MRI monitoring of lesion production in the brain by focused ultrasound enhanced by an ultrasound contrast agent in rats

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Introduction: In this work, we investigated the use of focused ultrasound exposures in the presence of an ultrasound contrast agent to produce local lesions in the brain under MRI guidance. The presence of the microbubbles in the vasculature has been shown to greatly reduce the threshold for tissue damage (1), making focused ultrasound surgery more practical in targets such as the brain that are shielded by bone, which is highly absorbing of ultrasound and can limit ultrasound surgery due to excessive heating.

Methods: Twenty-five locations in the brains of 10 rats were targeted with focused ultrasound exposures through the intact skull. The transducer characteristics were: ROC/diameter=8 cm/10 cm; frequency=1.5 MHz. Sonications were pulsed (pulse length: 1 ms, repetition frequency: 1 Hz, duration: 60 s). The acoustic power ranged from 3.5-35 W (measurement in water). An ultrasound contrast agent (Optison®) was injected (0.2 mL/kg, IV) through the tail vein. Half of the injection was given at the start of sonication, half 30 s later. MRI was used to target the locations and to detect the resulting tissue effects. The brains were removed either 4h or 7 days after sonication and were examined under light microscopy (serial section stained with H&E). Imaging was performed immediately after sonication, and at 4 days (N=1) and at 7 days after sonication. T2-weighted fast spin echo imaging (TR/TE: 2000/85 ms, echo train length: 8) and T1-weighted imaging (TR/TE: 500/17 ms, echo train length: 4) was performed (field of view: 8 cm, slice thickness: 1.5 mm, matrix: 256×256). T1-weighted imaging was repeated after an injection of MR contrast agent (MAGNEVIST®, Berlex Laboratories, Inc., Wayne NJ, dosage).

Results: Immediately after sonication, the lesions appeared as hyperintense spots in T1-weighted imaging. After contrast injection, slight enhancement was observed around the edge of the lesion, which slowly filled in over time. In T2-weighted imaging, the lesions appeared hypointense with hyperintense regions surrounding the lesions. Four days after sonication, the lesion appeared hyperintense in both T2 and T1-weighted imaging. At seven days, the lesions were hypointense in T2-weighted imaging and no or very little contrast enhancement was observed. At this time, some cases were hypointense in T1-weigthed imaging, and in some cases, hyperintense central regions were observed. An example is shown in Fig. 1. In histology, multiple hemorrhages were observed in the lesion at four hours, and most neurons appeared dark stained. At seven days, extensive macrophage infiltration and glial activation was seen.

Discussion: This technique greatly reduces the power needed to produce lesions, which may be useful for focused ultrasound surgery through the intact skull (2-5). Mechanical effects of the ultrasound and the interaction with the microbubbles in the vasculature (cavitation) presumably produced the lesions. Such effects may prove useful for ablation and could provide a different method for tissue death other than thermal ablation. The MR images of these lesions indicate an interesting progression over time.

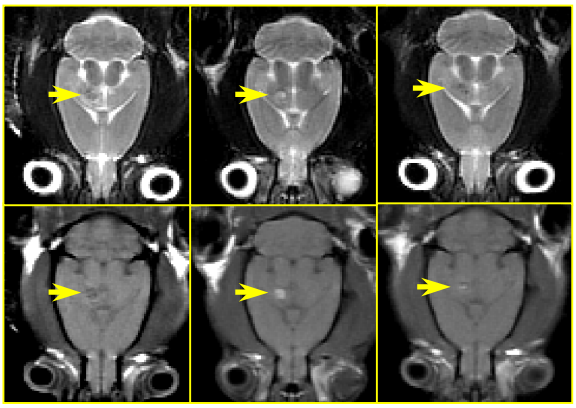

Fig 1: T2 (top) and T1 (bottom) weighted fast spin echo images of a lesion in a rat brain produced in the presence of Optison®. Left: Immediately after sonication; center: four days after sonication: right: seven days after sonication.

References
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