Neurosurgery

Nexstim

SmartFocus® E-field nTMS for Preoperative Planning

A new paradigm in the functional mapping of the brain.

As a world leader, we combine nTMS with 3D imaging and enable noninvasive mapping of eloquent brain areas that are closely linked with motor and language functions.

"What makes this so special is the ability for it to define very small, precise cortical regions on the surface of the brain, and define individual components of function which is something we never could do before."

Mitchel Berger, M.D., Chairman of the Department of Neurological Surgery, Director of the Brain Tumor Surgery Program, University of San Francisco, USA.

Indications of Use

Nexstim NBS System and NexSpeech are cleared by the Food and Drug Administration (FDA K112881).

The Nexstim Navigated Brain Stimulation (NBS) System 5 is indicated for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. The Nexstim NBS System 5 provides information that may be used in the assessment of the primary motor cortex for pre-procedural planning.

Nexstim NexSpeech®, when used together with the NBS System 5, is indicated for non-invasive localization of cortical areas that do not contain essential speech function. NexSpeech® provides information that may be used in pre-surgical planning in patients undergoing brain surgery. Intra-operatively, the localization information provided by NexSpeech® is intended to be verified by direct cortical stimulation.

The Nexstim NBS System 5 and NBS System 5 with NexSpeech® are not intended to be used during a surgical procedure.

The Nexstim NBS System 5 and NBS System 5 with NexSpeech® are intended to be used by trained clinical professionals.

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Nexstim SmartFocus® nTMS – a Uniquely Precise and Reliable Tool for Neurosurgery

1 Success Story

The introduction of transcranial magnetic stimulation (TMS) in 1985 was revolutionary. The new ability to elicit visible muscle responses, without pain or side effects, simply by placing an electromagnetic coil held over the head led to a rapid dissemination of the technique in neuroscientific research.

What turned a research technique into a prospective clinical tool for neurosurgery was incorporating another breakthrough, MRI-based stereotaxy. With new coil designs, TMS could be readily combined with stereotaxy from the 1990s onwards. However, merely knowing the location of the TMS coil relative to the scalp (line navigation) proved to be insufficient for a precise preoperative planning. It was only the pioneering work done by Nexstim to model the true location of the coil's induced electric field (E-field) on the individual brain anatomy which allowed for accurate and reliable TMS mapping.[1] This breakthrough navigated TMS technology is today known as SmartFocus® nTMS. With E-field navigation, the nTMS (navigated transcranial magnetic stimulation) has proven to be a very versatile and useful technology in neurosurgery.

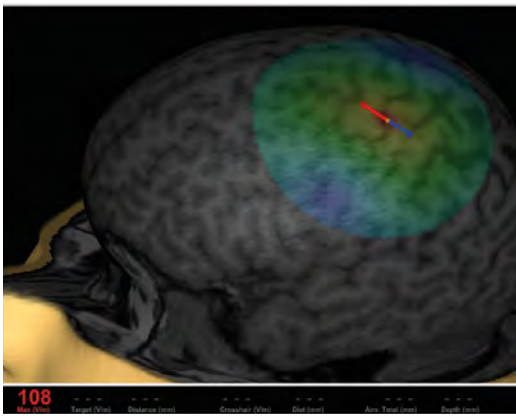


Image: The Nexstim nTMS shows the location, intensity and orientation of the electric field in the cortex during stimulation with the TMS coil.

2 Convincing Clinical Evidence

There is now a scientific consensus that Nexstim SmartFocus® nTMS is a robust and reliable clinical application for the mapping of motor areas of the human cortex prior to surgery. The Nexstim NBS system, using SmartFocus® technology, has been used in Europe under the CE mark since 2003 and was cleared by the FDA in 2009 for use in the USA.[2]

The data supplied to the FDA compared the agreement between nTMS localization of the primary motor cortex (M1) with M1 localization by direct cortical stimulation (DCS) after craniotomy—in the same patients. The data showed excellent agreement between nTMS and DCS localization, better than that previously found with other noninvasive methods like fMRI or MEG. These findings have been replicated in numerous clinical studies and the consequent benefits have been reaffirmed by very experienced DCS users.[3] Nexstim nTMS continues to be the subject of intensive research outside its clinically-validated indications.

[1] E-field vs line navigation: Krieg SM (editor) Navigated Transcranial Magnetic Stimulation in Neurosurgery, p 14-18 Springer, 2017.

[2] FDA, CDRH Office of Device Evaluation K091457 Dec 2009.

[3] Berger MS, presentation, 2018 Annual Meeting of the German Society of Neurosurgery (DGNC)

[4] Frey D Navigated transcranial magnetic stimulation improves the treatment outcome in patients with brain tumors in motor eloquent locations Neuro Oncol. 2014 Oct; 16(10): 1365–1372.

[5] Frey D et al. A new approach for corticospinal tract reconstruction based on navigated transcranial stimulation and standardized fractional ansiotrophy values. Neuroimage 2012, 62(3):1600-9

[6] Picht T 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.

4 Neurophysiologically-Based Fiber Tract Imaging

According to the recent findings, nTMS data provides far more reliable regions of interest (ROI) for diffusion tensor imaging-based visualization of fiber tracts than traditional methods. The nTMS analysis defines more exact seeding points for the DTI software and thus allows reliable and standardized representation of results of tractography.

