Feasibility and Safety of Focused Ultrasound-Enabled Brain Tumor Liquid Biopsy (FUS-LBx) in a Porcine Model

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Background, Motivation and Objective

Although blood-based liquid biopsy is a promising non-invasive technique to detect cancer-specific biomarkers (e.g., DNAs, RNAs, and proteins), there has been limited progress for brain tumor applications partially due to the blood-brain barrier (BBB). The low permeability of the BBB hinders the release of tumor biomarkers from the brain into the blood circulation. In our previous study using murine glioma models, we developed a novel technique called focused ultrasound-enabled brain tumor liquid biopsy (FUS-LBx) that increases the BBB permeability and enhances the release of tumor biomarkers into the bloodstream. The objective of this study was to develop a FUS system for FUS-LBx application in a large animal model for future clinical translation.

Statement of Contribution/Methods

A magnetic resonance (MR)-compatible FUS system dedicated for FUS-LBx was developed (Fig 1A-B). This system was comprised of a FUS transducer (frequency: 0.65 MHz, aperture: 65 mm, focal length: 65 mm), a motor to move the transducer, and a frame to stabilize anesthetized pig heads. Passive cavitation detection sensors were integrated with the transducer to validate sufficient acoustic coupling between the transducer and pig head and effective FUS sonication. Software was developed to target a specific brain location under MR guidance. FUS sonication was performed after intravenous injection of microbubbles. After sonication, contrast-enhanced MR images were acquired to evaluate BBB permeability. Blood was collected and brain-specific biomarkers were analyzed using enzyme-linked immunosorbent assay.

Results/Discussion

Contrast-enhanced T1-weighted MR images confirmed BBB opening (Fig. 1C). The average blood concentration of three brain-specific biomarkers, glial fibrillary acidic protein (GFAP), myelin basic protein (MBP), and S100 calcium-binding protein B (S100B), increased respectively by a factor of 2.5, 4, and 3 after FUS sonication compared with before (Fig. 1D). This study established a tool for FUS-LBx that enhances brain-specific biomarker release into the bloodstream of a porcine model. This system can be translated to the clinic for diagnosing various brain cancers.

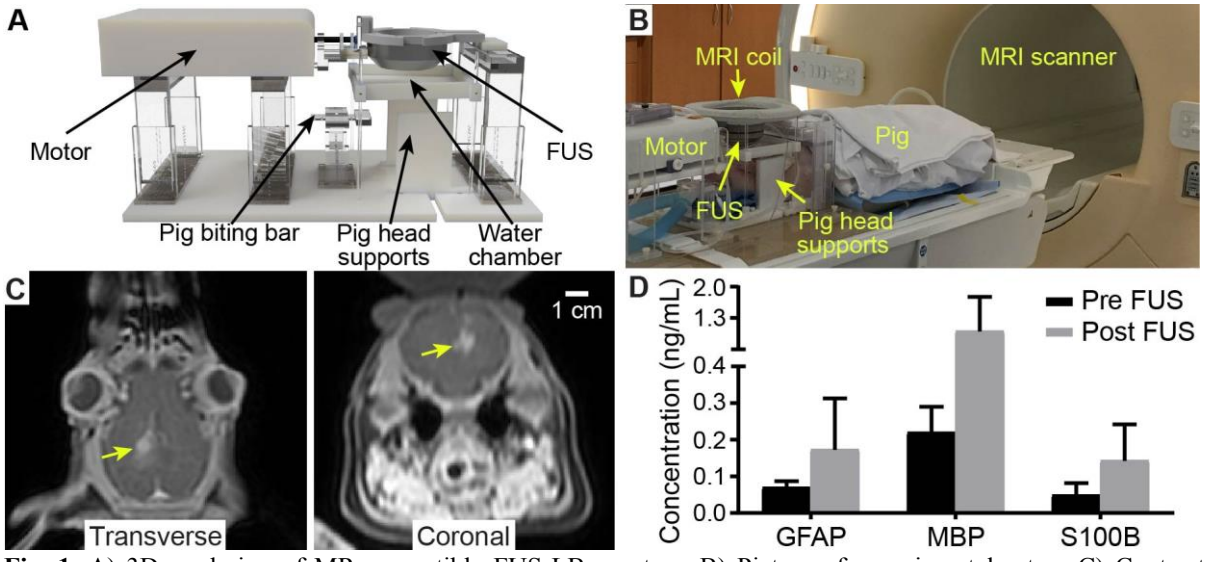

Fig. 1. A) 3D rendering of MR-compatible FUS-LBx system. B) Picture of experimental setup. C) Contrast-enhanced T1-weighted MR images verified successful BBB opening (yellow arrow). D) FUS-LBx enhanced the release of brain-specific biomarkers (GFAP, MBP, and S100B).