

TRANSCRANIAL MAGNETIC STIMULATION

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[Instructions for Use](#) ⓘ

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Related Commercial Policies
<ul style="list-style-type: none"> Deep Brain and Cortical Stimulation Vagus Nerve Stimulation
Community Plan Policy
<ul style="list-style-type: none"> Transcranial Magnetic Stimulation
Related Optum Guideline
<ul style="list-style-type: none"> Transcranial Magnetic Stimulation (TMS)

COVERAGE RATIONALE

The following are unproven and not medically necessary due to insufficient evidence of efficacy:

- Transcranial magnetic stimulation for treating all medical (i.e., non-behavioral) conditions including but not limited to:
 - Alzheimer’s disease
 - Chronic neuropathic pain
 - Dystonia
 - Epilepsy
 - Headaches
 - Parkinson’s disease
 - Stroke
 - Tinnitus
- Navigated transcranial magnetic stimulation (nTMS) for treatment planning or for diagnosing motor neuron diseases or neurological disorders

For Behavioral Disorders, refer to the Optum Behavioral Clinical Policy titled *Transcranial Magnetic Stimulation at Optum Provider Express > Clinical Resources > Guidelines/Policies/Manuals > Behavioral Clinical Policies*.

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

CPT Code	Description
64999	Unlisted procedure, nervous system
90867	Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; initial, including cortical mapping, motor threshold determination, delivery and management
90868	Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent delivery and management, per session
90869	Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent motor threshold re-determination with delivery and management

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DESCRIPTION OF SERVICES

Transcranial magnetic stimulation (TMS) is a method of delivering electrical stimulation to the brain. In general, single-pulse TMS is used to explore brain functioning and repetitive TMS (rTMS) is used to induce changes in brain activity that lasts beyond the stimulation period (Klomjai et al. 2015). Single-pulse TMS was originally introduced in 1985 as a noninvasive and safe way to stimulate the cerebral cortex. Activation of the motor cortex by transcranial magnetic stimulation produces contralateral muscular-evoked potentials (MEPs), thus providing a valuable tool for functional mapping of the motor cortex. Technological advances introduced generators capable of producing rapid, repetitive pulses of magnetic stimulation. The magnetic field pulses pass unimpeded through the hair, skin, and skull and into the brain where they induce an electrical current to flow inside the brain without seizures or need for anesthesia. The amount of electricity created is very small and cannot be felt by the individual, but the electric charges cause the neurons to become active and are thought to lead to the release of neurotransmitters such as serotonin, norepinephrine and dopamine. Repetitive TMS (rTMS) is currently under investigation as a treatment for several disorders originating in the cerebral cortex including pain, dystonia, epilepsy, headaches, Parkinson's disease, stroke, and tinnitus. TMS is delivered by various available devices, and treatment has been tested using a variety of protocols, including high frequency delivered over the left dorsolateral prefrontal cortex, low frequency delivered over the right or left dorsolateral prefrontal cortex, bi-lateral delivery, and deep TMS in which deeper prefrontal regions are stimulated.

Navigated transcranial magnetic stimulation (nTMS) is being studied as a diagnostic tool to stimulate functional cortical areas at precise anatomical locations to induce measurable responses. This technology is being investigated to map functionally essential motor areas for diagnostic purposes and for treatment planning.

CLINICAL EVIDENCE

Therapeutic Transcranial Magnetic Stimulation

Systematic Reviews and Meta-Analyses for Parkinson's Disease

Yang et al. (2018) performed a meta-analysis to evaluate the optimal rTMS parameters for motor recovery of Parkinson's disease (PD). Electronic databases were searched for studies investigating the therapeutic effects of rTMS on motor function in patients with PD. Twenty-three studies with a total of 646 participants were included. The pooled estimates of rTMS revealed significant short-term and long-term effects on motor function improvement of PD. Subgroup analysis observed that high-frequency rTMS (HF-rTMS) was significant in improving motor function, but low-frequency rTMS (LF-rTMS) was not. In particular, when HF-rTMS targeted over the primary motor cortex (M1), in which the bilateral M1 revealed a larger effect size than unilateral M1. Compared to single-session, multi-session of HF-rTMS over the M1 showed significant effect size. In addition, HF-rTMS over the M1 with a total of 18,000-20,000 stimulation pulses yielded more significant effects than other dosages. According to the authors, these results suggest that rTMS might be helpful in improving the motor deficits of PD patients. The authors stated that there are limitations of this meta-analysis. First, the experimental designs of the included studies were not homogenous (e.g., randomized controlled trials versus crossover design). Second, the selected participants varied in age, disease stage, and other biological characteristics that may have confounded the results.

