Laser treatment of benign prostate enlargement—which laser for which prostate?

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Abstract | Laser-based prostatectomy for benign prostatic obstruction has emerged over the past decade as a treatment alternative to transurethral resection of the prostate (TURP) and open prostatectomy. These techniques set new standards in minimally invasive surgery and aim to obviate the complications of open surgery while ensuring durability of outcomes. Enucleation, which mimics open prostatectomy in that the whole prostate adenoma is removed, and vaporization, which involves ultra-rapid heating of superficial tissue layers and subsequent ablation, are the most often used surgical techniques in laser prostatectomy. The wavelength and the power output of the laser influence the tissue–laser interactions, which determine the physical properties and the safety profile of the technique. Holmium laser enucleation of the prostate (HoLEP) and GreenLight™ laser vaporization of the prostate are the two reference techniques for laser prostatectomy, both of which have been shown to be as effective as TURP, while offering advantages in the safety profile in various randomized trials. Thulium laser enucleation of the prostate (ThuLEP) shares similarities with HoLEP and has shown encouraging results. However, more controlled trials with longer follow-up assessment are needed. Diode lasers come in various wavelengths and fibre designs and have been used for vaporization and enucleation, but require high-quality data to support their clinical use.

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Introduction

For decades, urologists presumed that 'complete' removal of adenomatous prostatic tissue was the only way to provide symptom relief for patients with benign prostatic obstruction (BPO). Accordingly, much effort was put into developing surgical techniques; the invention, development and widespread adoption of transurethral resection of the prostate (TURP) represented an important paradigm shift in urology.[1–3] During this procedure, a wire loop with an electrical current flowing in one direction (that is, monopolar TURP) is used to cut the prostatic tissue through a resectoscope; bipolar TURP uses bipolar current to remove the tissue. TURP was accepted as a minimally invasive alternative to open prostatectomy without any supporting data from randomized trials. Further reflecting the field's interest in minimally invasive surgery, ongoing technical progress over the past several decades has led to the development of small transistors, microchips and video-based techniques in endourology, which were all 'stepping stones' to modern laser-based applications in urological surgery.

The gold-standard method for the surgical treatment of male lower urinary tract symptoms (LUTS) due to urethral obstruction is TURP for prostates <80 ml in volume and open prostatectomy for prostates >80–100 ml in volume.[4] However, these techniques can be associated with significant morbidity and mortality. For example, TUR syndrome occurs after the absorption of irrigating fluid during surgery, which can cause hyponatraemia leading to dizziness, vomiting and seizure; its incidence in contemporary series of monopolar TURP is low (<1%) and has not been reported for bipolar TURP.[5,6] Clot retention has been reported to occur in approximately 6% of patients after both monopolar TURP and bipolar TURP.[5] In contemporary series, the mortality rate after open prostatectomy has been reported to be <0.25%, blood transfusions are required in 7–14% of patients and late complications, including urinary incontinence, bladder neck stenosis and urethral stricture, occur in fewer than 10% of men.[4,7–11]

Although complications with TURP are rare, improving safety while maintaining surgical efficacy is a priority in endourology. To that end, laser techniques for the treatment of BPO have been actively pursued, particularly in the past decade, as they offer increased safety and surgical efficacy. Early neodymium-doped yttrium aluminium garnet (Nd:YAG)-based laser systems were developed for visual laser ablation of the prostate and interstitial laser coagulation of the prostate (Box 1), but were unable to immediately ablate prostatic tissue.[12,13]

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Competing interests
A.B. is a company consultant for American Medical Systems, Orion Pharma, Schering, Olympus, and Caris Life; receives company speaker honoraria from American Medical Systems, Ferring, and Bayer; participates in trials for AstraZeneca, Pfizer, and American Medical Systems; and receives research grants from AstraZeneca and Pfizer. M.R. declares no competing interests.

Key points

- Laser techniques are increasingly being used in favour of transurethral resection of the prostate (TURP) and open prostatectomy as a treatment for benign prostatic obstruction
- Several laser-based surgical methods have been developed, using different wavelengths of light that have different physical properties and, accordingly, different uses in the clinic
- Laser enucleation with the holmium laser and green light laser vaporization lead to immediate improvement of voiding symptoms and parameters comparable to TURP
- With regard to intra-operative safety, green light laser vaporization seems to be superior to TURP
- Thulium laser enucleation shows encouraging results regarding efficacy and safety and early functional outcomes appear comparable to TURP
- Early diode lasers were associated with increased postoperative complications; in later models a trend towards enucleating techniques with less morbidity can be noticed

Box 1 | Key terms in laser-based surgery of the prostate

Visual laser ablation
Early and largely abandoned laser technique to ablate prostate tissue by heating the tissue with a laser beam

Interstitial laser coagulation
Early and largely abandoned laser technique where laser probes were introduced into prostatic tissue to induce coagulation necrosis

Enucleation
Surgical removal of the entire adenomatous tissue of the prostate

Vaporization
Surgical removal of prostate tissue by heating above the boiling point of water

Morcellation technique
Surgical technique that uses a device to crush and remove enucleated prostate tissue

Vaporesection
Surgical removal of prostate chips by incisions with a laser that also vaporizes prostate tissue

Vapoenucleation
Surgical removal of the entire adenomatous tissue of the prostate with a laser that also vaporizes prostate tissue to some extent

Furthermore, deep tissue necrosis led to long-lasting storage symptoms, such as frequency and urgency, and high reoperation rates; thus, these early laser techniques have been abandoned. The currently available laser systems differ strongly from these early techniques as they offer immediate tissue ablation. Every available system has an individual laser–tissue interaction, such that the common nomenclature of 'laser prostatectomy' should be avoided. In reality, contemporary surgical techniques can be divided into two major approaches: enucleation and vaporization. Enucleation mimics the technique of open prostatectomy, as tissue dissection is close to the surgical capsule of the prostate, whereas vaporization induces ultra-rapid heating of superficial tissue layers with subsequent ablation.

