Neuronavigation-guided focused ultrasound for non-invasive blood-brain barrier opening in the prefrontal cortex of Alzheimer's disease patients with real-time cavitation monitoring

A.N. Pouliopoulos[1], R. Ji[1], Maria M. Murillo[1], Rebecca L. Noel[1], Rachel Weber[1], Lawrence S. Honig[2], and Elisa E. Konofagou[1,3]

[1]Department of Biomedical Engineering, [2]Department of Neurology, [3]Department of Radiology

Columbia University, New York City, NY 10032, USA

Objective

FUS-induced blood-brain barrier (BBB) opening is rapidly expanding into clinical applications. Our group has developed a neuronavigation-guided clinical system prototype, which under an IDE by the FDA was applied in Alzheimer's disease (AD) patients. Here, we present preliminary findings from the first AD patient treated in the prefrontal cortex (PFC).

Methods

A 0.25-MHz FUS transducer (Sonic Concepts) was mounted onto a robotic arm (figure 1A). A 1.5-MHz transducer was used for real-time monitoring of cavitation emissions. Treatment planning in the BrainSight neuronavigation system included selection of a PFC location and a beam trajectory at normal incidence with the 12-mm-thick frontal skull. Modeling in k-wave was used to estimate an attenuation coefficient, which was 84±3%. The treatment was conducted using FDA-approved parameters (derated PNP: 200 kPa, MI: 0.4, PL: 10 ms, PRF: 2Hz, duration: 2min). T1-weighted MRI and amyloid PET images before and after the treatment were used for confirming the BBB opening and amyloid plaque load, respectively.

Results

We observed a localized 4.3-cm^3 BBB opening within the PFC following FUS using contrast-enhanced MRI (figure 1B). The subject reported no symptoms during or after the FUS procedure. Cavitation emissions were detected through the human skull and included harmonics and limited broadband signal at higher frequencies, with a harmonic-to-broadband dose ratio of 10. Amyloid PET 3 days post-FUS showed a 14% signal decrease in the targeted region.

Conclusion

Neuronavigation-guided BBB-opening in the PFC of an AD patient was shown to be feasible and initial findings in reduction of the detected amyloid PET signal were obtained.

Word count: 250/250 words