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REVIEW ARTICLE

Critical review of lasers in benign prostatic hyperplasia (BPH)

Stavros Gravas, Alexander Bachmann*, Oliver Reich†, Claus G. Roehrborn‡, Peter J. Gilling§ and Jean De La Rosette¶

*Departments of Urology, University of Thessaly, Larissa, Greece; *University Hospital Basel, Basel, Switzerland; †Ludwig-Maximilians-University, Munich, Germany; ‡Univeristy of Texas South-western Medical Centre, Dallas, TX, USA; §Tauranga Hospital, Tauranga, New Zealand, and ¶Academisch Medisch Centrum (AMC) University Hospital, Amsterdam, the Netherlands*

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What's known on the subject? and What does the study add?

Laser technology has been applied to treat LUTS secondary to BPH for >15 years. Some of the early approaches failed to fulfil our expectations and have been abandoned, but technological advancements and growing clinical experience have produced more refined techniques and devices with clinical outcomes that seem to challenge transurethral resection of the prostate.

Using an evidence-based approach, this review explains the basic principles of lasers and updates our knowledge on the progress of laser technology and the role of different laser techniques and types in the treatment of LUTS due to BPH in both the general population and specific groups of patients. The study also documents the need for better quality data to increase the level of evidence for each laser treatment.

- Laser treatment of benign prostatic hyperplasia has challenged transurethral resection of the prostate (TURP) due to advances in laser technology, better understanding of tissue–laser interactions and growing clinical experience.
- Various lasers have been introduced including neodymium: yttrium aluminium garnet (YAG), holmium (Ho) : YAG, potassium titanyl phosphate : YAG, thulium(Tm) and diode laser. Based on the different wave-length dependent laser–prostatic tissue interactions, the main techniques are coagulation, vaporization, resection and enucleation.
- The present review aims to help urologists to distinguish and to critically evaluate the role of different laser methods in the treatment by using an evidence-based approach. It also details further evidence for use in specific patient groups (in retention, on anticoagulation) and addresses the issues of cost and learning curve.
- Coagulation-based techniques have been abandoned; holmium ablation/resection of the prostate has been superseded by the enucleation technique Ho-laser enucleation of the prostate (HoLEP). The short-term efficacy of the emerging laser treatments such as diode and Tm prostatectomy has been suggested by low quality studies. HoLEP and photoselective vaporization of the prostate (PVP) represent valid clinical alternatives to TURP. HoLEP is the most rigorously analysed laser technique with durable efficacy for any prostate size and low early and late morbidity. PVP has grown in acceptance and popularity but long-term results from high quality studies are pending.

KEYWORDS laser prostatectomy, benign prostatic hyperplasia, holmium (Ho) laser, KTP laser, thulium (Tm) laser, diode laser

INTRODUCTION

Laser technology has been used to treat LUTS secondary to BPH for >15 years, initially with very high expectations. Some of the early laser procedures were abandoned because of the need for prolonged catheterization, unpredictable results, and high re-operation rates. However, advances in laser technology, better understanding of tissue–laser interactions, technical improvements (e.g. higher power setting, fibre improvements) and growing clinical experience have produced more refined techniques and devices that challenge TURP.

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Various lasers have been introduced as alternatives to TURP, mainly neodymium: yttrium aluminium garnet (Nd : YAG), holmium : YAG (Ho : YAG), potassium ('kalium' in Latin) titanyl phosphate : YAG (KTP : YAG), thulium- (Tm) and diode-laser. Techniques consist of coagulation, vaporization, resection, and enucleation, depending on the wavelength, power, and type of laser emission (continuous or pulsed). All these different laser treatment methods are included under the umbrella of the generic term 'laser prostatectomy'. However, this term may be misleading as the currently available lasers and laser techniques differ significantly in terms of handling, and laser–tissue interactions.

The aim of the present review is to provide all the necessary information to help urologists distinguish one laser from another and to critically evaluate the role of different laser methods in the treatment of LUTS due to BPH by using an evidence-based approach.

