Chapter 8
Surgical Treatment: Green Light Laser

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8.1 Introduction

Transurethral photoselective vaporization of the prostate (PVP) has evolved as an electrosurgical adaptation of the classical transurethral resection of the prostate (TURP) in the management of bladder outflow obstruction (BOO). Improvements in Light Amplification by Stimulated Emission of Radiation (laser) technology have shown potential for excellent haemostasis, a reduction in morbidity and good functional outcomes. The increasing role of PVP as a true 'day case' procedure has made it an attractive focus for clinicians and hospital managers in the age of healthcare economics.

The application of lasers in urology has been recognised and incorporated into the EAU and AUA guidelines in selected patients with BOO. TURP remains the transurethral standard for comparison, but in larger prostates, a prolonged resection time is invariably required. Historically, many surgeons would choose an open prostatectomy (OP) in this patient group to avoid the morbidity relating to bleeding and/or possible development of TUR syndrome.

This chapter will address the emerging utility, safety and efficacy profile of PVP as a valid alternative treatment of BOO in men with large prostates, including those over 100 mL, and the challenges that this modality presents.

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8.2 Mechanism of Action

Potassium-titanyl-phosphate (KTP) laser prostatectomy was first described by *Kuntzman* and colleagues in a comparative functional study against a Neodymium:Yttrium-Aluminum-Garnet (Nd:YAG) laser in canines in 1996 [1]. KTP vaporization was found to be significantly superior, with instantaneous reduction in prostate volume and spontaneous post-operative voiding. This was unlike the coagulative necrosis triggered by the Nd:YAG laser: which took weeks for the prostatic tissue to slough off and was often associated with storage symptoms.

GreenLight laser vaporisation differs in technique to laser enucleation of the prostate. Prostatic tissue is entirely vaporised, rather than enucleated and mechanically morcellated. The 532 nm wavelength generated by the KTP crystal falls within the visible green zone of the electromagnetic spectrum; hence 'GreenLight' laser. This accounts for its near exclusive absorption by haemoglobin, and not water; thus its enhanced ability to secure haemostasis within highly vascularised prostatic tissue [2].

The feasibility of the 80 W KTP PVP was subsequently trialled in humans (prostate volumes of 24–76 mL) with BPH by Malek et al. in 1998 [3]. This was replaced by the high-performance system (HPS) GreenLight 120 W (532 nm) laser which was introduced in 2006. GreenLight HPS used a Lithium Triborate (LBO) crystal in the place of KTP [4]. It has been further superseded by the 180 W GreenLight Xcelerated Performance System (XPS) in 2010 (American Medical Systems, Minnetonka, MI). Unlike earlier generations, the MoXy fibre within the XPS is a 750 nm side-firing laser with a 70° forward deflection. It also includes a steel-tipped cap and fibre cooling to prevent overheating and optimise fibre durability (i.e. one fibre per case). Compared to the HPS, the beam surface area is augmented from 0.28 to 0.44 mm^2 [5]. The laser is fired in a quasi-continuous wave laser rapid pulse to elicit vaporisation through a 23–26F cystoscope with normal saline irrigation fluid on continuous flow [6]. Compared to GreenLight HPS in prostate volumes of >80 mL, similar amounts of energy are used in significantly less time ($P = 0.001$) [7]. The ease at which an operative working channel can be created, reduces the risk of excess fluid absorption and dilutional hyponatraemia in these patients.

8.3 Operative Technique

GreenLight PVP can be performed under light general or regional anaesthesia; as there is no risk of TUR syndrome, even in massive prostates [8]; most experts avoid spinal anaesthesia. Unlike TURP, there is not always tissue for histopathological examination at the end of the procedure (transperineal biopsy is simple however if clinically indicated). The technique is non-contact (optimum fibre tissue distance = 1–2 mm). The pilot beam is used to guide the dissemination of energy evenly by a systematic "three-dimensional, sagittal, rotating and lateral motion of the fibre" [6]. An appropriate sweep speed is required to prevent carbonisation and ineffective ablation. Failure to do so may result in overheating and damage of the fibre and/or scope from heat reflection. The vaporisation results in vapour bubbles, which are carried away by the continuous flow setup with gravity inflow and outflow.

There is an increasing availability of validated computer simulation programmes to promote a sustained and standardised level of procedural excellence in GreenLight laser prostatectomies. Training and assessment of operative technique can be undertaken safely for small, medium and large glands (Figs. 8.1 and 8.2). The learning curve of proficiency for GreenLight prostatectomy builds upon fundamental principles of safe transurethral electrosurgical techniques and is comparably less technically challenging than HoLEP [9].

