# MRI-GUIDED TRANSURETHRAL ULTRASOUND ABLATION IN PATIENTS WITH LOCALIZED PROSTATE CANCER: 3-YEAR OUTCOMES OF A PROSPECTIVE PHASE I STUDY

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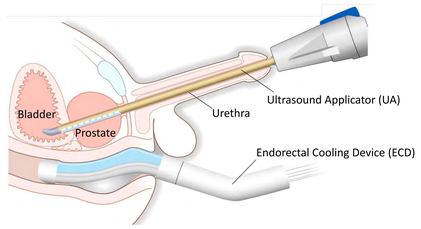
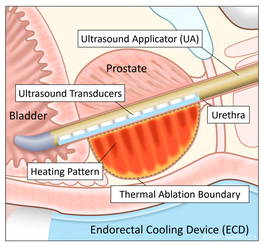
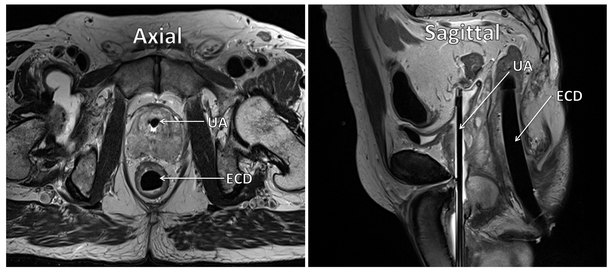
## INTRODUCTION

- 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




### Treatment Planning Images (T2w MRI)




## MATERIALS AND METHODS

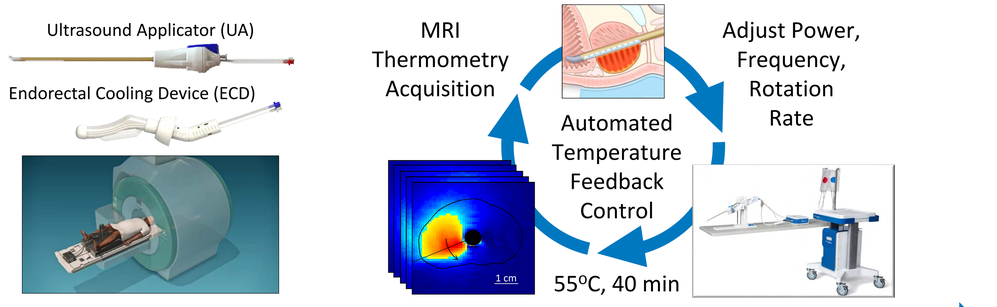
**Study Design**
- Prospective, multi-centre, single-arm trial to evaluate safety and feasibility of MRI-TULSA (TULSA-PRO, Profound Medical Inc.)
- Clinical trial sites in 3 jurisdictions, all under same protocol

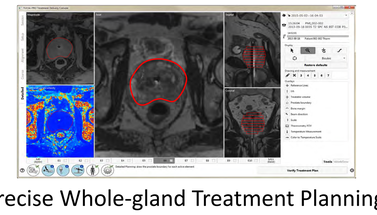
**Inclusion Criteria**
- Age ≥ 65 years; Biopsy-proven prostate cancer (cT1c-T2a)
- PSA ≤ 10 ng/ml; Gleason score 3+3 (3+4 in Canada only)
- Prostate size: ≤ 5 cm sagittal length & ≤ 6 cm axial diameter
- Eligible for MRI and general anesthesia; No prior PCa treatment

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

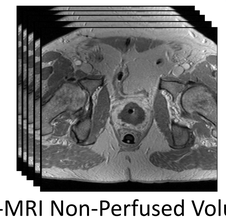
**Exploratory Endpoints (5-year follow-up)**
- Efficacy: PSA response and biopsies at 1 and 3 years
- Quality of life: IPSS, IIEF, Bowel habits domain of UCLA-PCI-SF