In this Review, we provide a comprehensive, evidence-based overview of laser treatment for men with BPO. We describe the physical properties of lasers that lend themselves to prostatic surgery and describe the clinical differences between the techniques. Patient selection is also described, as each laser-based technique has implications pertinent to individual patients' risk profiles.

Laser physics

Laser is an acronym of 'light amplification by stimulated emission of radiation'. Laser radiation is characterized as having a defined wavelength and direction, and can be generated by various materials. In the treatment of BPO, that material is either a crystal—such as holmium:yttrium aluminium garnet (Ho:YAG), thulium:yttrium aluminium garnet (Tm:YAG), potassium titanyl phosphate and lithium triborate—or a semiconductor (that is, diode lasers). The medium and the excitation source (electric current) determine the wavelength and the emission mode of each laser type, which can be either continuous or pulsed.[14] The optical fibre delivers the laser radiation to the tissue. Depending on the type of laser and fibre, the laser beam either leaves the fibre at the tip (front-firing fibre) or on the side (side-firing fibre; that is, deflected by 70°).

The interactions between the laser and tissue depend on the wavelength of the laser radiation, which in turn determines how much energy is absorbed by the tissue.[15] Energy is absorbed by the tissue via its relevant chromophores, which in the prostate are water and haemoglobin. The absorption coefficients of water and haemoglobin change according to the laser wavelength, which results in differing energy absorption between laser types. The energy absorbed by prostatic tissue leads to intracellular temperature increases, which, depending on speed and resultant temperature, can result in coagulation, vaporization or carbonization of tissue. For example, a high absorption coefficient leads to an ultra-quick increase in temperature at the tissue surface, which in turn results in disruption of cell structures owing to the increased intracellular pressure (vaporization).[14] By contrast, a low absorption coefficient leads to a less-intense temperature increase and results in coagulation.[14] Every laser that is used in the treatment of BPO can in fact vaporize and coagulate the tissue; however, the rate of induced vaporization and coagulation differs significantly between laser sources owing to the physical properties of each laser (Figure 1 and Table 1). For laser systems operating near the infrared end of the spectrum (1,064 nm)—that is, at long wavelengths—the tissue penetrance is deeper than for lasers that operate at shorter or longer wavelengths.

Clinical application of lasers

Aside from important theoretical laser characteristics associated with wavelength, many additional factors influence the clinical suitability and applicability of a laser for transurethral laser prostatectomy. During surgery, the laser fibre is positioned at variable distances relative to the tissue surface, which is determined by surgical technique. Furthermore, the tissue surface itself changes in appearance depending on how it reacts to the laser; which might lead to changes in laser–tissue interaction. In addition, the temperature of the irrigation fluid, the maximum power used and the speed of cutting (or vaporization) influence the clinical use of each laser.

Compared with outdated laser techniques, the current generation of lasers is high powered and able to ablate

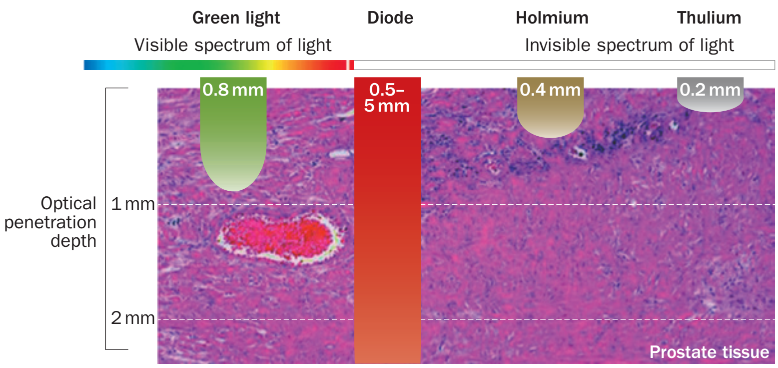

Figure 1 | Optical penetration depth of different lasers in prostate tissue. The penetration depth of each laser depends on laser–tissue interaction, which is determined by various factors such as laser wavelength and power output. Thulium-based lasers have the shallowest penetration depth, whereas diode lasers penetrate the deepest.

prostatic tissue immediately. The two reference lasers most often used in clinical practice and in academic research are the holmium laser, which is optimized for tissue incision, and the GreenLight™ (American Medical Systems, Minnetonka, USA) laser, which is optimized for tissue vaporization. With both systems, immediate de-obstruction of the prostatic urethra can be achieved. Other laser systems, such as the thulium or diode lasers, can be used in hybrid techniques with a mixture of incision, coagulation or vaporization, but neither of these lasers are comparable to the cutting-optimized holmium laser or the vaporization-optimized GreenLight™ laser.

