

Policy Number	MED205.037
Policy Effective Date	10/15/2024
Policy End Date	12/31/2025

Navigated Transcranial Magnetic Stimulation (nTMS)

Table of Contents
<u>Coverage</u>
<u>Policy Guidelines</u>
<u>Description</u>
<u>Rationale</u>
<u>Coding</u>
<u>References</u>
<u>Policy History</u>

Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

This medical policy has become inactive as of the end date above. There is no current active version and this policy is not to be used for current claims adjudication or business purposes.

Navigated transcranial magnetic stimulation (nTMS) is considered experimental, investigational and/or unproven.

Policy Guidelines

There is no specific CPT code for this procedure. CPT code 64999 may be used.

Description

Navigated transcranial magnetic stimulation (nTMS) is a noninvasive imaging method for evaluating eloquent brain areas (e.g., 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.

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 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 patients 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. (1) 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 TMS 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 (e.g., 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.

Regulatory Status

The Nexstim Navigated Brain Stimulation (NBS) System 5 Motor Mapping System and NBS 5 Speech Mapping System with NexSpeech® were cleared for marketing by the United States Food and Drug Administration (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

This medical policy was created in July 2014 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through April 25, 2024.

Medical policies assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Medical policies assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these policies, and credible information on technical reliability is available from other sources.

Preoperative Localization Of Eloquent Areas Of The Brain

Clinical Context and Test Purpose

The purpose of navigated transcranial magnetic stimulation (nTMS) in individuals who have brain lesions is to aid in the localization of eloquent areas of the brain to reduce damage to verbal and motor functions during surgery.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals who have brain lesions and are undergoing surgery that could harm eloquent areas of the brain (e.g., those controlling motor or language function).

Interventions

The intervention of interest is nTMS, a noninvasive imaging method for evaluating eloquent brain areas.

Comparators

Several tools are used for the noninvasive localization of brain functions, including functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG). Whether noninvasive presurgical tools are used, direct cortical stimulation (DCS) is usually performed during surgery to confirm the brain locations associated with specific functions.

Outcomes

The outcomes of interest are surgical improvement in survival or in functional measures such as speaking and walking or in a reduction in morbidity.

Study Selection Criteria

For the evaluation of clinical validity of the nTMS, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores);
- Included a suitable reference standard (DCS, fMRI, or MEG);
- Patient/sample clinical characteristics were described;
- Patient/sample selection criteria were described.

Several studies were excluded from the evaluation of the clinical validity of the nTMS test because they did not use the marketed version of the test, did not use an appropriate reference standard or reference standard was unclear, did not adequately describe the patient characteristics, or did not adequately describe patient selection criteria.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Language Mapping

Systematic Review

Jeltema et al. (2020) published a systematic review of articles that compared nTMS to intraoperative DCS for mapping of motor or language function. (2) Among 8 articles which evaluated mapping language function, sensitivity ranged from 10% to 100% and specificity ranged from 13.3% to 98% when nTMS was compared to DCS. The positive predictive value (PPV) ranged from 17% to 75% and the negative predictive value ranged from 57% to 100%.

Observational Studies and Case Series

Most studies of nTMS are case series or cohort studies evaluating patients with brain tumors, (3-5) cavernous angiomas, (6) arteriovenous malformations, (7) gliomas, (8, 9) or other brain lesions; case series are not ideal studies to ascertain diagnostic characteristics. A number of small nTMS studies have also evaluated healthy volunteers, but they do not add substantially to the evidence base. (6, 10-14) Studies comparing nTMS with DCS, MEG, and/or fMRI and/or using DCS as the reference standard are described next.

Distance Between Navigated Transcranial Magnetic Stimulation and Direct Cortical Stimulation Hotspots

Several small studies have evaluated the accuracy of nTMS by measuring the distance between nTMS "hotspots" (the point at which stimulation produced the largest electromyographic response in the target muscles) during preoperative cortical mapping and the gold standard of intraoperative DCS hotspots.

