Photoselective vaporization of the prostate: application, outcomes and safety

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Introduction: *Open prostatectomy and transurethral resection of the prostate (TURP) has been the gold standard therapy for moderate to severe lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). In recent years, laser vaporization technologies have now been recognized by international guidelines as an effective treatment alternative to TURP for treating BPH.*
Materials and methods: *In this contemporary review, we aim to discuss the application, outcomes and safety of photoselective vaporization of the prostate (PVP), specifically with the GreenLight laser. We also discuss the properties and evolution of the GreenLight laser as understanding the basic principles of this laser system.*
Results: *GreenLight PVP is a durable and effective alternative to TURP, especially in high-risk patients on systemic anticoagulation. Aside from providing similar efficacy and safety, the GreenLight PVP also allows for decreased hospitalization times, catheterization times and subsequently decreased healthcare costs. The latest generation laser, 180W XPS system, is found to be more cost-effective and efficacious in tissue vaporization when compared to previous laser generations.*
Conclusions: *Laser vaporization is a safe and effective option to treating LUTS secondary to BPH. A patient-centered approach considering patient preference and preoperative parameters should be employed to determine the ideal treatment option for each individual patient.*

Key Words: GreenLight, PVP, BPH, LUTS, photoselective vaporization of prostate

Introduction

Benign prostatic hyperplasia (BPH) is one of the most common diseases affecting the aging man and its prevalence rises markedly with increasing age. An estimated 90% of men is thought to be affected by BPH by the age of 85, of which, 25%-30% eventually require treatment.[1,2] For many decades, open prostatectomy and transurethral resection of the prostate (TURP) have been the gold standard therapy for moderate to severe lower urinary tract symptoms (LUTS) secondary to BPH.[3,4] In recent years, however, an effort has been made to further improve the clinical outcomes and efficacy of treatment options offered to patients suffering from this highly prevalent disease. The primary goal is to develop an alternative therapy that can not only effectively relieve symptomatic LUTS, but also be a tolerable and feasible option in high-risk patients, all while reducing patient morbidity, length of hospital stay and medical costs.[5]

With strong evidence from longitudinal cohort studies and meta-analyses, laser vaporization technologies have now been recognized by the American Urological Association (AUA) and European Association of Urology (EAU) as an effective treatment alternative to TURP for treating BPH.[3,4] There are currently four approved and commonly utilized laser systems among the urology community, namely the GreenLight, holmium, thulium and diode laser. Each individual system possesses distinct characteristics suitable for a large gamut of applications. Ultimately, the goal of these laser therapies is to relieve bladder outlet obstruction by means of reducing the prostate size via vaporization, resection or enucleation techniques.[5] In this contemporary review, we discuss the application, outcomes and safety of photoselective vaporization of the prostate (PVP), specifically with the GreenLight laser (Boston Scientific, Marlborough, MA, USA).

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Evolution of the GreenLight laser: from 60W to 180W in 10 years

The GreenLight laser is a non-contact, side-firing laser system that operates in a near continuous mode.[6] Since its introduction in the late 1990s by Kuntzman as the 60W potassium-titanyl-phosphate (KTP) laser, the GreenLight laser has undergone extensive studies and advancements over the decades to continuously improve its efficacy and safety for the treatment of BPH.[7] Following their initial experience, they subsequently described the utility of the first generation 80W KTP laser PVP in 1998 together with its 5 year postoperative outcomes.[8] In 2006, the first 2090 laser fiber and the 120W HPS GreenLight laser was developed by combining the neodymium:YAG laser resonator with a lithium triborate (LBO) crystal in place of the KTP. The next upgrade was the introduction of the side-firing, 600µm silica Mojo fiber which allowed for increased power output from 275kJ to 400kJ when compared to the 2090 fiber.[9] Next came the 180W XPS (LBO) laser system and the MoXy liquid-cooled, steel-capped laser fiber in 2010 which allowed for increased power, speed and efficiency to vaporize tissue.[10] With the latest XPS/MoXy system, both the power output and area of laser beam were increased by 50% while the depth of optical penetration remained the same at 1-2 mm. This improvement in technology allowed for increase in speeds and efficiency of tissue vaporization while minimizing complications such as thermal tissue injury or capsular perforation.[11] Moreover, the MoXy fiber optic also offers improved hemostatic properties, reduction of tissue debris devitrification and has increased fiber longevity compared to previous fibers, allowing for additional cost savings. Its Active Cooling Cap technology increases fiber protection by preventing overheating of the laser via a temperature feedback mechanism, such that when used correctly, only a single MoXy fiber is required for an entire case, regardless of prostate size.[12,13] Overall, comprehensive research comparing the outcomes of lasers with different power outputs have demonstrated each generation of laser being more efficacious and advantageous than the next. As such, with its comparable postoperative outcomes and superior intraoperative safety profile, international guidelines have approved the GreenLight PVP as an alternative to TURP for the treatment of LUTS secondary to BPH.[3,4]