Holmium laser enucleation of the prostate

The Ho:YAG laser operates at a wavelength of 2,140 nm in a pulsed mode with a front-firing fibre. The shallow penetration depth of 0.4 mm leads to a high energy density in the superficial prostate tissue and enables precise tissue incision. Use of the Ho:YAG laser in prostate surgery was first introduced in 1996 for holmium laser resection of the prostate.[16] The first report on the morcellation technique was published 2 years later, making holmium laser enucleation of the prostate (HoLEP) possible.[17] Adenoma enucleation might be considered the ideal technique for entire adenomatous prostate tissue removal, given that all adenomatous tissue is removed, but it remains debatable whether complete removal of the gland is necessary. Although HoLEP has been investigated in multiple studies,[18] the majority of these publications are based on repetitive data collection from a few centres worldwide.[18,19] Furthermore, none of these studies was powered to assess long-term outcomes. Accordingly, numerous studies, often covering the same patient cohorts, have compared HoLEP with monopolar TURP,[20–33] bipolar TURP,[34,35] open prostactectomy,[7,8,25,36] thulium laser enucleation of the prostate (ThuLEP),[37] holmium laser bladder neck incision[38] and photoselective vaporization (Table 2).[39]

Meta-analyses uniformly favour HoLEP over TURP with respect to catheterization time, length of hospital stay, blood loss and requirement for blood transfusion, but operative time is longer and postoperative dysuria occurs more frequently after HoLEP.[18,40,41] The functional outcomes after HoLEP—including symptom improvement, maximum urine flow (Q_{max}) and post-void residual volume (PVR)—are at least comparable to TURP.[18] One study has provided long-term evidence of HoLEP efficacy and safety, with a follow-up duration of 7 years for 31 of 61 patients enrolled.[23] According to this limited data pool, no significant differences were observed regarding symptom improvement, but reoperation rate was higher in the TURP arm (no reoperations versus three reoperations).[23] The incidence of erectile dysfunction was comparable after 1 year of follow-up monitoring and after 7 years. Although this single study clearly does not fulfil the criteria for high-level

Table 1 | Laser types and techniques for laser prostatectomy

Wavelength (nm)	Mode of operation	Optical penetration depth (mm)	Predominant surgical technique	Brand name, manufacturer
Ho:YAG				
2,140	Pulsed	0.4	Enucleation	VersaPulse® PowerSuite™, Lumenis (Palo Alto, USA); Auriga® XL, StarMedTech (Starnberg, Germany)
Tm:YAG				
2,000	Continuous	0.2	Enucleation; vapoenucleation	RevoLix®, LISA Laser (Katlenburg, Germany)
1,900	Continuous	0.2	Enucleation; vapoenucleation	Vela® XL, StarMedTech (Starnberg, Germany)
Green light				
532	Quasicontinuous; continuous	0.8	Vaporization	GreenLight™ KTP, HPS and XPS, all American Medical Systems, (Minnetonka, USA); Greenlaser, Realton (Beijing, China)
Diode				
980, 1,318 or 1,470	Continuous	0.5–5.0	Vaporization; enucleation	Diolas, Limmer Laser (Berlin, Germany); Ceralas®, Biolitec (Jena, Germany); Eraser, Rolle and Rolle (Salzburg, Austria)

Abbreviations: Ho:YAG, holmium:yttrium aluminium garnet; Tm:YAG, thulium:yttrium aluminium garnet.

Table 2 | Selected randomized trials of HoLEP

Study	Study design (*n*)	Follow-up (months)	Intraoperative complications	Reintervention or reoperation	Functional outcomes		
					IPSS	PVR	Q_{max}
Ahyai *et al.* (2007)[20,33]	HoLEP (100) vs monopolar TURP (100)	36	Comparable	HoLEP: 8.2% TURP: 6.6%	Comparable	Favours HoLEP	Comparable
Gilling *et al.* (2012)[23,31,32]	HoLEP (14) vs monopolar TURP (17)	84	Comparable	HoLEP: 0% TURP: 17.6%	Comparable	Comparable	Comparable
Gupta *et al.* (2006)[24]	HoLEP (50) vs monopolar TURP (50) vs TUVRP (50)	12	Comparable	HoLEP: 2% TURP: 4% TUVRP: 2%	Comparable	Comparable	Comparable
Montorsi *et al.* (2008)[21,27,28,30]	HoLEP (52) vs monopolar TURP (48)	12	Comparable	HoLEP: 3.8% TURP: 10.4%	Comparable	NR	Comparable
Chen *et al.* (2013)[34]	HoLEP (140) vs bipolar TURP (140)	24	Comparable	HoLEP: 0.7% TURP: 1.4%	Comparable	Comparable	Comparable
Fayad *et al.* (2011)[35]	HoLEP (30) vs bipolar TURP (30)	6	Comparable	NR	Comparable	Comparable	Comparable
Kuntz *et al.* (2008)[7,25,36]	HoLEP (60) vs OP (60)	60	Favours HoLEP	HoLEP: 15% OP: 15%	Comparable	Comparable	Comparable
Naspro *et al.* (2006)[8]	HoLEP (41) vs OP (39)	24	Favours HoLEP	HoLEP: 10.8% OP: 8.5%	Comparable	NR	Comparable
Zhang *et al.* (2012)[37]	HoLEP (62) vs ThuLEP (71)	18	Comparable	HoLEP: 0% ThuLEP: 0%	Comparable	Comparable	Comparable
Elmansy *et al.* (2012)[39]	HoLEP (43) vs 120 W GLV (37)	12	Comparable	HoLEP: 0% GLV: 5.4	Comparable	Favours HoLEP	Favours HoLEP

Abbreviations: GLV, GreenLight™ vaporization; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; NR, not reported; OP, open prostatectomy; PVR, postvoid residual volume; Q_{max}, maximum urine flow; ThuLEP, thulium laser enucleation of the prostate; TURP, transurethral resection of the prostate; TUVRP, transurethral vaporesection of the prostate.

evidence, intermediate follow-up[7,20] data of another study suggest that no worsening of symptoms is expected after 10 years.

