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Pulse inversion therapy for improved monitoring of blood-brain barrier opening

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Microbubble-based ultrasound therapy has enabled the non-invasive and reversible opening of the blood-brain barrier (BBB). However, the skull limits our ability to monitor the microbubble activity due to high attenuation and beam aberrations. In ultrasound imaging, pulse inversion is used to cancel echoes from linear scatterers by summing the signal obtained from consecutive positive (phase: 0° degrees) and negative (phase: 180° degrees) pulses, thus facilitating imaging of non-linear scatterers such as microbubbles. Here, we adapt the pulse inversion technique to improve monitoring of BBB opening, by treating with consecutive therapeutic pulses of inversed polarity. Pulse inversion therapy (PIT) was achieved by synchronizing the emission of inverted short pulses (pulse length: 2-3 cycles, PRF: 2 kHz, pressure: 400 kPa) through a focused 0.5 MHz therapeutic transducer driven by two function generators. An inserted and co-aligned P12-5 linear array was used to passively capture the microbubble emissions. Absolute time-of-flight information was introduced in the beamforming since emission and reception were synchronous. PIT suppressed the signal from linear scatterers within the focal area up to 6dB in a gelatine phantom, compared to positive-only pulses. In ongoing *in vivo* work, BBB opening volume is being correlated with the microbubble signal harvested through PIT.

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