MRI-Controlled Focused Ultrasound Blood–Brain Barrier Opening in Rats.

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The delivery of therapeutic agents to the central nervous system (CNS) remains limited by the restrictive nature of the blood–brain barrier (BBB), which prevents most molecules exceeding ~400 Da from reaching neural tissue. This barrier represents a major obstacle in the treatment of disorders such as Alzheimer's disease and gliomas. MRI-guided focused ultrasound (FUS) combined with intravenous microbubbles offers a noninvasive and spatially targeted strategy to transiently disrupt the BBB (FUS-BBBO), enabling localized drug delivery while maintaining tissue integrity. This project aims to develop and optimize a safe and effective MRI-controlled FUS protocol for BBB opening in a rat model for therapeutic agent delivery. Four different levels of acoustic pressure were applied with the intravenous administration of microbubbles in order to open the BBB. Acoustic emissions from oscillating microbubbles were monitored during sonication to assess treatment response and correlate physical signals with biological outcomes. BBB permeability was evaluated using dynamic contrast-enhanced MRI on a 7 T Bruker BioSpec 70/30 USR scanner with an 86-mm volume Tx/Rx coil, following intravenous gadolinium contrast administration at 0.2 mmol/kg. The immediate post-FUS protocol started within several to ~15 minutes after sonication and included repeated short T1-weighted FLASH scans (TE/TR = 4/18 ms, FA = 12°, 0.3 × 0.3 × 0.3 mm^3, TA = 3 min 42 s), followed by a higher-resolution T1-weighted FLASH scan (TE/TR = 6/50 ms, FA = 18°, 0.15 × 0.15 × 0.5 mm^3, TA = 10 min 14 s). Pre-FUS MRI included anatomical T2-weighted imaging and T1 mapping, while follow-up scans at 6, 24, 48 and 72 h will be used to monitor BBB closure. Evans blue was used to verify the size of the BBB opening and its correlation with MRI contrast enhancement. Preliminary results indicate reliable MRI visualization of BBB opening shortly after FUS (15-30 min.), with concordant Evans blue extravasation visible post-mortem. Higher acoustic parameters were associated with minor hemorrhagic effects detectable on MRI and histology, underscoring the importance of parameter optimization. This study contributes to refining MRI-guided FUS-BBBO as a controlled and translatable platform for CNS drug delivery.