



# Magnetic resonance imaging-guided transurethral ultrasound ablation of prostate tissue in patients with localized prostate cancer: single-center evaluation of 6-month treatment safety and functional outcomes of intensified treatment parameters

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## Abstract

**Objectives** To evaluate the effect of intensified treatment parameters on safety, functional outcomes, and PSA after MR-Guided Transurethral Ultrasound Ablation (TULSA) of prostatic tissue.

**Patients and methods** Baseline and 6-month follow-up data were collected for a single-center cohort of the multicenter Phase I ( $n = 14/30$  at 3 sites) and Pivotal ( $n = 15/115$  at 13 sites) trials of TULSA in men with localized prostate cancer. The Pivotal study used intensified treatment parameters (increased temperature and spatial extent of ablation coverage). The reporting site recruited the most patients to both trials, minimizing the influence of physician experience on this comparison of adverse events, urinary symptoms, continence, and erectile function between subgroups of both studies.

**Results** For Phase I and TACT patients, median age was 71.0 and 67.0 years, prostate volume 41.0 and 44.5 ml, and PSA 6.7 and 6.7 ng/ml, respectively. All 14 Phase I patients had low-risk prostate cancer, whereas 7 of 15 TACT patients had intermediate-risk disease. Baseline IIEF, IPSS, quality of life, and pad use were similar between groups. Pad use at 1 month and quality of life at 3 months favored Phase I patients. At 6 months, there were no significant differences in functional outcomes or adverse events.

**Conclusion** TULSA demonstrated acceptable clinical safety in Phase I trial. Intensified treatment parameters in the TACT Pivotal trial increased ablation coverage from 90 to 98% of the prostate without affecting 6-month adverse events or functional outcomes. Long-term follow-up and 12-month biopsies are needed to evaluate oncological safety.

**Keywords** TULSA · MRI-guided · Outcome · Phase I · Pivotal

## Abbreviations

CEM43	Cumulative equivalent minutes at 43 °C
IIEF	International index for erectile function
IPSS	International prostate symptom score
IQR	Interquartile range
MRI	Magnetic resonance imaging

PCa	Prostate cancer
PS	Positioning system
QoL	Quality of life
TACT	TULSA-PRO Ablation Clinical Trial
TULSA	Transurethral ultrasound ablation
UA	Ultrasound applicator

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## Introduction

The incidence and prevalence of prostate cancer (PCa) have risen in recent decades due to changes in demographics, and improvements in diagnosis and screening [1]. For men with very low-risk PCa, active surveillance is an option to reduce overtreatment [2]. Patients who do not qualify for active surveillance or are unwilling to undergo active surveillance

require definitive treatment options for localized PCa such as radical prostatectomy or radiotherapy [2]. These definitive treatment options have shown excellent tumor control and minimal adverse events in competence centers and are, therefore, considered as gold standard in the treatment of localized PCa [3]. Beside these options, alternative treatment methods have emerged aiming local tumor control with reduced procedure-related side-effects. Still in their infancy, these techniques lack long-term data, and their efficacy and safety are matter of recent studies [2].

Magnetic resonance imaging (MRI)-guided transurethral ultrasound ablation (TULSA) is a novel therapeutic tool for thermal ablation of prostatic tissue with the advantages of MRI planning and live MRI thermometry feedback/guidance. A recent Phase I trial demonstrated the clinical feasibility and safety of TULSA in 30 patients with localized PCa at three institutions [4], and the subsequent TULSA-PRO Ablation Clinical Trial (TACT) Pivotal study is investigating efficacy and safety in 115 men across 13 sites. The Phase I safety and feasibility trial intentionally used conservative treatment margins, sparing 3 mm of untreated prostate tissue at the apex, along with a 3-mm margin of untreated prostate tissue peripherally at the inside of the prostate capsule. This was expected to leave 10% of the prostate volume untreated, and the resulting risk of residual disease was willingly accepted. While not a primary endpoint of the Phase I study, 12-month biopsy identified clinically significant PCa in 31% of patients, and any disease in 55% of patients. For the TACT trial, treatment parameters were intensified towards the goal of achieving complete whole-gland ablation with reduced prostate tissue sparing, accepting the risk of increased treatment-related side effects. The results of follow-up biopsy are pending.

