

KTP Laser versus Transurethral Resection: Early Results of a Randomized Trial

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ABSTRACT

Background and Purpose: Many technologies have been mooted as equal to transurethral resection of the prostate (TURP) without gaining widespread acceptance because of the lack of randomized trials. The Greenlight® laser system (Laserscope, San Jose, Ca.), an 80 W system for photovaporization of the prostate (PVP), was compared with TURP in such a trial.

Patients and Methods: A series of 120 patients was randomized to undergo TURP or PVP after evaluation, which was repeated at 1, 3, 6, and 12 months after treatment. Irrigation use, length of catheterization (LOC), length of hospital stay (LOS), postvoiding residual volume, sexual function, blood loss, cost, and operative time also were assessed.

Results: To date, 76 patients are evaluable. Both groups showed a significant ($P < 0.5$) increase in maximum flow rate from baseline. In the TURP group, flow increased from 8.7 to 17.9 mL/sec (149%) and in the PVP group from 8.5 to 20.6 mL/sec (167%). The International Prostate Symptom Score decreased from 25.4 to 12.4 (50.23%) in the TURP group and from 25.7 to 12.0 (49.83%) in the PVP group. Postvoiding residual volumes also showed significant decreases. Similar trends were seen in relation to bother and quality of life scores. There was no difference in sexual function as measured by a questionnaire. The LOC was significantly less in the PVP group ($P < 0.001$), the mean being 12.2 hours (range 0–24 hours) versus 44.5 hours for TURP (range 6–192 hours). A similar situation was seen in relation to LOS ($P < 0.0001$), with the mean of the PVP group being 1.08 days (range 1–2 days) and the mean for the TURP group being 3.4 days (range 3–9 days). Adverse events were less frequent in the PVP group, and the costs were 22% less.

Conclusions: This trial demonstrates that PVP is effective compared with TURP, producing equivalent improvements in flow rates and IPSS with markedly reduced LOS, LOC, and adverse events. Long-term follow-up is being undertaken to assess the durability of these results.

INTRODUCTION

TRANSURETHRAL RESECTION OF THE PROSTATE (TURP) has been the most durable and reliable endoscopic method of relieving lower urinary-tract symptoms (LUTS) caused by bladder outlet obstruction (BOO) secondary to benign prostatic hyperplasia (BPH). The procedure markedly improves both objective (flow rates) and subjective (International Prostate Symptom score [IPSS]) measures of BOO, by 90% to 175% and 53% to 81%, respectively.¹ This surgical procedure is one of the most commonly performed today, with an estimated 400,000 TURPs being performed annually in the U.S. in the early 1990s, at a cost of approximately \$5 billion.² How-

ever, TURP is not without its problems. Complications occur in as many as 20% of patients, including need for blood transfusion, along with infections, strictures, bladder-neck stenosis, sexual problems, and urinary retention and incontinence.³ Allied with this, many men find the procedure, subsequent catheterization, and postoperative period painful and limiting from a quality of life point of view, and many are not satisfied with their result. In most hands, the procedure requires an inpatient stay of at least overnight, if not longer, with significant patient inconvenience and cost to the healthcare system.

Given these limitations in what is an extremely common procedure, many alternatives have been looked at over the last 15 years. The most promising comes from the field of laser tech-

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nology, with various manifestations and delivery systems having been well studied and some forms being subjected to randomized trials. These techniques include visual laser ablation of the prostate (VLAP)⁴ and holmium enucleation of the prostate (HoLEP).⁵ Newer energy sources, laser technologies, and methods of delivery should be evaluated in a similar manner.

The technique of photoselective vaporization of the prostate (PVP) was pioneered by Malek and coworkers in the Mayo Clinic, first at a 28 W power setting, then at 60 W, and now at 80 W, and is now available commercially.^{6,7,9} The Greenlight[®] laser system (San Jose, CA) utilizes a potassium titanyl phosphate (KTP) crystal to produce a light beam at a wavelength of 532 nm, which is preferentially taken up by the red heme moiety at a power level of 80 W. This creates tissue photovaporization, giving the procedure the name "photoselective vaporization of the prostate" (PVP). As well as vaporization of tissue, the system causes tissue coagulation, but only to a depth of 1 to 2 mm, as its effective depth of action is 0.8 mm.⁸ This system has been used to great effect for as long as 7 years, with excellent functional results, short catheterization times and inpatient stays, and minimal complications.¹² However, to date, there has not been a formal randomized trial comparing the results of this technology with those of TURP. We undertook such a trial.