Adding purely anatomical DTI imaging offers valuable information about the functionality of the displayed tracts. Only with a standardized combination of functional and structural analysis, does DTI imaging unfold its full potential in clinical practice. Functionally relevant white matter can be distinguished from the irrelevant and, importantly, the vulnerability of white matter near a tumor can be assessed. Using nTMS data, interventional strategy and risk* can now be determined individually and precisely.[4, 5]

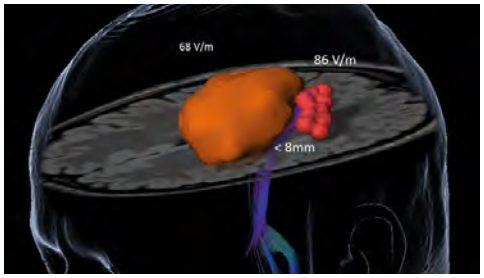


Image: Integration of MR and nTMS data into Brainlab planning software. The NBS mapping results were exported in DICOM format. Seeding points (red) used for DTI-based fiber network elucidation (blue green). The tumor mass is shown in orange.

This patient was deemed to be a very high-risk case since the distance between tumor and corticospinal tract (CST) is less than 8mm and cortical excitability, determined by nTMS motor threshold measurement, was markedly different between the hemispheres (non-affected: 68 V/m vs. tumor-affected: 86 V /m).

Source: PD Dr.med. Thomas Picht, Charité, Berlin.

3 Preoperative Mapping of the Language Network

Similarly to intraoperative awake language mapping, repetitive TMS (rTMS) can also temporarily disable cortical areas allowing the Nexstim SmartFocus® nTMS to be used for the preoperative mapping of language function, prior to confirmation by DCS** during surgery. nTMS language mapping creates a map of positive responses, as well as a map of negative responses, indicating areas safe to resect. By using nTMS language hotspots as a starting point for intraoperative awake mapping, a physician no longer needs to "hunt" for functional areas and can minimize the time when a patient may be awake.

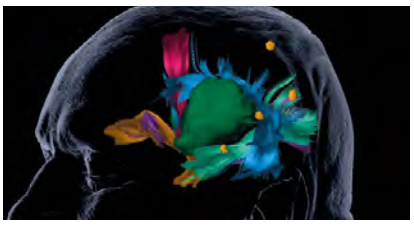
Studies have demonstrated good overall correlation between repetitive nTMS and DCS in language mapping. Additionally, in awake surgery, nTMS language mapping not only helps with the surgery itself but also prepares the patient for intraoperative language assessment, as well as assessing a patient's suitability for the technique.[6] nTMS-guided language fibertracking is a unique tool typically not available to neurosurgeons offering valuable information with regard to planning approaches, extent of surgical resection, and any need for re-mapping mid-resection. Pre-operative language mapping may also be the only language mapping tool available for those populations unable to co-operate sufficiently to undergo awake intraoperative mapping.

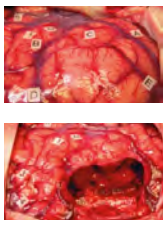
Image left: Craniotomy planning with Brainlab planning software with presentation of the language-positive areas determined with nTMS in conjunction with the tractography. While the upper language-positive area is not connected to the language network and is therefore of secondary relevance, the lower three language-positive areas are part of the network and can be considered to be clinically relevant.

Image above right: Before tumor resection.

Image below right: After tumor resection.

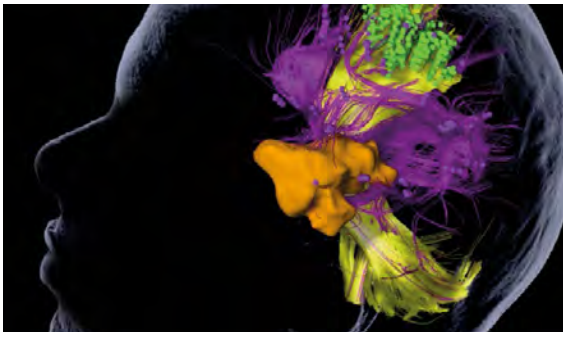
Source: PD Dr. med. Thomas Picht, Charité, Berlin.





Use of the language-positive areas determined by nTMS as seeding regions for the representation of the result of tractography

Source: PD Dr. med. Sandro Krieg, TU Munich.



* Please see text for "Risk Stratification Models" on page 7

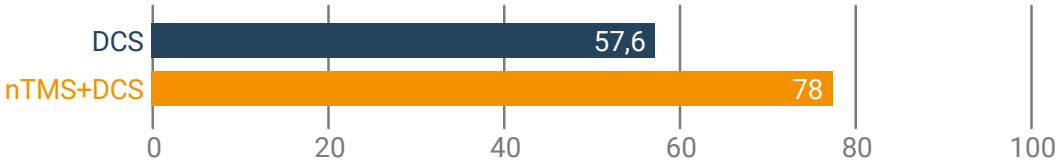
** Please see NexSpeech® Indications for use on page 2

5

Completing Intraoperative Monitoring

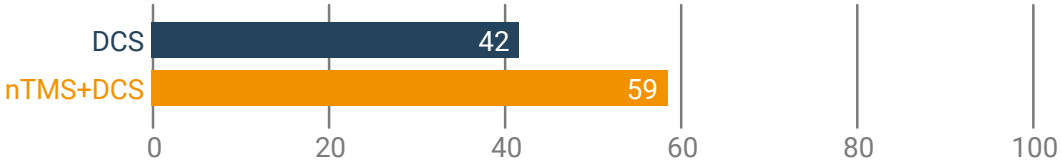
Prior to surgery, accurate assessment of surgical risk with SmartFocus® nTMS data may modify the indication for intraoperative neurophysiological monitoring (IONM), case-specifically.
Robust nTMS maps may be fused with additional imaging modalities on surgical navigation systems to guide surgical resection or optimize placement of grids and depth electrodes. E-field navigated TMS works synergistically with intraoperative monitoring, expediting DCS motor mapping and facilitating communication between surgeon and clinical neurophysiologist. Topographic and neurophysiological preoperative nTMS analysis may also facilitate interpretation of intraoperatively-evoked neurophysiological phenomena.
By accurately assessing the surgical risk with nTMS data, the indication for intraoperative neurophysiological mapping and monitoring (IONM) can be planned case-specifically. During surgery, the cortical nTMS data and subcortical nTMS-DTI data help to target and more effectively perform the intraoperative mapping. For example, a phase reversal to determine the central sulcus after prior nTMS mapping can be dispensed with. On the other hand, topographic and neurophysiological preoperative nTMS analysis help better interpret intraoperatively-evoked neurophysiological phenomena.[7]

35 % Increase in Gross Total Resection Rate, n=200*



* Krieg, Sandro M, et al. "Preoperative Motor Mapping by Navigated Transcranial Magnetic Brain Stimulation Improves Outcome for Motor Eloquent Lesions." Neuro-Oncology 16.9 (2014):1274-282.

