Name of Policy:
Navigated Transcranial Magnetic Stimulation (nTMS)

Policy #: 556
Category: Medicine
Latest Review Date: July 2016
Policy Grade: C

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**
Navigated transcranial magnetic stimulation (nTMS) is a noninvasive imaging method for the evaluation of eloquent brain areas (e.g., controlling motor or language function). nTMS is being evaluated as an alternative to other noninvasive cortical mapping techniques for presurgical identification of eloquent areas.

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 considered to be most accurately achieved with DCS, an intraoperative procedure that increases operating time and requires a wide surgical opening. Even if they are not completely accurate compared to DCS, preoperative techniques that map brain functions may aid in planning the extent of resection and the operative 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.

The most commonly used tool for the noninvasive localization of brain functions is functional magnetic resonance imaging (fMRI). fMRI identifies regions of the brain where there are changes in localized cortical blood oxygenation, which correlates with neuronal activity associated with a specific motor or speech task being performed as the image is obtained. The accuracy and precision of fMRI is dependent 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 for 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. reviewed several studies comparing fMRI and DCS of language areas and found large variability in sensitivity and specificity of fMRI. The discussion also points out a major conceptual point in how fMRI and DCS “map” language areas. fMRI findings reflect 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) also is used to map brain activity. In this procedure, electromagnetic recorders are attached to the scalp. In contrast to 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 improved spatial resolution. MEG is conducted in a magnetically shielded room to screen out environmental electric or magnetic noise that could interfere with the MEG recording.

Navigated transcranial magnetic stimulation (nTMS) is a noninvasive imaging method for the evaluation of 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 imaging (MRI) image of the patient’s brain. Surface electromyography (EMG) electrodes are attached to various limb muscles of the patient. Moving the magnetic stimulation source to various parts of the brain causes EMG 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. nTMS can be considered a noninvasive alternative to DCS, in which electrodes are directly applied to the surface of the cortex during craniotomy. nTMS is being evaluated as an alternative to other noninvasive cortical mapping techniques, such as fMRI and MEG, for presurgical identification of cortical areas involved in motor and language functions.

Policy:
Navigated transcranial magnetic stimulation does not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for all purposes, including but not limited to the preoperative evaluation of patients 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 and is considered investigational.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member’s contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:
This policy was updated using references identified in the MEDLINE database through April 25, 2016.

Diagnostic Accuracy of nTMS in Patients with Brain Lesions
Most studies of nTMS are small case series of patients with brain tumors, cavernous angiomas, arteriovenous malformations, or other brain lesions; these are not ideal studies to ascertain diagnostic characteristics. Because of the use of nTMS and/or other methods to identify motor or language centers in the cortex to determine surgical approach, the reference standard of direct cortical stimulation (DCS) may be biased; that is, the DCS procedure may be limited or altered because of the tumor resection or other surgical factors. It is not possible to verify all nTMS sites identified, because the surgical field is limited. Because of this necessarily limited verification, it is difficult to ascertain diagnostic characteristics of nTMS. There are also a number of small studies in healthy volunteers but these do not add substantially to the evidence base. Studies evaluating nTMS and compared findings with DCS are described next.

Distance Between nTMS and DCS Hotspots
Picht et al (2011) evaluated 17 patients with brain tumors with both nTMS and DCS. Both techniques were used to elicit “hotspots,” the point at which either nTMS or DCS produced the largest electromyographic response in the target muscles. Target muscles were selected based on the needs of each particular patient in regard to tumor location and clinical findings. The intraoperative DCS locations were chosen independently of nTMS, and the surgeon was not
aware of the nTMS hotspots. There were 37 muscles in the 17 patients for which both nTMS and DCS data were available. The mean (SE) distance between the nTMS and DCS hotspots was 7.83 (1.18) mm for the abductor pollicis brevis muscle and 7.07 (0.88) mm for the tibialis anterior muscle. The 95% confidence interval for the mean distance was 5.31 to 10.36 mm. When DCS was performed during surgery, there was large variation in the number of stimulation points, and the distance between nTMS and DCS was much less when a larger number of points were stimulated.

Forster et al (2011) performed a similar study in 11 patients. fMRI was also performed in these patients. The distance between corresponding nTMS and DCS hotspots was 10.49 (5.67) mm. The distance between the centroid of fMRI activation and DCS hotspots was 15.03 (7.59) mm. However, it is not clear whether there were hotspots with either device that cannot be elicited with the other. In at least 2 excluded patients, hotspots were elicited in which DCS but not by nTMS.

