



# Operative time comparison of aquablation, greenlight PVP, ThuLEP, GreenLEP, and HoLEP

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## Abstract

**Introduction** The BPH surgical armamentarium is composed of a rapidly expanding number of technologies and techniques. These include greenlight photovaporization of the prostate (PVP), greenlight enucleation of the prostate (GreenLEP), holmium laser enucleation of the prostate (HoLEP), thulium laser enucleation of the prostate (ThuLEP) and, more recently, the aquablation procedure. To the best of our knowledge, no direct comparison in operative time has been performed.

**Methods** Data for this study were pooled from five sources. For aquablation, patient-level data from four studies of the aquablation procedure were provided by the device manufacturer as well as from a high-volume commercial user. PVP, GreenLEP, HoLEP, and ThuLEP were performed by high-volume, experienced experts. Endpoints included total operative time, resection time, and proportion of total operative time for resection. General linear models were used to evaluate the relationship between prostate volume (or other continuous predictors) and procedure time.

**Results** Total procedure time was related to prostate size. Except for the small prostate size range (size < 40 cc), at any given prostate volume, procedure time was highest for PVP, intermediate for LEPs, and lowest for Aquablation. The relationship between procedure time and prostate size (i.e., slope of the fitted lines) was 0.16 min/g for aquablation, 0.32 min/g, 0.28 min/g and 0.32 min/g for GreenLEP, HoLEP and ThuLEP, respectively, and 0.63 min/g for PVP.

**Conclusion** In our analysis of pooled data of multi-surgical techniques and technologies, aquablation provided the lowest operative time across all prostate volumes. PVP had the longest procedure time for prostates > 40 cc.

**Keywords** Operative time · HoLEP · GreenLEP · ThuLEP · Greenlight PVP · Aquablation

## Introduction

Benign prostatic hyperplasia (BPH) is a histologic diagnosis of smooth muscle and epithelial cell proliferation within the prostatic transition zone [1]. It is the most common benign urologic disease in men. Its incidence is age-related—as the population ages, its prevalence will continue to increase, particularly increasing in incidence after age 50 [2].

Surgery is indicated for lower urinary tract symptoms (LUTS) attributed to BPH and unresponsive to conservative (primarily medication) treatment, provided the patient's comorbidities do not preclude this approach [3]. In accordance with current national guidelines, the BPH surgical ablative armamentarium is composed of a number of technologies and techniques [3–5] However, only a few can be considered for treating small to very large prostates with TURP-like efficacy. These include greenlight photovaporization of the prostate (PVP), greenlight

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enucleation of the prostate (GreenLEP), holmium laser enucleation of the prostate (HoLEP), thulium laser enucleation of the prostate (ThuLEP) and, more recently, aquablation.

HoLEP harnesses the well-established, globally available 2140 nm pulsed holmium:yttrium–aluminum–garnet (Ho:YAG) laser to assist with mechanical enucleation of the prostate. This wavelength is strongly absorbed by water (and water-rich tissues) with good hemostasis [6]. Enucleation, having been well established and studied since initially described by Gilling et al. [7] allows the surgeon to follow anatomic planes to separate entire lobes of the prostate, mimicking the action of the index finger in open simple prostatectomy. In general, these lobes are then liberated into the bladder with subsequent morcellation. HoLEP has been well demonstrated to be safe, effective and durable in all prostate volumes [8–10].

Similar to HoLEP, ThuLEP combines the blunt mechanical enucleation of tissue with a different wavelength to remove the prostatic adenoma. Thulium laser works at a wavelength of 2010 nm in continuous wave mode [11]. ThuLEP has been shown to have similar outcomes to HoLEP with the exception of hemostasis [12].

Moreover, greenlight XPS uses a unique 532 nm KTP-LBO (potassium–titanyl–phosphate–lithium triborate) length laser. This wavelength freely travels through water (therefore, a non-contact procedure) and is selectively absorbed by hemoglobin which acts as an intravascular target for the light energy which greatly improves hemostasis [13]. Studies have demonstrated that greenlight PVP is safe and effective with significantly shorter catheterization and hospitalization times than TURP [14–16]. Greenlight can also be used for enucleation [17]. GreenLEP has been shown to be safe with similar effectiveness in the treatment of BPH when compared to HoLEP [18].