Here we evaluate the impact of intensified treatment parameters on treatment safety by comparing adverse events, functional outcomes, and PSA course for Phase I and TACT patients treated at an experienced single center that enrolled patients to both studies.

## Patients and methods

The Phase I trial (NCT01686958) recruited 30 men  $\geq 65$  years with biopsy-proven PCa (Gleason score 3+3 or 3+4, PSA  $\leq 10$  ng/ml, clinical stage T1c–T2a, N0, M0) across three centers. The TACT Pivotal study (NCT02766543) recruited 115 patients  $\geq 45$  years with biopsy-proven PCa (Gleason score 3+3 or 3+4, PSA  $\leq 15$  ng/ml, clinical stage T1c–T2a, N0, M0) across 13 centers. In Germany, recruitment of men with Gleason 3+4 was not allowed for the Phase I trial. Both trials were approved by the respective ethics boards, and written informed consent was obtained from all study participants.

As the aim of this analysis was to evaluate the effect of intensified treatment parameters on safety and functional outcomes, the influence of physician experience was minimized by only including patients treated at a single experienced center (University of Heidelberg; Germany) that enrolled the most patients to both studies. All patients at this center were treated by the same physicians for both trials: 14 patients in Phase I, and 15 in the TACT study.

## MRI-guided TULSA procedure

The TULSA-PRO investigational device (Profound Medical Inc., Toronto, Canada) was described previously [4–7]. All TULSA procedures were performed under general anesthesia. A suprapubic catheter was inserted before the procedure. The rigid transurethral ultrasound applicator (UA) was inserted over a nitinol guidewire and mounted to a positioning system (PS) that provided remote linear and rotational motion of the UA. The UA consisted of 10 independent ultrasound transducers that emitted directional high-intensity ultrasound for thermal ablation of prostatic tissue. To protect the prostatic urethra, the UA was cooled by flowing water to preserve 1–2 mm of tissue around the array. To protect the rectal wall, a passive endorectal cooling device was used.

Treatment took place in a 3 Tesla MRI (Phase I: Magnetom Trio, Siemens, Munich, Germany; TACT: Magnetom Prisma, Siemens, Munich, Germany). The UA was positioned within the prostatic urethra under MRI guidance. The urologist and radiologist defined treatment plans by delineating the outer boundaries of the prostate on high-resolution T2-weighted MRI images acquired in alignment with each individual UA transducer element. In both studies, treatment plans spared a 3-mm safety margin of untreated tissue towards the external rhabdosphincter. A second safety margin of spared prostate tissue along the inner edge of the prostate capsule was defined differently between the Phase I and TACT studies as described below. Treatment of the prostate was done under live MRI thermometry feedback control of ultrasound power to each element during a complete rotation of the UA [4].

## Treatment differences between the Phase I study and the TACT pivotal study

In the Phase I safety and feasibility study, the treatment controller aimed to deliver temperatures  $\geq 55$  °C from the urethra out to a margin set 3 mm inside of the prostatic capsule. Histological studies of MRI–TULSA predict acute cell kill of tissues whose temperature measured by MR thermometry exceeds 55 °C [5, 8]. Delayed cell kill was expected to migrate outward an additional 1–3 mm [8], correlating with an isoeffective thermal dose of 240 cumulative equivalent

minutes at 43 °C (CEM43) [9], a widely accepted predictor of the extent of thermal coagulation [5, 10]. With a control temperature of 55 °C set 3 mm inside the capsule, the total volume of acute and delayed cell kill was expected to cover 90% of the gland, sparing a rim of viable prostate tissue at the periphery. These controller parameters were chosen to enable MR thermometry measurement of the spatial treatment precision and the expected extent of delayed cell kill within the prostate [11].

In the TACT study, the treatment control parameters were intensified for complete prostate ablation by delivering higher temperatures closer to the capsule. As thermal dose is a function of temperature and exposure time, the controller aimed to deliver  $\geq 57$  °C at a margin set 2 mm inside the capsule, and the minimum rotational speed was reduced from 8 to 4 degrees per minute. Simulations predicted these changes would deliver acute cell kill  $\geq 55$  °C to within 1 mm of the prostate capsule [6], with the total volume of acute and delayed cell kill covering 99% of the targeted prostate volume (Fig. 1).