METHODS

An electronic search (MEDLINE) over the last 15 years was carried out to identify publications in the English language on laser treatment in men with BPH using the keywords: laser, prostate, BPH, holmium, photoselective vaporization of the prostate (PVP), GreenLight KTP, lithium triborate (LBO), thulium and diode. We also searched the proceedings of recent conferences (last 5 years) of the European Association of Urology, AUA and Endourological Society. Using an evidence-based approach, our search focused on the highest quality studies for each of the treatment options moving from available meta-analyses to randomized clinical trials (RCTs), and to larger case studies and was also based on systematic review articles that have already been published. The available type of study also indicates how extensively each of these different laser prostatectomies have been studied.

LASER PHYSICS

Basic principles

The acronym LASER stands for 'Light Amplification by Stimulated Emission of Radiation'. Laser is characterized by being a monochromatic, collimated, coherent light that is emitted from an energized laser material (semiconductor, crystal, gas, or dye). The key determinant of laser application is based on the interaction between the laser beam and target tissue that depends on reflection, scattering, and absorption [1]. Absorption is the most important component in the light–tissue interaction process and is essential for the conversion of light to thermal energy. The thermal conversion of laser results in the elevation of target tissue temperature and can produce either coagulation or vaporization. Laser coagulation occurs when tissue is heated to below the boiling/vaporization temperature but above that required to denature protein, resulting in coagulative necrosis, with a potential for delayed anatomical debulking. Laser vaporization occurs when the tissue is evaporated by being heated to above the vaporization/boiling temperature using higher-density laser thermal energy. To achieve absorption a chromophore is required such as melanin (not important for urological applications), oxyhaemoglobin and water. With laser prostatectomy in general, the used energy has to lead to an immediate tissue removal. Thus, the absorption coefficient represents a very important characteristic of the interaction between laser wavelengths and the available chromophores. A high absorption coefficient means the given laser wavelength is well absorbed in the selected medium. A low absorption coefficient corresponds to a greater degree of tissue transparency allowing the light to penetrate deeper into the medium.

> 'Absorption is the most important component in the light–tissue interaction process'

Another key characteristic of laser is the optical penetration depth into tissue of each specific wavelength. For this reason, the concept of extinction length (defined as the depth until which 90% of the incident laser beam is absorbed and is converted into heat) was introduced. Extinction length is very important because a laser with shorter length will transfer more energy per unit area into the tissue. This means that at the same power level a laser wavelength with a long extinction length will diffuse power delivered and create a deep necrosis whereas a laser wavelength with a much shorter extinction length allows a more concentrated delivery of light energy leading to an increase of temperature above boiling point and to immediate vaporization of tissue.

Characteristics of common lasers

The Nd : YAG (crystal) laser produces energy at a wavelength of 1064 nm. The low-absorption coefficient in most tissues with a tissue penetration depth of >1 cm at this wavelength resulted in low-energy density leading to a deep coagulative necrosis of the tissue and more thermal injury.

The Ho : YAG laser is a pulsed solid-state laser that produces energy at a wavelength of 2140 nm with a pulse duration of 350 ms. Due to these properties, the laser energy of

TABLE 1 Main characteristics of different lasers

Type of laser	Wavelength, nm	Chromophore	Penetration depth, mm	Mode	Application
Nd : YAG	1064	Water and haemoglobin	10	Pulsed or continuous	Coagulation
Ho : YAG	2100	Water	0.4	Pulsed	Vaporization, resection, enucleation
KTP (LBO)	532	Haemoglobin	0.8	Quasi-continuous	Vaporization
Tm	2000	Water	0.25	Continuous	Vaporization, resection, enucleation
Diode	940 980 1470	Water and haemoglobin	Various	Pulsed or continuous	Vaporization

the Ho : YAG laser is promptly absorbed by water and water containing tissues, resulting in rapid dispersion of heat. The penetration depth in prostatic tissue is 0.4 mm and the resulting high-energy density creates vaporization without a deep coagulation zone (thermal damage is limited in the contiguous 0.5–1 mm). The Ho : YAG laser requires contact with target tissue and the prostatic tissue can be precisely incised, dissected and enucleated. Dissipating heat causes simultaneous coagulation of small- and medium-sized vessels to a depth of 2–3 mm, resulting in excellent haemostasis. The Ho : YAG laser system is optimized for cutting of prostate tissue, providing efficient haemostatic properties.