Picht et al. (2011) evaluated 17 patients with brain tumors using nTMS and DCS. (15) Both techniques were used to elicit hotspots. Target muscles were selected based on the needs of each patient concerning tumor location and clinical findings. Intraoperative DCS locations were chosen independently of nTMS, and the surgeon was unaware of the nTMS hotspots. For 37 muscles in 17 patients, nTMS and DCS data were both available. Mean distance between nTMS and DCS hotspots was 7.83 mm (standard error, 1.18) for the abductor pollicis brevis muscle (95% confidence interval [CI], 5.31 to 10.36 mm) and 7.07 mm (standard error, 0.88) for the tibialis anterior muscle. When DCS was performed during surgery, there were large variations in the numbers of stimulation points, and the distance between nTMS and DCS was much smaller when a larger number of points were stimulated.

Forster et al. (2011) performed a similar study in 11 patients. (16) Functional MRI also was performed in this study. The distance between corresponding nTMS and DCS hotspots was 10.49 mm (standard deviation [SD], 5.67). The distance between the centroid of fMRI activation and DCS hotspots was 15.03 mm (SD=7.59). However, it was unclear whether hotspots elicited by 1 device could be elicited by the other and vice versa. In at least 2 excluded patients, hotspots were elicited by DCS but not by nTMS.

Tarapore et al. (2012) evaluated the distance between nTMS and DCS hotspots. (17) Among 24 patients who underwent nTMS, 18 of whom also underwent DCS, 8 motor sites in 5 patients corresponded. The median distance between nTMS and DCS hotspots was 2.13 mm (standard error of the mean [SEM], 0.29). In the craniotomy field where DCS mapping was performed, DCS elicited the same motor sites as nTMS. The study also evaluated MEG; the median distance between MEG motor sites and DCS sites was 12.1 mm (SEM, 8.2).

Mangravati et al. (2013) evaluated the distance between nTMS and DCS hotspots in 7 patients. (4) It is unclear how many hotspots were compared or how many potential comparisons were unavailable due to a failure of either device to find a particular hotspot. It appears that the mean distance between hotspots was based on locations of hotspots for 3 different muscles.

The overall mean difference between nTMS and DCS was 8.47 mm, which was less than the mean difference between the fMRI centroid of activation and DCS hotspots (12.9 mm).

Krieg et al. (2012) compared nTMS with DCS in 14 patients. (18) Interpreting this study is difficult because the navigation device employed appeared to differ from the U.S. Food and Drug Administration–approved device. Additionally, the comparison of nTMS to DCS used a different methodology. Both nTMS and DCS were used to map the whole volume of the motor cortex, and a mean difference between the borders of the mapped motor cortex was calculated. The mean distance between the 2 methods was 4.4 mm (SD=3.4).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

The ideal study to determine whether nTMS improves health outcomes in patients being considered for surgical resection of brain tumors would be an RCT comparing nTMS with strategies that do not use nTMS. There are challenges in the design and interpretation of such studies. Given that results of diagnostic workups of brain tumor patients may determine which patients undergo surgery, the counseling given to patients, and the type of surgery performed, it would be difficult to compare outcomes for groups of patients with qualitatively different outcomes. For example, it is difficult to compare the health outcomes of a patient who ends up not having surgery, who conceivably has a shorter overall lifespan but a short period of very high quality of life, with a patient who undergoes surgery and has some moderate postoperative disability but a much longer lifespan.

Systematic Reviews

No RCTs were identified. However, controlled observational studies are available. Raffa et al. (2019) published a systematic review and meta-analysis of observational studies in patients with motor-eloquent brain tumors who underwent presurgical nTMS motor mapping compared to patients without nTMS. (19) Eight observational studies with 1031 patients were included in the analysis (n=593 with preoperative nTMS mapping and n=438 without nTMS mapping). Included patients had low and high grade gliomas, glioblastoma, brain metastasis, vascular malformations, and cavernous and artero-venous malformations. In pooled analyses, use of nTMS was associated with a lower risk of postoperative new permanent motor deficits (odds ratio [OR], 0.54; 95% CI, 0.37 to 0.79; p=.001), a higher probability of achieving the gross total resection rate (removal of 100% of tumor tissue at early postoperative magnetic resonance scan) (OR, 2.32; 95% CI, 1.73 to 3.1; p<.001), and reduced craniotomy size (-6.24 cm²; p<.001). Length of surgery was non-significantly lower with nTMS (-10.3 minutes; p=.38).

