Navigated Transcranial Magnetic Stimulation

Policy # 00407
Original Effective Date: 03/19/2014
Current Effective Date: 10/09/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Magnetoencephalography/Magnetic Source Imaging is addressed separately in medical policy 00082.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers navigated transcranial magnetic stimulation (nTMS) for all purposes, including but not limited to the preoperative evaluation of individuals being considered for brain surgery, when localization of eloquent areas of the brain (e.g., controlling verbal or motor function) is an important consideration in surgical planning to be **investigational.***

Background/Overview

Management of Brain Tumors

Surgical management of brain tumors involves resecting the brain tumor and preserving essential brain function. "Mapping" of brain functions, such as body movement and language, is most accurately achieved with direct cortical stimulation (DCS), an intraoperative procedure that lengthens operating times and requires a wide surgical opening. Even if not completely accurate compared with DCS, preoperative techniques that map brain functions may aid in planning the extent of resection and the surgical approach. Although DCS is still usually performed to confirm the brain locations associated with specific functions, preoperative mapping techniques may provide useful information that improves patient outcomes.

Noninvasive Mapping Techniques

The most commonly used tool for the noninvasive localization of brain functions is functional magnetic resonance imaging (fMRI). Functional MRI identifies regions of the brain where there are changes in localized cortical blood oxygenation, which correlate with the neuronal activity associated with a specific motor or speech task being performed as the image is obtained. The accuracy and precision of fMRI depend on the patient's ability to perform the isolated motor task, such as moving the single assigned muscle without moving others. This may be difficult in individuals in whom brain tumors have caused partial or complete paresis. The reliability of fMRI in mapping language areas has been questioned. Guissani et al (2010) reviewed several studies comparing fMRI with DCS of language areas and found large variability in the sensitivity and specificity rates of fMRI. Reviewers also pointed out a major conceptual point in how fMRI and DCS "map" language areas: fMRI identifies regional oxygenation changes, which show that a particular region of the brain is involved in the capacity of interest, whereas DCS locates specific areas in which the activity of interest is disrupted. Regions of the brain involved in a certain activity may not necessarily be required for that activity and could theoretically be safely resected.

Magnetoencephalography (MEG) is also used to map brain activity. In this procedure, electromagnetic recorders are attached to the scalp. Unlike electroencephalography, MEG records magnetic fields generated by electric currents in the brain, rather than the electric currents themselves. Magnetic fields tend to be less distorted by the skull and scalp than electric currents, yielding an improved spatial resolution. MEG is conducted in a magnetically shielded room to screen out environmental electric or magnetic noises that could interfere with the MEG recording.

Navigated transcranial magnetic stimulation (nTMS) is a noninvasive imaging method for evaluating eloquent brain areas. Transcranial magnetic pulses are delivered to the patient as a navigation system calculates the strength, location, and direction of the stimulating magnetic field. The locations of these pulses are registered to a magnetic resonance image of the patient's brain. Surface electromyography electrodes are attached to various limb muscles of the patient. Moving the magnetic stimulation source to various parts of the brain causes electromyography electrodes to respond, indicating the part of the cortex involved in particular muscle movements. For evaluation of language areas, magnetic stimulation areas that disrupt specific speech tasks are thought to identify parts of the brain involved in speech function. Navigated TMS can be considered a noninvasive alternative to DCS, in which electrodes are directly applied to the surface of the cortex during craniotomy. Navigated TMS is being evaluated as an alternative to other noninvasive cortical

mapping techniques (eg, fMRI, MEG) for presurgical identification of cortical areas involved in motor and language functions. Navigated TMS, used for cortical language area mapping, is also being investigated in combination with diffusion tensor imaging tractography for subcortical white matter tract mapping.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

The Nexstim Navigated Brain Stimulation System (NBS) 5 Motor Mapping System and NBS 5 Speech Mapping System with NexSpeech®‡ were cleared for marketing by the FDA through the 510(k) process for noninvasive mapping of the primary motor cortex of the brain to its cortical gyrus and for localization of cortical areas that do not contain speech function for preprocedural planning.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Navigated transcranial magnetic stimulation (nTMS) is a noninvasive imaging method for evaluating eloquent brain areas (eg, those controlling motor or language function). Navigated TMS is being evaluated as an alternative to other noninvasive cortical mapping techniques for presurgical identification of eloquent areas.

Summary of Evidence

For individuals who have brain lesion(s) undergoing preoperative evaluation for localization of eloquent areas of the brain who receive navigated transcranial magnetic stimulation (nTMS), the evidence includes systematic reviews, observational studies, and case series. Relevant outcomes are overall survival (OS), test accuracy, morbid events, and functional outcomes. Several studies have evaluated the distance between nTMS hotspots and direct cortical stimulation (DCS) hotspots for the same muscle. Although the average distance in most studies is 10 mm or less, this does not take into account the error margin in this average distance or whether hotspots are missed. It is difficult to verify nTMS hotspots fully because only exposed cortical areas can be verified with DCS. Limited

studies of nTMS evaluating language areas have shown high false-positive rates (low specificity) and sensitivity that may be insufficient for clinical use. Several controlled observational studies have compared outcomes in individuals undergoing nTMS with those (generally pre-TMS historical controls) who did not undergo nTMS. Findings of the studies were mixed. A meta-analysis of observational studies found improved outcomes with preoperative nTMS mapping in individuals with motor-eloquent brain tumors. However, in individual observational studies, outcomes were not consistently better in individuals who underwent presurgical nTMS. For example, OS did not differ significantly between groups in 2 studies. The controlled observational studies had various methodologic limitations and, being nonrandomized, might not have adequately controlled for differences in patient groups, which could have biased outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2013 Input

In response to requests, input was received from 1 physician specialty society (2 reviewers) and 2 academic medical centers while this policy was under review in 2013. Most reviewers considered navigated transcranial magnetic stimulation to be investigational.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information’ if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

No guidelines or statements were identified.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04062305	nTMS in Planning Stereotactic Radiosurgery in Individuals With Brain Metastases in the Motor Cortex	22	May 2023
NCT02741193[a]	Validation of Presurgical Motor Mapping With Transcranial Magnetic Stimulation (TMS) in Individuals With Epilepsy	14	Dec 2023
Unpublished			
NCT03974659	Through the Navigation Transcranial Magnetic Stimulation Over the Language Key Areas of Cerebellar to Enhance Language Function Recovery After Brain Tumor Resection	106	Oct 2021
NCT02879682	Randomized Controlled Multicenter Trial on the Impact of Presurgical Navigated Transcranial Magnetic Stimulation for Motor Mapping of Rolandic Lesions	330	Feb 2022

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Policy History

Original Effective Date: 03/19/2014
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03/06/2014	Medical Policy Committee review
03/19/2014	Medical Policy Implementation Committee approval. New policy.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
08/06/2015	Medical Policy Committee review
08/19/2015	Medical Policy Implementation Committee approval. Updated rationale and references. Coverage eligibility unchanged.
08/04/2016	Medical Policy Committee review
08/17/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
08/03/2017	Medical Policy Committee review
08/23/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2018	Coding update
08/09/2018	Medical Policy Committee review

08/15/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/02/2021	Medical Policy Committee review
09/08/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/01/2022	Medical Policy Committee review
09/14/2022	Medical Policy Implementation Committee approval. Investigational statement terminology changed from "patients" to "individuals". Coverage eligibility unchanged.
09/07/2023	Medical Policy Committee review
09/13/2023	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 09/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	64999
HCPCS	No codes
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.