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Aquablation Therapy in Large Prostates (80-150 mL) for Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: Final WATER II 5-Year Clinical Trial Results

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Purpose: We report 5-year safety and efficacy outcomes of the Aquablation procedure for the treatment of men with symptomatic benign prostatic hyperplasia and large-volume prostate glands.

Materials and Methods: A total of 101 men with moderate to severe benign prostatic hyperplasia symptoms and prostate volumes between 80 and 150 mL underwent a robotic-assisted Aquablation procedure in a prospective multicenter international trial (NCT03123250). Herein we report the final 5-year results.

Results: The study successfully met its safety and efficacy performance goal, which was based upon transurethral resection of the prostate outcomes typically done in smaller prostates, at 3 months. Mean prostate volume was 107 mL (range 80-150) at baseline. Patient symptoms showed a significant improvement

Submitted February 27, 2023; accepted April 10, 2023; published 000.

Support: The clinical study was funded by PROCEPT BioRobotics.

Conflict of Interest: Kevin C. Zorn, Mo Bidair, Eugene Kramolowsky, Mihir Desai, Dean Elterman, Claus Roehrborn, and Naeem Bhojani have had in the past or currently have a consulting agreement with PROCEPT BioRobotics. Leo Doumanian, Ronald P. Kaufman Jr, Gregg Eure, Gopal Badlani, Mark Plante, Edward Uchio, Greg Gin, Ryan Paterson, Alan So, Mitch Humphreys, Steven Kaplan, and Jay Motola have no disclosures with PROCEPT BioRobotics. Gregg Eure serves as a trainer at the AUA hands-on BPH course.

Ethics Statement: This study received Institutional Review Board approval (IRB No. G170027). All procedures performed to gather the data presented here 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 was obtained from all individual participants included in the study.

Author Contributions: All Authors on the manuscript were involved with recruiting, treating patients, and data collection. Naeem Bhojani and Mitch Humphreys led the manuscript effort.

Data Availability: The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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where the mean (SD) International Prostate Symptom Score of 22.6 (6.4) at baseline to 6.8 (4.6) at 5 years, resulting in a change score of 15.9 (7.7, $P < .001$). Uroflowmetry measurements also demonstrated improvement where the mean maximum urinary flow rate increased from 8.6 (SD 3.4) to 17.1 (9.8) mL/s at 5 years, resulting in a change score of 9.2 (11.1) mL/s at 5 years ($P < .001$). A regression analysis evaluating change in PSA as a function of baseline PSA across all time points out to 5 years resulted in a 50% reduction. A prespecified subgroup analysis using a baseline prostate volume cutoff of 100 mL showed no difference in efficacy outcomes through 5 years. Freedom from a secondary benign prostatic hyperplasia procedure at 5 years was 96.3% based on Kaplan-Meier.

Conclusions: At 5-years of prospective follow-up, the Aquablation procedure was shown to be safe with durable efficacy and low rates of retreatment in men with large prostates (80-150 mL).

Key Words: prostatic hyperplasia, lower urinary tract symptoms, robotic surgical procedures

THERE has been significant evolution in the surgical management of benign prostatic hyperplasia (BPH) over the past 2 decades. "Gold standard" treatment has changed from the early beginnings of open simple prostatectomy to transurethral resection of the prostate to endoscopic enucleation. There are very few surgical modalities that are size agnostic and can treat both small (≤80 mL) and large (>80 mL) prostates. Currently the only options are simple prostatectomy with its inherit risks/complications and prostate enucleation with its steep learning curve. Unfortunately, all other surgical options cannot treat large prostate glands without increased retreatment rates.[1] More recently Aquablation has emerged as an innovative technology that could potentially treat both small and large glands.[2-6] Aquablation is a real-time image-guided and robot-executed procedure combining multidimensional imaging, automated tissue removal, and a heat-free cavitating water jet.

With so many surgical BPH options available, it has become increasingly difficult for both patients and urologists to decide what the best surgical option is for each individual patient. Furthermore, with so many BPH surgical options available, it is becoming increasingly difficult to offer all BPH surgical treatment options while maintaining excellence and proficiency. Urologists need to decide which surgical options (if any) can treat the highest number of patient objectives/values while achieving the best possible functional outcomes.

The following study details the final 5-year multi-institutional clinical trial data from the WATER II: Aquablation therapy in large prostates (80-150 mL) for lower urinary tract symptoms due to BPH.[7]

