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## Safety of 1 Hz repetitive transcranial magnetic stimulation (rTMS) in patients with titanium skull plates

In the context of rTMS safety guidelines, we would like to bring to the readership's attention a brief report of uncomplicated rTMS of six patients with titanium (Ti) skull plates in the region of the TMS coil.

In an earlier study, we measured whether Ti skull plates could be appreciably heated or displaced by 1 Hz rTMS at 100% machine output (MO). The rationale for that experiment was to identify potential health risks for patients who may have had a craniotomy, and now are scheduled for low frequency rTMS. Included in this group are patients with epilepsy where craniotomy may be performed for placement of intracranial electrodes, seizure focus resection, or lesion biopsy. The safety of rTMS over Ti skull plates may also be relevant for other patient populations, including those with severe head trauma where skull repair may be necessary. Encouragingly, our data showed that Ti skull plates, even if positioned directly beneath the TMS coil, were minimally heated and unlikely to be displaced by a conventional low frequency rTMS protocol (Rotenberg et al., 2007).

Since publication of our ex vivo data, we have applied rTMS to six patients (age 12–47 years) with intractable epilepsy, frequent (>7 per week) seizures, and past craniotomy where the bone flap was secured with Ti skull plates. In all instances, the seizure focus was in the craniotomy region and the skull plates were in close proximity to the TMS coil. All patients were referred for rTMS by their primary epileptologist. The risks of the procedure, including those potentially related to rTMS over Ti skull plates were explained to each patient or the patient's guardian, and written consent was obtained in every case.

Repetitive TMS was applied in daily sessions of 1800 pulses at 1 Hz over the seizure focus with a figure-8 coil ($n = 5$) or with alternating figure-8 and circular coils ($n = 1$) in an instance of a patient with a broad bilateral seizure focus. Stimulation intensity ranged from 55% to 100% MO. Two stimulators were used in this series: (1) a Magstim Rapid$^2$ with a circular (P/N D0029) coil cooled by refrigeration or a figure-8 (P/N 1640-00) air-cooled coil (Magstim Company, Whitland, UK), and (2) a MagPro X100 with a liquid-cooled Cool Coil B-65 (P/N 9016E0491) (Tonica Electronik, Farum, Denmark).

All patients tolerated 1 Hz rTMS well. Physical exam by the TMS operator did not reveal any tenderness, warmth or skin changes around the craniotomy region. No patient complained of focal pain or discomfort in the region of the Ti skull plates during the procedure. Similarly, none complained of pain or discomfort immediately after rTMS, or on any follow up visit (range: 2–36 months) after rTMS. Upon rTMS completion (four or more consecutive sessions) seizure frequency improved in four of six patients, and was unchanged in the remaining two after rTMS. As there were no complications referable to the Ti skull plates in this group, follow-up radiographs were not obtained to confirm that there was no skull plate displacement.

To our knowledge, this is the first series documenting the absence of adverse events related to Ti skull plates in patients undergoing 1 Hz rTMS. Our observation in clinical practice is consistent with the ex vivo data which indicate low Ti plate heating by induced eddy currents, and insufficient force to displace Ti skull plates from secured position in the skull by the interaction of these eddy currents with the external magnetic field. Although the present data are limited to 1 Hz rTMS protocols, a natural extension of our observation is that lower rTMS frequencies (<1 Hz) are also likely to be well-tolerated in the post-craniotomy patient population.

More data will be required to conclude that rTMS in patients with Ti skull plates is definitively minimal risk, and we suggest that the potential health risks of rTMS in the region of implanted metallic cranial components should be included in the standard consent forms. We also encourage our colleagues who have experience with rTMS in patients with implanted cranial metallic components to report their observations so that collective experience may shape future safety guidelines.

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