MRI-Guided Transurethral Ultrasound Therapy with Real-Time Feedback – A Human Study

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Introduction

Image-guided therapy of prostate cancer has been studied using a variety of delivery mechanisms including cryotherapy, brachytherapy, laser thermal ablation, high intensity focused ultrasound (HIFU) with guidance typically being provided with ultrasound. These techniques are being translated to MRI-guided approaches as it is becoming increasingly recognized that MRI offers the best definition of prostate boundaries and identification of tumor targets. Thermal approaches with MRI are particularly attractive as MR thermography can be used to guide and monitor treatment. The ideal approach would offer complete coagulation of the target with the lowest morbidity in a very short period of time. Issues of target motion and deformation during treatment delivery remain difficult problems. HIFU is attractive in that it has the potential to deliver energy less invasively however it can be time consuming. By placing an ultrasound delivery device in the urethra and planning therapy at the same sitting as treatment delivery, MRI-guided transurethral ultrasound therapy with real-time thermometry feedback has the potential to become a mainstream therapeutic technology for prostate cancer [1]. This technology has been under development within our group in preclinical studies and has demonstrated the ability to coagulate large volumes of tissue in a short time [2-4]. To our knowledge this is the first report of the use of this technology in human subjects.

Methods

This study was approved by the institutional research ethics board and informed consent was obtained. Men with low to intermediate risk prostate cancer (T1/T2A, PSA<15 ng/ml, Gleason<7 (3+4)) who were scheduled for radical prostatectomy were enrolled. MRI-guided transurethral ultrasound therapy with real-time temperature feedback was performed immediately prior to radical prostatectomy. Patients underwent spinal anesthesia and were placed in a semirecumbent position on a removable MRI table. The transurethral device was placed outside the MRI suite and coupled to an MRI-compatible positioning system with a rotational motor. A rectal fiber-optic temperature sensor was also placed. Imaging was performed in a clinical 1.5T MR imager (Signa, GE Healthcare, USA) using an 8-channel cardiac phased array coil. FSE T2 images planning images were acquired to measure the location of the ultrasound transducer in relation to the prostate. Position changes were facilitated by adjustment controls on the in-bore motor. Oblique-axial FSE T2-weighted images were acquired orthogonal to the device to select a 180-degree arc within the gland for treatment. Ultrasound energy was delivered to the prostate while MR images were acquired continuously (FSPGR, FOV=26cm, 128x128, slice=10mm, TE=9ms, TR=40ms) at 5-second intervals and the spatial temperature distribution was calculated by phase subtraction using the PRF-shift method of thermometry. The rate of rotation and output power of the ultrasound applicator were adjusted by computer control in order to elevate the temperature along the boundary of the target boundary to 55°C. Ultrasound was delivered from a 10mm long by 3.5mm wide planar transducer operating at 8MHz, with an acoustic intensity of 10W/cm2. After the completion of heating, contrast-enhanced images were acquired (3D FGRE, TE=min full, flip=13°, slice=2mm, 256x256, FOV=26cm) after intravenous injection of 0.1mmol/kg of Omniscan (GE Healthcare, USA). Once subjects were removed from the MRI, they were immediately sent for radical prostatectomy. The prostate specimen was sectioned in the plane of imaging and assessed for thermal damage using techniques described previously[5].

Results

To date two patients have undergone the procedure with continuing accrual expected. The spinal anesthetic was well tolerated by both subjects. The transurethral device was inserted easily with a single pass into both patients without incident. Actual thermal treatment times were 9 and 10 minutes. Total MRI time was two hours with much of the time being spent planning and confirming treatments plans. Radii for ablation were between 10 and 18mm (Figure 1). The maximum temperature distribution (Figure 2) depicted the expected continuous region of heating within the target boundary (55°C boundary) matching the histologic section showing necrosis (Fig 3). The mean targeting error was <2 mm (~1 pixel in temperature images). In one patient there was rectal gas deforming the prostate boundary and potentially resulting in susceptibility artifact that could have affected the thermography. A rectal tube was inserted (Figure 1) which resolved the problem. Post-treatment contrast-enhanced imaging revealed regions of non-enhancement within the target boundary; however, agreement between non-enhancing regions and pathological necrosis was poor with some enhancement seen within necrotic regions (Figure 3). The radical prostatectomy for both patients was unaffected by the procedure.

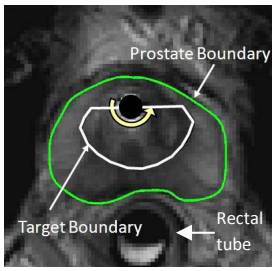

Figure 1: Target boundary selected for treatment

Discussion

We have demonstrated the feasibility of an MRI-compatible real-time-feedback transurethral approach for prostate coagulation in humans. This approach is scalable for whole prostate ablation through the use of multiple transducers which is particularly relevant as prostate cancer is often multifocal. With this approach one can envision quick treatment times (<1 hour depending on prostate size and geometry). Accrual continues in this trial which will enable further refinement of this technology for clinical application to either whole prostate ablation or targeted ablation of sites suspicious for cancer based on MRI findings.

Conclusion

It is feasible to perform accurate spatial heating of the prostate in humans using MRI-guided transurethral ultrasound in a closed bore system.

References

1. Chopra *et al*, Med Phys, 2008. 2. Burtnyk *et al*, Int J Hyperthermia, 2009. 3. Tang *et al*, Phys Med Biol, 2007. 4. Chopra *et al*, Phys Med Biol, 2009. 5. Boyes *et al*, J Urol, 2007

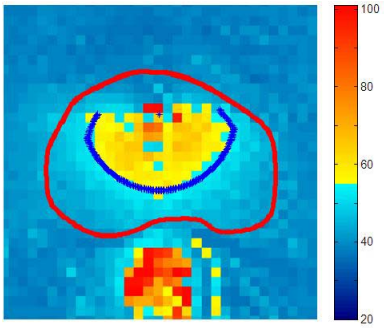

Fig 2: Maximum temperature distribution measured during treatment

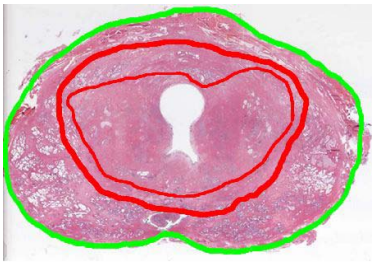

Fig 2: H&E stained section showing inner and outer boundary of thermal damage (red lines)

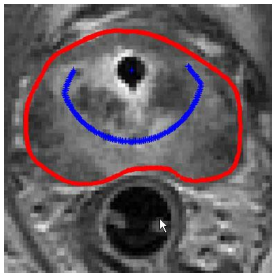

Fig 4: Contrast enhanced image obtained after treatment