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NexTalk EUROPE

Leading the Way in Non-Invasive, Navigated Brain Stimulation

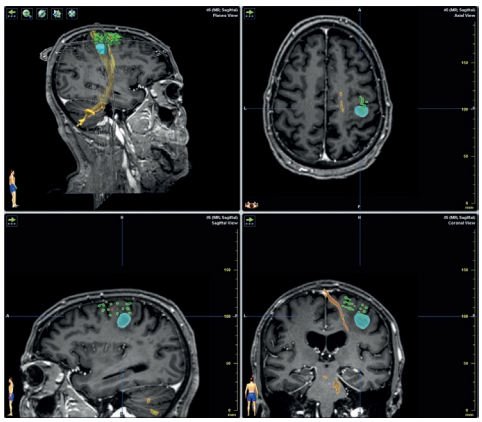
Large TUM study proves that preoperative nTMS mapping leads to better patient outcomes

The neurosurgery team led by Professor Bernhard Meyer at the Technische Universität München (TUM), Germany have had their poster entitled **Preoperative motor mapping by navigated transcranial magnetic brain stimulation improves outcome for motor eloquent lesions** accepted for the 5th International Symposium on NBS in Neurosurgery.

In a large study comparing a prospective cohort of 100 nTMS-mapped patients with a 100-patient historical control arm, the clinicians found that patients in the nTMS group showed a significantly lower rate of residual tumor on postoperative MRI (OR 0.3828; 95% CI 0.2062 – 0.7107). All patients in both groups had motor eloquently located supratentorial lesions.

Of the patients in the nTMS group, 12% had improved postoperative motor function on long-term follow-up, while in the non-nTMS group only 1% had an improvement. Of the patients in the nTMS group, 13% experienced a deterioration in postoperative motor function, compared to 18% in the non-nTMS group. 75% and 81% of patients in the nTMS and non-nTMS groups, respectively, had unchanged motor function after surgery (p=0.0057). Additionally, the nTMS group benefited from significantly smaller craniotomies (nTMS 22.4 ± 8.3 cm2; non-nTMS 26.7 ± 11.3 cm2; p=0.0023).

In their conclusion, the neurosurgeons state, ***"This is the first study to actually prove the value of preoperative motor mapping by nTMS for rolandic lesions in a group comparison study. This work therefore increases the level of evidence for this new modality and we strongly advocate nTMS to become increasingly used for these lesions."***



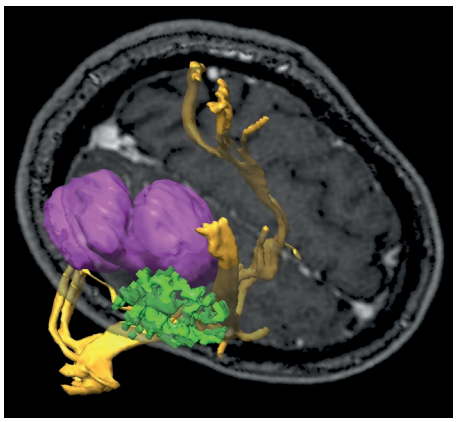


Figure: nTMS mapping results (NBS System, Nexstim Oy) imported into a surgical navigation system for preoperative planning. The tumor volume is drawn in purple/blue and the motor responses to stimulation are indicated by the green markers. The nTMS data visualized even severely impaired functional anatomy, including the corticospinal tract (in yellow), despite the considerable tumor mass.

Images and poster data courtesy of: Jamil Sabih, Lucia Bulubasova, Thomas Obermüller, MD, Chiara Negwer, MD, Insa Janssen, MD, Ehab Shiban, MD, Bernhard Meyer, MD, Florian Ringel, MD and Sandro M. Krieg, MD. Department of Neurosurgery, Klinikum rechts der Isar, Technische Universität München, Munich, Germany.

Potential of Nexstim technology recognized by Finnish Ministers

Navigated Brain Stimulation caught well-deserved attention both by current Finnish Minister for Health and Social Services, Paula Risikko, and Minister for European Affairs and Foreign Trade Alexander Stubb, in separate meetings. Recently, an informational event on stroke was hosted by former government Minister Pertti Savolainen at the Parliament building in Finland. Every year, 14,600 people suffer a stroke for the first time in Finland and 25,000 people live with the effects of stroke. A forerunner in treatment of acute stroke, Finland is today ranked highest in the effective use of thrombolytic therapy in ischemic stroke.

Mr. Stubb, a well-known Finnish, and European first adopter of twitter, tweeted: "Met reps from Nexstim. Ground breaking technology linked to brain stimulation. Impressive, really impressive."

