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Rapid transcranial magnetic stimulation for stroke rehabilitation

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PRIORITISING SUMMARY

REGISTER ID: **000291**

NAME OF TECHNOLOGY: **RAPID TRANSCRANIAL MAGNETIC STIMULATION FOR STROKE REHABILITATION**

PURPOSE AND TARGET GROUP: **TREATMENT FOR MOTOR FUNCTION IN STROKE PATIENTS**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☒	Yes	ARTG number	23492
☐	No		
☐	Not applicable		

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United Kingdom	✓		
Korea	✓		
Italy	✓		
Japan	✓		

IMPACT SUMMARY:

This prioritising summary presents results of the use of rapid transcranial magnetic stimulation (rTMS) with the Magstim Rapid^2 device for the treatment and rehabilitation of stroke patients. This device is manufactured by Magstim Company Ltd and is approved for clinical research use in the United States (personal communication, Magstim). The Magstim Rapid^2 is currently available in Australia for research purposes only.

BACKGROUND

An important factor in the recovery of motor function after stroke is central nervous system reorganisation, a process termed plasticity. rTMS may speed up or enhance plasticity, improving recovery by the induction of electrical activity on the surface of the brain (cortex). Magnetic stimulators induce electrical currents in tissues using a non-invasive stimulating coil at frequencies of up to 100Hz. The stimulating coil is placed near the intended site of stimulation and brief magnetic pulses are emitted

(Magstim 2007). When the brain is stimulated transcranially in this manner a complex sequence of events occur with excitatory and inhibitory effects on the corticospinal or corticocortical pathways (Alisauskliene et al 2005). Brain activity is triggered or modulated by rTMS without the need for surgery or external electrodes.

When utilised for stroke rehabilitation, rTMS is delivered to the brain by passing a strong brief electrical current through an insulated wired coil placed on the skull. The current generates a transient magnetic field in the brain inducing electric currents in the cortex that flow parallel to the coil.

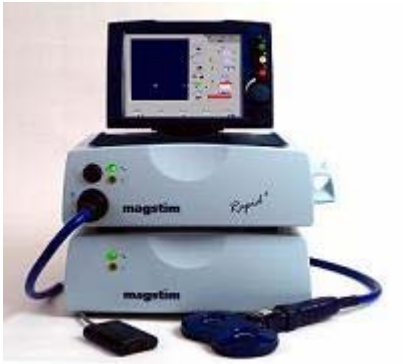

Figure 1 The Magstim Rapid² (printed with permission Magstim Company Ltd)

Depending on the frequency, duration of the stimulation, the shape of the coil, and the strength of the magnetic field, rTMS can activate or suppress activity in cortical regions inducing both short- and long-term changes of cortical activity (Hummel and Cohen 2006 and Alisauskiene et al 2005). A variety of standard stimulating coils, custom coils and output waveforms are available to suit different areas of application (Magstim 2007).

CLINICAL NEED AND BURDEN OF DISEASE

Stroke poses a significant burden on patients and their families as well as on the health system and aged care services. In 2003, there were 9,006 deaths from stroke in Australia accounting for approximately 7 per cent of all deaths. There is no national information on the incidence of stroke. In 2003 there were an estimated 346,700 survivors of stroke with approximately 146,400 of these individuals experiencing a disability as a result of stroke. In 2002–03 there were 68,866 hospital separations with a principal diagnosis of stroke; its sequelae, and rehabilitation for stroke or its sequelae, accounting for 1,073,645 patient days. There were an estimated 269,000 general practice visits for stroke associated conditions per year over the period April 1998–March 2004. It is expected that the ageing of the Australian population will result in an increase in the number of strokes in the future (AIHW 2006).

DIFFUSION

Currently, in Australia, the use of rTMS is limited to research purposes and has not yet diffused into clinical practice.

COMPARATORS

There are several electromagnetic brain stimulation techniques available which employ both invasive and non-invasive delivery methods. These include electroconvulsive therapy, transcutaneous electrical nerve stimulation, vagus nerve stimulation, deep brain stimulation and transcranial direct current stimulation. However, these techniques are not employed for stroke rehabilitation.

Rehabilitation in stroke patients aims to both prevent deterioration of, and improve, motor function and promote the highest possible level of physical, psychological and social independence. It involves the combined use of medical, nursing and allied health services, along with social, educational and vocational services to provide individual assessment, treatment, regular review, discharge planning and follow-up (AIHW 2006).

EFFECTIVENESS AND SAFETY ISSUES

Four high level studies (level II intervention evidence) were identified that assessed the effectiveness of rTMS on the damaged brain cortex for the improvement of motor recovery after stroke. The patient's ability to perform different physical tasks was the main form of assessment. There are some methodological concerns with some of the trials due to the small numbers of patients and the physical task training techniques patients underwent. It is acknowledged that the effect of practice of these physical tasks in stroke patients might be greater when compared to healthy controls (Mansur et al 2005).

A small study of 20 stroke patients (level II intervention evidence) compared the effect of rTMS with the Magstim at 1Hz (n=10) on hand function, to a control group (n=10) who received sham stimulation (Takeuchi et al 2005). Patients were tested ≥6 months post stroke. Prior to randomisation patients were given motor training (pinch force and acceleration) to be assessed at baseline, post-training, pre-rTMS and post-rTMS (immediately after and at 30 minutes post-rTMS). The maximum pinch force of the affected hand was measured using a pinch gauge and movement acceleration was measured with a monoaxial accelerometer. A repeated measure ANOVA for motor function showed no difference between the rTMS and control group in motor training. No adverse side effects were reported during the course of the study.

