Cigna Medical Coverage Policy

Subject **Transcranial Magnetic Stimulation**

Effective Date **1/15/2014**
Next Review Date **1/15/2015**
Coverage Policy Number **0383**

Table of Contents

Hyperlink to Related Coverage Policies

Attention-Deficit/Hyperactivity Disorder (ADHD): Assessment and Treatment
Complementary and Alternative Medicine
Deep Brain and Motor Cortex Stimulation
Electrical Stimulators
Vagus Nerve Stimulation (VNS)

INSTRUCTIONS FOR USE

*The following Coverage Policy applies to health benefit plans administered by Cigna companies. Coverage Policies are intended to provide guidance in interpreting certain **standard** Cigna benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supersedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of Cigna. Copyright ©2014 Cigna*

Coverage Policy

Cigna does not cover transcranial magnetic stimulation (TMS) for any indication, including depression or treatment of migraine, because it is considered experimental, investigational or unproven

Cigna does not cover navigated transcranial magnetic stimulation (nTMS) for any indication, including preoperative treatment planning and diagnostic testing of motor function, because it is considered experimental, investigational or unproven.

General Background

Therapeutic Transcranial Magnetic Stimulation for Depression

Though the majority of individuals treated for depression respond to standard treatments for depression, some do not benefit, or cannot tolerate, interventions such as psychotherapy, pharmacotherapy, or electroconvulsive therapy (ECT). Alternate approaches to treat depression are being investigated, including transcranial magnetic stimulation (TMS), vagal nerve stimulation, cranial electrical stimulation and herbal/homeopathic remedies (Miniussi, et al., 2005).

TMS uses brief magnetic field pulses to stimulate nerve cells in the brain. Standard TMS is mostly applied with an electromagnetic coil called a figure-of-eight coil (8-coil). Deep TMS can be applied with different types of coils: the H-coil, the C-core coil and the circular crown coil. The only deep TMS coil whose safety and effectiveness has been tested in clinical trials is the H-coil. During the TMS procedure, clinicians place a large electromagnetic coil on the patient's scalp near the forehead. The electromagnetic current switches on and off repeatedly, up to 10 times per second, to produce the pulses. To determine the therapeutic magnetic strength,

the amount of magnetic energy is adjusted until the motor threshold is reached (i.e., the patient's fingers or hands start to twitch). Treatment generally lasts about 40 minutes, and the entire session takes about two hours. The procedure does not require anesthesia and can be performed in a doctor's office. Sessions are typically administered five times a week over four to six weeks. It has been proposed that the stimulation is intended to alter brain activity in areas responsible for mood. The procedure is less invasive than vagal nerve stimulation and is not intended to induce seizures like ECT; it may cause some short-term side effects such as headache, tingling of facial muscles, scalp discomfort, lightheadedness, or discomfort because of the noise the device makes. Hearing loss and seizures have been reported as uncommon side effects. Symptom relief may not take place for several weeks (ECRI, 2013; Bersani, et al., 2013).

While the majority of clinical trials on TMS have evaluated its use in depression, numerous other conditions have also been studied, including, but not limited to, Parkinson's disease, post-traumatic stress disorder, acute ischemic stroke, obsessive-compulsive disorders and schizophrenia, alcohol dependence, tinnitus, migraines, chronic neuropathic pain, spinal cord injury. Ongoing research supports continued investigation of the usefulness of rTMS in the treatment of depression, although effect sizes vary and are modest. Studies have typically used high-frequency rTMS for a minimum of two weeks. Study designs have been both open and sham-controlled. Sample sizes have been relatively small. Few patients were without psychotropics or were followed for any substantial period. There have been a few direct comparisons of ECT and rTMS. Such comparisons have not favored rTMS. Studies have not shown the intervention to be effective for psychotic illness. As well, it may be less effective in elderly patients because of increased distance of brain tissue (associated with age) from the skull and, hence, from the magnetic field generated. rTMS has the advantages of being a subconvulsive and focal treatment, thus eliminating the need for anesthesia, and having minimal to no noticeable cognitive side effects. It has been reported that TMS does carry a very small risk of seizures, and it is recommended that patients be monitored for this adverse effect during the procedure (Machii, et al., 2006; Prudic, 2005; Gooch and Pullman, 2005).

A recent review of the evidence for TMS treatment of depression states that studies are being conducted to test a weak oscillating TMS device that is proposed to not cause seizures and therefore might enable home delivery of TMS for the treatment of schizophrenia and depression (George, et al., 2013).

U.S. Food and Drug Administration (FDA)
On December 13, 2013, a TMS device, The Cerena Transcranial Magnetic Stimulator (TMS) (eNeura Therapeutics, Sunnyvale, CA) received FDA approval thru the de novo premarket review pathway to market the Cerena TMS device. This is the first device to relieve pain caused by migraine headaches that are preceded by an aura: a visual, sensory or motor disturbance immediately preceding the onset of a migraine attack (FDA, 2013).

On January 7, 2013, a TMS device, The Brainsway Deep TMS System (Brainsway Ltd., Jerusalem, Israel) received 510(k) FDA approval as substantially equivalent to the predicate rTMS device (NeuroStar™ TMS System). The FDA indications for use state, "The Brainsway Deep TMS System is indicated for the treatment of depressive episodes in adult patients suffering from Major Depressive Disorder who failed to achieve satisfactory improvement from previous anti-depressant medication treatment in the current episode". The Brainsway Device TMS System is substantially equivalent to the Neurotar TMS Therapy & System).

On October 8, 2008, a TMS device, NeuroStar™ TMS System from Neuronetics, Inc. (Malvern, PA) received 510(k) approval for use by the FDA. The FDA determined that the NeuroStar TMS System is indicated for the treatment of Major Depressive Disorder (MDD) in adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode and can be classified in class II with the establishment of special controls. The FDA states that class II special controls provide reasonable assurance of the safety and effectiveness of the device type. Risks involved with the use of the device type include (FDA, 2008):

- usage outside of labeled patient population
- ineffective treatment
- seizure
- scalp discomfort, scalp burn or other adverse events
- magnetic field effects on functioning of other medical devices

- adverse tissue reaction
- hazards associated with electrical equipment
- hazards caused by electromagnetic interference and electrostatic discharge hazards
- hearing loss

In 2007, the FDA's Neurological Devices Panel reviewed the research comparing the NeuroStar TMS Therapy System device with electroconvulsive therapy (ECT) and concluded that the research did not establish a risk to benefit profile that was comparable to the risk to benefit profile of the predicate device, ECT, because effectiveness had not been demonstrated. The Panel agreed that the safety profile of the device was better than of ECT devices, but the Panel concluded that additional study was necessary to establish the device's effectiveness (FDA, 2007).

In July 2011, the FDA issued a guidance document detailing special controls that should be combined with general controls to ensure safety and effectiveness of rTMS systems for treatment of patients with MDD (FDA, 2011).

Literature Review–Depression
Published clinical trials evaluating the efficacy of TMS to date have generally involved small numbers of patients with major depression as the focus of treatment. The studies include varied diagnostic groups on and off pharmacotherapy. Studies have varied in terms of interval of treatment, degree and placement of stimulation and tend to be of short duration with limited follow-up intervals.

Mantovani et al. (2012a) studied the long-term durability of clinical benefit from TMS using a protocol-specified TMS taper and either continuation pharmacotherapy or naturalistic follow-up. Patients were remitters from an acute double-blind sham-controlled trial of TMS (n=18), or from an open-label extension in patients who did not respond to the acute trial (n=43). Long-term durability of TMS acute effect was examined in remitters over a 12-week follow-up. Relapse, defined as 24-item Hamilton Depression Rating Scale (HDRS-24) ≥20, was the primary outcome. Of 61 remitters in the acute trial, five entered naturalistic follow-up and 50 entered the TMS taper. Thirty-two patients completed TMS taper and 1-, 2-, and 3-month follow-up. At 3-month visit, 29 of 50 (58%) were classified as in remission (HDRS-24 ≤10), two of 50 (4%) as partial responders (30%≤ HDRS-24 reduction <50% from baseline), and one of 50 (2%) met criteria for relapse. During the entire 3-month follow-up, five of the 37 patients relapsed (relapse rate=13.5%), but four of them regained remission by the end of the study. The average time to relapse in these five patients was 7.2 ± 3.3 weeks. Patients who relapsed had higher depression scores at one month. The authors concluded that although one third of the sample was lost to follow-up, the results demonstrate that most patients contributing to observations experienced persistence of benefit from TMS followed by pharmacotherapy or no medication. This study was limited by small sample size and short-term follow-up. Longer follow-up is needed to explore the long-term durability of remission produced by TMS.

In a randomized clinical trial, Ray et al. (2011) studied the efficacy of adjunctive left prefrontal high-frequency rTMS treatment in depression patients as compared to sham stimulation. A total of 45 right handed moderate to severe depression patients were randomized to receive daily sessions of active or sham rTMS (10Hz, 90% of resting MT, 20 trains, 6s duration, 1200 pulses/day) over the right dorsolateral prefrontal cortex for 10 days. Depression and psychosis was rated using Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D) and Brief Psychiatric Rating Scale (BPRS) respectively before and after rTMS. For SIGH-D scores, repeated measures ANOVA showed a significant effect of treatment over time as shown by interaction effect (Pillai's Trace F [1/38]=56.75, $p<0.001$, $\eta(2)=0.60$). For BPRS, repeated measures ANOVA showed a significant interaction effect of treatment over time (Pillai's Trace F [1/38] = 39.87, $p<0.001$, $\eta(2)=0.51$). In psychotic depression patients, repeated measures ANOVA showed a significant effect of treatment over time for SIGH-D scores (Pillai's Trace F [1/25]=43.04, $p<.001$, $\eta(2)=0.63$) and BPRS scores (Pillai's Trace F [1/25]=42.17, $p<0.001$, $\eta(2)=0.63$). The reported limitations of this study were small sample size and lack of rater blinding which may induce bias. The authors reported that studies are required to optimize rTMS parameters in patients with psychotic depression.

Triggs et al., (2010) conducted a prospective, randomized, sham-controlled, double blind, parallel group study of right or left pre-frontal rTMS in 48 subjects with medication-resistant depression. Two thousand (50×8- s trains of 5 Hz) stimuli at measure motor evoked potential (MEP) threshold were delivered each weekday for two

weeks. A sham coil and simultaneous electrical stimulation of the scalp to simulate rTMS was used. Mean (±S.D.) reductions in the HAMD-24 from baseline to three months were not significantly different between rTMS and sham treatment groups. Right cranial stimulation (sham or rTMS) was significantly more effective than left cranial stimulation (sham or rTMS) (p=0.012). Mean (±S.D.) reductions in the HAMD from baseline to three months were: left: 28.1 (±5.36) to 19.2 (±11.2); and right 27.2 (±4.2) to 11.5 (±9.4). Left rTMS achieved a reduction in HAMD 9.5 points greater than that achieved by left sham. The authors reported that they did not find an rTMS effect, although they can not rule it out, particularly when it is applied to the left hemisphere, and future studies need to consider the possible value of rTMS applied at other sites, possibly at different frequencies, and ultimately, tailored to specific patients.

In a prospective study, Janicak et al. (2010) assessed the durability of antidepressant effect after acute response to TMS in patients with major depressive disorder (MDD) using protocol-specified maintenance antidepressant monotherapy. Three hundred one patients were randomly assigned to active or sham TMS in a 6-week, controlled trial. Nonresponders could enroll in a second, 6-week, open-label study. Patients who met criteria for partial response (i.e., >25% decrease from the baseline HAMD 17) during either the sham-controlled or open-label study (n=142) were tapered off TMS over three weeks, while simultaneously starting maintenance antidepressant monotherapy. Patients were then followed for 24 weeks in a naturalistic follow-up study examining the long-term durability of TMS. During this durability study, TMS was readministered if patients met prespecified criteria for symptom worsening (i.e., a change of at least one point on the CGI-S scale for two consecutive weeks). Relapse was the primary outcome measure. Ten of 99 (10%; Kaplan-Meier survival estimate =12.9%) patients relapsed. Thirty-eight (38.4%) patients met criteria for symptom worsening and 32/38 (84.2%) reachieved symptomatic benefit with adjunctive TMS. Safety and tolerability were similar to acute TMS monotherapy. Limitations of this study include the lack of a controlled comparison. The two groups were no longer fully randomized after entry in the long-term trial, inferential statistical comparisons are not appropriate. Further, all patients, regardless of whether they benefited from active or sham TMS during acute treatment, were continued on antidepressant medication monotherapy as a primary maintenance strategy during the 24-week follow-up. Hence, the acute sham responder group was not followed as a ‘‘pure’’ sham responder (or no treatment) extension cohort, because these patients may have received clinical benefit from the introduction of antidepressant medication.

In a prospective, multi-site, randomized, active sham-controlled (1:1 randomization) study, George et al. (2010) examined if daily left pre-frontal rTMS safely and effectively treats major depressive disorder. Approximately 860 outpatients were screened, yielding 199 antidepressant drug-free patients with unipolar non-psychotic major depressive disorder. The researchers delivered rTMS to the left pre-frontal cortex at 120 % motor threshold (10 Hz, 4-second train duration, and 26-second intertrain interval) for 37.5 minutes (3000 pulses per session) using a figure-eight solid-core coil. Sham rTMS used a similar coil with a metal insert blocking the magnetic field and scalp electrodes that delivered matched somatosensory sensations. In the intention-to-treat sample (n=190), remission rates were compared for the two treatment arms using logistic regression and controlling for site, treatment resistance, age, and duration of the current depressive episode. Patients, treaters, and raters were effectively masked. Minimal adverse effects did not differ by treatment arm, with an 88% retention rate (90% sham and 86% active). Primary efficacy analysis revealed a significant effect of treatment on the proportion of remitters (14.1% active rTMS versus 5.1% sham) (p=0.02). The odds of attaining remission were 4.2 times greater with active rTMS than with sham (95% CI, 1.32-13.24). The number needed to treat was 12. Most remitters had low antidepressant treatment resistance. Almost 30% of patients remitted in the open-label follow-up (30.2% originally active and 29.6% sham). There are several limitations reported with the study. As a consequence of the extensive work in designing a sham system, which delayed the start of the trial, the study failed to enroll the projected 240 subjects suggested by the initial power analysis. This power issue may be the reason why the treatment condition effect on remission rate in the fully adherent sample analysis was not statistically significant. Treaters were able to guess randomization assignment better than chance, without much confidence, which was not explained by covarying for clinical benefit. Although the treatment effect was statistically significant on a clinically meaningful variable (remission), the overall number of remitters and responders was less than one would like with a treatment that requires daily intervention for three weeks or more, and it is unclear how long the clinical benefit lasts once achieved.