PATIENTS AND METHODS

The trial was designed in accordance with the American Urological Association guidelines on establishment of new technologies in the treatment of BPH.¹⁰ After clearance was obtained from the hospital ethics committee, 120 patients in total are to be recruited, randomized to PVP or TURP, and evaluated in a prospective manner. All patients are being recruited from those referred with LUTS to the urology outpatient department of a major urban university hospital beginning in January 2004. Patients are screened to assess eligibility, and those suitable are counseled as to the nature of the trial. After fully informed consent is obtained, they are randomly assigned to TURP or PVP. Inclusion and exclusion criteria are listed in Table 1. In short, patients have to have a peak voiding flow rate (Q_{max}) ≤ 15 mL/sec and an IPSS of ≥ 12 . Platelet inhibitor use is not an exclusion criterion if the medication can be stopped safely 10 days preoperatively. Patients with suspicion of prostate cancer (raised serum prostate specific antigen concentration or abnormal digital rectal examination) must have cancer ruled out by biopsy prior to enrollment. Those who meet the initial inclusion criteria undergo estimation of prostate gland size by transrectal ultrasonography (TRUS) and full urodynamic evaluation, including analysis of definitive obstruction using an Abrams-Griffiths (A-G) nomogram. All patients undergo full blood count, urea and electrolyte measurement, and midstream urine testing. Preoperative bother scores, quality of life (QoL) scores, and baseline sexual function questionnaire (BSFQ) data also are collected.

All operative procedures were performed by registrars in training or fellows in the department, all of whom had performed between 35 and 325 TURPs and < 5 laser prostatectomies each. This was done to remove the expert bias that can

TABLE 1. INCLUSION AND EXCLUSION CRITERIA FOR PVP STUDY

<i>Inclusion criteria</i>	
Age	> 50 years
	Referred by family physician for LUTS
Flow rate	≤ 15 mL/sec
IPSS	≥ 12
Gland	15–85 cm ³ on TRUS
	Obstructed on A-G nomogram
	Able to complete QoL, Bother Score, and BSFQ questionnaires
	Able to give fully informed consent
<i>Exclusion criteria</i>	
	Neurogenic bladder
	Known or suspected prostate cancer
	Chronic retention
	Taking α -blocker ^a or herbal medication believed active in prostate ^b
	Permanently on anticoagulant
	Taking finasteride or dutasteride

^aUnless use is stopped at least 2 weeks before study entry.

^bUnless use is stopped at least 1 month before study entry.

be experienced in trials of new surgical procedures and to try to assess the ease of mastery of the PVP technology by the average urologist. The TURP was undertaken in the standard manner through a 25F resectoscope sheath using a ValleyLab diathermy machine with passage of a three-way 22F Foley catheter postoperatively that was on continuous irrigation with saline. Irrigation was stopped when deemed appropriate by the registrar of the unit when the irrigant was rosé colored or clearer, and catheter removal was undertaken at the clinical discretion of the registrar, usually on the second postoperative morning. The PVP was performed using an 80 W KTP laser using a Greenlight system and a StarPulse quasi-continuous-wave laser (Laserscope) emitting green light at a wavelength of 532 nm. A 600- μ m laser fiber with a 70° lateral deflecting quartz element was used through the working channel of a 22.5F continuous-flow laser cystoscope using saline for irrigation. A single fiber was used for each procedure. Catheters were left *in situ* at the discretion of the operating surgeon.

Intraoperative and postoperative parameters measured included the length of the operation, the amount of irrigation, the number of bladder washouts, postoperative hemoglobin concentration, length of catheterization (LOC), and length of inpatient stay (LOS). Both groups of patients received antibiotics at induction and a nonsteroidal anti-inflammatory drug on discharge for use as needed.

All patients were followed up in the clinic at 6 weeks and 3, 6, and 12 months by the same investigator. Repeat Q_{max} and IPSS, as well as QoL scores and bother and BSFQ scores were obtained at each visit, and a record of complications was noted. Prostate volume (measured by TRUS) and urodynamic studies were repeated at 6 months. Recently, we have begun to measure serum PSA concentrations at 6 months.

Results were recorded on a Microsoft Excel spreadsheet (Microsoft, Seattle, WA USA). Statistical analysis was undertaken again using Microsoft Excel software. Results are expressed as the mean \pm SD of the group, and the statistical tool used is the

Student *t*-test, either paired or unpaired as appropriate. Statistical significance is assumed if *P* is <0.05.

