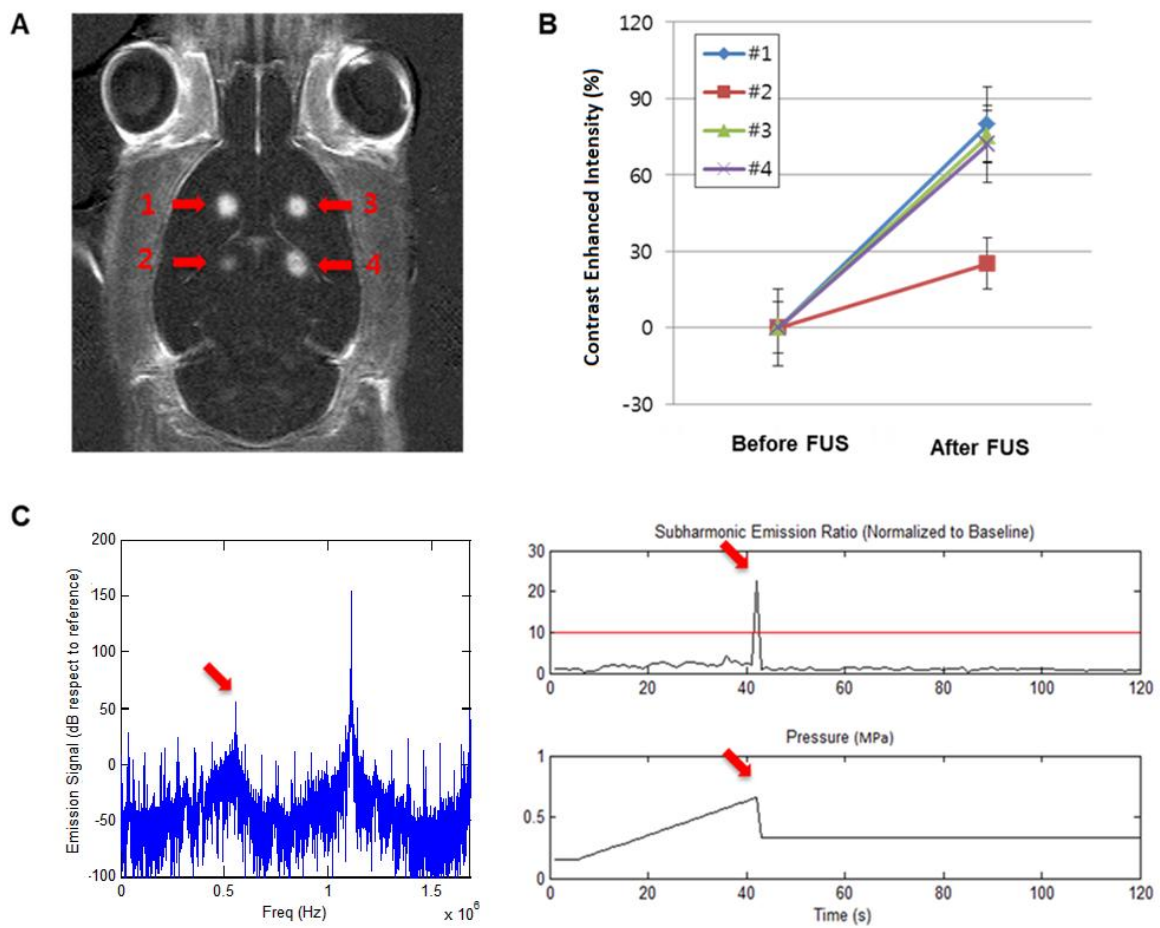


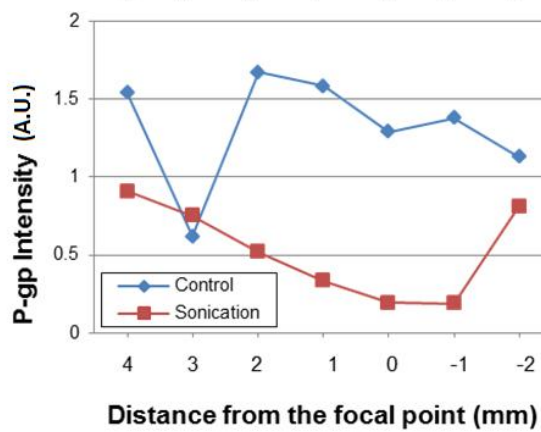
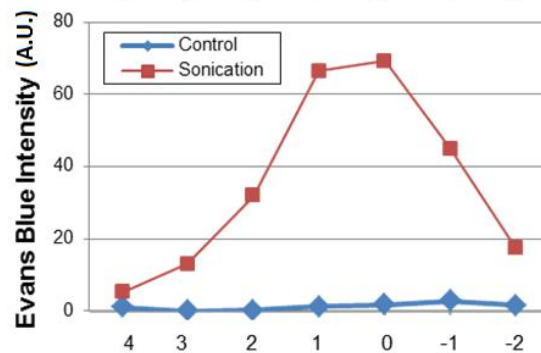
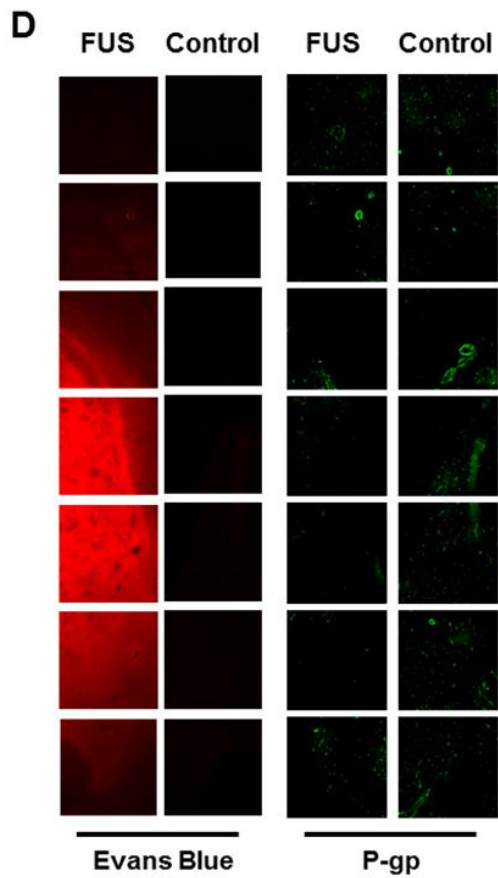
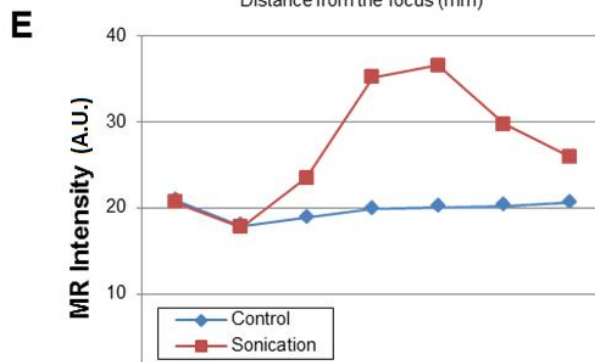
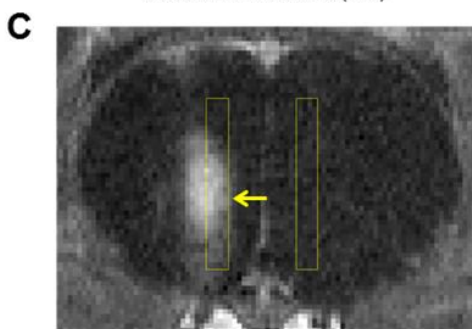