**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



Precise Whole-gland Treatment Planning



CE-MRI Non-Perfused Volume

## RESULTS

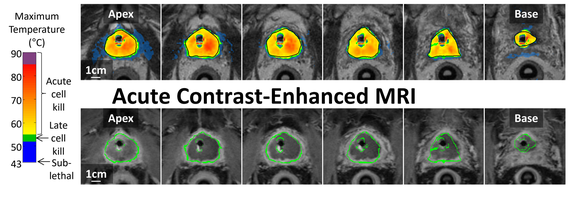
### Safety (NCI CTCAE v4)

- 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, median suprapubic catheterization time was 2.2 wk as per protocol

### Feasibility

- Accurate and precise prostate heating: 0.1 ± 1.3 mm, n=30
- Prostate volume mean 47 cc (95% CI 41–54, range 21–95)
- Treatment time 36 min (95% CI 32–40, range 24–61)
- Acute cell kill on MR thermometry matches the Non-Perfused Volume on acute Contrast-Enhanced MRI

**Maximum Temperature**



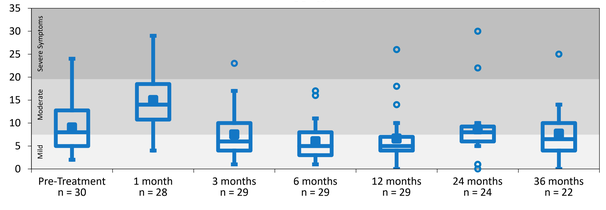

### 12-Month MRI and Biopsy

- Significant disease: 9/29 pts (31%), any disease: 16/29 pts (55%)
- 61% reduction in total cancer length (reduced cancer burden)
- 88% prostate volume reduction (enhancing volume less fibrosis)

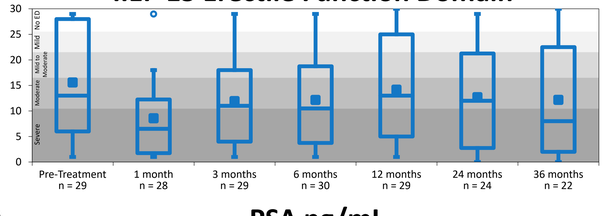
### 3-Year Biopsy

- 1/13 pts negative at 12-mo upgraded to 3+3 disease
- 1/9 remaining pts positive at 12-mo upgraded to 3+4 disease
- 4/9 remaining pts positive at 12-mo down to 3+3 or neg biopsy

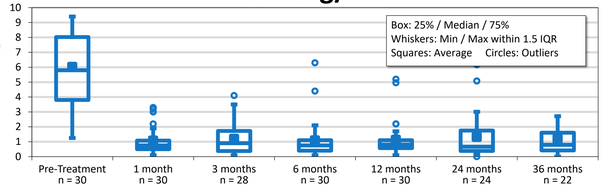
**IPSS**




**IIEF-15 Erectile Function Domain**

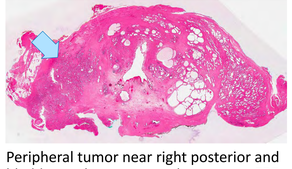



**PSA ng/mL**




### Salvage Prostatectomy

- Within 36 mo, salvage prostatectomy in 6 pts, EBRT in 1, FLA in 1
- 4 RP at 1 site: difficulty comparable to post-RT, extensive fibrosis
- Whole mount histology showed 2 pT2b and 2 pT3a consistent with persistent cancer in untreated peripheral safety region



Peripheral tumor near right posterior and bladder neck margins, with extensive EPE

| | |
|---|---|
| Mean operating time (min) | 191 (165-217) |
| Blood loss (ml) | 900 (700-1000) |
| Length of stay (days) | 3.5 (2-6) |
| Perioperative complications | None |
| Tumor Stage<br>Tumor Grade | pT2b (1/4), pT3a (3/4)<br>4+3 (1/4), 3+4 (3/4) |
| Stress urinary incontinence<br>Erect Dys. unresponsive to PDE-5i | Mild 2/4, Moderate 1/4<br>4/4 |
| PSA progression to salvage RT | 2/4 |

## 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
- A ***larger multicenter TULSA-PRO Ablation Clinical Trial (TACT)***, ***with reduced safety margins***, completed enrolment Feb 2018

Chin *et al*. European Urology 2016;70:447-455.