40 % Increase in Gross Total Resection Rate, n=365**



** Frey, Dietmar, et al. "Navigated Transcranial Magnetic Stimulation Improves the Treatment Outcome in Patients with Brain Tumors in Motor Eloquent Locations." Neuro Oncology (2014):nou110v1-nou110.

← Image: The presentation of the nTMS mapping results allow for a better discussion between the doctor and the patient about possible treatment options.

7

Decision making

Nexstim SmartFocus® nTMS data is easy to interpret and, with DICOM compatibility, can be easily integrated with other diagnostic results. nTMS data is the foundation for a comprehensive preoperative evaluation and helps the entire team involved in determining the treatment strategy, including a “tumor board”. One of the key features of Nexstim nTMS is that the data are displayed in a universally familiar context, the MR image. With the nTMS and MR-data rendered into a 3D model, the results of mapping are intuitive enough to facilitate treatment counselling, allowing patients and their families to be well informed and involved in treatment decision-making.

6

Support Throughout the Course of Treatment

Nexstim nTMS data adds value throughout the entire treatment process: preoperative examination and intraoperative guidance.

- Before the operation: nTMS helps support the best treatment decision, providing objective information to get the right balance between maintaining quality of life and the most extensive resection—using standardized risk stratification.* Pre-procedural nTMS disproves involvement of the primary motor cortex in 25% of cases, expands resection plans in 35% of cases, restricts resection plans in 4% of cases, and leads to a complete reversal from biopsy/no surgery to an indication for surgical resection in 15% of cases.[4]
- During the procedure: nTMS can guide DCS, saving time and cost of materials. Studies also show that the preoperative nTMS analysis in combination with nTMS-based DTI improves deliniation of safe resection limits and results in better resection outcomes.

7 Krieg SM, et al. 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.

* Risk Stratification Models

Motor system: Three independent factors have been found to significantly increase the risk of new postoperative motor deficits: tumor infiltration of the primary motor cortex, a distance less than 8 mm between the tumor margin and the pyramidal tract and pathological excitability of the motor system. Taken together, these three factors constitute a prognostic risk score (Rosenstock, Picht et al., J Neurosurg, 2017).

Language function: Hemispheric language mapping gives hints as to the vulnerability of the left hemisphere—the more speech errors from rTMS mapping in the right hemisphere, the lower the risk of new language deficits after left perisylvic surgery. Combined rTMS mapping and DTI fiber tract imaging indicate an increased risk of new postoperative language deficits when TMS-induced speech disturbances are in close proximity to the tumor. (Sollmann N, et al., Journal of Neurosurgery JNS, 2019)

nTMS in planning Epilepsy surgery

Studies have shown that nTMS mapping provides accurate functional information for pre-operative planning of epilepsy surgery. In a study of 10 patients, SmartFocus® nTMS information was regarded as essential or beneficial in the localization of M1 in relation to the lesions in 6 patients.[8] In addition, information on the location of primary motor representation areas can be used to guide subdural monitoring grid deployment.[9]

8 Säisänen L. et al. Non-invasive preoperative localization of primary motor cortex in epilepsy surgery by navigated transcranial magnetic stimulation. Epilepsy Res, 2010, 92:134-144.

9 Vitikainen A-M, et al. Applicability of nTMS in locating the motor cortical representation areas in patients with epilepsy. Acta Neurochir Epub 2013

nTMS in Arteriovenous Malformation (AVM) treatment planning

As AVMs are often inductors of functional plasticity & their vasculature makes standard functional imaging difficult, nTMS allows for detailed delineation of eloquent areas even within hypervascularized cortical areas.[10] nTMS data also allows a more objective decision-making regarding the treatment of AVMs: In a case series of 34 patients, SmartFocus® nTMS data’s influence on decision-making for or against treatment of AVMs was examined by confirming/disproving presumed motor or language eloquence. The decision for or against microsurgical resection of the AVM was affected by the results of the respective nTMS mapping in 21 cases (62%).[11]

10 Kato N, et al. Functional brain mapping of patients with arteriovenous malformations using navigated transcranial magnetic stimulation: first experience in ten patients. Acta Neurochir 2014 May; 156(5):885-95.

11 Ille S, et al. The impact of nTMS mapping on treatment of brain AVMs. Acta Neurochir. 2018 Jan 24.

SmartFocus® nTMS by Nexstim: Preserving What's Essential in Neurosurgery

One of the most crucial pieces of information needed for neurosurgery is the tumor's location in relation to essential functional tissue.

SmartFocus® nTMS mapping is used when the tumor is thought to be close to the functional areas of the brain, such as those responsible for limb movement or speech production. It is not uncommon for treatment plans to change after analysing pre-operative nTMS data, modifying planned extent of resection or even complete reversal on whether to operate at all.

