

Transcranial MRI-guided focused ultrasound surgery of brain tumors: Initial findings in patients

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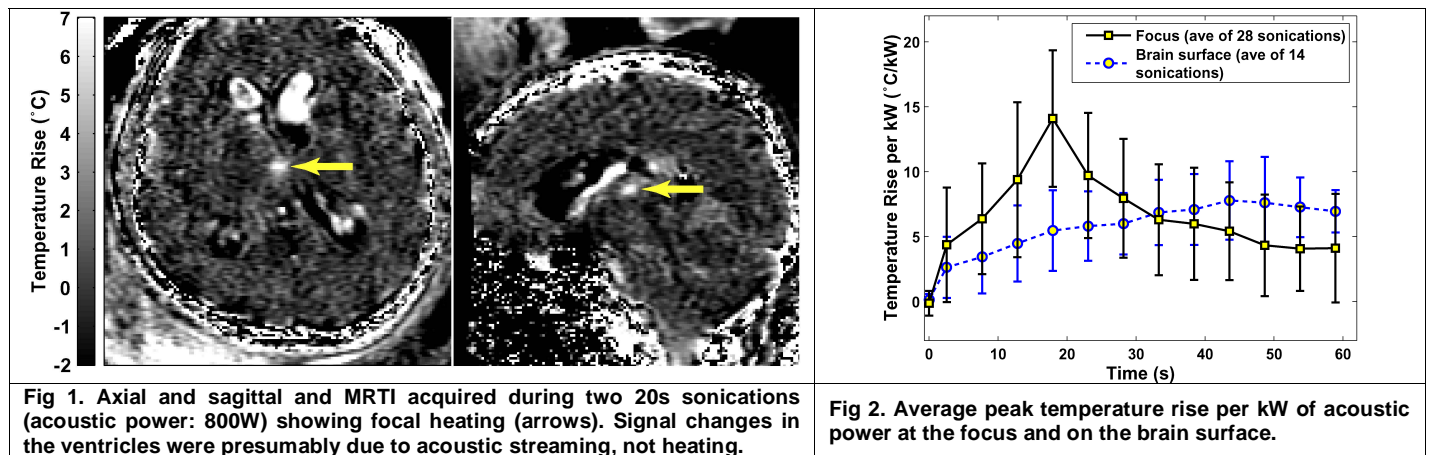
Introduction: Previously, an MRI-guided focused ultrasound (MRgFUS) system was described that aims to use transcranial ultrasound exposures to noninvasively thermally ablate targets in the brain (1-3). This system uses acoustic models, geometric and density information derived from CT scans, and a phased array transducer to correct for skull-induced aberrations of the ultrasound beam (4). Here we present initial technical results of this device from patient treatments.

Methods: The treatments were approved by our local IRB and we obtained informed consent. Three men with glioblastoma were treated with MRgFUS as part of a phase I clinical trial. The device tested was the ExAblate 3000 MRgFUS system (InSightec, Haifa, Israel), which consists of a 30 cm diameter hemispherical 512 element phased array transducer operating at 670 kHz coupled with a water cooling/circulation/degassing system and a clinical 1.5T MRI unit. Imaging was performed using the body coil. Before treatment, the patients' heads were shaved, coupled to the device with chilled and degassed water, and fixed in place using a thermoplastic mask. The treatments were performed under conscious sedation.

During treatment, the acoustic power was slowly increased over several 20s sonications until focal heating was observed in MR temperature imaging (MRTI) (5) to verify the target location within the tumor. After such verification, the acoustic power was increased further over additional sonications to the device's maximum level (800W). The maximum temperature rise achieved at each visible focal hotspot was calculated and compared to the heating on the outer brain surface induced by ultrasound absorption in the skull. To quantify this skull-induced heating, the mean temperature of the hottest 5% of the voxels within 7 mm of the outer brain surface were identified on coronal and sagittal images. This procedure was chosen to present a conservative estimate of skull-induced heating.

Results: Focal heating was readily observed in the tumor in MRTI (Fig 1) during 3/12, 14/16, and 11/17 of the sonications delivered in patients 1, 2, and 3, respectively. The maximum focal temperature achieved during a 20s sonication was approximately 51°C, near but not clearly above the threshold for thermal damage in the brain (6). Changes resulting from treatment were not evident in the tumor or brain in post-MRgFUS MRI. Average temperature measurements (normalized by acoustic power) over time at the focus and in hottest regions near the brain surface are shown in Fig 2. The average ratio between focal heating to brain surface heating was approximately 2. Severe instabilities observed in the phase difference images used for MRTI were removed by fitting non-heated regions of the brain to a smooth surface and extrapolation. A signal void in a large part of the tumor in patient 3 limited the use of MRTI in that region, presumably due to blood products from a prior biopsy.

Discussion: The study shows for the first time that ultrasound can be focused in the brain noninvasively through the intact skull in patients. While sufficient power was not available to us to clearly achieve thermal coagulation, these findings are a major step forward in producing a completely noninvasive alternative to surgical resection for brain disorders. Extrapolation of the mean temperatures achieved during these treatments suggests that with sufficient power, one could achieve thermal coagulation at the focus without overheating the brain surface. However, the safety window appears to be relatively narrow and could limit the extent of the brain that can be targeted without overheating the skull. Because of these limitations, the manufacturer has made substantial changes to the device and treatment strategy (7) to be used subsequent patient treatments in this trial. Results of treatments with this new version of the MRgFUS system will be presented separately.



References (1) Hynynen K, et al. *Magn Reson Med* 2004; 52:100-7. (2) Clement GT, et al. *J Ultrasound Med* 2005; 24:1117-25. (3) Hynynen K, et al. *Eur J Radiol* 2006; 59:149-56. (4) Clement GT, et al. *Phys Med Biol* 2002; 47:1219-36. (5) Ishihara Y, et al. *Magn Reson Med* 1995; 34:814-23. (6) McDannold N, et al. *Magn Reson Med* 2004; 51:913-23. (7) McDannold, N, et al. *Proc ISMRM* 2008.

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