In a three-group, three week double-blind, randomized controlled trial, Pallanti et al. (2010) compared unilateral low frequency, sequential bilateral rTMS treatment and sham in patients with treatment resistant depression (TRD) under stable pharmacological treatment. Sixty patients were assigned to receive either low-frequency rTMS over the right dorsolateral prefrontal cortex (DLPFC) (140s x1 Hz) followed by controlateral sham

(unilateral group, n=20), low frequency right DLPFC rTMS followed by left DLPFC high frequency rTMS (5s x 10 Hz) (bilateral group, n=20), or bilateral sham (sham group, n=20). The primary outcome variable was the score on Hamilton Depression Scale (HAM-D). Low frequency right-sided and sequential bilateral stimulation showed different antidepressant efficacy at three weeks and across the full duration of the study, only the unilateral method appearing significantly more effective than sham at the end of the trial, and correlated to the higher percent of remitters (30% of the group versus 10% -bilateral- and 5% -sham). Unilateral stimulation, but not bilateral, showed higher antidepressant efficacy compared to sham stimulation. The data suggest that right-sided low frequency stimulation may be a first line treatment alternative in resistant depression. The authors report that to confirm and extend these findings further studies require a longer follow-up period.

Mogg et al. (2008) conducted a randomized clinical trial with four month follow-up to evaluate the effectiveness of rTMS for major depression. Fifty-nine patients with major depression were randomly assigned to a 10-day course of either real (n=29) or sham (n=30) rTMS of the left dorsolateral prefrontal cortex. Primary outcome measures were the 17-item Hamilton Depression Rating Scale (HAMD) and proportions of patients meeting criteria for response (≥ 50% reduction in HAMD) and remission (HAMD ≤ 8) after treatment. Secondary outcomes included mood self-ratings on Beck Depression Inventory-II and visual analogue mood scales, Brief Psychiatric Rating Scale (BPRS) score, and both self-reported and observer-rated cognitive changes. Patients had six-week and four-month follow-ups. Overall, HAMD scores were modestly reduced in both groups but with no significant group x time interaction (p=0.09) or group main effect (p=0.85); the mean difference in HAMD change scores was -0.3 (95% CI -3.4 to 2.8). At end-of-treatment time-point, 32% of the real group were responders compared with 10% of the sham group (p=0.06); 25% of the real group met the remission criterion compared with 10% of the sham group (p=0.2); the mean difference in HAMD change scores was 2.9 (95% CI -0.7 to 6.5). There were no significant differences between the two groups on any secondary outcome measures. Blinding was difficult to maintain for both patients and raters. Four patients did not complete the full treatment course, of whom two were lost to follow-up. The authors reported that adjunctive rTMS of the left dorsolateral prefrontal cortex could not be shown to be more effective than sham rTMS for treating depression.

O'Reardon et al. (2007) conducted a multi-site, randomized, double-blind, controlled study examining whether TMS over the left dorsolateral prefrontal cortex (DLPFC) is effective and safe in the acute treatment of major depression. FDA-clearance of the NeuroStar™ TMS System was based on this study. In this multicenter study, 301 medication-free patients with major depression who had not benefited from prior treatment were randomized to active (n=155) or sham TMS (n=146) conditions. The patients had a current episode duration of three years or less. Patients were required to have failed at least one but no more than four adequate antidepressant treatments in this or the most recent episode. Patients were eligible if they had marked intolerance to antidepressants as indicated by four failed attempts to tolerate an adequate medication trial during their lifetime. Exclusionary criteria for study participation included a lifetime history of psychosis, bipolar disorder, or obsessive–compulsive disorder; posttraumatic stress disorder and eating disorders (if present in the past year); lack of response to an adequate trial of ECT; prior treatment with TMS or a vagus nerve stimulator implant; pregnancy; a personal or close family history of a seizure disorder; presence of neurologic disorder or medication therapy known to alter seizure threshold; or presence of ferromagnetic material in or in close proximity to the head.

The study had three phrases: a one week lead in phase with no treatment, a six week acute treatment phase with daily treatment with sham or TMS, and a taper phase consisting of three weeks of reduced frequency of TMS or sham and start of antidepressant. Sessions were conducted five times per week with TMS at 10 pulses/sec, 120% of motor threshold, 3000 pulses/session, for 4–6 weeks. Primary outcome was the symptom score change as assessed at week four with the Montgomery–Asberg Depression Rating Scale (MADRS). Response was defined as at least 50% reduction from baseline score. Remission was defined by an absolute scale-specific score. Secondary outcomes included changes on the 17- and 24-item HAMD and response and remission rates with the MADRS and HAMD.

Loss to follow-up was similar in the two groups, with 301 (92.6%) patients completing at least one post-baseline assessment and an additional 8% of patients from both groups dropping out before the four week assessment, which then become an open-label study. A dropout rate of 4.5% was reported for transient scalp discomfort or pain. Subjects in the TMS group exhibited improvement on several secondary outcome measures, but antidepressant effects did not reach statistical significance for the primary outcome measure, the MARDS. Baseline symptom scores MARDS (active 32.8 versus sham 33.9, p=0.36). Week four symptom scores MARDS

(active 27 versus sham 29.8, p=0.57). Week six symptom scores MARDS (active 26.8 versus sham 30, p=0.58). There was no long-term follow-up in this study. No outcomes were reported beyond six weeks.

Avery et al. (2008) provided further analysis of the open-label extension study of active rTMS for patients from the O'Reardon et al. (2007) study who did not benefit from the initial four week course of rTMS. As with O'Reardon's study, Avery used a sham-controlled design. They noted that patients who had failed only one adequate trial of an antidepressant were more likely to achieve a favorable response than those who had more than one treatment prior to rTMS. In those patients who received sham in the preceding randomized controlled trial (n=85), the mean reduction in MADRS scores after six weeks of open-label active TMS was -17.0 (95% CI = -14.0 to -19.9). Further, at six weeks, 36 (42.4%) of these patients achieved response on the MADRS, and 17 patients (20.0%) remitted (MADRS score < 10). For those patients who received and did not respond to active TMS in the preceding randomized controlled trial (n=73), the mean reduction in MADRS scores was -12.5 (95% CI = -9.7 to -15.4), and response and remission rates were 26.0% and 11.0%, respectively, after 6 weeks of additional open-label TMS treatment. The authors acknowledged that the response and remission rates at six weeks were probably higher than they actually were given that it was an open-label extension study, and there likely was a placebo effect related to expectations of a positive treatment outcome. Avery compared the data with the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) results (Rush, et al., 2006), also an open-label trial. They compared remission rates after 1—2 unsuccessful courses of antidepressants to be similar to those of the current study of TMS, and conclude that their data suggested the efficacy of rTMS to be comparable to that of second or third line pharmaceutical strategies. Avery did not note that the STAR*D study had a much larger sample size (n=4041 versus 158), or that they were comparing data that included two full 6 week courses of rTMS for 73 patients. The lack of a control treatment condition limits the interpretation of the data.

In a randomized clinical trial, Herwig et al. (2007) evaluated whether the application of rTMS in a routine clinical setting as an additional strategy to standard antidepressant medication would enhance the clinical improvement of depression compared with sham treatment with regard to the number of responders and the decrease in depression rating scores. A total of 127 patients were randomized to rTMS group (n=62) duration of current episode eight weeks or less in 25 pts, longer in 36 patients. The sham group (n=65) duration of current episode eight weeks or less in 24 patients, longer in 41 patients. The patients ranged in age from 18–75 years with a diagnosis of major depressive episode with Diagnostic and Statistical Manual of Mental Disorders Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria including bipolar affective disorder, score of ≥ 18 points on at least two of three depression rating scales. rTMS used as adjunct to venlafaxine or mirtazapine therapy or as monotherapy when no medication was possible. Patients stable on lithium therapy for at least three months prior to study entry were allowed to continue taking lithium. The rTMS group, received rTMS on the left side (position F3 according to international 10–20 system for electroencephalography electrode placement) with frequency 10 Hz and intensity 110% motor threshold (MT); 2000 stimuli/session times 15 daily sessions. The sham group received therapy with the coil placed 5 cm lateral to position F3 at an angle of 45°; intensity reduced to 90% MT for 15 daily sessions. Outcomes were measured at baseline, weeks one, two, three, and six. Response rate (response defined as ≥ 50% improvement in scores on at least two depression scales [MADRS; HAMD, Beck Depression Inventory (BDI)] after three wks of therapy); secondary outcome was overall change in depression rating score. Remission was defined as a score of 10 points or below in all three scales. No difference was found in the responder rates of the real and the sham treatment groups (31% in each) or in the decrease of the scores on the depression rating scales. The authors reported that the data do not support previous reports from smaller samples indicating an augmenting or accelerating antidepressant effect of rTMS.

Loo et al. (2007) studied the efficacy and safety of twice-daily rTMS over two weeks. A total of 38 patients with depression enrolled in a sham-controlled trial of twice-daily rTMS (left prefrontal cortex, 10 Hz, 110% intensity, 1500 stimuli per session) over two weeks. Mood and neuropsychological functioning were assessed weekly by blind raters, using the MADRS as the primary outcome measure, plus HAMD and self-report measures. Two subjects, one sham and one active, withdrew before completion of the two- week blind phase. After the blind period, 22 subjects continued with once-daily rTMS to receive a total of six weeks of active rTMS. The patients were moderately treatment-resistant. Active treatment resulted in significantly greater improvement than sham over the two-week blind period on one outcome measure only (MADRS $p<0.05$). Subjects showed further improvement over the six weeks of active rTMS. Neuropsychological test scores did not change significantly. The authors reported a limitation of this study is the direct lack of comparison with rTMS given once daily. Also, subjects in this study were not medication–free, although the antidepressants during the trial were medications

to which the subjects had failed to respond and were maintained at stable doses over the study period. The authors reported that rTMS given twice daily was effective and safe, with no adverse neuropsychological effects, although further investigations are needed to compare the efficacy of once daily and twice daily rTMS within a single study.

In a six-week randomized sham-controlled trial (n=50) Fitzgerald et al. (2006a) studied the efficacy of sequential bilateral rTMS combining both high-frequency left-sided stimulation (i.e., 15 trains of five seconds' duration at 10 Hz) with low-frequency right-side rTMS (i.e., three trains of 140 seconds' duration at 1 Hz). Forty-two patients had a diagnosis of major depressive episode (unipolar), and eight had a diagnosis of bipolar I disorder, depressive episode (four in each group). Twenty-five patients were in each arm of the study. All patients (unipolar and bipolar) had failed to respond to a minimum of two courses of antidepressant medications for at least six weeks. These courses were required to be at a standard minimum effective dose (e.g., 20 mg/day of fluoxetine, paroxetine, or citalopram; 150 mg/day of a tricyclic antidepressant; or 125 mg/day of venlafaxine). There was no difference in the proportions of patients taking any of the medication types between the two groups. Patients were not withdrawn from medication prior to treatment. Their dosage of medication was not allowed to change four weeks prior to and during treatment. Twenty patients reported at least one previous ECT treatment course. Half of these patients reported a previously favorable response to ECT, seven reported no response, and three reported a course limited by cognitive side effects. Patients with significant medical illness, neurological disorders, or other axis I psychotic disorders were excluded. For five consecutive days per week, all patients received ten outpatient treatment sessions. After the tenth session, a blind assessment was made classifying patients as initial responders if they achieved a > 20% reduction in score on the MADRS. If the patients met the > 20% reduction in MADRS score, they received another week of rTMS. The patients were assessed on a weekly basis and received further rTMS if they achieved an additional 10% reduction in MADRS score up to a maximum of six weeks of total treatments. Open-label active rTMS under the same treatment conditions was offered for those patients receiving sham stimulation. Five patients in the active group and two patients in the sham group reported a brief headache after one or more treatment sessions. In the active group, three patients reported brief nausea. No adverse events were reported. In the active group, 10/25 patients finished after two weeks, two continued for three weeks, two for four weeks, and 11 for the full six weeks. In the sham group, only seven continued for longer than 2 weeks. Two of these continued into week four, but none progressed further than week four in the study. The response rate in the active group was 44% (11/25) and 8% in the sham group (2/25); ($p<0.05$). Clinical remission in the active group was 6% (9/25) and in the sham group 0% (0/25); ($p=0.005$). Therapeutic response increased over a period of six weeks. The study limitations included: small sample size; lack of long-term follow-up period; heterogeneous patient population; slow-responding patients were excluded after two weeks; there was not good information as to the integrity of the blinding after two weeks of treatment, and the clinicians providing treatment were not blind to group; interpretation of the results of this study is complicated by the concurrent medication treatment of most subjects.

Fitzgerald et al. (2006b) conducted a randomized controlled trial of the efficacy of 1 Hz versus 2 Hz right prefrontal cortex rTMS. A total of 130 patients with treatment-resistant depression were randomized to either 1 or 2 Hz rTMS over the right prefrontal cortex for two weeks with a possible further two-week extension. Nonresponders were randomized to either 5 or 10 Hz left prefrontal cortex rTMS. Overall, 66 patients (51%) achieved response and 35 (27%) remission criteria. For right-sided treatment, depression significantly improved, but there was no between-group difference. Twenty-eight (42%) patients in the 1 Hz group and 33 (53%) patients in the 2 Hz group achieved response criteria ($p>0.05$). Depression symptom scores also improved for patients who crossed over to left-sided treatment, but there was no significant difference in response between 5 and 10 Hz rTMS. The authors reported that, despite a heterogeneous sample, a significant proportion of patients met clinical response criteria following treatment, but response to 1 and 2 Hz did not differ. Two Hz right prefrontal cortex rTMS has antidepressant properties but offers no advantage over 1 Hz despite doubling pulse number.

In a sham-controlled study, Avery et al. (2006) investigated the clinical efficacy of TMS using a more aggressive treatment protocol than was used in previous sham-controlled studies by utilizing a greater intensity of stimulation, greater number of sessions and total pulses. An Investigational Device Exemption was received from the FDA. There were multiple patient exclusions including, but not limited to: patients with active suicide ideation or recent suicide attempt; patients with a history of ECT therapy nonresponse; and chronically depressed patients. Patients had to be age 21–65 and have a diagnosis of major depressive disorder. The patients had to have failed, or been unable to respond to, at least two previous antidepressant trials. Patients had to have a 17-item HAMD score of 17 or more at both screening and treatment day one with a decrease of

no more than 20% between these two visits. There were no significant differences between subjects randomized to receive TMS (n=35) and those randomized to receive sham (n=33). The patients received 15 sessions of active or sham rTMS delivered to the left dorsolateral prefrontal cortex at 110% the estimated prefrontal threshold. Each session consisted of 32 trains of 10 Hz rTMS delivered in five-second trains. The primary end point was treatment response defined as a ≥ 50% decrease in HAMD score at one and two weeks following the final rTMS treatment. Remission was defined as an HAMD score less than eight. Forty-one percent of the TMS group reported pain at the site of stimulation. The response time for the TMS group was 30.6% (11/35) greater than the 6.1% (2/33) rate in the sham group (p=0.008). The remission rate for the TMS group was 20% (7/35) greater than the 3% (1/33) for the sham group (p=0.033). Of the 11 responders to TMS, five did not relapse during the six-month follow-up. Mean HAMD score at six months was 4.6. Of the five active TMS responders, one each relapsed at months one, two, three, four, and five. The authors reported that with this study, and the following study by Fitzgerald et al. (2003), clinically relevant antidepressant responses can be obtained in TMS studies if higher intensities and more sessions are used. The authors do state more research is needed with larger sample sizes and higher intensities to determine the efficacy of TMS treatment.

