Fast adaptive control for MRI-guided ultrasound hyperthermia treatment for prostate disease: *in vitro* and *in vivo* results

L. Sun[1], C. M. Collins[2], M. B. Smith[2], N. B. Smith[1,3]

[1]Bioengineering, The Pennsylvania State University, University Park, PA, United States, [2]Radiology, The Pennsylvania State University Colllege of Medicine, Hershey, PA, United States, [3]Graduate Program in Acoustics, The Pennsylvania State University, University Park, PA, United States

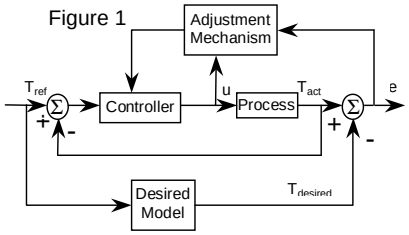
INTRODUCTION

Previous researchers have successfully demonstrated the application of temperature feedback control for thermal treatment of disease using MR thermometry (1-4). Using the temperature-dependent proton resonance frequency (PRF) shift, ultrasound heating for hyperthermia to a target organ (such as the prostate) can be tightly controlled. However, the response of the target to ultrasound heating varies in type, size, location, shape, stage of growth, and proximity to other vulnerable organs. To adjust for clinical variables, a novel adaptive feedback control system has been designed utilizing real-time, on-line MR thermometry by adjusting the output power to an ultrasound array to quickly reach the hyperthermia target temperatures. The advantages of this fast adaptive control method are that there is no need of *a priori* knowledge of the initial tissue properties and it can quickly reach the steady state target temperature by adaptively changing the output power according to the dynamic tissue properties (e.g. thermal conductivity, blood perfusion). To rapidly achieve and manage therapeutic temperatures from an ultrasound array, this research was conducted to utilize closed loop MRI guided temperature control using a novel adaptive feedback system with *in vitro* and *in vivo* experiments.

MATERIALS AND METHODS

Fast adaptive MRI control system: To shorten hyperthermia treatment time, previous researchers have evaluated several control schemes (1, 4, 5). Although the controllers initially operated well, some controllers had undesirable overshoots and oscillations (1, 5). The rapid adaptive control approach used here was designed to track an exponential target temperature with a very fast time constant and to avoid overshoots and oscillations. This robust control system had an ordinary feedback loop composed of the hyperthermia process and a second feedback loop that adjusted the controller parameters (Fig. 1). The mechanism for adjusting the parameters in a model reference adaptive system can be obtained in gradient method by applying Lyapunov stability theory (6). Three dimensional finite difference time domain computer simulations based on Pennes' bioheat transfer equation were conducted to determine the initial values of the control parameters.

Figure 1



Ultrasound hyperthermia system: For treatment of prostate disease, the ultrasound hyperthermia system consisted of a transrectal intracavitary array with 16 elements operating at 1.5 MHz. To drive the array, a multi-channel programmable ultrasound phased array driving system operating between 1-2 MHz and capable of 60W per channel was used. Verification of the temperature change within the target used a multi-channel fiber optic (Luxtron®) thermometer probe to provide a reference for the MR temperature map results.

In vitro and in vivo experiments: Nine *in vitro* adaptive control experiments were conducted using bovine muscle phantom within the Nine *in vitro* adaptive control experiments were conducted using bovine muscle phantom within the 3 Tesla Bruker S-300 MRI scanner using the ultrasound array. using the ultrasound array. The tissue was coupled to the ultrasound through a circulating water filled bolus surrounding the applicator. MR temperatures in a region of interest (ROI) where selected from the tissue from pre-treatment images were used as feedback thermometry data to the controller. Using rabbit thigh muscle (New Zealand white), *in vivo* animal experiments were conducted using a similar procedure as the phantom experiments with the animal anesthetized using ketamine (40 mg/kg) and xylazine (10 mg/kg). Both the animal and phantom experiments used a 26 cm diameter birdcage coil. For rapid hyperthermia heating, the time constant (target temperature) was selected to be less than 2 minutes for a total experiment of 25 minutes.