RESULTS

To date, 95 patients have been randomized, and 76 are evaluable at least 6 weeks postoperatively. Thus, the study has not yet achieved sufficient numbers to show the equivalence that it is powered to do, so these data can be viewed as only preliminary. However, statistical analysis is provided for these interim data. All 76 patients are evaluable at 6 weeks, 68 at 3 months, 57 at 6 months, and 44 at 12 months. Three patients dropped out after randomization but prior to surgery but are included in the statistical analysis. The two groups are well matched for age (TURP 66.23 years, range 55–80 years, versus PVP 65.23 years, range 51–81 years) and prostate volume (TURP 33.22 cc, range 15.4–67.5 cc, versus PVP 42.44 cc, range 16.52–82.6 cc). Although prostatic volume was greater in the PVP group, this difference was not statistically significant. Resection times were equal in the two groups (TURP 31.33 minutes, range 5–70 minutes, versus PVP 30.24 minutes, range 9–70 minutes).

The outcomes are shown in Table 2. In summary, both groups showed a significant increase in Q_{\max} ($P < 0.0005$), and there was no statistical difference between the groups. The two groups also showed a decrease of approximately 50% in IPSS from baseline ($P < 0.0005$). Similar trends were seen in both and QoL scores, with the groups showing equivalent improvement. There was no difference in sexual function, as measured by BSFQ, between preoperative and postoperative evaluation, nor between TURP and PVP. Postvoiding residual volumes were equivalent in the two groups, averaging 119 mL preoperatively in the TURP group and 147 mL in the PVP group, with reductions to 37 mL and 27 mL, respectively ($P < 0.0005$ for both groups). Data from TRUS volumes, repeat urodynamics,

and PSA concentrations at 6 months are not mature enough for inclusion in this analysis.

The LOC, LOS, liters of irrigant used, blood loss, and overall cost are summarized in Table 3. In summary, LOC (defined as time to initial removal of the catheter) was significantly less in the PVP group ($P < 0.001$). A similar situation was seen in relation to LOS, with the mean of the PVP group being 1.08 days and that of the TURP group 3.4 days ($P < 0.00001$). Irrigant usage was markedly less in the PVP group, being 6.9 L (range 2–30 L) as against 23.1 L (range 10–64 L) in the TURP group ($P < 0.00001$). Blood loss, as measured by serum hemoglobin values on the first postoperative morning, showed that both procedures had blood loss that was statistically significant (TURP 1.46 g/dL, PVP 0.45 g/dL) but that the change was statistically less with PVP ($P < 0.005$).

Figure 1 illustrates the complications in the two groups by patients and by number of events. There were more significant complications in the TURP group. These complications included 10 instances of clot retention on one or more occasions in the early postoperative period that necessitated manual bladder washouts. One of these patients required a blood transfusion. Eight patients in the TURP group and five in the PVP group had submeatal/urethral strictures or bladder-neck stenosis. All were treated easily with dilatation or bladder-neck incision as appropriate, except for one patient from the TURP group, who required a meatotomy and has withdrawn from further follow-up. Three of the TURP patients failed their trial of voiding and required recatheterization for a further 4 weeks, after which, they voided without difficulty. This complication occurred in three patients in the PVP group, but they all had their catheters removed 48 hours later. Eight members of both groups complained of dysuria significant enough to warrant being mentioned at the clinic at 6 weeks, and four patients (three TURP, one PVP) had a secondary hemorrhage necessitating recatheterization and inpatient admission. Two PVP patients underwent

TABLE 2. MEAN CHANGES IN FLOW RATES, IPSS, QoL AND BOTHER SCORE AFTER PVP OR TURP (RANGE)

	TURP (N = 38)	PVP (N = 38)	P value, change within group ^a	P value, comparison between groups ^a
Increase in flow (mL/sec)	8.56 ± 9.08 (-8-30.9)	11.96 ± 8.23 (-4.2-32.3)	<0.0005	NS
% change	149.01 ± 231.8 (-19.1-1041.1)	167.37 ± 146.36 (-35-725)	<0.0005	NS
Decrease in IPSS	12.9 ± 10.6 (-4-32)	14.0 ± 9.8 (-5-32)	<0.000001	NS
% decrease	50.23 ± 39.7 (-18.5-97.0)	49.82 ± 36.19 (-76.1-98.5)	<0.000001	NS
Decrease in QoL score	2.91 ± 2.04 (-1-6)	2.65 ± 2.1 (-1-6)	<0.00005	NS
Decrease in bother score	1.61 ± 1.22 (-1-3)	1.91 ± 1.29 (0-3)	<0.000001	NS
Decrease in PVR ^b (mL)	86 ± 124.38 (-216-319)	125 ± 198 (-243-770)	<0.0005	NS

^aPaired and unpaired Student *t*-test.

