Pre-clinical testing of a phased array ultrasound system for MRI-guided noninvasive surgery of the brain - A primate study

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Introduction: Applying focused ultrasound surgery in the brain has been hampered in the past by the presence of the skull, which distorts the ultrasound beam and heats excessively due to its high absorption. Recently a technique was introduced that uses a large ultrasound phased array and CT derived information skull parameters to correct for the wave propagation and allows for trans-cranial focusing without overheating the skull (1). A complete system based on this array technology designed for clinical focused ultrasound surgery has been developed, and it was tested here in non-human primates to establish the clinical feasibility of the approach. Due to the small size of the primate head these experiments were designed to establish the maximum intensity levels that could be delivered through the living skull bone.

Methods: The ultrasound system (ExAblate 3000^{TM}, InSightec) consisted of a hemispherical ultrasound array with 512 equal area elements and radius of curvature of 15 cm (frequency =670kHz) the array elements were driven with a separate RF line with independent amplitude and phase control. The hemispherical array was positioned on its side and connected to a three dimensional manual positioning device that allowed the focal point of the array to be aimed within the target volume.

The MRI guided focused ultrasound system was tested in three rhesus monkeys. The monkeys were anesthetized with a mixture of ketamine and xylazine, the hair on the head of each monkey was removed with clippers and hair-removing lotion. The animal was positioned on its back, and its head was held in place with an acrylic holder so that the brain was centered in the ultrasound array. A latex membrane was secured to the edges of the array. The head was inserted through a hole in this membrane, which was slightly smaller in diameter than the head. Thus, a watertight compartment between the array surface and the membrane and the skin on the head was created. This space was filled with temperature controlled, degassed, circulating water to couple the ultrasound array to the head and to cool the skin and the skull (Fig. 1).

The algorithm for focusing through the skull utilized CT-derived information of the skull geometry (2) and its localization from a digitized profile of the skull obtained using a Siemens SOMATOM CT Scanner (FOV = 20 cm, slice thickness = 1 mm). A bone reconstruction kernel (AH82) was used to acquire image intensities proportional to the bone density. The CT and MRI images were co-registered by using an overlay display that allowed visual inspection and alignment.

Experiments were performed by focusing the beam in locations within the brain while imaging the temperature elevation with the MRI. Temperature images were acquired in one plane from phase-difference images of a fast spoiled gradient echo sequence (3) (TR/TE = 39.3/19.3 ms, flip angle = 30°, bandwidth = 3.57 kHz, FOV = 32 cm, slice thickness = 3 mm, matrix size = 256x128, scan time = 5.3 s). A temperature sensitivity of –0.010 ppm/°C was used (4). A time series of temperature maps were produced. In addition small thermocouple probes (wire diameter 0.05 mm, bare junction) were inserted under the skin on the skull surface.

Results: The thermocouple probes on the skull surface under the skin demonstrated that the skull surface temperature could be reduced to less than 20°C by circulating cooled water in the array (12-15°C). The surface temperatures increased during the sonication and then cooled back to baseline over the next 5-7 min. The MRI derived temperature agreed well with the temperature rise measured with the thermocouples (Fig. 2).

The outside surface of the brain was also heated by thermal conduction from the skull. The temperature elevation in all of the sonications is summarized in Fig. 3 as a function of the applied spatial average ultrasound intensity on the skull surface. Due to the fact that the monkey head is much smaller than that of a human, the brain surface heating reached the tissue coagulation limit before focal tissue coagulation could be achieved.

Discussion: These results continue to support that ultrasound induced completely noninvasive thermal ablation may be feasible. By cooling the coupling water the outer skull surface temperatures can be kept acceptable and the brain surface temperatures become the limiting factor. When the results are scaled to human size, it appears that focal coagulation is possible with the proposed method without damaging the brain surface, bone or the skin.

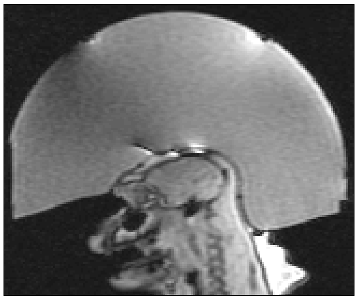

Fig 1: Gradient echo image of the monkey head within the ultrasound device. The thermocouple probe is visible as well.

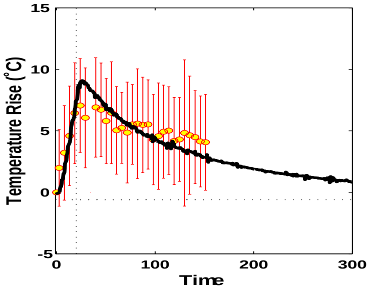

Fig. 2: Temperature vs. time plot for MR voxels outside the skull (circles, error bars: ±1 S.D) and for thermocouple measurements (solid line).

References

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Fig. 3: Temperature rise outside the skull as a function of ultrasound intensity on the skull surface.