

# TRANSCRANIAL MAGNETIC STIMULATION

**Policy Number:** BEHAVIORAL 025.9 T2

**Effective Date:** March 1, 2017

Table of Contents	Page
<a href="#">INSTRUCTIONS FOR USE</a> .....	1
<a href="#">APPLICABLE LINES OF BUSINESS/PRODUCTS</a> .....	1
<a href="#">BENEFIT CONSIDERATIONS</a> .....	1
<a href="#">NON-COVERAGE RATIONALE</a> .....	2
<a href="#">APPLICABLE CODES</a> .....	2
<a href="#">DESCRIPTION OF SERVICES</a> .....	2
<a href="#">CLINICAL EVIDENCE</a> .....	3
<a href="#">U.S. FOOD AND DRUG ADMINISTRATION</a> .....	8
<a href="#">REFERENCES</a> .....	8
<a href="#">POLICY HISTORY/REVISION INFORMATION</a> .....	11

- Related Policies**
- [Deep Brain and Cortical Stimulation](#)
  - [Vagus Nerve Stimulation](#)
- Related Optum Guideline**
- [Transcranial Magnetic Stimulation \(TMS\)](#)

## INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines 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.

## APPLICABLE LINES OF BUSINESS/PRODUCTS

This policy applies to Oxford Commercial plan membership.

## BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

### **Essential Health Benefits for Individual and Small Group**

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits (“EHBs”). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

## NON-COVERAGE RATIONALE

### **Transcranial magnetic stimulation is unproven and not medically necessary for treating all conditions including the following:**

- Chronic neuropathic pain
- Dystonia
- Epilepsy
- Headaches
- Parkinson's disease
- Stroke
- Tinnitus

**For behavioral disorders**, refer to the Optum Behavioral Solutions Coverage Determination Guideline titled *Transcranial Magnetic Stimulation (TMS)* at [Optum Provider Express > Clinical Resources > Guidelines/Policies/Manuals > Coverage Determination Guidelines](#).

Some studies have examined the use of transcranial magnetic stimulation for treating disorders such as pain, dystonia, epilepsy, headaches, Parkinson's disease, stroke, and tinnitus. However, because of limited studies and small sample size there is insufficient data to conclude that transcranial magnetic stimulation is beneficial for treating these conditions.

### **Navigated transcranial magnetic stimulation (nTMS) is unproven and not medically necessary for treatment planning or for diagnosing motor neuron diseases or neurological disorders.**

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

## 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 may apply.

CPT Code	Description
0310T	Motor function mapping using non-invasive navigated transcranial magnetic stimulation (nTMS) for therapeutic treatment planning, upper and lower extremity
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

*CPT® is a registered trademark of the American Medical Association*

## DESCRIPTION OF SERVICES

Single-pulse transcranial magnetic stimulation (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 patient, 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 also 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 Review and Meta-Analyses for Parkinson's Disease***

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.

In a systematic review and meta-analysis, Chou et al. (2015) evaluated the repetitive transcranial magnetic stimulation (rTMS) effects on motor dysfunction in patients with Parkinson's disease (PD). Eligible studies included sham-controlled, randomized clinical trials of rTMS intervention for motor dysfunction in patients with PD. Relevant measures were extracted independently by 2 investigators. Standardized mean differences (SMDs) were calculated with random-effects models. Twenty studies with a total of 470 patients were included. Random-effects analysis revealed a pooled SMD of 0.46, indicating an overall medium effect size favoring active rTMS over sham rTMS in the reduction of motor symptoms. Subgroup analysis showed that the effect sizes estimated from high-frequency rTMS targeting the primary motor cortex and low-frequency rTMS applied over other frontal regions were significant. Using the Grading of Recommendations, Assessment, Development, and Evaluation criteria, the authors characterized the quality of evidence presented in this meta-analysis as moderate quality. The authors concluded that the pooled evidence suggests that rTMS improves motor symptoms for patients with PD. According to the authors, one of the limitations of this meta-analysis was that the results could be constrained by the unclear risk of bias on certain domains owing to incomplete data in a few studies. In addition, several uncontrolled variables, such as medication use, disease stage, side of onset, side of rTMS stimulation, age, and sex, existed and may have confounded the results of the analysis.

