Preclinical testing of a second-generation MRI-guided focused ultrasound system for transcranial brain tumor ablation

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Introduction: Previously, an MRI-guided focused ultrasound (MRgFUS) system was described that uses noninvasive transcranial ultrasound exposures to thermally ablate brain tumors (1-3). That system uses acoustic models based on information derived from CT scans to correct for skull-induced focal distortion (4). Based on initial clinical experience with the system was upgraded to use lower frequency and pulsed sonication to enhance the focal heating (5). Here, we describe preclinical tests of this device at our institution.

Methods: The device tested was the ExAblate 4000 MRgFUS system (InSightec, Haifa, Israel). It consists of a hemispherical 1000 element phased array transducer operating at 220 kHz coupled with a water circulation/degassing system and a clinical 1.5T MRI unit. Tests were performed in cadaver skulls (N=5) and tissue mimicking phantoms with acoustic properties similar to soft tissue. Focal heating produced by high power sonications (for tissue ablation; pulsed mode at 50% duty cycle, acoustic power up to 2475 W) and lower-power sonications (for target verification; continuous wave, acoustic power up to 396 W) was compared to the skull heating. Temperature was measured using MR temperature imaging (6) during 260 sonications. Experiments were performed to determine (a) at how many locations cavitation-enhanced heating could be observed (for ablation); (b) at how many locations heating *without* cavitation could be performed with a peak temperature rise of at least 5°C (to verify focal point); and (c) the ratio between focal heating to skull-induced heating for sonications with and without cavitation enhancement. The geometric focus was targeted near the center of the skull cavity and locations within ±3 cm of this point were targeted via electronic beam steering.

Results: The average ratio between focal temperature rise per kJ and skull-induced heating per kJ on neighboring phantom was 15.6 ± 5.6 when cavitation enhanced heating was evident during high power sonication. Example heating and thermal dose contours are shown in Fig. 1. When cavitation was not evident during high-power sonication this ratio was 1.6 ± 0.8. It was 3.1 ± 1.2 during lower power verify sonications. Heating of at least 18°C (to produce a peak temperature in vivo of 55°C assuming a body temperature of 37°C) was possible during sonication in 50/55 locations tested where multiple sonications were delivered up to the system maximum power (electronic steering up to ±3 cm from the geometric focus). Heating of at least 5°C was possible in 47/57 locations sonicated at low power. Cavitation produced no obvious artifacts to the thermal imaging during these sonications.

Discussion: These results indicate that this system has substantially improved the ability to steer the focal point away from the geometric focus without substantial skull heating compared to the previous clinical system (1-3). Thus, larger regions of the brain will be accessible by the device without overheating the skull and the brain surface. If cavitation enhancement similar to what was observed in the phantoms is observed in the brain, a wider range of patients will be targetable with this noninvasive technology.

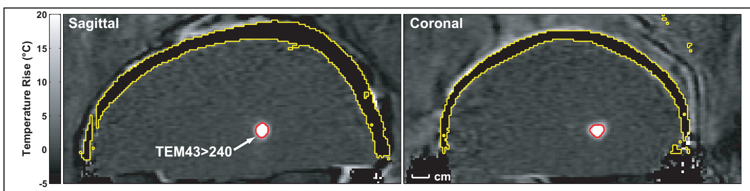

Fig 1. Sagittal and coronal temperature maps during high-power sonications in the brain phantom (acoustic power/duration: 1500 W/10s in sagittal example, 1000W/10s in coronal example). Segmentation of the skull bone is shown as well as thermal dose contours indicating regions that would receive at least 240 TEM43°C (assuming 37°C body temperature).

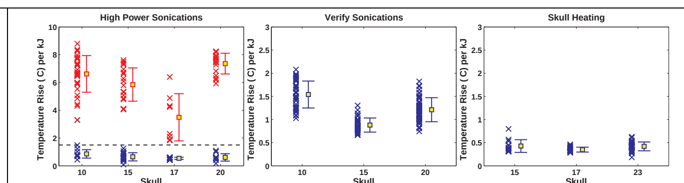

Fig 2. Temperature rise per kJ of acoustic energy for high power (ablation) sonications, low power sonications to verify focal coordinate, and for skull heating for all locations tested. For the high-power sonications, the measurements above the dotted line were assumed to be cavitation-enhanced.

References

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This work was supported by NIH Grant U41RR019703