Historically, surgical treatment of men with prostates larger than 80–100 ml was limited to open prostatectomy. Because open prostatectomy has been associated with significant morbidity, two groups have compared HoLEP with open prostatectomy in patients with prostate volumes >70 ml[8] and >100 ml,[7,36] reporting results 6 months,[36] 2 years[8] and 5 years[7] after the procedures. Catheterization time and hospital stay were significantly shorter, and blood loss and the need for blood transfusions significantly lower, after HoLEP than the open procedure; however, again, operative time was longer for, and postoperative dysuria more frequently reported after, HoLEP. Improvements in symptoms, Q_{max} and PVR were comparable; the 5-year reoperation rate was 5% and 6.7% after HoLEP and open prostatectomy, respectively.[7] However, these figures do not include additional reoperations owing to arterial bleeding in the early postoperative phase, which occurred in 5% of the patients undergoing HoLEP and 5% of those undergoing open prostatectomy.[7,36] Finally, the postoperative changes in erectile function over the course of 2 years were comparable.[8] Thus, HoLEP can be regarded as a safe and effective treatment option for men with large prostates.

In a prospective randomized trial comparing HoLEP and ThuLEP, 133 patients were randomly assigned and followed-up for 18 months.[37] Although the mean operating time was approximately 10 minutes longer with ThuLEP, the functional outcomes of the patients were comparable between techniques. Another prospective randomized trial compared HoLEP with GreenLight™ vaporization of the prostate (GLV; using the 120 W GreenLight™ HPS laser) in 80 patients with a prostate volume >60 ml.[39] Operative time and catheterization time were comparable; however, conversion to TURP or HoLEP because of bleeding was necessary in 21.6% of the GLV cases, whereas no conversion was necessary in those undergoing HoLEP. As these results differ considerably from previously published GLV series,[42] this single-centre study should be interpreted with caution. Finally, within a follow-up period of 1 year, symptom improvement was comparable between the HoLEP and GLV groups, but improvements in Q_{max} and PVR were higher after HoLEP.[39]

The largest single-centre experience encompassing 1,065 patients treated with HoLEP within a time span of 11 years reported a total intraoperative and early postoperative complication rate of 2.3%.[43] Another HoLEP single-centre study including 330 consecutive patients reported bladder mucosa injury in 5.7%, reintervention for bleeding in 2.4%, persistent stress incontinence in 0.6% and reintervention for residual adenoma in 2.7% of the patients.[44] These positive results were confirmed by another cohort study including 949 patients; bladder neck contracture, urethral stricture and reoperation owing to residual adenoma developed in 0.8%, 1.6% and 0.7% of patients, respectively (Table 3).[45]

HoLEP has also been reported in patients who are at increased risk of bleeding (Table 4). In a retrospective

Table 3 | Selected case series of laser prostatectomy

Study	*n*	Mean prostate volume (ml)	Mean follow-up (months)	Urinary retention (%)	Perioperative complications	Surgical reintervention	Functional outcomes
HoLEP							
Elmansy *et al.* (2011)[45]	949	81	62	36	Blood transfusion: 0.4%	Urethral stricture: 1.6% Bladder neck contracture: 0.8% Adenoma: 0.7%	IPSS, QoL, Q_{max} and PVR improved
Krambeck *et al.* (2013)[43]	1,065	99	9.5	38.7	Clot retention: 0.7%	Urethral stricture: 1% Bladder neck contracture: 0.7% Adenoma: 0.1%	IPSS, QoL, Q_{max} and PVR improved
Vavassori *et al.* (2008)[44]	330	62	36	11.5	Blood transfusion: 0%	Bleeding: 2.4% Urethral stricture: 3% Bladder neck contracture: 0.6% Adenoma: 2.7%	IPSS, QoL, Q_{max} and PVR improved
ThuVEP							
Gross *et al.* (2013)[52]	1,080	51	NR	21.6	Blood transfusion: 1.7% Clot retention: 3.5%	Bleeding: 2.0% Adenoma: 2.7%	Q_{max} and PVR improved
GLV							
Bachmann *et al.* (2012)[72*]	201	68	5.8	25.4	Blood transfusion: 0% Clot retention: 0%	Bleeding: 0% Urethral stricture: 1.3% Bladder neck contracture: 0% Adenoma: 0.5%	IPSS, QoL, Q_{max} and PVR improved
Hai *et al.* (2009)[61‡]	246	55	60	NR	NR	Bladder neck contracture: 1.2% Adenoma: 7.7%	IPSS, QoL, Q_{max} and PVR improved
Ruszat *et al.* (2008)[42‡]	500	56	30	11	Blood transfusion: 0.4%	Bleeding: 0.6% Urethral stricture: 4.4% Bladder neck contracture: 3.6% Adenoma: 6.8%	IPSS, QoL, Q_{max} and PVR improved
DiVAP							
Erol *et al.* (2009)[85§]	47	51	6	NR	Blood transfusion: 0%	Bleeding: 2.2% Urethral stricture: 0% Bladder neck contracture: 0% Adenoma: 0%	IPSS, QoL, Q_{max} and PVR improved
Ruszat *et al.* (2009)[80||]	55	65	6	29	Blood transfusion: 0% Clot retention: 0%	Bleeding: 0% Urethral stricture: 0% Bladder neck contracture: 15% Adenoma: 0% Necrosis: 18%	IPSS, QoL, Q_{max} and PVR improved
Yang *et al.* (2013)[83#]	120	63	7	NR	Blood transfusion: 1.3%	Bleeding: 1.3% Urethral stricture: 1.3% Bladder neck contracture: 0.8%	IPSS, Q_{max} and PVR improved

*180 W GreenLight™. ‡80 W GreenLight™. §Laser at 132 W and 980 nm. ||Laser at 200 W, 980 nm. #Laser at 80 W, 980 nm. Abbreviations: DiVAP, diode laser vaporization of the prostate; GLV, GreenLight™ vaporization; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; NR, not reported; PVR, postvoid residual volume; Q_{max}, maximum urine flow; QoL, quality of life; ThuVEP, thulium laser vapoenucleation of the prostate.

study of 76 patients—25 of whom were taking aspirin, 13 were taking coumadin and one was taking clopidogrel—the complication rates were comparable between the groups. Notably, the study is limited by the fact that all but two patients taking coumadin had an international normalized ratio (INR) <2.0; thus, further data supporting the safety of HoLEP in patients at increased risk of bleeding are definitely required.[46] The risk of capsule perforation caused by the fibre and subsequent bleeding control in these patients—and the limited coagulation capacity of the HoLEP wavelength compared with other lasers—is the reason why HoLEP is not regarded as the ideal technique in this cohort. On the basis of published data, HoLEP is suited as surgical treatment for prostates of all sizes. However, experience is limited in patients at high risk of bleeding.