Miniussi et al. (2005) studied the efficacy of a five-day treatment regimen with high and low TMS rates in a population of depressed patients. Additionally, the TMS-induced changes in plasma levels of neurotransmitters were evaluated. Seventy-one drug-resistant depressed patients were randomly assigned to low (1 Hz) or high (17 Hz) rate TMS, applied for five days over the left dorsolateral prefrontal cortex. Two study designs were used. One group of 20 patients received active treatment, while the other group entered a double-blind, placebo-controlled, crossover design. Pre- and post-treatment blood samples were taken to evaluate plasma levels of serotonin and dopamine. The authors reported that using the treatment schedule of one week, rTMS produced an antidepressant effect that is not distinguishable from a placebo effect. Also, differences in the type of treatment or clinical response do not correlate with changes in plasma levels of neurotransmitters implicated in mood control. The authors stated that further studies with larger patient populations, and for longer treatment periods, are required to assess the potential benefit of TMS in the treatment of depression.

In a five-week, randomized placebo-controlled trial, Rossini et al. (2005) investigated the efficacy of high frequency rTMS directed to the left prefrontal cortex in drug-resistant depressed patients. Fifty-four patients were randomized to 10 daily applications of real or sham rTMS. Subjects receiving active stimulation were further randomized into subgroups according to the intensity of stimulation: 80% versus 100% of motor threshold. Two patients dropped out of the study due to withdrawal and the other, from the 80% sham group, due to worsening of clinical condition during the first week of treatment. At the end of the study, the response rates were 61.1%, 27.8%, and 6.2% for the 100% motor threshold group, 80% motor threshold group, and sham group, respectively. A significant difference was found between the sham and 100% motor threshold groups, while the 80% motor threshold group did not differ significantly from the sham group.

In a single-center, prospective, double-blind, sham-controlled “add on” trial, Hausmann et al. (2004) concluded that rTMS as an “add on” in the stimulation of depression did not exert an additional antidepressant effect. The efficacy of high-frequency, left-sided repetitive TMS and low-frequency, right-sided TMS to the right prefrontal cortex in treatment-resistant depression was evaluated in a double-blind, randomized, sham-controlled trial conducted by Fitzgerald et al. (2003). Sixty patients were divided into three groups of 20 that did not differ in age, sex, or any other clinical variables. The researchers reported a significant difference in response among the three groups, with a substantial difference between the high-frequency, left-sided repetitive TMS and low-frequency, right-sided TMS groups and the sham group but not between the treatment groups.

In a double-blind controlled study, Loo et al. (1999) examined the efficacy and safety of left prefrontal rTMS for treating resistant major depression. Eighteen subjects were randomly assigned to two weeks of real or sham rTMS, and then permitted up to four weeks of real rTMS. Mood, electroencephalogram (EEG), hearing and neuropsychological function were assessed. The results after two weeks showed no significant difference between groups. The researchers found that four weeks of rTMS yielded progressive improvement and was safe.

TMS and Electroconvulsive Therapy (**ECT):** In a randomized study, Keshtkar et al. (2011) compared the efficacy of rTMS (n=33) and ECT (n=40) in adult patients with refractory major depressive disorder (MDD). Both ECT and rTMS significantly improved depression and suicidal behavior scores. However, ECT reduced depression and suicidal behavior scores more than rTMS. There were no significant adverse effects in the rTMS group. The authors reported that both ECT and rTMS improved MDD in the short term, but the antidepressant

efficacy of ECT was greater than rTMS. Moreover, ECT led to greater reductions in suicidal behavior than rTMS. The authors reported that additional studies are needed to compare ECT and rTMS in terms of the long-term relapse rate and quality of life.

In a randomized study, Hansen et al. (2011) compared the antidepressant efficacy and adverse effects of right prefrontal low frequency rTMS with that of ECT. A total of sixty inpatients with major depression were randomized to 15 days of 1-Hz right prefrontal rTMS or nine unilateral ECTs. Depressive symptoms and adverse effects were recorded using the Hamilton Scale for Depression and the Udvalg for Kliniske UndersLgelser side effect scale, supplied by neuropsychological assessment of cognitive functions. The authors reported that rTMS was significantly less effective than ECT.

A randomized clinical trial conducted for the National Coordinating Center for Health Technology Assessment (NCCHTA) found that ECT is a more effective antidepressant treatment than three weeks of rTMS (McLoughlin, et al., 2007). Forty-six patients with major depression were randomized to receive a 15-day course of rTMS (n=24) or a course of ECT (n=22). One patient was lost to follow-up at end of treatment and another eight at six months. The end-of-treatment HRSD scores were lower for ECT (95% confidence interval (CI) 3.40–14.05, p=0.002), with 13 (59%) achieving remission compared with four (17%) in the rTMS group (p=0.005). However, HRSD scores did not differ between groups at six months. Beck Depression Inventory-II, visual analogue mood scales (VAMS), and Brief Psychiatric Rating Scale scores were lower for ECT at the end of treatment and remained lower after six months. Improvement in subjective reports of side-effects following ECT correlated with antidepressant response. There was no difference between the two groups before or after treatment on global measures of cognition. The investigators reported that there was also no difference in gain in quality adjusted life years (QALYs) for ECT and rTMS patients. It should be noted that rater blinding was not maintained and is a potential source of bias. However, similar results were obtained on both observer- and self-rated measures. The optimal parameters for administering rTMS to achieve an antidepressant effect are not yet known.

In a randomized single-blind study, Rosa et al. (2006) compared the efficacy of rTMS and ECT. Forty-two patients between 18 and 65 years of age, referred to ECT due to unipolar non-psychotic depression refractoriness, entered the trial. They were randomly assigned to receive either rTMS or ECT. Depressive symptom changes were blindly measured by HAMD, visual analogue scale for depression and Clinical Global Impression at baseline, after two and four weeks of treatment. There was no difference in the antidepressant efficacy of ECT and rTMS. Response rates were relatively low in both groups (40% and 50% respectively), with no significant difference between them (p=0.55). Remission rates were also low for both groups (20% and 10% respectively), also with no significant difference (p=0.631). There was no significant difference in the neuropsychological test performance after either one of these therapies. The authors reported that both treatments were associated with a degree of improvement in refractory depression and therefore add to the literature that rTMS can be an effective option to ECT. The authors reported that the limitations of this study were the lack of a placebo group, small sample size, and their neuropsychological battery might not have been adequate to detect memory changes following ECT treatment, especially with unilateral ECT (deficits of orientation, anterograde memory and delayed recall of non-verbal material), or the sample was too small to show this difference.

Eranti et al. (2007) conducted a multicenter randomized controlled trial to test the equivalence of rTMS with ECT. A total of 107 patients met the inclusion criteria with 61 patients declining participation in the study due to clinical decision or they did not want to participate in research. Forty-six patients with major depression referred for ECT were randomly assigned to either a 15-day course of rTMS of the left dorsolateral prefrontal cortex (n=24) or a standard course of ECT (n=22). The primary outcome measures were the score on the 17-item HAMD and the proportion of patients with remissions (Hamilton score, ≤8) at the end of treatment. Secondary outcomes included mood self-ratings on the Beck Depression Inventory-II and visual analogue mood scales, Brief Psychiatric Rating Scale score, and both self-reported and observer-rated cognitive changes. Follow-up was after six months. Five of the rTMS patients stopped treatment within two weeks because of a perceived lack of benefit. A total of 23 patients were analyzed for primary outcome in the rTMS group. Two patients were lost to follow-up, and one death was noted due to previously diagnosed prostate cancer. A total of 22 patients were analyzed for primary outcome in the ECT group. Six patients were lost to follow-up. The HAMD scores at the end of treatment were significantly lower for ECT, with 13 patients (59.1%) achieving remission in the ECT group and four (16.7%) in the rTMS group. However, at six months, the HAMD scores did not differ between groups. Beck scale, visual analogue mood scale, and Brief Psychiatric Rating Scale scores were lower for ECT at the end of treatment and remained lower after six months. Self- and observer-rated cognitive measures were

similar in the two groups. The authors reported that rTMS was not as effective as ECT, and ECT was substantially more effective for the short-term treatment of depression.

Janicak et al. (2002) compared rTMS to ECT in severely ill, depressed patients in a randomized clinical trial. Twenty-five patients with major depression (i.e., unipolar or bipolar) were randomly assigned to rTMS or a course of ECT. The primary outcome measure was the 24-item HAMD. The authors reported that rTMS and ECT had comparable therapeutic effects. Similar conclusions were reported in studies by Grunhaus et al. (2003) and Pridmore et al. (2000).

Literature Review-Safety of TMS: Machii et al. (2006) conducted a review of the literature and their own data to assess the safety of rTMS to non-motor areas. The authors identified 173 articles, published between 1998 and 2003, that applied rTMS to non-motor areas. Also, they analyzed data on 249 patients from their own studies between 1997 and 2003. The authors found 74 articles in which the authors reported the presence or absence of adverse events. Overall, headache was the most common adverse event, occurring in 23% of the patients, and more frequently with frontal rTMS. Serious adverse events were rare and consisted of four cases of psychotic symptoms and two seizures induced by rTMS to the dorsolateral prefrontal cortex in patients with depression. The authors concluded that rTMS, as currently applied to non-motor areas, appears to be safe with few adverse events.

Agency for Healthcare Research and Quality (AHRQ): The 2011 comparative effectiveness review on nonpharmacological interventions for treatment-resistant depression (TRD) in adults concludes that “Our review suggests that comparative clinical research on nonpharmacologic interventions in a TRD population is early in its infancy, and many clinical questions about efficacy and effectiveness remain unanswered. Interpretation of the data is substantially hindered by varying definitions of TRD and the paucity of relevant studies. The greatest volume of evidence is for ECT and rTMS. However, even for the few comparisons of treatments that are supported by some evidence, the strength of evidence is low for benefits, reflecting low confidence that the evidence reflects the true effect and indicating that further research is likely to change our confidence in these findings. This finding of low strength is most notable in two cases: ECT and rTMS did not produce different clinical outcomes in TRD, and ECT produced better outcomes than pharmacotherapy. No trials directly compared the likelihood of maintaining remission for nonpharmacologic interventions. The few trials addressing adverse events, subpopulations, subtypes, and health-related outcomes provided low or insufficient evidence of differences between nonpharmacologic interventions. The most urgent next steps for research are to apply a consistent definition of TRD, to conduct more head-to-head clinical trials comparing nonpharmacologic interventions with themselves and with pharmacologic treatments, and to delineate carefully the number of treatment failures following a treatment attempt of adequate dose and duration in the current episode” (Gaynes, et al., 2011.

In June 2012, the New England Comparative Effectiveness Public Advisory Council (CEPAC), an AHRQ funded, independent body composed of public representatives and clinicians and led by a research team at the Institute for Clinical and Economic Review (ICER) at the Massachusetts General Hospital, published a coverage policy analysis addressing repetitive transcranial magnetic stimulation (rTMS). In December 2011, CEPAC reviewed the 2011 AHRQ evidence review on rTMS along with supplementary information. The authors reported that the supplementary analysis is not meant to revisit the core scientific findings and conclusions of the AHRQ review on “Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults” but is intended to supplement those findings with updated information on the patient management options for treatment-resistant depression published since the AHRQ review. CEPAC voted that the evidence was adequate to demonstrate that (rTMS), was as good as or better than usual care for patients with treatment-resistant depression. CEPAC members voted on questions concerning the comparative clinical effectiveness of the treatment options discussed: 1) repetitive transcranial magnetic stimulation (rTMS) and 2) electroconvulsive therapy (ECT).

- Comparative clinical effectiveness of rTMS versus usual care (i.e., general supportive psychotherapy with or without continued use of antidepressant medication). A majority of CEPAC voted (10 to 5) that for patients with TRD, the evidence is adequate to demonstrate that rTMS provides a net health benefit equivalent or superior to usual care. CEPAC members split (5 to 5) on whether rTMS has a net health benefit that is superior or equivalent to usual care.

- Comparative clinical effectiveness of rTMS versus electroconvulsive therapy (ECT). A majority of CEPAC members voted (9 to 6) that for patients with TRD, the evidence is adequate to demonstrate that rTMS provides a net health benefit equivalent to ECT.

The questions and discussions section of the coverage policy analysis lists the following comments:

- "CEPAC desired greater clarity on the ideal number of treatment failures required before rTMS is used, since standard practice differs from the FDA label (one failed trial of antidepressants).
- Although the majority of CEPAC voted that the evidence is adequate to suggest that rTMS is more effective than usual care, comments from some CEPAC members noted the need for more data on which patients are ideal candidates for rTMS.
- Some members expressed concern about the potential for overutilization of rTMS without a standard definition of the ideal patient population.
- Many CEPAC members who voted that the evidence was inadequate to determine if rTMS is as effective or better than usual care cited the dearth of evidence on the benefits of rTMS beyond the initial 4-6 week treatment phase."

Meta-analyses and Reviews: In a systematic review and meta-analysis, Berlim et al. (2013b) compared the efficacy and acceptability of high frequency repetitive transcranial magnetic stimulation (HF-rTMS) and electroconvulsive therapy (ECT) for treating major depression (MD).The authors searched the literature for randomized trials from January 1995 through September 2012. The main outcome measures were remission rates, pre-post changes in depression ratings, as well as overall dropout rates at study end. Data were obtained from seven randomized trials, totaling 294 subjects with MD (Grunhaus, et al., 2000; Pridmore, et al., 2000; Janicak, et al., 2002; Grunhaus, et al., 2003; Rosa, et al., 2006; Eranti, et al., 2007; Keshtkar, et al., 2011). After an average of 15.2 HF-rTMS and 8.2 ECT sessions, 33.6% (38/113) and 52% (53/102) of subjects were classified as remitters (p=0.04), respectively. The associated needed to treat for remission was six and favored ECT. Also, reduction of depressive symptomatology was significantly more pronounced in the ECT group (p=0.007). No differences on dropout rates for HF-rTMS and ECT groups were found. The authors concluded that ECT seems to be more effective than HF-rTMS for treating MD, although they did not differ in terms of dropout rates. Additional comparative trials with larger sample sizes and better matching at baseline, longer follow-ups and more intense stimulation protocols are needed.