> 'Tm-laser may be suitable for transurethral vaporization, resection or enucleation of the prostate'

The KTP : YAG laser is a derivative of the Nd : YAG laser. The Nd : YAG laser beam is passed through a KTP (or LBO) crystal resulting in doubling of the frequency and halving of the wavelength from 1064 nm to 532 nm. KTP laser energy is selectively absorbed within the tissue by haemoglobin, which acts as an intracellular chromophore, and not by the water. The penetration depth into tissue is only 0.8 mm and the system is considered a quasi-continuous wave laser due to the fact that the coherently emitted laser beam pulses last >0.25 s. Based on these characteristics, increased absorption from haemoglobin leads to trapping of the energy in the superficial layers of tissue with high haemoglobin, like prostatic tissue, which is photothermally vaporized rapidly with only a 1 ± 0.2-mm rim of coagulation. The heat-induced coagulation of superficial blood vessels explains the enhanced haemostatic properties of the KTP laser. The KTP and LBO lasers produce the same 532 nm light beam. The GreenLight laser is optimized for vaporization of prostate tissue.

The Tm : YAG laser operates at a wavelength of 2000 nm and is delivered as a continuous wave. Similarly to Ho-laser, the Tm-laser offers complete absorption of laser energy in water. Furthermore, due to the slightly shorter wavelength of thulium the depth of penetration is decreased to 0.25 mm leading to rapid vaporization of the tissue; however, the visible tissue effect is completely different to holmium because of the continuous rather than pulsed nature of the device. The Tm-laser may be suitable for transurethral vaporization, resection or enucleation of the prostate. The Tm-laser provides a continuous visible laser beam, which is not visible with the Ho : YAG.

Diode lasers use a special diode for energy generation. Thus, based on the semiconductor industry, various wavelengths of 940, 980 or 1470 nm are available for the application in diode-laser prostatectomy [2]. These wavelengths are all near the infrared electromagnetic spectrum and therefore absorbed by both water and haemoglobin and are supposed to combine good haemostatic properties with tissue vaporization. *Ex vivo* studies showed that all diode lasers have improved haemostatic characteristics compared to the 120-W LBO laser [2,3]. Data about the penetration depths of diode lasers differed considerably between distinct reports.

Table 1 shows the main characteristics of the above mentioned lasers.

CURRENT LASER TECHNIQUES

The main categories of laser technique include coagulation, vaporization, resection and enucleation. Based on the described principles, it is not surprising that not all of the lasers can be used for all the laser techniques.

(1) Coagulation

The initial application of the Nd : YAG laser in the management of BPH was accompanied by great enthusiasm. But, based on the clinical results obtained, Nd : YAG lasers were not able to remove tissue immediately. Lasers using Nd : YAG near wave lengths resulted in deep coagulative necrosis with delayed (4–8 weeks) sloughing and secondary ablation of the obstructive tissue. No tissue was available for histological examination.

The main representatives of laser coagulation are visual laser ablation of the prostate (VLAP) and interstitial laser coagulation (ILC). A systematic review of the available randomized clinical trials comparing VLAP with TURP and reviews of the available studies (mostly open-label studies) on ILC showed that both treatments are effective for subjective and objective improvement [4–6]. In addition, VLAP provided a similar improvement in symptoms compared with TURP but was less effective for maximum urinary flow rate (Q_{max}).

Operative morbidity of VLAP and ILC is almost non-existent and no blood transfusion is required. However, the early postoperative morbidity is high with the most bothersome and distressing adverse events (AEs) being early postoperative dysuria, urgency and other storage symptoms often called collective ‘post-laser voiding syndrome’ and the need for prolonged catheterization due to retention [4–6]. Another limitation of VLAP and ILC was the reported re-operation rates of 7.5–20% and 0–15.4% at 12 months, respectively. The re-operation rate reached 26.7% at 24 months after VLAP [7]. In a study with longer follow-up of median (range) 54 (46–61) months, it was reported that half of the patients that had ILC received re-treatment [8]. Because of the unacceptable AEs, high re-operation rate and the emergence of more efficient and technically improved laser systems both VLAP and ILC have been abandoned.