A 2012 study by Tarapore et al evaluated distance between nTMS and DCS hotspots. Among 24 patients who underwent nTMS, 18 of whom underwent DCS, 8 motor sites in 5 patients were corresponding. The median distance between nTMS and DCS hotspots was 2.13 (0.29) mm. In the craniotomy field in which DCS mapping was performed, DCS did not find any new motor sites that TMS failed to identify. The study also evaluated magnetoencephalography (MEG); the median distance between MEG motor sites and DCS was 12.1 (8.2) mm.

Mangravati et al (2012) also evaluated the distance between nTMS and DCS hotspots in 7 patients. It is unclear how many hotspots are compared and how many potential comparisons were unavailable due to failure of either device to find a particular hotspot. It appeared that the mean distance between hotspots was based on the 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 of 12.9 (5.7) mm.

Krieg et al (2012) also evaluated nTMS in comparison to DCS in a study of 14 patients. However, the navigation device employed appears to be different than the FDA-approved device. Additionally, the comparison of nTMS to DCS uses a different methodology. Both nTMS and DCS were used to map out the whole volume of the motor cortex, and a mean difference between the borders of the edge of the mapped motor cortex was calculated. The mean distance between the 2 methods was 4.4 (3.4) mm.

These studies assessing the distance between nTMS and DCS hotspots appear to show that stimulation sites in which responses can be elicited from both techniques tend to be mapped within 1 cm 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, in terms of the utility of the information, on presurgical planning.

**nTMS for Language Mapping**

A 2013 study by Picht et al attempted to evaluate the accuracy of nTMS for identifying language areas. Twenty patients underwent evaluation of language areas over the whole left hemisphere, which was divided into 37 regions. DCS was necessarily performed only in areas accessible in
the craniotomy site. Data for both methods were available in 160 regions in the 20 patients. Using DCS as the reference standard, there were 46 true positives, 83 false positives, 26 true negatives, and 5 false negatives. Considering the analysis as 160 independent data points for each brain region, nTMS had a sensitivity of 90%, specificity of 24%, positive predictive value of 36% and negative predictive value (NPV) of 84%. An analysis of regions considered to be in the classic Broca area showed a sensitivity of 100%, specificity 13.0%, positive predictive value of 57%, and negative predictive value of 100%.

A 2013 study by Tarapore et al also evaluated nTMS for identifying language areas (N=12). MEG was also evaluated. A total of 183 regions were evaluated with both nTMS and DCS. In these 183 regions, using DCS as the reference standard, there were 9 true positives, 4 false positives, 169 true negatives and 1 false negative. This translates to a sensitivity of 90%, specificity of 98%, a positive predictive value of 69% and a NPV of 99%.

A research group in Germany published 2 studies of nTMS for mapping cortical language sites, 1 in healthy volunteers and one in patients with brain tumors. In a case series of 10 healthy volunteers, nTMS test-retest reliability varied across error type (e.g., neologism, semantic error) and cortical region (i.e., anterior or posterior), but overall, both intra- and interobserver reliability were low (range of concordance correlation coefficients: intraobserver, -0.222 to 0.505; interobserver, -0.135 to 0.588). In a case report of three patients with language-eloquent brain tumors who underwent nTMS and DCS for both initial surgery and repeat surgery for recurrence, nTMS performance characteristics varied by definition of a positive nTMS finding (i.e., a language error made in response to stimulation). For positivity defined by error rates (percentage of stimulations that produced errors) ranging from 5% to 25%, sensitivity was 90% to 10%, specificity was 28% to 89%, PPV was 21% to 17%, and NPV was 93% to 82%. Plasticity of language areas in both healthy volunteers and in patients with brain lesions was identified as a source of variation in nTMS studies across time. As noted in one review, the language network appears to spread over both hemispheres, increasing the complexity of presurgical language mapping.

The 2013 study by Picht et al showing the very high number of false positives raises concerns about the utility of nTMS for identifying language areas. Even if nTMS is used to rule out areas in which language areas are unlikely, the sensitivity of 90% may result in some language areas not appropriately identified.

**Safety of nTMS**

In 2016, Tarapore et al evaluated the safety of nTMS in a large multicenter series of 733 patients. Patients had tumors in eloquent or perieloquent regions of the brain and underwent nTMS as part of presurgical planning. nTMS frequencies of 5, 7 and/or 10 Hz were used. A total of 537 patients underwent single pulse motor mapping, 38 had repetitive-pulse language mapping, and 158 had both of these. nTMS was successfully completed in all patients. No seizures (focal, complex or generalized) were reported and no patients reported hearing changes, cognitive or neuropsychological changes, or other transient adverse effects. Headache, reported by 28 patients (6%), was the most commonly reported adverse effect. A total of 141 of 196 patients (72%) completed questionnaires after the procedure and 131 of these (93%) reported discomfort during
Using a visual analogue scale (VAS) of 1 to 10, 33 of 131 (25%) patients reported a VAS of 1-3 and the remaining 98 (75%) reported a VAS >3.

