EXPANDING THE TREATMENT ENVELOPE FOR TRANSCRANIAL MR-GUIDED FOCUSED ULTRASOUND WITH A 256-ELEMENT CLINICAL TRANSDUCER

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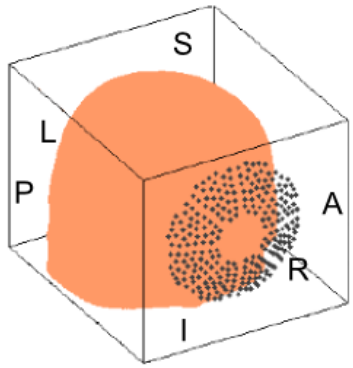
TARGET AUDIENCE: Clinicians and researchers who wish to use MR-guided high intensity focused ultrasound (MR-HIFU) in the brain, in the superficial cortex and near the skull base.

PURPOSE: MR-HIFU has demonstrated great promise for treating targets near the geometric center of the skull, such as the thalami[1]. However, with current clinical hemispherical transcranial MR-HIFU systems, it is difficult to develop spatially compact sonication foci that are suitable for clinical applications in the superficial brain or near the skull base[2]. We sought to determine whether a non-hemispherical clinical MR-HIFU transducer, whose sonication isocenter can be moved with respect to the subject, could develop spatially compact transcranial sonication foci within these clinically relevant locations.

METHODS: The Sonalleve V2 clinical transducer (256 elements, 3.3 mm element radius, 14 cm focal length, 13 cm diameter; Philips Healthcare, Vantaa, Finland) was modeled in MATLAB (Mathworks, Natick, MA) using the k-Wave Toolbox (University College of London, UK) at 800 kHz frequency. 3D Simulations were completed on a computer running Xubuntu 14.04 LTS, with 16 GB RAM, an Intel i7-3520M 2.9 GHz processor, and 128 GB SSD storage. Simulation grids and medium were matched to an anonymized normal head CT that was subsampled to 0.4 mm isotropic voxel size. The transducer position was moved to colocalize the transducer isocenter and the sonication target (Fig. 1). The transducer was oriented along the left-right axis for each position, except for sonication of the pons when the transducer was oriented superiorly-inferiorly. Phase aberrations induced by skull were measured using a point acoustic source placed at the target, using the transducer as the sensor elements. Transducer source timeseries were then corrected, with each element's phase set to the negative of the calculated phase delay.

Figure 1: Typical transducer (dark gray) configuration relative to the head (orange-pink) used in the simulations.



RESULTS: Without intervening skull, a sonication focus of 2.8 x 2.8 x 20.8 mm full width at half maximum (FWHM) was generated at the transducer isocenter. With skull included, an attenuated yet intact sonication focus could be developed within clinically interesting sites of the superficial cortex (superior temporal and inferior frontal gyri) and nearer the skull base (hippocampus, amygdala, nucleus accumbens, BA25 and pons; Fig. 2). FWHM of the transcranial sonication focus was on average 1.4 x 1.6 x 7.7 mm. Peak pressure relative to no skull was on average 53.4%, -2.7 dB (Table 1).

Figure 2: Sonication foci (red) for each target location, above a half of peak pressure threshold, overlaid onto a 1 cm white box centered on the sonication target and the relevant axial CT section. Axial and sagittal sections are displayed for the pons sonication focus, which is magnified 2x relative to the other foci.

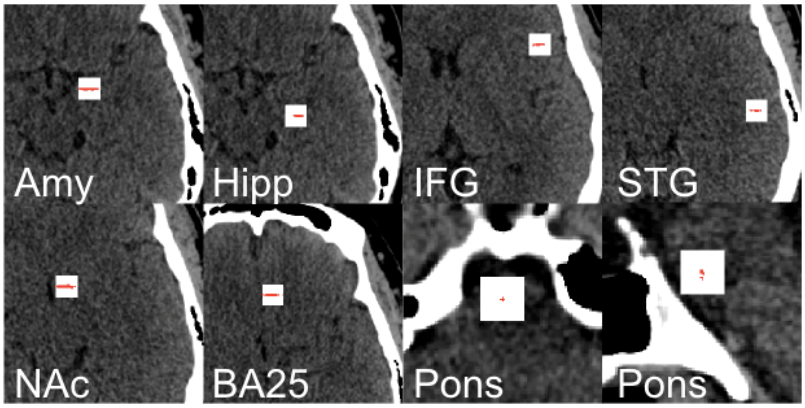


Table 1: Full width at half maximum (FWHM) and peak pressure (relative to the no skull condition) for each simulated transcranial sonication focus

Location	FWHM (mm)	Peak Pressure (Rel.)	
Amygdala (Amy)	1.6 x 2.0 x 9.2	48.2%	-3.17 dB
Hippocampus (Hipp)	1.2 x 1.2 x 5.2	44.2%	-3.55 dB
Nucleus Accumbens (NAc)	2.0 x 2.0 x 12.0	47.6%	-3.22 dB
Subgenual cingulate (BA25)	1.2 x 2.0 x 10.4	47.4%	-3.24 dB
Inferior Frontal Gyrus (IFG)	1.6 x 1.2 x 8.4	53.0%	-2.76 dB
Superior Temporal Gyrus (STG)	1.2 x 1.6 x 5.6	56.4%	-2.49 dB
Pons	1.2 x 1.2 x 2.8	77.2%	-1.12 dB
No skull	2.8 x 2.8 x 20.8	100%	0.00 dB

DISCUSSION: We were able to demonstrate *in silico* that a 256-element non-hemispherical clinical transducer may develop transcranial sonication foci at clinically relevant locations in the superficial cortex and near the skull base, as the isocenter of this transducer may be moved with respect to the subject. The focus FWHM was typically half in each dimension compared to sonication without intervening skull. The calculated reflection loss due to skull of approximately -3 dB agrees with that reported for reflection loss of human skull samples[3]. The differences in peak pressure and FWHM for the pons sonication compared to the others is likely due to the altered skull geometry and thickness of the cranial dome versus the lateral frontal and temporal bones. Given the expected attenuation loss of skull (-10-15 dB at 800 kHz[3]) and the maximal acoustic powers of this clinical transducer, these results suggest that the most successful such transcranial applications would be lower pressure ones like blood-brain barrier (BBB) disruption for drug delivery or neuromodulation, which require ~0.5 MPa acoustic pressure.

CONCLUSION: We have *in silico* evidence that a 256-element non-hemispherical clinical transducer can transcranially sonicate clinically relevant foci in the superficial cortex and near the skull base, particularly for applications such as BBB disruption for drug delivery and neuromodulation. Experimental validation of this study is underway in phantoms and animal models, using ARFI-based autofocusing algorithms[4].

REFERENCES: 1. Elias et al. (2013) NEJM. 369:640. 2. Eames et al. (2012) AIP Conf Proc. 1503:181. 3. Fry. 1977. Ultrasound Med Biol. 3:179. 4. Grissom et al. (2012) AIP Conf Proc. 1503:162. *Funding: NIH 5T32EB006351; Philips Healthcare; The Walter and Mary Ciceric Foundation*