Event to highlight stroke care and rehabilitation arranged at the Parliament building, Finland.

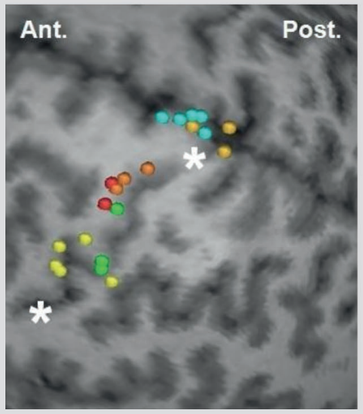
ALSO IN THIS ISSUE

Epilepsy workshop shared latest findings on NBS

In September, Helsinki University Central Hospital (HUCH) hosted a special workshop on the use of NBS in epilepsy surgery, bringing together 20 experts in the field to share their experiences and plans for the future. HUCH has extensive experience in pediatric epilepsy surgery, having operated on more than 250 pediatric patients since 1991. Pediatric neurologist Eija Gaily, Associate Professor, Chief of the HUCH Epilepsy Unit and Dr. Jyrki Mäkelä, Head of Biomag Laboratory, HUS Medical Imaging Center - and one of the world's most experienced NBS-users - summarized their experiences with NBS motor and speech mapping in epilepsy. Neurosurgeon Aki Laakso, Associate Professor in Neurosurgery and Neurobiology reviewed the positive contribution NBS has made to surgical planning and workflow at HUCH Department of Neurosurgery.

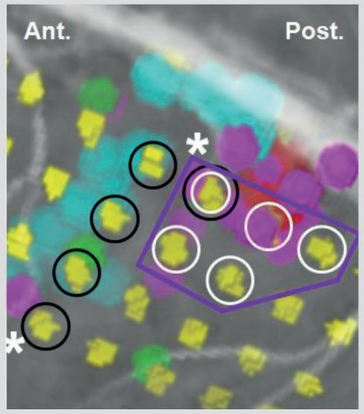
Also in epilepsy patients, it was reported that good concordance has been found between NBS and direct stimulation in motor mapping. The preliminary results of NBS speech mapping in pediatric patients have also shown good concordance with invasive mapping. Epilepsy can potentially impact NBS: in one patient a frequently discharging epileptic focus confounded the mapping results due to inhibition of nearby motor cortex.

NBS, MEG and ECS investigations in a 16-year-old girl scheduled for epilepsy surgery.

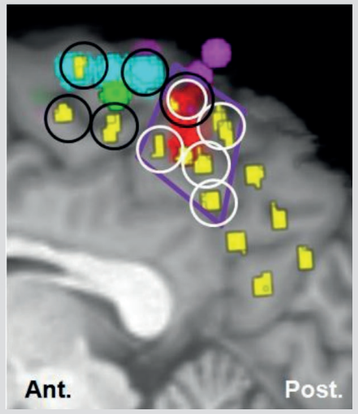


Results from NBS mapping

The colored dots indicate muscle representation areas in the cortex determined by NBS-evoked motor responses. The red, orange, yellow and green dots indicate representation areas of various muscles of the hand.
Responses evoked from the leg are indicated by turquoise, and responses from the foot by light orange.
The central sulcus is marked by white asterisks (also in center image).



MRI reconstruction in lateral (side) view



MRI reconstruction in cross-sectional view

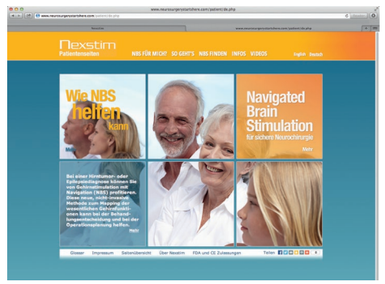
Views of the results of the NBS, MEG and ECS investigations reconstructed with an image of the ECS electrode locations, marked in yellow.
The NBS-determined muscle representation areas are all colored turquoise.
From the MEG investigation results, the epileptic area is marked in purple and the right median (arm) and tibial (leg) nerve representation areas are both marked in green.
The electrodes eliciting either motor or sensory responses to stimulation are circled in black, and those eliciting habitual seizures in white.
The lesion is colored red and the area to be resected is demarcated by the purple lines, in both images.

NBS: Navigated Brain Stimulation, MEP: Motor Evoked Potential, MEG: Magnetoencephalography, ECS: Electro-cortical Stimulation.