In a comparative review, Minichino et al. (2012) compared the efficacy and of ECT, rTMS, and deepTMS in drug-free patients with pharmacoresistant unipolar depression. The first outcome was the clinical response to the three different techniques defined as a percentage improvement of Hamilton Depression Rating Scale (HDRS). The second outcome was the evaluation of their neuropsychological effects. The third outcome was the evaluation of the number of remitted patients; remission was defined as an absolute HDRS-24 score of ≤11 or as an absolute HDRS-17 score of ≤8. Tolerability was the fourth outcome; it was evaluated by examining the number of dropped-out patients. The comparative evaluation of HDRS percentage variations shows ECT as the most effective method after four weeks of therapy; on the other hand, a better efficacy is obtainable by deepTMS after two weeks of therapy. DeepTMS was the technique that gave the best improvement of cognitive performances. The percentage of remitted patients obtained with ECT treatment is the same obtained in the deepTMS group. Both techniques have a remitted patients percentage two times larger than the rTMS. DeepTMS shows a tolerability, measured by the number of dropped-out patients, worse than ECT. The authors confirmed the therapeutic power of ECT. DeepTMS seems to be the only therapy that provides a substantial improvement of both depressive symptoms and cognitive performances; nevertheless it is characterized by a poor tolerability. rTMS seems to provide a better tolerability for patients, but its therapeutic efficacy is lower. Reported limitations of this study include lack of data regarding the long-term effects of rTMS and deepTMS, small sample sizes, and the absence of double-blind studies using ECT or deepTMS in drug-free unipolar depressed patients limits the possibility of achieving a definitive conclusion.

Dell'osso et al. (2011) conducted a meta-analysis of meta-analytic studies to review the optimal parameters of stimulation of rTMS in MD and TRD. A total of 15 meta-analyses were included from 2001-2011. The authors found mixed results with more recent meta-analytic studies seem to support the antidepressant efficacy of the technique to a greater extent in light of longer periods of stimulation (e.g. > 2 weeks). The authors concluded that rTMS seems to be an effective and safe brain stimulation technique for the treatment of medication

refractory depression. Nevertheless, further studies are needed to better define specific stimulation-related issues, such as duration of treatment as well as durability of effects and predictors of response.

In a meta-analysis, Allan et al. (2011) examined TMS in the treatment of depression. A literature search was performed from 1996 until 2008 for randomized sham-controlled trials, with patients and investigators blinded to treatment, and outcome measured using a version of the Hamilton Depression Rating Scale (or similar). Thirty-one studies were suitable for inclusion, with a cumulative sample of 815 active and 716 sham TMS courses. Nine studies included follow-up data with an average follow-up time of 4.3 weeks; there was no mean change in depression severity between the end of treatment and follow-up and no heterogeneity in outcome. The authors stated that "TMS appears to be an effective treatment; however, at 4 weeks' follow-up after TMS, there had been no further change in depression severity. Problems with finding a suitably blind and ineffective placebo condition may have confounded the published effect sizes. If the TMS effect is specific, only further large double-blind randomized controlled designs with systematic exploration of treatment and patient parameters will help to define optimum treatment indications and regimen."

In a meta-analysis, Slotema et al. (2010) examined if rTMS is effective for various psychiatric disorders. A literature search was performed from 1966 through October 2008. Data were obtained from randomized, sham-controlled studies of rTMS treatment for depression (34 studies, n=751 rTMS and n=632 sham), auditory verbal hallucinations (AVH, seven studies), negative symptoms in schizophrenia (seven studies), and obsessive-compulsive disorder (OCD, three studies). Studies of rTMS versus electro-convulsive therapy (ECT, six studies) for depression. Standardized mean effect sizes of rTMS versus sham were computed based on pre-treatment versus post-treatment comparisons. The mean weighted effect size of rTMS versus sham for depression was 0.55 ($p<0.001$). Monotherapy with rTMS was more effective than rTMS as adjunctive to antidepressant medication. ECT was superior to rTMS in the treatment of depression (mean weighted effect size -0.47, $p=0.004$). In the treatment of AVH, rTMS was superior to sham treatment, with a mean weighted effect size of 0.54 ($p<0.001$). The mean weighted effect size for rTMS versus sham in the treatment of negative symptoms in schizophrenia was 0.39 ($p=0.11$) and for OCD, 0.15 ($p=0.52$). Side effects were mild, yet more prevalent with high-frequency rTMS at frontal locations. The authors stated that although the efficacy of rTMS in the treatment of depression and AVH may be considered proven, the duration of the effect is as yet unknown. Effect sizes were measured immediately after the cessation of rTMS treatment. There are indications that the effects of rTMS may last for several weeks to months. The authors reported that although rTMS cannot replace ECT in depressive patients, there may be subgroups in which rTMS can replace antidepressant medication.

A random effects meta-analysis by Schutter et al. (2009) was performed to investigate the clinical efficacy of rTMS over the left dorsolateral prefrontal cortex (DLPFC) in depression. This meta-analysis included 30 double-blind sham-controlled trials with 1164 patients. The clinical trial by O'Reardon et al. (2007) was included in this assessment and is included in this meta-analysis contributing to over one-fourth of the total number of patients. The authors concluded that, "The results show that fast frequency rTMS over the left DLPFC is superior to sham and may be as effective as at least a subset of commercially available antidepressant medications. In addition, TMS is a safe method and because of its few side-effects is well tolerated by patients. However, at this point caution should be exercised because the integrity of blinding and the lack of a proper control condition are considered limitations of rTMS trials. In addition, age bias, medication, suboptimal stimulation parameters, lack of biological information and follow-up assessments may stand in the way of exploiting the effects of rTMS. Nevertheless, ongoing methodological innovations and technological advancements in the field will without doubt further improve the quality and therapeutic efficacy of future rTMS trials. All in all, the present findings suggest that rTMS treatment may be an alternative for patients suffering from major (non-psychotic) depression, and especially for those patients who do not tolerate the side-effects associated with regular pharmacological treatment."

Lam et al. (2008) conducted a systematic review of randomized controlled trials of active rTMS compared with a sham in patients with treatment resistant depression (i.e., at least one failed trial). The primary outcome was clinical response as determined from global ratings, or 50% or greater improvement on a rating scale. Other outcomes included remission and standardized mean differences in end point scores. Meta-analysis was conducted for absolute risk differences using random effects models. Sensitivity and subgroup analyses were also conducted to explore heterogeneity and robustness of results. A total of 24 studies (n=1092 patients) met criteria for quantitative synthesis. Active rTMS was significantly superior to sham conditions in producing clinical response, with a risk difference of 17% and a number-needed-to-treat of 6. The pooled response and remission rates were 25% and 17%, and 9% and 6% for active rTMS and sham conditions, respectively. Sensitivity and

subgroup analyses did not significantly affect these results. Dropouts and withdrawals owing to adverse events were very low. For patients with treatment resistant depression, rTMS appears to provide significant benefits in short-term treatment studies. However, the relatively low response and remission rates, the short durations of treatment, and the relative lack of systematic follow-up studies suggest that further studies are needed before rTMS can be considered as a first-line monotherapy treatment for treatment resistant depression or less refractory cases of depression.

Gross et al. (2007) performed a systematic review and a meta-analysis of the rTMS studies on depression published in the past 12 months comparing these results with an earlier meta-analysis that analyzed the results of the initial rTMS studies on depression. The inclusion criteria included the meta-analysis of Martin et al. (2003) that included 13 studies (324 patients) and five studies for the recent meta-analysis (274 patients). The pooled effect size (standardized mean difference between pretreatment versus post-treatment) from the random effects model was -0.76 (95% confidence interval, CI, -1.01 to -0.51). This result was significantly larger than that of the earlier meta-analysis -0.35, (95% CI) -0.66 to -0.04). The authors concluded that the recent rTMS clinical trials have shown larger antidepressant effects when compared with the earlier studies but larger multicenter studies are still necessary to confirm these trends.

Hermann et al. (2006) conducted a meta-analysis that included prospective studies investigating the effects of rTMS on depressive symptoms in patients. Thirty-three studies met the inclusion criteria. Studies had to be randomized parallel or crossover design with sham control, with both patients and investigators unaware of whether patients were receiving real or sham rTMS. Patients were required to have a diagnosis of depression (i.e., major depressive disorder or bipolar disorder). The studies were required to report their findings using either the HAMD or the MADRS. The authors concluded that studies that have examined rTMS efficacy in the treatment of depression are heterogeneous in terms of outcome, sample characteristics, and treatment parameters. Most of the studies have a small number of participants. Strict double-blinding often cannot be guaranteed because of sham conditions that may be detected by patients. The authors reported that there is as yet no compelling evidence regarding the most effective combination of rTMS parameters and that larger controlled trials are needed with more knowledge regarding the characteristics of patients who benefit from this treatment and the size and persistence of clinical outcomes.

A 2003 Cochrane review assessed the efficacy of rTMS in treating depression. After a systematic review and meta-analysis of published randomized controlled trials comparing rTMS with sham in patients with depression, a total of 16 trials were included in the review, with 14 containing data in a suitable form for quantitative analysis. The HAMD showed an effect that favored rTMS compared to sham after two weeks of treatment, but this was not significant at the two-week follow-up. The authors concluded that current trials are of low quality and provide insufficient evidence to support the use of rTMS in the treatment of depression (Martin, et al., 2003). The Cochrane review conclusion is in accordance with the conclusions from the systematic and meta-analysis of TMS for the treatment of depression conducted by Couturier (2005) and Gershon et al. (2003).

Kozel and George (2002) conducted a meta-analysis to determine whether the literature supports the use of left prefrontal rTMS as a treatment option for depression. Ten of 14 studies (n=230) were suitable for analysis. The authors concluded that, as of the date of this meta-analysis, double-blind published rTMS literature supports the use of left prefrontal rTMS to improve depressive symptoms. The authors discuss that multiple TMS parameters have been used with varying protocol designs. It is not known which TMS parameters maximize effectiveness. The duration of improvement after acute treatment, or whether maintenance rTMS could be used to prolong the benefits of rTMS, is unknown. Also, the relationship between medication use and rTMS is unknown.

Technology Assessment
In April 2012, ECRI updated the emerging evidence report on repetitive transcranial magnetic stimulation (NeuroStar System) for major depressive disorder. The findings to their key questions are as follows:
“Key Question 1: Does rTMS alone improve response rates (i.e., symptoms), remission (absence of symptoms) rates, or quality of life (QOL) compared to sham rTMS alone for adults with MDD?

The available evidence is insufficient to definitively conclude whether rTMS alone produces a clinically meaningful or statistically significant improvement in response, remission, or QOL compared to sham. Two multicenter randomized controlled trials (RCTs) reported slightly higher short-term response rates (i.e., improved depression severity scores for a small proportion [<20%] of patients) in the active rTMS groups than in the sham rTMS groups. However, standard definitions of clinical significance are not available for response, remission, or

QOL. Clinicians may see any possibility for improvement in response as important in this treatment population given the risk of suicide, even though rTMS studies showed relatively low response (19.4% in O'Reardon et al., 15.2% in George et al.) and remission rates (9.0% in O'Reardon et al., 14.1% in George et al.). In both RCTs, between-group differences in response rates were statistically significant, but only one RCT demonstrated a statistically significant difference between groups for remission. In addition, the studies defined response and remission differently. The RCTs also had additional limitations, including lack of testing for blinding integrity in one study and inappropriate post hoc analysis in one study. In one study, a significant portion of patients in the active rTMS group, which was blinded from knowledge of treatment assignment, decided after four weeks to move to the "active" treatment group in the open-label study, which suggests they did not perceive benefit even though they had unknowingly received active rTMS from the start. No data were available to assess QOL in either study.

Key Question 2: Does rTMS plus first-line therapy improve response rates, remission rates, or improve QOL compared to sham rTMS plus first-line therapy for adults whose MDD has not responded to first-line therapy?
Our searches did not identify any studies that met our inclusion criteria and addressed this question.
Key Question 3: Does rTMS alone reduce symptoms, improve the remission rate, or improve QOL compared to first-line therapy alone for adult patients with MDD?
Our searches did not identify any study that met our inclusion criteria and addressed this key question.
Key Question 4: Does rTMS alone improve response rates, remission rates, or QOL compared to second-line therapies (i.e., additional antidepressants, increased dose of antidepressants, other medications used to augment the effects of antidepressants, electroconvulsive therapy) for adults with MDD?
Our searches did not identify any studies that met our inclusion criteria and addressed this key question.
Key Question 5: How do adverse events (AEs) reported with rTMS compare to AEs reported with sham or second-line therapies for treatment of MDD in adults?
The available evidence from two RCTs suggests that active rTMS produces similar, relatively mild AEs (application site discomfort and pain) compared to sham rTMS; 5.4% or fewer patients in either study stopped treatment due to AEs. No deaths or seizures occurred in either study, although seizure is stated as a potential risk of treatment. Our searches did not identify any studies comparing AEs from active rTMS to other second-line therapies.
Key Question 6: What AEs have been reported during rTMS treatment when used as second-line therapy for adults with MDD?

The most common device-related AEs reported in the open-label extensions of rTMS were application site discomfort or pain, headache, muscle twitching, and skin pain. The only serious AE reported in these studies that was deemed to be related to rTMS was one case of temporary left-sided facial numbness" (ECRI, 2012).

The Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) published a Technology Assessment on TMS for depression in November 2009 followed by an update in July 2011. In 2009 TMS was "judged to not meet TEC criteria based on insufficient evidence of treatment effect, especially following the acute treatment period." For the update a search of the peer-reviewed literature was completed for the period up through January 2011. The 2011 TEC Assessment included six recent meta-analyses (Schutter, et al., 2009; Lam, et al., 2008; Gross, et al., 2007; Couturier, et al., 2005; Martin, et al., 2003), the largest evaluating 30 double-blind sham-controlled trials with a total of 1383 patients (Slotema, et al., 2010). Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel made the following judgments concluding that TMS for the treatment of depression does not meet the Blue Cross and Blue Shield Association TEC criteria.

- "An important limitation of the evidence is lack of information beyond the acute period of treatment. Most of the clinical trials evaluate the outcomes at the point of the last TMS treatment, between 1 and 4 weeks. Very few studies evaluated patients beyond this time period. Recent clinical trials have not shown statistically significant results at follow-up points out to 12 weeks beyond treatment. Although meta-analyses are consistent with short-term antidepressant effects, the clinical significance of the effect is uncertain. The large clinical trial of TMS reviewed in this assessment did not unequivocally demonstrate efficacy, as the principal endpoint was not statistically significant at 4 weeks, and some results were sensitive to the methods of analysis. A subsequent clinical trial using the same device and similar treatment protocol showed statistical significance and the remission of depression at the end of TMS treatment. The patients in whom TMS is indicated are usually treated with a second course of

antidepressant therapy. The clinical trial, which was sham controlled without active treatment, cannot determine whether TMS would be more or less successful than this standard treatment."

