Clinical Outcome Comparison of GreenLight KTP-532 Laser (80 W) Prostatectomy Versus Transurethral Resection of the Prostate (TURP)

Introduction: Transurethral resection of the prostate (TURP) has long been regarded as the gold standard treatment for benign prostatic hyperplasia (BPH). The popularity of TURP was cultivated by reported symptomatic and functional improvements repeatedly documented in clinical trials. However, TURP has also been associated with well-documented, significant peri- and post-operative risks.[1,2,3] Nevertheless, TURP has remained the standard against which all other BPH treatments are measured.

Despite the clinical successes of TURP, the degree and severity of the peri-operative and post-operative complications have driven the development of alternative, minimally invasive surgical tools for BPH. Historically, laser treatments for BPH failed, primarily because the clinical outcomes were inferior to TURP. Technical evolution of laser systems yielded laser treatments now capable of challenging the standard set by TURP.

One such technology is the 532 nm laser, also known as the KTP laser, or greenlight laser. The 532 nm laser is effective for elimination of tissue because it is highly and selectively absorbed by the hemoglobin-rich prostatic tissue (optical penetration depth, 0.8mm). The absorption of the laser light results in trapped thermal energy. The release of this energy produces vapor bubbles within the tissue. The bubbles disrupt the cellular matrix of the tissue which then erupts releasing tissue and vapor bubbles.[4] This mechanism, coined "greenlight photoselective vaporization of the prostate" or greenlight PVP,[5] was developed by Malek in 1997 using a prototype 60 W laser generator. Subsequently, a higher power 80W generator was introduced and more recently a High Performance System providing 120W(GreenLight-PV and Greenlight HPS, Laserscope/ American Medical Systems, Inc., Minnetonka, Minn.).

Recent reviews of 532 nm laser results (including data obtained using a 60 W prototype as well as from 80 W devices) have raised the question of whether laser prostatectomy with a 532 nm laser may represent a viable challenge to TURP in the treatment of obstructive BPH.[5,6,7] However, as Ahmed et al.[6] have pointed out, most studies of KTP laser prostatectomy have been on small cohorts with generally short follow-up, and with no element of randomization and direct comparison against TURP. To evaluate in further detail whether the 532 nm, or Greenlight, laser does indeed meet or exceed the standards of TURP, a compilation of all comparative study data is reviewed.

Methods and Materials: A literature search using PubMed was done using the search terms (greenlight OR KTP OR PVP OR photoselective) AND (BPH OR prostate OR prostatic) AND TURP. The search results were reviewed to identify all published papers and as many abstracts as possible comparing the use of GreenLight 80W and TURP in the same study. Meeting abstracts from the *Journal of Urology, Urology, European Urology and Lasers in Surgery and Medicine* were included. A total of 13 citations, four papers and nine abstracts, provided usable data. Among these, two of the papers and one of the abstracts are from randomized trials.[8,9,10] It should be noted that not all papers or abstracts provide data for each of the discussion points below.

Results:

Procedure Time and Preoperative Gland Size

One criticism of lasers is that procedure times are longer than TURP.[10] Ahmed et al.[6] point out though, that many believe TURP is limited to those men with a gland size below 80g due to the risk of increased operative time leading to absorption of irrigating fluid and hence hyponatremia and the TUR syndrome. As such, it is necessary to compare not just procedure time, but also mean prostate size.

Table 1 presents mean procedure time as well as mean preoperative gland size for those publications providing these data.

Despite variability in results between studies, the data on the following page suggest a comparable length of procedure, particularly when accounting for differences in gland size between groups. Five of the citations show similar or proportional procedure times between PVP and TURP when accounting for gland size. Of the four remaining articles, 2 favor TURP and 2 show significantly faster procedure times for PVP. It is critical to note that without post-operative prostate volumes, it is impossible to determine whether the procedures resulted in similar volumes of prostate removal, which would be a better comparison for the efficiency of the procedures.