Thulium laser vaporesection and enucleation

The emitted wavelength of Tm:YAG lasers is approximately 2,000 nm and can be used for both resection and enucleation of the prostate. The target chromophore of the laser is water, and its penetration depth of only 0.2 mm results in high energy density in the tissue, leading to rapid vaporization and carbonization.[14] The laser operates with a front-firing fibre and has a continuous wave mode, which enables precise incision of the tissue. Unlike HoLEP, the Tm:YAG laser fibre has a red tip that is visible to the naked eye and does not use pulsation, which increases its ease of use. Several techniques have been described for the application of the thulium laser in prostate surgery: vaporization (ThuVaP), vaporesection (ThuVaRP), vapoenucleation (ThuVEP) and enucleation (ThuLEP).[47] No one

Table 4 | Safety of laser prostatectomy in patients at increased risk of bleeding

Study	Technique	*n*			Perioperative blood transfusion			Surgical revision*		
		Aspirin	Clopidogrel	Coumadin	Aspirin (%)	Clopidogrel (%)	Coumadin (%)	Aspirin (%)	Clopidogrel (%)	Coumadin (%)
Tyson *et al.* (2009)[46]	HoLEP	25	1	13	0	0	0	0	0	0
Netsch *et al.* (2013)[54]	ThuVEP	32	8	16	6.3	12.5	6.25	9.4	12.5	25
Chung *et al.* (2011)[67]	GLV‡	101	19	31	0	0	6.5	2.0	5.3	6.5
Ruszat *et al.* (2007)[63]	GLV§	71	9	36	0	0	0	0	0	0
Woo *et al.* (2011)[71,78]	GLV‡	NR	18	43	NR	0	0	NR	0	2.3
Ruszat *et al.* (2009)[80]	DiVaP‖	20	6	26	0	0	0	0	0	0

*Or readmission within 3 months of surgery due to bleeding. ‡Laser at 80 W and 120 W. §Laser at 80 W. ‖Laser at 200 W, 980 nm. Abbreviations: DiVAP, diode laser vaporization of the prostate; GLV, GreenLight™ vaporization; HoLEP, holmium laser enucleation of the prostate; NR, not reported; ThuVEP, thulium laser vapoenucleation of the prostate.

technique has been shown to be superior so far. However, a trend towards increased use of enucleating techniques has been noted,[47] probably because the continuously operating laser beam makes for simple handling during enucleation.

Prospective randomized trials have been reported that compare ThuVaRP and monopolar TURP,[48,49] ThuVaRP and bipolar TURP,[50] ThuLEP and bipolar TURP[51] and ThuLEP and HoLEP (Table 5).[37] Additionally, large case series have reported outcomes from experienced centres.[52,53] As many of these studies have methodological flaws, such as lack of sample size calculation, these results must be interpreted with caution. Another major drawback is the lack of data from prospective randomized trials with >18 months of follow-up monitoring. Given these caveats, some conclusions can be drawn regarding safety. Compared with monopolar TURP, ThuVaRP was shown in one study to be superior in terms of catheterization time, hospital stay and drop in haemoglobin levels, whereas operating times were comparable.[48] Furthermore, two patients required blood transfusion and one experienced TUR syndrome after monopolar TURP, whereas none of these events occurred after ThuVaRP. The functional outcomes and sexual function at 1 year were comparable between techniques.[48] Another study randomly assigned 100 men with BPO to either ThuVaRP or bipolar TURP and followed-up the participants for 3 months. Although the researchers found operating time to be longer with ThuVaRP than TURP, catheterization time and hospital stay were approximately 1 day shorter for those undergoing ThuVaRP; functional results at 3 months were comparable.[50] The prospective randomized study with the longest follow-up data (18 months) compared ThuLEP with bipolar TURP and included 158 consecutive patients. ThuLEP required a longer operating time, but a shorter catheterization time and hospital stay.[51] Additionally, functional outcomes were comparable, and no urethral or bladder neck strictures were observed during follow-up monitoring in both groups.[51]

Aside from these randomized trials, case series have confirmed the safety and efficacy of interventions with the Tm:YAG laser in the treatment of symptomatic prostate enlargement (Table 3). In 2013, Gross *et al.*[52] reported their single-centre experience with 1,080 patients who were treated with ThuVEP between 2007 and 2012. Common complications that were encountered included acute urinary retention after catheter removal (9%), surgical revision owing to incomplete morcellation (1.5%), residual prostate tissue (2.7%) and clot retention (2.0%). No association between urinary retention, surgical revision, significant UTI or transfusion rate and prostate size could be determined.[52] The overall complication rate decreased significantly over time at the centre, from 41.7% for the first 216 cases to 19.4% for the subsequent 216 cases, reflecting the learning curve of the institution.[52] In a subgroup analysis of data from the same centre, encompassing 90 patients with a prostate >80 ml (mean volume 108.6 ml), two patients required a blood transfusion and 10 patients experienced postoperative stress urinary incontinence, which resolved in all but two patients within the first year of surgery.[53]

The safety of ThuVEP in patients at increased risk of bleeding was retrospectively analysed in a small cohort of 56 patients who were taking aspirin (57%), clopidogrel or aspirin and clopidogrel (14%) or coumadin (29%) (Table 4).[54] Postoperative blood transfusions were required in 7.1% of the patients, clot retention without surgical revision occurred in four of the eight patients on clopidogrel or aspirin and clopidogrel and six of the 16 patients on coumadin.[54] In summary, all thulium-laser-based techniques seem to be suitable for men with symptomatic prostate enlargement. A clear trend towards enucleation can be noticed. A drawback is the lack of long-term outcomes from randomized controlled trials.