Zanjani et al. (2015) examined the effects of repetitive transcranial magnetic stimulation (rTMS) targeting the primary motor cortex (M1) in the treatment of motor signs in Parkinson's disease (PD). Studies meeting inclusion criteria were analyzed using meta-analytic techniques and the Unified Parkinson's Disease Rating Scale (UPDRS) sections II and III were used as outcome measures. Compared with sham rTMS, active rTMS targeting the M1 significantly improved UPDRS III scores at the short-term follow-up. When the long-term follow-up UPDRS III scores were compared with baseline scores, the standardized effect size between active and sham rTMS did not reach significance. No significant improvement in the UPDRS II was found. According to the authors, rTMS over the M1 may improve motor signs. The authors stated that further studies are needed to provide a definite conclusion.

### ***Systematic Review and Meta-Analyses for Pain***

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.

In an updated version of the original Cochrane review published in 2010, O'Connell et al. (2014) evaluated the efficacy of non-invasive brain stimulation techniques in chronic pain. The update included a total of 30 rTMS studies. Meta-analysis of studies of rTMS (involving 528 participants) demonstrated significant heterogeneity. Pre-specified subgroup analyses suggested that low-frequency stimulation is ineffective (low-quality evidence) and that rTMS applied to the dorsolateral prefrontal cortex is ineffective (very low-quality evidence). The authors found a short-term effect on pain of active high-frequency stimulation of the motor cortex in single-dose studies (low-quality evidence). This equates to a 12% reduction in pain, which does not exceed the pre-established criteria for a minimal clinically important difference. Evidence for multiple-dose studies was heterogenous but did not demonstrate a significant effect (very low-quality evidence). The authors concluded that single doses of high-frequency rTMS of the motor cortex may have small short-term effects on chronic pain. However, it is likely that multiple sources of bias may exaggerate this observed effect. The authors state that the effects do not meet the predetermined threshold of minimal clinical significance and multiple-dose studies do not consistently demonstrate effectiveness. According to the authors, the available evidence suggests that low-frequency rTMS and rTMS applied to the pre-frontal cortex are not effective in the treatment of chronic pain.

Marlow et al., (2013) systematically reviewed the literature to evaluate the use of repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) for patients with fibromyalgia syndrome (FMS). The authors concluded that rTMS/tDCS showed analogous pain reductions as well as considerably fewer side effects compared to U.S. Food and Drug Administration (FDA) approved FMS pharmaceuticals. The authors stated that further work into optimal stimulation parameters and standardized outcome measures is needed to clarify associated efficacy and effectiveness.

### ***Systematic Review and Meta-Analyses for 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. (2015) 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.

Ren et al. (2014) performed a meta-analysis of studies that explored the effects of low-frequency rTMS on aphasia in stroke patients. Seven eligible studies involving 160 stroke patients were identified to be included in the meta-analysis. A significant effect size of 1.26 was found for the language outcome severity of impairment (95% CI=0.80 to 1.71) without heterogeneity ( $I^2=0\%$ ,  $P=0.44$ ). The effect size did not change significantly even when any one trial was eliminated. None of the patients from the 7 included articles reported adverse effects from rTMS. The authors concluded that low frequency rTMS with a 90% resting motor threshold that targets the triangular part of the right inferior frontal gyrus has a positive effect on language recovery in patients with aphasia following stroke. According to the authors, further well-designed studies with larger populations are required to determine the effect duration and long-term impact of rTMS in aphasia treatment.