Goodwill et al. (2017) conducted a meta-analysis that quantified the effectiveness of repetitive transcranial magnetic stimulation (rTMS) to improve motor and cognitive dysfunction in Parkinson's disease (PD). A total of 24 rTMS with a sham control group were included in the analyses. The results showed an overall positive effect in favor of rTMS compared with sham stimulation on motor function. The use of rTMS did not improve cognition. No effects for stimulation parameters on motor or cognitive function were observed. The authors acknowledged several limitations. Studies evaluating rTMS demonstrated modest effect sizes (0.4-0.6) and large heterogeneity between studies. Clinical and lifestyle variables including PD-related comorbidity, physical activity levels and other mental health conditions were not accounted for in the subgroup analyses, which may have influenced the responsiveness to non-invasive brain stimulation (NBS).

In a systematic review and meta-analysis, Wagle Shukla et al. (2016) reviewed the literature on clinical repetitive transcranial magnetic stimulation (rTMS) trials in Parkinson's disease to quantify the overall efficacy of this treatment. Prospective clinical trials were included that had an active arm and a control arm and change in motor scores on Unified Parkinson's Disease Rating Scale as the primary outcome. The authors pooled data from 21 studies that met these criteria and analyzed separately the effects of low- and high-frequency rTMS on clinical motor improvements. Repetitive transcranial magnetic stimulation therapy demonstrated benefits at short-term follow-up (immediately after a treatment protocol) with a pooled mean difference of 3.4 points as well as at long-term follow-up (average follow-up 6 weeks) with mean difference of 4.1 points. The authors concluded that rTMS therapy results in mild-to-moderate motor improvements and has the potential to be used as an adjunct therapy for the treatment of Parkinson's disease. According to the authors, future large, sample studies should be designed to isolate the specific clinical features of Parkinson's disease that respond well to rTMS therapy. The authors indicated that the literature on the use of rTMS for

levodopa-induced dyskinesia, objective bradykinesia, and gait measures is sparse and that on the basis of the current available information, the results are conflicting, and no clear treatment protocol has yet been defined.

Chung and Mak (2016) conducted a systematic review to examine the efficacy of rTMS on improving physical function and motor signs over the short- and long-terms in people with Parkinson's disease (PD). Twenty-two randomized placebo-controlled trials comprising 555 people with PD were included. Pooled estimates of effect of rTMS indicated significantly improved short-term upper limb function, short-term and long-term walking performance, short-term and long-term unified Parkinson's disease rating scale (UPDRS) III scores. Subgroup analyses suggest a more prominent effect for primary motor cortex (M1) stimulation. Meta-regression revealed that a greater number of total stimulation pulses were associated with more UPDRS III improvements over the long-term. The authors concluded that the pooled evidence suggests that rTMS improves upper limb function in the short-term, and walking performance and UPDRS III in the short- and long-terms in PD sufferers. According to the authors, the limitations of this review included the following: the insignificant long-term effect of rTMS on upper limb bradykinesia results should be interpreted with caution due to small number of studies. Second, the effects of rTMS targeting frontal areas other than M1, low frequency rTMS and TBS remain inconclusive due to an insufficient number of research studies. Third, the followup period for the included trials was relatively short considering that PD is a chronic degenerative disease. The lack of studies with a longer duration of follow-up, such as 6–12 months, limited this analysis.

Systematic Reviews and Meta-Analyses for Pain

In an updated version the Cochrane review published in 2014, O'Connell et al. (2018) evaluated the efficacy of non-invasive brain stimulation techniques in chronic pain. The update included a total of 42 rTMS studies. The meta-analysis of rTMS studies versus sham for pain intensity at short-term follow-up (0 to < 1 week postintervention), (27 studies, involving 655 participants), demonstrated a small effect with heterogeneity. This equates to a 7% reduction in pain, or a 0.40 point reduction on a 0 to 10 pain intensity scale, which does not meet the minimum clinically important difference threshold of 15% or greater. The authors concluded that there is very low-quality evidence that single doses of high-frequency rTMS of the motor cortex may have short-term effects on chronic pain and quality of life. However, multiple sources of bias exist that may have influenced the observed effects. The authors stated that they did not find evidence that low-frequency rTMS or rTMS applied to the dorsolateral prefrontal cortex are effective for reducing pain intensity in chronic pain. According to the authors, there remains a need for substantially larger, rigorously designed studies, particularly of longer courses of stimulation.