Laser vaporization with the GreenLight™ laser

The GreenLight™ laser operates at a wavelength of 532 nm (green light) at which the energy of the laser is strongly absorbed by haemoglobin, but not by water. This physical property led to the term 'photoselective vaporization' but does not reflect the reality of the surgery. Owing to the high energy density applied by the laser, tissue ablation is ongoing even if the surface does not 'shine red'. The high energy density in prostate tissue leads to the rapid vaporization of the superficial tissue and a small 'rim' of coagulated tissue. In the past decade, technical advances have improved the technique, including an increase in the

Table 5 | Selected randomized trials of thulium and diode lasers*

Study	Study design (*n*)	Follow-up (months)	Reintervention or reoperation	Functional outcomes		
				IPSS	PVR	Q_{max}
Xia *et al.* (2008)[48]	ThuVaRP (52) vs monopolar TURP (48)	12	ThuVaRP: 1.9% TURP: 6.3%	Comparable	Comparable	Comparable
Yan *et al.* (2013)[49]	ThuVaRP (40) vs monopolar TURP (40)	3	ThuVaRP: 0% TURP: 0%	Comparable	NR	Comparable
Peng *et al.* (2013)[50]	ThuVaRP (50) vs bipolar TURP (50)	3	NR	Comparable	Comparable	Comparable
Yang *et al.* (2013)[51]	ThuLEP (79) vs bipolar TURP (79)	18	ThuLEP: 0% TURP: 0%	Comparable	Comparable	Comparable
Lusuardi *et al.* (2011)[82]	DiLEP (30) vs bipolar TURP (30)	6	DiLEP: 0% TURP: 0%	Comparable	Comparable	Comparable

*Intraoperative complications were comparable between the arms of each study. Abbreviations: DiLEP, diode laser enucleation of the prostate; IPSS, International Prostate Symptom Score; NR, not reported; PVR, postvoid residual volume; Q_{max}, maximum urine flow; ThuLEP, thulium laser enucleation of the prostate; ThuVaRP, thulium laser vaporesection of the prostate; TURP, transurethral resection of the prostate.

maximum power output of the GreenLight™ from 80 W to 180 W. Importantly, fibre design has improved, resulting in faster tissue vaporization via a larger laser beam area.[55,56] Furthermore, fibre degradation leading to a loss in power output is no longer observed with the latest GreenLight™ XPS model.[57] Thus, clinical data obtained using different types of GreenLight™ laser are usually comparable in terms of safety and outcome, but not in terms of efficiency.[55] The majority of available data are based on the former 80 W[42,58–64] and 120 W[39,65–71] systems and only a few articles have reported on the contemporary 180 W GreenLight™ laser system.[55,72] Notably, a 160 W laser system operating at the same wavelength has been developed by another manufacturer (LITEA laser system, Realton, Beijung, China). However, this system has only been evaluated in one prospective case series to date.[73]

Seven randomized controlled trials have been reported that compare TURP with GLV, using either the 80 W or 120 W laser.[59,62,65,66,68–70] In addition, one trial compared open prostatectomy to GLV (using the 80 W laser in men with prostate volumes >80 ml),[58,64] one study compared HoLEP with GLV (using the 120 W laser in men with a prostate volume >60 ml)[39] and another trial compared holmium laser ablation of the prostate (HoLAP) with GLV with the 80 W laser in patients with prostate volume <60 ml (Table 6).[60] A meta-analysis that included data from trials comparing TURP with GLV, demonstrated that catheterization time and hospitalization time were shorter with GLV, whereas operating time was shorter with TURP[74]—as was observed with other laser-based procedures. The risk of postoperative blood transfusion and clot retention was significantly reduced in patients undergoing GLV. The incidences of other complications, such as postoperative retention, UTI, gross haematuria, urethral stricture and bladder neck stricture, were also comparable between techniques.[74] However, when analysing the results of the trial with the longest available follow-up data, the 3-year reoperation rate was significantly higher after 120 W GLV than TURP.[65] Regarding functional outcomes, one study[62] showed TURP to be superior to GLV in terms of International Prostate Symptom Score (IPSS), quality of life (QoL) and PVR improvement, whereas six other studies did not detect any statistically significant differences in these outcomes between the two techniques.[59,65,66,68–70] Furthermore, no difference regarding urodynamic de-obstruction, erectile function and sexual satisfaction could be detected between the techniques within 1 year of follow-up monitoring in one study.[69]

When comparing HoLAP with GLV (80 W laser), one trial in 109 patients with prostate volumes <60 ml showed operating time to be shorter with GLV, whereas catheterization time and hospital stay were comparable.[60] Both techniques were associated with significant improvements in symptoms, Q_{max} and PVR during the 7-year follow-up duration. The retreatment rate was 19.2% for patients who underwent HoLAP and 25% for those who were treated with GLV (P >0.05).[60] In another trial, patients with prostate volumes >80 ml who underwent GLV had a longer operating time than those who underwent open prostatectomy, but a shorter catheterization time and hospital stay. Blood loss and the need for perioperative blood transfusions was significantly higher in the open prostatectomy arm of the study.[58] After 18 months, no significant differences in improvement of IPSS, Q_{max} and PVR could be detected.[64]