Two studies included in the systematic review by Raffa et al. (2019) included survival as an outcome. Krieg et al. (2015) prospectively enrolled 70 patients who underwent nTMS and matched them with a historical control group of 70 patients who did not have preoperative nTMS. (20) All patients had motor eloquently located supratentorial high-grade gliomas and all underwent craniotomy by the same surgeons. Patients were matched by tumor location, preoperative paresis, and histology; the primary outcome was not specified. Outcome assessment was blinded. Median overall survival (OS) was 15.7 months (SD=10.9) in the nTMS group and 11.9 months (SD=10.3) in the non-nTMS group, which did not differ significantly between groups ($p=.131$). Mean survival at 3, 6, and 9 months was significantly higher in the nTMS group than in the non-nTMS group but did not differ statistically between groups at 12 months.

Frey et al. (2014) enrolled 250 consecutive patients who underwent nTMS preoperative mapping and identified 115 historical controls who met the same eligibility criteria. (21) Criteria included being evaluated for surgery for a tumor in a motor eloquent area and without seizures more than once a week or cranial implants. Fifty-one percent of the nTMS group and 48% of controls had World Health Organization grade II, III, or IV gliomas; remaining patients had brain metastases from other primary cancers or other lesions. Intraoperative motor cortical stimulation to confirm nTMS findings was performed in 66% of the nTMS group. The Medical Research Council scale and Karnofsky Performance Status were used to assess muscle strength and performance status, respectively. Outcomes were assessed at postoperative day 7 and then at 3-month intervals. Progression-free survival (PFS) and OS were reported for patients with glioma only (128 nTMS patients, 55 controls). At a mean follow-up of 22 months (range, 6-62 months) in the nTMS group and 25 months (range, 9-57 months) in controls, mean PFS was similar between groups (mean PFS, 15.5 months [range, 3-51 months] for nTMS vs. 12.4 months [range 3-38 months] for controls; not significantly different). In the subgroup of patients with low-grade (grade II) glioma (38 nTMS patients, 18 controls), mean PFS was longer in the nTMS group (mean PFS, 22.4 months; range, 11-50 months) than in the control group (15.4 months; range, 6-42 months; $p<0.05$). Overall survival did not differ statistically between treatment groups.

Observational Studies

Three additional observational studies were not included in the systematic review by Raffa et al. (2019) because they did not evaluate motor mapping or did not include relevant outcome data. Hendrix et al. (2017) reported on 20 consecutive patients with malignant brain tumors and lesions in language-eloquent areas who underwent preoperative nTMS and matched them to patients treated in the pre-nTMS era. (22) Patients were matched on tumor location, tumor and edema volume, preoperative language deficits, and histopathology. The primary efficacy outcome was not specified. Patients underwent clinical language assessments before and after surgery at postoperative day 1 and weeks 1, 6, and 12 postsurgery. Language performance status was characterized as no language deficit (grade 0), mild deficit (grade 1), medium deficit (grade 2), and severe deficit (grade 3). The complication rates, gross resection rates, and residual tumor volumes on fMRI did not differ significantly between groups. The group that had

presurgical nTMS had shorter surgery durations than patients treated pre-nTMS (mean, 104 minutes and 135 minutes, respectively, $p=0.039$) and a shorter inpatient stay (mean, 9.9 days vs 15 days, $p=0.001$). Language deficits did not differ between groups preoperatively, or at postoperative day 1, week 1, or week 12. For example, at week 12, 15 patients in the nTMS group and 14 patients in the pre-TMS group had a grade 0 deficit ($p=0.551$). There was a statistically significant difference at week 6 ($p=0.048$); the p value was not adjusted for multiple comparisons (i.e., assessment at multiple time points). Groups might have differed in other ways that affected outcomes and procedures might have changed over time in ways that affected surgical duration, complication rates, and inpatient stays.