### Evaluated parameters and follow-up

At the baseline visit, all patients underwent physical examination, transrectal ultrasound, and blood chemistry. PSA values were determined at treatment day and during follow-up. The first follow-up was after 2 weeks to evaluate micturition and remove the suprapubic catheter. Detailed follow-up visits at 1, 3, and 6 months included physical examination, blood samples including PSA values, and evaluation

for adverse events using Common Terminology Criteria for Adverse Events v.4 [12]. All patients completed standardized questionnaires at the baseline visit and follow-up including the international index for erectile function (IIEF-15) questionnaire, and the international prostate symptom score (IPSS) and quality of life (QoL) questionnaire. Urinary continence was evaluated by interview and pad use. Ablation coverage (measured by MR thermometry) was calculated for all patients and compared between groups [11].

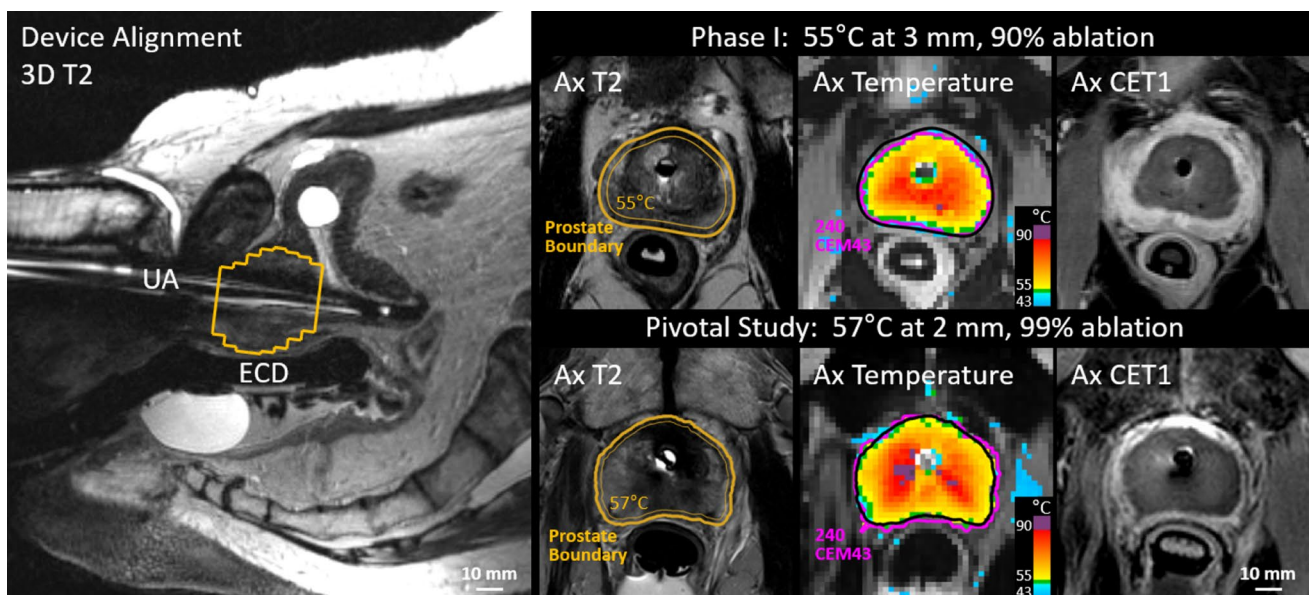
### Statistical analysis

Descriptive statistics for the evaluated parameters were reported by their median and inter-quartile range. Comparisons between the Phase I and TACT study patients used Chi square tests for categorical variables, and Mann–Whitney *U* tests for continuous variables, with a significance threshold of  $p < 0.05$ . All statistical analyses were carried out using IBM SPSS software package version 25.

## Results

### Patient characteristics

Baseline clinical data are given in Table 1. In Phase I, 12/14 patients had an MRI/TRUS fusion biopsy [13] for diagnosis of PCa, and 2/14 had a transrectal, TRUS-guided biopsy. In the TACT study, 10/15 patients had a baseline MRI/TRUS fusion biopsy [13], 5/15 had a TRUS-guided biopsy. All



**Fig. 1** MRI-guided TULSA workflow. Device alignment within the prostate under MR visualization (left), along with treatment planning (Ax T2), live MR Thermometry (Ax Temperature), and post-treat-

ment contrast-enhanced imaging (Ax CET1) for Phase I and Pivotal (TACT) study patients

