Characterizing the mechanism of FUS-BBBO at pre-clinically and clinically relevant frequencies

Objectives

To assess the frequency dependence of focused ultrasound blood-brain barrier opening (FUS-BBBO) volume and cavitation mechanism through BBBO volume and closing.

Methods

A 0.5-MHz single-element FUS transducer (H-204, Sonic Concepts) was driven at 0.5 MHz and 1.5MHz (MI=0.4) (Fig. A). A phased array (P4-2, ATL Phillips, f_c=2.5 MHz, # elements:64) for acquisition of B-mode images for targeting and cavitation doses with a research ultrasound system (Vantage 256, Verasonics). 1:10 lipid-shelled microbubbles were administered in young, female transgenic microglia-knockout mice towards assessment of immune response changes at n=2/frequency. Contrast-enhanced T1-weighted MRI was used for BBBO and closing (BBBC).

Results

Average initial BBBO was 89.09 ± 21.99 mm^3 and 36.69 ± 4.75 mm^3, respectively (Fig. C)**.** The BBBC timeline at each frequency indicated BBBO at 1.5 MHz closed 2 days earlier than 1.5 MHz according to when 95% reduction of the initial BBBO volume was achieved. Linear regression fits indicated that the larger BBBO volume at 0.5 MHz also closed twice as fast as that at 1.5 MHz.

Conclusions

BBBO incurred 2.4x larger volumes and 20 dB higher cavitation doses at 0.5 MHz. BBBC occurred at faster rates at 0.5 MHz but lasted 3 days longer than at 1.5 MHz. FUS-BBBO characteristics of opening and closing are highly dependent on frequencies and should be considered for clinical translation.

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