Graef et al. (2016) performed a systematic review with meta-analysis to investigate the effects of rTMS combined with upper-limb training versus sham rTMS combined with upper-limb training on the upper-limb recovery after a stroke. Eleven studies were included in the review. The meta-analysis included eight studies with 199 participants and did not show any difference between groups, neither for upper-limb function nor for spasticity. The authors concluded that the current state of the literature is not enough to support the hypothesis that a combination of rTMS and upper-limb training has a stronger effect on upper-limb function than upper-limb training alone.

In a Cochrane review, Hao et al. (2013) assessed the efficacy and safety of rTMS for improving function in people with stroke. The review included 19 trials involving a total of 588 participants. Two heterogenous trials with a total of 183 participants showed that rTMS treatment was not associated with a significant increase in the Barthel Index score. Four trials with a total of 73 participants were not found to have a statistically significant effect on motor function. The authors concluded that current evidence does not support the routine use of rTMS for the treatment of stroke. According to the authors, further trials with larger sample sizes are needed to determine a suitable rTMS protocol and the long-term functional outcome.

### ***Systematic Review and Meta-Analyses for Other Conditions***

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.

In a Cochrane review, Fang et al. (2013) evaluated the clinical efficacy and safety of rTMS for treating amyotrophic lateral sclerosis (ALS). Three randomized, placebo-controlled trials with a total of 50 participants were included in the review. All the trials were of poor methodological quality and were insufficiently homogeneous to allow the pooling of results. The authors concluded that there is currently insufficient evidence to draw conclusions about the efficacy and safety of rTMS in the treatment of ALS.

## **Randomized Controlled Trials and Other Technology Assessments**

Several randomized controlled trial and comparative studies with small patient populations suggest that TMS treatment may improve conditions such as the following:

- Stroke (Zheng et al., 2015, n=108; Chieffo et al., 2014, n=10; Kim et al., 2014, n=32)
- Alzheimer's disease (Eliasova et al., 2014, n=10; Ahmed et al., 2012, n=45; Rabey et al., 2013, n=15)
- Aphasic stroke (Du et al., 2016; Rubi-Fessen et al., 2015; Tsai et al., 2014, n=56; Barwood et al. 2011, n=12; Khedr et al., 2014, n=30)
- Cigarette consumption, dependence and craving (Dinur-Klein et al., 2014, n=115)
- Fibromyalgia (Short et al., 2011, n=20; Mhalla et al., 2011, n=30; Lee et al. 2013, n=15; Boyer et al. 2014, n=38)
- Focal hand dystonia (Rosset-Llobet et al., 2015; Borich et al., 2009, n=15)
- Headaches (Rocha et al., 2015, n=19; Misra et al., 2013, n=50)
- Multiple sclerosis (Mori et al. 2009, n=20)
- Parkinson's disease (Brys et al., 2016; Li et al., 2015)
- Paretic hand after stroke (Takeuchi et al., 2009, n=30; Gillick et al., 2014, n=19)
- Spinal cord injury spasticity (Kumru et al., 2013, n=17)

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 (Seynaeve et al., 2016; Cincotta et al., 2016; de Oliveira et al., 2014; Benninger et al., 2012; Seniów et al., 2012; Shirota et al., 2013; Langguth et al., 2012; Plewnia et al., 2012; Wrigley et al., 2013; Conforto et al., 2014).

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)***

Crucca 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. (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.

Krieg et al. (2015) prospectively enrolled 70 patients with supratentorial motor eloquently located high-grade glioma (HGG) undergoing preoperative nTMS and matched these patients with 70 HGG patients who did not undergo preoperative nTMS. On average, the overall size of the craniotomy was significantly smaller for nTMS patients when compared to the non-nTMS group. Furthermore, residual tumor tissue (nTMS: 34.3%; non-nTMS: 54.3%) and unexpected tumor residuals (nTMS: 15.7%; non-nTMS: 32.9%) were less frequent in nTMS patients. Regarding the further clinical course, median inpatient stay was 12 days for the nTMS and 14 days for the non-nTMS group. Sixty percent of patients of the nTMS group and 54.3% of patients of the non-nTMS group were eligible for postoperative chemotherapy, while 67.1% of nTMS patients and 48.6% of non-nTMS patients received radiotherapy. Moreover, 3, 6, and 9 months survival was significantly better in the nTMS group. The authors concluded that with the limitations of this study in mind, the data show that HGG patients might benefit from preoperative nTMS mapping. The lack of randomization was regarded by the authors as the major limitation of this study.