Table 1: Mean Procedure Time and Preoperative Gland Size for GL-PV and TURP

Reference (Mean of follow ups)	Tx	N	Mean Procedure Time(min)	p-value*	Mean Pre-Op. Prostatic Size, cc (range or SD)	p-value*
Bachmann et al.[11] _ (≥12 mos)	GL-PV	147	75	<0.001	72	0.002
	TURP	87	53		50	
Bachmann et al.[12] (6 mos)	GL-PV	64	59.6	0.047	65.1	Tend to be larger volumes in GL-PV group"
	TURP	37	49.4		48.9	
Bouchier-Hayes et al.[8] (≥6 wks)	GL-PV	38	30.24	"equal"	42.4 (16.52-82.6)	"matched"
	TURP	38	31.33		33.2 (15.4-67.5)	
Bouchier- Hayes[9] (12 mos)	GL-PV	60	30.4	"equal"	39.4 (19.86-82.6)	"matched"
	TURP	50	34.1		33.5 (15.4-60.9)	
Park et al.[15] _ (6 mos)	GL-PV	87	51.5	<0.001	45.0+22.5	ns*
	TURP	33	74.2		46.8+17.5	
Ruszat et al.[13] _ (N/A)	GL-PV	77	54	0.011	--	--
	TURP	28	66		--	
Sarica and Altay[10] _ (12 mos)	GL-PV	28	99.6	<0.05	89.1+4.0 (83-142)	"similar"
	TURP	32	68.7		91.8+3.6 (82-135)	
Sulser et al.[16] _ (> 6 mos)	GL-PV	61	53	ns*	63 (20-130)	--
	TURP	38	55		57 (18-90)	
Tugcu et al.[17] _ (24 mos)	GL-PV	112	59	<0.001	--	--
	TURP	98	45		--	

* p-value represents the difference between GL-PV and TURP
ns = not significant
_ = abstract

Qmax

Maximum urinary flow rate (Qmax, ml/sec), is widely recognized as an essential functional measure of lower urinary tract obstructive disease. The results reported for each citation providing Qmax data are reported in Table 2. When numerical data were not present, the authors' verbiage from the articles was included.

Of nine articles, seven reported non-significant clinical and statistical differences between TURP and PVP. In one of the seven neutral articles, the difference in the mean change from baseline between PVP and TURP was actually 4.5 ml/sec in favor of PVP though this failed to reach statistical significance. Statistical superiority for TURP was reported in the remaining two articles.

International Prostate Symptom Score (IPSS)

The IPSS and AUA Symptom Score are commonly used to evaluate the burden of obstructive symptoms and their resulting effects on quality of life. Post-treatment, only two of nine citations showed significant differences between GL-PV and TURP. The other seven articles reported non-significant differences (6) or no conclusion (1).

Hospitalization Time and Catheterization Time

Two claims made in support of PVP are shorter hospitalization and catheterization times. In the seven studies with data reported on hospitalization times, differences between the mean hospitalization times of PVP and TURP ranged from 0.91 and 3.4 days, with PVP having significantly shorter hospitalization times in all studies. Of the eight studies reporting catheterization times, the range of differences in mean PVP and TURP catheterization times was 1.1–2.0 days. All studies showed significantly shorter catheterization times for PVP. It is clear that PVP is indeed associated with significantly reduced hospitalization and catheterization times when compared to TURP.

Table 2: Change in Qmax after GL-PV and TURP

Reference (Mean of follow ups)	Tx	N	Mean Qmax (ml/s)			
			Before	p-value*	After	p-value*
Bachmann et al.[11] _ (≥12 mos)	GL-PV	147	7.6		19	<0.05
	TURP	87	9.6	0.71	24.1	
Bachmann et al.[12] (6 mos)	GL-PV	64	6.9		18.1	ns
	TURP	37	6.9	ns	19.1	
Bouchier-Hayes et al.[8] (≥6 wks)	GL-PV	38	N/A	--	↑167.37%±146.36%	ns
	TURP	38	N/A	--	↑149.01%±231.8%	
Bouchier- Hayes[9] (12 mos)	GL-PV	60	8.8		18.7	ns
	TURP	50	8.9	--	18.5	
Han et al.[14] (≥6 mos)	GL-PV	53	N/A		Significant↑	ns
	TURP	14	N/A	--	Significant↑	
Park et al.[15] _ (6 mos)	GL-PV	87	10.8		17	ns
	TURP	33	8.7	ns	17.8	
Sarica and Altay, 2007[10] _ (12 mos)	GL-PV	28	N/A		PVP < TURP	"significant"
	TURP	32	N/A	"similar"		
Sulser et al.[16] _ (> 6 mos)	GL-PV	61	6		19	ns
	TURP	38	7	--	20	
Tugcu et al.[17] _ (24 mos)	GL-PV	112	6.9		16.8	"similar"
	TURP	98	7.3	"similar"	12.8	