Aquablation (AQUABEAM System, PROCEPT BioRobotics, Inc., USA) is a robotically executed, surgeon-guided, high-velocity waterjet technology integrating real-time ultrasonography. Studies have shown the non-inferior symptom relief benefit of aquablation as compared to TURP, but with considerably lower resection times and low risks of sexual side effects, specifically ejaculatory function [19]. Aquablation's effectiveness has also been shown in large prostates with analyses of trial data showing that the benefits observed in smaller prostates transfer to larger ones.

In this study, given the paucity of comparative performance between technologies, we sought to compare the procedural outcomes of high-volume, expert surgeons of each technique and mid-term improvement in international prostate symptom scores (IPSS) of aquablation, greenlight PVP, GreenLEP, HoLEP, and ThuLEP.

## Methods

### Data sources

Data for this study were pooled from five sources (further details below). All men had comparable diagnostic work-up for BPH according to EAU/AUA guidelines with preoperative assessment of symptom scores (IPSS), uroflow measures, post-void residual (PVR), cystoscopy and transrectal ultrasound (TRUS) for prostate volume assessment. Long-term outcomes were not included due to lack of consistent data collection.

*Aquablation* Individual patient-level data from the following four studies of the aquablation procedure were provided by the device manufacturer/study sponsor: (1) WATER (NCT02505919) [20], a double-blinded prospective international multicenter clinical trial of the aquablation procedure vs. standard transurethral resection of the prostate (TURP) in prostates measuring between 30 and 80 cc, (2) WATER II (NCT03123250) [21], a prospective international single-arm clinical study of the aquablation procedure in men with larger (80–150 cc) prostates, (3) WATER FRANCAIS (NCT03191734) [22], a prospective 3-center single-arm clinical trial conducted in France, and (4) Open WATER (NCT02974751), a prospective registry of outcomes of Aquablation in the commercial setting, conducted at five centers in the UK, Germany, Australia, New Zealand and Lebanon (enrollment complete and follow-up ongoing, unpublished). Additionally, data from the commercial experience of one high-volume user (TB) were added (unpublished full data set, but partial data set published on first 118 patients [23]).

*Photo-vaporization of the prostate* Patients undergoing standardized anatomic PVP with greenlight XPS at the University of Montreal Hospital Center between February 2011 and March 2019 were included. All procedures were performed by a single surgeon (KCZ) with greenlight laser experience since 2005. All greenlight XPS cases were conducted as previously described as outpatient, same-day surgery [24].

*Greenlight laser enucleation of the prostate* Patients underwent GreenLEP at Clinique Pasteur (Toulouse, France) between June 2013 and March 2019. The procedure, executed as described by Gomez-Sancha et al. [25], was performed by a single surgeon (VM) who has had laser experience since 2011.

*Holmium laser enucleation of the prostate* Patients underwent HoLEP at Indiana University Health Methodist Hospital (Indianapolis, USA) between April 2016 and April 2018. All procedures were performed by a single surgeon (JEL) who performed the first holmium enucleation prostatectomy in the United States in 1998 and completed > 2000 HOLEPs.

*Thulium laser enucleation of the prostate* Patients underwent ThuLEP at Asklepios Hospital Harburg (Hamburg, Germany) between January 2017 and March 2019 as described initially by Bach et al. in 2009 [12]. All procedures were performed by a single surgeon (TB), with enucleation experience since 2007.

Men with prostate volumes < 30 cc (5% for Aquablation, 2.7% for PVP, 0.5% for GreenLEP, 1% for HoLEP and 11.4% for thulium) were excluded from the analysis.