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.

Picht et al. (2013) conducted a cohort study that compared the safety and effectiveness of preoperative nTMS with direct cortical stimulation (DCS) mapping during awake surgery for the identification of language areas in patients with left-sided cerebral lesions. Twenty patients with tumors in or close to left-sided language eloquent regions were examined by repetitive nTMS before surgery. During awake surgery, language-eloquent cortex was identified by DCS. nTMS results were compared for accuracy and reliability with regard to DCS by projecting both results into the cortical parcellation system. Presurgical nTMS maps showed an overall sensitivity of 90.2%, specificity of 23.8%, positive predictive value of 35.6%, and negative predictive value of 83.9% compared with DCS. For the anatomic Broca's area, the corresponding values were a sensitivity of 100%, specificity of 13.0%, positive predictive value of 56.5%, and negative predictive value of 100%, respectively. The authors concluded that good overall correlation between repetitive nTMS and DCS was observed. According to the authors, noninvasive inhibition mapping with nTMS is evolving as a valuable tool for preoperative mapping of language areas. The low specificity in posterior language areas in the current study necessitates further research to refine the methodology.

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.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm378608.htm>

[http://www.accessdata.fda.gov/cdrh\\_docs/pdf13/K130556.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf13/K130556.pdf)

[http://www.accessdata.fda.gov/cdrh\\_docs/reviews/K130556.pdf](http://www.accessdata.fda.gov/cdrh_docs/reviews/K130556.pdf)

(Accessed November 4, 2016)

In 2009, the FDA approved the Navigated Brain Stimulation System (NBS) System 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 Web Site for more information: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf9/K091457.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf9/K091457.pdf). (Accessed November 4, 2016)

#### **Additional Products**

Neuralieve TMS device

#### REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealthcare Medical Technology Assessment Committee. [2017T053I]

Ahmed MA, Darwish ES, Khedr EM, et al. Effects of low versus high frequencies of repetitive transcranial magnetic stimulation on cognitive function and cortical excitability in Alzheimer's dementia. *J Neurol*. 2012 Jan; 259(1):83-92.

Barwood CH, Murdoch BE, Whelan BM, et al. The effects of low frequency Repetitive Transcranial Magnetic Stimulation (rTMS) and sham condition rTMS on behavioural language in chronic non-fluent aphasia: Short term outcomes. *NeuroRehabilitation*. 2011; 28(2):113-28.

Benninger DH, Iseki K, Kranick S, et al. Controlled study of 50-Hz repetitive transcranial magnetic stimulation for the treatment of Parkinson disease. *Neurorehabil Neural Repair*. 2012 Nov-Dec; 26(9):1096-105.

Borich, M, Arora, S, and Kimberley, TJ. Lasting effects of repeated rTMS application in focal hand dystonia. *Restor Neurol Neurosci*. 2009;27(1):55-65.

Boyer L, Dousset A, Roussel P, et al. rTMS in fibromyalgia: a randomized trial evaluating QoL and its brain metabolic substrate. *Neurology*. 2014 Apr 8;82(14):1231-8.

Brys M, Fox MD, Agarwal S, et al. Multifocal repetitive TMS for motor and mood symptoms of Parkinson disease: A randomized trial. *Neurology*. 2016 Oct 5.



