Brain-Mapping using robotized TMS

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Abstract— We present first results of brain-mapping using robotic Transcranial Magnetic Stimulation. This non-invasive procedure enables the reliable detection of the representation of individual muscles or muscle groups in the motor-cortex. The accuracy is only exceeded by direct electrical stimulation of the brain during surgery. Brain-mapping using robotic TMS can also be used to detect displacements of brain regions caused by tumors. The advantage of TMS is that it is non-invasive. In this study, we compare results from statistical mapping with robotic TMS to results achieved from direct stimulation done during tumor surgery. To our knowledge this is the first study of this type. We mapped the representation of three muscle groups (forearm, pinky and thumb) in tumor patients with the robot-aided TMS protocol and with direct stimulation. The resulting maps agree within 5mm.

I. INTRODUCTION

Transcranial magnetic stimulation (TMS) is based on the principle of induction. A strong electrical impulse is sent through a coil, producing a rapidly changing magnetic field. The magnetic field passes the skull nearly undisturbed and induces a current flow in the superficial brain tissue [1].

The underlying biophysical processes leading to a macroscopic response to the stimulation are not completely understood.

Conventional brain imaging techniques like functional MRI (fMRI) or Positron Emission Tomography (PET) measure changes in metabolic activity when performing specific tasks compared to rest. TMS directly stimulates nervous tissue [2]. Thus, we can examine the brain by stimulating it and testing which muscle responds when placing the stimulation coil at different spots around the head.

Today, fMRI is still the most common procedure for non-invasive functional brain-mapping. However, it does not completely meet the needs of neurosurgeons, because its metabolic-based nature makes it difficult to distinguish functional response areas from erratic high metabolic tissue such as tumors. Furthermore, MRI images are prone to susceptibility caused geometric distortion [3]. TMS allows direct stimulation of functional areas without being influenced by tumors or suffering from distortions in any imaging process. Hence, by measuring the muscle twitching strength when placing the stimulating TMS coil at several positions around the motor cortex, one can infer the location of the motor-cortex does also trigger muscle twitching. This can be used to create a map of the motor-cortex by measuring the muscle twitching at several positions. We improve the stimulation accuracy with a robot which positions the coil and compensates the head motion.

We propose a procedure for brain mapping with TMS, based on robotized navigated stimulation and statistic evaluation of the motor responses. Hereby, the robot aided system allows precise stimulation of the planned target region. The statistical mapping algorithm employs a functional model of the stimulation and uses the exact coil positions and orientations, the stimulation responses, and the characteristic field of the TMS coil to predict the most likely area of representation. Using this set-up we mapped 6 patients and compared the mapping with direct electrical stimulation performed during a neurosurgical procedure.

II. METHODS

A. SET-UP OF THE EXAMINATION

The system for robot-guided TMS contains six main components (Fig. 1): TMS coil (a), robot (b), robot controller (c), computer (d), tracking camera (e) and headband (f). In our experiment, we used (a) a standard figure-of-eight coil (The Magstim company Ltd, Spring Gardens, Whitland, UK), (b,c) an Adept Viper s850 robot (Adept Technology, Inc. Livermore, CA, USA), (d) a standard PC with 2.8GHz, (e) a Polaris infrared stereooptical tracking system (Northern Digital Inc., Waterloo, Ontario, Canada), (f) a self made rubber headband with three passive Polaris markers on a plastic frame.

The robot and the tracking camera are registered to each other before the experiment to a common coordinate system using standard algorithms [9]. The TMS coil is attached to the robot using a aluminium clamp. The coil coordinate system is defined by pointing to three predefined points (at the centre, the front, and the left side) on the underside of the coil with a tracked pointer. This also determines the static representation of the muscle in the brain [4], [5]. Traditional TMS mapping algorithms like center of gravity calculations implicitly use a very coarse model of the TMS stimulation principle and the electromagnetic field produced by the coil and have been shown to be accurate only within centimeter range [6]. Furthermore, the resulting cranial maps need to be projected to the cortex, causing further problems [7].

TMS is an established technique and used for neurological diagnostics and for the treatment of neurological disorders such as tinnitus [8] where the magnetic coil is positioned manually by the surgeon. The magnetic stimulation of the motor-cortex does also trigger muscle twitching. This can be used to create a map of the motor-cortex by measuring the muscle twitching at several positions. We improve the stimulation accuracy with a robot which positions the coil and compensates the head motion.