### Procedural outcomes

The procedural rate (operative minutes per cc TRUS prostate volume) was calculated as operative time divided by measured TRUS baseline prostate volume. For aquablation, the total operative time was defined as the number of minutes from either the insertion of the TRUS probe or insertion of the aquablation handpiece (using the earlier of the two) to the catheter placement or removal of the TRUS probe (using the later of the two). This calculation was available in WATER, WATER II, and WATER FRANÇAIS studies as well as in commercial procedures. For Open WATER, total procedure time was estimated as minutes from handpiece in to catheter in. For PVP, total procedure time was calculated from camera entry to Foley placement. For the enucleation procedures (HoLEP, ThuLEP, and GreenLEP), total procedure time was calculated from the insertion of the scope to the completion of morcellation.

### International prostate symptom score

IPSS were collected at baseline and at all post-operative follow-up visits. Unfortunately, not all centers used the same timepoints for IPSS assessments post-operatively. Given the variation in surgeon follow-ups, analysis of IPSS score changes was performed in patients with both baseline and follow-up scores where the follow-up score used was the latest of post-operative scores collected at least 1 month

following surgery but not more than 12 months after surgery. Mean IPSS follow-up time was 8.7 months for aquablation, 2 months for GreenLEP, 8.5 months for HoLEP, 12 months for thulium and 7.6 months for PVP.

### Statistical analysis

General linear models were used to evaluate the relationship between prostate volume (or other continuous predictors) and procedure time or other continuous outcome measures. Multivariate models were also used. A  $p$  value  $\leq 0.05$  was considered statistically significant. All statistical analyses were performed using R on the R studio platform.

### Results

Compared to aquablation, those undergoing GreenLEP, HoLEP and ThuLEP were slightly older (by 1.2, 2.1, and 3.7 years, respectively). Men undergoing aquablation, PVP, GreenLEP, HoLEP, and ThuLEP had mean prostate volumes of 71.7 cc, 79.6 cc, 97.4 cc, 116.1 cc and 75.7 cc, respectively (Table 1).

### Procedural outcomes

Total procedure time was strongly related to prostate size ( $p < 0.0001$ , Fig. 1); except for the small prostate size range (size < 40 cc), at any given prostate volume, procedure time was highest for PVP, intermediate for LEPs, and lowest for aquablation. Procedure time of the approach and prostate size can be found in Table 2. The relationship between procedure time and prostate size (i.e., slope of the fitted lines) was 0.16 min/g for aquablation, 0.32 min/g, 0.28 min/g and 0.32 min/g for GreenLEP, HoLEP and ThuLEP, respectively, and 0.63 min/g for PVP.

After controlling for prostate volume, the addition of baseline PSA, age, and body mass index to statistical models did

**Table 1** Baseline demographic characteristics of men undergoing aquablation procedure, PVP or GreenLEP

	Aquablation ( $n=608$ )	PVP ( $n=565$ )	GreenLEP ( $n=365$ )	HoLEP ( $n=221$ )	Thulium ( $n=272$ )
Age (years) <sup>a</sup>	67.4 (7.6) [38–86]	67.9 (8.7) [47–94]	68.7 (6.6) [50–89]	69.6 (7.2) [51–89]	71.2 (7.9) [53–89]
Prostate volume (cm <sup>3</sup> )	71.7 (32.5) [30–280]	79.6 (37.3) [30–275]	97.4 (38.3) [30–280]	116.1 (54) [31–361]	75.7 (39.5) [30–220]
PSA (ng/dL)	5.1 (4.9) [0.1–36]	5.9 (15.3) [0.14–326]	7.2 (5.3) [0.44–33]	7.7 (9.3) [0.75–94]	6.6 (9.3) [0.19–116]
International prostate symptom score <sup>b</sup>	21.9 (6.7) [0–35]	25.9 (6.5) [10–35]	17.6 (5.5) [6–30]	20.2 (6.2) [7–34]	18.1 (7.6) [0–34]
Catheter at time of surgery <sup>c</sup>	97/608 (16%) <sup>†</sup>	195/565 (35%)	102/365 (28%)	28/221 (13%)	114/272 (42%)