Chen R, Spencer DC, Weston J, et al. Transcranial magnetic stimulation for the treatment of epilepsy. *Cochrane Database Syst Rev.* 2016 Aug 11;(8):CD011025.

Chieffo R, De Prezzo S, Houdayer E, et al. Deep repetitive transcranial magnetic stimulation with H-coil on lower limb motor function in chronic stroke: a pilot study. *Arch Phys Med Rehabil.* 2014 Jun; 95(6):1141-7.

Chou YH, Hickey PT, Sundman M, et al. Effects of repetitive transcranial magnetic stimulation on motor symptoms in Parkinson disease: a systematic review and meta-analysis. *JAMA Neurol.* 2015 Apr; 72(4):432-40.

Chung CL, Mak MK. Effect of Repetitive Transcranial Magnetic Stimulation on Physical Function and Motor Signs in Parkinson's Disease: A Systematic Review and Meta-Analysis. *Brain Stimul.* 2016 Jul-Aug;9(4):475-87.

Cincotta M, Giovannelli F, Chiaramonti R, et al. No effects of 20 Hz-rTMS of the primary motor cortex in vegetative state: A randomised, sham-controlled study. *Cortex.* 2015 Oct;71:368-76.

Conforto AB, Amaro E Jr, Gonçalves AL, et al. Randomized, proof-of-principle clinical trial of active transcranial magnetic stimulation in chronic migraine. *Cephalalgia.* 2014 May; 34(6):464-72.

Cruccu G, Garcia-Larrea L, Hansson P, et al. EAN guidelines on central neurostimulation therapy in chronic pain conditions. *Eur J Neurol.* 2016 Oct;23(10):1489-99.

de Oliveira RA, de Andrade DC, Mendonça M, et al. Repetitive transcranial magnetic stimulation of the left premotor/dorsolateral prefrontal cortex does not have analgesic effect on central poststroke pain. *J Pain.* 2014 Dec; 15(12):1271-81.

Dinur-Klein L, Dannon P, Hadar A, et al. Smoking cessation induced by deep repetitive transcranial magnetic stimulation of the prefrontal and insular cortices: a prospective, randomized controlled trial. *Biol Psychiatry.* 2014 Nov 1; 76(9):742-9.

Du J, Yang F, Liu L, et al. Repetitive transcranial magnetic stimulation for rehabilitation of poststroke dysphagia: A randomized, double-blind clinical trial. *Clin Neurophysiol.* 2016 Mar;127(3):1907-13.

ECRI Institute. Product Brief. Cefaly Supraorbital Transcutaneous Neurostimulator (Cefaly-Technology) for Preventing and Treating Migraine Headache. April 2014.

ECRI Institute. Product Brief. Cerena Transcranial Magnetic Stimulator (eNeura Therapeutics, LLC) for Treating Migraine Headache with Aura. March 2014. Archived.

Eliasova I, Anderkova L, Marecek R, et al. Non-invasive brain stimulation of the right inferior frontal gyrus may improve attention in early Alzheimer's disease: a pilot study. *J Neurol Sci.* 2014 Nov 15; 346(1-2):318-22.

Fang J, Zhou M, Yang M, et al. Repetitive transcranial magnetic stimulation for the treatment of amyotrophic lateral sclerosis or motor neuron disease. *Cochrane Database Syst Rev.* 2013 May 31; 5:CD008554.

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.* 2014 Oct; 16(10):1365-72.

Galhardoni R, Correia GS, Araujo H, et al. Repetitive transcranial magnetic stimulation in chronic pain: a review of the literature. *Arch Phys Med Rehabil.* 2015 Apr; 96(4 Suppl):S156-72.

Gillick BT, Krach LE, Feyma T, et al. Primed low-frequency repetitive transcranial magnetic stimulation and constraint-induced movement therapy in pediatric hemiparesis: a randomized controlled trial. *Dev Med Child Neurol.* 2014 Jan; 56(1):44-52.

