MRI Monitoring of Skull-Base Heating in Transcranial Focused Ultrasound Ablation

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Introduction
The skull presents a major obstacle for focused ultrasound (FUS) ablation of the brain since it blocks most of the ultrasound energy and generates significant skull heating (1,2). In clinical trials, a craniotomy was often needed to provide an acoustic window for the ultrasound beam, which limited the attractiveness of FUS as a non-invasive surgical tool (3). This issue was greatly lessened lately by a hemispherical design of phased-array transducers to deliver the energy over the maximum available skull surface area, and by active cooling of the skull surface with water circulation (4,5). However, the potential heating of the skull base, which sits on the other side of the brain relative to the outer skull surface, has not been brought into much attention. If the targeted location is close to the skull base, a significant amount of energy may be deposited at the bone after passing through the focus. The lack of active cooling may result in a temperature elevation significant enough to cause damage to adjacent tissue and nerves. In this work, experiments were performed with a MR-guided transcranial FUS system on a full human skull sample to investigate the heating of the skull base. MR thermometry was applied to measure the temperature change during the phantom adjacent to the skull base. The distance of the foci to the bone was varied to measure a safety margin for avoiding significant skull base heating.

Methods
A prototype MR-guided FUS brain system (ExAblate 4000, Insightec, Tirat Carmel, Israel) was used with a 3T MR scanner (Signa MR750, GE Healthcare, Milwaukee, WI, USA). The FUS transducer consists of a 1000-element hemispherical phased-array with a diameter of 30 cm and a central frequency of 650 kHz. A full human skull was filled with gel phantom made by 50% of agar and 50% of milk. Ethylene Diamine Tetraacetic Acid (EDTA) and copper II chloride were added to adjust the MR properties (6). Acoustic and T1, T2 values of the phantom were tuned to be similar to that of human brain tissue. Fig.1 shows the skull setup in the transducer. CT data of the human skull was acquired prior to the experiment and registered to the MR coordinate for the ultrasound re-focusing correction used by this transcranial FUS system (Fig.2). 10 sec sonifications with 900 W acoustic power were applied to various locations close to the skull base. 5 min intervals were allowed between sonifications for the cooling of the skull. Active water cooling (~20 °C) to the outer skull surface with circulated water was applied between sonifications. Proton resonance frequency (PRF)-based MR thermometry was used to measure the temperature change during and after sonifications. Sagittal images were applied to cover the cross-section of the skull base with a slice thickness of 3.3 mm and a temporal resolution of 3.5 sec. A 3x3 ROI at the hottest area adjacent to the bone was manually chosen to measure the temperature elevation of the skull base.

Results
The acoustical attenuation of the phantom was measured as 3.8 Np/m/MHz and the sound speed was 1400 m/s. T1 and T2 values at 3T were around 900 ms and 133 ms, respectively. These values were close to that of human brain tissues. MR temperature images showed significant heating of the skull base. When the focus was 15 mm from the bone, the temperature increase of the skull was 8 °C, which was equal to the temperature elevation at the focus (Fig.3). When the focus was electrically steered away from the bone, the heating of the skull base was reduced (Fig.4).

Discussion
To our knowledge, heating of the skull base in transcranial FUS ablation has not been previously reported in research and clinical studies. This could be either due to that the targets in previous studies were mostly away from the skull base, therefore the MR thermometry imaging plane did not cover the bones, or because in the in situ situation, blood perfusion helps to dissipate the heat quickly. Perfusion was not present in our ex vivo study and could reduce the significance of the heating issue in situ. Nonetheless, our data suggests the heating of the skull base should be considered when targets are close to bone (<2 cm) and further in vivo animal studies are needed.

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References