Focused Ultrasound-Enabled Brain Tumor Liquid Biopsy (FUS-LBx) for Noninvasive, Safe, and Effective Brain Tumor Biomarker Detection

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Background, Motivation and Objective

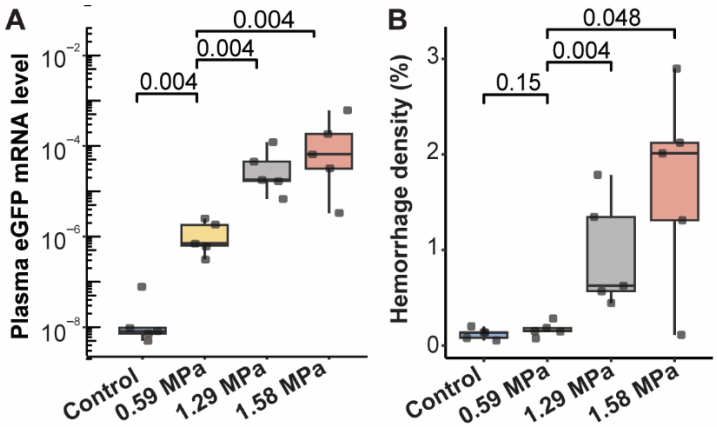
The development of noninvasive approaches for brain tumor diagnosis and monitoring continues to be a major medical challenge. We proposed the focused ultrasound-enabled brain tumor liquid biopsy (FUS-LBx) technique in our previous publication (Zhu et al. Sci. Rep. 2018; 8). FUS-LBx uses FUS to enable the release of tumor-specific biomarkers into the blood circulation for the diagnosis of brain tumors through blood-based liquid biopsies. The objective of this study was to investigate the feasibility of FUS-LBx for noninvasive, safe, and effective brain tumor biomarker detection.

Statement of Contribution/Methods

Mice with orthotopic implantation of enhanced green fluorescent protein (eGFP)-transfected glioblastoma cells were noninvasively sonicated by FUS in the presence of systemically-injected microbubbles at three different peak negative pressures (0.59 MPa, 1.29 MPa, and 1.58 MPa). The sonication was performed by a clinical magnetic resonance (MR)-guided FUS system (Sonalleve V2, Profound Medical Inc.) integrated with a clinical MR scanner (Ingenia 1.5T, Philips Healthcare). Blood was collected immediately after the FUS sonication. eGFP mRNA, which was specific to the tumor model used in this study, was selected to represent tumor-specific biomarkers. Plasma eGFP mRNA levels were quantified using quantitative polymerase chain reaction (qPCR). The safety of the FUS-LBx technique was evaluated by the quantification of hemorrhage density in *ex vivo* brain slices.

Results/Discussion

FUS at 0.59 MPa achieved an increase in plasma eGFP mRNA level that was comparable to those at higher acoustic pressures (1.29 MPa and 1.58 MPa) (Fig. A). Hemorrhage density associated with FUS at 0.59 MPa was significantly lower than that with the two higher acoustic pressures and not significantly different from the control group (Fig. B). These findings suggest that FUS-LBx is a promising technique for noninvasive, safe, and effective brain tumor biomarker detection.



(A) Plasma levels of eGFP mRNA in the control and FUS-sonicated groups with different pressure levels.
(B) Hemorrhage density quantification in the control and FUS-sonicated groups.