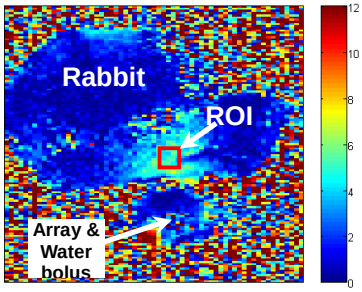


Figure 2

MR temperature imaging: The proton resonant frequency shift was evaluated by using a spoiled gradient echo (SPGR) sequence with the following imaging parameters: TR = 100 ms, TE = 15 ms, flip angle = 30°, data matrix 64 x 64, field of view (FOV) = 14 x 14 cm, slice thickness = 8 mm and bandwidth = 61.7 kHz. These parameters were chosen to maximize the temperature dependent phase shift, while maintaining a high temporal resolution. A baseline scan was acquired before ultrasound heating and subsequent temperature measurement scans were obtained every 19.7 seconds. Phase subtraction was conducted on-line in real-time to calculate the PRF shift (7). The temperature elevation was obtained using the temperature dependence for muscle $\alpha(t) = -0.00909$ ppm/°C by averaging temperatures within a 4 x 3 pixel region located at least 1 cm above the bolus-tissue interface.

RESULTS

Robust adaptive MR temperature control has been demonstrated for both the *in vitro* and *in vivo* experiments. A temperature map (Fig. 2) using phase subtraction images from an *in vivo* rabbit experiment can be seen with a color bar indicating the temperature change within the selected heating ROI from the array below. Since the desired target temperature profile was 38°C for all nine *in vitro* experiments, Fig. 3(a) plots nine averaged MR temperature results (mean ± s.d.) which were consistent with the controller target temperature (solid line) and comparable with the Luxtron® results (x-marks). Consistently starting with an initial phantom temperature of 28°C, the controller achieved the steady state temperature within 6 minutes and deviation from the target profile was no greater than ± 1.37°C. Similar to the *in vitro* results, *in vivo* temperature control can be seen in Fig. 3(b) where the rabbit thigh muscle was heated initially from about 36.5°C for 25 minutes. For this experiment, the target temperature was 44.5°C and was achieved in 8 minutes. From other *in vivo* experiments, the maximum variation from the desired temperature profile was -3.9°C; after reaching steady state, tissue temperature was maintained at 44.5°C ± 1.2°C.

Figure 3(a) In vitro control results

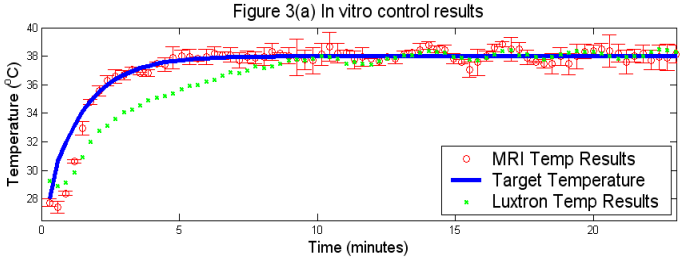
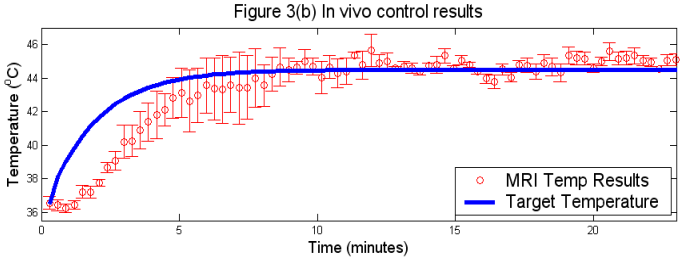


Figure 3(b) In vivo control results



DISCUSSION AND CONCLUSION

Dynamic MR temperature control for hyperthermia is necessary for fast effective thermal treatments while eliminating the risk of permanently damaging healthy tissue due to overheating. Integration of ultrasound hyperthermia and MR thermometry with robust adaptive control between the modalities has clinical applications. Considering that the accuracy of PFR technique is approximately ± 1°C, the adaptive control system works well to effectively track the reference by adjusting the transducer power according to dynamic tissue properties such as blood perfusion rate.

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