A retrospective cohort study by Schiller et al. (2020) evaluated pediatric and adult patients with epilepsy or brain tumor who underwent TMS language mapping and fMRI language mapping as part of a presurgical evaluation. (23) There were 106 patients with complete TMS language maps that were identified; of those patients, 84 also underwent functional MRI language mapping. The overall accuracy of TMS across all language areas when compared to functional MRI was 71% (which was mainly due to its high specificity of 83%), with a diagnostic odds ratio of 1.27; TMS was more accurate in determining the dominant hemisphere for language as well (diagnostic OR, 6). TMS was able to reliably localize cortical areas that are not essential for speech function, however, TMS demonstrated only slight concordance between TMS and fMRI-derived language areas, which demonstrated low accuracy in localization of specific language cortices.

One nonrandomized study used concurrent controls. Sollmann et al. (2015) matched 25 prospectively enrolled patients who underwent preoperative nTMS but whose results were not available to the surgeon during the procedure (group 1) to 25 patients who underwent preoperative nTMS whose results were available to the surgeon (group 2). (13) All patients had language eloquently located brain lesions within the left hemisphere. Primary outcomes were not specified. Three months postsurgery, 21 patients in group 1 had no or mild language impairment and 4 patients had moderate-to-severe language deficits. In group 2, 23 patients had no or mild language impairment and 2 patients had moderate-to-severe deficits. The difference between groups in postoperative language deficits was statistically significant ($p=0.015$). Other outcomes, including duration of surgery, postoperative Karnofsky Performance Status scores, the percentage of residual tumor, and peri- and postoperative complication rates did not differ significantly between groups.

Picht et al. (2012) assessed whether a change in management occurred as a result of knowledge of nTMS findings. (24) In this study, surgeons first made a plan based on all known information without nTMS findings. After being informed of nTMS findings, the surgical plan was reformulated if necessary. Among 73 patients with brain tumors in or near the motor cortex, nTMS was judged to have changed the surgical indication in 2.7%, changed the planned extent of resection in 8.2%, modified the approach in 16.4%, added awareness of high-risk areas in 27.4%, added knowledge not used in 23.3%, and only confirmed the expected anatomy in 21.9%. The first 3 surgical categories, judged to have been altered because of nTMS findings, were summed to determine “objective benefit” of 27.4%.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility. Current evidence on clinical validity does not permit construction of a chain of evidence to support the use of nTMS for presurgical mapping of eloquent areas of the brain.

Section Summary: Preoperative Localization of Eloquent Areas of the Brain

The studies assessing the distance between nTMS and DCS hotspots appear to show that stimulation sites eliciting responses from both techniques tended to be mapped within 10 mm of each other. This distance tends to be less than the distance between fMRI centers of activation and DCS hotspots. It is difficult to assess the clinical significance of these data for presurgical planning. The available studies of the diagnostic accuracy of nTMS evaluating language areas have shown a sensitivity range of 10% to 100% and specificity range of 13.3% to 98%. The PPV ranged from 17% to 75% and the negative predictive value ranged from 57% to 100%. Even if nTMS were used to rule out areas in which language areas are unlikely, the sensitivity of 10% to 100% might result in some language areas not appropriately identified.

No RCTs have compared health outcomes in patients who did and did not have presurgical nTMS before brain surgery. There is direct evidence from several nonrandomized comparative studies of patients undergoing nTMS, mainly compared with historical controls. A meta-analysis of observational studies found that use of nTMS improved outcomes, including risk of postoperative new permanent motor deficits, gross total resection rate, and craniotomy size, in patients with motor-eloquent brain tumors who underwent preoperative nTMS mapping compared to those who did not undergo nTMS mapping. Two observational studies reported survival rates. In both, OS did not differ significantly between groups. One of the studies found significantly higher mean survival rates in the nTMS group at 3, 6, and 9 months postsurgery but not at 12 months. Limitations of all studies discussed in this section include the single-center settings (because nTMS is an operator-dependent technology, applicability may be limited), lack of randomization and/or use of historical controls (surgeon technique and practice likely improved over time), selective outcomes reporting (survival outcomes in glioma patients only), and uncertain validity of statistical analyses (primary outcome not identified and no correction for multiple testing). Additionally, studies either matched patients to controls on a few variables, or used controls who met similar eligibility criteria. These techniques may not adequately control for differences in patient groups that may affect outcomes.