8.4 Adverse Events and Sexual Function

The search for alternative surgical modalities for BPH relates to the ongoing rate of morbidity associated with TURP. Teng et al. undertook a comparative systematic review and meta-analysis of RCTs and non-RCTs (n = 9) evaluating TURP and GreenLight laser PVP outcome data. Overall, the rates of bleeding (requiring

Fig. 8.1 Theatre set up of GreenLight Laser

Fig. 8.2 Creating the working channel with GreenLight Laser intra-operatively

transfusion RR =5.88, 95% CI:1.92–18.3, P = 0.002) capsular perforation (RR = 9.28, 95%CI: 2.79–30.88, P = 0.001) and TUR syndrome (RR =5.31, 95% CI:1.18–23.94, P = 0.003) were shown to be considerably lower in the PVP groups than for those undergoing TURP [10].

Another recent meta-analysis identified six RCTs evaluating PVP with GreenLight HPS 120 W device against monopolar TURP (697 patients). Statistical significance was demonstrated with reduced peri-procedural transfusion rate (OR: 0.10; $P < 0.00001$) and reduced duration of post-operative catheterisation following PVP (mean difference: 32.36 h; $P < 0.00001$). Accordingly, the length of stay was shorter relative to the TURP patients (mean difference: 32.36 hours; $P < 0.00001$). Post-procedural re-catheterisation and urinary tract infection rates were comparable in the two groups [11]. Long-term comparative outcome data were not available between the two groups beyond 12 months in these series. Very few prospective studies have addressed this in large prostates over 100 mL.

A prospective multicentre non-randomised study of GreenLIght XPS showed excellent outcomes and safety in a group of over 200 patients of whom the majority were on some form of ongoing anticoagulation and over a quarter had prostate volumes greater than 80 mL [12].

Skolarikos et al. report outcomes of GreenLight laser prostatectomy (n = 65) compared against a control arm of OP (n = 60) for patients with prostate volumes greater than 80 mL in their prospective RCT. 7.7% of the GreenLight laser group required additional intraoperative conversion to TURP for haemostasis. Overall 18-month follow-up results corroborated with earlier data showing a statistically significant shorter period of hospitalisation and catheterisation post-procedure, with non-inferior functional outcomes for GreenLight laser [13].

One concern is the perceived need for 'retreatment' of patients undergoing GreenLight laser prostatectomy. An RCT by Al-Ansari et al. cited re-operation rates of as high as 11% over 36 months; all were in prostate volumes greater than 80 mL [14]. However the energy used in this study was not reported. Interestingly, 3-year outcome data from an American multicentre evaluation of the technique demonstrated a re-intervention rate for Greenlight HPS of 4.3%, however there was no sub-group analysis of the effect of prostate volume on this rate [15].

The meta-analysis by Teng et al. confirmed a higher re-intervention rate than those in the TURP groups studied (RR = 0.24, 95% CI: 0.10–0.59, $P = 0.002$) [10]. It should be noted however, that although bigger glands may display a correlation with a higher rate of retreatment in initial series, the question for future trials (assessing XPS) should address whether adequate energy per mL of prostate tissue was delivered.

The topic of sexual dysfunction in relation to GreenLight laser prostatectomy in large glands over 100 mL is poorly characterised in the literature. As with all surgical modalities for BOO, this is in part related to the co-existence of LUTS and erectile dysfunction. Theoretically, efficacious bladder outflow obstruction surgery relieves LUTS and thus the need to take 5-ARI and/or alpha blockers, which are associated independently with libido reduction and retrograde/anejaculation respectively. The randomised prospective trial by Horasanli et al. (n = 81) demonstrated similar rates of retrograde ejaculation rates in TURP (56.7%) and GreenLight laser groups (49.9% p = 0.21) at 36-months follow-up [16]. In comparison with HoLEP, the rate of retrograde ejaculation in previously sexually active patients within a prospective RCT was significantly lower in GreenLight PVP (28.5% vs. 88%) [17]. The authors felt this reflected the extent of tissue removal in the two groups.

It has been postulated that laser ablation of prostatic tissue, which requires augmented laser energy per unit of prostate, may have a detrimental effect on adjacent cavernous nerves and thus influence sexual function. This is thought to be due to increased transmitted heat which may extend beyond the penetration depth of the laser [18]. Capsular perforation is known to be an independent risk factor for erectile dysfunction in prostatic resection; the extent of penile nerve damage has been established in previous studies evaluating TURP with neurophysiological testing [19].

