MRI-GUIDED TRANSURETHRAL ULTRASOUND PROSTATE ABLATION IN PATIENTS WITH LOCALIZED PROSTATE CANCER: 12-MONTH OUTCOMES OF A PROSPECTIVE PHASE I CLINICAL TRIAL

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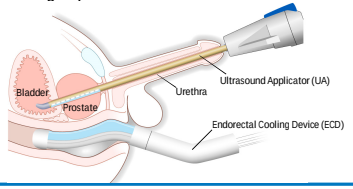
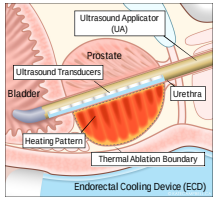
INTRODUCTION

- MRI-guided transurethral ultrasound ablation (MRI-TULSA) is a ***new minimally-invasive modality*** to ablate the prostate in patients with localized prostate cancer (PCa)
- This novel approach has the potential to offer disease control of localized PCa with a ***low morbidity profile***
- MRI-TULSA consists of a ***transurethral ultrasound applicator*** generating a precise volume of thermal ablation shaped to patient-specific prostate anatomy, using ***real-time active MRI thermometry feedback control***
- A multi-centre ***Phase I Clinical Trial*** of MRI-TULSA was performed, which enrolled patients between March 2013 and March 2014
- The aim of this Phase I study was to determine clinical ***safety*** and ***feasibility*** of MRI-TULSA for whole-gland prostate ablation in the primary treatment setting of patients with localized PCa





MATERIALS AND METHODS

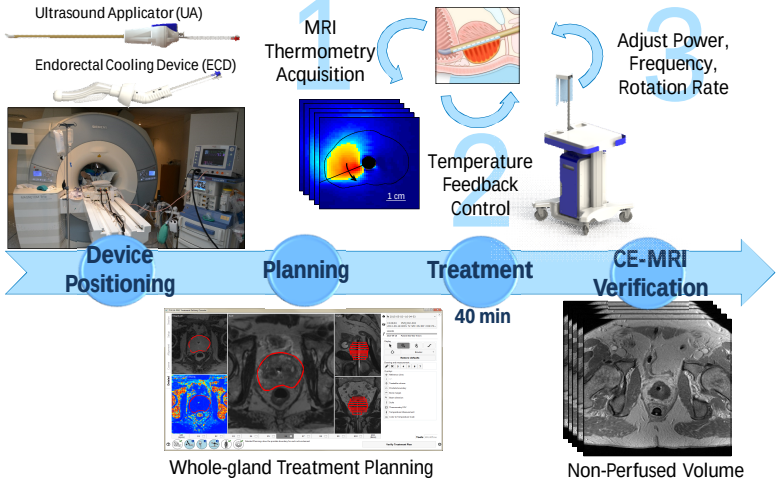
Study Design
- Prospective, multi-centre, single-arm trial to evaluate safety and feasibility of MRI-TULSA (TULSA-PRO, Profound Medical Inc.)
- Clinical trial sites in 3 jurisdictions, all under same protocol

Inclusion Criteria
- Age ≥ 65 years; Biopsy-proven prostate cancer (cT1c-T2a)
- PSA ≤ 10 ng/ml; Gleason score 3+3 (3+4 in Canada only)
- Prostate size: ≤ 5 cm sagittal length & ≤ 6 cm axial diameter
- Eligible for MRI and general anesthesia; No prior PCa treatment

Primary Endpoints (1-year follow-up)
- Safety: Frequency and severity of treatment related AE
- Feasibility: Accurate & precise conformal heating of the prostate

Exploratory Endpoints (5-year follow-up)
- Efficacy: PSA response and biopsies at 1 and 3 years
- Quality of life: IPSS, IIEF, Bowel habits domain of UCLA-PCI-SF

Treatment Planning
- Therapeutic intent of conservative whole-gland ablation
- 3 mm safety margins at the gland periphery
- 10% residual viable prostate expected around the capsule