**Test-Retest Reliability in Healthy Volunteers**

In some studies, navigated transcranial magnetic stimulation (nTMS) has been repeated in subjects over a relatively short interval in time to evaluate whether the test is reliable; that is, produces a similar result. In these studies, it is assumed that nothing in the subject has changed, and any difference in result is due to variations in the testing procedure and any natural variability in the subject.

In a 2013 study by Forster et al, 12 healthy participants underwent nTMS in 2 different sessions, separated in time an average of 10 days. Five muscle groups in the upper and lower extremity in each subject were stimulated, and the hotspots (points of optimal stimulation) and center of gravity (amplitude-weighted center of area sensitive to stimulation) for each subject were identified. The mean distance between these points between sessions for each muscle were calculated. The intraclass coefficient in the \( x \) axis (mediolateral) and the \( y \) axis (anteroposterior) for each muscle was calculated. Overall, across all muscles, the mean difference (SD) in hotspot location between sessions was 0.79 (0.47) cm. The mean difference in center of gravity location was 0.57 (0.32) cm. The intraclass coefficients in the anteroposterior axis ranged from 0.54 to 0.89, consistent with moderate to excellent reliability. In the mediolateral axis, intraclass coefficients ranged from 0.11 to 0.89, with several of the coefficients less than 0.49, which is generally regarded as poor reliability.

A 2013 study by Weiss et al also evaluated the reliability of nTMS and functional MRI in ten healthy subjects. Muscles in the hand, foot and face were evaluated. nTMS was not feasible in a high proportion of subjects for evaluating the face and tongue due to technical constraints and other artifacts. Functional magnetic resonance imaging (fMRI) on the other hand, produced interpretable findings for all muscle groups in all sessions. The mean difference (SD) in hotspot location, as identified by nTMS between sessions was 10.8 (1.9) mm. The mean difference in maximum activation, as identified by fMRI between sessions was 6.2 (1) mm, thus showing that fMRI was more reliable than nTMS in locating a specific point associated with a particular muscle. In another type of analysis in which the spatial extent of a particular muscle activity was mapped by either nTMS or fMRI, neither technique yielded reliable results. The extent of spatial overlap between sessions was very low for either technique (less than 32% for both) and the intraclass correlation coefficients were also both less than 50%, indicating poor reliability.

Schmidt et al (2014) in Germany designed a study to examine confounding factors that affect nTMS performance. In a three-part design, investigators differentiated variance due to physiological factors (e.g., tissue conductivity, brain rhythms, cognitive state, peripheral sensory input, pre-innervation, brain dysfunction) from physical variation of the nTMS device (i.e., coil location, orientation, and tilt, stimulation strength). Twenty healthy volunteers participated in 2 experiments to compare targeted stimulation (optimal stimulus location, orientation, and tilt parameters) with nontarget-controlled stimulation. Four healthy volunteers participated in a third experiment of maximal physiological confounding variance (e.g., patients were instructed to maximally contract the target muscle). Spatial resolution of nTMS (defined as variation in the area of cortical stimulation that leads to maximum muscle contraction) was found to be
approximately 5 mm so that “even small physical fluctuations can confound the statistical comparison of corticospinal excitability measurements.” The authors recommended stepwise regression to partition physical from physiological variance in nTMS results and to produce more interpretable data.

**Studies of nTMS in Brain Tumor Patients**

Most studies of nTMS are small case series of brain tumor patients, which are not ideal studies to ascertain diagnostic characteristics. Due to the use of nTMS and/or other methods to identify the motor or language centers in the cortex and determine the surgical approach, the reference standard of direct cortical stimulation (DCS) may be biased. The DCS procedure may be limited or altered because of the tumor resection or other surgical factors. It is not possible to verify all the nTMS sites identified, because the surgical field is limited. Because of this necessarily limited verification, it is difficult to ascertain diagnostic characteristics of nTMS.