Elshal et al., in a longitudinal study, propose that post-operative erectile dysfunction is perceived to be more significant in patients with previously normal function prior to GreenLight Laser prostatectomy [18]. This effect has not been confirmed in other multicentre studies which have stringently assessed sexual function. Contemporary erectile dysfunction rates are reported as less than 1% with GreenLight PVP [12, 20] a rate which is reflected in our own clinical practice. We do however support the role of pre-operative sexual function assessment and counselling for all patients.

8.5 Photoselective Vaporization of the Prostate in the Very Large Prostate

There remains distinct heterogeneity in the literature regarding the exact definition of a 'large' prostate. Big glands are associated with a rapid rate of adenomatous enlargement [21, 22]. There is no consensus on exactly how prostate volume should determine surgical approach.

Data specifically examining the use of PVP in the larger prostate is limited. Rajbabu et al. published a contemporary prospective series of 54 patients with BOO whose prostates were greater than 100 mL in size (mean: 135 mL, range 100–300 mL). Their results confirmed that the 80 W KTP laser PVP led to sustained improvements in flow rate. The mean (SD) improvement in Qmax was 8.0 (3.1) to 18.2 (8.1), 18.5 (9.2), 17.9 (7.8) and 19.3 (9.8) mL/s at 3, 6, 12 and 24 months respectively. The IPSS and Quality of life scores demonstrated a similarly favourable trend post-procedure [23]. Despite using only the 80 W laser and despite many of these patients having significant co-morbidities, excellent safety and medium-term results were demonstrated.

At the time of writing, the GOLIATH study is the only published multicentre, multinational RCT to evaluate the XPS 180 W PVP. This was found to be non-inferior to TURP in relation to functional outcomes of IPSS, Qmax and complication rates at 6 months [24]. Subsequent 2-year follow up data [20] confirmed consistent durable effectiveness and safety compared to TURP, irrespective of prostate size. It should be noted however, that men with prostates larger than 100 mL were excluded from this study on the basis of TURP being potentially unsafe for them. GLXPS (n = 136): mean prostate volume: 48.6 mL ± 19.2 mL (SD) versus TURP (n = 133) mean volume: 46.2 ± 19.1 mL (SD). Nonetheless, bleeding related complications and recovery were significantly better in the GreenLight laser group.

Early results from a small (n = 35), single centre series using 180 W GreenLight PVP in prostates greater than 100 mL (median: 132, Range: 118-157 mL) retrospectively reported promising equivalent outcomes to previous trials comparing PVP with the other modalities of TURP and OP at 3 and 6 months. Of note, 31% of this cohort were taking anticoagulants (which were not withheld). There were no blood transfusions required in this series [25].

Araki et al. undertook a prospective evaluation of GreenLight laser in patients on medical therapy for BPH. It has previously been suggested that the downregulation of prostatic angiogenesis in patients on long term 5-alpha reductase inhibitors may affect the efficiency of GreenLight laser usage. This study demonstrated no significant difference in laser time/total energy usage and comparable outcomes in the presence and absence of 5-ARI supplementation [26].

The effectiveness of GreenLight in patients on anticoagulation has generated interest amongst researchers. Sandu et al. undertook a retrospective cohort analysis of 24 men with a mean prostate volume of 82 cc (range 34–164 cc). Each was in receipt of anticoagulation and underwent GreenLight laser PVP. Warfarin was held for 2 days pre-operatively, aspirin and clopidogrel were not stopped in the remaining patients. None of these high-risk cardiac patients had clinically significant haematuria, clot retention or thromboembolic events post-operatively. All patients were discharged within 23 h and 92% of men had successful trial without catheter prior to discharge [27].

More recently, the outcome data from GreenLight laser PVP in specific patient groups was published from a larger multi-centre prospective study (n = 305) by Woo et al.; it included anticoagulated patients (n = 62) and those with prostate volumes of >80 mL (n = 52); (mean = 118.4 mL, SD = 34.9 mL). There was a 233.3% improvement in Qmax for patients with prostate volumes greater than 80 mL (mean: 5.8 mL/s SD: 3.4) at baseline compared to follow up at mean follow up of 4.2 months (mean: 19.7 mL/s SD: 9.1). 185% improvement was reported in those with a prostate volume of less than 80 mL at baseline (mean: 7.6 mL/s SD 4.4) and at follow up (mean: 21.7 mL/s SD: 10.3).

