An MR-Compatible Hydrophone for Ultrasound Monitoring of MRI-Guided Transcranial Focused Ultrasound Therapy

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Introduction

MRI-guided transcranial ultrasound therapy shows great promise for the non-invasive treatment of a range of brain diseases. MRI provides useful information regarding the bioeffects that occur as a result of therapy, however it does not provide information regarding the generated acoustic field. One of the most promising applications for transcranial ultrasound therapy is in the disruption of the blood-brain barrier (BBB) for the targeted delivery of therapeutics in the brain [1-3]. Disruption of the BBB is assisted by ultrasound microbubble contrast agents, and one study has also shown a correlation between acoustic emissions and BBB disruption [3]. This study presents an MR compatible hydrophone to monitor acoustic emissions during MR-guided transcranial therapy, with the aim of identifying further parameters to better control therapy.

Methods

An MR-compatible hydrophone (fig.1) was constructed by clamping a piece of polyvinylidene fluoride (PVDF) film with NiCu electrodes between inner (signal) and outer (ground) pieces of brass tubing. The PVDF film had a thickness of 110μm and a diameter of 4.8 mm. A preamplifier providing 20 dB of gain, with board dimensions of 7.1 x 1.8 mm was constructed in-house and enclosed within the brass tubing to drive the long cables required to reach outside the MRI. The sensitivity of the hydrophone was characterized over a range of frequencies using a calibrated transducer. The frequency dependence of the preamplifier and its cable driving abilities were measured. The hydrophone was tested for MR compatibility in a 1.5 T MRI (Signa 1.5 T, GE Healthcare, Milwaukee, WI, USA). MR images of the hydrophone were captured to determine the extent, if any, to which the hydrophone contributed signal artifacts. To examine the effects of the MRI on the hydrophone, ultrasound pulse-echo signals were captured in the MR bore both with the MR idle, and while capturing MR images. Finally, the hydrophone was mounted on an existing pre-clinical MRI guided ultrasound positioning system [4], and was used to monitor BBB disruption in rats.

Sonications ranging in *in situ* acoustic pressure from 0.10 MPa to 0.24 MPa were performed at 4 locations in each of 6 rats (Wistar; 303-380 g). In two rats, after the first location was sonicated at low-power and BBB disruption was not observed, a second sonication at a higher power at the same location was performed. A total of 26 sonications were performed at 24 different locations. Sonications consisted of 0.558 MHz 10 ms bursts at a repetition frequency of 1 Hz for 2 minutes. Definity (Lantheus Medical Imaging, MA, U.S.A.) contrast agent (0.02 ml/kg) was injected simultaneously with the start of sonications. The hydrophone was aimed at the focus of the therapy transducer and waveforms were captured every three seconds for the duration of the sonications using a LeCroy WavePro 715Zi oscilloscope (LeCroy, Chestnut Ridge, NY, USA). BBB disruption was confirmed by contrast enhanced T1-weighted imaging (FSE, TE=10 ms, TR=500 ms, ETL=4, FOV=6 cm x 6 cm, 128x128, slice thickness=1 mm) and T2-weighted images (FSE, TE=60.6 ms, TR=2000 ms) were used to check for edema.

Results

The hydrophone demonstrated high sensitivity (e.g. 1.62 ± 0.09 V/MPa at 306 kHz; 1.38 ± 0.16 V/MPa at 830 kHz) with a negative 3 dB point around 4 MHz. The preamplifier roll-off occurred around 1 MHz, and correction for the preamplifier response yielded a flat hydrophone trend over the range of 0.306 – 4.589 MHz. The preamplifier was able to drive cable lengths of 8.5 m without loss of signal strength, sufficient to reach outside the MRI. The MRI artifacts caused by the hydrophone were small and deemed negligible relative to the distance of the hydrophone from the transducer focus (greater than 10 cm). Ultrasound A-mode images taken in the bore with the MRI off produced clear signals. When the MRI was scanning, some distortion was added to the ultrasound signals. However, the signals were still discernable and the frequency spectra showed minimal change.

In the *in vivo* experiments, BBB-opening was observed after 23 of the 26 sonications. Figure 2 and 3 show the T1-weighted and T2-weighted images of a rat brain sonicated in four locations with increasing acoustic power applied from location 1 to location 4, and figure 4 shows the corresponding frequency spectra. In figure 2, enhancement indicating BBB opening is visible in all four locations. In figure 3, two locations show edema. There were 13 instances of edema. In 12 locations which had edema, acoustic sub-harmonics and ultra-harmonics were detected by the hydrophone. No sub or ultra-harmonics were detected without the presence of edema. In 5 of the locations experiencing edema, an increase in broadband noise was detected (figure 4.4), indicating inertial cavitation.

Discussion

An MR compatible hydrophone was successfully built. The detection of different acoustic emissions at the onset of edema demonstrates that the hydrophone is sufficiently sensitive to detect differences in the acoustic field from sonications producing different bioeffects. In this study, a single hydrophone was used to monitor a pre-clinical experiment. Construction of an array of hydrophones, which would allow 3-D mapping of signals, holds promise for real-time monitoring of MR guided transcranial therapy, and comparison of acoustic emissions with MR data could provide new information on the mechanisms behind observed bio-effects.

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References

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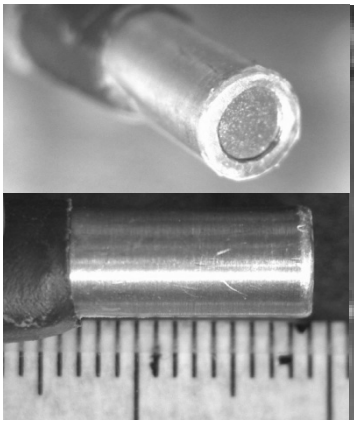

Fig.1 – MR compatible hydrophone

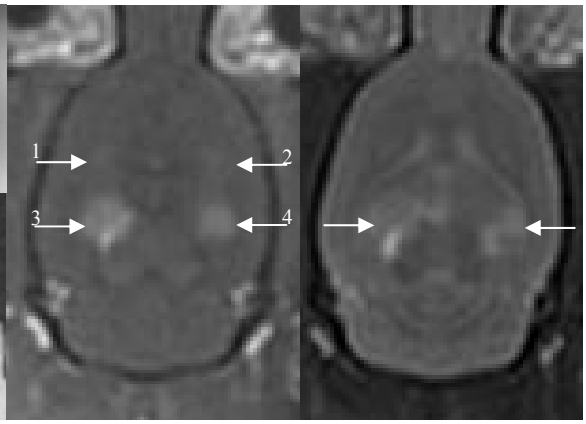

Fig.2 – T1w image showing enhancement at the four sonication locations

Fig.3 – T2w image showing edema at two locations

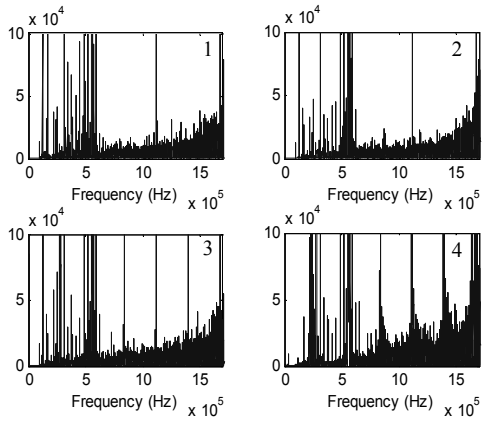

Fig.4 – Frequency spectra for sonication locations 1-4