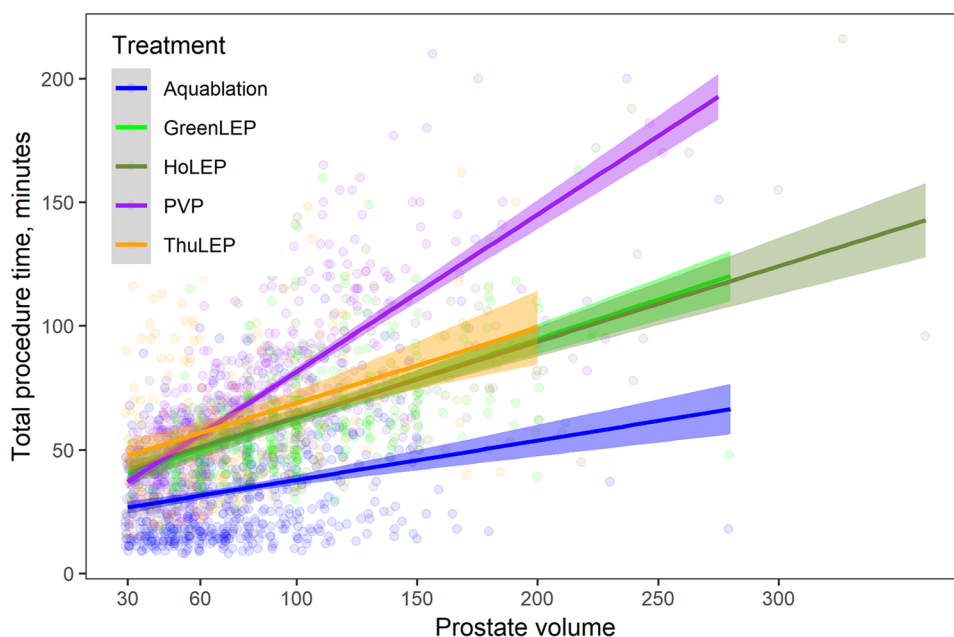
<sup>a</sup>Mean (SD) [range]; NA not available

<sup>b</sup>Amongst those with baseline and 12-month follow-up

<sup>c</sup>Used catheter in 45 days prior to consent

<sup>†</sup>Patients in retention at baseline were excluded from WATER and FRANCAIS WATER Studies accounting for 162 subjects

**Fig. 1** Total procedure time by prostate volume and treatment. Each dot represents an individual patient. Lines/shaded regions represent linear fit with 95% confidence interval



**Table 2** Observed total procedure minutes by treatment and prostate size category

Treatment	Prostate volume (cc)					
	30–80		80–150		> 150	
	N	Mean OR time (min)	N	Mean OR time (min)	N	Mean OR time (min)
Aquablation	410	30.1	182	40.7	7	24.6
Anatomic greenlight XPS PVP	331	51.8	198	87.6	26	136
GreenLEP	150	51.2	176	67.3	27	88.9
HoLEP	60	53.6	107	67.1	44	92.1
Thulium	157	54	68	71.6	11	91.8