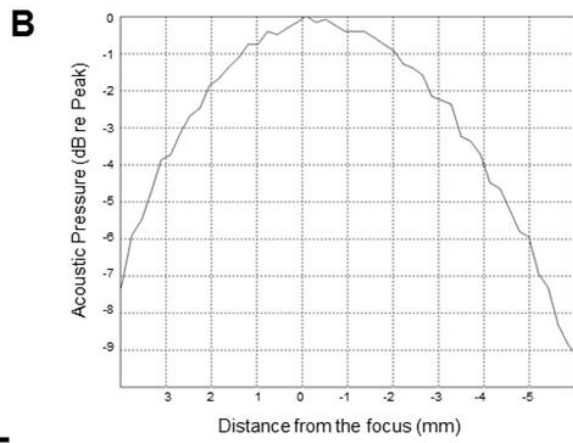
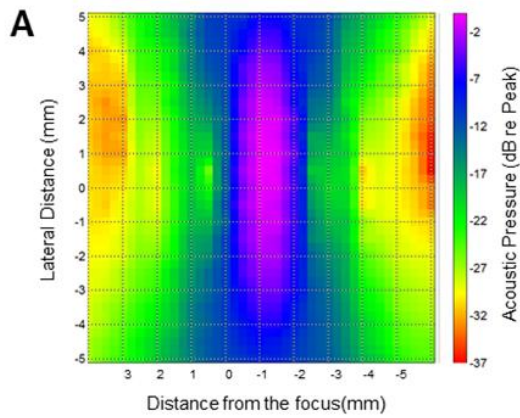
# Localized Down-regulation of P-glycoprotein by Focused Ultrasound and Microbubbles induced Blood-Brain Barrier Disruption in Rat Brain