Alongside the high-level evidence obtained from these randomized controlled studies, several case series confirm the safety and efficacy of GLV (Table 3). In one single-surgeon series of GLV with the 80 W laser, 246 of 321 patients were available for 5-year follow-up assessment. Symptoms, Q_{max} and PVR were significantly improved in this time frame, and the overall reoperation rate was 8.9%.[61] Another case series included 500 patients who were treated with the 80 W laser between 2002 and 2007 by seven different surgeons at the same institution.[42] Of these patients, 15% had prostate volumes >80 ml, for whom early postoperative haematuria was significantly more common; patients with prostates <40 ml reported significantly more dysuria. The incidence of all other intraoperative and early

Table 6 | Selected randomized trials of GLV

Study	Study design (*n*)	Follow-up (months)	Intraoperative complications	Reintervention or reoperation	Functional outcomes		
					IPSS	PVR	Q_{max}
Al-Ansari *et al.* (2010)[65]	120 W GLV (60) vs monopolar TURP (60)	36	Favours GLV	GLV: 18.5% TURP: 5.4%	Comparable	Comparable	Comparable
Bouchier-Hayes *et al.* (2010)[59]	80 W GLV (59) vs monopolar TURP (50)	12	Comparable	GLV: 16.9% TURP: 12%	Comparable	Comparable	Comparable
Capitán *et al.* (2011)[66]	120 W GLV (50) vs monopolar TURP (50)	24	Comparable	GLV: 12% TURP: 2%	Comparable	Comparable	Comparable
Horasanli *et al.* (2008)[62]	80 W GLV (39) vs monpolar TURP (37)	6	Favours GLV	GLV: 23.1% TURP: 8.1%	Favours TURP	Favours TURP	Favours TURP
Kumar *et al.* (2013)[68]	120 W GLV (58) vs monopolar TURP (60) vs bipolar TURP (57)	12	Favours GLV and bipolar TURP	GLV: 3.4% Monopolar TURP: 1.7% Bipolar TURP: 1.8%	Comparable	Comparable	Comparable
Lukacs *et al.* (2012)[69]	120 W GLV (69) vs monopolar TURP (70)	12	Comparable	GLV: 1.4% TURP: 0%	Favours TURP	Comparable	Comparable
Pereira-Correia *et al.* (2012)[70]	120 W GLV (10) vs monopolar TURP (10)	24	Comparable	GLV: 0% TURP: 0%	Favours TURP	Comparable	Comparable
Skolarikos *et al.* (2008)[58,64]	80 W GLV (65) vs open prostatectomy (60)	18	Favours GLV	GLV: 4.6% Open prostatectomy: 5%	Comparable	Comparable	Comparable
Elshal *et al.* (2013)[60]	80 W GLV (52) vs HoLAP (57)	70	Comparable	GLV: 25% HoLAP: 19.2%	Comparable	Comparable	Comparable

Abbreviations: GLV, GreenLight™ vaporization of the prostate; HoLAP, holmium laser ablation of the prostate; IPSS, International Prostate Symptom Score; PVR, postvoid residual volume; Q_{max}, maximum urine flow; TURP, transurethral resection of the prostate.

postoperative complications did associate with prostate size. The overall retreatment rate was 15.4%. However, it is important to note that only 27 of 500 patients were available for 5-year follow-up assessment.[42] Other case series have also confirmed the efficacy and safety of GLV.[72,75,76]

The physical properties of lasers operating at 532 nm include the ability to ablate the tissue at the centre of the beam area and coagulate the tissue at the outer area of the beam, which make GLV ideal for patients who are at increased risk of bleeding (Table 4). Indeed, several case series have illustrated the safety and efficacy of GLV in patients taking aspirin, clopidogrel or coumadin.[63,67,71,77–79] In a retrospective study comparing outcomes of 80 W GLV in 116 patients at increased risk of bleeding—61% of whom were taking aspirin, 31% taking coumadin and 8% taking clopidogrel—and a control group of 92 patients, haematuria with transient bladder irrigation occurred significantly more often in patients on anticoagulants.[63] The 2-year functional outcomes and the reoperation rate were comparable. Similar results were obtained in a cohort of 162 patients who underwent GLV (80 W or 120 W laser) over a period of 6 years. Of these patients, 62% were on aspirin, 19% on coumadin, 12% on clopidogrel and 7% were taking two or more anticoagulants.[67] Within the first 30 days after the procedure, delayed bleeding occurred in six (4%) patients, three of whom required blood transfusion and one of whom required reoperation.[67] In summary, GLV is suitable for patients with all prostate sizes; however, long-term evidence is lacking for patients with large prostates. The technique is also ideal for patients with increased risk of bleeding.

Diode laser vaporization and enucleation

Diodes are semiconductors with the ability to generate and emit monochromatic light. This light is passed through a crystal, which leads to the final wavelength. Diode lasers are available in various wavelengths and fibre designs (that is, side-firing and end-firing). With the development of fairly cheap semiconductors in the 1990s, Nd:YAG-based laser systems (1,064 nm) gained wide acceptance.[12] However, unfavourable functional outcomes led to their abandonment. The major disadvantage of these lasers is the near-infrared wavelength, with its physically defined deep optical penetration that causes coagulation necrosis. This necrotic tissue leads to dysuria, sloughing and long-lasting storage symptoms.[80] New diode-based laser systems are designed to overcome these disadvantages by modulating frequency, pulsation, maximum power or fibre design to reduce penetration depth. Importantly, other laser systems also use diodes to generate monochromatic light, but differ in the crystal used—for example, the GreenLight™ laser uses a lithium triborate crystal whereas the holmium lasers all use Ho:YAG crystals.