TRIAL DESIGN AND PARTICIPANTS

WATER II (NCT03123250) was a prospective, multicenter clinical trial conducted at 16 centers in the U.S. and Canada that examined safety and feasibility data from men with large-gland BPH. Adult men aged 45-80 years were included if they had a prostate volume between 80 and 150 mL by transrectal ultrasound, baseline International Prostate Symptom Score (IPSS) ≥12, a maximum urinary flow rate (Qmax) <15 mL/s, a serum creatinine <2 mg/dL, a history of inadequate or failed response to medical therapy, and the mental capability and willingness to participate in the study. Men were excluded if they had a body mass index ≥42 kg/m^2, a history of prostate or bladder cancer, a concomitant bladder calculus or clinically significant bladder diverticulum, active urinary infection, previous urinary tract surgery, indwelling urinary catheter for 90 or more days consecutively, chronic pelvic pain, history of clinically significant urethral stricture, meatal stenosis or bladder neck contracture, current use of anticholinergic agents, or other general conditions that could prevent adequate study follow-up. Patients with prior prostate surgery were not excluded. Each center obtained Institutional Review Board/Ethics Committee approval prior to the initiation of the study. There was no washout period for patients on BPH medical therapy prior to treatment in the study. Te et al reported no differences in overall outcomes comparing Aquablation and TURP in patients who truly failed medical therapy.[8] Overall, 101 men were enrolled in the original study at 16 sites. The initial 1-year study was extended during follow-up to include visits annually out to 5 years. The study was sponsored by the device manufacturer.

At baseline and selected follow-up visits, participants completed the following questionnaires: IPSS, Incontinence Severity Index, Pain Intensity Scale, International Index of Erectile Function, the Male Sexual Health Questionnaire—Ejaculatory Function domain, PSA, uroflowmetry, and post-void residual (PVR) volume measurements. Scheduled 5-year follow-up visits included PSA, uroflowmetry and PVR, IPSS questionnaires, and adverse event assessment.

The primary end points were based on objective performance criteria published on TURP assessment at 3 months.[7] Although TURP is typically used

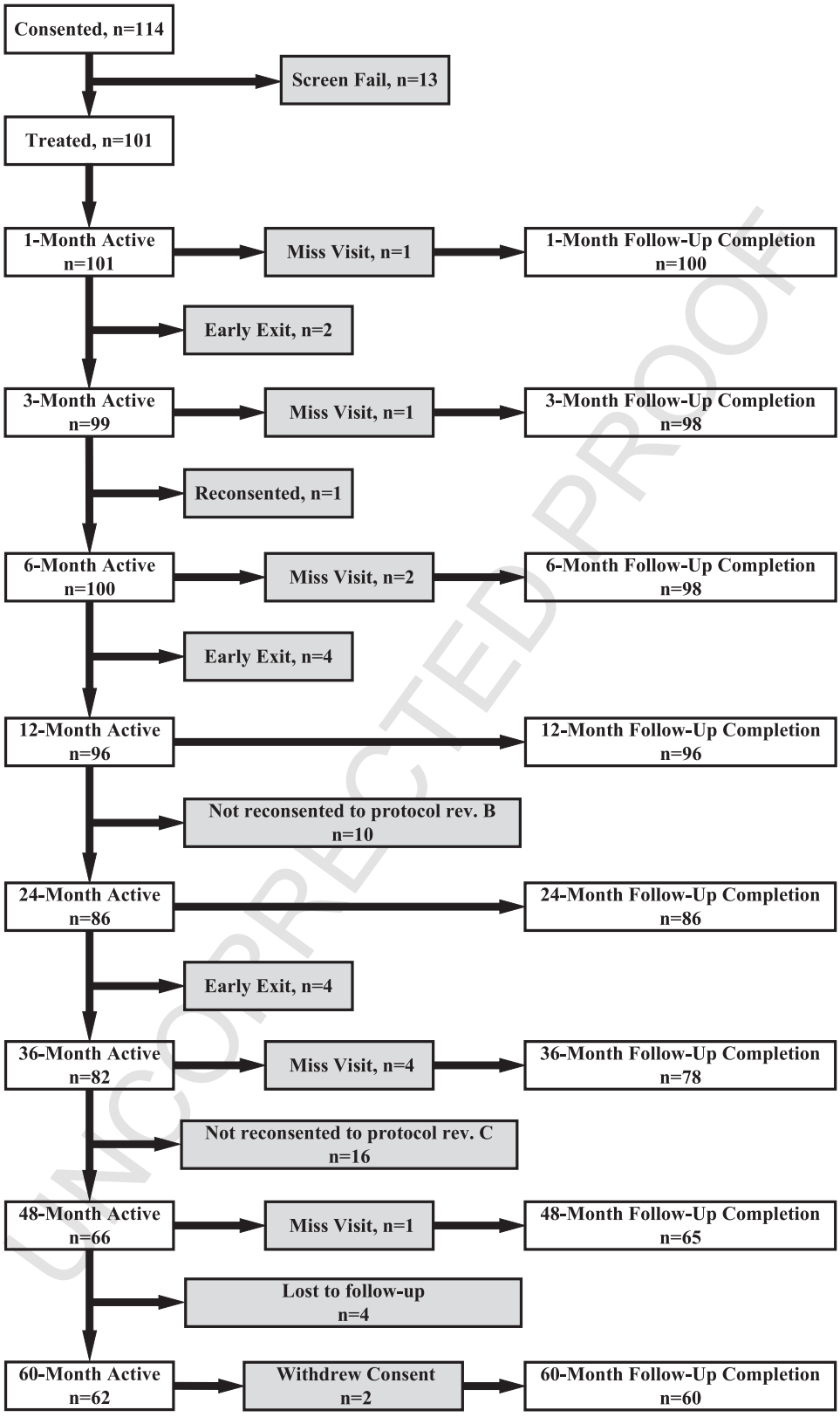

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram.rev.indicatesrevision.