Clavien-Dindo complications (>2) were comparable in prevalence in both small and larger prostates. There was no statistical difference in functional outcome between those taking versus not taking anticoagulation. There was a 50.8% reduction in prostate volume for those on anticoagulation (mean 72.7 mL SD 36.8 at baseline and 35.8 SD16.2 at follow up), and a 44.2% reduction for those not on anticoagulation (mean: 58.2 SD 33.1 and 32.5 SD 17.4 at baseline and follow up respectively). There was no significant difference in length of stay and period of catheterisation post-procedure between prostate volume groups [28].

Although this study was limited by its mean follow-up time of 4.2 months, it was concluded that unlike TURP, anticoagulation is not a contraindication for GreenLight laser prostatectomy and should be considered routinely in high risk cardiac patients.

In our experience, increasing prostate size correlates with an increase in operative duration and energy utilisation with GreenLight Laser PVP. This has significantly improved with the introduction of the 180 W XPS laser fibre and will continue to do so with ongoing modifications. We believe that the key technical consideration in managing prostates >100 cc is the creation of the working channel to optimise irrigation flow and thus vision (Fig. 8.3). This can be achieved following early vaporisation of occlusive lateral lobes. If a significant middle lobe is evident, avoid undue pivotal movements at the bladder neck as this can precipitate bleeding and impair the visual field. Sometimes, visualisation of the ureteric orifices must be deferred until the middle lobe has been reduced.

We believe that any surgeon proficient in TURP would find it straightforward to adapt to the GreenLight laser technique, following demonstration of competency in the simulation setting. It is important that the surgeon is patient when commencing GreenLight laser, as the sweep speed required is slower and working distance increased compared to that associated with a loop resectoscope. The mechanics of the technique involve co-ordination of the dominant and non-dominant hands to control the scope and fibre respectively. We recommend from experience that larger glands should not be tackled until fully confident operating on smaller prostates.

The EAU guidelines support GreenLight laser as a “safe method for volume reduction in large sized prostate glands” and “safe and effective for patients receiv-

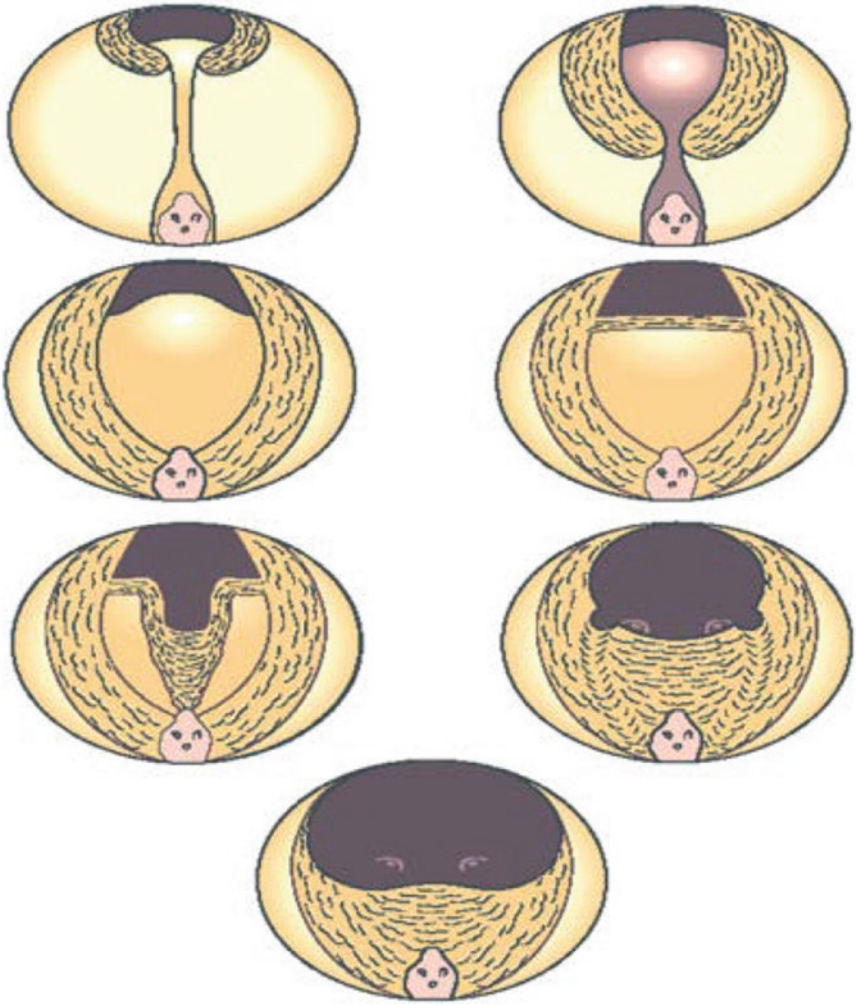

Fig. 8.3 Schematic for creating the working channel with GreenLight laser: An adaptation of the IGLU (International GreenLight Users group) modular technique [4]

ing anticoagulation medication or patients in retention" [29]. In 2016, The National Institute of Health and Clinical Excellence (NICE) issued a resource impact report in which GreenLight XPS was compared with TURP. Cost-modelling analysis estimated a cost-reduction potential of £60 per GreenLight patient. Extrapolating their data on the basis of proportional day case procedures in low-risk patients for both modalities, they predicted an annual saving with PVP of £2.3 million in NHS England [30]. Table 8.1 describes the advantages and disadvantages of GreenLight PVP compared to conventional TURP.