Graef P, Dadalt ML, Rodríguez DA, et al. Transcranial magnetic stimulation combined with upper-limb training for improving function after stroke: A systematic review and meta-analysis. *J Neurol Sci.* 2016 Oct 15;369:149-58.

Hao Z, Wang D, Zeng Y, Liu M. Repetitive transcranial magnetic stimulation for improving function after stroke. *Cochrane Database Syst Rev.* 2013 May 31; 5:CD008862.

Hayes Inc. Hayes Search and Summary. Navigated Transcranial Magnetic Stimulation for Pre-Surgical Planning. Lansdale, PA: Hayes. October 13, 2016.

Jin Y, Xing G, Li G, et al. High Frequency Repetitive Transcranial Magnetic Stimulation Therapy For Chronic Neuropathic Pain: A Meta-analysis. *Pain Physician.* 2015 Nov;18(6):E1029-46.

Khedr, E, Abo-Elfetoh, N. Therapeutic role of rTMS on recovery of dysphagia in patients with lateral medullary syndrome and brain stem infarction. *J Neurol Neurosurg Psychiatry.* 2009.

Kim WS, Jung SH, Oh MK, et al. Effect of repetitive transcranial magnetic stimulation over the cerebellum on patients with ataxia after posterior circulation stroke: A pilot study. *J Rehabil Med.* 2014 May;46(5):418-23.

Krieg SM, Sabih J, Bulbasova L, et al. Preoperative motor mapping by navigated transcranial magnetic brain stimulation improves outcome for motor eloquent lesions. *Neuro Oncol.* 2014 Sep;16(9):1274-82.

