MRI-Guided Transurethral Ultrasound Therapy of the Prostate Gland using Real-Time Thermal Mapping: An Analysis of Technical Accuracy and Immediate Postinterventional Assessment of Tissue Destruction via CE-MRI

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PURPOSE: Providing good local disease control while causing low morbidity are goals of minimally-invasive, image-guided therapies for localised prostate cancer (PCa) [1]. They are attractive treatment alternatives to active surveillance and radical treatments, such as surgery and radiation. One such promising minimally-invasive treatment method is MRI-guided transurethral ultrasound ablation (MRgTULSA). Using high intensity ultrasound delivered from a transurethral device, and real-time MR-Thermometry (MRT) active temperature feedback control [2], a continuous and conformal volume of thermal coagulation is generated and shaped to the prostate. Additionally, MRI-guidance enables accurate treatment planning and visualization of treatment success by means of an immediate post-interventional contrast-enhanced MR (CE-MRI). To evaluate this method, a prospective, multi-institutional phase I safety and feasibility trial was conducted. The feasibility endpoint was to assess the accuracy and precision of the thermal pattern shaped to the pre-defined acute ablation boundary (MRT vs. T2-planning) using linear and volumetric metrics of targeting accuracy as well as the Dice Similarity Coefficient (DSC). Additionally, conformal thermal coagulation of the prostate was confirmed by comparing the MRT images to the non-perfused volume (NPV) determined on CE-MRI.

METHODS: This ethics-approved study enrolled 26 patients with biopsy-proven, low-risk PCa (age ≥ 65y, T1c/T2a, PSA ≤ 10ng/ml, Gleason 6 (3+3)). MRgTULSA (TULSA-PRO, Profound Medical Inc., Canada) targeted conservative whole-gland ablation. A 3 Tesla clinical magnet (Magnetom Trio, Siemens Healthcare, Germany) with a 16-channel phased-array coil were used for MR guidance and imaging. Exact positioning of the transurethral device was achieved using an MRI-compatible positioning system and MR image guidance. Treatment planning entailed the exact delineation of the outer prostate boundary on oblique-axial T2-weighted images acquired transverse to the ultrasound device (Fig. 1a, black line). A safety margin of 3 mm from the outer boundary defined the region of acute ablation inside the prostate (Fig. 1a, yellow to red temperatures), which was targeted to 55°C [2]. Late cell kill is expected to migrate an additional 1-3 mm towards the prostate capsule [2,3] (Fig. 1, green temperatures) Ultrasound treatment was delivered in one single session under active MRT feedback control: EPI sequence, FOV=26cm, matrix=128x128, slice=4mm, gap=1mm, TE=8ms, TR=350ms. Every 5.9 s a new set of up to 12 slices were acquired to allow for real-time assessment of a 3D temperature volume. The MRT spatial temperature distribution was calculated by phase subtraction using the PRF-shift method and a multi-point phase drift correction, arriving at a temperature uncertainty of ±1°C. With every new set of MRT images, the rotation rate of the transurethral device as well as the ultrasound power and frequency of the individual transducer elements were adjusted automatically (10 independent, planar, rectangular transducers, each 4.5 x 5.0 mm^2, operating 4 or 14 MHz, with an acoustic intensity up to 20 W/cm^2). This was done to shape the thermal pattern and heat the acute ablation boundary to 55°C. Following completion of heating, CE-MRI images were acquired (3D FGRE, TE=min, flip=13°, slice=5 mm, matrix=256x256, FOV=23.4 cm) after weight adjusted intravenous injection of 0.1 mmol/kg of a gadolinium-based contrast agent. Target planning accuracy was evaluated by spatially comparing the resulting 55°C isotherm MRT to the pre-defined acute ablation boundary (T2-planning) using linear and volumetric metrics as well as DSC. Treatment success in terms of thermally coagulated tissue was confirmed by visually comparing MRT images to non-perfused volume (NPV) as obtained from post-interventional CE-MRI (Fig. 1b).

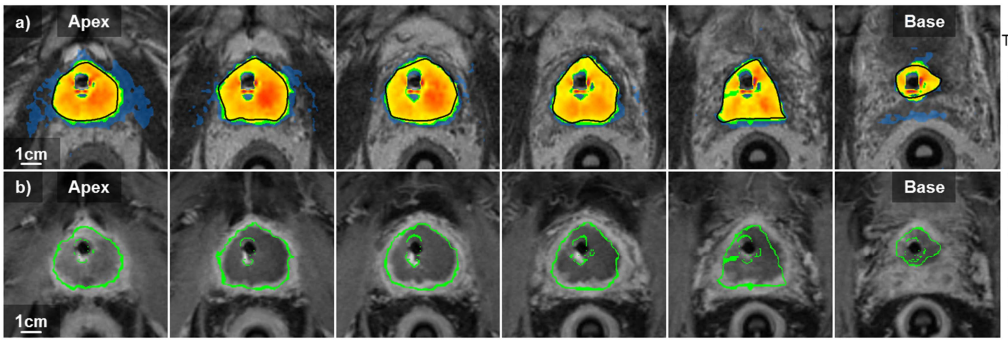

Fig. 1: Example clinical treatment, illustrating the accuracy and precision of MRgTULSA. (a) Maximum temperature measured by MRT overlaid on the T2-planning images, with pre-defined acute ablation boundary (black line). (b) Expected late cell kill (52-55°C, green region) overlaid on the immediate post-interventional CE-MRI, showing good concordance between the thermal pattern and the peripheral region of enhancement surrounding the non-perfused volume.

Tab. 1: Conformal heating results (MRT vs T2-planning)

n = 26	MEDIAN	MIN	MAX
Prostate Volume (ml)	48.6	28.2	94.7
Treatment Time (min)	36.3	23.8	61.0
DSC	0.94	0.91	0.96
Over-Targeted Volume (ml)	0.65	0.07	2.56
Under-Targeted Volume (ml)	0.93	0.07	4.83
Linear Targeting Accuracy (mm)	0.1	-0.6	1.1
Linear Targeting Precisoin (mm)	1.3	0.7	2.4

RESULTS: Median treatment time and prostate volume were 36 min (range, 24 - 61 min) and 49 ml (range, 28 – 91 ml), respectively. Average spatial control of the thermal ablation was within 0.1±1.4 mm, with average over- and under-targeted volumes of 0.8 and 1.0 ml, respectively, and a mean DSC of 0.94 (range 0.91 – 0.96) (Tab. 1). Immediate post-treatment cell kill, as visualized by the peripheral region of enhancement surrounding the NPV, showed a good concordance with the acute cell kill regions as measured by MR-Thermometry (Fig. 1).

CONCLUSION: MRgTULSA real-time thermometry and MR-guidance offers accurate treatment planning and active control of the ablation volume, as shown in high median DSC and targeting accuracy metrics. Treatment success is further confirmed through immediate postinterventional CE-MRI visualization of acute tissue destruction, which was demonstrated to be in concordance with the MR-Thermometry maps.

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