to treat prostates less 80 mL, the performance goals were chosen to prove Aquablation could demonstrate reproducible results as seen in the WATER study but in larger prostates. Prior studies have demonstrated that IPSS scores are reduced by approximately 16 points after Aquablation, values

Table 1. *Baseline Demographics of the Initial WATER II Cohort and Those Available at 60 Months of Follow-up*

Characteristic	Aquablation at baseline N = 101	Aquablation at 60 mo N = 62
Age, y		
No.	101	62
Mean±SD	67.5±6.6	67.5±6.7
Median (IQR)	68.0 (63.0, 72.0)	67.0 (63.0, 72.0)
Minimum, maximum	52.0, 79.0	52.0, 79.0
Body mass index		
No.	101	62
Mean±SD	28.3±4.1	28.3±4.0
Median (IQR)	27.5 (24.9, 30.7)	28.5 (25.4, 30.6)
Minimum, maximum	21.8, 40.8	21.8, 40.8
% Race		
Asian	5.0 (5/101)	4.8 (3/62)
Black	5.9 (6/101)	3.2 (2/62)
White	87 (88/101)	91 (57/62)
Other	2.0 (2/101)	0.0 (0/62)
% Ethnicity		
Hispanic or Latino	8.9 (9/101)	6.5 (4/62)
Non-Hispanic or Latino	91 (92/101)	93 (58/62)
Prostate-specific antigen (ng/mL)		
No.	100	61
Mean±SD	7.1±5.9	7.3±6.4
Median (IQR)	5.2 (2.6, 10.2)	5.5 (2.5, 10.2)
Minimum, maximum	(0.3, 29.3)	(0.3, 29.3)
% Use of catheters 45 days prior to enrollment	16 (16/101)	16 (10/62)
Prostate size on TRUS, (mL)		
No.	101	62
Mean±SD	107.4±20.2	108.1±20.6
Median (IQR)	105.0 (90.7, 120.0)	105.8 (89.8, 120.0)
Minimum, maximum	80.0, 149.7	80.0, 149.7
% Middle lobe	83 (84/101)	86 (53/62)
% Intravesical component	80 (81/101)	82 (51/62)
Intravesical protrusion, (mm)		
No.	81	51
Mean±SD	1.8±0.8	1.7±0.6
Median (IQR)	1.7 (1.4, 2.1)	1.7 (1.3, 2.0)
Minimum, maximum	0.7, 6.8	0.7, 3.5
Baseline questionnaires		
IPSS score		
No.	101	62
Mean±SD	23.2±6.3	22.6±6.4
Median (IQR)	24.0 (18.0, 28.0)	22.5 (17.0, 28.0)
Minimum, maximum	12.0, 35.0	12.0, 35.0
IPSS QoL		
No.	101	62
Mean±SD	4.6±1.0	4.6±1.0
Median (IQR)	4.0 (4.0, 5.0)	4.0 (4.0, 6.0)
Minimum, maximum	(2.0, 6.0)	(2.0, 6.0)
MSHQ-EjD in sexually active men	78% (77/99)	78% (47/60)
No.	75	45
Mean±SD	8.1±3.9	8.5±3.7
Median (IQR)	9.0 (5.0, 11.0)	9.0 (7.0, 11.0)
Minimum, maximum	(1.0, 15.0)	(1.0, 15.0)
IIEF-5 in sexually active men		
No.	76	46
Mean±SD	14.8±7.7	15.0±7.7
Median (IQR)	15.0 (7.5, 22.5)	15.5 (8.0, 24.0)
Minimum, maximum	(2.0, 25.0)	(2.0, 25.0)
% Antithrombotic use		
Anticoagulant	4.0 (4/101)	3.2 (2/62)
Antiplatelet/NSAID including high dose aspirin	21 (21/101)	18 (11/62)
Aspirin	18 (18/101)	16 (10/62)
Any of above	43 (43/101)	37 (23/62)
% BPH medication use		
Alpha-blocker	41 (41/101)	39 (24/62)
5-ARI	4.0 (4/101)	1.6 (1/62)
Alpha-blocker/5-ARI	29 (29/101)	27 (17/62)
Any of above	73 (74/101)	68 (42/62)

Abbreviations: 5-ARI, 5-alpha reductase inhibitor; BPH, benign prostatic hyperplasia; IIEF-5, International Index of Erectile Function; IPSS, International Prostate Symptom Score; IQR, interquartile range; MSHQ-EjD, Male Sexual Health Questionnaire—Ejaculatory Function domain; NSAID, nonsteroidal anti-inflammatory drug; QoL, quality of life; SD, standard deviation; TRUS, transrectal ultrasound.