HongSeok Cho, Hwa-Youn Lee, Mun Han, Jong-ryul Choi, Sanghyun Ahn, Taekwan Lee, Yongmin Chang, Juyoung Park

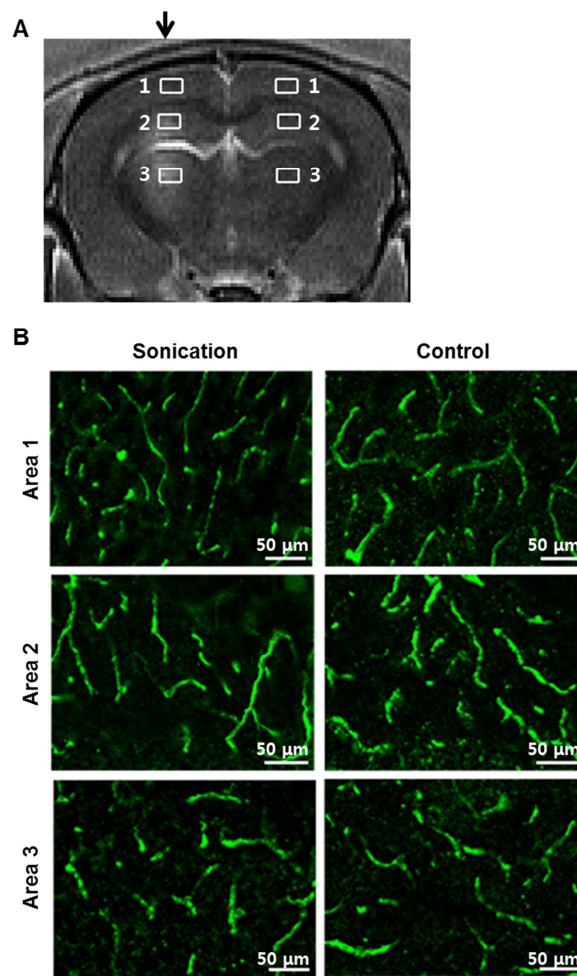
## Supplementary Materials



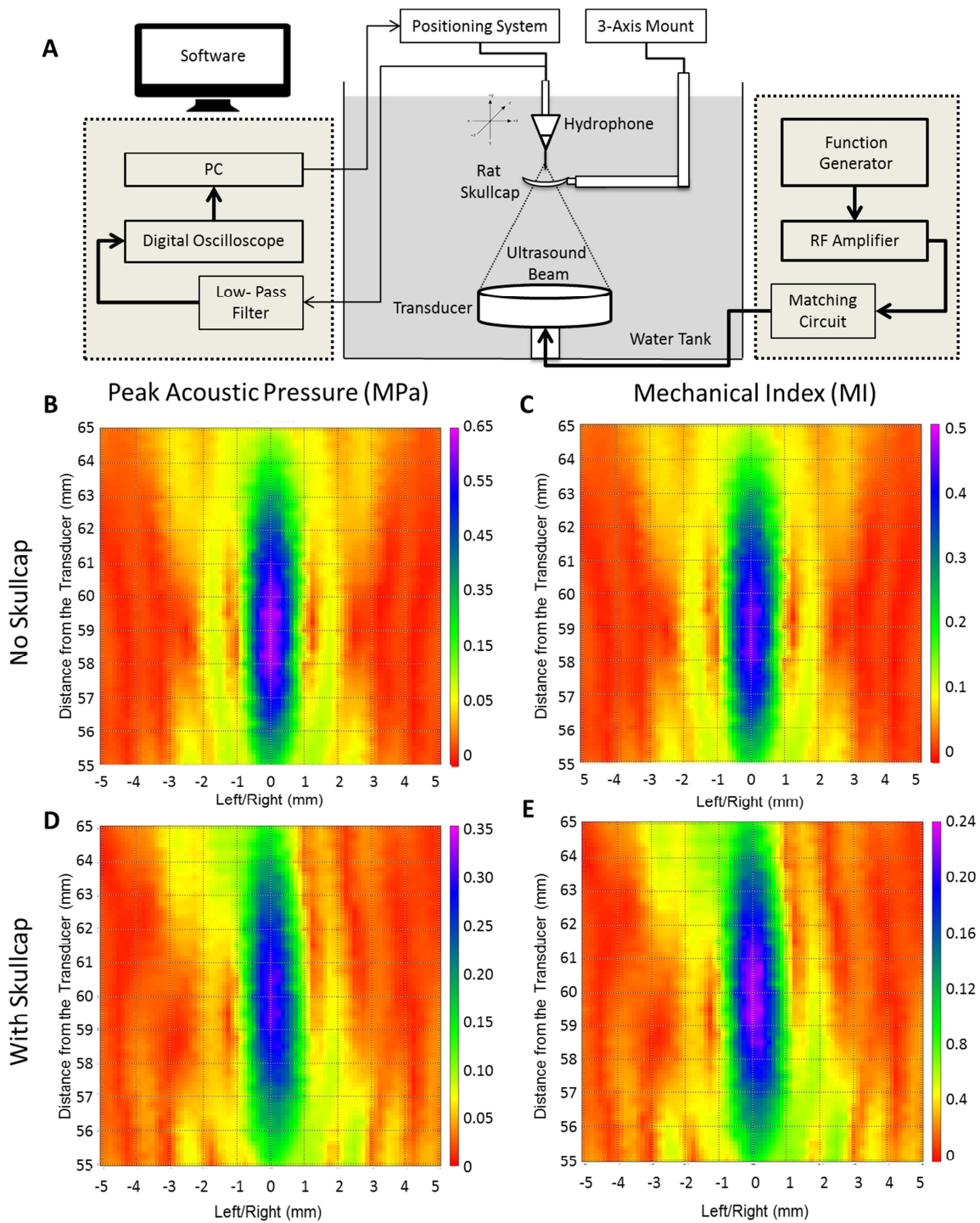
**Fig. S1:** BBB disruption results from the pilot study. (A) T1-weight contrast enhanced MR image showing four targets with different magnitude of BBB disruptions (B) MR contrast intensity increase at the target due to BBB disruptions. (C) Acoustic emission data acquired during sonication at target 1. The rise in subharmonic signal is noted with a red arrow (left), indicating active oscillation of microbubble. The acoustic pressure threshold was noted at the time of the rise in subharmonics (around 0.6 MPa).



**Fig. S2:** (A) Acoustic pressure map generated from focused ultrasound. (B) Acoustic Pressure gradient along axial line around focal point (dB respect to peak pressure). (C) A Contrast enhanced T1-weighted MR Image of the rat brain at sonication region. Yellow squares indicate areas selected for fluorescence microscopy for P-gp expression and Evans Blue. Yellow arrow indicates the focal point of focused ultrasound. (D) Fluorescence microscopy images of the Evans Blue (Red) and the P-gp expression (Green). The sonication region (left column) and the control region (right column) are compared. (E) Line plot comparing the sonicated region and the