Saltychev and Laimi (2017) investigated whether there is evidence of repetitive transcranial magnetic stimulation (rTMS) being effective in decreasing the severity of pain among patients with fibromyalgia. Seven trials were included in the meta-analysis. The risk of bias was considered low for seven studies. Pain severity before and after the last stimulation decreased by -1.2 points on 0-10 numeric rating scale. Pain severity before and 1 week to 1 month after the last stimulation decreased by -0.7 points. Both pooled results were below the minimal clinically important difference of 1.5 points. The authors did not find evidence of clinically significant effectiveness of rTMS in decreasing the severity of fibromyalgia pain immediately after the treatment as well as in short-term follow-up.

Goudra et al. (2017) evaluated the role of repetitive transcranial magnetic stimulation (rTMS) in the treatment of chronic pain. Studies comparing rTMS and conventional treatment for chronic pain were searched. The comparison was made for decrease in the pain scores with and without (sham) the use of rTMS after a follow-up interval of 4-8 weeks. All reported pain scores were converted into a common scale ranging from "0" (no pain) to "10" (worst pain). Nine trials with 183 patients in each of the groups were included in the analysis. The decrease in pain scores with rTMS was 1.12 and in sham-rTMS was 0.28. The pooled mean drop in pain scores with rTMS therapy was higher by 0.79. The duration and frequency of rTMS were highly variable across trials. Publication bias was unlikely. The authors concluded that the use of rTMS improves the efficacy of conventional medical treatment in chronic pain patients. This treatment is not associated with any direct adverse effects. However, according to the authors, the duration and frequency of rTMS therapy is presently highly variable and needs standardization. According to the authors, availability of a limited number of trials examining the usefulness of rTMS is an important drawback of the current meta-analysis.

In a systematic review of controlled clinical trials, Shirahige et al. (2016) evaluated the efficacy of noninvasive brain stimulation (NIBS) on pain control in migraine patients. Eight studies were included in the quantitative analysis with 153 migraine patients who received NIBS and 143 patients who received sham NIBS. In the overall meta-analysis, the authors did not find significant results for pain intensity, for migraine attacks, and for painkiller intake. However, subgroup analysis considering only transcranial direct current stimulation (tDCS) effects demonstrated a decrease for pain intensity, migraine attacks, and painkiller intake. Subgroup analysis for TMS did not reveal significant effects for any outcome. The authors concluded that this review failed to find support for the superiority of NIBS over sham treatment. According to the authors, there is a need for larger controlled trials with methodological rigor, which could increase the power of result inference.

Jin et al. (2015) conducted a meta-analysis that examined clinical trials (randomized sham-controlled or self-controlled trials; double-blind or single-blind; parallel or cross-over study designs) involving the analgesic efficacy of high frequency repetitive transcranial magnetic stimulation (HF-rTMS) for neuropathic pain (NP). Twenty-five studies (including 32 trials and 589 patients) were selected for the meta-analysis. All 3 HF-rTMS treatments (5, 10, and 20 Hz) produced pain reduction, while there were no differences between them, with the maximal pain reduction found after one and 5 sessions of rTMS treatment. Further, this significant analgesic effect remained for one month after 5 sessions of rTMS treatment. There are limitations of this meta-analysis. For example, the long-term analgesic effects of different HF-rTMS and low frequency (LF) rTMS sessions, including the single session of rTMS on different NP of varying origins have yet not been evaluated; the full degree of pain relief is still unclear for many rTMS studies. The authors concluded that HF-rTMS stimulation on primary motor cortex is effective in relieving pain in NP patients. Although 5 sessions of rTMS treatment produced a maximal analgesic effect and may be maintained for at least one month, further large-scale and well-controlled trials are needed to determine if this enhanced effect is specific to certain types of NP such as post-stroke related central NP. According to the authors, there is not enough clinical evidence to determine the long-term effect of rTMS therapy (longer than 2 months post-treatment).

In a meta-analysis, Galhardoni et al. (2015) reviewed the literature on the analgesic effects of repetitive transcranial magnetic stimulation (rTMS) in chronic pain according to different pain syndromes and stimulation parameters. A total of 33 randomized trials were found. Many studies reported significant pain relief by rTMS, especially high-frequency stimulation over the primary motor cortex performed in consecutive treatment sessions. Pain relief was frequently >30% compared with control treatment. Neuropathic pain, fibromyalgia, and complex regional pain syndrome were the pain syndromes more frequently studied. However, among all published studies, only a few performed repetitive sessions of rTMS. The authors concluded that TMS has potential utility in the management of chronic pain; however, studies using maintenance sessions of rTMS and assessing the effects of rTMS on the different aspects of chronic pain are needed to provide a more solid basis for its clinical application for pain relief.