- 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*. 2015 Apr 8;15:231.
- Kumru H, Benito J, Murillo N, et al. Effects of high-frequency repetitive transcranial magnetic stimulation on motor and gait improvement in incomplete spinal cord injury patients. *Neurorehabil Neural Repair*. 2013 Jun;27(5):421-9.
- Kumru H, Murillo N, Samsó JV, et al. Reduction of spasticity with repetitive transcranial magnetic stimulation in patients with spinal cord injury. *Neurorehabil Neural Repair*. 2010 Jun;24(5):435-41.
- Langguth B, Landgrebe M, Frank E, et al. Efficacy of different protocols of transcranial magnetic stimulation for the treatment of tinnitus: Pooled analysis of two randomized controlled studies. *World J Biol Psychiatry*. 2012 Aug 22.
- Lee SJ, Kim DY, Chun MH, et al. The effect of repetitive transcranial magnetic stimulation on fibromyalgia: a randomized sham-controlled trial with 1-mo follow-up. *Am J Phys Med Rehabil*. 2012 Dec;91(12):1077-85.
- Leung, A, Donohue, M, Xu, R, et al. rTMS for suppressing neuropathic pain: a meta-analysis. *J Pain*. 2009;10(12):1205-1216.
- Li Y, Qu Y, Yuan M, et al. Low-frequency repetitive transcranial magnetic stimulation for patients with aphasia after stroke: A meta-analysis. *J Rehabil Med*. 2015 Sep 3;47(8):675-81.
- Li ZJ, Wu Q, Yi CJ. Clinical efficacy of istradefylline versus rTMS on Parkinson's disease in a randomized clinical trial. *Curr Med Res Opin*. 2015 Nov;31(11):2055-8.
- Marlow NM, Bonilha HS, Short EB. Efficacy of transcranial direct current stimulation and repetitive transcranial magnetic stimulation for treating fibromyalgia syndrome: a systematic review. *Pain Pract*. 2013 Feb;13(2):131-45.
- Martelletti P, Jensen RH, Antal A, et al. Neuromodulation of chronic headaches: position statement from the European Headache Federation. *J Headache Pain*. 2013 Oct 21;14(1):86.
- Misra UK, Kalita J, Bhoi SK. High-rate repetitive transcranial magnetic stimulation in migraine prophylaxis: a randomized, placebo-controlled study. *J Neurol*. 2013 Nov;260(11):2793-801.
- Mori, F, Codeca, C, Kusayanagi, H, et al. Effects of intermittent theta burst stimulation on spasticity in patients with multiple sclerosis. *Eur J Neurol*. 2009.
- National Institute for Health and Care Excellence (NICE). (2014) Transcranial magnetic stimulation for treating and preventing migraine.
- O'Connell NE, Wand BM, Marston L, et al. Non-invasive brain stimulation techniques for chronic pain. *Cochrane Database Syst Rev*. 2014 Apr 11;4:CD008208.
- Pichora-Fuller MK, Santaguida P, Hammill A, et al. Evaluation and Treatment of Tinnitus: Comparative Effectiveness. Comparative Effectiveness Review No. 122. (Prepared by the McMaster University Evidence-based Practice Center under Contract No. 290-2007-10060-I.) AHRQ Publication No. 13-EHC110-EF. Rockville, MD: Agency for Healthcare Research and Quality; August 2013.
- Picht T, Krieg SM, Sollmann N, et al. A comparison of language mapping by preoperative navigated transcranial magnetic stimulation and direct cortical stimulation during awake surgery. *Neurosurgery*. 2013 May;72(5):808-19.
- Pisegna JM, Kaneoka A, Pearson WG Jr, et al. Effects of non-invasive brain stimulation on post-stroke dysphagia: A systematic review and meta-analysis of randomized controlled trials. *Clin Neurophysiol*. 2016 Jan;127(1):956-68.
- Plewnia C, Vonthein R, Wasserka B, et al. Treatment of chronic tinnitus with  $\theta$  burst stimulation: a randomized controlled trial. *Neurology*. 2012 May 22;78(21):1628-34.
- Rabey JM, Dobronevsky E, Aichenbaum S, et al. Repetitive transcranial magnetic stimulation combined with cognitive training is a safe and effective modality for the treatment of Alzheimer's disease: a randomized, double-blind study. *J Neural Transm*. 2013 May;120(5):813-9.
- Ren CL, Zhang GF, Xia N, et al. Effect of Low-Frequency rTMS on Aphasia in Stroke Patients: A Meta-Analysis of Randomized Controlled Trials. *PLoS One*. 2014 Jul 18;9(7):e102557.
- Rocha S, Melo L, Boudoux C, et al. Transcranial direct current stimulation in the prophylactic treatment of migraine based on interictal visual cortex excitability abnormalities: A pilot randomized controlled trial. *J Neurol Sci*. 2015 Feb 15;349(1-2):33-9.
- Rosset-Llobet J, Fàbregas-Molas S, Pascual-Leone Á. Effect of Transcranial Direct Current Stimulation on Neurorehabilitation of Task-Specific Dystonia: A Double-Blind, Randomized Clinical Trial. *Med Probl Perform Art*. 2015 Sep;30(3):178-84.
- Rubi-Fessen I, Hartmann A, Huber W, et al. Add-on Effects of Repetitive Transcranial Magnetic Stimulation on Subacute Aphasia Therapy: Enhanced Improvement of Functional Communication and Basic Linguistic Skills. A Randomized Controlled Study. *Arch Phys Med Rehabil*. 2015 Nov;96(11):1935-44.e2.

Sedlackova, S, Rektorova, I, Srovnalova, H, et al. Effect of high frequency repetitive transcranial magnetic stimulation on reaction time, clinical features and cognitive functions in patients with Parkinson's disease. *J Neural Transm.* 2009;116(9):1093-1101.

Seniów J, Bilik M, Leśniak M, et al. Transcranial magnetic stimulation combined with physiotherapy in rehabilitation of poststroke hemiparesis: a randomized, double-blind, placebo-controlled study. *Neurorehabil Neural Repair.* 2012 Nov-Dec;26(9):1072-9.