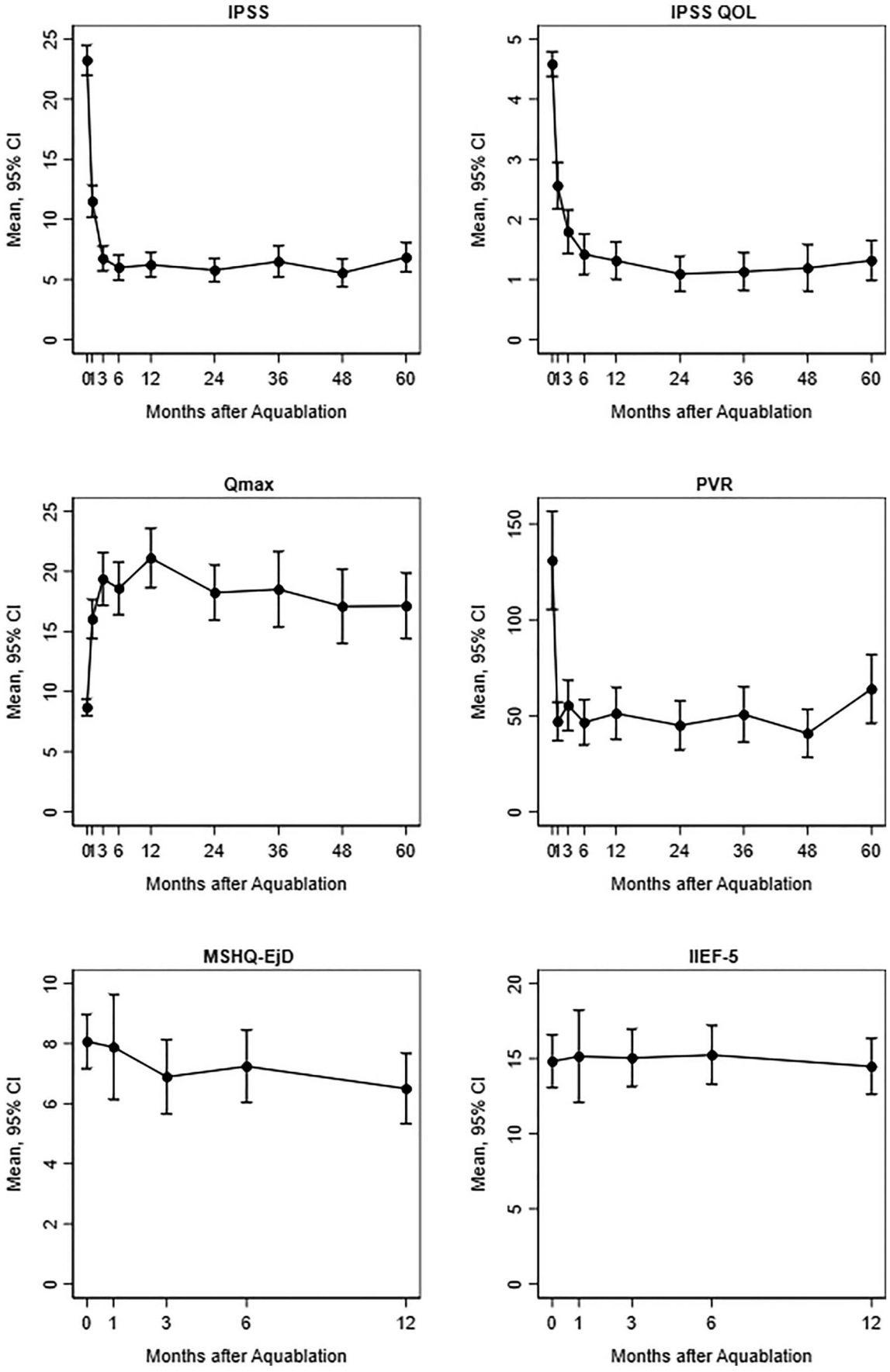

Figure 2. Clindicates confidence interval; IPSS, International Prostate Symptom Score; PVR, post-voidresidual; Qmax, maximumurinary flowrate; QOL, quality of life.

Table 2. *Site-reported Long-term Follow-up Urological Events Summary*

	12-24 Mo rate (% subjects N=86)	24-36 Mo rate (% subjects N=82)	36-48 Mo rate (% subjects N=66)	48-60 Mo rate (% subjects N=62)
Chronic cystitis	1.2	-	-	-
Ejaculatory dysfunction (nonprocedure-related)	1.2	1.2	-	-
Erectile dysfunction (nonprocedure-related)	1.2	1.2	1.5	1.6
Hematospermia	-	-	1.5	-
Hematuria	3.5	2.4	4.5	1.6
LUTS	3.5	4.9	1.5	1.6
Nocturia	-	3.7	-	-
Urinary urgency	1.2	1.2	-	-
Mixed or nonspecified symptoms	2.3	1.2	1.5	1.6
Other[a]	2.3	4.9	-	1.6
Prostate cancer	-	-	1.5	1.6
Prostatitis	1.2	1.2	1.5	-
Rising PSA	2.3	4.9	1.5	3.2
Transient urinary incontinence	1.2	-	-	-
Urinary retention	1.2	1.2	1.5	-
Urinary tract infection	1.2	3.7	3.0	3.2

Abbreviations: LUTS, lower urinary tract symptoms; PSA, prostate-specific antigen.
[a]Other includes penile curvature, microscopic hematuria, kidney stones, kidney dysfunctions.