Systematic Reviews and Meta-Analyses for Stroke

In a systematic review, Sebastianelli et al. (2017) summarized the evidence for the effectiveness of low-frequency (LF) repetitive transcranial magnetic stimulation (rTMS) in promoting functional recovery after stroke. Sixty-seven studies were included in the review. The authors observed considerable heterogeneity across studies in the stimulation protocols. According to the authors, the use of different patient populations, regardless of lesion site and stroke etiology, different stimulation parameters and outcome measures means that the studies were not readily comparable, and estimating real effectiveness or reproducibility was very difficult. The authors concluded that LF rTMS over unaffected hemisphere may have therapeutic utility, but the evidence is still preliminary and the findings need to be confirmed in further randomized controlled trials.

Dionísio et al. (2017) conducted a systematic review to provide information regarding the application of repetitive transcranial magnetic stimulation (rTMS) in stroke patients and to assess its effectiveness in clinical rehabilitation of motor function. Seventy trials were included in the review. The majority of the articles reported rTMS showing potential in improving motor function, although some negative reports, all from randomized controlled trials, contradicted this claim. According to the authors, future studies are needed because there is a possibility that a bias for non-publication of negative results may be present.

In a meta-analysis and systematic review, McIntyre et al. (2017) evaluated the effectiveness of repetitive transcranial magnetic stimulation (rTMS) in improving spasticity after stroke. A literature search of multiple databases was conducted for articles published in English from January 1980 to April 2015 using select keywords. Studies were included if: 1) the population included was >50% stroke patients; 2) the sample size included ≥ 4 subjects; 3) the intervention applied was rTMS; and 4) upper extremity spasticity was assessed pre and post intervention. Randomized controlled trials (RCTs) were assessed for methodological quality using the Physiotherapy Evidence Database (PEDro) tool. The main outcome measurement was the Modified Ashworth Scale (MAS). Ten studies met the inclusion criteria: two RCTs (PEDro scores 8-9) and eight pre-post studies. Meta-analyses of primarily uncontrolled pre-post studies found significant improvements in MAS for elbow, wrist, and finger flexors. However, a meta-analysis of the two available RCTs failed to find a significant rTMS treatment effect on MAS for the wrist. The authors concluded that there is limited available evidence to support the use of rTMS in improving spasticity post stroke. Despite the positive findings reported, better powered and appropriately controlled trials are necessary.

In a systematic review and meta-analysis, Zhang et al. (2017) evaluated the short- and long-term effects as well as other parameters of repetitive transcranial magnetic stimulation (rTMS) on upper limb motor functional recovery after stroke. Thirty-four studies with 904 participants were included in the systematic review. Pooled estimates show that rTMS significantly improved short-term and long-term manual dexterity. More pronounced effects were found for rTMS administered in the acute phase of stroke, subcortical stroke, 5-session rTMS treatment and intermittent theta burst stimulation. Only three studies reported mild adverse events such as headache and increased anxiety. The authors concluded that five-session rTMS treatment could best improve stroke-induced upper limb dyskinesia acutely in a long-lasting manner and intermittent theta burst stimulation is more beneficial than continuous theta burst stimulation.

Studies with larger sample sizes are needed to further investigate the use of rTMS for upper limb motor functional recovery after stroke.

Pisegna et al. (2016) conducted a systematic review and meta-analysis of randomized controlled trials to evaluate the effects of non-invasive brain stimulation, including transcranial magnetic stimulation on post-stroke dysphagia. Eight randomized controlled trials were included in the review. This review found evidence for the efficacy of non-invasive brain stimulation on post-stroke dysphagia. A significant effect size resulted when stimulating the unaffected rather than the affected hemisphere. This finding is in agreement with previous studies implicating the plasticity of cortical neurons in the unaffected hemisphere. According to the authors, non-invasive brain stimulation appears to assist cortical reorganization in post-stroke dysphagia but emerging factors highlight the need for more data. The authors indicated that based on this preliminary review, non-invasive brain stimulation facilitated recovery in post-stroke dysphagia but should not yet be considered for clinical use outside of clinical trials.

Li et al. (2015a) performed a meta-analysis of studies investigating the effects of low-frequency repetitive transcranial magnetic stimulation on post-stroke aphasia. Of the 879 articles identified, 4 RCTs were included in the final analysis. Data synthesis showed that low-frequency repetitive transcranial magnetic stimulation was beneficial for post-stroke patients in terms of naming and changes in brain excitability. However, the changes in repetition and comprehension after stimulation were not significant. No adverse effects were reported. The included studies were of high methodological quality. The authors concluded that these findings indicate that low-frequency repetitive transcranial magnetic stimulation is an effective treatment for recovery of naming. According to the authors, due to the limited number of included studies, as well as the small sample sizes, the statistical power of the meta-analysis was moderate. The authors also indicated that although rTMS is considered a promising therapy, the specific mechanism underlying its success is unknown. Further investigations should evaluate the different types and phases of aphasia.