Photoselective vaporization: principles and properties of the GreenLight

The two primary mechanisms of laser therapy in BPH surgery is to induce thermal injury via laser coagulation and laser vaporization. When the laser beam is concentrated on targeted prostatic tissue, the optical energy is converted to thermal energy, which gradually heats the tissue. During laser coagulation, prostatic tissue is heated with temperatures below 100°C to induce tissue coagulation necrosis, causing sloughing of the prostatic urothelium which ultimately leads to delayed anatomical debulking. Conversely, tissue vaporization occurs when temperatures exceeds 100°C and is usually evidenced by the formation of bubbles during the procedure. Additionally, varying extents of coagulation necrosis is observed beneath the vaporized area as the temperature gradually decreases with increasing distance from the laser source.[14]

Utilizing a 532-nm wavelength emission, the GreenLight laser is preferentially absorbed by oxyhemoglobin and has a lower affinity towards water, allowing vaporization of the highly vascularized transitional zone of the prostate, permitting differentiation with the more avascular prostatic capsule.[15] It has a penetration depth of approximately 0.8 mm and majority of the laser energy is concentrated to the superficial tissues, preventing it from penetrating deep into targeted prostatic tissue. It also has a coagulation depth of 1-2 mm around the areas of vaporization, which is ideal such that it is not too shallow, giving rise to its beneficial and adequate hemostatic properties, but also not too deep allowing for excellent efficacy and decreased postoperative complications. Deep coagulation has been associated with an increased risk of dysuria, irritative symptoms, and bladder neck contractures secondary to tissue sloughing, edema and scarring.[7,16]

Outcomes of the GreenLight PVP

The first 80W KTP prototype showed significant and durable improvements in voiding parameters in BPH patients durable up to 5 years post-procedure.[17] Although retreatment rates were observed at 6.8%-8.9%, initial experience by Ruszat et al further reported that PVP can be safely performed in patients who are on systemic anticoagulation.[18,19] Subsequent upgrading to the 120W HPS and 180W XPS also showed consistent improvements in the International Prostate Symptom Score (IPSS), Quality of Life (QoL), maximum urinary flow rate (Qmax) and post-void residual volume (PVR) parameters regardless of prostate sizes. Furthermore, as described by Spaliviero, PVP was successfully performed as an outpatient procedure in all patients in their series with 70% of patients being discharged home catheter-free.[16,20,21]

When comparing amongst the different GreenLight laser systems, the most recent 180W system has shown to provide more efficient tissue vaporization when compared to earlier generation lasers. While there were no significant differences among postoperative parameters between the 180W XPS and 120W HPS laser, operative and catheterization times appeared shorter among the XPS group.[22,23] Mean quantity of fiber and 3 L saline bags used were also significantly lower in the 180W XPS group.[15] These results suggest that while both GreenLight systems were able to provide safe and effective tissue vaporization with clinical relief of BPH obstruction, the 180W XPS system allows for increased cost savings with regards to both intraoperative materials utilized as well as reduced operative, hospitalization and catheterization times. Indeed, a systematic review by Brunken et al also revealed that among all GreenLight generations, the 180W XPS offered the greatest efficiency of energy and resource utilization, decreased operative times and increased tissue removal, all while minimizing complication rates.[24]

Subsequently, randomized controlled trials comparing the outcomes and safety of the GreenLight to current BPH treatment options have also been extensively conducted. Accruing over 290 patients among 29 sites in nine European countries, the GOLIATH study remains the largest, prospective, randomized controlled trial to date, comparing the 180W XPS PVP to the gold standard TURP. Their study reported comparable and durable outcomes between the GreenLight XPS to TURP with regards to IPSS, Qmax, complication-free rates and storage symptoms even after 2 years. Reintervention rates between the two treatment modalities were also similar at 9.0% for the GreenLight XPS and 7.6% for TURP. Furthermore, patients treated with PVP were found to have a significantly shorter median length of catheterization, hospitalization times and time until stable health while patients undergoing TURP resulted in 5 times more surgical interventions to resolve postoperative bleeding.[25,26]

Other randomized trials comparing the older generation PVP lasers to TURP have also demonstrated similar improvements in Qmax, IPSS, QoL and PVR parameters with maintenance of sexual function.[27] However, when compared to TURP, PVP was found to be cheaper, had shorter catheterization and hospital stays and had fewer perioperative adverse events. In a study by Al-Ansari et al, there were no major intraoperative complications reported or blood transfusions required with the PVP procedure, but among the TURP cohort, 20% required transfusions, 17% suffered capsular perforations and 5% developed TUR syndrome.[28] Ultimately, a meta-analysis conducted by Cornu et al assessing the outcomes and complication rates of transurethral procedures for BPH found that the functional outcomes, namely IPSS, Qmax and PVR, after the 120W PVP procedure were similar to that of the monopolar TURP. However, the PVP has a lower transfusion rate and shorter hospitalization and catheterization time compared to TURP.[29] Table 1 summarizes the available clinical data to date for the GreenLight PVP.