nTMS is being studied as a technique to augment preoperative detection of motor corticospinal tracts (CSTs), which are currently identified using diffusion tensor imaging (DTI), an MRI technique. Conti et al (2014) compared the size and location of (cortical) motor maps determined by the cortical end of CSTs, identified using DTI only and nTMS-DTI, to nTMS maps. Twenty patients who underwent brain surgery at a single center in Italy were prospectively enrolled. All brain lesions (70% brain tumors [glioma, astrocytoma, glioblastoma multiforme], 20% cavernous angioma, 10% metastasis) were located within 10 mm of the motor cortex. nTMS-DTI was performed the day before surgery, and standard DTI was obtained after surgery using preoperative imaging data. Direct subcortical stimulation (functional tractography) was applied to confirm tract location. Overlap between nTMS cortical maps and cortical end-regions of CSTs was greater with nTMS-DTI compared with standard DTI (90% vs 58%). Direct subcortical stimulation confirmed CST location in all patients. A potential limitation of the study is lack of DCS to confirm nTMS-determined motor maps. Larger comparative studies with clinical outcomes are needed to assess the clinical relevance of these results.

**Clinical Utility**

The ideal study would be a randomized controlled trial (RCT) comparing health outcomes after nTMS versus other strategies without nTMS in patients being considered for surgical resection of brain tumors. 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 of groups of patients with very qualitatively different outcomes. For example, it is difficult to compare the health outcome of a patient who ends up not being operated on, who conceivably has a shorter overall lifespan but a short period of very high quality of life, with a patient who undergoes operation but has some moderate postoperative disability, but a much longer lifespan.

No RCTs were identified. However, controlled observational studies are available. Several studies matched patients who underwent presurgical nTMS with similar historical controls who did undergo nTMS. Krieg et al (2014) enrolled 100 consecutive patients who underwent nTMS preoperative mapping and identified 100 historical controls who were matched for tumor location, preoperative paresis, and histology.22 Most patients had glioblastoma (37%), brain
metastasis (24%), or astrocytoma (29%). Data analysis was performed blinded to group assignment. The primary efficacy outcome was not specified. Median follow-up was 7.1 months (range, 0.2-27.2 months) in the nTMS group and 6.2 months (range, 0.1-79.4 months) in controls. Incidence of residual tumor by postoperative MRI was less in the nTMS group compared with controls (22% vs 42%; odds ratio [OR], 0.38; 95% CI, 0.21 to 0.71). Incidence of new surgery-related transient or permanent paresis did not differ between groups. However, “when also including neurological improvement [undefined] in the analysis,” more patients in the nTMS group improved (12% nTMS vs 1% controls), and similar proportions of patients worsened (13% nTMS vs 18% controls) or remained unchanged (75% nTMS vs 81% controls; Mann-Whitney-Wilcoxon test, p=0.006). Limitations of this study include the use of historical control, uncertain outcome assessments (“neurological improvement” not defined), and uncertain validity of statistical analyses since the primary outcome was not specified and there was no correction for multiple testing).

A second study by this research group, with some overlap in enrolled patients, was published by Krieg et al in 2015. This study prospectively enrolled 70 patients who underwent nTMS and matched them with a historical control group of 70 patients who did not have preoperative nTMS. All patients had motor eloquently located supratentorial high-grade gliomas (HGG) and they all underwent craniotomy in the single department by the same group of surgeons. As in the 2014 study by Krieg et al, patients were matched by tumor location, preoperative paresis and histology, and the primary outcome was not specified. Outcome assessment was blinded. Craniotomy size was 25.3 cm² (SD: 9.7cm) in the nTMS group and 30.8 cm² (SD: 13.2) in the non-nTMS group; the difference in size was statistically significant, p=0.006. There was not a statistically significant difference between groups in the rate of surgery-related paresis, rate of surgery-related complications on MRI or the degree of motor impairment during follow-up. Median overall survival was 15.7 months (SD: 10.9) in the nTMS group and 11.9 months (SD: 10.3) in the non-nTMS group which was not significantly different between groups (p=0.131). Mean survival at 3, 6 and, 9 months was significantly higher in the nTMS group compared with the non-nTMS group and mean survival at 12 months did not differ significantly between groups.

Frey et al (2014) enrolled 250 consecutive patients who underwent nTMS preoperative mapping and identified 115 similar historical controls who met the same eligibility criteria. Fifty-one percent of the nTMS group and 48% of controls had WHO Grade II to 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. British Medical Research Council and Karnofsky scales were used to assess muscle strength and performance status, respectively. Outcomes were assessed at postoperative day seven and then at three-month intervals. At 3-month follow-up, 6.1% of the nTMS group and 8.5% of controls had new postoperative motor deficits (p=NS); changes in performance status postoperatively also were similar between groups. Other outcomes were reported for patients with glioma only (128 nTMS patients, 55 controls). Based on postoperative MRI, gross total resection was achieved in 59% of nTMS patients and in 42% of controls (2 test, p<0.05). At mean followup of 22 months (range, 6-62) in the nTMS group and 25 months (range, 9-57) in controls, mean PFS was similar between groups (mean PFS, 15.5 months [range, 3-51] nTMS vs 12.4 months [range, 3-38] controls; statistical test for survival outcomes not specified, p=NS). 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] nTMS vs 15.4 months [range, 6-42] controls; p<0.05), and new postoperative motor deficits were similar (7.5% vs 9.5%, respectively; 2 test, p=NS). Overall survival did not differ statistically between treatment groups.