Systematic Reviews and Meta-Analyses for Other Conditions

Dong et al. (2018) conducted a systematic review and meta-analysis to evaluate the efficacy and safety of repetitive transcranial magnetic stimulation (rTMS) in Alzheimer's disease (AD). Five randomized controlled trials (RCTs) involving 148 participants were included in this review. Compared with sham stimulation, high-frequency rTMS led to a significant improvement in cognition as measured by Assessment Scale-cognitive subscale (ADAS-cog), but not (Mini-Mental State Examination) MMSE. High-frequency rTMS also improved the global impression in comparison to the placebo. There was no significant difference in mood and functional performance between high-frequency rTMS and sham groups. Only one trial included low-frequency rTMS reported no significant improvement in cognition, mood and functional performance. Few mild adverse events were observed in both the rTMS and sham groups. The authors concluded that rTMS is relatively well tolerated, with some promise for cognitive improvement and global impression in patients with AD. According to the authors, a limitation of this meta-analysis is that the sample size was too small to ensure adequate power to detect a significant difference in primary outcomes among groups.

In a Cochrane review, Chen et al. (2016) assessed the evidence for the use of TMS in individuals with drug-resistant epilepsy compared with other available treatments in reducing seizure frequency and improving quality of life. Seven randomized controlled trials that were double-blinded, single-blinded or unblinded, and placebo, no treatment, or active controlled were included in the analysis. The total number of participants in the seven trials was 230. Two of the seven studies analyzed showed a statistically significant reduction in seizure rate from baseline (72% and 78.9% reduction of seizures per week from the baseline rate, respectively). The other five studies showed no statistically significant difference in seizure frequency following rTMS treatment compared with controls. The authors judged the quality of evidence for the primary outcomes of this review to be low. According to the authors, there is evidence that rTMS is safe and not associated with any adverse events, but given the variability in technique and outcome reporting that prevented meta-analysis, the evidence for efficacy of rTMS for seizure reduction is still lacking despite reasonable evidence that it is effective at reducing epileptiform discharges.

Soleimani et al. (2016) conducted a systematic literature review and meta-analysis on the effect of repetitive transcranial magnetic stimulation (rTMS) compared with sham in chronic tinnitus patients. For the meta-analysis weighted mean differences (and standard deviations) of Tinnitus Questionnaire (TQ) and Tinnitus Handicap Inventory (THI) scores were determined. Therapeutic success was defined as difference of at least 7 points in the THI score between baseline and the follow-up assessment after treatment. Results from 15 RCTs were analyzed. For THI, the data of mean difference score in two groups, 1 and 6 month after intervention, was 6.71 and 12.89, respectively. According to the authors, these data underscore the clinical effect of rTMS in the treatment of tinnitus. The authors reported that there is high variability of studies design and reported outcomes. Replication of data in multicenter trials with a large number of patients and long-term follow-up is needed before further conclusions can be drawn.

Randomized Controlled Trials and Other Technology Assessments

Several randomized controlled trial and comparative studies with small patient populations evaluated whether TMS improves conditions such as the following:

- Stroke (Watanabe et al., 2018; Long et al., 2018; Zheng et al., 2015; Kim et al., 2014)

- Aphasic stroke (Du et al., 2016; Rubi-Fessen et al., 2015; Tsai et al., 2014; Barwood et al., 2011; Park et al., 2017)
- Cigarette consumption, dependence and craving (Sheffer et al., 2018; Dinur-Klein et al., 2014)
- Headaches (Rocha et al., 2015; Misra et al., 2013)
- Multiple sclerosis (Elzamarany et al., 2016)
- Parkinson's disease (Brys et al., 2016; Li et al., 2015b)

The limited data from these studies do not allow definitive conclusion regarding the possible benefits of TMS. Many of these studies were feasibility studies with methodological limitations including small patient populations and short-term follow-up. The findings of these studies need to be validated by randomized trials with larger patient numbers and long-term follow-up.

Other randomized trials have found that TMS may be not be as effective as or superior to placebo or that TMS has no significant effect on symptoms for various conditions (Cohen et al., 2018; Lozeron et al., 2017; Sahlsten et al., 2017; Seynaeve et al., 2016; Cincotta et al., 2015; de Oliveira et al., 2014; Shirota et al., 2013; Wrigley et al., 2013; Conforto et al., 2014).

According to the National Institute for Health and Care Excellence (NICE) Guideline for Dementia: assessment, management and support for people living with dementia and their carers (2018), non-invasive brain stimulation (including transcranial magnetic stimulation) should not be offered to treat mild to moderate Alzheimer's disease, except as part of a randomized controlled trial.