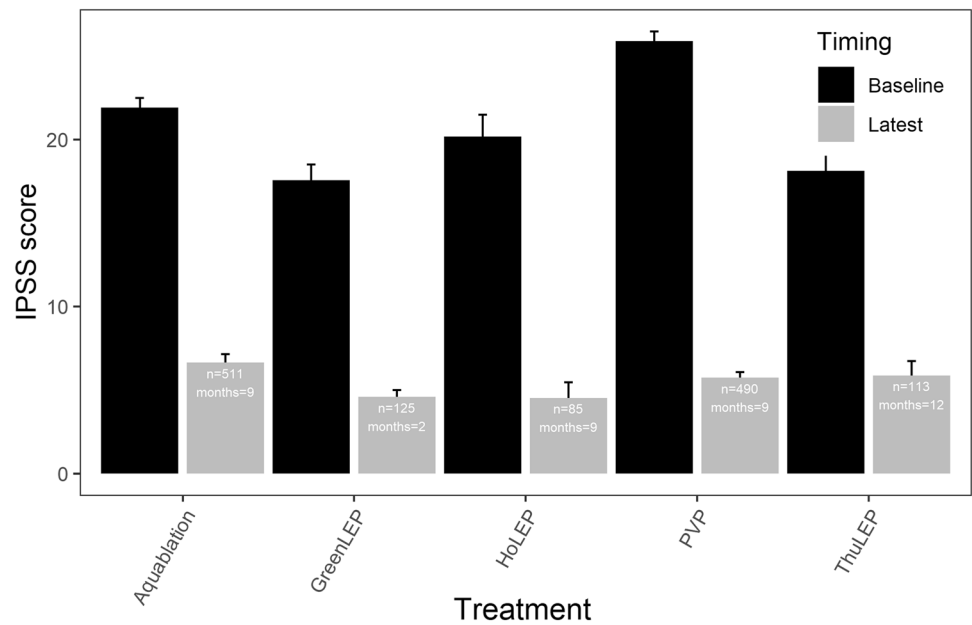
not further predict procedure time. In stepwise selection models, prostate volume was the strongest predictor of total procedure time for each procedure ( $p < 0.0001$  for all procedures except thulium, where  $p = 0.0021$ ).

IPSS scores were available at both baseline and follow-up (minimum 1 month, maximum 12 months) in 511/608 (84%) of treated aquablation patients, 490/608 (81%) PVP patients, 125/365 (34%) GreenLEP patients, 85/221 (38%) HoLEP patients and 113/272 (42%) thulium patients. Baseline scores were highest for the PVP group and lowest for the GreenLEP group (Fig. 2); follow-up scores were low in all groups. All change scores were highly statistically significant ( $< 0.001$ ) (Fig. 3).

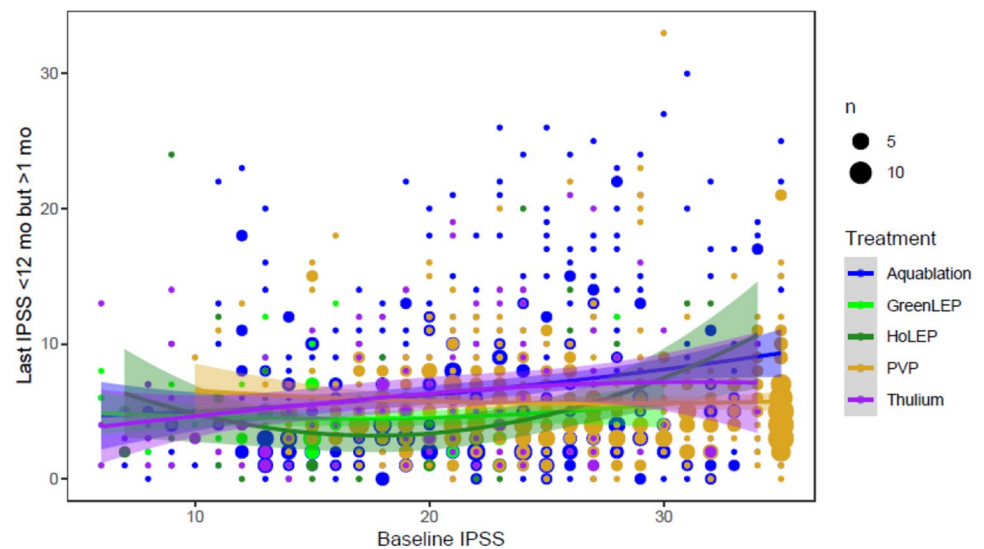
## Discussion

In this study, we compared procedural parameters and mid-term improvement in IPSS of four commonly performed procedures (Greenlight PVP, GreenLEP, HoLEP, and ThuLEP) and a newer procedure, aquablation. The aquablation procedure had the lowest total procedure time across all prostate sizes and the lowest slope (i.e., increase in procedure time per extra gram of tissue). ThuLEP and Greenlight PVP had the longest procedures for prostate sizes  $< 40$  cc and  $> 40$  cc, respectively.