Use of Nexstim's NBS System with SmartFocus® nTMS in presurgical mapping has been reported to increase progression free survival by 46% in patients with low grade gliomas.[12]

nTMS in Neurosurgery:

- Reduces risk in performing brain surgeries and leads to increased resection rates, thus saving the costs for a second surgery or surgery-related complications (e.g., paresis, neurological deficits).[13]
- Increases progression free survival in patients with low grade gliomas which also results in decreased health care costs.[12]
- Early and non-invasive identification of non-operable tumors avoids unnecessary and ineffective brain surgeries.[13]
- Allows patient access to innovative, low-risk and individualized health-care (personalized medicine).[13]

Nexstim NBS system is the only FDA cleared and CE marked navigated TMS system for presurgical mapping of the speech and motor cortices of the brain.

[12] Dietmar Frey, Peter Vajkoczy, and Thomas Picht. Navigated transcranial magnetic stimulation improves the treatment outcome in patients with brain tumors in motor eloquent locations Neuro Oncology 2014: nou110v1-nou110.

[13] Analysis and estimates of LinkCare GmbH based on the following publications:

Krieg S, et al. Changing the clinical course of glioma patients by preoperative motor mapping with navigated transcranial magnetic brain stimulation. BMC Cancer. 2015 Apr 8; 15(1):231. [Epub ahead of print]

Ille S, et al. The impact of nTMS mapping on treatment of brain AVMs. Acta Neurochirurgica 160 (2018): 567-578.

Rosenstock T, et al. Risk stratification in motor area-related glioma surgery based on navigated transcranial magnetic stimulation data. J Neurosurg. 2016 Jun 3:1-11. [Epub ahead of print]

nTMS Workflow

Importing the MRI images → NBS mapping → NBS map & Fibertracking (pre-op surgical planning) → Tumorboard and surgery

* Image: Courtesy of Kuopio University Hospital

nTMS Mapping with SmartFocus® for Safer Radiation Therapy

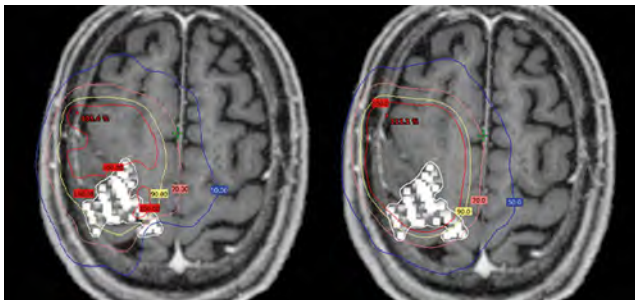
For patients undergoing radiotherapy or radiosurgery for brain metastases, it is important to preserve quality of life after a course of therapy.

Ionizing radiation is effective in treating tumor tissue because it damages the cells, slowing growth of the tumor—and at high doses can cause the cancerous cells to die. However, the radiation beams can also cause undesirable toxicity to other, healthy areas of the brain. Unlike in surgical resection, which can be guided by direct electrocortical stimulation (DES), with radiotherapy there is no way to be sure of the location of the individual patient's motor areas, unless pre-procedural brain mapping is used.

Brain mapping with Nexstim's SmartFocus® nTMS technology accurately defines the areas in the brain responsible for motor function—non-invasively. nTMS differs from fMRI by being a direct, causal method and there is a wealth of clinical data showing good concordance of nTMS mapping with DES.[14]

The SmartFocus® nTMS functional maps allow the radiotherapist to modify the dose plan in order to minimize undesired dosing of eloquent motor areas which need to be preserved.

High doses of radiation are associated with cell death and high doses of radiation to motor areas are associated with a deterioration in patient's motor function post-therapy.



On the left, isodose plan made with nTMS and on the right side isodose plan without nTMS. (Image courtesy of Maximilian Schwendner/ TU Munich)

Studies have shown that using nTMS to guide the orientation of the applied radiation beam allows for significantly reduced dosing to motor areas (-18.1%). Importantly, this reduction is achieved without compromising treatment of the tumors.[15]

It has been shown also that SmartFocus® nTMS mapping data can be easily and reliably integrated into GammaKnife treatment plans by the standard GammaPlan software. In a study of 8 patients, when compared with plans without nTMS data, treatment plans with integration of cortical nTMS mapping data showed a 2% to 78% (mean, 35.2% ± 22.7%) lower 12-Gy volume within the motor cortex without reduction of the dose applied to the tumor.[16]

