MR-guided focused ultrasound ablation of the rat liver

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Introduction MR-guided therapeutic ultrasound, specifically high intensity focused ultrasound (HIFU), has become increasingly prominent among the range of treatments for localized tumors. This technique is used clinically for the treatment of uterine fibroids, prostate and liver cancer. To study hepatocellular carcinoma an appropriate animal model must be established. Rodent models are preferred to larger animals because of the cost associated with survival studies, convenience of experimental setup, and available tumor cell lines. We propose that the rat could be a viable model for HIFU therapy. In previous FUS studies the rat liver has been exteriorized to allow access to the tissue [1]. However, to be a useful model, the effects of the ribcage, including the bone and cartilage, on the ultrasound beam must be able to be ignored without exteriorizing the liver. In the following study we show that it is possible to sonicate through the ribcage of the rat and create *in vivo* thermal lesions localized to the liver with no resulting skin burns. By limiting the motion of the rat, treatment monitoring using MR thermal imaging is also possible.

Methods All the experiments in this study were performed on the InSightec (Haifa, Israel) MR-guided focused ultrasound system, ExAblate 2000. The animals used in this study were Sprague-Dewey rats placed head first in prone position on the therapy table inside the MRI (3 Tesla, GE Signa) using a standard GE (Milwaukee, WI) 3-inch surface coil attached under the rat so that the abdomen is suspended through the coil into a water bath This water bath is used to achieve acoustic coupling between the animal and the transducer (Fig. 1). *In vivo* rats (n=2) were anesthetized using 1.5%-2.0% isoflourine, 2 L/min Oxygen while their heart rate and oxygen saturation were monitored. The abdomens of the rats were shaved to remove most of the hair; the remaining hair was removed with a chemical depilatory (Nair, Church and Dwight Co., Lakewood, NJ). Sonications were performed using 1.35 MHz and energy levels of 716-797 Joules. Temperature measurements were made with PRF-thermometry (gradient echo, TE=6, FOV= 14cm, slice thickness=3mm, matrix= 128x128, BW= 31.25 kHz). Necropsy samples were frozen and 1mm slices were photographed from which lesion volumes were calculated. Volumes from MR images were calculated using non-enhancing regions of the lesion corresponding to non-perfused ablated areas.

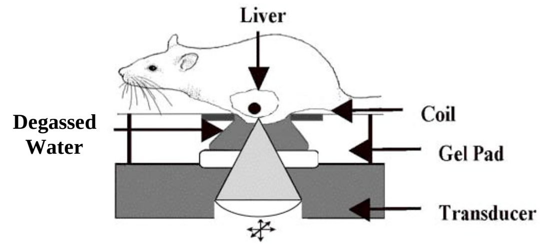

FIGURE 1. Schematic of experimental setup (not to scale)

Results and Discussion In this *in vivo* study, we found it was possible to create thermal lesions localized to the liver of rats by sonicating directly through the ribcage. Respiratory and bowel motion, as well as flow artifact from the cardiovascular system of the rat were minimized in several ways. The suspension of the abdomen through the MRI coil reduced the motion of the liver from the rat's respiration. By keeping the phase encode direction of the MR system in the R/L direction, flow artifacts from the heart and cardiovascular system are limited to the area superior to the liver. Finally, bowel motion was greatly reduced by fasting the animals for twelve hours before the experiment. Using all these techniques we were able to limit the motion and obtain MR temperature profiles during treatment (Fig. 2). No thermal burns were observed by visual inspection on the skin. *In situ* skin lesions were observed at energies levels above 1393 Joules. This was used as the threshold for the *in vivo* experiments; during which thermal lesions were created in the liver of the rat while no skin burns were observed. Lesions size was determined using T1 contrast (Magnevist, Montville, NJ) enhanced images. Resulting lesion volume from the MR contrast enhanced images, compared to the lesion size obtained during necropsy can be seen in Table 1. Size of ablated volume is slightly overestimated when calculating volume using the MR contrast enhanced images. This may be due to a difference in slice thickness between the MR images and the necropsy images.

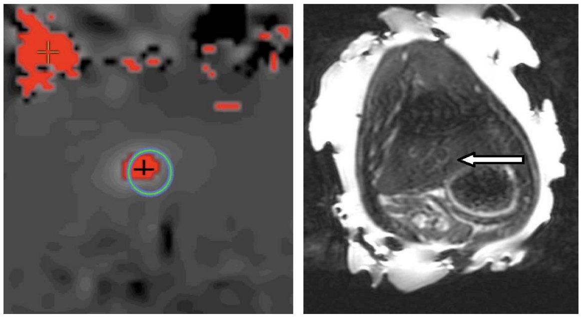

FIGURE 2. MR temperature profile during HIFU ablation of a rat liver performed *in vivo*. The crosshairs indicate a peak temperature of 88°C with an average of the surrounding pixels of 77°C (left). T2 weighted image after the same sonication (right). The liver shows minimal physiological motion. Arrow indicates resulting lesion.

Necropsy Volume (cm^3)	MRI Volume (cm^3)
1.1	1.3
2.2	2.7

Table 1. Volume of HIFU lesion compared from gross examination during necropsy and MR T1 contrast-enhanced images.

Conclusions In this study we have shown that the rat can be a feasible model for MR guided HIFU liver treatments. It is possible to ignore the effect of the ribs and the sternum in rats and create *in vivo* thermal lesions localized to the liver of the rat. By limiting motion artifacts this ablative treatment can be performed while acquiring MR temperature data, and the resulting temperature maps can be used to monitor the HIFU treatment. Such models are needed for the advancement of patient procedures.

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References [1] L. Chen, et al, Ultrasound in Med Biol, 1999; 5; PP 847