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 small 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 patients 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 patients with motor-eloquent brain tumors. However, in individual observational studies, outcomes were not consistently better in patients 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.

Practice Guidelines and Position Statements

No guidelines or statements were identified.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this medical policy are listed in Table 1.

Table 1. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT04062305	Feasibility of Navigated Transcranial Magnetic Stimulation (nTMS) of Patients Treated With Stereotactic Radiosurgery for Brain Metastases in the Motor Cortex: A Comprehensive Cross-Sectional Assessment	22	May 2025
<i>Unpublished</i>			
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	Apr 2023

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	64999
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

References

1. Giussani C, Roux FE, Ojemann J, et al. Is preoperative functional magnetic resonance imaging reliable for language areas mapping in brain tumor surgery? Review of language functional magnetic resonance imaging and direct cortical stimulation correlation studies. *Neurosurgery*. Jan 2010; 66(1):113-120. PMID 19935438
2. Jeltema HR, Ohlerth AK, de Wit A, et al. Comparing navigated transcranial magnetic stimulation mapping and "gold standard" direct cortical stimulation mapping in neurosurgery: a systematic review. *Neurosurg Rev*. Aug 2021; 44(4):1903-1920. PMID 33009990
3. Rizzo V, Terranova C, Conti A, et al. Preoperative functional mapping for rolandic brain tumor surgery. *Neurosci Lett*. Nov 07 2014; 583:136-141. PMID 25224631
4. Mangraviti A, Casali C, Cordella R, et al. Practical assessment of preoperative functional mapping techniques: navigated transcranial magnetic stimulation and functional magnetic resonance imaging. *Neurol Sci*. Sep 2013; 34(9):1551-1557. PMID 23266868
5. Opitz A, Zafar N, Bockermann V, et al. Validating computationally predicted TMS stimulation areas using direct electrical stimulation in patients with brain tumors near precentral regions. *Neuroimage Clin*. May 2014; 4:500-507. PMID 24818076
6. Forster MT, Limbart M, Seifert V, et al. Test-retest reliability of navigated transcranial magnetic stimulation of the motor cortex. *Neurosurgery*. Mar 2014; 10 Suppl 1:51-55; discussion 55-56. PMID 23842557
7. Kato N, Schilt S, Schneider H, et al. Functional brain mapping of patients with arteriovenous malformations using navigated transcranial magnetic stimulation: first experience in ten patients. *Acta Neurochir (Wien)*. May 2014; 156(5):885-895. PMID 24639144
8. Baro V, Sartori L, Caliri SL, et al. Navigated Transcranial Magnetic Stimulation Motor Mapping and Diffusion Tensor Imaging Tractography for Diencephalic Tumor in Pediatric Patients. *Brain Sci*. Jan 30 2023; 13(2):234. PMID 36831777
9. Ille S, Kelm A, Schroeder A, et al. Navigated repetitive transcranial magnetic stimulation improves the outcome of postsurgical paresis in glioma patients - A randomized, double-blinded trial. *Brain Stimul*. 2021; 14(4):780-787. PMID 33984536

