A high precision MR-compatible positioning system for focused ultrasound experiments in small animal models

A. C. Waspe[1,2], A. Chau[1], R. Chopra[1,2], and K. Hynynen[1,2]
[1]Imaging Research Discipline, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada, [2]Department of Medical Biophysics, University of Toronto, Toronto, Ontario, Canada

Introduction:
Magnetic resonance guided focused ultrasound (MRgFUS) therapy is a non-invasive technique for targeted blood-brain barrier disruption, site-specific delivery of pharmaceuticals, and controlled heating and coagulation of tissues [1, 2]. However, the translation of this technology into clinical practice still requires extensive testing in preclinical rodent models, yet the small size of mice and rats makes implementation of focused-ultrasound experiments using clinically approved MRgFUS systems difficult. In order to implement this technology at spatial scales appropriate for small animals, a dedicated small animal system that is capable of delivering ultrasound sonications with a spatial resolution of approximately 0.25 – 0.5 mm in tissues is required. In addition, the capability to operate this system within an MR imager enables precise image-guided targeting of tissue structures. MR-compatible positioning systems have been built previously for focused ultrasound experiments in both humans and animals. However, many of these systems are integrated with particular MR vendors and have not been designed with the intention of delivering exposures to small targets in rodent models [2, 3]. The objective of this research is to develop a high precision, MR-compatible, vendor-independent positioning system for focused-ultrasound sonications in small animal models, and to evaluate its performance in closed-bore 1.5 and 3.0 T clinical MR scanners.

Methods:
A three-axis positioning system was built using non-magnetic components, such as aluminum, brass, plastic, ceramics, and glass. Horizontal motion is controlled with linear piezoelectric ultrasonic actuators (HR4, Nanomotion Ltd., Israel) and position is measured using sinusoidal-wave linear optical encoders (LIA20, Numerik Jena, Germany). Precise horizontal motion is achieved by driving the actuators along ceramic strips that are mounted on linear ball-slides. Vertical motion is achieved by driving a leadscrew-based stage with a rotary piezoelectric ultrasonic motor (USR60-S3N, Shinsei Corp., Japan). A third linear encoder mounted on a brass support beam of the stage measures position along the vertical axis. The transducer is attached to the positioning system by a rigid arm and is submerged within a closed water tank. The arm passes into the tank through flexible bellows to ensure that the system remains sealed. A photograph of the positioning system placed on the couch of a 3.0 T Siemens TIM Trio MR scanner is shown in Figure 1. The electrical cables powering the motors and encoders are passed into the magnet room through low-pass filtered connectors on a grounded RF penetration panel. An RF coil acquires high-resolution images in the vicinity of the target tissue. The subject is placed on top of an acoustic window centered about the RF coil to enable ultrasound transmission from below the body. Spatial registration between ultrasound and MR coordinates involves sonicating a Zerdine® temperature-sensitive phantom and measuring the centroid of the thermal focal zone in 3D with MR thermometry. Figures 2(a) and 2(b) show sagittal and coronal planes of a T_1-weighted image of the transducer positioned directly under the phantom. Figures 2(c) and 2(d) show the corresponding planes from an MR thermometry image. The 3D centroid of the thermal focal zone is determined manually from these two orthogonal planes. The positioning accuracy of the system was measured on the bench top and the range of motion and velocities achievable with the system were tested. MR imaging and thermometry were performed with the positioning system off, with the positioning system stationary with motors engaged but not moving, and with the positioning system moving in order to determine whether the positioning system degrades SNR or biases temperature measurements during image acquisition or MR thermometry. SNR was evaluated on magnitude images from T_1 and T_2 weighted acquisitions of an ultrasound standoff. A small section of the phantom was removed to allow background noise to be measured in the same field of view. A correction factor of 0.655 was applied to all SNR calculations to account for the SNR being measured from magnitude images [4].

Results:
Bench top tests revealed that linear ranges of over 5 cm with a positioning resolution of 0.1 mm were achievable for each axis. Horizontal and vertical velocities up to 10 mm/s and 5 mm/s respectively were also achievable. The entire system was constructed with non-magnetic components and operation of the positioning system and transducer within the bore of clinical MRI scanners of different manufacturers was feasible. Simultaneous motion and sonication during MR imaging and thermometry did not result in any mutual interference, image artifacts or temperature measurement errors. SNR dropped by less than 20% between operation of the motors and baseline images for both T_1 and T_2 weighted sequences. This allows for multi-point sonications to be performed while measuring the localized temperature deposition, increasing the throughput of small animal experiments.

Conclusions:
An MR-compatible focused ultrasound system has been developed that is capable of sonicating anatomical targets in small animals with high precision within the bore of clinical MR imagers. The system has sufficient travel length for use in localized drug delivery and thermal ablation in small rodents and larger animals as well. The absence of interference on MR imaging during operation of the motors and the transducer indicates a high level of MR compatibility enabling simultaneous sonication, transducer positioning and MR thermometry. The system enables high throughput ultrasound-enhanced therapies involving large numbers of small animals.

References:
[1] K. Hynynen, "Focused ultrasound for blood-brain disruption and delivery of therapeutic molecules into the brain," *Expert Opin. Drug Deliv.* 4, 27-35 (2007).
[2] C. Damianou, K. Ioannides, V. Hadjisavvas, *et al.*, "In vitro and in vivo brain ablation created by high-intensity focused ultrasound and monitored by MRI," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 56, 1189-1198 (2009).
[3] R. Chopra, L. Curiel, R. Staruch, *et al.*, "An MRI-compatible system for focused ultrasound experiments in small animal models," *Med. Phys.* 36, 1867-1874 (2009).
[4] R.M. Henkelman, "Measurement of signal intensities in the presence of noise in MR images," *Med. Phys.* 12, 232-233 (1985).

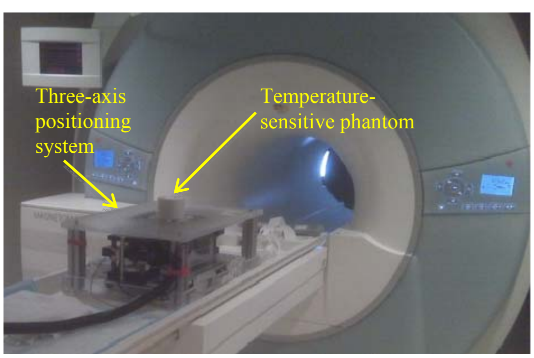

Figure 1: Photograph of the focused ultrasound system installed on a 3.0 T Siemens TIM Trio MR scanner.

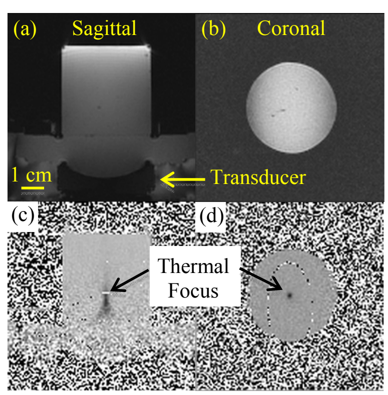

Figure 2: T_1-weighted images depict the ultrasound transducer positioned directly under the temperature-sensitive phantom in the (a) sagittal and (b) coronal planes. Corresponding MR thermometry images depict the location of the centroid of the thermal focal zone within the phantom in (c) sagittal and (d) coronal planes.