Open-Source Small-Animal MR-Guided Focused Ultrasound System

Megan E Poorman[1,2], Vandiver L Chaplain[2,3], Ken Wilkens[2], Shantanu Majumdar[2], William A Grissom[1,2], and Charles F Caskey[1,2]
[1]*Biomedical Engineering, Vanderbilt University, Nashville, TN, United States,* [2]*Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States,* [3]*Computational and Physical Biology, Vanderbilt University, Nashville, TN, United States*

Target audience: MR and Ultrasound scientists interested in hardware and software systems for pre-clinical MR-guided focused ultrasound studies.

Purpose: MRgFUS is a rapidly developing field that is increasingly being explored in cross-disciplinary applications, such as enhanced drug delivery, disruption of the blood brain barrier, and immunomodulation. Despite burgeoning interest in using MRgFUS, access to MRgFUS systems remains limited due to the technical difficulties associated with developing these systems and limited deployment of commercial MRgFUS solutions. The lack of well-described, accessible preclinical MRgFUS systems may limit progress and repeatability of new developments in FUS therapies. In this work, we present an open-source preclinical MRgFUS hardware and software system that can deliver repeatable and quantifiable thermal and mechanical FUS over an extended period in small animals.

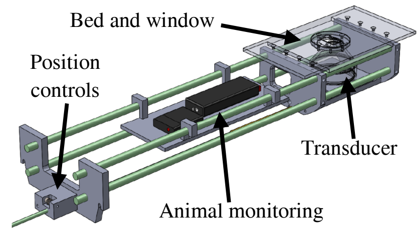

Figure 1*: Thermometry delivery table for 30cm bore Varian 4.7 Tesla MRI.*

Methods: A hardware and software platform was developed to provide fine control over FUS-induced temperature rise in a small-animal model via MR temperature feedback and closed-loop control of FUS sonication. The Solidworks hardware drawings and software are available on Github at {https://github.com/poormanme}.

Hardware: A plexiglass thermotherapy delivery table was constructed (Fig. 1) to be compatible with a 30cm bore Varian 4.7 T animal scanner (Agilent, Santa Clara, CA, USA) and designed to hold a small animal, associated monitoring equipment, MR RF surface coil, and FUS transducer (Sonic Concepts H-101MR single element, 1.1 and 3.3 MHz operation, 400W, Sonic Concepts, Bothell, WA, USA). Surface coils are interchangeable, and the system has been tested with both 2 cm and 5 cm diameter Tx/Rx surface coils, centered perpendicular to the transducer above a 2.54cm FUS delivery window. Translation of the transducer is controlled by a rack and pinion mechanical positioning system that extends outside the magnet bore for optimal positioning of the acoustic focus. The delivery table was placed within the bore of the magnet and the transducer driven by the described software connected to an Agilent 33511B waveform generator and a Panametrics 5072 pulser/receiver.

Figure 2: *Graphical user interface for the control and monitoring software.*

Software: Thermal monitoring A single-slice, gradient echo (GRE) imaging sequence for proton resonance frequency shift (PRF shift) MR temperature measurements was implemented [1] on the 4.7T scanner to obtain high SNR dynamic images at the focus. A closed-loop, real-time image and temperature map reconstruction method was implemented in MATLAB on the MR host PC (Fig. 2). The program continuously polls the MR raw data file for new data and reconstructs an image from which temperature maps are derived in real-time. The focus temperature is controlled by a tuned proportional, integral, derivative (PID) controller that adjusts the FUS transducer output based on the calculated temperature rise to allow for controllable temperature increase. Prior to sonicating, PID parameters are auto-tuned to the tissue of interest using an ultrasound test shot to obtain coefficients for the Pennes bioheat transfer equation in our heating simulation [2]. The temperature rise is fit to the ideal with a Runge-Kutta method to obtain the PID parameters. Baseline field drift correction is performed on images prior to temperature reconstruction by subtracting out a baseline phase obtained from an ROI in the tissue outside of the FUS focus. Future iterations of the software will implement a multi-echo water/fat processing method being explored in the lab for improved accuracy in fatty tissues [3]. A full suite of other scans are also available for planning with this system including a gradient echo implementation of MR-ARFI for visualization of the focus and guiding mechanical FUS [4].

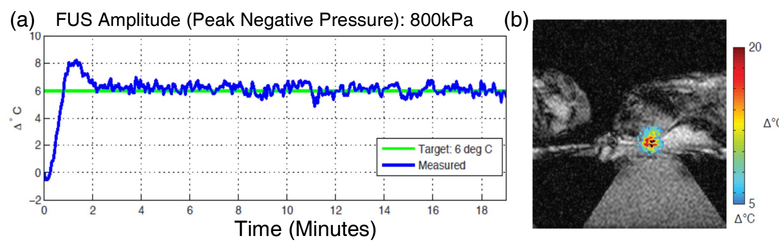

Figure 3*: (a) Sample 20 minute, controlled sonication at 6 ºC in a phantom. (b) Representative temperature map during an in vivo experiment overlayed on base image.*

Hyperthermia Validation: The system was tested on phantoms and *in vivo*. Tofu and graphite agar phantoms were placed on the FUS bed and acoustically coupled to the transducer. Sustained sonications controlled by the feedback system we performed at varied set points between 2-10ºC for up to 20 minutes and MR thermometry calculations were validated with an optical temperature probe. The same procedure was performed *in vivo* in a murine model where manual sonication was performed first followed by closed-loop controlled sonication.

Results: Temperature rises in phantoms from 2-10ºC were successfully sustained for periods from 5 to 20 minutes (bias = 0.1ºC, σ = 0.34ºC) (fig 3a). Optical probe temperature readings over time matched the same trend as those obtained with MR thermometry but were slightly lower due to being placed outside the ultrasound focus to avoid disturbances. Closed-loop, *in vivo* sonication performed with the system successfully generated heat in the targeted tissue (Fig. 3b). A temporal resolution of 4.8 seconds was achieved with SNR of 15:1. Sonication was aborted for safety after the temperature rise reached greater than 10ºC. PID parameters were tuned in subsequent studies to avoid target overshoot. Further *in vivo,* closed-loop sonications are currently underway. Thermal dosages were successfully calculated for all sonications.

Discussion/Conclusion: An open source MRgFUS treatment system has been developed to be capable of accurate, precise, and controllable heating in a target tissue over an extended time period. This has been demonstrated in both phantom and *in vivo* experiments. Future work will focus on additional software developments to improve the temporal resolution and expand the open source effort to other platforms. While the system described here is basic compared to commercial options, the availability of a robust, cost-effective, MRgFUS system will lower the barrier for the increasing number of cross-disciplinary researchers who wish to enter this rapidly evolving field.

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