* p-value represents the difference between GL-PV and TURP
ns = not significant
_ = abstract

Intra, Peri and Post-Operative Complications:

While the above data is focused on the functional improvements in patient outcomes, clinical complications and procedural risks drove development of alternatives to TURP. The incidences of specific AEs have been broken out below, based on those events that are of greatest concern or of greatest frequency for either treatment. Five publications reviewed complications, which include: [8,11,12,16,17]

• ***Capsular perforation*** – Of the articles reporting complications, the range of reported capsular perforation rates were from 2.5-5% for TURP and did not occur for PVP. In addition, Park et al.[18] stated that more capsule perforations occurred in the TURP group than in the GL-PV group. These rates are slightly elevated over historical reported rates for TURP, of 1-2%.[6] This complication is rare but expected with TURP while this is considered very rare with PVP.

• ***Clot retention requiring bladder washout*** – Clot retention again was mentioned in several of the articles, including rates for TURP of 2.3%, 2.5%, 5.0%, and 26.2% while this was not reported in any of the PVP groups.

• ***Urinary tract infection*** – UTI incidence was reported in four articles, all with comparable occurrence rates between the two groups which would be expected.

• ***Stricture*** – Stricture rates were highly variable with rates between 2.7% and 21% for TURP, and 2.0%-13.2% for PVP. Three articles reported rates similar between groups, while two others showed some difference between groups, one favoring TURP and one favoring PVP. Outside of one outlier, all studies reported rates consistent with non-comparative study results.

• ***TUR Syndrome, Hyponatremia*** – TUR Syndrome was reported in only two studies, each with single occurrences (1%, 2.6%) for TURP patients, and no occurrences were reported for PVP patients; these rates are consistent with other TURP specific literature.

• ***Excessive bleeding*** – Excessive bleeding is defined as bleeding that required active management or stoppage of the procedure, but without requiring transfusion. The incidence rates for TURP ranged from 10.5%-18%, while this was not reported in any PVP group. The decrease in bleeding for PVP is primarily driven by the way that green light interacts with tissue.

Table 3: Change in IPSS after GL-PV and TURP

Reference (Mean of follow ups)	Tx	N	Mean Qmax (ml/s)			
			Before	p-value*	After	p-value*
Bachmann et al.[11] _ (≥12 mos)	GL-PV	147	N/A	--	5.3	ns
	TURP	87	N/A		5.4	
Bachmann et al.[12] (6 mos)	GL-PV	64	18.1±5.9	ns	5.2	ns
	TURP	37	17.3±6.3		4.8	
Bouchier-Hayes et al.[8] (≥6 wks)	GL-PV	38	N/A	--	↓49.82%±36.19%	ns
	TURP	38	N/A		↓50.23%±39.7%	
Bouchier- Hayes[9] (12 mos)	GL-PV	60	25.3	--	9.5	ns
	TURP	50	25.4		10.2	
Han et al.[14] (≥6 mos)	GL-PV	53	N/A	comparable	"significantly improved"	ns
	TURP	14	N/A		"significantly improved"	
Park et al.[15] _ (6 mos)	GL-PV	87	21.7	ns	12.5	ns
	TURP	33	24.2		11.2	
Sarica and Altay[10] _ (12 mos)	GL-PV	28	N/A	"similar"	↓PVP < ↓TURP	"significant"
	TURP	32	N/A			
Sulser et al.[16] _ (> 6 mos)	GL-PV	61	17	ns	6	ns
	TURP	38	18		6	
Tugcu et al.[17] _ (24 mos)	GL-PV	112	17.9	"similar"	3.1	--
	TURP	98	17.7		2.9	

* p-value represents the difference between GL-PV and TURP
ns = not significant
_ = abstract

• ***Impotence/Erectile Dysfunction*** – Two studies reported the incidence of ED, at 0% and 2.7% for TURP, while no incidents or ED were reported for PVP.