(2) Non-contact laser ablation or vaporization

This is the most current basic laser technique and all lasers can be used to perform a contactless ablation or vaporization of the prostate. Recently, because of the improved technical advantages and increased power outputs, the ‘ablation’ is transferred more and more to ‘vaporization’, because with vaporization an immediate tissue removal is visible during surgery.

The laser beam is directed by a bare fibre straight or sideways onto the prostate tissue by the use of a side-firing fibre. Usually a channel of evaporated tissue is created through the prostate. No tissue is available for histological examination.

Ho-laser ablation of the prostate (HoLAP)

HoLAP was first reported in 1994 using a 60-W Ho-laser. The interest in pure HoLAP faded away with the development of holmium resection and enucleation techniques. However, HoLAP has regained attention with the recent introduction of the high-powered 100-W Ho-laser but still sufficient data is lacking.

Efficacy and morbidity: HoLAP has been compared with TURP in only one small RCT that showed a similar improvement in International Prostate Symptom Score (IPSS) and Q_{max} between the two groups at 12 months follow-up [9]. Catheterization and hospitalization times were shorter for the patients that had HoLAP. Kumar [10] reported the preliminary results using 100-W HoLAP in patients with large prostates (>80 mL). The short-term efficacy in terms of the AUA-symptom score (SS) and Q_{max} improvement was shown and insignificant blood loss, no stress incontinence and short catheterization and hospitalization was reported. Recently, Elzayat *et al.* [11] performed a RCT comparing HoLAP (80–100 W) and PVP of the prostate (80 W). Functional outcomes improved significantly and were comparable at 12 months postoperatively. Moreover, there was no significant difference in complications rates between the procedures and only operative time was in favour of PVP. Table 2 [9–16] presents clinical data on HoLAP.

Durability: Tan *et al.* [17] reported the long-term results of 34 patients with a median follow-up of 7.4 years. Subjective and objective voiding variables were durable with a 47% reduction in AUA-SS and an 83% increase in Q_{max} from baseline. The re-operation rate was 15% after 7 years.

PVP

PVP using the 80-W KTP laser (GreenLight PV) was first reported in 2003 [18]. Since then, a rapid adoption and diffusion of this laser technique has been witnessed due to the promising results and rigorous marketing. A higher-powered 120-W LBO laser (GreenLight HPS) was developed and more recently the 180-W LBO system (GreenLight XPS) has been marketed to further improve vaporization speed [19].

Efficacy and morbidity: Only three RCTs were available comparing GreenLight PV with TURP and only one RCT was available comparing GreenLight PV with open prostatectomy (OP) [20–23]. Bouchier-Hayes *et al.* [20] showed that the improvement of voiding variables was similar in the two groups with a mean increase in Q_{max} of 136% and a 61% mean IPSS improvement for the 80-W GreenLight laser group (Table 3) [19–27]. However, one study with patients with large prostates reported a significant difference in IPSS and Q_{max} at 6 months in favour of TURP [21]. When compared with OP, 80-W GreenLight laser showed similar improvement in IPSS score, quality of life (QOL), and Q_{max}, whereas there was a statistically significantly greater reduction of prostate volume after OP [22]. Several large cases studies showed the efficacy and low morbidity of GreenLight PV [24,25,28]. Data from the largest case studies are also presented in Table 3.

> ‘HoLAP has regained attention with the recent introduction of the high-powered 100-W Ho-laser’

Rieken *et al.* [29] reviewed the recent data on complications of laser prostatectomy and indicated that GreenLight PV had low intraoperative morbidity and early postoperative complications comparable with OP or TURP. As also shown in Table 3, the comparison with TURP is favourable, due to significantly less blood loss and significantly shorter duration of catheterization and hospital stay. One study reported a significantly greater risk of postoperative clot retention in patients treated with TURP (34%) compared with the GreenLight PV group (5.1%) [20]. Catheterization time is generally <24 h, while in one study 44 patients (32%) were left without a catheter at the end of the procedure [30]. In addition, no transurethral resection (TUR)-syndrome rate was reported in any study. The most frequent complications include re-catheterization (range from 1.7% to 15.3%), dysuria (from 8.5% to 20%) and minor haematuria (up to 18%; Table 3).