**Table 1** Characteristics of Phase I and TACT patients

	Phase I <i>N</i> =14	TACT <i>N</i> =15	<i>p</i> value
Age, median (IQR)	71.0 (69.2–73.0)	67.0 (64.9–71.9)	0.10
Charlson comorbidity index, median (IQR)	5 (4–5)	4 (4–5)	0.48
Prostate volume, median (IQR)	41.0 (33.8–65.7)	44.5 (33.4–54.5)	0.76
PSA, median (IQR)	6.7 (3.8–8.1)	6.7 (4.7–7.3)	0.84
Gleason score			<b>0.04</b>
Gleason 3+3	14	10	
Gleason 3+4	0	5	
Risk classification			<b>0.01</b>
Low risk	14	8	
Intermediate risk	0	7	
IIEF, median (IQR)	11.5 (3.8–26.5)	22.5 (5.0–28.8)	0.21
IPSS, median (IQR)	8.5 (5.0–15.5)	10.0 (5.5–14.8)	0.74
Quality of life, median (IQR)	2.5 (1.8–4.0)	3.0 (2.0–3.8)	0.91
Number of pads, median (IQR)	0 (0–0)	0 (0–0)	1.00

Groups were compared by Chi square tests for categorical variables and Mann–Whitney-*U* tests for continuous variables.  $p < 0.05$  was considered statistically significant

**Table 2** Baseline and follow-up PSA for Phase I and TACT patients

	Phase I <i>N</i> =14	TACT <i>N</i> =15	<i>p</i> value
PSA, median (IQR)			
Baseline	6.7 (3.8–8.1)	6.7 (4.7–7.3)	0.84
1 month	0.9 (0.5–1.9)	1.0 (0.5–1.6)	0.78
3 months	0.9 (0.3–1.7)	0.7 (0.2–1.3)	0.13
6 months	0.7 (0.4–1.2)	0.9 (0.5–1.4)	0.60
PSA Nadir at 6 months	0.7 (0.2–0.8)	0.5 (0.2–1.2)	0.42
Time to PSA nadir	3.0 (1.0–6.0)	3.0 (3.0–4.5)	0.45

Groups were compared by Mann–Whitney-*U* test.  $p < 0.05$  was considered statistically significant

TACT patients had a protocol-mandated pre-intervention MRI of the prostate to rule out advanced disease.

Comparison of ablation coverage measured by MR thermometry revealed that 90% (IQR 88–92%) and 98% (IQR 97–99%) of the gland reached a lethal thermal dose of 240 CEM43 in the Phase I and TACT trials, respectively ( $p < 0.01$ ). The PSA nadirs in Phase I and TACT patients were 0.7 ng/ml (IQR 0.2–0.8) and 0.5 ng/ml (IQR 0.2–1.2), respectively ( $p > 0.05$ ), reached in a median of 3 months (Table 2).

### Functional outcomes

At 6 months, functional outcomes in patients from the Phase I and TACT studies were similar in terms of urinary symptoms, incontinence, and erectile function. The suprapubic catheter was removed 14.5 days (median; IQR 13.0–25.0) and 20.0 days (median; IQR 10.3–42.0) after treatment in Phase I and TACT patients, respectively

**Table 3** Micturition data for Phase I and TACT patients

	Phase I <i>N</i> =14	TACT <i>N</i> =15	<i>p</i> value
Catheter indwelling time, median (IQR)	14.5 (13.0–25.0)	20.0 (10.3–42.0)	0.18
IPSS, median (IQR)			
Baseline	8.5 (5.0–15.5)	10.0 (5.5–14.8)	0.74
1 month	15.5 (11.0–21.0)	14.5 (11.5–18.5)	0.84
3 months	5.0 (3.0–10.0)	7.5 (3.5–10.0)	0.38
6 months	5.0 (3.0–7.0)	7.0 (2.0–9.0)	0.50
Quality of life, median (IQR)			
Baseline	2.5 (2.0–4.0)	3.0 (2.0–3.5)	0.91
1 month	4.0 (2.0–4.0)	4.0 (3.0–6.5)	0.12
3 months	2.0 (1.0–2.0)	3.0 (1.5–3.0)	<b>0.01</b>
6 months	2.0 (1.0–2.0)	2.0 (1.0–3.0)	0.11
Number of pads (IQR; range)			
Baseline	0 (0–0; 0–0)	0 (0–0; 0–0)	1.00
1 month	0 (0–0; 0–0)	0 (0–0; 0–2)	<b>0.04</b>
3 months	0 (0–0; 0–0)	0 (0–0; 0–1)	0.33
6 months	0 (0–0; 0–0)	0 (0–0; 0–0)	1.00

