Feasibility study of a new system for MR-guided scanned focused ultrasound hyperthermia in small animals

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INTRODUCTION: Localized hyperthermia using focused ultrasound (FUS) has been suggested as a noninvasive method for achieving locally enhanced drug delivery and triggering temperature-sensitive drug release, but many questions remain regarding the optimization of hyperthermia protocols for drug delivery in vivo. Our group has been developing MR-guided scanned focused ultrasound systems for use in preclinical drug delivery experiments, designed to achieve temporally and spatially uniform temperature elevations of 5-10°C in targets measuring up to 2.0 cm in diameter. The purpose of this study is to present a motorized transducer positioning system capable of modulating ultrasound power along a rapidly scanned circular heating trajectory during MR temperature imaging, and to demonstrate its ability to achieve temporally and spatially uniform heating in tissue using MR temperature images for single and multi-point proportional-integral (PI) feedback control.

METHODS: In order to be used during imaging, the MR-guided scanned focused ultrasound system uses MR-compatible ultrasonic motors and is constructed almost entirely of non-metallic components. The system operates under computer control, and is used to rapidly position a single-element focused ultrasound transducer (2.787 MHz, 5 cm aperture, 10 cm radius).

Previous iterations of the scanned focused ultrasound system showed periodic phase artifacts related to the magnetic susceptibility of the positioning system as it was scanned along a circular trajectory near the imaging plane. Prior to performing sonications under MR control, scanning-induced baseline temperature drift was characterized using the same sequences to be used for MR thermometry during controlled heating (FSPGR, TE = 10 ms, TR = 38.6 ms, flip angle = 30°, matrix size = 128 x 128, FOV = 10-14 cm, slice thickness = 3 mm, proton resonance frequency temperature coefficient α = -0.0097 ppm/°C). This allowed the selection of scan radii and speeds with acceptable levels of temperature artifact for controlled heating.

During heating experiments, the treatment control software produces temperature maps from complex images passed directly from the MR imager, and calculates a new series of acoustic output powers for each control point based on the specified control algorithm, which are buffered by the motor control software. When the transducer reaches each control point along the scan trajectory, the corresponding output voltage is sent to the function generator, updating the acoustic power applied by the transducer.

Table 1. Baseline temperature variations during simultaneous imaging & transducer motion.

Motion Parameters		ROI Temperature Change (°C)		
Radius	Period	Min	Max	Mean ± SD
Static		-0.66	0.16	-0.168 ± 0.26
2.5 mm	1.0 s	-0.61	0.33	-0.075 ± 0.22
5.0 mm	1.0 s	-1.38	0.93	-0.583 ± 0.59
10.0 mm	2.0 s	-2.16	2.96	0.840 ± 1.58

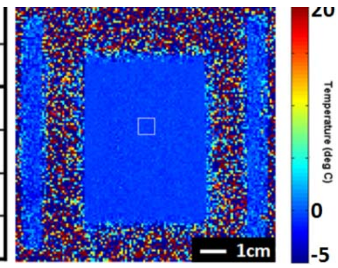

Figure 2. Coronal temperature map with 5mm ROI for baseline temperature measurements.

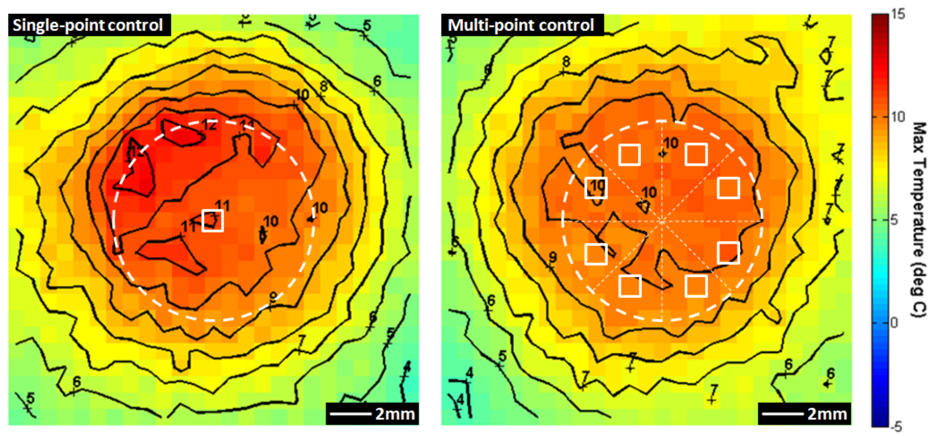

Figure 2. Maximum temperatures observed during MR-guided scanned focused ultrasound heating of a circular trajectory with radius 5mm and 1 rotation per second. Control points for single-point control (left) and multi-point control (right) are shown.

Numerical simulations of scanned FUS hyperthermia based on the bioheat transfer equation and ultrasound field calculations were used to identify appropriate PID gains for the specific transducer, imaging sequences and experimental setup used. The single-point controller was implemented with a proportional gain Kp = 0.050 and integral gain Ki = 0.001. Multi-point control was achieved as the application of several identical single-point controllers operating independently around the scanning trajectory. The feasibility of MR-guided scanned heating using this system, and the relative efficacy of single- and multi-point control algorithms were compared in ex vivo heating experiments using degassed turkey breast.

RESULTS: Baseline temperature artifacts caused by circular scanning of the transducer setup were measured in a 5mm region of interest (outlined in Figure 1) for several sets of motion parameters. Each set of motion parameters was used for 2 minutes, and the ROI mean was compared over the resulting 24 images, with the range, mean and standard deviation summarized in Table 1. Temperature variations observed for 2.5 mm and 5 mm scans (approximately ± 1°C) were deemed to be sufficiently low to use for hyperthermia control. Figure 2 shows the maximum temperatures in a 2 cm region of interest during scanned FUS heating of a circular region with 5 mm radius at 1 revolution per second under single-point (left) and multi-point (right) feedback control. The multi-point controller exhibits better spatial uniformity across the heated region.

DISCUSSION: The results from ex vivo heating confirm the feasibility of using MR-guided scanned focused ultrasound to produce temporally and spatially uniform hyperthermia in small targets. Minimal artifacts of [±1°C] were observed in MR temperature maps acquired while rapidly scanning the transducer along a circular trajectory below the focal plane, which did not prevent the use of MR-guided temperature control. The use of multiple rapidly switched single-point controllers achieved better spatial temperature distributions than a single point.