Data on sexual function after GreenLight laser are scarce. Between 36% and 52% of sexually active men had retrograde ejaculation after treatment in case studies [30,31]. The reported rate of retrograde ejaculation was 56.7% and 49.9% ($P = 0.21$) for patients that underwent TURP and GreenLight PV, respectively; in one RCT [21], while no difference could be detected between patients undergoing OP/TURP and GreenLight PV concerning erectile function (EF) [20,22]. Using the International Index of Erectile Function, Bruyere *et al.* [32] evaluated 149 patients treated with either the 80-W (63 cases) or the 120-W GreenLight laser (86 cases). Sexual function seemed to be maintained after GreenLight laser vaporization, although in patients with normal preoperative EF there was a significant decrease in EF. There was no difference in EF between patients who underwent an 80-W or 120-W procedure.

TABLE 2 *Studies on efficacy and morbidity of laser ablation [mean values (SD)]*

Study	Type	LoE	Treatment	Pts, *n*	FU, mo	bIPSS	IPSS	bQ_{max}, mL/s	Q_{max}, mL/s	DoC, days	LoS, days	Blood trans., %	Dysuria, %	Re-cath., %	Strictures, %	Re-operation, %
Mottet *et al.* [9]	RCT	1b	HoLAP	17	12	21.7	6.5	8.8	19.9	2.2	1.6	0	NA	0	0	5.9
			TURP	13		23.7	4.7	7.7	17.6	2.1	3.1	0	NA	0	15.4	0
Elzayat *et al.* [11]	RCT	1b	HoLAP	57	12	20 (6.8)	6.2 (3.9)	6.7 (3.9)	17.2 (8.4)	2.1 (2.7)	0.9 (0.3)	0	22.8	12.2	5.2	3.5
			PVP	52		18.4 (6.6)	8.2 (6.2)	6.4 (3.9)	18.4 (8.4)	1.7 (1.6)	1.0 (0.3)	0	19.2	11.5	13.4	1.9
Kumar [10]	Case series	4	HoLAP 100 W	17	3.3	20.4 (5.3)	5.7 (2.2)	6.9 (5.7)	15.1 (7.6)	2.1 (1–5)	1.3 (1–3)	5.9	11.8	23.6	5.9	0
Erol *et al.* [13]	Case series	4	980 nm Diode laser	47	6	21.9 (4.9)	9.9 (3.2)	8.9 (2.2)	18.3 (3.9)	1.0	NA	0	23.4	4.2	NA	NA
Ruszat *et al.* [12]	Case control	3	980 nm Diode laser	55	6	18.7 (7.9)	4.5 (2.5)	10.7 (5.4)	15.8 (5.1)	1.8 (1.2)	3.4 (1.9)	0	23.6	20.0	14.5	18.2
			120-W HPS	62		20.9 (6.6)	8.8 (5.3)	12.4 (6.1)	23.7 (9.1)	2.3 (1.0)	3.7 (2.6)	1.6	17.7	8.0	1.6	1.6
Chen *et al.* [15]	Case series	4	980 nm Diode laser	55	6	20.1 (5.2)	4.9 (5.2)	5.5 (5.4)	19.2 (7.9)	34.8 h (30.1)	2.8 (1.8)	0	18.0	10.9	7.3	7.3
Leonardi [14]	Case series	4	980 nm Diode laser	52	12	18.4 (5.8)	6.0 (0.6)	7.5 (4.1)	19.7 (1.4)	24.0 h (16.9)	5.0 h (2.0)	0	0.0 significant	5.8	NA	NA
Seitz *et al.* [16]	Case series	4	1470 nm Diode laser	10	12	16.3 (2.2)	5.0 (1.6)	8.9 (2.9)	22.4 (4.3)	49.8 h (46.0)	4.7 (2.3)	0	20.0	20.0	0	20.0

