MRI monitoring of focused enhanced ultrasound heating in the presence of an ultrasound contrast agent in the rabbit brain

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Introduction: In this work, we used MR imaging and thermometry to investigate the effects of a commercially available ultrasound contrast agent that consists of preformed gas bubbles (Optison®, Malinckrodt Inc., St. Louis, MO) on focused ultrasound exposures in the brain. The presence of the microbubbles in the vasculature reduces the threshold for tissue damage (1,2), making focused ultrasound surgery more practical in targets such as the brain that are shielded by bone. Because the heating induced will depend on both the acoustic parameters and the local supply of agent, monitoring of the exposures will be crucial.

Methods: Fifty-seven locations in fifteen rabbit brains were targeted with unfocused ultrasound exposures through a craniotomy. A spherical focused transducer was used (ROC/diameter: 8 cm/10 cm; frequency: 1.5 MHz; acoustic power 8.2 - 16.5 W; duration: 10-20s). Sonications were performed continuous wave (23 locations) and at a 50% duty cycle (repetition frequency 1Hz, 34 locations). The acoustic power ranged from 0.35-14W. Before the sonications, a bolus of Optison® (0.05 mL/kg) was injected through the ear vein. During the sonications, temperature was monitored with MRI thermometry (PRF technique (3), FSPGR sequence, parameters: TR/TE: 39.5/19.3 ms, flip angle: 30°, bandwidth: 3.57 kHz, FOV: 10 × 7.5 cm, slice thickness: 3 mm, 256×96 matrix, scan time: 4 s). After the sonications, T2 and contrast-enhanced T1-weighted fast spin echo images were obtained to observe the tissue effects (T2/T1 parameters: TR: 2000/15, TE: 90/15 ms, echo train length: 8/4, NEX: 2/4, FOV: 10 cm, slice thickness: 1.5 mm, 256×256 matrix).

Results: The temperature distributions were visible in the MR thermometry, which did not appear to contain artifacts due to the sonications or the contrast agent (Figure 1 A,C). In some cases, heating at the focal plane rapidly progressed to heating along the entire beam path. Focal heating could be more reliably produced with the sonications with a 50% duty cycle. In some cases hot spots were observed outside the focal region, presumably due to the presence of large blood vessels. Tissue changes were observed in contrast enhanced T1-weighted imaging at all power levels tested and matched the shape of the temperature distributions seen in MRI (Figure 1 B,D). Tissue damage was also observed in many cases in T2-weighted imaging.

Discussion: The threshold for tissue damage was reduced by approximately a factor of ten below that found in the same experimental conditions without the contrast agent (4,5). Pulsing the sonication is needed to reduce the chance of pre-focal heating, and care should be used to ensure that the beam path avoids large blood vessels. This technique greatly reduces the power needed to produce lesions, which may be useful for focused ultrasound surgery through the intact skull (6-8). Both thermal and mechanical effects of the ultrasound presumably produced the lesions. The measured temperature information may be useful to monitor online the progression of such lesions and perhaps even to predict their extent. Such monitoring will be necessary since the temperature distribution and lesion formation will depend on the local distribution of the microbubbles in addition to the acoustic and tissue properties (as is the case in thermal ablation not enhanced by the microbubbles). The tissue acoustic properties and local blood supply are unknowns for a given treatment.

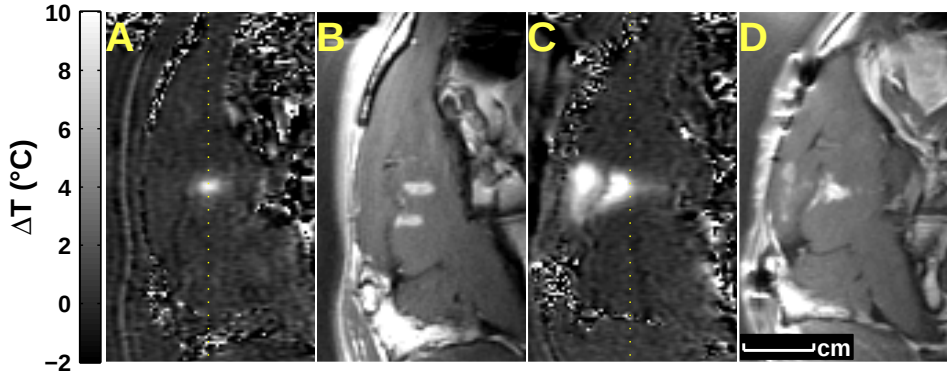

Figure 1: Sagital images of a rabbit brain showing (A,C) temperature maps acquired during sonication in the presence of Optison® and (B,D) contrast-enhanced T1-weighted images acquired after the sonications. The sonication that produced the heating shown in (A) was delivered at a duty cycle of 50%, and the heating was contained to the area around the focal plane (indicated by the dotted line). The sonication that produced the heating shown in (C) was continuous wave, and the heating was observed along the entire beam path. The tissue effects matched the shape of the heating.

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