A CLINICAL SYSTEM FOR NON-INVASIVE BLOOD-BRAIN BARRIER OPENING USING A NEURONAVIGATION-GUIDED SINGLE-ELEMENT TRANSDUCER

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OBJECTIVES

Blood-brain barrier (BBB) opening clinical trials using focused ultrasound (FUS) are conducted with either an implanted transducer or a multi-element array within an MRI system. Here, we describe a clinical system based on a neuronavigation-guided FUS transducer that can achieve a large treatment envelope non-invasively while eliminating the need of on-line MRI.

METHODS

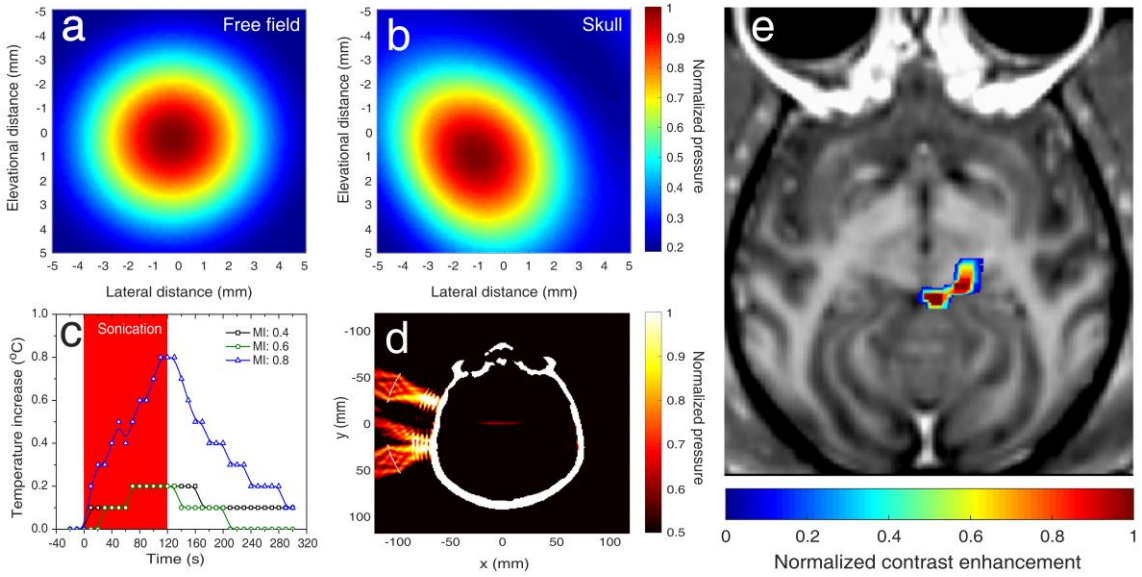
A 0.25-MHz, single-element FUS transducer was developed for clinical BBB opening applications. Human skull-induced beam aberrations and temperature increase were estimated during therapeutic sonication (MI: 0.4-0.8). K-Wave simulations were performed to determine whether the system was able to reach the human brain midline. *In vivo* feasibility was shown in a non-human primate (NHP) at MI of 0.4 (PL: 10 ms, PRF: 2 Hz) and 1x Definity microbubbles.

RESULTS

Numerical simulations showed that the system can target the human midbrain. Transcranial transmission through a human skull caused a 1-mm lateral and 3-mm axial focal shift. A temperature increase of 0.2-0.8°C was measured within the MI range of 0.4-0.8. Contrast-enhanced T_1-weighted imaging revealed a 150 mm^3 BBB opening in the NHP caudate at a MI of 0.4, without damage as assessed by susceptibility- and T_2-weighted imaging.

CONCLUSIONS

The neuronavigation-guided, single-element FUS system transcranially induced a safe BBB opening in a NHP brain with minimal distortion at clinically-relevant ultrasound parameters and FDA-approved Definity microbubble dosage.



CAPTION: a)-b) Beam transverse profile in free field and through a human skull. c) Skull heating. d) Numerical simulations of ultrasound propagation through a human skull. e) BBB opening at MI of 0.4 and Definity microbubbles at clinical dose.