on
health outcomes has suggested that, although bilateral activation patterns in fMRI cannot be
conclusively interpreted, fMRI in patients who are to undergo neurosurgery for seizures or brain
tumors may help to define eloquent areas, reduce surgical time, and alter treatment decisions.

Localization of Seizure Focus with Simultaneous Electroencephalography and fMRI
Some small studies have evaluated surgical outcomes following use of simultaneous
electroencephalography (EEG) and fMRI to identify seizure focus. For example, in a 2007 report,
the preoperative localization of epileptic focus was assessed in 29 complex patients (unclear
focus and/or multifocality) not deemed to be candidates for epilepsy surgery.14 Patients were
selected if they had no contraindications for MRI, had more than 10 interictal discharges in 40
minutes of a previously recorded EEG, and if the reason for denial of surgery was the inability to
localize a single source with EEG. The results of the fMRI were considered robust if a consensus-
defined interictal electrical discharge was associated with a significant fMRI response. In 8 (28%)
patients, a robust fMRI response was considered to be topographically related to interictal
electrical discharges. As a result of the testing, 4 (14%) patients were considered to be surgical
candidates, and 1 of the 4 had undergone surgery at the time of publication. Moeller et al
(2009) reported on an EEG-fMRI study for the workup of 9 patients with refractory frontal lobe
epilepsy who did not have a clear lesion or seizure focus.15 The number of interictal discharges
recorded during the fMRI session ranged from 9 to 744. There was concordance between spike
localization and positive fMRI response in 8 patients; surgery was subsequently performed on 2
patients, one of whom was seizure-free at the time of publication.

A 2011 multicenter study compared presurgical interictal discharge-related blood oxygen
level-dependent (BOLD) signal changes with intracranial EEG and postoperative outcomes in 23
patients with refractory epilepsy.16 The 23 patients were selected based on a diagnosis of focal
cortical dysplasia from structural MRI or histology. The EEG-fMRI results were not used in the
planning of intracranial EEG or surgical resections. In the 11 patients with a BOLD response, fMRI
results were concordant with the intracranial EEG-determined seizure onset zone in 5 (45%)
patients. The other 6 of 11 patients had widespread or discordant regions of fMRI signal change,
and 5 had either a poor surgical outcome or a widespread seizure onset zone that precluded
surgery. This study should be considered exploratory. Another 2011 study from many of the same
investigators described a newer method to evaluate simultaneous EEG-fMRI results in the
absence of visually identifiable interictal epileptiform spikes.17

In a 2013 study, van Houdt et al conducted a retrospective comparison of presurgical EEG-fMRI
with invasive electrocorticographic data and surgical outcomes in 16 patients.18 Patients were
selected based on the following criteria: if they had interictal epileptiform activity during fMRI
acquisition, if they had acceptable EEG and fMRI data, and if they were candidates for surgery.
In each patient, at least one of the simultaneous EEG-fMRI areas was concordant with an
interictally active electrocorticographic anatomic brain region. For areas covered with subdural
grids, 76% of the BOLD regions were concordant with interictally active electrocorticographic
electrodes. However, due to limited spatial sampling, 51% of the active BOLD regions were not
covered with electrodes. Simultaneous EEG-fMRI BOLD areas included the resected area in 93% of
the cases.
Research is ongoing to improve the identification of seizure focus with simultaneous EEG-fMRI, including occasions without intrascanner interictal epileptic discharges.\textsuperscript{19,20}

**Section Summary: Localization of Seizure Focus with Simultaneous Electroencephalography and fMRI**

Several small studies identified have evaluated seizure focus with simultaneous EEG plus fMRI. This is a relatively recent area of research, which has followed the development of MRI-compatible EEG electrodes. Current research is attempting to improve the identification of seizure focus with this technique, particularly when there are no interictal epileptic discharges during the fMRI session. There are very few data on the effect of this procedure on health outcomes.

**Summary of Evidence**

For individuals who have epilepsy or brain tumors who are undergoing presurgical mapping of the eloquent cortex who receive fMRI, the evidence includes studies on diagnostic accuracy and clinical utility. Relevant outcomes are test accuracy, morbid events, functional outcomes, and quality of life. The diagnostic accuracy of fMRI has been compared with the Wada test and intracortical mapping to evaluate postoperative language changes. Sensitivity and specificity depend on the specific task but have been shown to be predictive of hemispheric dominance in a substantial percentage of patients. According to findings from health outcomes, fMRI has several benefits for patients who are to undergo neurosurgery for seizures or brain tumors; these benefits are: the potential to define eloquent areas (e.g., controlling verbal or motor function), and the ability to reduce surgery time and alter treatment decisions. Because of the highly detrimental impact of resecting the eloquent cortex, fMRI may be considered complementary to the Wada test and direct electrical stimulation when the lesion is in close proximity to an eloquent area of the brain. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have epilepsy who are being evaluated for localization of seizure focus who receive simultaneous electroencephalography and fMRI, the evidence includes a limited number of small studies. Relevant outcomes are test accuracy, morbid events, functional outcomes, and quality of life. The objective of current research is to improve the identification of seizure focus with this technique, particularly when there are no interictal epileptic discharges during an fMRI session. There are very few data on the effect of this procedure on health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Supplemental Information**

**Practice Guidelines and Position Statements**

The American College of Radiology, American Society of Neuroradiology, and Society for Pediatric Radiology jointly published 2014 guidelines (revised in 2017), which state that “Functional magnetic resonance imaging (fMRI) using blood oxygen level dependent imaging (BOLD) technique is a proven and useful tool for localizing eloquent cortex in relation to a focal brain lesion, such as neoplasm or vascular malformation.”\textsuperscript{21} The guidelines’ primary indications for fMRI included “[p]resurgical planning and operative risk assessment, [a]ssessment of the eloquent cortex ... in relation to a tumor or another focal lesion, [s]urgical planning (biopsy or resection), [e]valuation of preserved eloquent cortex, [a]ssessment of eloquent cortex for epilepsy surgery” and therapeutic follow-up.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

There is no national coverage decision specifically for fMRI.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.
Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01534104</td>
<td>Using Functional MRI and Diffusion Imaging of Eloquent Brain Areas to Optimize Brain Tumor Resection Planning</td>
<td>250</td>
<td>Feb 2018</td>
</tr>
<tr>
<td>NCT02107989</td>
<td>Noninvasive Pre-surgical Evaluation of Patients With Focal Epilepsy</td>
<td>250</td>
<td>Jul 2020</td>
</tr>
<tr>
<td>NCT02795338</td>
<td>Multi-modality Localization of Eloquent Brain Function—A Comparison of Technologies for Improved Applicability</td>
<td>80</td>
<td>Oct 2021</td>
</tr>
</tbody>
</table>

NCT: National Clinical Trial.

References


### Documentation for Clinical Review

**Please provide the following documentation (if when requested):**
- History and physical and/or consultation notes including:
  - Reason for functional MRI of the brain
- Previous imaging studies pertaining to request

**Post Service**
- Functional MRI of the brain report

### Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

**MN/IE**

The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT®</td>
<td>70554</td>
<td>Magnetic resonance imaging, brain, functional MRI; including test selection and administration of repetitive body part movement and/or visual stimulation, not requiring physician or psychologist administration</td>
</tr>
</tbody>
</table>
### Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

### Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.
Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.