Comparisons of catheter indwelling time, IPSS, quality of life, and pad use at baseline and follow-up were made by Mann–Whitney-*U* test.  $p < 0.05$  was considered statistically significant

( $p = 0.18$ ). Micturition during follow-up was evaluated by IPSS and QoL questionnaires (Table 3). Patients from both trials showed an increase in IPSS score after 1 month, with improvements from baseline at 3 and 6 months, and no statistical difference between groups ( $p > 0.05$ ). None of the Phase I patients reported urinary leakage or pad use at baseline or follow-up. Among TACT patients, at the 1-month visit three patients needed 1 pad/day (significant difference



to Phase I,  $p=0.04$ ) and one patient needed 2 pads/day. At the 3-month visit, one patient required 1 pad/day. At the 6-month visit, none of the TACT patients required pads. Quality of life was better in Phase I patients at 3 months ( $p=0.01$ ) and was comparable between groups at baseline, 1 month, and 6 months. Erectile function was evaluated using question two of the IIEF questionnaire (erections sufficient for penetration) as the ability to penetrate in more than 50% of attempts. At baseline, 40% and 60% of Phase I and TACT patients had good erectile function ( $p=0.36$ ). At 6 months, 29% and 47% of Phase I and TACT patients reported good erectile function, respectively ( $p=0.32$ ). IIEF scores were comparable between groups, with a decline at 1 month followed by recovery at 3 and 6 months (Table 4).

### Adverse events

Adverse events of any grade were experienced by 11/14 patients in Phase I (78.5%) and 12/15 patients in TACT (80.0%). There were no intraoperative complications, no rectal injuries or fistulae, and no cases of severe urinary incontinence. There were no grade 4 or higher adverse events. In both groups, all patients were discharged 1 day after the procedure. Aside from one attributable grade 3 adverse event in Phase I, and one in TACT, all adverse events were grade 1 or 2. Both grade 3 adverse events were epididymitis, resolved with hospitalization and intravenous antibiotic therapy (Phase I and TACT) and vasectomy (TACT). Other

adverse events mainly consisted of urinary tract infection [Phase I: 6/14 (43%); TACT: 10/15 (66.6%);  $p=0.229$ ], epididymitis with outpatient antibiotic treatment [Phase I: none; TACT: 3/15 (20%)], bladder outlet obstruction [Phase I: 6/14 (43%); TACT: 2/15 (13%)] or urgency [Phase I: 5/14 (36%); TACT: 3/15 (20%)]. All grade 1 and 2 adverse events could be managed with outpatient treatment, medication, or catheterization. All adverse events occurred during the first 3 months and resolved with adequate treatment (Table 5).

### Discussion

MRI-guided TULSA has demonstrated clinical safety and feasibility in a Phase I trial [4]. In contrast to other ablative therapies like transrectal HIFU or cryotherapy, TULSA treatment is planned and delivered under live MRI visualization and MRI thermometry. Thereby, treatment planning, heat delivery, and ablation extent can be controlled precisely [4]. In the Phase I trial, the treatment controller was designed to deliver temperatures  $\geq 55$  °C up to a 3-mm margin inside of the prostate capsule. In concordance with the treatment plan, a lethal thermal dose ( $\geq 240$  CEM43 [9]) was achieved in 90% of the gland [11]. This was confirmed by an 88% reduction in viable prostate tissue volume measured using 12-month MRI and biopsy data [11]. To increase ablation coverage, treatment parameters in the TACT study were modified to deliver higher temperatures ( $\geq 57$  °C) closer to the prostate capsule (2 mm interior margin). In our patients, this increased the extent of lethal thermal dose from 90% of the prostate volume in Phase I, to 98% coverage

**Table 4** Comparison of erectile function data from the IIEF questionnaire at baseline and during follow-up for Phase I and TACT patients