10. Weiss C, Nettekoven C, Rehme AK, et al. Mapping the hand, foot and face representations in the primary motor cortex - retest reliability of neuronavigated TMS versus functional MRI. *Neuroimage*. Feb 1 2013; 66:531-542. PMID 23116812
11. Schmidt S, Bathe-Peters R, Fleischmann R, et al. Nonphysiological factors in navigated TMS studies; confounding covariates and valid intracortical estimates. *Hum Brain Mapp*. Jan 2015; 36(1):40-49. PMID 25168635
12. Sollmann N, Ille S, Boeckh-Behrens T, et al. Mapping of cortical language function by functional magnetic resonance imaging and repetitive navigated transcranial magnetic stimulation in 40 healthy subjects. *Acta Neurochir (Wien)*. Jul 2016; 158(7):1303-1316. PMID 27138329
13. Sollmann N, Tanigawa N, Tussis L, et al. Cortical regions involved in semantic processing investigated by repetitive navigated transcranial magnetic stimulation and object naming. *Neuropsychologia*. Apr 2015; 70:185-195. PMID 25731903
14. Schramm S, Albers L, Ille S, et al. Navigated transcranial magnetic stimulation of the supplementary motor cortex disrupts fine motor skills in healthy adults. *Sci Rep*. Nov 28 2019; 9(1):17744. PMID 31780823
15. Picht T, Schmidt S, Brandt S, et al. Preoperative functional mapping for rolandic brain tumor surgery: comparison of navigated transcranial magnetic stimulation to direct cortical stimulation. *Neurosurgery*. Sep 2011; 69(3):581-588; discussion 588. PMID 21430587
16. Forster MT, Hattingen E, Senft C, et al. Navigated transcranial magnetic stimulation and functional magnetic resonance imaging: advanced adjuncts in preoperative planning for central region tumors. *Neurosurgery*. May 2011; 68(5):1317-1324; discussion 1324-1315. PMID 21273929
17. Tarapore PE, Tate MC, Findlay AM, et al. Preoperative multimodal motor mapping: a comparison of magnetoencephalography imaging, navigated transcranial magnetic stimulation, and direct cortical stimulation. *J Neurosurg*. Aug 2012; 117(2):354-362. PMID 22702484
18. Krieg SM, Shiban E, Buchmann N, et al. Utility of presurgical navigated transcranial magnetic brain stimulation for the resection of tumors in eloquent motor areas. *J Neurosurg*. May 2012; 116(5):994-1001. PMID 22304452
19. Raffa G, Scibilia A, Conti A, et al. The role of navigated transcranial stimulation for surgery of motor-eloquent brain tumors: a systematic review and meta-analysis. *Clin Neurol Neurosurg*. May 2019; 180:7-17. PMID 30870762
20. Krieg SM, Sollmann N, Obermueller T, et al. Changing the clinical course of glioma patients by preoperative motor mapping with navigated transcranial magnetic brain stimulation. *BMC Cancer*. Apr 2015; 15:231. PMID 25884404
21. Frey D, Schilt S, Strack V, et al. Navigated transcranial magnetic stimulation improves the treatment outcome in patients with brain tumors in motor eloquent locations. *Neuro Oncol*. Oct 2014; 16(10):1365-1372. PMID 24923875
22. Hendrix P, Senger S, Simgen A, et al. Preoperative rTMS language mapping in speech-eloquent brain lesions resected under general anesthesia: a pair-matched cohort study. *World Neurosurg*. Apr 2017; 100:425-433. PMID 28109861

23. Schiller K, Choudhri AF, Jones T, et al. Concordance Between Transcranial Magnetic Stimulation and Functional Magnetic Resonance Imaging (MRI) Derived Localization of Language in a Clinical Cohort. *J Child Neurol.* May 2020; 35(6):363-379. PMID 32122221
24. Picht T, Schulz J, Hanna M, et al. Assessment of the influence of navigated transcranial magnetic stimulation on surgical planning for tumors in or near the motor cortex. *Neurosurgery.* May 2012; 70(5):1248-1256; discussion 1256-1247. PMID 22127045

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <<https://www.cms.hhs.gov>>.

Policy History/Revision	
Date	Description of Change
12/31/2025	Document became inactive.
10/15/2024	Document updated with literature review. Coverage unchanged. No new references added.
12/01/2023	Document updated with literature review. Coverage unchanged. References 8, 9, 14 and 23 added.
08/15/2022	Document updated with literature review. Coverage unchanged. Reference 2 and 16 added.
09/15/2021	Reviewed. No changes.
10/15/2020	Document updated with literature review. Coverage unchanged. No new references added.
09/15/2019	Reviewed. No changes.
01/15/2019	Document updated with literature review. Coverage unchanged. Reference 18 added.
10/15/2017	Reviewed. No changes.
01/01/2017	Document updated with literature review. Coverage unchanged.
04/15/2015	Reviewed. No changes.
07/01/2014	New medical document. This topic was previously addressed on PSY301.015 Transcranial Magnetic Stimulation. Coverage is unchanged: Navigated transcranial magnetic stimulation (nTMS) remains experimental, investigational and/or unproven.