similar to those observed after TURP. The assumption used to establish the efficacy end point was a change of 16 points and a change score standard deviation of 7.5 points. Therefore, showing a mean reduction in IPSS scores that statistically exceeds 11 points will be interpreted as study success using a one-way statistical test (alpha = .025 for interpretation). The primary safety end point was the proportion of subjects with adverse events rated as probably or definitely related to the study procedure classified as Clavien-Dindo grade 2 or higher or any grade 1 event resulting in persistent disability (incontinence, ejaculatory disorder, or erectile dysfunction) evidenced through 3 months posttreatment. The WATER study (IDE No. G150089) used an assumption that a TURP rate for the same safety definition provided in this protocol would be 65% for prostates sized between 30-80 mL. The same safety target will be used for this protocol treating large prostates of 80-150 mL. The study design had 99% power to detect an improvement in efficacy greater than 11 IPSS points and 80% power to detect the safety rate was less than 65%. Five-year outcomes for IPSS, IPSS quality of life (QoL), Qmax, PVR, and adverse events were collected. A prespecified subgroup efficacy analysis for baseline prostate volumes above and below 100 mL was performed.

The Aquablation procedure was performed using the AquaBeam Robotic System.[9] Briefly, after induction of general or spinal anesthesia, a 24F single-use handpiece was inserted into the prostatic urethra and secured into place using a bed-mounted arm. Using real-time transrectal ultrasound guidance, the surgeon defined the target anatomy creating a resection contour plan on a computer console. Contours were selected to avoid damage to the bladder neck, ejaculatory ducts, and urinary sphincter. Furthermore, apical treatment was also planned ipsilaterally to ensure no injury to the verumontanum and its underlying ejaculatory ducts (butterfly cut). Tissue was then treated utilizing an automated, robotic-executed, high-velocity water jet with up to 2.4 cm of treatment depth. For larger prostates, the Aquablation procedure typically required 2 or more treatment passes of the AquaBeam probe for tissue removal.

Post-Aquablation, the bladder was irrigated using a resectoscope sheath along with a Toomey syringe. Thereafter, hemostasis was delivered via low-pressure tamponade with a Foley balloon catheter inflated to 40-80 cc at the bladder neck (98 cases) or within the prostatic fossa (3 cases), followed by continuous bladder irrigation as previously described, in addition to the use of the continuous traction device. Unlike the contemporary Aquablation treatment procedure that uses focal bladder neck cautery,[10] it is noteworthy that no cases utilized electrocautery for hemostasis.

DATA MONITORING

All study data were collected using an electronic data capture system. Study data were 100% source verified by study monitors up to 24 months. Risk-based monitoring was implemented for the 36- through 60-month data verification due to the COVID-19 pandemic. An independent adjudication committee evaluated all adverse events for Clavien-Dindo classification.[11]

STATISTICAL ANALYSIS

Changes between baseline and 5 years for IPSS, IPSS QoL, Qmax, and PVR were assessed using paired *t*-tests. A subgroup analysis using a baseline prostate volume cutoff of 100 mL was also conducted to compare IPSS, IPSS QoL, Qmax, and PVR