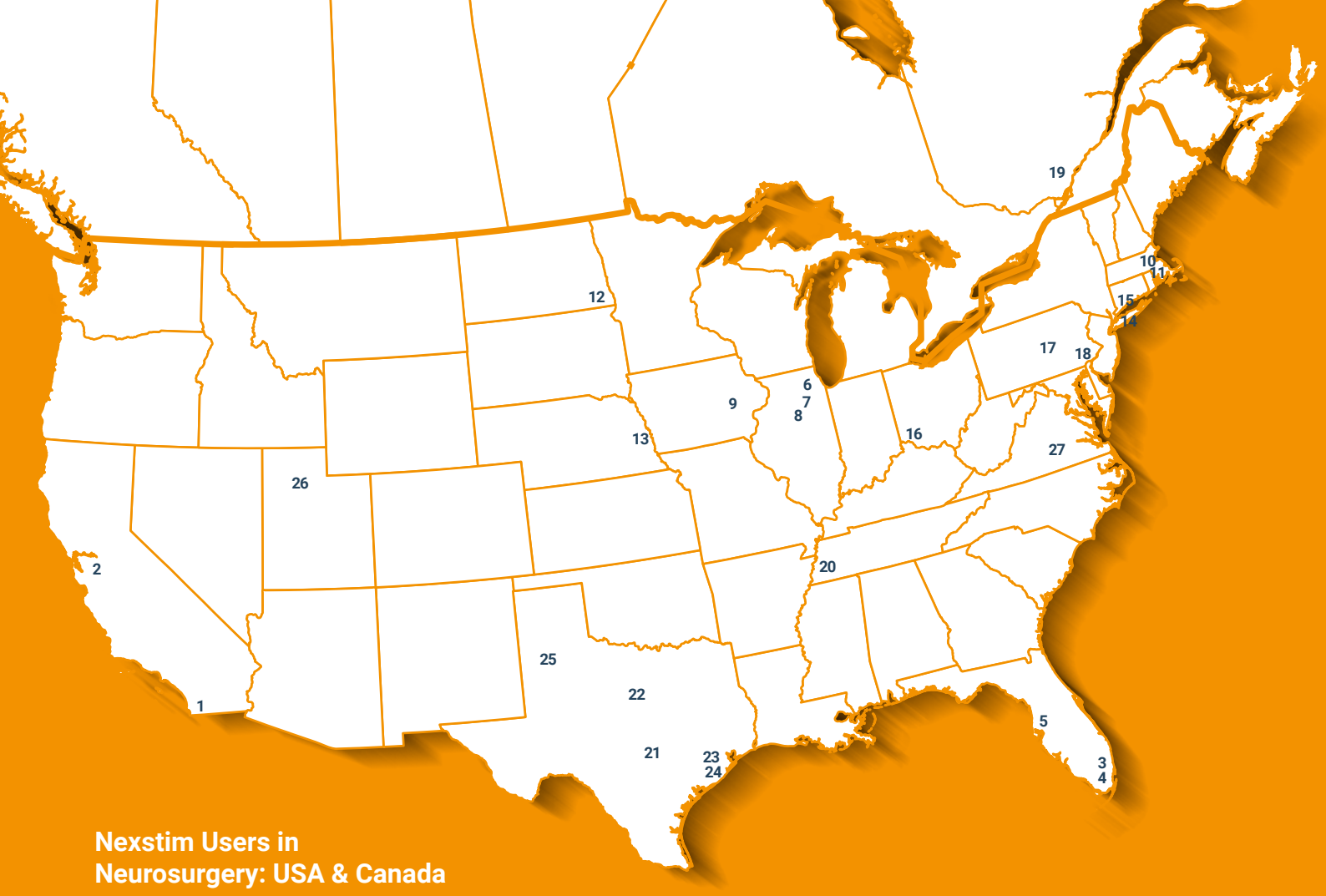
nTMS offers radiotherapists a new, non-invasive treatment approach. nTMS complements the use of non-surgical (non-invasive) treatment approaches. DICOM tools allow for direct export of nTMS results into dose planning software for visualization.

Nexstim's NBS System with SmartFocus® nTMS gives radiotherapists the ability to accurately and reliably modify dosing to help preserve motor function and potentially the quality of life of their patients.

14 Tarapore P, et al. Preoperative multimodal motor mapping: a comparison of magnetoencephalography imaging, navigated transcranial magnetic stimulation, and direct cortical stimulation. J Neurosurg. 2012 Aug; 117(2).

15 Schwendner MJ, et al. The Role of Navigated Transcranial Magnetic Stimulation Motor Mapping in Adjuvant Radiotherapy Planning in Patients With Supratentorial Brain Metastases. Front Oncol. 2018 Oct 2; 8:424.

16 Tokarev AS et al. Appliance of Navigated Transcranial Magnetic Stimulation in Radiosurgery for Brain Metastases. Journal of Clinical Neurophysiology, July 2019



Nexstim Users in Neurosurgery: USA & Canada

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2. San Francisco, California
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4. Miami, Florida
5. Tampa, Florida
6. Chicago, Illinois
7. Chicago, Illinois
8. Winfield, Illinois
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10. Boston, Massachusetts
11. Boston, Massachusetts
12. Rochester, Minnesota
13. Omaha, Nebraska
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15. White Plains, New York
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18. Philadelphia, Pennsylvania
19. Laval, Québec
20. Memphis, Tennessee
21. Austin, Texas
22. Fort Worth, Texas
23. Houston, Texas
24. Houston, Texas
25. Lubbock, Texas
26. Salt Lake City, Utah
27. Richmond, Virginia

Nexstim Users in Neurosurgery: Europe

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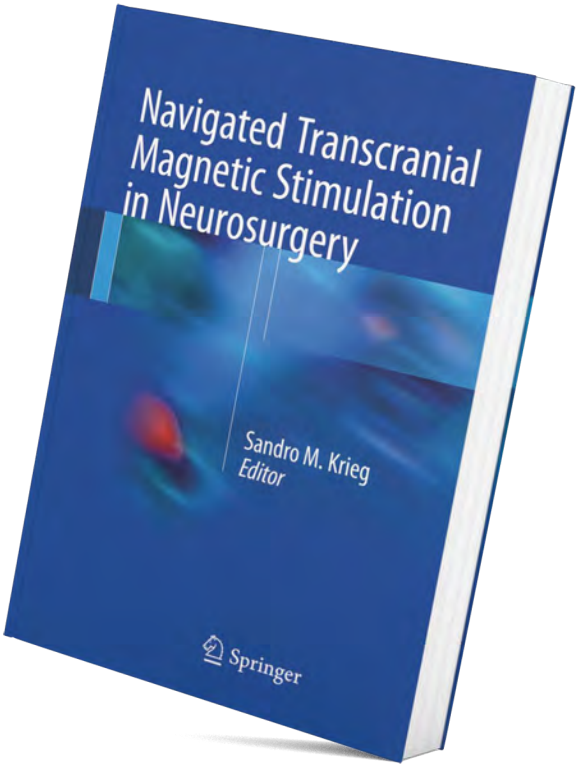
Navigated Transcranial Magnetic Stimulation in Neurosurgery

This book is the first comprehensive work summarizing the advances that have been made in the neurosurgical use of navigated transcranial magnetic stimulation (nTMS) in neurosurgery over the past ten years. It offers essential and detailed information for both new and experienced users of nTMS.