According to the National Institute for Health and Care Excellence (NICE) Guideline for transcranial magnetic stimulation for treating and preventing migraine (2014), evidence on the efficacy of TMS for the treatment of migraine is limited in quantity and for the prevention of migraine is limited in both quality and quantity. Evidence on its safety in the short and medium term is adequate but there is uncertainty about the safety of long-term or frequent use of TMS. Therefore, according to NICE, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

In an Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review for the evaluation and treatment of tinnitus, the evidence was rated as insufficient for repetitive transcranial magnetic stimulation (Pichora-Fuller et al., 2013).

Professional Societies

European Academy of Neurology (EAN)

Cruccu et al. (2016) conducted a systematic review and meta-analysis of trials to update previous European Federation of Neurological Societies guidelines on neurostimulation for neuropathic pain. The GRADE system was used to assess quality of evidence and propose recommendations. Weak recommendations were given for the use of primary motor cortex (M1) rTMS in neuropathic pain and fibromyalgia and inconclusive recommendations were given regarding complex regional pain syndrome (CRPS). There were inconclusive recommendations regarding rTMS of the dorsolateral prefrontal cortex (DLPFC) in fibromyalgia and neuropathic pain.

European Headache Federation

In a position statement for neuromodulation of chronic headaches, the European Headache Federation states that application of the noninvasive rTMS in chronic headaches is not yet evidence based, given the poor amount of controlled data (Martelletti et al. 2013).

American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS)

In a clinical practice guideline for tinnitus, the American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) Guideline Development Panel indicated that clinicians should not recommend TMS for the treatment of patients with persistent, bothersome tinnitus (Tunkel et al., 2014).

Diagnostic Transcranial Magnetic Stimulation

Takahashi et al. (2013) conducted a systematic review to evaluate spatial accuracy and clinical usefulness of navigated transcranial magnetic stimulation (nTMS) in brain tumor surgery in or near the motor cortex. A total of 11 studies that evaluated nTMS prior to surgery in adults were included in the review. Quality criteria consisted of documentation of the influence of nTMS brain mapping on clinical decision making in a standardized prospective manner and/or performance of intraoperative direct electrical stimulation (DES) and comparison with nTMS results. Cross-observational assessment of nTMS accuracy was established by calculating a weighted mean distance between nTMS and DES. All studies reviewed concluded that nTMS correlated well with the "gold standard" of DES. The mean distance between motor cortex identified on nTMS and DES by using the mean distance in 81 patients described in 6 quantitatively evaluated studies was 6.18 mm. The nTMS results changed the surgical strategy based on anatomical

imaging alone in 25.3% of all patients, based on the data obtained in 87 patients in 2 studies. The authors conclude that the nTMS technique spatially correlates well with the gold standard of DES. Its functional information benefits surgical decision making and changes the treatment strategy in one-fourth of cases. The studies included in the review were limited by small sample sizes.

Primary Studies Not Included in the Systematic Review

Sollmann et al. (2018) evaluated a novel multimodal setup consisting of preoperative navigated transcranial magnetic stimulation (nTMS) and nTMS-based diffusion tensor imaging fiber tracking (DTI FT) as an adjunct to awake surgery. Sixty consecutive patients suffering from highly language-eloquent left-hemispheric low- or high-grade glioma underwent preoperative nTMS language mapping and nTMS-based DTI FT, followed by awake surgery for tumor resection. Both nTMS language mapping and DTI FT data were available for resection planning and intraoperative guidance. Clinical outcome parameters, including craniotomy size, extent of resection (EOR), language deficits at different time points, Karnofsky Performance Scale (KPS) score, duration of surgery, and inpatient stay, were assessed. According to postoperative evaluation, 28.3% of patients showed tumor residuals, whereas new surgery-related permanent language deficits occurred in 8.3% of patients. KPS scores remained unchanged. According to the authors, this is the first study to present a clinical outcome analysis of this modern approach, which is increasingly applied in neuro-oncological centers worldwide. The authors indicated that although human language function is a highly complex and dynamic cortico-subcortical network, the presented approach offers excellent functional and oncological outcomes in patients undergoing surgery of lesions affecting this network. According to the authors, a limitation of this study is that it analyzed clinical outcome without a control group; thus, follow-up studies that include randomized controlled trials are needed to prove the optimized outcome in comparison to patients who do not undergo such an extensive preoperative workup.