	Phase I $N=14$	TACT $N=15$	$p$ value
IIEF, median (IQR)			
Baseline	11.5 (3.8–26.5)	22.5 (5.0–28.8)	0.21
1 month	3.0 (1.0–9.3)	3.5 (1.3–13.8)	0.56
3 months	11.5 (4.8–16.5)	13.0 (1.0–27.3)	0.52
6 months	11.0 (5.3–20.0)	11.0 (1.8–24.0)	0.98
IIEF Q2 erection sufficient for penetration			
Baseline	2.5 (0.8–5.0)	4.0 (0.0–5.0)	0.69
1 month	0.0 (0.0–1.5)	0.0 (0.0–1.8)	0.57
3 months	2.0 (0.0–3.3)	2.5 (0.0–4.8)	0.37
6 months	2.5 (1.0–4.3)	2.5 (0.0–4.8)	0.95
IIEF Q2 erection sufficient for penetration (no of patients)			
Baseline	6/14 (40%)	9/15 (60%)	0.36
1 month	1/14 (7%)	3/15 (20%)	0.32
3 months	3/14 (21%)	7/15 (47%)	0.15
6 months	4/14 (29%)	7/15 (47%)	0.32

Groups were compared by Mann–Whitney- $U$  test for continuous variables and Chi square for categorical variables.  $p < 0.05$  was considered statistically significant

**Table 5** Adverse events for Phase I and TACT patients

Adverse event	Phase I $N=14$	TACT $N=15$	$p$ value
Haematuria			0.316
Grade 1	2/14 (14.3%)	1/15 (6.7%)	
Grade 2	0/14 (0.0%)	2/15 (13.3%)	
Urinary tract infection			0.229
Grade 1	0/14 (0.0%)	2/15 (13.3%)	
Grade 2	6/14 (42.9%)	8/15 (53.3%)	
Epididymitis/Orchitis			0.208
Grade 2	0/14 (0.0%)	3/15 (20.0%)	
Grade 3	1/14 (7.1%)	1/15 (6.7%)	
Bladder outlet obstruction			0.075
Grade 2	6/14 (42.9%)	2/15 (13.3%)	
Urgency			0.067
Grade 1	1/14 (7.1%)	3/15 (20.0%)	
Grade 2	4/14 (28.6%)	0/15 (0.0%)	

Attributable adverse events of the same name are reported once per patient using the highest attributable grade. Groups were compared by Chi square test.  $p < 0.05$  was considered statistically significant

in the TACT study. We observed some evidence that PSA nadir at 6 months was lower in TACT, but the difference did not reach significance in our single-center subsets. Preliminary data for the whole patient collective of the TACT trial showed a significant difference in PSA decline at 6 months compared to Phase I [14]. As previously demonstrated, PSA nadir is a prognostic parameter for disease-free survival in patients undergoing HIFU treatment [15, 16] with the lowest risk for disease recurrence in patients with the lowest PSA nadir. However, longer follow-up including prostate biopsy is mandatory to assess whether the modified treatment parameters affected oncological safety for TULSA treatment as PSA nadir is only a surrogate parameter.

The therapeutic benefits of increasing the treatment temperature and ablation extent were expected to be accompanied by an increased risk of side effects. The main purpose of this study was to evaluate whether the intensified TULSA treatment parameters in the TACT study affected the previously demonstrated clinical safety of the Phase I trial. As the experience of the physician can also have an effect on treatment outcomes, this analysis only included data from patients treated at one experienced institution [17].

There were no significant differences in treatment safety between Phase I and TACT patients. However, due to the small group sizes, some potentially important differences did not meet statistical significance. In particular, patients in TACT had to tolerate their catheter a median of 1 week longer than in Phase I. As prostate volumes were comparable between groups, we attribute this difference to increased swelling of the prostate due to the increased temperature and treatment volume. The correlation of higher obstruction rates with increased treatment volume has been described for transrectal HIFU [18]. Bladder outlet obstruction is a typical side effect of transrectal HIFU. Without prior transurethral resection, up to 50% of HIFU patients develop bladder outlet obstruction with the need for surgical intervention [19, 20], with a reported median time to bladder outlet obstruction of 6 months after a single HIFU session [20]. None of the patients treated with TULSA required surgical intervention for bladder outlet obstruction during 6 months follow-up, and the number of bladder outlet obstruction events was lower in TACT patients. Further, evaluation of IPSS scores even showed that micturition symptoms improved after 3 months, suggesting a simultaneous therapeutic effect on benign prostatic enlargement and derived symptoms. The transurethral access, non-focused delivery of thermal energy, and lower peak treatment temperature seem to have a different effect than transrectal HIFU, making TULSA more comparable to other transurethral BPH treatments like transurethral needle ablation or transurethral microwave ablation [21].

