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Transcranial magnetic resonance guided focused ultrasound for non-invasive treatment of brain diseases

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1) WM description

Transcranial magnetic resonance (MR)-guided focused ultrasound (tcMRgFUS) has become a promising technology for non-invasive treatment of brain diseases. However, its treatment planning and monitoring phase is hampered by the lack of reliable predictability and embedded automation. A safe treatment is currently possible, but very challenging and time consuming. Here, we summarize the state-of-the-art workflow of clinically applied tcMRgFUS and highlight enabling technologies in the field of MR thermometry. The presented MR methods are not limited to tcMRgFUS and could also support applications such as RF hyperthermia. One objective is to form a consortium of interdisciplinary research expertise aiming for a grant submission in which the existing problems are targeted.

2) Comprehensive review (state-of-the-art)

TcMRgFUS is a non-invasive therapy with the potential to treat several types of brain diseases hopefully replacing some of the open craniotomies or particularly minimally invasive approaches in functional neurosurgery [1-4]. Unlike established treatment options such as deep brain stimulation, tissue resection, or invasive tissue coagulation, tcMRgFUS does not require invasive procedures that carry high risks of complications including damage of healthy tissue around the surgical area, infection and hemorrhages. Furthermore, in contrast to non-surgical cancer treatment modalities like radiation therapy, tcMRgFUS does not use ionizing radiation. This allows for multiple treatment sessions without increased risks of collateral damage to remaining healthy tissues.

TcMRgFUS procedures can be divided into two phases: (i) precise treatment planning and (ii) treatment monitoring. The former involves transducer parameter optimization based on CT data by calculating phase-aberrations in the human skull and by adjusting phase and amplitude of the ultrasound transducer elements to achieve a high focal gain. Pre-acquired CT images are registered with MR images and based on a brain atlas, the surgeon identifies the treatment area. One of the key advantages of MR imaging in thermal treatment is its capability of a non-invasive, direct assessment of local temperatures using inherent physical temperature dependencies of the MR signal. Treatment monitoring is based on a planning phase where low-power sonications together with MR thermometry help the surgeons to correctly position the focal spot of the treatment. In parallel, it is verified that no other areas than the treatment region are heated, i.e. through acoustic energy absorption in the skull or secondary foci. The final ablation is guided and monitored under the surveillance of MR thermometry.

The ultrasound applicator of the InSightec ExAblate 4000 Neuro system (InSightec Ltd., Tirat Carmel, Israel) consists of a hemispherical 1024-element phased-array transducer operating at 650 kHz [2]. The transducer setup is interfaced to an MR scanner (Discovery MR750w 3.0T, GE Healthcare, Waukesha, WI) and is integrated into a patient table that can be docked to the MR system. The patient's head is fixed inside a stereotactic frame and placed inside the transducer. During the treatment, the skull surface is cooled with water.

With a frequency of 650 kHz, deep brain targets such as the thalamus and sub thalamus are reached. The transducer parameters are adjusted according to CT-based modeling. The hot spot can be electronically shifted by 1 cm isotropic with a fixed transducer and according to skull properties, head positioning and tissue properties, enough focal gain is available for sonication. With this transducer, a focal spot of 2 - 6 mm and temperatures up to 60 °C are created. MR thermometry is achieved by techniques based on the temperature-dependent proton resonance frequency shift (PRFS) phenomenon [5-9]. Today, only single slice phase images from a gradient echo-based (GRE) sequence are acquired at the location of the hot spot [10] with a temporal resolution of about 3 s and a spatial resolution of about 2 mm isotropic. Temporal phase differences of the MR signal are utilized to calculate the relative temperature change, whereas the magnitude images give the T1 weighted soft tissue contrast information on which the thermal maps are superimposed.

One key goal of MR thermometry is to provide a highly spatiotemporally resolved temperature update. Multiple approaches have been proposed, such as parallel imaging [11-14], compressed sensing [15, 16], advanced temperature dependent reconstruction algorithms [17], or by simply applying fast single-shot MR sequences such as echo-planar imaging [18-[22], each of them owing their potentials and limitations. All these advanced techniques have in common that they have not found their way into clinical application yet, probably due to their technical complexity, but also regulatory impediments and financial restrictions may limit their success.