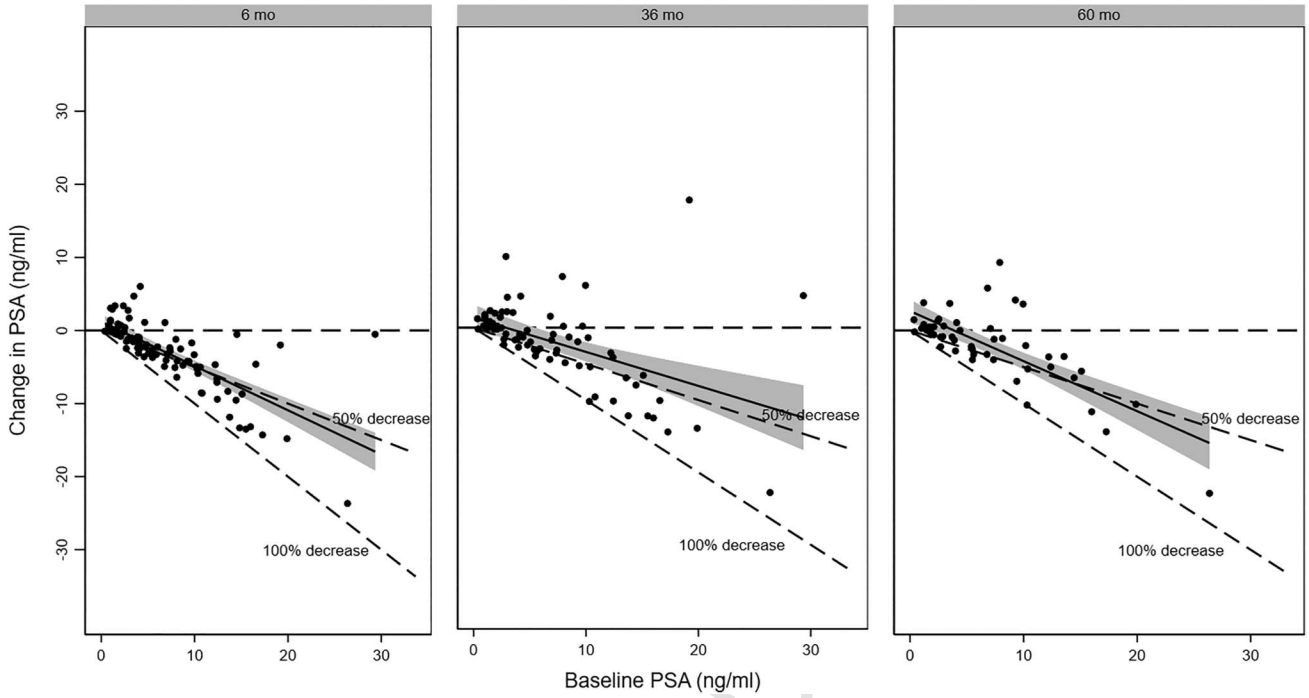

Figure 3. Clindicates confidence interval; IPSS, International Prostate Symptom Score; PVR, post-voidresidual;Qmax, maximumurinary flowrate; QOL, quality of life.

through 5 years. Linear regression of change in PSA as a function of baseline PSA was performed at 6 months, 36 months, and 60 months. The Kaplan-Meier method was used to estimate freedom from a secondary BPH procedure. All statistical analysis was performed using Stata 17.0[12] and a P value $< .05$ was considered clinically significant.

RESULTS

One hundred and one men were enrolled and treated at 16 sites by 24 surgeons between September and December 2017 in the WATER II study (Figure 1). Aquablation experience prior to the start of the study was an average of 0.5 procedures per surgeon. Sixty subjects completed their 60-month visit. Approximately half of the subjects who did not make it to the fifth year of the study could be linked to the impact of COVID-19 (ie, patients declining to consent or research departments closing). The balance of subjects left the study for various reasons such as prostate cancer treatment (n=2), unreachable by research staff (n=6), or no longer interested in participating in research (n=8). Baseline patient characteristics of the enrollment cohort and the subset that completed the 5-year follow-up are summarized in Table 1 and showed no differences. A subgroup analysis was conducted to ensure the patient cohorts (no follow-up beyond 1 year [n=15], no follow-up beyond 3 years [n=20], and those participating beyond 3 years [n=66]) with shorter follow-up participation did not have different IPSS outcomes. The IPSS scores at 1 year across all 3 cohorts were 6.9, 6.7, and 6.0, respectively, and were not statistically different. Mean age was 68 years (range 52-79) and baseline IPSS was 23 (12-35). Among all the treated patients, 16 (16%) had used a urinary catheter in the 45 days prior to enrollment. Mean prostate volume was 107 mL (range 80-150). A median lobe was present in 83% of cases with an average intravesical prostatic protrusion distance of 1.8 cm (range 0.7-6.8). Study procedures were performed under general and spinal anesthesia in 18% and 82% of cases, respectively. Mean operative time, Aquablation treatment time, and average number of treatment passes were 55 minutes (range 25-111), 8 minutes (3-17), and 1.8 passes (34% 1 pass, 56% 2 passes, and 10% 3 or more passes), respectively. Procedure-related erectile and ejaculatory dysfunction at 6 months was 0% and 15%, respectively. Stable Male Sexual Health Questionnaire and International Index of Erectile Function results are shown in Figure 2.

The long-term urological event rates were low and consistent with previously published data at 1- and 3-year follow-up (Table 2).[3,13] There were no bladder neck contractures reported in any of the patients seen at the 5-year follow-up visit, and there were no occurrences of urethral stricture or meatal stenosis reported during the 60-month follow-up. One report of transient incontinence (1.2%) beyond 1 year was reported that resolved with medication. There were no reports of transfusion or fulguration beyond 30 days through 60-month follow-up.