As the treatment is performed in a MRI suite under live MRI-thermometry, ablation extent can be monitored

during treatment and real-time adjustments can be made for complete treatment of the intended target volume [5, 6, 22]. MRI guidance also facilitates sparing of surrounding sensitive structures. In Phase I, none of our patients experienced incontinence, and erectile function returned to baseline levels after 6 months. No significant differences were observed in TACT study patients at 6 months. However, 4 of 15 (26.6%) and 1 of 15 (6.7%) TACT patients used pads due to urgency and mild incontinence at 1 and 3 months, respectively. This may have influenced transient differences in quality of life, favoring Phase I patients at 3 months. Median IIEF scores had not yet returned to baseline in TACT patients after 6 months as in Phase I, but there were no significant differences in the number of patients with erections sufficient for penetration between groups, or between baseline and 6 months for either group. We attribute the observed differences to the reduction of the safety margin from the prostatic capsule and the subsequently increased treatment volume and delivered energy.

During the Phase I trial, a high rate of urinary tract infections across all three study centers was a matter of concern and attributed to the preoperative cystoscopy, the suprapubic catheter, or insertion of the transurethral ultrasound device [4]. At our institution infections occurred more often in TACT patients, but this difference was not statistically significant. The rate of epididymitis was also higher in TACT patients. Urinary tract infections attributed to necrosis caused by thermoablative treatments of the prostate are not uncommon and have been described extensively for transurethral needle ablation [23], transurethral microwave thermotherapy [24, 25], transurethral laser coagulation [26], and transrectal HIFU [19]. The higher rates of urinary tract infections in TACT patients may, therefore, be attributed to increased necrosis as a result of the higher energy delivered to a larger treatment volume. As infection rates are a matter of concern, action should be taken to overcome this issue. In transrectal HIFU, the combination with TURP to remove debris reduced the infection rate significantly [27], but is also used to overcome high rates of obstructive micturition and bladder neck obstructions. As described by Chaussy et al., the use of low-dose antibiotic prophylaxis also resulted in significantly lower urinary infection rates after HIFU [18]. In our collective, all patients with symptomatic urinary tract infections were treated successfully by antibiotics. To overcome the high rates of urinary tract infections observed in TULSA throughout the Phase I and TACT trials, extension of antibiotic prophylaxis from a solely perioperative course to several weeks after TULSA should be considered.

Limitations of this study include the small number of patients and the short follow-up of 6 months. Although early clinical safety can be evaluated at 6 months, evidence of oncological efficacy for TACT patients requires further follow-up including prostate biopsy at 12 months, and

long-term evaluation of clinical safety is needed to rule out late toxicity.

## Conclusion

TULSA is a safe and well-tolerated treatment for transurethral ablation of prostatic tissue, as demonstrated in a Phase I safety and feasibility trial. For the subsequent TACT Pivotal study of safety and efficacy, intensified treatment parameters increased ablation extent from 90 to 98% coverage of the prostate. Comparing adverse events and functional outcomes in subgroups of patients from the Phase I and TACT trials who were treated at a single experienced institution demonstrated that clinical safety was not affected by these changes to the treatment algorithm.

**Author contribution** GH: project development, data collection, data analysis, manuscript writing and editing. VP: data collection, data analysis. DB: data collection, data analysis, manuscript writing and editing. MB: project development, data analysis, manuscript writing and editing. RS: project development, data analysis, manuscript writing and editing. SP: project development, data collection, data analysis. GT: data collection, data analysis. JPR: data analysis, manuscript writing and editing. JM: data collection, supervision. HPS: project development, supervision, critical revision of manuscript. MH: project development, manuscript writing and editing, supervision, critical revision of manuscript. JNN-D: data analysis, manuscript writing and editing, supervision, critical revision of manuscript.

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## Compliance with ethical standards

**Conflict of interest** R. Staruch and M. Burtnyk are employees of Profound Medical and receive a salary and stock options. The other authors declare, that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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