MR GUIDANCE OF TMS FOR A PATIENT SPECIFIC TREATMENT PLAN:MR BASED TMS FIELD MEASUREMENTS AND ELECTROMAGNETIC SIMULATIONS

S. Mandija[1], P. Petrov[2], S.W.F. Neggers[2], A.D. de Weijer[3], P.R. Luijten[1], and C.A.T. van den Berg[1]

[1]Imaging Division, UMC Utrecht, Utrecht, Netherlands, [2]Brain Center Rudolf Magnus, UMC Utrecht, Utrecht, Netherlands, [3]FMRIB Center, University of Oxford, Oxford, United Kingdom

Introduction: Transcranial magnetic stimulation (TMS) is a non-invasive neuro-stimulation method. For this purpose, a TMS coil applies a focal, time-varying incident magnetic field to a specific target region inducing an electric field and causing neuronal activation by locally exceeding the neuronal depolarization threshold[1]. The less painful inductive current generation makes this technique attractive to treat neurological disorders. Although a TMS-MRI setup already exists for fMRI studies, the positioning and power calibration of the TMS coil is still performed in a very simple way. The TMS power is increased until the thumb movement in response to a TMS pulse applied on the motor cortex is observed[2]. Here we demonstrate that MRI can provide guidance and dosimetry of the TMS treatment by mapping and quantifying the incident TMS magnetic field (B_{TMS}). For this purpose, we first describe a new combined TMS-MRI setup and MR sequence that allow us to map B_{TMS}. Then, starting from this map, we simulate the TMS induced electric field employing a patient specific brain model generated by automated segmentation of pre-treatment MR images. In this way, we can verify whether the TMS magnetic field focus overlays the target area. Subsequently, by means of the subject specific modelling we can quantify the electric field at the target area.

Materials and Methods: A TMS machine (Rapid, Magstim Company, Whitland, UK) is here integrated into a 3T MR scanner (Achieva, Philips, Best, The Netherlands) using different components to safely apply a TMS pulse.

Combined TMS-MRI setup: In fig.1, starting from the top left corner, for each 90° pulse of a Multi-SpinEcho sequence a TTL pulse is sent to a control box. This box synchronizes the TMS machine with the MR scanner triggering the TMS control signal. Every time a TMS pulse has to be delivered, the control box sends a pulse to a safety box that controls both the TMS machine and the relay box (Rapid, Magstim Company, Whitland, UK) enabling the closing of the relay that connects the TMS machine to the coil. Particular attention is paid to the time the relay takes:

- to close (15 ms), otherwise it will break due to the high level of current (15000 A) ;
- to open (2ms), to prevent image distortions by electrically disconnecting the TMS simulator from the coils.

All the signal time responses are verified using an oscilloscope (Fig. 2) to ensure the absence of delays in transmitting the signals between all the components shown in fig. 1. Finally, we use a dedicated TMS coil holder (Fig. 1.5) that enable placement of the TMS coil in different positions, paying attention not to exceed an angle of 30° between the coil plane and the B0 field to keep the Lorentz forces into mechanically tolerable limits[3].

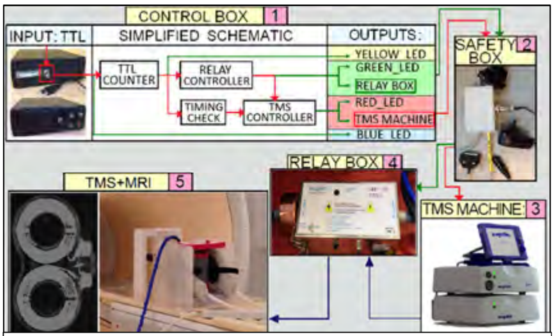

Figure 1: TMS-MRI setup: different components, MRI holder, CT scan of the TMS coil (resolution 1mm).

Measurements: We investigate the effect of a TMS pulse applied before the readout gradient in a conductive phantom (r = 12,5 cm, L = 20 cm, σ = 1.6 S/m: Agar 20 gr/L, NaCl 9.3 gr/L). In fig. 2, we show a Multi-SpinEcho sequence with the TMS integrated control signals: TR=1 sec, TE=50 ms, FOV= 160x160x88, RES=2.5x2.5x2.5 mm, G_x=29mT/m, slew rate=188 T/m/s. To safely apply a TMS pulse, a free gradient window is needed. Since we need 17 ms for the relay to open and close, this window is available only before the readout gradient. The measured accumulated phase at the spin echo is[4]:

$$\phi_{acc} = \phi_{RF} + \gamma \int_0^{TE} \Delta B_{0,eddy\_current}(\vec{r},t)dt + \gamma \int_0^{T_{TMS\_pulse}} \Delta B_{TMS,z}(\vec{r},t)dt\,.$$

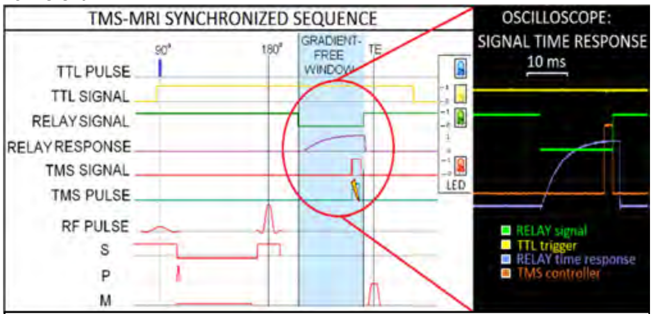

Figure 2: TMS-MRI integrated sequence and oscilloscope measurements.