TABLE 1. **Summary table of clinical data to date for GreenLight photoselective vaporization of the prostate**

Endpoint	Time point	Clinical outcomes
IPSS	Baseline	21.2 ± 5.9
	24 mo	6.9 ± 6.0
IPSS-QoL	Baseline	4.6 ± 1.1
	24 mo	1.3 ± 1.2
Qmax (mL/s)	Baseline	9.5 ± 3.0
	24 mo	21.6 ± 10.7
PVR (mL)	Baseline	110.1 ± 88.5
	24 mo	45.6 ± 65.5
Prostate volume (mL)	Baseline	48.6 ± 19.2
	24 mo	23.9 ± 13.0
PSA (ng/mL)	Baseline	2.7 ± 2.1
	24 mo	1.4 ± 1.7
OABq-SF symptoms	Baseline	44.2 ± 20.5
	24 mo	15.3 ± 16.7
OABq-SF health	Baseline	59.0 ± 21.9
	24 mo	88.5 ± 15.8
ICIQ-UI SF	Baseline	3.9 ± 4.7
	24 mo	2.8 ± 4.1
IIEF-5	Baseline	13.2 ± 7.6
	24 mo	12.9 ± 7.5
Complication-free	24 mo	83.6%
Retrograde ejaculation	6 mo	30%-67.1%
Urinary incontinence	12 mo	1%

IPSS = International Prostate Symptom Score
Qmax = maximum urinary flow rate
PVR = post-void residual urine
PSA = prostate-specific antigen
OABq-SF = overactive bladder questionnaire-short form
ICIQ-US SF = International Consultation on Incontinence Questionnaire-Urinary Incontinence short form
IIEF-5 = International Index of Erectile Function-5

Safety profile, durability and adverse events

The main advantage of the GreenLight laser is its effective hemostatic properties and low bleeding rates. This allows it to be a viable treatment option for high-risk patients who are on anticoagulation. While ongoing oral anticoagulation portends a much higher risk of bleeding and is relatively contraindicated in electrocautery TURP or open prostatectomy, GreenLight PVP does not concur that risk.

A study by Ruszat et al reported no occurrence of bleeding complications necessitating blood transfusions in 116 men who underwent PVP on anticoagulation. Postoperative hemoglobin was also not significantly decreased in men on anticoagulation when compared to those who were not.[30] A comparable study by Sandhu et al also demonstrated the safety of PVP among men on systemic anticoagulation with no cases of blood transfusions, hematuria or clot retentions being reported. In their study, serum hematocrit was also not significantly decreased after the procedure (40.0% to 38.3%, $p > 0.05$).[31]

While similar studies have also proven the safety of PVP in men on anticoagulation, Yuan et al performed the PVP among 128 high-risk men and found no major complications or mortalities in men who had high cardiovascular risk, high pulmonary risk, were receiving anticoagulant medication or had a coexisting bleeding disorder.[32-34] Thus, the evidence suggests that the GreenLight PVP procedure can be a suitable and effective treatment option in men on systemic anticoagulation who are at high-risk of significant bleeding.

With regards to durability, functional outcomes after GreenLight PVP has shown to be stable even up to a mean follow up of 5 years with reoperation rates being reported to be as low as 4.8% with the XPS system.[35] Retreatment rates for the 80W KTP and 120W HPS laser, however, were slightly higher (8.9%-14.8%) further suggesting the inefficiency of earlier generation lasers to provide immediate tissue removal.[18,19,28] It is also important to note that addressing larger prostates with the GreenLight PVP requires a certain level of expertise as a high TURP conversion rate has been reported in these patients.[20]

One of the disadvantages to the PVP procedure is that tissue analysis for pathology evaluation is often unavailable due to its vaporization techniques. Conceptually, the risk of missing undiagnosed prostate cancer does exist. However, a recent analysis of the SEER database by Meeks et al found that when patients are screened appropriately with serum prostate-specific antigen (PSA) levels, the risk of missing clinically significant prostate cancer is as low as 0.26%.[36] As such, digital rectal exams, serum PSA screening and prostate biopsies should be performed prior to PVP in patients who at risk for prostate cancer.

Conclusions

Overall, the GreenLight PVP has been shown to be a durable and effective treatment option in treating LUTS secondary to BPH and is especially safe in men on anticoagulation who are at higher risk of bleeding. As such, current consensus guidelines have recommended this procedure in patients on anticoagulants or in high-risk surgical candidates.[3,4] The PVP also has the added advantage of cost savings with decreased catheterization time, hospital stay and can also be performed as an outpatient procedure.

Nevertheless, surgeons should note that being familiar with one laser system may not necessarily translate to expertise with another laser and that techniques and surgical approaches vary widely among different laser systems. However, with the new and improved training curriculum for the GreenLight simulator, trainees can potentially acquire the necessary skills and knowledge to a predetermined level of proficiency.

While ongoing trials and research continue to develop better and improved technologies for the treatment of this highly prevalent disease, the ultimate goal as physicians is to acquire an individualized, shared decision-making process with each patient to determine the ideal treatment option based on patient preference and preoperative parameters.

Disclosures

Dr. Jaspreet S. Sandhu and Joon Yau Leong have no disclosures.
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