To Characterize the Safety Window of Focused Ultrasound when applied to Blood-Brain Barrier Disruption

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Introduction

High-intensity focused ultrasound has been used to locally and reversibly increase the permeability of the blood–brain barrier (BBB)[1], which can be confirmed by contrast enhanced T1 weighted MRI (CE-MRI)[2]. However, side effects such as microhemorrhage, erythrocyte extravasations, or extensive hemorrhage prevent it from further applications. Current efficacy of CE-MRI in detecting the induced tissue hemorrhage remains limited. In this study, effort has been made to characterize the extent of tissue hemorrhage by susceptibility-weighted imaging (SWI), which provided an *in-vivo* imaging protocol to define a secure ultrasound energy level.

Material and Methods

Sprague-Dawley rats were subjected to the sonications unilaterally under various HIFU power. Craniotomy was performed and the microbubble (SonoVue®, Bracco, Milan, Italy) was IV administered before the ultrasound sonication. Animals were placed directly under the water tank with heads tightly attached to the window. The concentrated ultrasound energy was generated with diameter = 60 mm, radius of curvature = 80 mm, frequency = 1.5 MHz. The ultrasound power amplifier operated in a burst mode (burst length = 10 ms, PRF = 1s, total time = 30s), producing a focal zone of approximately 10 mm. Four acoustic pressure amplitudes of 0.78, 1.1, and 2.45 MPa were tested, which either induced BBB disruption alone or accompanied with hemorrhage. MRI images were acquired on a Siemens 3-T scanner using a house made surface coil. Contrast enhanced T1-weighed TSE images were acquired (TR/TE = 534 /11 ms, voxel size = 0.3×0.3×1.5 mm^3, ETL = 5) followed by SWI (TR/TE/flip angle = 28 ms/20 ms/15°, voxel size = 0.3×0.3×0.7 mm^3). An ROI of 3×3 voxels was selected from the T1-weighted images.

Result

Figure 1 showed that when at a lower sonication power (0.78 and 1.1 MPa, upper panel), an enhancement was noticed in CE-MRI but not in the corresponding SWI, indicating a safe BBB disruption process without hemorrhage occurred. When using a higher power of 2.45 MPa.(lower panel), an restricted area of enhancement than CE-MRI was noted in SWI, indicating the area of hemorrhage in the core of BBB disruption region. Histology confirmed the above findings, which was not shown here.

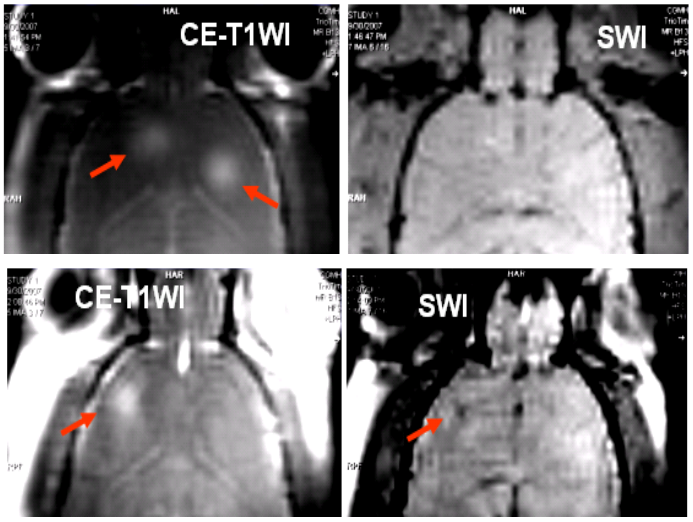

Fig. 1. MRI at low (left two) and high (right two) power.

Discussion and conclusion

The study showed that T1-weighted CE-MRI detected the local disruption of BBB, but was unable to distinguish from the induced hemorrhage. SWI provided complimentary information for in-vivo real-time monitoring of the presence of hemorrhage. When combining both, MRI provides a safe operation power window for HIFU, which is essential to the potential clinical applications.

References

[1] Hynynen et al, Acta Neurochir Suppl, pp. 555-8, 2003. [2] Treat et al. Int J Cancer, pp. 901-7, 2007.