One study used concurrent controls, but did not randomize patients to treatment group. Sollman et al (2015) matched 25 prospectively enrolled patients who underwent preoperative nTMS but whose results were not available to the surgeon during the operation (group 1) to 25 patients who underwent preoperative nTMS and results were available to the surgeon (group 2). All patients had language eloquently located brain lesions within the left hemisphere. Primary outcomes were not specified. Three months after surgery, 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 post-operative language deficits was statistically significant (p=0.0153). Other outcomes, including duration of surgery, post-operative scores on the Karnofsky performance status scale, percent residual tumor, and peri- and postoperative complication rates did not differ significantly between groups.

Limitations of all of the studies discussed above in this section include the single-center setting (because nTMS is an operator-dependent technology, applicability may be limited), use of historical controls (surgeon technique and practice likely improved over time), selective outcome reporting (survival outcomes in glioma patients only), and uncertain validity of statistical analyses (primary outcome not identified, no correction for multiple testing). In addition, 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.

One study was identified that assessed whether a change in management occurred as a result of knowledge of nTMS findings. In this study, published in 2012 by Picht et al, surgeons first made a surgical 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 that was not used in 23.3%, and only confirmed the expected anatomy in 21.9%. The first 3 categories in which it was judged that the surgery was altered because of nTMS findings were summed up to determine “objective benefit,” which was 27.4%.

**Summary of Evidence**

For individuals who have brain lesions undergoing preoperative evaluation for localization of eloquent areas of the brain who receive navigated transcranial magnetic stimulation, the evidence includes controlled observational studies and case series. Relevant outcomes are overall survival, 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 1 cm or less, this does not take into account the degree of error in this average distance, or whether there are missed hotspots. It is
difficult to fully verify nTMS hotspots because only exposed cortical areas can be verified with DCS. Limited studies of nTMS to evaluate language areas show a high false positive rate (low specificity) and sensitivity that may be insufficient for clinical use. Several controlled observational studies compared outcomes in patients undergoing nTMS versus other mapping techniques. Most outcomes were similar between groups, such as post-surgical motor impairment, paresis and surgical complication rates. Overall survival did not differ significantly between groups. One study found significantly higher mean survival rates in the nTMS group at 3, 6 and 9 months (but not 12 months) post-surgery. The controlled observational studies had various methodological limitations and, being non-randomized, may not adequately control for differences in patient groups that may affect outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements
No guidelines or statements were identified.

U.S. Preventive Services Task Force Recommendations
No U.S. Preventive Services Task Force recommendations for navigated transcranial magnetic stimulation have been identified.

Key Words:
Navigated transcranial magnetic stimulation, nTMS, Nexstim®, Nexstim NBS System 4, NexSpeech®

Approved by Governing Bodies:
The Nexstim® (Helsinki, Finland) eXimia Navigated Brain Stimulation (NBS) System received FDA 510(k) marketing clearance in 2009 for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus for preprocedural planning.

Similarly, the Nexstim NBS System 4 and NBS System 4 with NexSpeech® received FDA 510(k) clearance in May 2012 for noninvasive mapping of the primary motor cortex and for localization of cortical areas that do not contain speech function, for the purposes of preprocedural planning.

Benefit Application:
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply.
FEP: Special benefit consideration may apply. Refer to member’s benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.
Current Coding:
CPT Codes: 0310T Motor function mapping using noninvasive navigated transcranial magnetic stimulation (nTMS) for therapeutic treatment planning, upper and lower extremity

References:
Policy History:
Medical Policy Panel, December 2013
Medical Policy Group, December 2013 (3): New policy; does not meet medical criteria for coverage and therefore considered investigational
Medical Policy Administration Committee, February 2014
Available for comment February 5 through March 21, 2014
Medical Policy Panel, December 2014
Medical Policy Group, February 2015 (6): Updated Key Points, Key Words, Approved by Governing Bodies and References; no change in policy statement.
Medical Policy Group, June 2016
Medical Policy Group, July 2016 (6): Updated Description of Procedure, Key Points, Key Words, Summary of Evidence, Approved by Governing Bodies and References; no change in policy statement.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.