^bPostvoiding residual volume.

TABLE 3. MEAN CHANGES IN LOC AND LOS, BLOOD LOSS, AND COST (RANGE)

	TURP (N = 38)	PVP (N = 38)	P value, change within group	P value, comparison between groups
LOC (hr)	44.52 ± 30.23 (6–192)	12.2 ± 8.6 (0–24)	NS	<0.0005
LOS (days)	3.39 ± 1.17 (2–9)	1.08 ± 0.28 (1–2)	NS	<0.0000001
Hemoglobin decrease (g/dL)	1.5 ± 0.15 (–0.3–6.3)	0.45 ± 0.7 (–0.7–1.5)	<0.05	<0.05
Cost per case (AU\$)	4291.68	3368.12	NS	<0.005

Paired and unpaired Student *t*-test.

TURP for persistent obstructive symptoms and with residual tissue noted on cystoscopy. A TURP was used even on those patients treated with PVP, as it is the reference standard operation in prostatectomy. Both of these patients were among the first 10 PVP patients operated on. One patient in the TURP group suffered from symptomatic TURP syndrome, with an immediate postoperative serum sodium concentration of 116 mmol/L but no long-term sequelae.

DISCUSSION

Transurethral resection has stood the test of time as an efficacious operative procedure for the relief of BOO secondary to BPH and is recognized, with good reason, as the gold standard in this regard. However, as mentioned earlier, it is not without its drawbacks. In general, at least a 1-night inpatient stay is required. Complication rates as high as 20% have been described.³ The procedure is not easy to learn, and most urologists would claim that one needs to have completed 20 or more TURPs before being comfortable with this technique. Many men suffer side effects, which urologists regard as nearly normal or expected, such as prolonged dysuria, hematuria, and retrograde ejaculation. (Retrograde ejaculation after PVP was not addressed as a specific outcome in this study.) The cost of the procedure plus inpatient stay is not inconsiderable.

With these points in mind, surgeons have attempted to harness different technologies to simulate the positive results from TURP but minimize the negative aspects of it. One of the most interesting of these has been the evolution of laser therapy as a proposed minimally invasive treatment. Early side-firing vaporization techniques, such as VLAP using the neodymium:YAG laser, described by Costello and colleagues,⁴ suffered from long postoperative catheterization times and extended tissue sloughing with dysuria and patient dissatisfaction. This technique also did not appeal to many urologists, as the final result of the therapy (i.e., a large prostatic cavity) could not be appreciated immediately, as it can be in TURP. Other forms of laser therapy have shown promise, most significantly the holmium laser for resection (HoLRP) or, more recently, for adenoma enucleation (HoLEP).⁵ Although these techniques have excellent results, as shown by rigorous studies, they have not achieved universal acceptance, as both procedures, especially

HoLEP, which is essentially an endoscopic Millin's prostatectomy, require considerable surgical skill, and the average urologist, it seems, has struggled to match the outstanding results of Gillig and other investigators without a considerable learning curve. The patients in the current study were all operated on by surgeons with minimal laser experience in order to show the ease of acquisition of the skills involved in PVP. Essentially, a short mentorship period usually is sufficient to be able to perform the procedure safely and, in general, effectively.

Overall, the preliminary data from this first randomized comparison of TURP and PVP are encouraging. Although firm conclusions cannot be drawn yet because of the early nature of the results and the relatively small population, what can be inferred is that PVP is equivalent to TURP in terms of decreasing IPSS and other measures of symptom severity and increases flow rates to a similar degree. These results are generally in line with those reported by Malek and associates in a setting of long-term (5-year) follow-up¹² and across multiple centers,¹³ although the improvements in flow rate and symptom score are not quite as pronounced as those from Malek et al.¹² This may reflect the relative inexperience of those performing PVP, especially in the early part of the series, but may be a better reflection of what the urologist who is not an expert in this area may hope to achieve. The procedure is day-case based, with much shorter admission times and LOC, with consequent real monetary savings despite the high cost of the equipment and consumables. Finally, the rate of significant complications is much less with PVP, and it is a safe and efficacious procedure, even in the hands of the relative novice.