Raffa et al. (2018) evaluated the impact of a non-invasive preoperative protocol for mapping the language network through the navigated transcranial magnetic stimulation (nTMS) and nTMS-based diffusion tensor imaging fiber tracking (DTI-FT) in patients not eligible for awake surgery and thereby operated under general anesthesia for suspected language-eloquent brain tumors. Twenty patients were enrolled in the study. All patients underwent nTMS language cortical mapping and nTMS-based DTI-FT of subcortical language fascicles. The nTMS findings were used to plan and guide the maximal safe resection of the tumor. The impact on postoperative language outcome and the accuracy of the nTMS-based mapping in predicting language deficits were evaluated. The nTMS-based reconstruction of the language network was successful in all patients. The nTMS mapping disclosed the true-eloquence of lesions in 12 (60%) of all suspected cases. In the remaining 8 cases (40%) the suspected eloquence of the lesion was disproved. The nTMS-based findings guided the planning and surgery through the visual feedback of navigation. This resulted in a slight reduction of the postoperative language performance at discharge that was completely recovered after one month from surgery. The accuracy of the nTMS-based protocol in predicting postoperative permanent deficits was significantly high, especially for false-eloquent lesions. The authors concluded that nTMS-based preoperative mapping allows for a reliable visualization of the language network, being also able to identify an intra-hemispheric tumor-induced cortical plasticity. It allows for a customized surgical strategy that could preserve postoperative language function. The authors indicated that despite the promising results provided by the preoperative nTMS-based language mapping, awake surgery and intraoperative neurophysiological monitoring and mapping (IONM), when possible, still remain the gold standards to achieve a safe tumor resection and a good language outcome in patients with tumors involving the language network.

Hendrix et al. (2016) evaluated preoperative navigated transcranial magnetic stimulation (nTMS) in cortical motor eloquent lesions with emphasis on metastasis. A total of 61 patients underwent nTMS before undergoing surgery for a motor eloquent brain lesion. Thirty patients (49.2%) presented with a preoperative motor deficit. One week after surgery, paresis had resolved or improved in 56.7% of the patients. Out of the patients with postoperative paresis, 89.5% experienced an improvement of motor status at follow-up. All metastatic lesions were completely resected compared to 78.9% of non-metastatic lesions. Only 4.3% of patients with a metastatic lesion, but 26.3% of patients with a non-metastatic lesion experienced deterioration of motor function after surgery. The authors concluded that preoperative nTMS is suitable for mapping of a variety of motor eloquent brain lesions resulting in favorable neurological outcome. Particularly in metastatic motor eloquent lesion, motor function appears to be preserved after surgery. The findings of this study need to be validated with a randomized trial comparing navigated transcranial magnetic stimulation with the gold standard of direct cortical stimulation intraoperative mapping.

Sollmann et al. (2015) enrolled 25 patients with language eloquently located brain lesions undergoing preoperative rTMS language mapping (GROUP 1), with the mapping results not being available for the surgeon, and matched those patients with 25 subjects who also underwent preoperative rTMS (GROUP 2), but the mapping results were taken into account during tumor resection. Additionally, cortical language maps were generated by analyzing preoperative rTMS and intraoperative direct cortical stimulation (DCS) data. Mean anterior-posterior craniotomy extents and overall craniotomy sizes were significantly smaller for the patients in GROUP 2. Postoperative language deficits were found significantly more frequently for the patients in GROUP 1, although the preoperative language status did not differ

between groups. Additionally, there was a trend towards fewer unexpected tumor residuals, shorter surgery duration, less peri- or postoperative complications, shorter inpatient stay, and higher postoperative Karnofsky performance status scale for the patients in GROUP 2. According to the authors, this study provides a first hint that the clinical course of patients suffering from brain tumors might be improved by preoperative rTMS language mapping. However, a significant difference between both groups was only found for craniotomy extents and postoperative deficits, but not for other clinical parameters, which only showed a trend toward better results in GROUP 2. The authors indicated that multicenter trials with larger sample sizes are needed to further investigate the distinct impact of rTMS language mapping on the clinical course of brain tumor patients.

Frey et al. (2014) evaluated whether the use of navigated transcranial magnetic stimulation (nTMS) had an impact on treatment and outcome in patients with brain tumors in motor eloquent locations. The study included 250 consecutive patients and compared their functional and oncological outcomes to a matched pre-nTMS control group (n = 115). Navigated transcranial magnetic stimulation mapping results disproved suspected involvement of primary motor cortex in 25.1% of cases, expanded surgical indication in 14.8%, and led to planning of more extensive resection in 35.2% of cases and more restrictive resection in 3.5%. In comparison with the control group, the rate of gross total resections increased significantly from 42% to 59%. Progression-free-survival for low grade glioma was significantly better in the nTMS group at 22.4 months than in control group at 15.4 months. Integration of nTMS led to a nonsignificant change of postoperative deficits from 8.5% in the control group to 6.1% in the nTMS group. The authors concluded that TMS provides crucial data for preoperative planning and surgical resection of tumors involving essential motor areas. According to the authors, expanding surgical indications and extent of resection based on nTMS enables more patients to undergo surgery and might lead to better neurological outcomes and higher survival rates in brain tumor patients. The findings of this study need to be validated with a randomized trial comparing navigated transcranial magnetic stimulation with the gold standard of direct cortical stimulation intraoperative mapping.