In another study (level II intervention evidence) fifteen patients who had experienced a stroke were instructed to perform a complex, sequential finger motor task either after rTMS at 10Hz or sham treatment over the contralateral primary motor cortex

(Kim et al 2006). An inclusion criterion for this study was that patients must have experienced a stroke at least three months prior to randomisation. This study differs to that conducted by Takeuchi et al in that it examined the effects of *high-frequency* rTMS (10Hz). Patients treated with Magstim rTMS demonstrated statistically significant faster and more accurate finger movement when compared to sham stimulated patients ($p<0.05$).

The largest study published to date reports on rTMS (10x ten second pulse of 3 Hz stimulation with 50 seconds between each pulse) applied daily in 26 patients and compared to 26 patients receiving sham treatment (level II intervention evidence). The application of rTMS was combined with normal rehabilitative treatment, including physical and drug therapies, for 10 days within the first two weeks after stroke (Khedr et al 2005). This study differs from those conducted by Takeuchi et al and Kim at al as the rTMS intervention was administered soon after stroke (within 2 weeks) rather than 3-6 months post stroke. Khedr et al suggests that rTMS would be more beneficial to patients immediately after stroke and may result in earlier discharge from hospital. This study reported that rTMS treated patients demonstrated a statistically significant improvement in motor control when compared to sham treated control patients when assessed by three disability scales ($p<0.0001$).[1]

In a smaller study, 10 stroke patients were given three sessions of rTMS at 1 Hz for ten minutes to the unaffected hemisphere over the primary motor cortex and results were compared to sham treatment in 16 *healthy* patients (level II intervention evidence) (Mansur et al 2005). Patients were studied within the first year after their stroke. All participants underwent four physical tests assessing reaction time and physical movement. Treatment with the Magstim demonstrated significant improvement in all four physical tasks ($p<0.05$) compared to no significant changes in any of the tasks in the healthy control group participants.

COST IMPACT

The cost of the Magstim device is approximately US$30-40,000. There are no data available on the cost impact of rTMS with the Magstim for rehabilitation after stroke.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified at the time of preparing this summary.

OTHER ISSUES

The use of rTMS is currently being investigated in numerous research studies and clinical trials are being conducted for various clinical applications including the treatment of depression (Eranti et al 2007, National Insitutes of Health 2007 and

[1] The scales were the Scandinavian Stroke Scale (SSS), the National Institute of Health (NIH) Scale and the Barthel Score (BS).

personal email communication Magstim). The manufacturer is also investigating the use of rTMS in the functional assessment of central motor pathways in adults and children and for the early diagnosis, assessment, prognosis and monitoring of nervous diseases such as multiple sclerosis, central motor disorders, motor neurone disease, epilepsy, cervical spondylosis and other spinal injuries (Magstim 2007).

CONCLUSION:

Stroke is a leading cause of adult motor disability with recovery of motor function usually incomplete. There is considerable interest in the use of rTMS in several clinical applications both in Australia and overseas with ongoing clinical trials.

HEALTHPACT ACTION:

An application is currently being considered by the MSAC for the Magstim device for the treatment of refractory depression. It is likely that the company will apply for public funding for the use of the Magstim device to treat stroke patients, therefore HealthPACT has recommended that further assessment of this technology is no longer warranted.

SOURCES OF FURTHER INFORMATION:

AIHW: Senes, S. (2006). *How we manage stroke in Australia. AIHW cat. no. CVD 31.* [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/publications/cvd/hmsa/hmsa.pdf [Accessed 16th January 2007].

Alisauskiene, M., Truffert, A. et al (2005). 'Transcranial magnetic stimulation in clinical practice', *Medicina (Kaunas),* 41 (10), 813-824.

Food and Drug Administration (2007). *510(k)s Final Decisions Rendered for December 2005*. [Internet]. United States Food and Drug Administration. Available from: http://www.fda.gov/cdrh/510k/sumdec05.html [Accessed 16th January 2007].

Hummel, F. C. & Cohen, L. G. (2006). 'Non-invasive brain stimulation: a new strategy to improve neurorehabilitation after stroke?' *Lancet Neurol,* 5 (8), 708-712.

Khedr, E. M., Ahmed, M. A. et al (2005). 'Therapeutic trial of repetitive transcranial magnetic stimulation after acute ischemic stroke', *Neurology,* 65 (3), 466-468.

Kim, Y. H., You, S. H. et al (2006). 'Repetitive transcranial magnetic stimulation-induced corticomotor excitability and associated motor skill acquisition in chronic stroke', *Stroke,* 37 (6), 1471-1476.

Magstim (2007) *Magnetic stimulators.* [Internet]. Available from: http://www.magstim.com/magneticstimulators.html [Accessed 16th Janaury 2007].

Mansur, C. G., Fregni, F. et al (2005). 'A sham stimulation-controlled trial of rTMS of the unaffected hemisphere in stroke patients', *Neurology,* 64 (10), 1802-1804.

National Institutes of Health (2007). *Search Clinical Research Studies Protocol Database* Available from: http://clinicalstudies.info.nih.gov/ [Accessed 16th January 2007].

Takeuchi, N., Chuma, T. et al (2005). 'Repetitive transcranial magnetic stimulation of contralesional primary motor cortex improves hand function after stroke', *Stroke,* 36 (12), 2681-2686.

LIST OF STUDIES INCLUDED

Total number of studies

Level II intervention evidence	4

SEARCH CRITERIA TO BE USED:

Brain Mapping
Motor Cortex/ physiopathology
Transcranial Magnetic Stimulation/ methods