control region along the axial direction (MR image contrast intensity, Evans Blue fluorescence intensity and P-gp fluorescence intensity, respectively)



**Fig. S3:** RECA-1 expression at the sonicated region (A) A contrast enhanced T1-weighted MR image of a rat brain at sonication region (the opposite hemisphere of the brain served as a control). Areas indicated with white squares were selected for fluorescence spectroscopy analysis. (B) The fluorescence intensity at the sonicated region and the control region is shown to compare RECA-1 expression intensities (green)



**Figure S4:** Measurement setup and acoustic output distribution at a focal zone **(A)** A schematic diagram of acoustic pressure distribution measurement with a rat skullcap **(B)** Peak acoustic pressure distribution without skull **(C)** Mechanical Index (MI) distribution without skull **(D)** Peak acoustic pressure distribution with a rat skullcap **(E)** MI distribution with a rat skullcap

**Table S1.** MR Imaging Parameters

<b>Sequence</b>	<b>Use</b>	<b>TR (ms)</b>	<b>TE (ms)</b>	<b>FOV (mm<sup>2</sup>)</b>	<b>Matrix Size</b>	<b>Slice Thickness (mm)</b>	<b>N E X</b>	<b>E T L</b>	<b>Band- width (kHz)</b>
<b>T1-weighted RARE (±Gd-DTPA)</b>	Detection of BBB Disruption	1500	6.5	40×40	256× 256	1.5	3	2	±15.6
<b>T2-weighted RARE</b>	Treatment Planning, Detection of edema	2500	33	40×40	256× 256	1.5	2	2	±15.6