- "The available evidence does not permit conclusions regarding the effect of TMS on health outcomes or compared with alternatives. Comparison to alternatives using other observational studies may not be valid due to unmeasured differences in severity of depression between studies and other differences in studies."

- "It has not yet been demonstrated whether TMS improves health outcomes in the investigational setting. Therefore, it cannot be demonstrated whether improvement is attainable outside the investigational settings."

Professional Societies/Organizations
The 2010 American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients with Major Depressive Disorder states that evidence for TMS is currently insufficient to support its use in the initial treatment of major depressive disorder. Electroconvulsive therapy (ECT) remains the treatment of best established efficacy against which other stimulation treatments (e.g., VNS, deep brain stimulation, TMS, other electromagnetic stimulation therapies) should be compared. A substantial number of studies of TMS have been conducted, but most have had small sample sizes, and the studies overall have yielded heterogeneous results. Further complicating the interpretation of the TMS literature is the variability in stimulation intensities (relative to the motor threshold), stimulus parameters (e.g., pulses/second, pulses/session), anatomical localization of stimulation, and number of TMS sessions in the treatment course. As an initial treatment in the acute phase of major depression the guideline reports, "Treatment in the acute phase should be aimed at inducing remission of the major depressive episode and achieving a full return to the patient's baseline level of functioning. Acute phase treatment may include pharmacotherapy, depression-focused psychotherapy, the combination of medications and psychotherapy, or other somatic therapies such as ECT, TMS, or light therapy" (Gelenberg, et al., 2010). There has been no update to this guideline since 2010.

Transcranial Magnetic Stimulation - Other Psychiatric or Neurological Disorders
Literature Review—Other Psychiatric or Neurological Disorders
There have been a number of studies and meta-analyses exploring the efficacy of TMS for a selection of neuropsychiatric-related disorders. Some of the methodological limitations of these studies include small sample size, limited follow-up intervals and varied diagnostic groups on and off pharmacotherapy. Therefore, the role of TMS in the treatment of other psychiatric or neurological disorders has not been clearly established. TMS has not been proven effective in the peer-reviewed published scientific literature for any of the following indications, including but not limited to:

- alcohol dependence (Mishra, et al., 2010)
- Alzheimer disease (Ahmend, et al., 2012; Cotelli, et al., 2010)
- amyotrophic lateral sclerosis (ALS) (Guo, et al., 2011; Di Lazzaro, et al., 2010)
- attention deficit hyperactivity disorder (ADHD) (Bloch, et al., 2010)
- auditory hallucinations in schizophrenia (Freitas, et al., 2011; Slotema, et al., 2011; Cordes, et al., 2010; Loo, et al., 2010; Freitas, et al., 2010; Dlabac-de Lange, et al., 2010; Fitzgerald, et al., 2005, Shonefldt-Lecuona, et al., 2004; Hoffman, et al., 2003; Aleman, et al., 2007)
- autism (Sokhadze et al., 2010)
- blepharospasm (Kahn, et al., 2010)
- bulimic disorders (Van den Eynde, et al., 2010)
- chronic pain (Taylor, et al., 2012; O'Connell, et al., 2011; Sampson, et al., 2011; 2010)
- chronic tinnitus (Meng, et al., 2011; Anders, et al., 2010; Lorenz, et al., 2010; Frank, et al., 2010; Rossi, et al., 2010; Marcondes, et al., 2010; Langrebe, et al., 2008; Khedr, et al., 2008; Kleinjung, et al., 2005; De Ridder, et al., 2005; Plewnia et al. 2003)
- epilepsy (Brodbeck, et al., 2010)
- fibromyalgia (Marlow, et al., 2012)
- focal dystonia (Schneider, et al., 2010)
- Huntington's disease (Medina, et al., 2010)
- migraine (Teepker, et al., 2010; Lipton, et al., 2010)

- obsessive-compulsive disorder (Berlim, et al., 2013c; Mansur, et al., 2011; Mantovani, et al., 2010; Rodriguez-Martin, et al., 2003)
- panic disorder (Mantovani, et al., 2012b)
- Parkinson's disease (Benninger, et al., 2011; Arias, et al., 2010; Hartelius, et al., 2010; Pal, et al., 2010; Filipović, et al., 2010; Fregni, et al., 2004)
- post-operative pain (Borckardt, et al., 2006; Khedr, et al., 2005)
- post-traumatic stress disorder (Boggio, et al, 2010; Cohen, et al., 2004)
- schizophrenia (Blumberger, et al., 2010; Matheson, et al., 2010; McNamara, et al., 2001)
- smell and taste dysfunction (Henkin, et al., 2011)
- spinal cord injury (Soler, et al., 2010; Kumru, et al., 2010)
- stroke (Avenanti, et al., 2012; Corti, et al., 2012; Weiduschat, et al., 2011; Emara, et al., 2010; Takeuchi, et al., 2010; Chang, et al., 2010; Kim, et al., 2010; Khaleel, et al., 2010; Lim, et al., 2010; Khedr, et al., 2009, 2010; Fregni, et al., 2006)
- tic disorders (Steeves, et al., 2012; Kwon, et al., 2011)

Professional Societies/Organizations
The American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients with Obsessive-Compulsive Disorder states that the use of somatic treatments such as TMS needs additional investigation (Koran, et al., 2007). There has been no update to this practice guideline since 2007.

The APA Practice Guideline for the Treatment of Patients with Schizophrenia states that although rTMS may share beneficial features of ECT and studies with rTMS have shown promising results in decreasing auditory hallucinations, rTMS has a lack of approval by the FDA for the treatment of psychosis, and additional research is recommended before its use in clinical practice (Lehman, et al., 2004). The updated APA Guideline Watch for the Treatment of Patients with Schizophrenia does not mention TMS (Dixon, et al., 2009). There has been no update to this guideline since 2009.

The American Academy of Neurology evidence-based practice parameter for the evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (2006) concludes that there is insufficient evidence to support or refute the efficacy of TMS or ECT in the treatment of depression associated with Parkinson disease (Miyasaki, et al., 2006). There has been no update to this practice parameter since 2006.

Diagnostic Navigated Transcranial Magnetic Stimulation (nTMS)
Navigated transcranial magnetic stimulation (nTMS) is being investigated as a noninvasive modality to map essential functional motor cortex areas for diagnostic indications and for preoperative treatment planning. It uses electromagnetic pulses to stimulate points of the patient's brain and then records the motor output (if any) on a standard electromyogram. Direct electrical stimulation (DES) is the gold standard for brain mapping and is used intraoperatively but is not used preoperatively. DES cannot be replaced by a noninvasive method due to its unique capability to stimulate subcortical structures accurately and to monitor function during surgery. Preoperative functional brain imaging is used widely in the context of rolandic brain tumor surgeries. The most widely adopted method is fMRI, but MEG, PET, and electroencephalography have also been used for preoperative mapping (Takahashi, et al., 2013; Pitch, et al., 2012).

U.S. Food and Drug Administration (FDA)
In 2009, the Nexstim eXimia Navigated Brain Stimulation System (NexStim, North Attelboro, MA) received 510(k) FDA approval. The 501(k) summary indications for use state, "The Nexstim eXimia Navigated Brain Stimulation System (NBS System) is indicated for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. The NBS System provides information that may be used in the assessment of the primary motor cortex for pre-procedural planning. The NBS System is not intended to be used during a surgical procedure. The NBS System is intended to be used by trained clinical professionals" (FDA, 2009).

Literature Review
There is limited evidence at this time to permit conclusions regarding the impact of nTMS testing on health outcomes. Several comparative studies with small sample sizes suggest that nTMS may be useful as a mapping modality of the motor cortex. Additional well-designed clinical studies with larger patient populations are required (Krieg, et al., 2013; Coburger, et al., 2013; Tarapore, et al., 2012; Forster, et al., 2012; Krieg, et al., 2012; Picht, et al,. 2012, Frey, et al., 2012; Makela, et al., 2012; Picht, et al., 2011).

In a systematic review of observational studies, Takahashi et al. (2013) studied the spatial accuracy and clinical utility of nTMS in rolandic brain tumor surgery in or near the motor cortex. A total of 11 reports published up to October 2012 in which adult patients were examined with nTMS prior to surgery met the inclusion criteria For mapping of the motor cortex, most studies used a biphasic TMS pulse (250–280 μsec pulse length) from a figure-eight coil with an outer diameter of 70 mm applied at 110% of the resting motor threshold and a maximum frequency of 0.25 Hz.2–5,7–9,12,14–17,20,21 For lower-extremity stimulation the intensity was adapted on an individual basis. 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 six 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 two studies. 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 include in the review were limited by small sample sizes. The impact of nTMS on the operation was not reported in the majority of the studies.

In a cohort study, Picht et al., (2013) compared the safety and effectiveness of preoperative nTMS with DCS mapping during awake surgery for the identification of language areas in patients with left-sided cerebral lesions. A total of 20 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 reported good overall correlation between repetitive nTMS and DCS, particularly with regard to negatively mapped regions. The authors reported that its low specificity in posterior language areas necessitates further research to refine the methodology.

Professional Societies/Organizations
Professional society opinion on this technology is lacking.

Use Outside of the US
National Institute for Health and Clinical Excellence (NICE): In November 2007, the NICE (United Kingdom) issued an interventional procedural guidance document on TMS for severe depression. The authors reported that there are no major safety concerns about TMS. However, there are uncertainties about how to achieve the best results from this procedure, in terms of what intensity of electromagnetic energy should be used, how frequently the procedure should be carried out, how long treatment sessions should last and whether both sides of the brain should be stimulated. For these reasons, NICE has reported that this procedure should only be carried out as part of a research or clinical study that looks at these questions. NICE reports that these research studies should consider how to decide whether the procedure is suitable for certain types of patients, whether other treatments patients are taking affect the results of the procedure, and the long term outcomes of electromagnetic stimulation of the brain.

The Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults recommends that rTMS is a second line therapy to ECT (Kennedy, et al., 2009).

The 2013 Royal Australian and New Zealand College of Psychiatrists position statement on repetitive transcranial magnetic stimulation states under clinical indication**:**

- Major Depression: rTMS should be offered in psychiatric clinical settings with appropriate protocols, training and equipment to appropriately selected patients with major depression.

- Refractory hallucinations in schizophrenia:rTMS may be offered on a restricted basis to carefully selected patients with schizophrenia who have auditory hallucinations that have not improved with adequate trials of antipsychotic medications. This should only be performed in tertiary referral centres with appropriate expertise.

- Other psychiatric disorders: Until further data are available, rTMS should only be used for the treatment of other psychiatric disorders within a research protocol which has had formal ethical review and approval.

Summary
Studies have been performed assessing TMS for the treatment of major depression disorder (MDD), schizophrenia and other psychiatric and neurological disorders. Evidence in the peer-reviewed literature has concluded that TMS is safe with few adverse events. While TMS is safe, the efficacy of TMS as compared to other treatments (e.g., psychotherapy, pharmacotherapy, electroconvulsive therapy) has not been established for any indication, including depression or other psychiatric disorders. The majority of clinical trials to assess TMS, including sham-controlled trials, have involved small numbers of patients with MDD as the focus of treatment. The majority of studies to date are not consistent in interval of treatment, degree and placement of stimulation and study length, tend to be of short duration with limited follow-up intervals and include varied diagnostic groups on and off pharmacotherapy. There is a lack of published data to determine if TMS significantly reduce symptoms or improve the remission rate compared to other second-line treatments for MDD. As well, no professional organizations have adopted standards for the administration of this treatment and do not recommend its use in routine clinical practice. Therefore, the role of TMS in the treatment of depression, or other psychiatric or neurological disorders, has not been clearly established.

Navigated transcranial magnetic stimulation (nTMS) is being investigated as a noninvasive modality to map essential functional motor cortex areas for diagnostic indications and for preoperative treatment planning. Several comparative studies with small sample sizes suggest that nTMS may be useful as a mapping modality of the motor cortex. Additional well-designed clinical studies with larger patient populations are required.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Experimental/Investigational/Unproven/Not Covered for any indication:

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

References

1. Ahmed MA, Darwish ES, Khedr EM, El Serogy YM, Ali AM. 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.

2. Aleman A, Sommer IE, Kahn RS. Efficacy of slow repetitive transcranial magnetic stimulation in the treatment of resistant auditory hallucinations in schizophrenia: a meta-analysis. J Clin Psychiatry. 2007 Mar;68(3):416-21.

3. Allan CL, Herrmann LL, Ebmeier KP. Transcranial magnetic stimulation in the management of mood disorders. Neuropsychobiology. 2011;64(3):163-9.

4. Alonso P, Pujol J, Cardoner N, Benlloch L, Deus J, Menchon JM, et al. Right prefrontal repetitive transcranial magnetic stimulation in obsessive-compulsive disorder: a double-blind, placebo-controlled study. Am J Psychiatry. 2001 Jul;158(7):1143-5.

5. American Psychiatric Association (APA) Practice Guidelines. Accessed December 9, 2013. Available at URL address: http://psychiatryonline.org/guidelines.aspx

6. Anders M, Dvorakova J, Rathova L, Havrankova P, Pelcova P, Vaneckova M, et al. Efficacy of repetitive transcranial magnetic stimulation for the treatment of refractory chronic tinnitus: a randomized, placebo controlled study. Neuro Endocrinol Lett. 2010;31(2):238-49.

7. Arias P, Vivas J, Grieve KL, Cudeiro J. Double-blind, randomized, placebo controlled trial on the effect of 10 days low-frequency rTMS over the vertex on sleep in Parkinson's disease. Sleep Med. 2010 Sep;11(8):759-65.

8. Avenanti A, Coccia M, Ladavas E, Provinciali L, Ceravolo MG. Low-frequency rTMS promotes use-dependent motor plasticity in chronic stroke: a randomized trial. Neurology. 2012 Jan 24;78(4):256-64.

9. Avery DH, Isenberg KE, Sampson SM, Janicak PG, Lisanby SH, Maixner DF, et al. Transcranial magnetic stimulation in the acute treatment of major depressive disorder: clinical response in an open-label extension trial. J Clin Psychiatry. 2008 Mar;69(3):441-51.

10. Avery DH, Holtzheimer PE 3rd, Fawaz W, Russo J, Neumaier J, Dunner DL, et al. A controlled study of repetitive transcranial magnetic stimulation in medication-resistant major depression. Biol Psychiatry. 2006 Jan 15;59(2):187-94.

11. Benninger DH, Berman BD, Houdayer E, Pal N, Luckenbaugh DA, Schneider L, et al. Intermittent theta-burst transcranial magnetic stimulation for treatment of Parkinson disease. Neurology. 2011 Feb 15;76(7):601-9.

