MRI-guided focused ultrasound (MRgFUS) system for thermal ablation of prostate cancer: Pre-clinical evaluation in canines

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Introduction: Focused ultrasound (FUS) has shown potential as a non-invasive alternative to existing prostate cancer treatments (1,2), which are often associated with severe side-effects. MRI offers substantial potential improvements in target identification and control over current FUS treatments, which are currently guided by ultrasound imaging. In addition, phased array technology may offer improved performance over existing fixed focus FUS systems (3). In this study, pre-clinical animal tests of a prototype transrectal phased array MRI-guided focused ultrasound (MRgFUS) system were performed.

Methods: We investigated a prostate MRgFUS system's (ExAblate 2000 Prostate, InSightec) ability to localize the focal point and ablate multiple locations, in 4 male dogs (14-30kg). The system combines a 2.3MHz, 1000 element/channel phased array transducer, robotic transducer positioning system, water chiller/degassing system (for acoustic coupling and to thermally protect the rectum), and a planning/thermal dosimetry workstation with a 3T MRI (GE Healthcare). The transducer was housed in a transrectal probe surrounded by a condom through which circulated temperature-controlled degassed water and was mounted to a housing unit on the MRI table. A targeted tissue volume was ablated by multiple overlapping 10-30 second sonications in one side of each gland. A similar sized volume on the opposite side was targeted using sublethal sonications to test our ability to reliably verify focal position. Temperature changes were monitored with single FSPGR or multi-slice 8-shot EPI MR temperature imaging (MRTI) (4) and an 8-channel clinical cardiac MRI coil (GE Healthcare). MRTI and thermal dose maps were used to fine-tune the system-generated treatment plan, sonication targeting and ultrasound exposure levels. Acute treatment effects were investigated after treatment with contrast-enhanced MRI and histology (TTC-staining and light microscopy). Small gland or local tissue motion during sonication was tracked in post-treatment analysis using 2D non-rigid registration on the magnitude reconstruction of the gradient echo images used for MRTI. This registration was then applied to the phase maps to observe the effects of prostate motion on the energy deposition.

Results: Every sonication delivered (N=155), including the 67 sublethal sonications, were readily visualized with MRTI (Fig 1, left). The mean peak temperature rise for treatment sonications was 25.3 ± 8.5 °C. Despite substantial variation between animals in the mean peak temperature (Fig 2), exposure levels could be adjusted based on MRTI feedback to create controlled ablated volumes (0.03-1.0 cm³). In dog 4, the ablated volume was significantly smaller (~90%) than planned, probably due to errors in the MRTI-based estimates of prostate cooling resulting from motion or undetected body cooling. Ablated volumes consistent with contrast MRI data were observed in histology, with a sharp boundary (~0.4mm) between ablated and normal tissues. Registration of the prostate motion appeared to elucidate the motion's influence on the energy delivery.

Discussion: MRTI is an excellent method for detecting focal thermal changes for this application and appears to correlate with necrosis as seen on contrast enhanced MRI and histology. Current challenges with these tests include tracking prostate motion over the entire treatment and reducing motion-induced artifacts in the MRTI used to monitor prostate cooling by the circulating water. While we do not anticipate large motion during clinical treatments, being able to track and compensate for even small motion of the gland will be advantageous for precise targeting next to critical structures, such as the rectum and the neurovascular bundles.

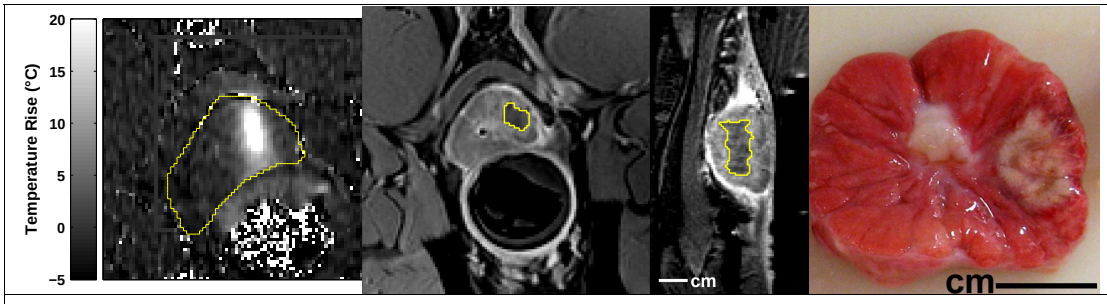

Fig 1. Left: MRTI at peak temperature rise during a 30s sonication in the prostate. The gland is outlined. Center: post-treatment contrast-enhanced T1-weighted imaging showing nonperfused volume (outlined). Right: gross histology showing small discrete ablated volume.

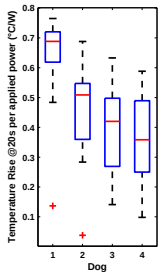

Fig 2. Average temperature rise per W of acoustic power at the focus at 20 s for each dog.

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Support: This work was funded by NIH grants R01CA109246, P01CA067165, U41RR019703. The authors thank Yongzhi Zhang, Vince Collucci and Jalil Afnan for their help with these experiments.