Table 8.1 Advantages of GreenLight PVP versus conventional TURP

Advantages	Disadvantages
True day case operation. Can treat large glands in single procedure	Long term follow up data awaited regarding sustained benefit of PVP
Safe in patients on anticoagulation	MoXy Fibre cannot be used for laser lithotripsy
No risk of TUR syndrome in spite of prolonged vaporisation time in large prostates	TURP skills not directly transferrable. Surgeons need additional simulation training to overcome the learning curve
Catheter free within 24 h	

8.6 Discussion

The ‘big prostate’ remains a significant benign urological pathology, commonly requiring surgical intervention. The number of patients referred for operative management is likely to increase with an ageing population. Within an elderly population, the proportion of men with significant comorbidities who need surgery is likely to increase. It is not uncommon that patients referred for surgery are on long-term anticoagulation. A modality such as GreenLight Laser, which affords a reduced risk of bleeding that negates the need for bridging therapy and demonstrates comparable functional outcomes in a day case setting is an exciting prospect.

In an ideal world, emerging prospective, well-designed RCTs would directly compare GreenLight laser prostatectomy against all operative modalities for large volume BPH. Funding and cohort heterogeneity make recruitment difficult. Current outcome data available support the efficacious, non-inferiority of laser ablative therapy in the management of large prostates in the long-term. Table 8.2 describes some of the main studies comparing Greenlight PVP with other treatment modalities for the large prostate.

As with the adoption of any new surgical technique, the use of simulation in the context of a formal, certified training programme with synchronous mentorship, is recommended to improve the procedure-specific aptitude, safety profile and confidence of the surgeon undertaking GreenLight laser prostatectomy in large prostates.

It could be argued that patients with very large prostates should only be managed in centres where a number of the modern management techniques for large prostates are offered. We believe that a bespoke approach respecting each patient’s status and aspirations will allow the best outcomes in this difficult group of patients.

8.7 Conclusion

GreenLight laser is a very safe option even for men with significant co-morbidities and can be offered to almost any man with LUTS or retention regardless of prostate size or general health status. In both of our centres it is routine to manage high risk and anticoagulated patients with prostates over 100 mL as outpatient day case

Table 8.2 Comparative GreenLight PVP studies in large prostates/high risk patients

Trial	Number of patients and trial design	Main inclusion/ exclusion criteria	Intervention(s)	Relevant outcomes
Bachmann et al., Thomas et al. (GOLIATH trial) 2014 and 2016 [20, 24]	n = 281 Multicentre Randomised, non-inferiority comparative trial	Prostates >100 cc excluded from trial	GreenLight XPS 180 W PVP or TURP	GLXPS non-inferior to TURP for IPSS, Qmax and complication rate at 6 and 24 month follow up
Woo et al. 2008 [28]	n = 305 Multicentre prospective study	Subgroup analysis: 63 patients in urinary retention, 70 patients on anticoagulation, 52 patients with prostate volume > 80 cc	GreenLight HPS 120 W	GLHPS is Safe and efficacious in patients on anticoagulation with comparable short term complication rates
Skolarikos et al. 2008 [13]	n = 125 Randomised prospective study	Prostates >80 cc included	GreenLight PVP or Open Prostatectomy (OP)	Shorter hospital stay, length of catheterization, perioperative blood loss and equivocal short term functional outcomes in GLPVP vs. OP
Rajbabu et al. 2007 [23]	n = 53 Single centre prospective study	Prostates >100 cc (mean 135, range 100–300) included	GreenLight KTP 80 W	Mean catheterization time 23 h (0–72 h) Sustained favourable IPSS and Qmax at 2 year follow up

procedures, often sending even these patients home without a catheter. Risks of bleeding, perforation and incontinence are very small. The early benefits need to be set against what will likely be a longer-term re-operation rate that is higher than for full laser enucleation. However for those more elderly men the rates of reoperation at 10–20 years may not be as important.

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