12. Berlim MT, McGirr A, Beaulieu MM, Turecki G. High frequency repetitive transcranial magnetic stimulation as an augmenting strategy in severe treatment-resistant major depression: a prospective 4-week naturalistic trial. J Affect Disord. 2011 Apr;130(1-2):312-7.

13. Berlim MT, Van den Eynde F, Daskalakis ZJ. A systematic review and meta-analysis on the efficacy and acceptability of bilateral repetitive transcranial magnetic stimulation (rTMS) for treating major depression. Psychol Med. 2013a Nov;43(11):2245-54.

14. Berlim MT, Van den Eynde F, Daskalakis ZJ. Efficacy and acceptability of high frequency repetitive transcranial magnetic stimulation (rTMS) versus electroconvulsive therapy (ECT) for major depression: a systematic review and meta-analysis of randomized trials. Depress Anxiety. 2013b Jul;30(7):614-23.

15. Berlim MT, Neufeld NH, Van den Eynde F. Repetitive transcranial magnetic stimulation (rTMS) for obsessive-compulsive disorder (OCD): an exploratory meta-analysis of randomized and sham-controlled trials. J Psychiatr Res. 2013c Aug;47(8):999-1006.

16. Bloch Y, Harel EV, Aviram S, Govezensky J, Ratzoni G, Levkovitz Y. Positive effects of repetitive transcranial magnetic stimulation on attention in ADHD Subjects: a randomized controlled pilot study. World J Biol Psychiatry. 2010 Aug;11(5):755-8.

17. BlueCross BlueShield Association Technology Evaluation Center. Transcranial Magnetic Stimulation for Depression. Assessment Program. 26(3). July 2011. Accessed December 9, 2013. Available at URL address: http://www.bcbs.com/blueresources/tec/vols/

18. BlueCross BlueShield Association Technology Evaluation Center. Transcranial Magnetic Stimulation for the Treatment of Schizophrenia. Assessment Program. 26(6). November 2011. Accessed December 9, 2013. Available at URL address: http://www.bcbs.com/blueresources/tec/vols/

19. Blumberger DM, Fitzgerald PB, Mulsant BH, Daskalakis ZJ. Repetitive transcranial magnetic stimulation for refractory symptoms in schizophrenia. Curr Opin Psychiatry. 2010 Mar;23(2):85-90.

20. Boggio PS, Rocha M, Oliveira MO, Fecteau S, Cohen RB, Campanhã C, et al. Noninvasive brain stimulation with high-frequency and low-intensity repetitive transcranial magnetic stimulation treatment for posttraumatic stress disorder. J Clin Psychiatry. 2010 Aug;71(8):992-9.

21. Borckardt JJ, Weinstein M, Reeves ST, Kozel FA, Nahas Z, Smith AR, et al. Postoperative left prefrontal repetitive transcranial magnetic stimulation reduces patient-controlled analgesia use. Anesthesiology. 2006 Sep;105(3):557-62.

22. Bretlau LG, Lunde M, Lindberg L, Undén M, Dissing S, Bech P. Repetitive transcranial magnetic stimulation (rTMS) in combination with escitalopram in patients with treatment-resistant major depression: a double-blind, randomised, sham-controlled trial. Pharmacopsychiatry. 2008 Mar;41(2):41-7.

23. Brodbeck V, Thut G, Spinelli L, Romei V, Tyrand R, Michel CM, et al. Effects of repetitive transcranial magnetic stimulation on spike pattern and topography in patients with focal epilepsy. Brain Topogr. 2010 Jan;22(4):267-80.

24. Burt T, Lisanby SH, Sackeim HA. Neuropsychiatric applications of transcranial magnetic stimulation: a meta analysis. Int J Neuropsychopharmacol. 2002 Mar;5(1):73-103.

25. Carpenter LL, Janicak PG, Aaronson ST, Boyadjis T, Brock DG, Cook IA, et al. Transcranial magnetic stimulation (TMS) for major depression: a multisite, naturalistic, observational study of acute treatment outcomes in clinical practice. Depress Anxiety. 2012 Jul;29(7):587-96. doi: 10.1002/da.21969.

26. Chang WH, Kim YH, Bang OY, Kim ST, Park YH, Lee PK. Long-term effects of rTMS on motor recovery in patients after subacute stroke. J Rehabil Med. 2010 Sep;42(8):758-64.

27. Coburger J, Musahl C, Henkes H, Horvath-Rizea D, Bittl M, Weissbach C, Hopf N. Comparison of navigated transcranial magnetic stimulation and functional magnetic resonance imaging for preoperative mapping in rolandic tumor surgery. Neurosurg Rev. 2013 Jan;36(1):65-75; discussion 75-6.

28. Cohen H, Kaplan Z, Kotler M, Kouperman I, Moisa R, Grisaru N. Repetitive transcranial magnetic stimulation of the right dorsolateral prefrontal cortex in posttraumatic stress disorder: a double-blind, placebo-controlled study. Am J Psychiatry. 2004 Mar;161(3):515-24.

29. Connolly KR, Helmer A, Cristancho MA, Cristancho P, O'Reardon JP. Effectiveness of transcranial magnetic stimulation in clinical practice post-FDA approval in the United States: results observed with the first 100 consecutive cases of depression at an academic medical center. J Clin Psychiatry. 2012 Apr;73(4):e567-73. doi: 10.4088/JCP.11m07413.

30. Cordes J, Thünker J, Agelink MW, Arends M, Mobascher A, Wobrock T, et al. Effects of 10 Hz repetitive transcranial magnetic stimulation (rTMS) on clinical global impression in chronic schizophrenia. Psychiatry Res. 2010 May 15;177(1-2):32-6.

31. Corti M, Patten C, Triggs W. Repetitive transcranial magnetic stimulation of motor cortex after stroke: a focused review. Am J Phys Med Rehabil. 2012 Mar;91(3):254-70.

32. Cotelli M, Calabria M, Manenti R, Rosini S, Zanetti O, Cappa SF, et al. Improved language performance in Alzheimer disease following brain stimulation. J Neurol Neurosurg Psychiatry. 2011 Jul;82(7):794-7.

33. Couturier JL. Efficacy of rapid-rate repetitive transcranial magnetic stimulation in the treatment of depression: a systematic review and meta-analysis. J Psychiatry Neurosci. 2005 Mar;30(2):83-90.

34. Cristancho MA, Helmer A, Connolly R, Cristancho P, O'Reardon JP. Transcranial magnetic stimulation maintenance as a substitute for maintenance electroconvulsive therapy: a case series. J ECT. 2013 Jun;29(2):106-8.

35. Dannon PN, Dolberg OT, Schreiber S, Grunhaus L. Three and six-month outcome following courses of either ECT or rTMS in a population of severely depressed individuals--preliminary report. Biol Psychiatry. 2002 Apr 15;51(8):687-90.

36. Dell'osso B, Camuri G, Castellano F, Vecchi V, Benedetti M, Bortolussi S, Altamura AC. Meta-Review of Metanalytic Studies with Repetitive Transcranial Magnetic Stimulation (rTMS) for the Treatment of Major Depression. Clin Pract Epidemiol Ment Health. 2011;7:167-77.

37. De Ridder D, Verstraeten E, Van der Kelen K, De Mulder G, Sunaert S, Verlooy J, et al. Transcranial magnetic stimulation for tinnitus: influence of tinnitus duration on stimulation parameter choice and maximal tinnitus suppression. Otol Neurotol. 2005 Jul;26(4):616-9.

38. Di Lazzaro V, Dileone M, Pilato F, Profice P, Cioni B, Meglio M, et al. Long-term motor cortex stimulation for amyotrophic lateral sclerosis. Brain Stimul. 2010 Jan;3(1):22-7.

39. Dlabac-de Lange JJ, Knegtering R, Aleman A. Repetitive transcranial magnetic stimulation for negative symptoms of schizophrenia: review and meta-analysis. J Clin Psychiatry. 2010 Apr;71(4):411-8.

40. Dixon L, Perkins D, Calmes C. Guideline Watch (November 2009) Practice Guideline for the Treatment of Patients with Schizophrenia. Accessed December 9, 2013. Available at URL address: http://www.psychiatryonline.com/pracGuide/pracGuideTopic_6.aspx

41. ECRI Institute. Repetitive transcranial magnetic stimulation using the NeuroStar System for treating major depressive disorder. [Emerging Technology evidence report]. Plymouth Meeting (PA): ECRI Institute; published 2009 February 6; updated 2010 September 21; updated 2012 April 26. Available at URL address: http://www.ecri.org

42. ECRI Institute. Hotline Response [database online]. Plymouth Meeting (PA): ECRI Institute; 2013 January 24. Repetitive transcranial magnetic stimulation versus electriconvulsive therapy for treatment-resistant depression. Available at URL address: http://www.ecri.org

43. Emara TH, Moustafa RR, Elnahas NM, Elganzoury AM, Abdo TA, Mohamed SA, et al. Repetitive transcranial magnetic stimulation at 1Hz and 5Hz produces sustained improvement in motor function and disability after ischaemic stroke. Eur J Neurol. 2010 Sep;17(9):1203-9. Epub 2010 Apr 8.

44. Eranti S, Mogg A, Pluck G, Landau S, Purvis R, Brown RG, et al. A randomized, controlled trial with 6-month follow-up of repetitive transcranial magnetic stimulation and electroconvulsive therapy for severe depression. Am J Psychiatry. 2007 Jan;164(1):73-81.

45. Filipović SR, Rothwell JC, Bhatia K. Slow (1 Hz) repetitive transcranial magnetic stimulation (rTMS) induces a sustained change in cortical excitability in patients with Parkinson's disease. Clin Neurophysiol. 2010 Jul;121(7):1129-37.

46. Fitzgerald PB, Benitez J, de Castella A, Daskalakis ZJ, Brown TL, Kulkarni J. A randomized, controlled trial of sequential bilateral repetitive transcranial magnetic stimulation for treatment-resistant depression. Am J Psychiatry. 2006a Jan;163(1):88-94.

47. Fitzgerald PB, Huntsman S, Gunewardene R, Kulkarni J, Daskalakis ZJ. A randomized trial of low-frequency right-prefrontal-cortex transcranial magnetic stimulation as augmentation in treatment-resistant major depression. Int J Neuropsychopharmacol. 2006b Dec;9(6):655-66.

48. Fitzgerald PB, Benitez J, Daskalakis JZ, Brown TL, Marston NA, de Castella A, et al. A double-blind sham-controlled trial of repetitive transcranial magnetic stimulation in the treatment of refractory auditory hallucinations. J Clin Psychopharmacol. 2005 Aug;25(4):358-62.

49. Fitzgerald PB, Brown TL, Marston NA, Daskalakis ZJ, De Castella A, Kulkarni J. Transcranial magnetic stimulation in the treatment of depression: a double-blind, placebo-controlled trial. Arch Gen Psychiatry. 2003 Oct;60(10):1002-8.

50. Forster MT, Senft C, Hattingen E, Lorei M, Seifert V, Szelényi A. Motor cortex evaluation by nTMS after surgery of central region tumors: a feasibility study. Acta Neurochir (Wien). 2012 Aug;154(8):1351-9.

51. Frank G, Kleinjung T, Landgrebe M, Vielsmeier V, Steffenhagen C, Burger J, et al. Left temporal low-frequency rTMS for the treatment of tinnitus: clinical predictors of treatment outcome--a retrospective study. Eur J Neurol. 2010 Jul;17(7):951-6.

52. Fregni F, Boggio PS, Valle AC, Rocha RR, Duarte J, Ferreira MJ, et al. A sham-controlled trial of a 5-day course of repetitive transcranial magnetic stimulation of the unaffected hemisphere in stroke patients. Stroke. 2006 Aug;37(8):2115-22.

53. Fregni F, Santos CM, Myczkowski ML, Rigolino R, Gallucci-Neto J, Barbosa ER, et al. Repetitive transcranial magnetic stimulation is as effective as fluoxetine in the treatment of depression in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry. 2004 Aug;75(8):1171-4.

54. Freitas C, Fregni F, Pascual-Leone A. Meta-analysis of the effects of repetitive transcranial magnetic stimulation (rTMS) on negative and positive symptoms in schizophrenia. Schizophr Res. 2009 Mar;108(1-3):11-24.

55. Freitas C, Pearlman C, Pascual-Leone A. Treatment of auditory verbal hallucinations with transcranial magnetic stimulation in a patient with psychotic major depression: one-year follow-up. Neurocase. 2012 Feb;18(1):57-65.

56. Frey D, Strack V, Wiener E, Jussen D, Vajkoczy P, Picht T. A new approach for corticospinal tract reconstruction based on navigated transcranial stimulation and standardized fractional anisotropy values. Neuroimage. 2012 Sep;62(3):1600-9.

57. Gaynes BN, Lux L, Lloyd S, Hansen RA, Gartlehner G, Thieda P, et al. Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults. Comparative Effectiveness Review No. 33. (Prepared by RTI International-University of North Carolina [RTI-UNC] Evidence-Based Practice Center under Contract No. 290-02-0016I.) AHRQ Publication No. 11-EHC056-EF. Rockville, MD: Agency for Healthcare Research and Quality. September 2011. Accessed December 9, 2013. Available at: http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1010&PC=mhb

58. Gelenberg AJ, Freeman MP, Markowitz JC, Rosenbaum JF, Thase ME, Trivedi MH, et al. American Psychiatric Association (APA). Practice guideline for the treatment of patients with major depressive disorder. 3rd Edition. November 2010. Accessed December 9, 2013. Available at URL address: http://psychiatryonline.org/guidelines.aspx

59. George MS, Lisanby SH, Avery D, McDonald WM, Durkalski V, Pavlicova M, et al. Left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: a sham-controlled randomized trial. Arch Gen Psychiatry. 2010 May;67(5):507-16.

60. George MS, Taylor JJ, Short EB. The expanding evidence base for rTMS treatment of depression. Curr Opin Psychiatry. 2013 Jan;26(1):13-8. doi: 10.1097/YCO.0b013e32835ab46d.

61. Gooch CL, Brannagan TH, Pullman SL, Weimer LH. Electromyography, nerve conduction studies, and magnetic stimulation. In: Rowland LP, editor. Merritt's Neurology. 12th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010. Ch. 16.

62. Grisaru N, Chudakov B, Yaroslavsky Y, Belmaker RH. Transcranial magnetic stimulation in mania: a controlled study. Am J Psychiatry. 1998 Nov;155(11):1608-10.

63. Gross M, Nakamura L, Pascual-Leone A, Fregni F. Has repetitive transcranial magnetic stimulation (rTMS) treatment for depression improved? A systematic review and meta-analysis comparing the recent vs. the earlier rTMS studies. Acta Psychiatr Scand. 2007 Sep;116(3):165-73.

64. Grunhaus L, Schreiber S, Dolberg OT, Polak D, Dannon PN. A randomized controlled comparison of electroconvulsive therapy and repetitive transcranial magnetic stimulation in severe and resistant nonpsychotic major depression. Biol Psychiatry. 2003 Feb 15;53(4):324-31.

