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# Blood-brain barrier disruption using a diagnostic scanner and Definity in mice

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Objective: To quantify localized disruption of the blood-brain barrier (BBB) in a murine model using focused, diagnostic ultrasound (at higher frequencies than previously studied) and contrast agent and to explore the optimal parameters for opening without causing irreversible damage. Methods: Definity (US contrast) and Magnevist (MR contrast) were injected before a custom ultrasound transmission sequence. The volume of tissue over which the BBB disruption allowed Magnevist to enter the brain was quantified by the contrast in T1-weighted MR images. Results: Preliminary results suggest increased BBB opening with decreased time between Definity injection and insonification. A range of typical diagnostic frequencies (e.g. 5-8 MHz) has shown BBB disruption, with maximum contrast occurring at 5.7 MHz. Increasing pressure had an apparent threshold for visible opening, while increasing F/# led to a larger region of BBB opening and increasing duty cycle produced more contrast. Histology showed blood cell extravasation from B-mode imaging (MI=1.5, duty cycle=0.4%), but no damage was noted after the low-pressure, custom sequences. Conclusions: This study has shown the ability of a diagnostic ultrasound system and contrast agent to open the BBB for nanometer-scale particles (possibly drugs) and examined the effects of various parameters on this opening.