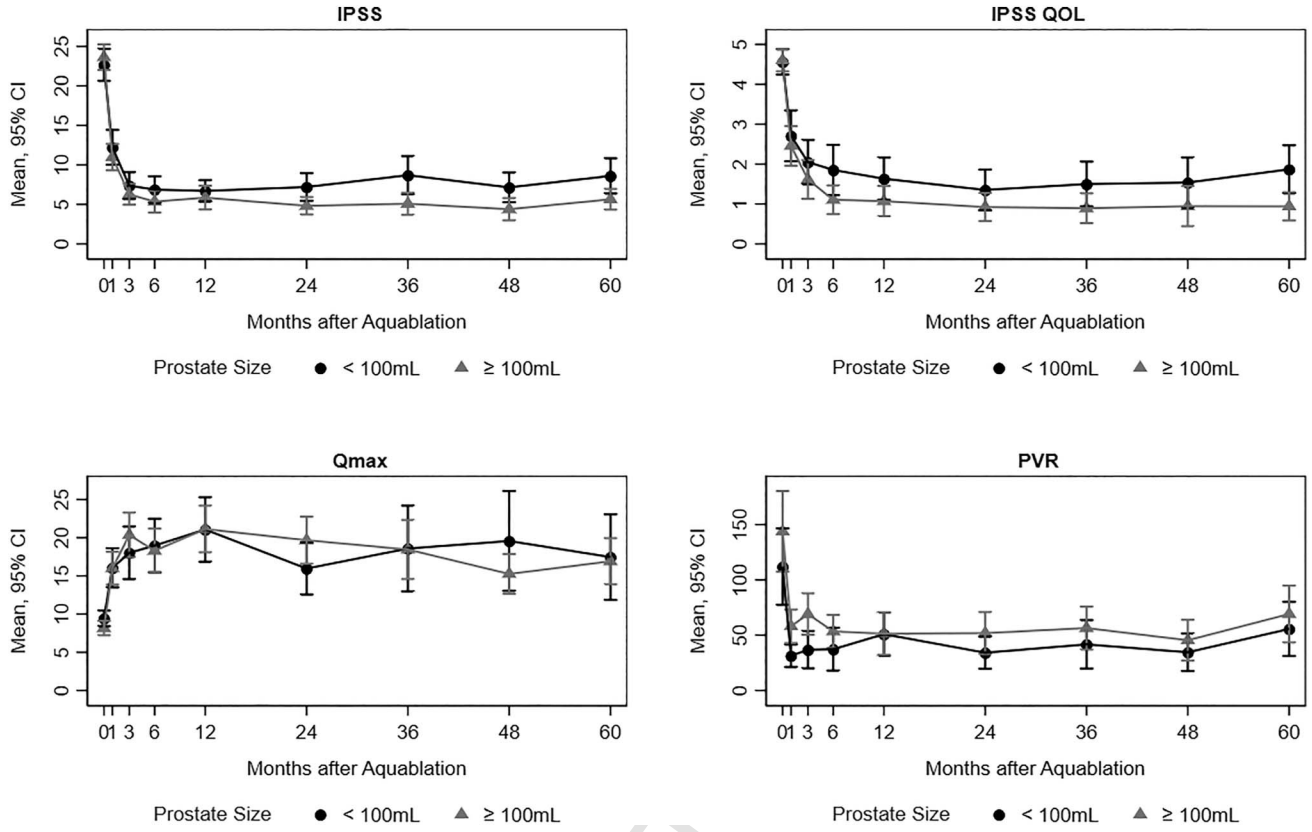

Figure 4. PSA indicates prostate-specificantigen.

For the patients who completed the 5-year visit, symptoms showed an improvement from a mean (SD) IPSS score of 22.6 (6.4) at baseline to 6.8 (4.6) at 5 years, resulting in a change of 15.9 (7.7, $P < .001$). The IPSS scores were independent of both baseline IPSS and prostate size. IPSS QoL decreased from 4.6 (SD 1.0) at baseline to 1.3 (1.3) at 5 years, resulting in a change of 3.3 (1.6, $P < .001$). Subjects observed an immediate improvement postoperatively with the maximum benefit seen at approximately 90 days postoperatively and sustained thereafter (Figure 2). Uroflowmetry measurements also showed a significant improvement where the mean Qmax increased from 8.6 (SD 3.4) to 17.1 (9.8) mL/s at 5 years, resulting in an improvement of 9.2 (11.1) mL/s at 5 years ($P < .001$). PVR urinary volume decreased from 141 (SD 140) mL at baseline to 64 (64) mL at 5 years ($P < .001$).

During the 5-year follow-up, 6% of patients were placed on BPH medications (3 on 5-alpha reductase inhibitor, 2 on alpha-blocker, and 1 on combination therapy 5-alpha reductase inhibitor/alpha-blocker) occurring on average 34 months after the initial procedure. An additional 3% required surgical retreatment for lower urinary tract symptoms occurring on average 25 months after their initial Aquablation procedure. A Kaplan-Meier analysis showed 96.3% of patients were free from a secondary BPH intervention at 5 years. There were no surgical retreatments occurring in year 4 or 5. A regression analysis evaluating change in PSA as a function of baseline PSA across all time points out to 5 years trended along a 50% reduction (Figure 3). The 9 patients who needed a surgical reintervention (n=3) or went back on BPH medication (n=6) did not show a correlation with PSA changes compared to the broader population. A prespecified subgroup analysis using a baseline prostate volume cutoff of 100 mL showed no difference in efficacy outcomes through 5 years (Figure 4).

DISCUSSION

The surgical management of BPH has undergone significant change over the past 20 years. There are many options available to patients and providers; however, most surgical options are limited in one way or another. The AUA guidelines on the surgical management of BPH stratify treatment by prostate size with few modalities being truly size independent other than prostate enucleation.[14] However, with real-time ultrasound guidance and robotic execution, Aquablation has the potential to treat prostates of nearly any size. The 5-year data validate the durability of Aquablation. This prospective

multicenter trial demonstrated that Aquablation is easily reproducible (implemented at 16 different sites) and clinically effective for the treatment of large prostate glands (80-150 mL). At 3 months, the study successfully met its powered primary end points against established performance goals.[7]