Editor: Krieg, Sandro (Ed.)
ISBN 978-3-319-54918-7

With the goal to achieve optimal precision and safety in the operating theater, a neurosurgeon must investigate not only the structure and vasculature of the brain but also its neural functions. The human central nervous system (CNS) is the single most complex organ in the known universe, and its functional networks are not yet perfectly understood. In this setting, in order to preserve the quality of life of patients who will undergo brain surgery, it is crucial to study the organization of neural circuits before removal of a part of the CNS affected by a cerebral disease, e.g., epilepsy or tumor. Due to a major interindividual anatomo-functional variability, especially in case of brain lesions, which can induce mechanisms of neuroplasticity, mapping techniques are very helpful to understand the distribution of cortical and subcortical pathways underlying motor, language, cognitive, and emotional functions at the individual level. To this end, intraoperative direct electrical stimulation (DCS) in awake patients remains the gold standard to optimize the extent of resection (EOR) while minimizing neurological morbidity. However, even though this method allows real-time anatomo-functional correlations throughout the surgical procedure, in order to detect and to preserve the structures crucial for brain functions, it is also important to benefit from complementary techniques that permit a noninvasive preoperative mapping. Functional neuroimaging has been extensively used in the past decade, but its main limitation is the impossibility to differentiate critical areas which should not be removed during surgery, to avoid permanent deficit, versus regions involved in a neural network but which can be compensated — and thus surgically resected.

In this state of mind, navigated transcranial magnetic stimulation (nTMS) represents an original tool opening new avenues in the exploration of the CNS, especially in brain-damaged patients. Indeed, as intraoperative DCS, nTMS offers the unique opportunity to create a transient virtual disruption of neural networks, with the aim to identify the cortical areas crucial for brainfunctions. However, contrary to DCS, nTMS is a noninvasive technique that can be used before surgery to map the eloquent cortex and to plan the resection accordingly. This is the reason why a textbook on nTMS in neurosurgery was desperately needed. Led by the editor, Sandro M. Krieg, this collective body of work will serve as a comprehensive textbook for all physicians with

an individualized personal approach of brain surgery. What makes this book so unusual is that it contains all required information to use nTMS in a department of neurosurgery and outlines pros and cons to other techniques. The approach the authors have taken in defining this new technology and its implication for neurosurgical management are quite unique and innovative, to say the least. The book is organized in a very logical and informative fashion, starting off with critically important chapters covering the basic principles of nTMS. The clinical aspects are further evoked in chapters on preoperative motor and language mapping. To this end, Dr. Krieg is a master at explaining and detailing how to use nTMS for surgical planning and how to combine this method with other techniques, as fiber tracking. I particularly like the way in which further brain functions can be mapped by nTMS and in which this methodology may be used in children—knowing that it is very difficult to achieve awake surgery in pediatric population, especially under 10 years. Interestingly, the fact that nTMS is also able to modulate neural networks for neurosurgical applications, as previously done in neuropsychiatry for depression, is depicted in a series of detailed chapters on these subjects. For example, nTMS can be helpful to treat chronic pain. In the future, this technique could also be considered to induce and canalize neuroplasticity, allowing an increase of the EOR or even an improvement of the neurological status — for example, by combining it with specific programs of rehabilitation in patients with neurological deficits. Finally, in the field of cognitive neurosciences, nTMS may represent a unique tool to investigate CNS processing in humans. Indeed, thanks to recent advances in the new science of connectomics, which aims to comprehensively map neural connections at both structural and functional levels, coordination of cognitive and behavioral domains is now attributed to parallel and intersecting large-scale neural circuits that contain interconnected cortical and subcortical components. In this context, a technique based on the concept of transitory disruption of neural circuits will undoubtedly provide new insights into the organization of such a networking brain. Yet, it is worth noting that nTMS can achieve only a mapping of the cortex, but it is not able to map the white matter tracts that nonetheless constitute a crucial part of the connectome. From a clinical point of view, preservation of subcortical pathways is essential during brain surgery, because the white matter connectivity is a well- known limitation of neuroplasticity. In other words, currently, nTMS should still be combined with other mapping techniques, especially intraoperative DCS, in order to be more extensively validated and to compensate its inability to investigate directly the function of the fibers.

It is crucial for modern clinical neuroscience, and especially for neurosurgery, to incorporate advances in this complex field of brain mapping in as timely a fashion as possible, so that patient care becomes guided by the latest increments of relevant technology and knowledge with regard to CNS processing. I have no doubt that this comprehensive volume edited by Dr. Krieg and his colleagues will serve this purpose with considerable distinction. All in all, this text is a major contribution that will be significant in the history of neurosurgery and cerebral mapping. If you only have one reference source on nTMS in brain surgery, this must be it!

Montpellier, France
Hugues Duffau, M.D., Ph.D.

Publications about nTMS in Neurosurgery

The topic of nTMS is of great scientific interest. There are already 79 publications with data from 3417 patients, both about the clinical as well as the economic benefits of preoperative nTMS mapping. Below is a selection of publications:

Relevance of Motor Mapping for the Clinical Outcome

Krieg SM, et al.
Preoperative motor mapping by navigated transcranial magnetic brain stimulation improves outcome for motor eloquent lesions. Neuro-Oncology 2014; 0, 1-9, doi: 10.1093 /neuonc/nou007.

Jung J, Lavrador J-P, Patel S, Giamouriadis A, Lam J, Bhangoo R, Ashkan K, Vergani F,
First UK experience of navigated Transcranial Magnetic Stimulation in pre-surgical mapping of brain tumors, World Neurosurgery (2018), doi: https://doi.org/10.1016/j.wneu. 2018.11.114.