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coordinate transformation from the robot end-effector to the coil, i.e. how the coil is attached to the robot.

The patient is equipped with the headband before the procedure starts. Three landmarks (outer eye canthi, tip of the nose) and about 300 surface points of the head are sampled using again the tracked pointer device. All points are referenced to the coordinate system defined by the headband marker. By registering these points with the reconstruction of the head outline from MRI data, we link the patient’s head with its model in the computer [10].

For stimulation, the coil target position is defined using the MRI data and the head reconstruction in the computer. A point on the virtual head surface is selected defining the target position of the coil center. Coil orientation is set tangential to surface and $45^\circ$ to sagittal plane. This virtual position is then transformed to robot coordinates using the tracking system and the pre-established registration. The robot then steers the coil to the corresponding target position on the patient’s head. The coil trajectory is divided into three parts: Away from the old position at the head - around the head along a circular trajectory - to the head to the new target position. The actual head position (determined using the headband marker) is always taken into account and the trajectory is adapted if the head moves. As soon as the target position is reached, a motion compensation module sets in and the robot follows any head movements. This guarantees that the coil is at its precise target position at all times.

The latency of the system, i.e. the time between a head movement and the reaction of the robot, was measured to be less than 50 milliseconds. Note that the time to restore the desired coil position after a head motion can be greater, depending on the amplitude and speed of the movement and the speed restrictions of the robot.

After stimulation, the motor evoked potentials (MEP) of three muscles (forearm, pinky and thumb) are recorded. The stimulation setup used was composed of a Medtronic MagPro X100 stimulator connected to a Medtronic Endeavor CR MEP recorder. The trigger signal given synchronously to the Endeavor for recording and to the stimulator came from a script on a laptop. The MEP signal was fed into the MEP recorder, filtered with a band pass of 2-2000Hz and sampled at 5000Hz.

B. BRAIN-MAPPING

For brain mapping a magnetic coil was placed above the motor cortex. By firing it, an electric field occurs which stimulates the central nervous system and causes a contraction of a muscle of the contralateral side of the body. The intensity of such muscle twitches was measured for five points in the expected muscle representation area. The intensity of the stimulation impulse was evaluated by the intensities of the muscle twitches at these five points. After that, the effective stimulation of up to 70 points was performed. The intensities of the muscle twitches of these 70 points were taken to identify the region in the brain where muscles are represented.

The coil itself influences the brain-mapping procedure because each coil has different effects to the brain. Therefore, the electromagnetic field of the coil has been measured and a grid representing the field strengths has been obtained (Fig. 3). The determination of the electromagnetic field was done in a previous experiment using the robot, a copper wire probe and a PCS100 8 bit digital oscilloscope (Velleman Components N.V., Gavere, Belgium) with a sampling frequency of 800kHz [11].

The precise knowledge of the stimulation points and the coil field characteristics enabled us to calculate the electric field distribution in the brain for each stimulation point. Assuming now an approximately functional relationship between the electric field strength at the representation of a muscle and its MEP response, we calculated the most likely representation point for the muscle using an adapted version of the Correlation Ratio statistic [11].

An image segmentation algorithm (SPM package for Mat- Lab) was used to obtain the surface of the grey matter. For this brain image, the measurements of the muscle’s twitch $Y = \{y_1, ..., y_N\}$ and the characteristic grid of the coil’s electromagnetic field $X = \{x_1(p), ..., x_N(p)\}$ are used to calculate the electric field strengths for all points $p$ on the brain’s surface for all stimulation positions. Let $Y = \{y_1, ..., y_N\}$ be the list of measured twitches. We use a discretized version of the Correlation Ratio $\eta$ to measure the functional dependence between the electric field strengths $X(p)$ at a brain point $p$ and the muscle responses $Y$:

$$\eta_y = \frac{\sum_{p \in P} x(p) y(p)}{\sqrt{\sum_{p \in P} x^2(p) \sum_{p \in P} y^2(p)}}$$
\[ \eta(y_1, \ldots, y_N | x_1(p), \ldots, x_N(p)) = \frac{1 - \sum_{j=1}^{N} y_j^2 - \sum_{i=1}^{N} \left( \sum_{j=1}^{N} y_j g_j(x_i) \right)^2}{\sum_{j=1}^{N} y_j^2 - \frac{1}{N} \left( \sum_{j=1}^{N} y_j \right)^2}, \]

(1)

where \( g_j \) are Gaussian windowing functions centered at \( x_j \) (see [12]). The correlation ratio is 1, if \( p \) is the point on the motor cortex from where the muscle is controlled. Otherwise, the correlation ratio is less than 1. The representation site of the muscle in the brain is thus found as the point \( p \) which maximizes (1).