Aquablation at 5 years in prostate glands between 80 and 150 mL maintained excellent clinical outcomes including a significant reduction in IPSS (mean reduction of 16 points), increase in Qmax (mean increase of 9.2 mL/s), and improvements in QoL (average reduction in IPSS QoL of 3.3). Moreover, these results were sustained during at least 5 years of follow up. These results are even more important, demonstrating no impact on erectile function and minimal impact on ejaculatory function or urinary continence. Furthermore, these outcomes are very similar to the results observed in smaller prostate glands, and therefore Aquablation is one of the few treatment modalities that can effectively treat prostate glands ranging from 30-150 mL with minimal impact on sexual function or urinary continence. While the investigators in the study had very little Aquablation experience, they were very experienced urological surgeons. As the technology expands, a number of commercial single-center experience publications are being published showing similar outcomes to the U.S. Food and Drug Administration (FDA) trials.[15-18]

Notably, Aquablation in large prostate glands confirmed excellent durability with only 3% of patients (n=3) requiring a second BPH surgical treatment during the 5 years. Unfortunately, there are no direct comparison publications where photovaporization of the prostate (PVP) or enucleation has shown results from a multicenter study in gland sizes >80 mL. However, examining the literature regarding the surgical management of large prostate glands, it is clear that Aquablation has the potential to treat glands as efficiently as both prostate enucleation and PVP. The surgical retreatment rate of Aquablation in this study (3%) is similar to Gilfrich et al's 5-year durability for laser enucleation (~7%) and TURP (~9%) but better than PVP (~14%).[1] In addition, the rare occurrence of urinary incontinence with Aquablation is reassuring to patients.

The main shortcoming of Aquablation in large prostate glands has been the associated bleeding in the early years of research. However, it should be considered that this study was the first FDA trial for Aquablation to be performed in prostates larger than 80 mL. Furthermore, adjunctive cautery was not permitted for this trial. Subsequent to this trial, newer protocols have been reported with Aquablation (bladder neck cautery) with a transfusion decline from 5.9% predischarge in this study to less than 1% in more than 2,000 procedures where the prostate size on average was 87 mL (range 20-363),[10] which is not too dissimilar to the prostate sizes treated in this study of 107 mL (80-150). Gloger et al compared Aquablation to enucleation across various prostate size subgroups, and the >80 mL group had 0% transfusions.[19] Helfand et al published on prostates >150 mL with no reports of transfusion.[20] Future randomized studies will further solidify the hemostasis findings in large prostates. Contemporary hemostasis techniques and methods have addressed the risk of bleeding since the era of no adjunctive cautery in the WATER II study.

It is important to recognize that with Aquablation there is a significant drop in PSA (~50%)[4] in these large prostate glands that is maintained out to 5 years. Comparatively, there is a paucity of data on PSA drop for other BPH surgical modalities in prostates between 80 and 150 mL. The durability question beyond 5 years remains based on the observed PSA decrease, which only time and additional experience will be able to answer. The only other surgical modality that clearly has a significantly larger PSA drop than Aquablation is simple prostatectomy or prostate enucleation.[21] However, prostate enucleation also has higher rates of ejaculatory dysfunction, especially in these larger prostate glands.

Finally, operating room time comes at a significant premium and must be used as efficiently as possible. Aquablation demonstrates a significant advantage where surgical time is only marginally impacted by prostate volume. This operating room efficiency has been compared to other surgical modalities and has been found to be significantly better, especially in large prostates.[22] In addition, the reproducibility of Aquablation with which prostate sizes small and large can be treated will allow more surgeons the ability to treat large prostates in a limited amount of time.

Despite the merits of the 5-year longitudinal data to assess Aquablation outcomes in men with large-gland BPH, this study has limitations. The main limitation is that this trial is a single-arm study without a control group, although a performance goal was used, preventing direct comparisons with other techniques. Future studies are warranted to compare Aquablation to other modalities for the surgical treatment of large prostates. An ongoing prospective randomized clinical trial comparing Aquablation to enucleation in large prostates is being conducted in Europe (WATER III, NCT04801381). Quintas et al compared concurrent enrollment of 100 subjects receiving either Aquablation or enucleation at 6 months.[23] Baseline characteristics were similar in both groups, including the

average prostate size of approximately 78 mL. There were no transfusions in either arm. The 6-month IPSS, IPSS QoL, Qmax, and PVR were similar across therapies. Ejaculatory dysfunction was 98% for enucleation and 0% for Aquablation.

The impact of COVID-19 on the patient follow-up warrants addressing. Treatment durability was assessed via Kaplan-Meier analysis. With a dynamically changing denominator over time, the authors felt this was the most robust way to present the data. We put the study fifth year of missing follow-up (ie, 40%) in comparison to 2 other contemporary FDA clinical studies that have reached 5-year follow-up, the LIFT study and the Rezūm pivotal trial. Their percentage of patients failing to meet the 5-year visit were 38%[24] and 43%,[25] respectively. While the follow-up rates of WATER II are similar to other FDA clinical trials, the authors believe the additional cohort analysis to show no difference in baseline and IPSS outcomes instills confidence in the overall study results and conclusions.

In conclusion, At 5 years of prospective follow-up, the Aquablation procedure was shown to be safe with durable efficacy and low rates of retreatment in men with large prostates (80-150 mL).

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