Diode laser vaporization of the prostate (DiVAP) or diode laser enucleation of the prostate (DiLEP), which has attracted increasing attention in recent years, can be performed. The surgical techniques are comparable to other vaporization or enucleation techniques. Although tissue incision is feasible with diode lasers, avoiding deep coagulation can be challenging. Unfortunately, the available evidence on diode lasers is primarily based on low-quality studies with small patient cohorts, and advantages over other established laser techniques, such as HoLEP or GLV, remain to be demonstrated.

The only prospective randomized trial available on any diode laser type compared bipolar TURP with DiLEP (at 1,318 nm)[81] in 60 patients with symptomatic prostate enlargement (Table 5).[82] Operating time was significantly longer with DiLEP than TURP, whereas catheterization and hospitalization were significantly shorter. No blood transfusions were necessary in either group and no reoperation was noted within the postoperative follow-up window of 6 months.[82] One case series including 120 consecutive patients treated with DiLEP (980 nm) between 2008 and 2012 analysed the impact of prostate volumes on outcomes and complications.[83] Functional results within 6 months were comparable between patients with prostate volumes <60 ml and volumes ≥60 ml. In the group with larger prostates, two patients required blood transfusions; postoperative urinary retention occurred significantly more often in patients with smaller prostates.

Two case series have compared laser vaporization between a diode (200 W, 980 nm) and green light (120 W, 532 nm) laser (Table 3). Operating time, catheterization time and hospitalization time were comparable, whereas impaired visibility owing to bleeding occurred more frequently with the green light procedure.[80,84] During the postoperative course, a significantly higher rate of dysuria, passing of sloughed tissue and reoperation owing to bladder neck stricture and obstructive necrotic tissue was reported after DiVAP.[80,84] By contrast, two cohort studies of DiVAP (980 nm) reported no reoperations after 3 months and 6 months.[85,86] Longer follow-up times for these series are needed for any conclusions to be drawn. Finally, after treatment with a 1,470 nm diode laser, reoperation was required in two of 10 patients within 12 months of surgery.[87]

Owing to the increased coagulation capacity of some diode laser systems, high rates of bladder neck stricture, tissue necrosis, postoperative storage symptoms and reoperation have been shown in several case series. In an effort to reduce the high reoperation rate caused by necrotic tissue observed with the 980 nm diode laser, a quartz head contact laser fibre was introduced with the intention of reducing penetration depth. This modification led to a reduction in the incidence of dysuria by >1 month, from 42% to 17%, and a reduction in the passage of significant tissue remnants (slough) from 52% to 16%.[88] Although promising, a comprehensive preclinical evaluation of diode lasers (and any such modification) is warranted before introducing them into routine clinical practice.

Conclusions

Lasers have become an established treatment alternative to TURP and open prostatectomy for men with BPO in the past decade. This development was primarily driven by the success of two different surgical techniques—namely, HoLEP with the Ho:YAG laser and GLV with the GreenLight™ laser. Facilitated by encouraging results from early studies and the economic success of these two laser types, Thu:YAG and diode lasers have also entered the market. Despite scepticism owing to unfavourable results of early laser techniques, such as laser vaporization with the Nd:YAG laser, lasers currently hold an established position in the surgical armamentarium that is reflected in current treatment guidelines.[4] The increasing number of different laser types and techniques often leads to confusion, and the evidence supporting the different lasers varies substantially. Thus, not every laser can be recommended for every patient.

For a patient with a small-to-medium-sized prostate (<80 ml in volume), HoLEP, GLV, ThuLEP and DiLEP have all shown superior safety and comparable efficacy in terms of early postoperative symptom improvement to TURP in at least one randomized controlled trial. The high reproducibility of improved safety and comparable efficacy has also been shown for HoLEP and GLV, such that these can be regarded as the techniques with the most supporting evidence. However, the maximum available follow-up data extends to 7 years for HoLEP and 3 years for GLV and no reported study of these techniques is adequately powered for long-term results.

For patients with large prostates (>80 ml in volume), randomized controlled trials have compared HoLEP and GLV with open prostatectomy. Both laser techniques were characterized by fewer perioperative complications than the open procedure. Functional results were comparable at 5 years postsurgery between HoLEP and open prostatectomy, but GLV was inferior to open prostatectomy at 18 months in terms of QoL improvement. Thus, only HoLEP currently provides, regardless of limitations in study design, comparable long-term results to open surgery.

For patients at increased risk of bleeding, case series have been published on HoLEP, GLV, ThuLEP and DiVaP. When critically analysing patient characteristics and associated complications, GLV has the most robust data supporting its safety and efficacy, especially in those taking coumadin, clopidogrel or combinations of anticoagulant drugs. Although some diode lasers seem to be superior to GLV in terms of haemostasis, their high rate of postoperative complications clearly stands against the application of these laser types in these patients.

Based on the evidence currently available, lasers are an established treatment option for BPO. Novel technical developments might lead to an increase in efficiency while maintaining safety. Future well-designed studies should focus on specific risk groups of patients as well as the long-term durability of outcomes.

Review criteria

Search of the peer-reviewed literature was conducted using the MEDLINE/PubMed databases. Articles published between January 2002 and June 2013 were identified using the terms "laser prostate", "laser enucleation" and "laser vaporization", which were individually combined with the following terms: "outcomes" and "complications". The reference lists of these articles were searched to identify articles that were of particular relevance to the topics of the current Review. Only full-text papers in English were selected.

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Author contributions

Both authors researched data for the article and discussed its content. M.R. wrote the manuscript, after which both authors edited it before submission.