65. Grunhaus L, Dannon PN, Schreiber S, Dolberg OH, Amiaz R, Ziv R, Lefkifker E. Repetitive transcranial magnetic stimulation is as effective as electroconvulsive therapy in the treatment of nondelusional major depressive disorder: an open study. Biol Psychiatry. 2000 Feb 15;47(4):314-24.

66. Guo J, Zhou M, Yang M, Zhu C, He L. Repetitive transcranial magnetic stimulation for the treatment of amyotrophic lateral sclerosis or motor neuron disease. Cochrane Database Syst Rev. 2011 Sep 7;9:CD008554.

67. Guse B, Falkai P, Wobrock T. Cognitive effects of high-frequency repetitive transcranial magnetic stimulation: a systematic review. J Neural Transm. 2010 Jan;117(1):105-22.

68. Hadley D, Anderson BS, Borckardt JJ, Arana A, Li X, Nahas Z,et al. Safety, tolerability, and effectiveness of high doses of adjunctive daily left prefrontal repetitive transcranial magnetic stimulation for treatment-resistant depression in a clinical setting. J ECT. 2011 Mar;27(1):18-25.

69. Hansen PE, Ravnkilde B, Videbech P, Clemmensen K, Sturlason R, Reiner M, et al. Low-frequency repetitive transcranial magnetic stimulation inferior to electroconvulsive therapy in treating depression. J ECT. 2011 Mar;27(1):26-32.

70. Hartelius L, Svantesson P, Hedlund A, Holmberg B, Revesz D, Thorlin T. Short-term effects of repetitive transcranial magnetic stimulation on speech and voice in individuals with Parkinson's disease. Folia Phoniatr Logop. 2010;62(3):104-9.

71. Hausmann A, Kemmler G, Walpoth M, Mechtcheriakov S, Kramer-Reinstadler KK, Lechner T et al. No benefit derived from repetitive transcranial magnetic stimulation in depression: a prospective, single center, randomized, double blind, sham controlled "add on" trial. J Neurol Neurosurg Psychiatry. 2004;75:320-2.

72. Henkin RI, Potolicchio SJ Jr, Levy LM. Improvement in smell and taste dysfunction after repetitive transcranial magnetic stimulation. Am J Otolaryngol. 2011 Jan-Feb;32(1):38-46.

73. Herwig U, Fallgatter AJ, Höppner J, Eschweiler GW, Kron M, Hajak G, et al. Antidepressant effects of augmentative transcranial magnetic stimulation: randomised multicentre trial. Br J Psychiatry. 2007 Nov;191:441-8.

74. Hoffman RE, Hawkins KA, Guorguieva R, Boutros NN, Rachid F, Carroll K et al. Transcranial magnetic stimulation of left temporoparietal cortex and medication-resistant auditory hallucinations. Arch Gen Psychiatry. 2003 Jan;60:49-56.

75. Janicak PG, Nahas Z, Lisanby SH, Solvason HB, Sampson SM, McDonald WM, et al. Durability of clinical benefit with transcranial magnetic stimulation (TMS) in the treatment of pharmacoresistant major depression: assessment of relapse during a 6-month, multisite, open-label study. Brain Stimul. 2010 Oct;3(4):187-99.

76. Janicak PG, Dowd SM, Martis B, Alam D, Beedle D, Krasuski J, et al. Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for major depression: preliminary results of a randomized trial. Biol Psychiatry. 2002; 51:659-67.

77. Janicak PG, O'Reardon JP, Sampson SM, Husain MM, Lisanby SH, Rado JT, et al. Transcranial magnetic stimulation in the treatment of major depressive disorder: a comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction treatment. J Clin Psychiatry. 2008 Feb;69(2):222-32.

78. Kennedy SH, Milev R, Giacobbe P, Ramasubbu R, Lam RW, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT). Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults. IV. Neurostimulation therapies. J Affect Disord. 2009 Oct;117 Suppl 1:S44-53.

79. Keshtkar M, Ghanizadeh A, Firoozabadi A. Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for the treatment of major depressive disorder, a randomized controlled clinical trial. J ECT. 2011 Dec;27(4):310-4.

80. Khaleel SH, Bayoumy IM, El-Nabil LM, Moustafa RR. Differential hemodynamic response to repetitive transcranial magnetic stimulation in acute stroke patients with cortical versus subcortical infarcts. Eur Neurol. 2010;63(6):337-42.

81. Khedr EM, Abo-Elfetoh N. Therapeutic role of rTMS on recovery of dysphagia in patients with lateral medullary syndrome and brainstem infarction. J Neurol Neurosurg Psychiatry. 2010 May;81(5):495-9.

82. Khedr EM, Ahmed MA, Fathy N, Rothwell JC. Therapeutic trial of repetitive transcranial magnetic stimulation after acute ischemic stroke. Neurology. 2005 Aug 9;65(3):466-8.

83. Khedr EM, Rothwell JC, Ahmed MA, El-Atar A. Effect of daily repetitive transcranial magnetic stimulation for treatment of tinnitus: comparison of different stimulus frequencies. J Neurol Neurosurg Psychiatry. 2008 Feb;79(2):212-5.

84. Khedr EM, Etraby AE, Hemeda M, Nasef AM, Razek AA. Long-term effect of repetitive transcranial magnetic stimulation on motor function recovery after acute ischemic stroke. Acta Neurol Scand. 2010 Jan;121(1):30-7.

85. Khedr EM, Abo-Elfetoh N, Rothwell JC. Treatment of post-stroke dysphagia with repetitive transcranial magnetic stimulation. Acta Neurol Scand. 2009 Mar;119(3):155-61.

86. Kim BR, Kim DY, Chun MH, Yi JH, Kwon JS. Effect of repetitive transcranial magnetic stimulation on cognition and mood in stroke patients: a double-blind, sham-controlled trial. Am J Phys Med Rehabil. 2010 May;89(5):362-8.

87. Kleinjung T, Eichhammer P, Langguth B, Jacob P, Marienhagen J, Hajak G, et al. Long-term effects of repetitive transcranial magnetic stimulation (rTMS) in patients with chronic tinnitus**.** Otolaryngol Head Neck Surg. 2005 Apr;132(4):566-9.

88. Koran LM, Hanna GL, Hollander E, Nestadt G, Simpson HB; American Psychiatric Association. Practice guideline for the treatment of patients with obsessive-compulsive disorder. Am J Psychiatry. 2007 Jul;164(7 Suppl):5-53.

89. Kozel FA, George MS. Meta-analysis of left prefrontal repetitive transcranial magnetic stimulation (rTMS) to treat depression. J Psychiatr Pract. 2002 Sep;8(5):270-5.

90. Kranz G, Shamim EA, Lin PT, Kranz GS, Hallett M. Transcranial magnetic brain stimulation modulates blepharospasm: a randomized controlled study. Neurology. 2010 Oct 19;75(16):1465-71.

91. Krieg SM, Shiban E, Buchmann N, Gempt J, Foerschler A, Meyer B, Ringel F. Utility of presurgical navigated transcranial magnetic brain stimulation for the resection of tumors in eloquent motor areas. J Neurosurg. 2012 May;116(5):994-1001.

92. Krieg SM, Shiban E, Buchmann N, Meyer B, Ringel F. Presurgical navigated transcranial magnetic brain stimulation for recurrent gliomas in motor eloquent areas. Clin Neurophysiol. 2013 Mar;124(3):522-7.

93. Kumru H, Murillo N, Samso JV, Valls-Sole J, Edwards D, Pelayo R, 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.

94. Kwon HJ, Lim WS, Lim MH, Lee SJ, Hyun JK, Chae JH, et al. 1-Hz low frequency repetitive transcranial magnetic stimulation in children with Tourette's syndrome. Neurosci Lett. 2011 Mar 29;492(1):1-4.

95. Lam RW, Chan P, Wilkins-Ho M, Yatham LN. Repetitive transcranial magnetic stimulation for treatment-resistant depression: a systematic review and metaanalysis. Can J Psychiatry. 2008 Sep;53(9):621-31.

96. Landgrebe M, Binder H, Koller M, Eberl Y, Kleinjung T, Eichhammer P, et al. Design of a placebo-controlled, randomized study of the efficacy of repetitive transcranial magnetic stimulation for the treatment of chronic tinntius. BMC Psychiatry. 2008 Apr 15;8:23.

97. Lehman AF, Lieberman JA, Dixon LB, McGlashan TH, Miller AL, Perkins DO, Kreyenbuhl J; American Psychiatric Association; Steering Committee on Practice Guidelines. Practice guideline for the treatment of patients with schizophrenia. 2004. Accessed December 9, 2013. Available at URL address: http://psychiatryonline.org/guidelines.aspx

98. Lim JY, Kang EK, Paik NJ. Repetitive transcranial magnetic stimulation to hemispatial neglect in patients after stroke: an open-label pilot study. J Rehabil Med. 2010 May;42(5):447-52.

99. Lipton RB, Dodick DW, Silberstein SD, Saper JR, Aurora SK, Pearlman SH, et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial. Lancet Neurol. 2010 Apr;9(4):373-80.

100. Lisanby SH, Husain MM, Rosenquist PB, Maixner D, Gutierrez R, Krystal A, et al. Daily left prefrontal repetitive transcranial magnetic stimulation in the acute treatment of major depression: clinical predictors of outcome in a multisite, randomized controlled clinical trial. Neuropsychopharmacology. 2009 Jan;34(2):522-34.

101. Loo CK, Mitchell PB, McFarquhar TF, Malhi GS, Sachdev PS. A sham-controlled trial of the efficacy and safety of twice-daily rTMS in major depression. Psychol Med. 2007 Mar;37(3):341-9.

102. Loo CK, Mitchell PB, Croker VM, Malhi GS, Wen W, Gandevia SC, Sachdev PS. Double-blind controlled investigation of bilateral prefrontal transcranial magnetic stimulation for the treatment of resistant major depression. Psychol Med. 2003 Jan;33(1):33-40.

103. Loo C, Mitchell P, Sachdev P, McDarmont B, Parker G, Gandevia S. Double-blind controlled investigation of transcranial magnetic stimulation for the treatment of resistant major depression. Am J Psychiatry. 1999 June;156(6):946-8.

104. Loo CK, Sainsbury K, Mitchell P, Hadzi-Pavlovic D, Sachdev PS. A sham-controlled trial of left and right temporal rTMS for the treatment of auditory hallucinations. Psychol Med. 2010 Apr;40(4):541-6.

105. Lorenz I, Müller N, Schlee W, Langguth B, Weisz N. Short-term effects of single repetitive TMS sessions on auditory evoked activity in patients with chronic tinnitus. J Neurophysiol. 2010 Sep;104(3):1497-505.

106. McDonald WM, Durkalski V, Ball ER, Holtzheimer PE, Pavlicova M, Lisanby SH, et al. Improving the antidepressant efficacy of transcranial magnetic stimulation: maximizing the number of stimulations and treatment location in treatment-resistant depression. Depress Anxiety. 2011 Nov;28(11):973-80. doi: 10.1002/da.20885.

107. McLoughlin DM, Mogg A, Eranti S, Pluck G, Purvis R, Edwards D, et al. The clinical effectiveness and cost of repetitive transcranial magnetic stimulation versus electroconvulsive therapy in severe depression: a multicentre pragmatic randomised controlled trial and economic analysis. Health Technol Assess. 2007 Jul;11(24):1-54.

108. McNamara B, Ray JL, Arthurs OJ, Boniface S. Transcranial magnetic stimulation for depression and other psychiatric disorders. Psychol Med. 2001;31(7):1141-6.

109. Machii K, Cohen D, Ramos-Estebanez C, Pascual-Leone A. Safety of rTMS to non-motor cortical areas in healthy participants and patients. Clin Neurophysiol. 2006 Feb;117(2):455-71.

110. Mäkelä JP, Vitikainen AM, Lioumis P, Paetau R, Ahtola E, Kuusela L, et al. Functional plasticity of the motor cortical structures demonstrated by navigated TMS in two patients with epilepsy. Brain Stimul. 2013 May;6(3):286-91.

111. Mansur CG, Myczkowki ML, de Barros Cabral S, Sartorelli Mdo C, Bellini BB, et al. Placebo effect after prefrontal magnetic stimulation in the treatment of resistant obsessive-compulsive disorder: a randomized controlled trial. Int J Neuropsychopharmacol. 2011 Nov;14(10):1389-97.

112. Mantovani A, Aly M, Dagan Y, Allart A, Lisanby SH. Randomized sham controlled trial of repetitive transcranial magnetic stimulation to the dorsolateral prefrontal cortex for the treatment of panic disorder with comorbid major depression. J Affect Disord. 2012b Aug 1. [Epub ahead of print]

113. Mantovani A, Pavlicova M, Avery D, Nahas Z, McDonald WM, Wajdik CD, et al. Long-term efficacy of repeated daily prefrontal transcranial magnetic stimulation (TMS) in treatment-resistant depression. Depress Anxiety. 2012a Oct;29(10):883-90. doi: 10.1002/da.21967.

114. Mantovani A, Simpson HB, Fallon BA, Rossi S, Lisanby SH. Randomized sham-controlled trial of repetitive transcranial magnetic stimulation in treatment-resistant obsessive-compulsive disorder. Int J Neuropsychopharmacol. 2010 Mar;13(2):217-27.

115. Marcondes RA, Sanchez TG, Kii MA, Ono CR, Buchpiguel CA, Langguth B, et al. Repetitive transcranial magnetic stimulation improve tinnitus in normal hearing patients: a double-blind controlled, clinical and neuroimaging outcome study. Eur J Neurol. 2010 Jan;17(1):38-44.

116. 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. 2012 May 28. doi: 10.1111/j.1533-2500.2012.00562.x. [Epub ahead of print]

117. Martin JLR, Barbanoj MJ, Schaelpfer TE, Thompson E, Pérez V, Kulisevsky J. Repetitive transcranial magnetic stimulation for the treatment of depression. Systematic review and meta-analysis. Br J Psychiatry. 2003b;182:480-91.

118. Matheson SL, Green MJ, Loo C, Carr VJ. Quality assessment and comparison of evidence for electroconvulsive therapy and repetitive transcranial magnetic stimulation for schizophrenia: a systematic meta-review. Schizophr Res. 2010 May;118(1-3):201-10.

119. Medina FJ, Túnez I. Huntington's disease: the value of transcranial meganetic stimulation. Curr Med Chem. 2010;17(23):2482-91.

120. Meng Z, Liu S, Zheng Y, Phillips JS. Repetitive transcranial magnetic stimulation for tinnitus. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD007946.

121. Minichino A, Bersani FS, Capra E, Pannese R, Bonanno C, Salviati M, et al. ECT, rTMS, and deepTMS in pharmacoresistant drug-free patients with unipolar depression: a comparative review. Neuropsychiatr Dis Treat. 2012;8:55-64.