Images courtesy of Dept. of Pediatric Neurology and BioMag Laboratory, HUCH, Finland. Case is fully described in: Vitikainen et al. Combined use of non-invasive techniques for improved functional localization for a selected group of epilepsy surgery candidates. Neuroimage, 2009

Patient Resource Center site now also in German

Nexstim has launched its Patient Resource Center website for Navigated Brain Stimulation in German. The website brings together information from physicians and feedback from patients to help explain the role NBS mapping can play in helping patients with a diagnosis of brain tumor or epilepsy. The primary goal of the sites is to help patients decide whether NBS mapping could help make the optimum treatment decision and where they can find institutions with an NBS device in clinical use. We welcome feedback to further develop communications with patients, relatives and support groups.



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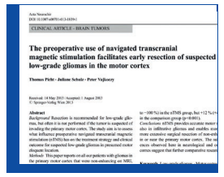
Clinical Spotlight

NBS facilitates early and more extensive resection of low-grade gliomas in the motor cortex

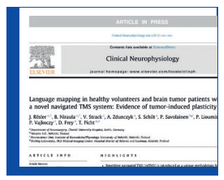

The preoperative use of navigated transcranial magnetic stimulation facilitates early resection of suspected low-grade gliomas in the motor cortex

Neurosurgeons compared their neurosurgical decison-making in suspected low-grade gliomas (LGG) in the motor cortex in patients treated prior to, and subsequent to, adopting NBS mapping. The nTMS group in their study comprised the first 11 patients since the adoption of routine nTMS mapping. The comparison group consisted of the 11 patients with the same diagnosis immediately prior to the availability of nTMS.

After the availability of nTMS mapping, all 11 LGG patients had surgical resection and in 6 of the 11 patients the nTMS mapping result changed the surgical plan towards early and more extensive resection. Prior to the availability of nTMS, glioma patients typically received only radiotherapy or chemotherapy – only 3 out of 11 patients had a surgical resection. From baseline to 1-year post-surgical assessment by MRI, there was a highly significant ($p < 0.001$) median change of tumor volume, from +12 % in the comparison group to -83 % in the nTMS group. In the nTMS-mapped patients, 1 out of 4 patients with pre-operative neurological deficits had an improved status at one year; whereas the historical comparison group had increased neurological deficits in 3 out of the 8 patients not offered surgical treatment at one year. The authors concluded that, "nTMS provides accurate motor mapping results also in infiltrative gliomas and enables more frequent and more extensive surgical resection of non-enhancing gliomas in or near the primary motor cortex."

Ref: Picht T, et al. The preoperative use of navigated transcranial magnetic stimulation facilitates early resection of suspected low-grade gliomas in the motor cortex. Acta Neurochir (Wien). 2013 Oct;155(10):1813-21.

Language mapping shows evidence of tumor-induced plasticity

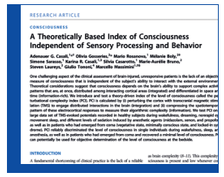

Clinical Neurophysiology

Language mapping in healthy volunteers and brain tumor patients with a novel navigated TMS system: Evidence of tumor-induced plasticity

Clinicians at the Department of Neurosurgery, Charité University Hospital, Berlin studied 15 right-handed healthy volunteers and 50 right-handed consecutive patients with left-sided gliomas using the NBS System with rTMS. In healthy subjects, language disturbances were almost exclusively induced in the left hemisphere, as expected. However, in the brain tumor patients language errors were not only more frequent, but also induced at a similar ratio over both left and right hemispheres. The authors conclude that the increased sensitivity of the right hemisphere to rTMS disturbance, suggests reorganization of language representation in brain tumor patients.

Ref: Rösler J, et al. Language mapping in healthy volunteers and brain tumor patients with a novel navigated TMS system: Evidence of tumor-induced plasticity. Clin Neurophysiol. 2013 Sep 16. pii: S1388-2457(13)01004-3.

NBS enables reliable measurement of consciousness in coma patients

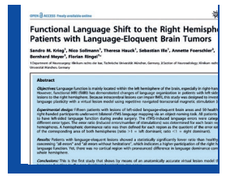

A Theoretically Based Index of Consciousness Independent of Sensory Processing and Behavior

The NBS-EEG technique has been shown to effectively measure the amount of information flow occurring in the brain in response to a stimulus. Clinical researchers have been able to discriminate between various levels of consciousness and developed a numerical index of human consciousness, the perturbational complexity index (PCI). In the study, measurements were initially made on 32 healthy subjects and subsequently on 20 brain-injured patients who had been in coma and subsequently recovered.