Some areas of this study in its present form can justifiably be criticized. Because this paper was an invited manuscript, it is presented before recruiting is complete, and the 1-year follow-up is not finished for many patients, which must be borne in mind when interpreting the data. Nevertheless, the data indicate interesting trends, which we feel are durable enough to be replicated in the full study, although that remains to be seen. Again, certain types of data, such as PSA values, urodynamic results, and TRUS volumes, are incomplete because of this restriction and thus are not presented. Moreover, the situation with larger glands and those in retention is not addressed, as our upper limit of size is 85 cc in order to allow TURPs to be completed within 60 minutes for obvious safety reasons. Also, this study was designed specifically to assess outcomes in sympto-

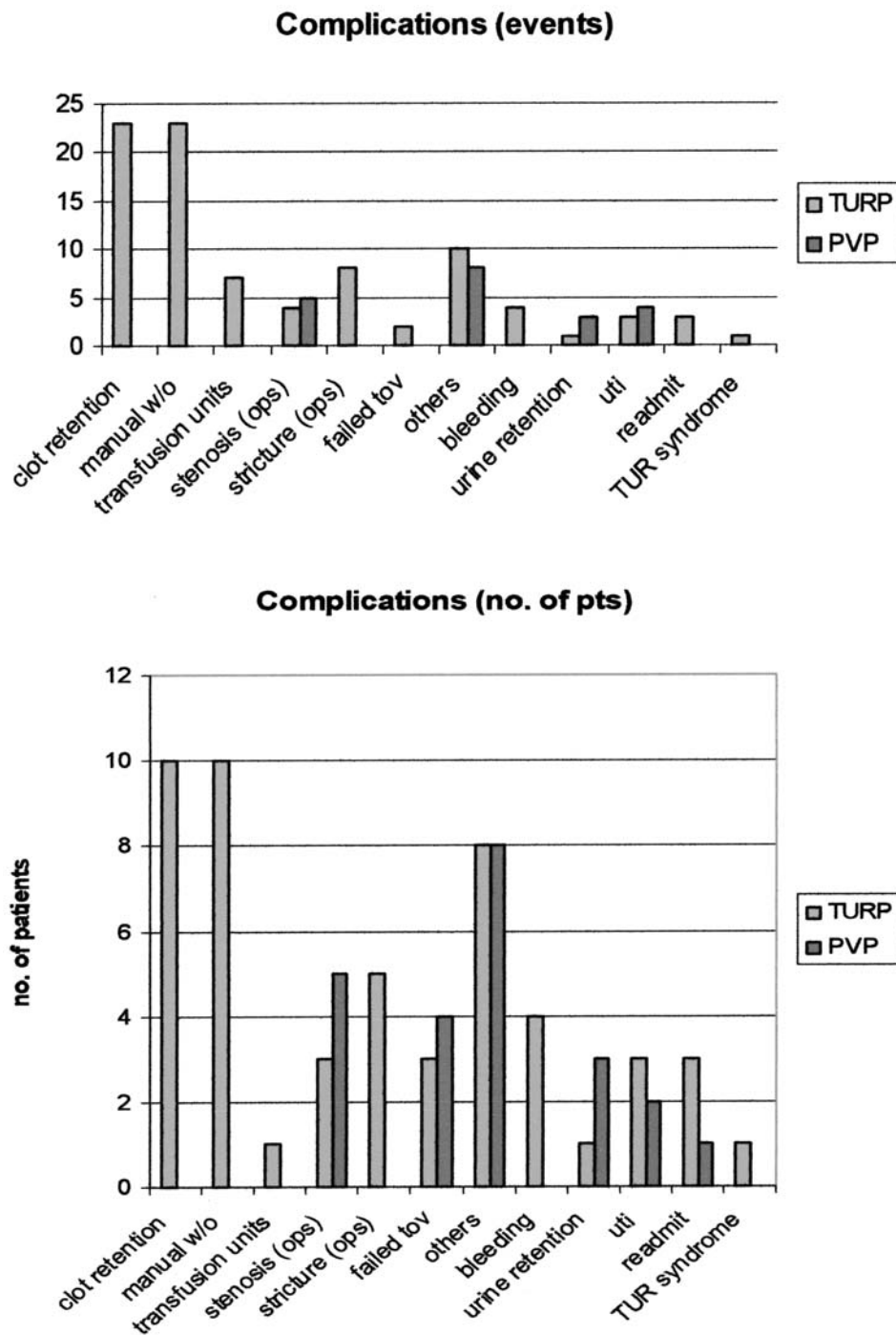


FIG. 1. Complications. w/o = washout; tov = trial of voiding; uti = urinary-tract infection.