• ***Retention requiring indwelling catheter*** – Of the four studies reporting on transient retention requiring placement of an indwelling catheter, all four reported rates higher in the PVP group. Rates for TURP ranged from 0%-3.4%, while PVP had a significantly higher rate, with ranges between 3.0%-8.2%.

• ***Bleeding requiring transfusion*** – In addition to the excessive bleeding, some cases are severe enough to require transfusion. Of the five papers, 2 reported no occurrence in either group, while the other three reported significantly greater rates in the TURP group with occurrences between 2.6%-3.4%.

All articles made statements like equivalent or reduced incidence of complications associated with PVP. Evaluating the complications above, it is clear that PVP does indeed have lower intra and peri-operative risks. Long-term risks such as stricture appear to be equivalent between the groups. Interestingly, retention requiring in-dwelling catheter placement occurred at higher frequency with PVP. Dysuria, hematuria and retrograde ejaculation surprisingly were not reported. All occur with both TURP and PVP and, based on occurrence rates, would have been expected. It is possible that these events were not included because they did not require additional medical intervention for resolution.

Discussion: In the assessment of the 532nm laser, despite the abundance of prospective single arm trials of PVP and the GreenLight laser, physicians insist that randomized controlled trials are necessary to prove equivalence or superiority of GreenLight over TURP. In an effort to compile the existing data on the subject, these articles provide direct side by side comparisons between GreenLight and TURP.

It seems clear that while GreenLight was once thought to be far slower and more tedious that TURP, the results are essentially inconclusive. Because PVP does not allow for measurement of resected tissue, and no post-operative TRUS data was presented, we must rely on baseline prostate volume and assume that all physicians would strive for

equivalent tissue removal. If that assumption is made, then the results suggest little to no difference between the two treatments. Regardless, it is clear that this area requires further study, particularly as higher power PVP technology is released. Additionally, as Ahmed, et al, point out, TURP is not generally appropriate for prostates greater than 80g because of TUR Syndrome, whereas PVP does not limit the treatable prostate size.

With Qmax, IPSS, catheterization and hospitalization times as the outcomes measured, PVP and TURP appear to have comparable impact. For Qmax only 2 of nine articles showed a significant difference when evaluating change from baseline. In the one negative article with data provided, PVP was associated with over 150% improvement in Qmax. All seven of the articles showed no statistically or clinically significant differences in Qmax. When evaluating IPSS, eight of the nine articles showed no difference in IPSS scores. The one article that did show a difference did not report the data. In addition, all articles showed significantly reduced catheterization and hospitalization times for PVP. While no tests for equivalence were performed, it is clear that PVP outcomes are comparable to TURP and that the degree of symptomatic and functional improvements are similar. It should be noted that no trial attempted to prove equivalence and as such, it cannot be said that outcomes are equivalent, but such a study would be provocative.

With the implied benefit of a laser technology on the potential risks associated with TURP, it is crucial to evaluate whether any new complications or risks arise with the technology. All the articles were reviewed for any event that occurred in either group. That list was then taken and rates from each study compiled. Interestingly absent from the list were common complications of dysuria, hematuria and retrograde ejaculation, perhaps because none of the events were considered severe or required subsequent medical therapy. Despite this, it should be noted that the events associated with PVP are all historically expected with TURP. In fact, other than transient retention, which was higher in PVP, all event rates are equivalent or decreased in all other complications observed with TURP. Several of the major complications, capsular perforation, transfusion and excessive bleeding were not observed for PVP in any of the trials.

Conclusions: PVP is associated with treatment outcomes similar to TURP with a more favorable risk profile, including significant reductions in capsular perforation, excessive or severe bleeding and elimination of TUR Syndrome. While procedure time may or may not be longer than TURP, catheterization time and hospitalization times after the procedure are significantly reduced.

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This white paper is authored by American Medical Systems, Inc. 2008

21500086B (02/08)