122. Miniussi C, Bonato C, Bignotti S, Gazzoli A, Gennarelli M, Pasqualetti P, et al. Repetitive transcranial magnetic stimulation (rTMS) at high and low frequency: an efficacious therapy for major drug-resistant depression? Clin Neurophysiol. 2005 May;116(5):1062-71.

123. Mishra BR, Nizamie SH, Das B, Praharaj SK. Efficacy of repetitive transcranial magnetic stimulation in alcohol dependence: a sham-controlled study. Addiction. 2010 Jan;105(1):49-55.

124. Mitchell J, Trangle M, Degnan B, Gabert T, Haight B, Kessler D, et al. Institute for Clinical Systems Improvement. Adult Depression in Primary Care. Updated September 2013.

125. Miyasaki JM, Shannon K, Voon V, Ravina B, Kleiner-Fisman G, Anderson K, et al.; Quality Standards Subcommittee of the American Academy of Neurology. Practice Parameter: evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Apr 11;66(7):996-1002.

126. Mogg A, Pluck G, Eranti SV, Landau S, Purvis R, Brown RG, et al. A randomized controlled trial with 4-month follow-up of adjunctive repetitive transcranial magnetic stimulation of the left prefrontal cortex for depression. Psychol Med. 2008 Mar;38(3):323-33.

127. National Alliance on Mental Illness. Treatment and Services.Transcranial Magnetic Stimulation (TMS). August 2012. Accessed December 9, 2013. Available at URL address: http://www.nami.org/Content/NavigationMenu/Inform_Yourself/About_Mental_Illness/About_Treatments_and_Supports/Transcranial_Magnetic_Stimulation_(rTMS).htm

128. National Institute for Excellence (NICE). Transcranial magnetic stimulation for severe depression. Interventional Procedure (IP) Number: 346 IP Guidance Number: IPG242. November 28, 2007. Accessed December 9, 2013. Available at URL address: http://www.nice.org.uk/

129. NeuroStar TMS Therapy® Accessed December 9, 2013. Available at URL address: http://www.neurostartms.com/Home.aspx

130. New England Comparative Effectiveness Public Advisory Council (CEPAC). Coverage Policy Analysis: Repetitive Transcranial Magnetic Stimulation (rTMS). Completed by the Institute for Clinical and Economic Review (ICER). June 2012. Accessed December 9, 2013. Available at URL address: http://cepac.icer-review.org/?page_id=140

131. New England Comparative Effectiveness Public Advisory Council (CEPAC). Repetitive Transcranial Magnetic Stimulation: Supplementary Data and Analyses to the Comparative Effectiveness Review of the Agency for Healthcare Research and Quality. December 22, 2011. Accessed December 9, 2013. Available at URL address: http://cepac.icer-review.org/?s=tms

132. O'Connell NE, Wand BM, Marston L, Spencer S, Desouza LH. Non-invasive brain stimulation techniques for chronic pain. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD008208.

133. O'Connell NE, Wand BM, Marston L, Spencer S, Desouza LH. Non-invasive brain stimulation techniques for chronic pain. A report of a Cochrane systematic review and meta-analysis. Eur J Phys Rehabil Med. 2011 Jun;47(2):309-26. Epub 2011 Apr 14.

134. O'Reardon JP, Solvason HB, Janicak PG, Sampson S, Isenberg KE, Nahas Z, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. Biol Psychiatry. 2007 Dec 1;62(11):1208-16.

135. Pal E, Nagy F, Aschermann Z, Balazs E, Kovacs N. The impact of left prefrontal repetitive transcranial magnetic stimulation on depression in Parkinson's disease: a randomized, double-blind, placebo-controlled study. Mov Disord. 2010 Oct 30;25(14):2311-7.

136. Pallanti S, Bernardi S, Di Rollo A, Antonini S, Quercioli L. Unilateral low frequency versus sequential bilateral repetitive transcranial magnetic stimulation: is simpler better for treatment of resistant depression? Neuroscience. 2010 May 5;167(2):323-8.

137. Picarelli H, Teixeira MJ, de Andrade DC, Myczkowski ML, Luvisotto TB, Yeng LT, et al. Repetitive transcranial magnetic stimulation is efficacious as an add-on to pharmacological therapy in complex regional pain syndrome (CRPS) type I. J Pain. 2010 Nov;11(11):1203-10.

138. Plewnia S, Bartels M, Gerloff C. Transient suppression of tinnitus by transcranial magnetic stimulation. Ann Neurol. 2003 Feb;53(2):263-6.

139. Picht T, Schmidt S, Brandt S, Frey D, Hannula H, Neuvonen T, et al. Preoperative functional mapping for rolandic brain tumor surgery: comparison of navigated transcranial magnetic stimulation to direct cortical stimulation. Neurosurgery. 2011 Sep;69(3):581-8; discussion 588.

140. Picht T, Schulz J, Hanna M, Schmidt S, Suess O, Vajkoczy P. Assessment of the influence of navigated transcranial magnetic stimulation on surgical planning for tumors in or near the motor cortex. Neurosurgery. 2012 May;70(5):1248-56; discussion 1256-7.

141. Picht T, Krieg SM, Sollmann N, Rösler J, Niraula B, Neuvonen T, 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.

142. Pridmore S, Bruno R, Turnier-Shea Y, Reid P, Rybak M. Comparison of unlimited numbers of rapid transcranial magnetic stimulation (rTMS) and ECT treatment sessions in major depressive episode. Int J Neuropsychopharmacol. 2000 Jun;3(2):129-134.

143. Rasmussen KG. Some considerations in choosing electroconvulsive therapy versus transcranial magnetic stimulation for depression. J ECT. 2011 Mar;27(1):51-4.

144. Ray S, Nizamie SH, Akhtar S, Praharaj SK, Mishra BR, Zia-ul-Haq M. Efficacy of adjunctive high frequency repetitive transcranial magnetic stimulation of left prefrontal cortex in depression: a randomized sham controlled study. J Affect Disord. 2011 Jan;128(1-2):153-9.

145. Rowny SB, Lisanby SH. Other brain stimulation methods. In: Sadock BJ, Sadock VA, editors. Kaplan Sadock Psychiatry. 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009. Part 31.34b.

146. Rodriguez-Martin JL, Barbanoj JM, Pérez V, Sacristan M. Transcranial magnetic stimulation for the treatment of obsessive-compulsive disorder. Cochrane Database of Systematic Reviews 2003, Issue 2. Art. No.: CD003387. DOI: 10.1002/14651858.CD003387.

147. Rosa MA, Gattaz WF, Pascual-Leone A, Fregni F, Rosa MO, Rumi DO, et al. Comparison of repetitive transcranial magnetic stimulation and electroconvulsive therapy in unipolar non-psychotic refractory depression: a randomized, single-blind study. Int J Neuropsychopharmacol. 2006 Dec;9(6):667-76.

148. Rosenberg O, Zangen A, Stryjer R, Kotler M, Dannon PN. Response to deep TMS in depressive patients with previous electroconvulsive treatment. Brain Stimul. 2010 Oct;3(4):211-7.

149. Rossi S, De Capua A, Ulivelli M, Bartalini S, Falzarano V, Filippone G, et al. Effects of repetitive transcranial magnetic stimulation on chronic tinnitus: a randomised, crossover, double blind, placebo controlled study. J Neurol Neurosurg Psychiatry. 2007 Aug;78(8):857-63.

150. Rossini D, Lucca A, Zanardi R, Magri L, Smeraldi E. Transcranial magnetic stimulation in treatment-resistant depressed patients: a double-blind, placebo-controlled trial. Psychiatry Res. 2005 Nov 15;137(1-2):1-10.

151. The Royal Australian and New Zealand College of Psychiatrists. Position Statement 79. Repetitive Transcranial Magentic Stimulation (TMS). Accessed December 9, 2013. Available at URL address: http://www.ranzcp.org/

152. Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, et al. Acute and longer-term outcomes in depressed outpatients requiring one of several treatment steps: A STAR*D report. Am J Psych, 2006 163, 1905-1917.

153. Sampson SM, Kung S, McAlpine DE, Sandroni P. The use of slow-frequency prefrontal repetitive transcranial magnetic stimulation in refractory neuropathic pain. J ECT. 2011 Mar;27(1):33-7.

154. Schneider SA, Pleger B, Draganski B, Cordivari C, Rothwell JC, Bhatia KP, et al. Modulatory effects of 5Hz rTMS over the primary somatosensory cortex in focal dystonia--an fMRI-TMS study. Mov Disord. 2010 Jan 15;25(1):76-83.

155. Schonfeldt-Lecuona C, Gron G, Walter H, Buchler N, Wunderlich A, Spitzer M et al. Stereotaxic rTMS for the treatment of auditory hallucinations in schizophrenia. Neuro Report. 2004 July 19; 15(10): 1669-73.

156. Schulze-Rauschenbach SC, Harms U, Schlaepfer TE, Maier W, Falkai P, Wagner M. Distinctive neurocognitive effects of repetitive transcranial magnetic stimulation and electroconvulsive therapy in major depression. Br J Psychiatry. 2005 May;186:410-6.

157. Schutter DJ. Antidepressant efficacy of high-frequency transcranial magnetic stimulation over the left dorsolateral prefrontal cortex in double-blind sham-controlled designs: a meta-analysis. Psychol Med. 2009 Jan;39(1):65-75.

158. Schutter DJ, van Honk J. A framework for targeting alternative brain regions with repetitive transcranial magnetic stimulation in the treatment of depression. J Psychiatry Neurosci. 2005 Mar;30(2):91-7.

159. Slotema CW, Blom JD, Hoek HW, Sommer IE. Should we expand the toolbox of psychiatric treatment methods to include Repetitive Transcranial Magnetic Stimulation (rTMS)? A meta-analysis of the efficacy of rTMS in psychiatric disorders. J Clin Psychiatry. 2010 Jul;71(7):873-84.

160. Slotema CW, Blom JD, de Weijer AD, Diederen KM, Goekoop R, Looijestijn J, et al. Can low-frequency repetitive transcranial magnetic stimulation really relieve medication-resistant auditory verbal hallucinations? Negative results from a large randomized controlled trial. Biol Psychiatry. 2011 Mar 1;69(5):450-6.

161. Sokhadze E, Baruth J, Tasman A, Mansoor M, Ramaswamy R, Sears L, et al. Low-frequency repetitive transcranial magnetic stimulation (rTMS) affects event-related potential measures of novelty processing in autism. Appl Psychophysiol Biofeedback. 2010 Jun;35(2):147-61.

162. Soler MD, Kumru H, Pelayo R, Vidal J, Tormos JM, Fregni F, Navarro X, Pascual-Leone A. Effectiveness of transcranial direct current stimulation and visual illusion on neuropathic pain in spinal cord injury. Brain. 2010 Sep;133(9):2565-77.

163. Steeves T, McKinlay BD, Gorman D, Billinghurst L, Day L, Carroll A, et al. Canadian guidelines for the evidence-based treatment of tic disorders: behavioural therapy, deep brain stimulation, and transcranial magnetic stimulation. Can J Psychiatry. 2012 Mar;57(3):144-51.

164. 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.

165. Takeuchi N, Tada T, Toshima M, Ikoma K. Correlation of motor function with transcallosal and intracortical inhibition after stroke. J Rehabil Med. 2010 Nov;42(10):962-6.

166. Tarapore PE, Tate MC, Findlay AM, Honma SM, Mizuiri D, Berger MS, Nagarajan SS. Preoperative multimodal motor mapping: a comparison of magnetoencephalography imaging, navigated transcranial magnetic stimulation, and direct cortical stimulation. J Neurosurg. 2012 Aug;117(2):354-62.

167. Taylor JJ, Borckardt JJ, George MS. Endogenous opioids mediate left dorsolateral prefrontal cortex rTMS-induced analgesia. Pain. 2012 Jun;153(6):1219-25.

168. Teepker M, Hötzel J, Timmesfeld N, Reis J, Mylius V, Haag A, et al. Low-frequency rTMS of the vertex in the prophylactic treatment of migraine. Cephalalgia. 2010 Feb;30(2):137-44.

169. Triggs WJ, Ricciuti N, Ward HE, Cheng J, Bowers D, Goodman WK, et al. Right and left dorsolateral pre-frontal rTMS treatment of refractory depression: a randomized, sham-controlled trial. Psychiatry Res. 2010 Aug 15;178(3):467-74.

170. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH Guidance for industry and Food and Drug Administration staff. Class II special controls guidance document: repetitive transcranial magnetic stimulation (rTMS) systems. Rockville (MD); 2011 Jul 26. Accessed December 9, 2013. Available at URL address: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM265272.pdf

171. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Search Devices@FDA. NeuroStar® TMS System. Neuronetics. K061053. Date approved October 7, 2008. Correction March 23, 2011. Accessed December 9, 2013. Available at: http://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/

172. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Search Devices@FDA. Brainsway Deep TMS System. K122288. Date approved January 7, 2013. Accessed December 10, 2013. Available at: http://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/

173. U.S. Food and Drug Administration (FDA). FDA Executive Summary. Neurological Devices Panel of the Medical Devices Advisory Committee. January 26, 2007.Accessed December 9, 2013. Available at: http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4273b1_01-FDAExecutiveSummary.pdf

174. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health. Brief Summary from the Neurological Devices Panel Meeting - January 26, 2007. Updated March 3, 2009. Accessed December 9, 2013. Available at URL address: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/NeurologicalDevicesPanel/ucm124779.htm

175. U.S. Food and Drug Administration (FDA). FDA News Release. December 13, 2013. FDA allows marketing of first device to relieve migraine headache pain. Accessed December 17, 2013. Available at URL address: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm378608.htm

176. U.S. National Institutes of Health (NIH). Transcranial magnetic stimulation: multiple clinical trials. Accessed December 9, 2013. Available at URL address: http://www.clinicaltrials.gov/ct/search?term=transcranial+magnetic+stimulation

177. Van den Eynde F, Claudino AM, Mogg A, Horrell L, Stahl D, Ribeiro W, et al. Repetitive transcranial magnetic stimulation reduces cue-induced food craving in bulimic disorders. Biol Psychiatry. 2010 Apr 15;67(8):793-5.

178. Weiduschat N, Thiel A, Rubi-Fessen I, Hartmann A, Kessler J, Merl P, et al. Effects of repetitive transcranial magnetic stimulation in aphasic stroke: a randomized controlled pilot study. Stroke. 2011 Feb;42(2):409-15.

179. Zheng H, Zhang L, Li L, Liu P, Gao J, Liu X, et al. High-frequency rTMS treatment increases left prefrontal myo-inositol in young patients with treatment-resistant depression. Prog Neuropsychopharmacol Biol Psychiatry. 2010 Oct 1;34(7):1189-95.