Krieg SM, et al.
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For questions about system prices, rent models as well as reimbursement in your country, please contact: **info@nexstim.com**

We would also be pleased to inform you about the other possible applications in neurosurgery, radiotherapy as well in neurology or psychiatry.

Health Economics

The Nexstim NBS system can help you improve diagnostics and increase the number of medically-necessary tumor surgeries while reducing the length of stay for your patients and thus reducing the overall cost burden to your clinic.

Using the Nexstim NBS System with SmartFocus® technology prior to any treatment decision can result in patients who were originally considered inoperable, to be considered for surgery.[17]

Your clinic also benefits financially by adding an NBS brain mapping service. It allows both higher hospital DRG revenue, through increased surgery volumes, as well as a reduction in the associated costs. Studies have shown that patients who went through nTMS mapping before the operation, experienced shorter in average in-hospital stay than those without nTMS mapping.[18] Hospitals can thus reduce their cost burden while improving operating results.

SmartFocus® nTMS can be utilized across multiple departments, including but not limited to neurosurgery and radiotherapy. In addition, Repetitive TMS (rTMS) is a recognized treatment for major depressive disorder, for example.

We would be pleased to assist you with questions related to financial issues. Contact us to discuss how Nexstim SmartFocus® can add value to your clinic.

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Marketing Support

Nexstim will assist you in marketing and communication activities to draw attention to the new services offered at your clinic.

1. Providing communication and marketing materials

We provide you with free materials that you can use in your own media channels (website, social media, brochures, flyers etc.). This includes the following materials:

- Texts with the most important information for patients (long and short versions, key messages and FAQs)
- Patient video about preoperative motor and language mapping
- Images (Photos of the NBS System 5, System Screen shots, Mood pictures and logos)

2. Clinic-specific patient brochure

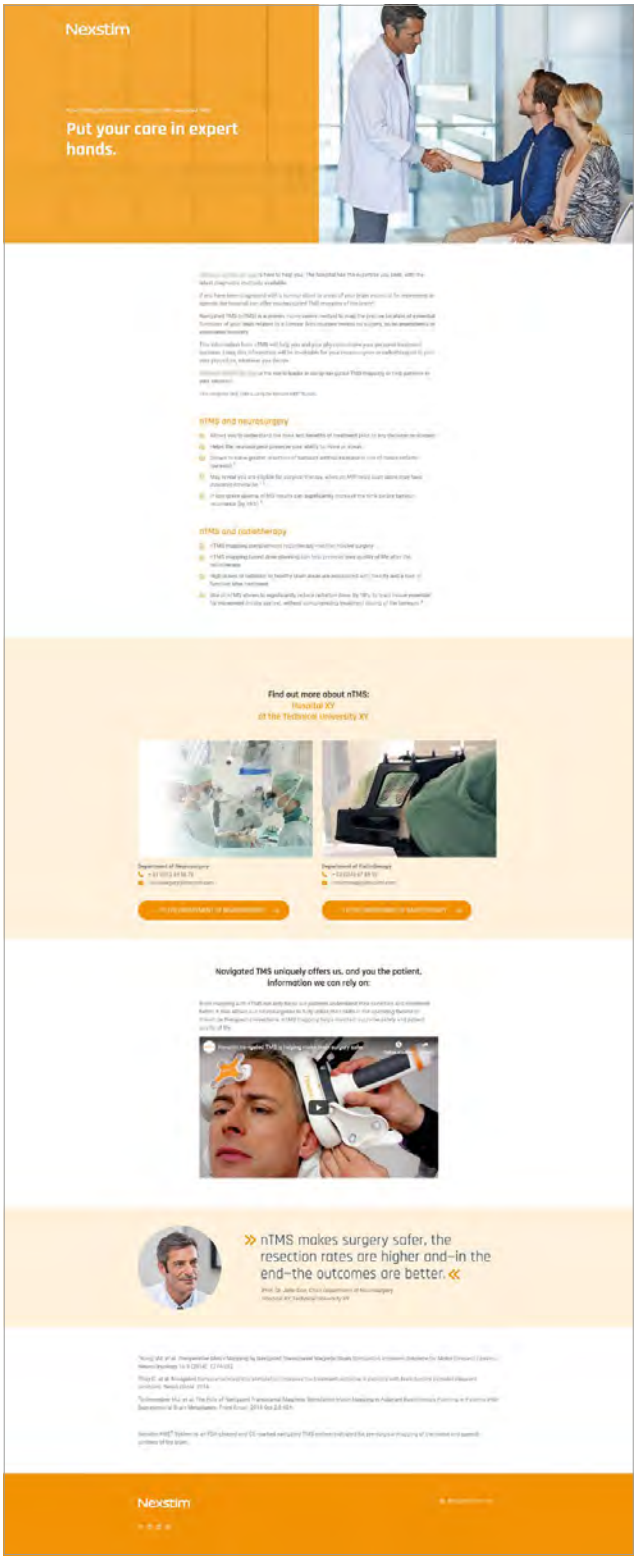
We create information brochure for patients with your clinic's logo and contact details.