PCI is calculated from principles derived from theoretical neuroscience. When TMS effectively elicits a significant cortical response it directly engages large portions of the thalamocortical system without requiring the patient to perform any tasks. A patient´s capacity for consciousness can then be assessed based on the complexity of induced cortical interactions, independent of the patient´s ability or willingness to react to external stimuli. Because the stimulus needs to be applied to structures of the brain which have not been structurally damaged, the researchers used the NBS System for guidance. The apparent usefulness of PCI supports the notion that consciousness is linked to complexity - measured as the information content of distributed causal interactions in the brain.

Ref: Casali AG et al., A theoretically based index of consciousness independent of sensory processing and behavior. Sci Transl Med. 2013 Aug 14;5(198):198ra105. doi: 10.1126/scitranslmed.3006294.

NBS reveals hemispheric language shift in patients with language-eloquent brain tumors


Functional Language Shift to the Right Hemisphere in Patients with Language-Eloquent Brain Tumors

Clinicians have shown that if regions of the brain involved in language in the language-dominant hemisphere are damaged, language processing can shift to the opposite hemisphere. Patients who had undergone brain surgery for tumor participated in the study that used the NBS System with the NexSpeech module. The 15 patients in the study were all confirmed to have had language lateralization on the left-side during awake surgery. After recovery, the clinicians later used the NBS System to identify cortical regions that are essential in language and not only in speech processing. In these 15 patients they were able to show that NBS mapping of corresponding right cortical regions caused a range of errors, especially no response and performance errors. The clinicians concluded that lesions within language-eloquent brain had induced plasticity, which resulted in a shift of language function to the non-dominant right hemisphere.

The clinical implications of these original findings may be significant: if NBS is able to reliably measure the degree of language shift in brain tumor patients, it may be able to perform more extensive tumor resection within perisylvian language regions - relying on brain plasticity to preserve language function

Ref: Krieg SM, et al. Functional language shift to the right hemisphere in patients with language-eloquent brain tumors. PLoS One. 2013 Sep 17;8(9):e75403.

NexTalk interviews Professor Belkin, Director of the Clinical Institute of the Brain, Yekaterinburg, Russia

Professor Andrey A. Belkin is the Chief Neurologist and Director of the Clinical Institute of the Brain in Yekaterinburg, a city in the center of the Ural Federal District of Russia. The institute has extensive experience with TMS and purchased an NBS System in 2008, becoming Nexstim's first customer in Russia. With no neurosurgical facility at the institute, the NBS System is primarily used for therapy. Still, around a 100 NBS mappings for presurgical planning are performed annually.

Q: How many stroke or brain trauma patients do you treat with rTMS?
A: With its ability to optimize cortical excitability for motor function rTMS is seen as a basic method to support kinesiotherapy at our institute. We therefore use rTMS for all our patients, around 40-50 per month.

Q: What are the treatment main indications?
A: Movement disorders are the most common indications for rTMS therapies, but we are also trying to improve the results of aphasia treatment.

Q: What have the results of rTMS therapy been like?
A: rTMS increases the rate of neural metabolism and, based on brain plasticity, we believe that it activates the repair processes in the brain. According to the subjective opinion of patients treated, rTMS is effective in 75-80% of cases. By objective measurements, the best results have been achieved in motor paresis as well as in improving the level of consciousness in vegetative-state patients.

Q: Can you reveal what kind of rTMS protocols you use?
A: Usually, we use 1Hz for motor stimulation in 10-15 sessions applying a total of 600-900 pulses per session.

Q: What kind of role do you envision for rTMS therapy in stroke rehabilitation on a wider scale?
A: rTMS deserves to become a routine treatment method for rehabilitation of nervous system disorders. In our Ural region, for example, we believe each department of neurology should be equipped with devices able to deliver rTMS therapy.

Q: Have you used rTMS therapy for other conditions?
A: Yes, we have experimented with NBS in also treating tinnitus, chronic pain and seasonal depression.

Q: What are the latest ideas for rTMS therapy research at your institute?
A: One area we are keenly interested in is the search for predictors of consciousness recovery in coma and vegetative-state patients. We have had an abstract of our work "Navigated Brain Stimulation in diagnosis of minimally conscious state" recently published in the European Journal of Anaesthesiology, where we reported that the ability of patients to perform mental imagery was a strong predictor of regaining consciousness. Three of our patients who scored positive for motor excitation, as measured by NBS, recovered consciousness in the subsequent 6 months. Since these patients were in a vegetative state fMRI had no value, but NBS with EMG can monitor for changes in motor excitation levels even without actual muscle movement.

Nexstim across the globe

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