The calculation of each brain-map took about one minute. Measuring the stimuli took about one minute at each position. A detailed description of brain mapping using Correlation Ratio is presented in [12].

### C. EXAMINATION OF PROBANDS

One healthy test person and six patients suffering from tumors (WHO grade I-IV) in or neighbouring the central region of one hemisphere were enrolled in this pilot study. First, they underwent a normal functional MRT-examination followed by the procedure explained in section II-A. The brain of all tumor patients who were operated was also stimulated directly during the operation.

Up to five spots have been stimulated with different intensities for a first survey to initially choose the stimulation intensity to use in order to avoid using a too strong pulse with the risk of overstressing the patients. The intensity chosen was the one which was able to deliver activations for the recorded muscles without provoking discomfort in the patients.

Ten pulses per stimulated spot have been delivered with an interstimulus interval of five seconds. The analysis of the peak-to-peak amplitudes of the motor evoked potentials recorded (MEPs) has been done online using the Medtronic Viasys software. The final value used for the scalp map at a given point has been calculated for the average of the MEP curves for that point.

The MRI data of the patient’s head is used for the TMS examination as well as for the intraoperative navigation. With the help of navigation markers the exact coordinates of the maximum stimulation point could be determined. These coordinates can be transferred to the navigation data for individual muscles easily. This simplifies the orientation during surgery. Therefore, several reference points were defined so that the coordinates of stimulated areas could be determined relative to these points. Difference vectors were calculated for each reference point and each muscle. These vectors were used to find the correct position of stimulated points during operation with the help of the navigation software (BrainLAB, Germany).

### III. RESULTS

The motor-cortex areas of individual muscles or muscle groups (m. abductor digiti minimi, m. abductor pollicis brevis and m. brachioradialis) were spatially clearly differentiated from one another (see Fig. 4). In addition to this, the functional data corresponded well to the classical anatomical mapping of segmented MRI (gyrus centralis, hand notch).
IV. DISCUSSION

Robotized transcranial magnetic stimulation is an appropriate non-invasive procedure for mapping the motor-cortex areas on the brain surface. With this it can be decided whether to remove diseased brain areas in order to reduce the tumor or to leave the tumor to avoid paralysis. An accuracy of about 5mm on the brain surface has been achieved compared to the direct stimulation. It provides a resolution of the motor-cortex areas of individual muscles and muscle groups and is superior to the functional MRI because fMRI also shows neighboring muscle groups and secondary motoric areas, which do not control the muscles themselves but are responsible for motion planning. The removal of such secondary motoric areas is not so bad because the functions of these areas can be adopted by other brain areas. In contrast to fMRI, our robotic TMS-System shows only brain areas which must not be removed. This makes our method more specific.

The intraoperative stimulation of three muscles (forearm, pinky and thumb) showed a good agreement with the target points of the praoperative stimulation. The configuration of robotic TMS makes it possible to transfer the position of maximum stimulation of single muscles to the navigation system used during operation. This enables a precise identification of important brain structures. In addition to this, it allows a accurate prediction of postions which have to be stimulated intraoperatively.

V. CONCLUSION AND FUTURE WORK

A. Conclusion

We presented first results of human brain mapping using a robotic TMS system. Individual muscles or muscle groups can be detected reliably and with high accuracy in the motor cortex of a patient’s brain. The quality of the map is comparable to fMRI and is only exceeded by the direct stimulation of the brain during surgery. The advantage of TMS brain-mapping is, that no other muscle groups or secondary motoric areas, which do not control the muscles themselves but are responsible for motion planning, are included in the map.

It was shown that the displacement of brain regions, which are responsible for the control of individual muscles in the motor-cortex, can be determined with the help of robotic TMS. This was confirmed by direct stimulation during the operation.

B. Future Work

For the future, we plan to extend this pilot study to include more patients. Especially, we are interested in measuring the extent of the motor representation area in the OR and compare it with our statistical TMS map. Further, we are working on statistical algorithms which require less mapping points than η, reducing the time requirements for the TMS mapping procedure.

REFERENCES