Human skull resolution dependence of the transcranial focused ultrasound propagation accuracy

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Background:
Blood-brain barrier (BBB) opening with focused ultrasound (FUS) is a noninvasive technique for delivering therapeutics to the brain parenchyma. The noninvasive nature of BBB opening in the clinic relies on transcranial acoustic propagation through the intact human skull. However, phase aberration, signal attenuation and beam distortion after transcranial transmission necessitates thorough treatment preplanning, including transcranial acoustic wave propagation simulation. Such *in silico* preplanning involves simulating the acoustic propagation through a model of the patient's skull derived from patient-specific computed tomography (CT) scans and observing the predicted beam distortion and attenuation profile. Since transcranial acoustic wave propagation depends on several skull properties including density, thickness, topographical irregularities and trabecular microstructure, we demonstrate the improved ability of high-resolution micro-CT over conventional CT to better replicate the human skull model *in silico*.

Materials and Methods:
The k-Wave MATLAB toolbox for time-domain modeling of acoustic wave propagation was used to simulate a 1.5 MHz focused transmit in 2D and 3D from a P4-1 phased array transducer through micro-CT and conventional CT scan-based models of the same fragment of human frontal and parietal skull bone. The computational grid resolution of the 2D and 3D simulation was 8 points/wavelength and 6 points/wavelength, respectively, while the resolutions of the micro-CT and conventional CT scans used in the simulation were 0.08 mm and 0.49 mm, respectively. Density, sound speed and absorption maps for both skull models were derived from the Hounsfield unit scale in each CT scan. The simulated P4-1 phased array (96 elements, 0.245 mm element width, 0.295 element spacing, 16 mm elevational aperture) was positioned ~5 mm from the skull surface and the beam was electronically focused at 60 mm in the 2D simulation and 35 mm in the 3D simulation.

Results:
Along with the fundamental increase in skull microstructure resolution (Fig. 1), simulations revealed differences in both beam distortion and attenuation profiles between transcranial focused transmits through the micro-CT and conventional CT-based human skull models when validated against in vitro measurements. 2D simulations revealed axial focal shifts of 4.25 mm and 1.38 mm, and lateral focal shifts of 0.5 and 0.75 mm from the free-field focal position after transmission through the micro-CT model and conventional CT model, respectively. Additionally, acoustic transmission through the micro-CT model yielded a 19.32% increase in signal attenuation over the conventional CT model. 3D simulations of transcranial propagation through the micro-CT model yielded axial, lateral and elevational focal shifts of 3.25, 1.0 and 0.25 mm, respectively (Fig. 3), along with a 95.51% signal attenuation. The micro-CT model yielded a marked improvement in representing the attenuation profile recorded *in vitro* at 1.5 MHz of 87.7%.

Conclusions:
This study demonstrated the importance of emphasizing human skull microstructure for accurate simulation of FUS transcranial propagation and proper treatment pre-planning. While the reported simulated attenuation profile of the micro-CT model in 2D may underestimate the overall signal attenuation, the simulated attenuation profile in 3D more closely aligns with the attenuation profile recorded *in vitro*.

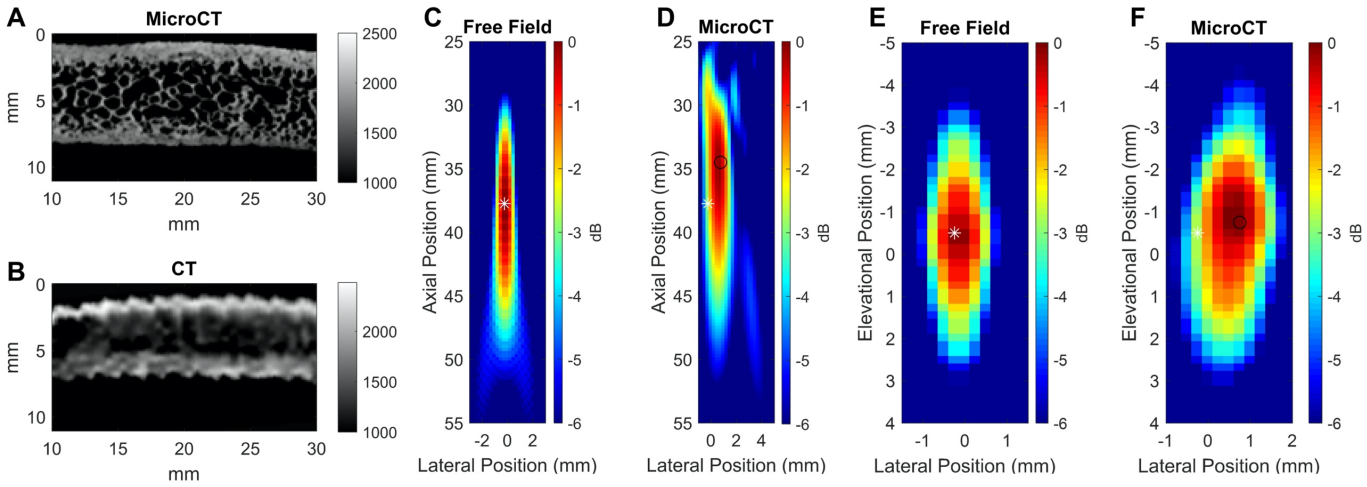
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Figure 1