In a prospective trial, Krieg et al. (2014) compared patients with motor eloquently located supratentorial lesions investigated with or without preoperative nTMS in terms of clinical outcome parameters. The trial included 100 patients with supratentorial lesions located in motor eloquent areas that was investigated by preoperative nTMS (2010-2013) and matched with a control of 100 patients who were operated on without nTMS data (2006-2010) by a matched pair analysis. Patients in the nTMS group showed a significantly lower rate of residual tumor on postoperative MRI. Twelve percent of patients in the nTMS and 1% of patients in the non-nTMS group improved while 75% and 81% of the nTMS and non-nTMS groups, respectively, remained unchanged and 13% and 18% of patients in the nTMS and non-nTMS groups, respectively, deteriorated in postoperative motor function on long-term follow-up. Moreover, the nTMS group showed smaller craniotomies. The authors concluded that this study increases the level of evidence for preoperative motor mapping by nTMS for rolandic lesions. The authors identify a need for a randomized trial comparing the gold standard of intraoperative mapping with navigated transcranial magnetic brain stimulation.

There is limited information from the peer-reviewed published medical literature to conclude that navigated transcranial magnetic stimulation is an effective clinical diagnostic test. Randomized controlled studies with large populations are needed to evaluate how this test can reduce clinical diagnostic uncertainty or impact treatment planning.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

On December 13, 2013, the Cerena™ Transcranial Magnetic Stimulator (TMS) (eNeura Therapeutics®) received FDA approval thru the de novo premarket review pathway, a regulatory pathway for low- to moderate-risk medical devices that are not substantially equivalent to an already legally marketed device. According to the FDA documents, the Cerena Transcranial Magnetic Stimulator is indicated for the acute treatment of pain associated with migraine headache with aura. See the following websites for more information:

- http://www.accessdata.fda.gov/cdrh_docs/pdf13/K130556.pdf
- http://www.accessdata.fda.gov/cdrh_docs/reviews/K130556.pdf

(Accessed November 13, 2018)

The SpringTMS (eNeura Therapeutics) has received multiple FDA 510(k) clearances. The initial clearance on May 21, 2014 was predicated on the Cerena device by the same manufacturer. Subsequent clearances were granted for modifications in the size and design of the device with no changes to the basic technology. See the following website for more information: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmnmn.cfm?ID=K140094>.

(Accessed October 18, 2018)

For a complete list of approved products for transcranial magnetic stimulator for headache, see the following websites (use product code OKP):

- <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>
- <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm>

(Accessed November 13, 2018)

In 2009, the FDA approved the eXimia Navigated Brain Stimulation System (NBS) System (Nexstim) for use in pre-surgical planning for patients undergoing brain surgery. The NBS uses transcranial magnetic stimulation (TMS) guided by standard MR-image data, a non-invasive direct technique for functional mapping of the motor cortex. See the following website for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf9/K091457.pdf. (Accessed November 13, 2018)

The Navigated Brain Stimulation (NBS) System (Nexstim) received 510(k) clearance on May 22, 2012. See the following website for more information: https://www.accessdata.fda.gov/cdrh_docs/pdf11/K112881.pdf. (Accessed November 13, 2018)

Additional Products

Neuralie TMS device

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for transcranial magnetic stimulation used in treatment of medical (i.e., non-behavioral) conditions.

Local Coverage Determinations (LCDs) exist. Refer to the LCDs for [Repetitive Transcranial Magnetic Stimulation \(rTMS\) in Adults with Treatment Resistant Major Depressive Disorder](#), [Transcranial Magnetic Stimulation](#), [Transcranial Magnetic Stimulation \(TMS\)](#) and [Transcranial Magnetic Stimulation for Major Depressive Disorder](#). (Accessed November 16, 2018)

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
02/01/2019	<ul style="list-style-type: none"> • Reorganized policy template: <ul style="list-style-type: none"> ○ Simplified and relocated <i>Instructions for Use</i> ○ Removed <i>Benefit Considerations</i> section • Simplified coverage rationale (no change to guidelines) • Updated supporting information to reflect the most current description of services, clinical evidence, FDA and CMS information, and references • Archived previous policy version 2018T0536K

INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.