MR-Guided Focused Ultrasound for the Treatment of Essential Tremor: Initial Experience on MR-Based Targeting and Temperature Monitoring

Yuexi Huang[1], Nir Lipsman[2], Michael L. Schwartz[3], Andres M. Lozano[2], and Kullervo Hynynen[1]

[1]Sunnybrook Research Institute, Toronto, ON, Canada, [2]Division of Neurosurgery, Toronto Western Hospital, Toronto, ON, Canada, [3]Division of Neurosurgery, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Introduction

Magnetic resonance guided focused ultrasound (MRgFUS) has been undergoing clinical trials in the treatment of various brain diseases, including neuropathic pain (1,2), brain tumor (3), and essential tremor (4). Ablating tissues in the brain requires spatial accuracy on the order of 1 mm to avoid damaging surrounding neurons and fibers. Here we summarized the initial findings on MR-based targeting and temperature monitoring in a phase-one clinical trial on essential tremor performed in 2012 at our hospital.

Methods

Four patients with medication-refractory essential tremor have been treated by a MRgFUS brain system (ExAblate 4000, 650kHz central frequency, Insightec, Tirat Carmel, Israel) with a 3 T MR scanner (MR750, GE Healthcare, Milwaukee, WI, USA). Treatment target was the ventralis intermediate nucleus (VIM) of the thalamus. Since the VIM cannot be directly identified in regular MR images, targeting was based on distance measurement from reference structures according to the stereotactic atlas (5). Measurement was performed on an oblique axial FRFSE T2 image crossing through the anterior commissure (AC) and posterior commissure (PC) (TR 3920 ms, TE 98.5 ms, slice thickness 2mm). The average location of the VIM was ~15mm lateral from the central line, and ~7 mm anterior from the PC (Fig.1). Minor adjustment (±1mm) for patient variance was added based on the measurement of the length and width of the third ventricle. Low energy sonications (250-350 W, 10s) were first applied to elevate the focal temperature to be over 40 ^{o}C. Temperature was mapped by proton resonance frequency (PRF)-based MR thermometry (TR 27.6 ms, TE 12.8 ms, slice thickness 3 mm, FOV 28cm, 256x128, temporal resolution 3.5s). If the actual heating volume mismatched the targeted location, corrections were applied by steering the ultrasound beam to the intended location. Corrections were performed on all three orthogonal planes across the focus. Power was then further increased to elevate focal temperature close to 50 ^{o}C. In case the patient had a sensory response, such as numbness of fingers during the sonication, the target location was adjusted accordingly to avoid the side effect. After confirming the target with no sensory response, power/sonication time were incrementally increased till the peak temperature was above 57 ^{o}C, or the thermal dose induced permanent lesions (750-1200 W, 10-30s). FRFSE T2 images were acquired between sonications to confirm the location/volume of the lesion. After each sonication, testing of the tremor was performed in the MR scanner. If some tremor symptoms remained, sonication was repeated at the same location to enlarge the lesion volume. For research purposes, diffusion tensor images (DTI) were acquired before and after treatment for retrospectively investigating diffusion-based image contrast in the thalamus for direct VIM targeting (b=1000, 2mm slice thickness, 68 diffusion directions).

Results

All four patients were successfully treated with significant reduction/removal of tremor symptoms. In two patients, the initial target based on distance measurement needed no adjustment (i.e. no sensory response). In the other two patients, targets were both moved 1mm anterior, and 1mm inferior / 1mm superior, respectively, based on sensory responses. Alignments of the ultrasound focal volume to the intended target location based on low-power heating were necessary on all four patients (±5mm maximum). Fig.2 is a post-treatment T2 image showing the lesion at the exact location as planned in Fig.1. Fractional anisotropy images generated from DTI showed hyper intensity signal next to the lesion location in all four patients (Fig.3). This hyper intensity structure and the margin of the internal capsule in fractional anisotropy images may potentially be useful for adjusting VIM targets for individual patients. In MR thermometry, background phase corrections were applied to remove flow/ brain motion induced phase errors. MR thermometry was performed on all three orthogonal planes with repeated sonications until the shape/location of the focal volume was confirmed.

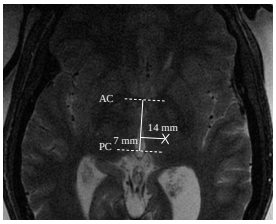

Fig.1 VIM targeting based on distance measurement from the AC-PC reference on an intraoperative T2 image.

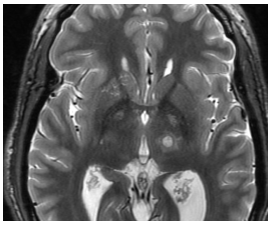

Fig.2 Post treatment T2 image shows the lesion at the intended target location.

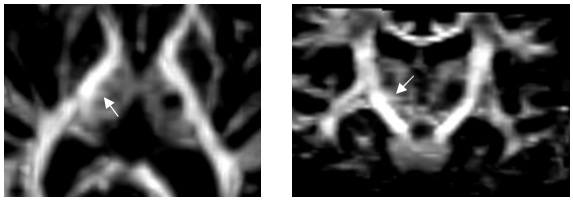

Fig.3 Post treatment (day7) fractional anisotropy images (axial and coronal) showing hyper intensity signal in the thalamus next to the corresponding lesion location on the contralateral side (arrows). This structure may potentially be useful as a landmark for targeting the VIM.

Discussion

VIM targeting based on distance measurement on T2 images appeared to be accurate in our four patients (within 1mm). Furthermore, patients' feedback from low/medium power sonications was very important in fine tuning the target location. The focus of ultrasound was 3 mm in diameter in the lateral dimension. However, to have significant reduction of tremor symptoms, the volume of the lesion needed to be about 6mm. This was achieved by sonications at higher powers and longer times so that heat diffused to a larger volume. It is important to keep in mind that potential side effects at high energy levels (larger lesion) might not be observed at the testing sonications at low energy levels (smaller lesion). Therefore, while patient feedback was extremely valuable, image-based direct targeting is still important to avoid sensitive structures. Fractional anisotropy images generated image contrast within the thalamus next to the VIM target, which may be useful for patient specific targeting.

On temperature monitoring, it is crucial to perform temperature mapping on all three orthogonal planes with repeated sonications to detect any irregular shape of the actual focal heating volume. In the future, multi-slice temperature mapping is desirable to monitor the 3D temperature distribution at the focal volume.

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