**Fig. 2** IPSS at baseline and last follow-up by treatment



**Fig. 3** Relationship between last IPSS and baseline IPSS and prostate volume by technology. Dot size is proportional to number of patients. Shaded regions represent 95% CI of smoothed fits



As expected, prostate volume was the strongest predictor of total procedure time. Greenlight PVP’s operative time was the most affected by an increase in prostate size, as shown by its highest slope value (0.63 min/g by TRUS volume). This can be explained by the greenlight energy being fully transmitted to tissue during vaporization. Aquablation’s operative time was the least affected by an increase in prostate size with a slope value of 0.16 min/g (3.93 times faster than PVP). This can be explained by the fact that the process to prepare to the resect tissue is the same regardless of prostate size. Then the tissue resection is performed robotically that takes approximately 5 minutes regardless of prostate size. This is in line with a previous analysis of aquablation surgical times comparing prostates < 100 cc and > 100 cc.

This analysis showed a volume-independent rapid ablation of prostate tissue with a mean resection time, for the smaller and larger prostates, of 6.4 min and 9.1 min, respectively [26]. In aquablation, the duration of resection is dictated by the length of the prostate. The waterjet rotates and transverses at a constant speed regardless of depth.

Across all prostate sizes, aquablation had significantly shorter operative time despite limited previous experience. All 14 WATER sites and 9 out of 16 WATER II sites had never performed an aquablation procedure before enrolling their first patient in these trials. This is in contrast with the other approaches analyzed in this study which were all executed by surgeons with significant expertise in each technique.

Advantages of our study include its large sample size and use of standardized measures (prostate volume as estimated by TRUS, symptom scores measured with IPSS). Disadvantages include its retrospective design. While comparative effectiveness was beyond the scope of this study and the focus of this paper was on short-term and procedural outcomes, additional limitations include the limited follow-up for long-term outcomes and heterogeneous data collection of long-term outcomes. Characterization of the median lobe and anticoagulation varied by data source, making it difficult for any analysis of its potential impact on procedure times and symptom responses. An additional limitation of our study is the different study designs pooled. For example, part of the data pooled for aquablation is from the WATER trials which had high considerations for accuracy than prospectively maintained institutional databases. Unfortunately, data collection methods were also too disparate to estimate the impact of technology choice on adverse event rates as well as consistent post-operative assessments with IPSS. As large tertiary centers were considered for procedural referral, the follow-up timepoints were not consistent at all centers. Additionally, pooling data from several centers in different countries further limits the generalizability of our results. Nevertheless, in expert hands, all technologies/techniques provided comparable significant IPSS improvements compared to baseline. Aquablation data came from > 20 surgeon users whereas PVP, GreenLEP, HoLEP and ThuLEP data were derived from highly experienced individual experts. Procedure times for these latter technologies could be longer for less experienced users. However, in the context of this study, these limitations do not impact the key findings considering that the quickest procedure was still the more recent aquablation.

## Conclusions

In our analysis of pooled data of multi-surgical techniques and technologies performed by high-volume experts, Aquablation demonstrated the lowest operative time across all prostate volumes. Such findings are valuable when counseling men and planning anesthesia time for respective BPH procedures; however, they need to be considered along with other factors such as complications and re-intervention rates.

**Author contributions** D-DN: protocol/project development, data analysis, manuscript writing. VM: data collection, manuscript editing. TB: data collection, manuscript editing. NB: manuscript editing. JEL: data collection, manuscript editing. DSE: manuscript editing. KCZ: protocol/project development, data collection, data management, manuscript editing.

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## Compliance with ethical standards

**Conflict of interest** Consultants and proctors for Boston Scientific for greenlight: KZ, DE, VM. Investigators and consultants for PROCEPT BioRobotics: VM, TB, NB, KZ. DDN were supported by a summer scholarship from the Endourological Society.

**Research involving human participants and/or animals** This research involves humans.

**Informed consent** Informed consent was obtained from all participants.

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