After unwrapping the phase images (Fig. 3, c-d), it is possible to calculate the TMS incident magnetic field strength. To isolate the TMS phase contribution from other SE phase contributions such as the RF phase and the eddy current phase we subtract the phase image acquired with non-zero and zero power of the TMS pulse. Then we retrieve the z component of the incident TMS magnetic field: $\Delta B_{TMS,z}(\vec{r}) = \frac{\phi_{acc}^{TMS\neq0}-\phi_{acc}^{TMS=0}}{\gamma\int_{t_{TMS\_pulse}} A(t)dt}$, where A(t) is the time integral over the TMS pulse waveform.

Simulations: Using SCIRun (SCI Institute's NIH/NIGMS CIBC Center, University of Utah, Utah), for the three different values of power we simulate $\Delta B_{TMS,z}$ to match the measured one. In this way, from these maps we can simulate the total electric field induced in the phantom (E_{ind}^{TMS}), assuming a quasi-static approximation (Fig. 3, m, n, o). By overlapping the electric field map on a pre-acquired anatomical image and on an anatomical image acquired during TMS session, we can precisely define the region that will be excited, since the electric field is very focal. Subtle changes in the position of the TMS coil allow us to target the focus of electric field to the region that has to be treated. Then, by changing the amount of current that runs into the TMS coil we can evaluate the minimum value needed to induce an E_{ind}^{TMS} capable to depolarize neuronal membranes inducing neuronal activation. In this way, we have created a very precise method to perform TMS magnetic field dosimetry.

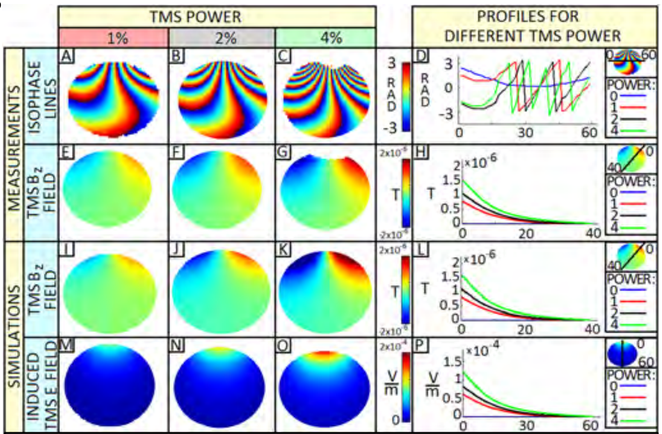

Figure 3: Measurements and simulations of the TMS incident magnetic field for three different intensities of the TMS pulse, and relative simulated induced electric fields.

Results: In fig. 3, a, b and c we clearly see both the increase of the phase wraps with higher TMS power values by a factor of $\sqrt{2}$ and a region closer to the TMS coil where intra-voxel dephasing occurs due to large intra-voxel ΔB_{TMS} field gradients. With the method described above, from measurements we retrieve the z component of the incident TMS magnetic field, the only measurable component (Fig. 3, e, f, and g). We can compare the measured magnetic fields maps with the simulated magnetic field maps (Fig. 3, i, j, k). As shown in fig. 3, the magnetic field drops approximately with $1/r^3$, where r is the distance from the coil, and it increases with the square root of the pulse power. As we can see, the region where E_{ind}^{TMS} is maximum is very constrained. Therefore guiding the positioning of the TMS coil with the MR scanner is crucial to precisely and correctly stimulate a predefined target brain area and subsequently quantify exactly the applied magnetic field at the focal region. An overlay of the measured magnetic field onto an anatomical scan acquired during TMS-MRI session records the applied treatment plan.

Conclusions: A precise MR based map of the TMS magnetic field, in combination with electromagnetic simulations and pre-acquired anatomical images, allows us to evaluate the behaviour of the induced TMS electric field and precisely target a certain functional area. In fact, with this new combined TMS-MRI setup we can now guide and provide dosimetry of TMS with the MR scanner for a patient specific treatment.

References: [1] D. E. Bohning et al, Neuroreport 1997, 8(11), 2535-2538. [2] M. Kobayashi, Lancet Neurology 2003, 2, 145-156. [3] A.D.de Weijer et al, Clin Neurophysiol 2014, 31(5), 474-487. [4] A. S. C. Peres et al, IFMBE Proceedings 2009, 25(7), 571-574.