3. Digital campaigning

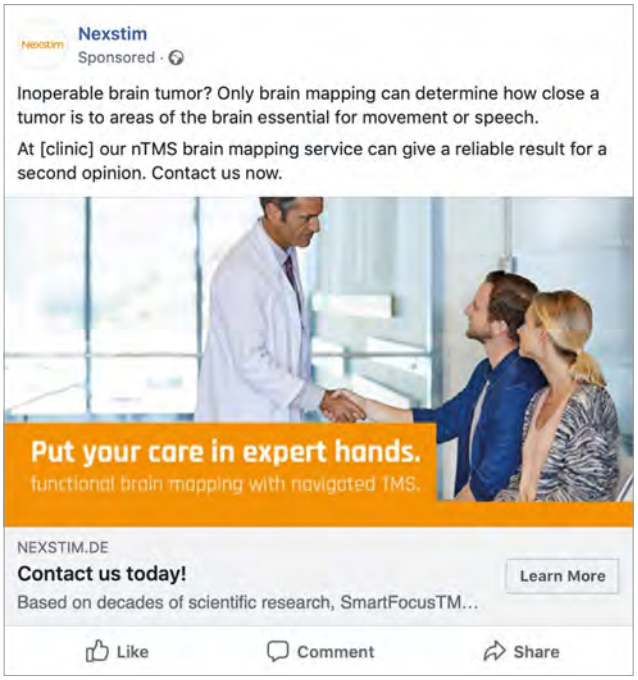
We support you with digital marketing campaigns targeted to your patient groups in your clinic's region. If a person clicks on an ad, it redirects to a landing page specifically tailored for your clinic. The tailored landing page highlights both nTMS mapping and your clinic's contact details. The financial support Nexstim can provide for the campaigns will be discussed separately with each clinic.

Marketing Material Examples

Landing page



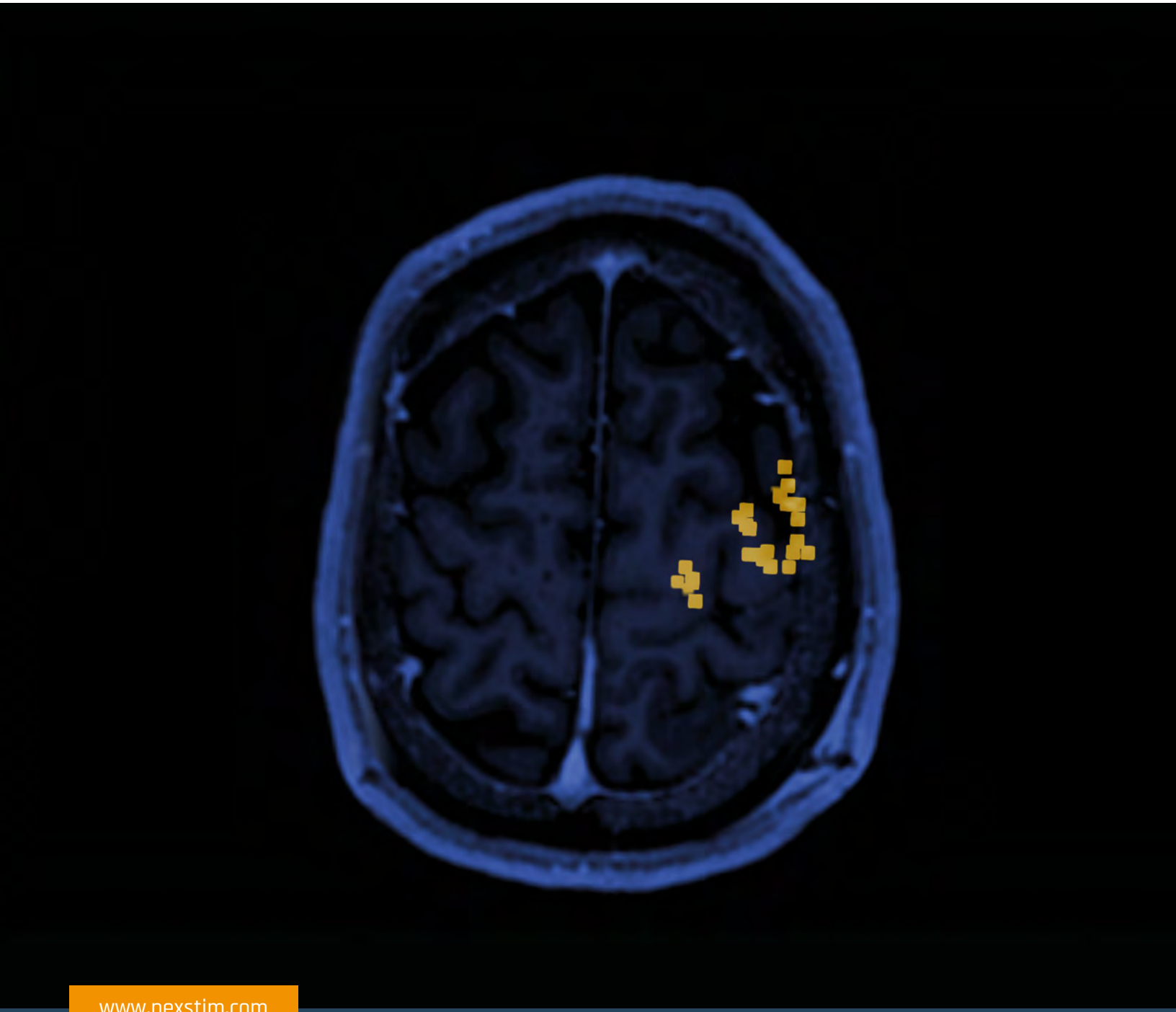
Facebook posts



Youtube video

Nexstim

SmartFocus™ TMS



www.nexstim.com

Certificate: Nexstim Plc is ISO-13485 certified. All Nexstim® products comply with the relevant safety standards. The Nexstim® NBS System 5 complies with the EU Medical Device Directive 93/42 / EEC IEC 60601-1 edition 3.1 (General requirements for safety and essential features) with the CE mark as medical device IEC 60601-1-2 (EMC).

Classification: FDA Class II (21 CFR 882.1870), MDD Class IIa (Rule 10), IP Classification: IPX0 Application Part Type: BF, Patient chair B.

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