Seynaeve L, Devroye A, Dupont P, et al. Randomized crossover sham-controlled clinical trial of targeted low-frequency transcranial magnetic stimulation comparing a figure-8 and a round coil to treat refractory neocortical epilepsy. *Epilepsia.* 2016 Jan;57(1):141-50.

Shirota Y, Ohtsu H, Hamada M, Enomoto H, Ugawa Y; Research Committee on rTMS Treatment of Parkinson's Disease. Supplementary motor area stimulation for Parkinson disease: a randomized controlled study. *Neurology.* 2013 Apr 9;80(15):1400-5.

Soleimani R, Jalali MM, Hasandokht T. Therapeutic impact of repetitive transcranial magnetic stimulation (rTMS) on tinnitus: a systematic review and meta-analysis. *Eur Arch Otorhinolaryngol.* 2016 Jul;273(7):1663-75.

Sollmann N, Ille S, Hauck T, et al. The impact of preoperative language mapping by repetitive navigated transcranial magnetic stimulation on the clinical course of brain tumor patients. *BMC Cancer.* 2015 Apr 11;15:261.

Takahashi S, Vajkoczy P, Picht T. Navigated transcranial magnetic stimulation for mapping the motor cortex in patients with rolandic brain tumors. *Neurosurg Focus.* 2013 Apr;34(4):E3.

Takeuchi, N, Tada, T, Toshima, M, et al. Repetitive transcranial magnetic stimulation over bilateral hemispheres enhances motor function and training effect of paretic hand in patients after stroke. *J Rehabil Med.* 2009;41(13):1049-1054.

Tsai PY, Wang CP, Ko JS, et al. The persistent and broadly modulating effect of inhibitory rTMS in nonfluent aphasic patients: a sham-controlled, double-blind study. *Neurorehabil Neural Repair.* 2014 Oct;28(8):779-87.

Tunkel DE, Bauer CA, Sun GH, et al. Clinical practice guideline: tinnitus. *Otolaryngol Head Neck Surg.* 2014 Oct;151(2 Suppl):S1-40.

Wagle Shukla A, Shuster JJ, Chung JW, et al. Repetitive Transcranial Magnetic Stimulation (rTMS) Therapy in Parkinson Disease: A Meta-Analysis. *PM R.* 2016 Apr;8(4):356-66.

Wrigley PJ, Gustin SM, McIndoe LN, et al. Longstanding neuropathic pain after spinal cord injury is refractory to transcranial direct current stimulation: a randomized controlled trial. *Pain.* 2013 Oct;154(10):2178-84.

Zanjani A, Zakzanis KK, Daskalakis ZJ, et al. Repetitive transcranial magnetic stimulation of the primary motor cortex in the treatment of motor signs in Parkinson's disease: A quantitative review of the literature. *Mov Disord.* 2015 May;30(6):750-8.

Zheng CJ, Liao WJ, Xia WG. Effect of combined low-frequency repetitive transcranial magnetic stimulation and virtual reality training on upper limb function in subacute stroke: a double-blind randomized controlled trial. *J Huazhong Univ Sci Technolog Med Sci.* 2015 Apr;35(2):248-54.

## POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
03/01/2017	<ul style="list-style-type: none"> <li>• Reformatted and reorganized policy; transferred content to new template</li> <li>• Updated benefit considerations; added instruction to check the member specific benefit plan document and any federal or state mandates, if applicable, before using this policy</li> <li>• Updated list of applicable codes: <ul style="list-style-type: none"> <li>○ Removed coding clarification language pertaining to unproven diagnoses for transcranial magnetic stimulation (addressed in coverage rationale)</li> <li>○ Modified table heading; removed descriptor classifying codes as "non-reimbursable"</li> </ul> </li> <li>• Updated supporting information to reflect the most current description of services, clinical evidence, and references</li> <li>• Archived previous policy version BEHAVIORAL 025.8 T2</li> </ul>