Whole-gland Treatment Planning

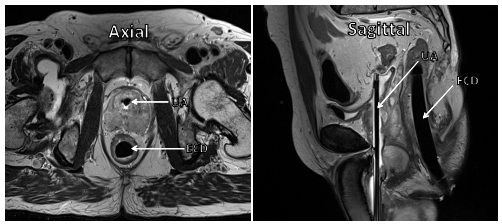
Non-Perfused Volume

RESULTS

Safety (NCI CTCAE v4)

- No cases of intraoperative complications, severe urinary incontinence, rectal injury or fistula
- No Grade (G) ≥ 4 AE's; Total of one attributable G3 AE
- Hematuria G1 (13 patients), G2 (2 patients), resolved
- UTI G2 (10 patients), resolved with oral antibiotics
- Epididymitis G3 (1 patient), resolved with IV-antibiotics
- Urinary retention G1 (3 patients) and G2 (5 patients), resolved with prolonged or re-catheterization
- All patients were discharged on or prior to POD1

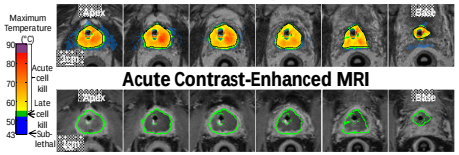
Treatment Planning Images (T2w MRI)



Feasibility

- Excellent conformal heating of prostate tissue: ± 1.3 mm
- Acute cell kill on MR thermometry matches the Non-Perfused Volume on acute Contrast-Enhanced MRI

Maximum Temperature



Acute Contrast-Enhanced MRI

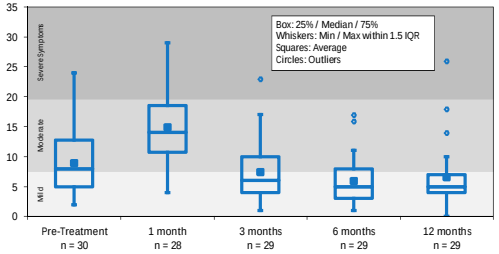
Conformal Heating Results Summary

PARAMETER (n=30)	MEAN	95% CI	RANGE
Prostate Volume (cc)	47 cc	41 – 54	21 – 95
Treatment Time (min)	36 min	32 – 40	24 – 61
Ablation Accuracy (mm)	0.1 mm	-0.1 – 0.2	-0.6 – 1.1
Ablation Precision (mm)	1.3 mm	1.2 – 1.5	0.7 – 2.4

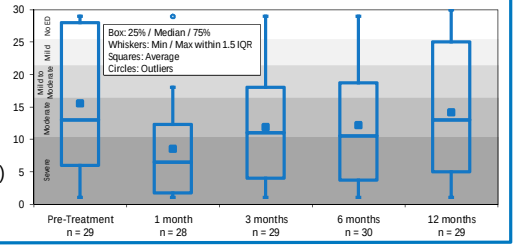
12-Month Biopsy

- Positive biopsy, clinically significant disease: 9/29 patients (31%)
- Positive biopsy, any disease: 16/29 patients (55%)
- 61% reduction in total cancer length (reduced cancer burden)

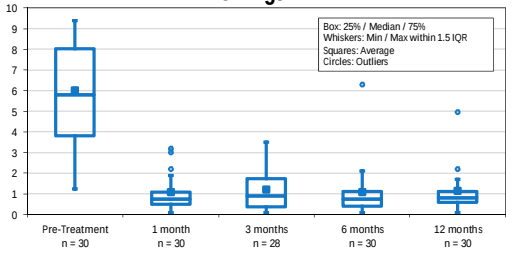
IPSS



IIEF-15 Erectile Function Domain



PSA ng/mL



CONCLUSIONS

- MRI-TULSA provides ***detailed planning***, ***real-time thermal dosimetry***, and precise ***feedback control*** of prostate ablation
- MRI-TULSA is a ***safe and well tolerated procedure*** with a ***low morbidity profile*** for a whole-gland ablation of PCa
- Phase I data are sufficiently compelling to study MRI-TULSA in a ***larger trial with reduced safety margins***, to begin in 2016
- Chin *et al*. European Urology 2016 (Jan 6 epub ahead of print)