matic voiding patients, not those in retention. Obviously, long-term data will need time to accrue, and it will be vital to observe the reoperation rate in both groups over the next 3 to 5 years or longer, as this is felt to be an area where PVP may be inferior to TURP, although there is no evidence of this to date.

Transurethral resection has served both urologists and their patients extremely well throughout the years. However, the rapid improvement in technology in every walk of life must

also transfer into the area of urology, especially with so common a procedure as TURP. It is our belief that PVP performed with the Greenlight[®] laser has significant potential and warrants further rigorous investigation for the treatment of men with troublesome voiding symptoms secondary to BPH. It is hoped that commercial considerations will not overcome the virtues of proper clinical research in this area, so that a correct, accurate, and unbiased appreciation of the role of this technol-

ogy in the treatment of the obstructing prostate can be achieved. It is hoped too that the early results of this study will be interpreted as just that: encouraging to date, but by no means complete, and to note that further publications concerning this trial will address these flaws and give a more accurate picture of the place of PVP in the urologist's armamentarium.

REFERENCES

1. Wasson JH, Reda DJ, Bruskwewitz RC, Elinson J, Keller AM, Henderson WG. A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia: The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. *N Engl J Med* 1995;332:75-79.
2. Brawer MK, McConnell JD, Oesterling JE. What will replace TURP? *Contemp Urol* 1992;4(2):30-40.
3. Mebust WK, Holtgrewe HL, Cockett AT, Peters PC, Writing Committee, the American Urological Association. Transurethral prostatectomy: Immediate and postoperative complications: Cooperative study of 13 participating institutions evaluating 3,885 patients. *J Urol* 1989;141:243-247.
4. Costello AJ, Bowsher WG, Bolton DM, Braslis KG, Burt J. Laser ablation of the prostate in patients with benign prostatic hypertrophy. *Br J Urol* 1992;69:603-608.
5. Tan AH, Gilling PJ, Kennett KM, Frampton C, Westenberg AM, Fraundorfer MR. A randomized trial comparing holmium laser enucleation of the prostate with transurethral resection of the prostate for the treatment of bladder outlet obstruction secondary to benign prostatic hyperplasia in large glands (40 to 200 grams). *J Urol* 2003;170:1270-1274.
6. Kuntzman RS, Malek RS, Barrett DM, Bostwick DG. High-power (60-watt) potassium-titanyl-phosphate laser vaporization prostatectomy in living canines and in human and canine cadavers. *Urology* 1997;49:703-708.
7. Kuntzman RS, Malek RS, Barrett DM, Bostwick DG. Potassium-titanyl-phosphate laser vaporization of the prostate: A comparative functional and pathologic study in canines. *Urology* 1996;48:575-583.
8. Jacques SL. Laser-tissue interactions: Photochemical, photothermal, and photomechanical. *Surg Clin North Am* 1992;72:531-558.
9. Hai MA, Malek RS. Photoselective vaporization of the prostate: initial experience with a new 80 W KTP laser for the treatment of benign prostatic hyperplasia. *J Endourol* 2003;17:93-96.
10. Roehrborn CG, McConnell JD, Barry MJ, et al. Guidelines on the Management of Benign Prostatic Hyperplasia. Linthicum, MD: American Urological Association, 2003, Chapter 4, appendix 4.
11. Das A, Kennett K, Fraundorfer M, Gilling, P. Holmium laser resection of the prostate (HoLRP): 2-year follow-up data. *Techn Urol* 2001;7:252-255.
12. Malek RS, Kuntzman RS, Barrett DM. Photoselective potassium-titanyl-phosphate laser vaporization of the benign obstructive prostate: Observations on long-term outcomes. *J Urol* 2005;174:1344-1348.
13. Te AE, Malloy TR, Stein BS, Ulchaker JC, Nseyo UO, Hai MA, Malek RS. Photoselective vaporization of the prostate for the treatment of benign prostatic hyperplasia: 12-month results from the first United States multicenter prospective trial. *J Urol* 2004;172:1404-1408.

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