3) Gaps and challenges

TcMRgFUS treatments usually take up to 6 hours and are restricted to certain areas in the brain. The treatable area is limited by the size of the focal spot achievable by the transducer. At any phase of the tcMRgFUS treatment, the surgeons need reliable guidance through the procedures and the confidence that the focal spot of the treatment is identical to the predefined target and that no other healthy tissue is getting harmed by the procedure.

CT data sets with 1 mm isotropic resolution are required for a reliable computation of phase aberration and transducer parameters. This diagnostically often redundant acquisition adds unnecessary exposure to ionizing ration for the patient.

With existing, state-of-the-art technologies for tcMRgFUS, about 30% of the patients are not treatable with the current procedure due to currently not accessible inter-individual differences in cortical bone structure and geometry. Thus, ultrasound wave-attenuation and propagation in the human skull will only become prominent during the already started therapy.

The tcMRgFUS target area is selected by the surgeon based on a brain atlas created from a small sample of brains (elderly adults) and where no individual adaptation is possible, i.e. pediatric or pathologic anatomy. Identification of local brain functionality through advanced MR imaging methods like functional MR imaging (fMRI) or diffusion tensor imaging (DTI).

Furthermore, only 2D MR images are acquired at the location of the hot spot every 3 s. To safely locate the sonication hot spot, 3D or at least multi-plane temperature updates are highly desirable. However, the currently available and certified temperature imaging sequences do not allow reaching the high spatiotemporal resolution one would aim for. Major research efforts are ongoing to provide fast and robust MR thermometry protocols, but implementing those into a clinical protocol is not resolved yet. One technically limiting aspect is the electro-magnetic interaction of the ultrasound transducer with the MR system, which currently limits fast MR acquisitions such as echo planar imaging for temperature mapping or the above mentioned fMRI and DTI techniques.

4) Objectives to be achieved

This WM is aiming for a transition of tcMRgFUS from a currently very complex, time consuming and in various aspects restricted research application to a state-of-the art procedure in standard clinical care.

On the hardware side, a redesign of the transducer could enable larger treatment areas or treatment areas closer to the proximity of the brain, i.e. by changing the amount of transducer elements, their arrangement, and the driving frequency. Another aspect of new transducer designs could focus on the MR compatibility of the transducer to enable state-of-the-art MR sequences for temperature mapping.

To simplify the treatment planning workflow and to eliminate the critical exposure of ionizing radiation, using a MR based phase aberration calculation could be performed. Additionally, a potential error source of registering CT and MR images would be removed. One objective of this WM could focus on the prediction of the tissue properties through simulation and how to use the information to reliably predict the treatability of the patients. A safe guidance of the surgeon by supporting the treatment identification based on brain atlas- probabilistic atlas or functional probing would be highly desirable.

Safety of and confidence in tcMRgFUS clinical procedures can be improved if volumetric temperature maps with sufficient temporal resolution become available. As such, fast MR thermometry techniques are highly desirable in clinical tcMRgFUS to reduce acquisition time and, thus, increase spatial coverage of the hot spot. To further simplify early stage prototyping, data evaluation platforms in terms of a research software tool would add high value.

Finally, reducing the treatment duration would increase the patient's comfort and clinical patient throughput, which is essential to establish the general acceptance of the technology from a patients but also the economical perspective.

5) Proposed research activities

The research activity proposed may be organized as follows:

- Implement a single modality planning workflow to overall shorten the treatment time and to replace the CT scan. This could be achieved by using zero TE bone imaging [23]. It is expected that the prediction of treatability by calculating phase-aberrations from the MR images with high bone contrast could be improved.
- Further investigate fast MR thermometry techniques, i.e. by calibrating the transducer with the help of a magnetic field camera (i.e. as provided by Skope, www.skope.ch) and by using the information in higher order eddy current compensated image reconstruction.
- Look at other MR signal contrasts to extract temperature information, i.e. proton density, T1/T2 relaxation properties, diffusion, or hybrid methods to obtain overall temperature map coverage.
- Develop MR thermometry platform for sequence exchange.
- Increase predictability of treatability by applying tissue property simulations.
- Support the surgeon in the treatment identification based on brain atlas- probabilistic atlas or functional probing would be highly desirable.
- Propose new transducer designs to increase MR compatibility in terms of minimizing conducting structures that produce eddy currents which create strong geometric distortions [24] to enable fast MR imaging sequences such as EPI.

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