LoE, level of evidence; Pts, patients; FU: follow-up; mo, months; bIPSS, baseline IPSS; bQ_{max}*: baseline* Q_{max}*; DoC, duration of catheterization; LoS, length of stay; Strictures: urethral, meatal, bladder neck; Re-operation, due to obstruction; NA: not available; trans., transfusion; Re-cath, re-catheterization.*

TABLE 3 *Studies on efficacy and morbidity of GreenLight laser [mean values (SD)]*

Study	Type	LoE	Treatment	Pts, *n*	FU, mo	bIPSS	IPSS	bQ$_{max}$, mL/s	Q$_{max}$, mL/s	DoC, days	LoS, days	Blood trans., %	Dysuria, %	Re-cath., %	Strictures, %	Re-operation, %
Bouchier *et al.* [20]	RCT	1b	80 W	59	12	25.3 (5.9)	8.9 (7.6)	8.8 (2.6)	18.6 (8.2)	13.8 h (9.6)	1.1 (0.4)	0	8.5	1.7	6.8	10.2
			TURP	50		25.4 (5.7)	10.9 (9.4)	8.9 (3.0)	19.4 (8.7)	44.2 h (33.6)	3.3 (1.0)	2.0	14.0	4.0	8.0	4.0
Horasanli *et al.* [21]	RCT	1b	80 W	39	6	18.9 (5.1)	13.1 (5.8)	8.6 (5.2)	13.3 (7.9)	1.7 (0.8)	2.0 (0.7)	0	NA	15.3	8.1	17.9
			TURP	37		20.2 (6.8)	6.4 (7.9)	9.2 (5.6)	20.7 (11.3)	3.9 (1.2)	4.8 (1.2)	8.1	NA	2.7	5.1	0
Alivizatos *et al.* [22]	RCT	1b	80 W	65	12	20.0	9.0	8.6	16.0	1.0	2.0	0	15.0	7.7	3.1	1.5
			OP	60		21.0	8.0	8.0	15.1	5.0	6.0	13.3	20.0	16.7	5.0	0
Al-Ansari *et al.* [23]	RCT	1b	120-W HPS	60	36	27.2 (2.3)	11.0 (2.4)	6.9 (2.2)	17.0 (1.8)	1.4 (0.6)	2.3 (1.2)	0	93.3*	NA	7.4	11.0
			TURP	60		27.9 (2.7)	9.0 (2.6)	6.4 (2.0)	20.0 (2.1)	2.7 (0.9)	4.1 (0.6)	20.0	31.7*	NA	3.6	1.8
Ruszat *et al.* [24]	Case series	4	80 W	500	12 (302) 60 (27)	18.3 (6.5)	6.4 (5.3) 7.6 (5.6)	8.4 (5.0)	18.6 (9.6) 17.5 (7.5)	1.8 (1.2)	3.7 (2.9)	0.4	14.8	11.0	8.0	6.8
Hai [25]	Case series	4	80 W	321	60	24.0 (5.3)	5.0 (3.0)	8.6 (3.5)	21.1 (6.3)	NA	NA	NA	NA	NA	1.2	8.9
Woo/Choi *et al.* [19,26]	Case series	4	120-W HPS	305	4.2	NA	NA	NA	NA	NA	NA	0.4	11.8	4.6	0.7	0.7
Spaliviero *et al.* [27]	Case series	4	120-W HPS	70	12	22.0	4.0	9.4	20.0	1.0 (0.5)	NA	0	0†	2.8	0	0

*LoE, level of evidence; Pts, patients; FU: follow-up; mo, months; bIPSS, baseline IPSS; bQ$_{max}$: baseline Q$_{max}$; DoC, duration of catheterization; LoS, length of stay; Strictures: urethral, meatal, bladder neck; Re-operation, due to obstruction; NA: not available; trans., transfusion; Re-cath, re-catheterization; h, hours. *Dysuria/urge; †bothersome.*

Only one RCT and a few case studies evaluating the safety and efficacy of the GreenLight HPS prostatectomy have been published. Al-Ansari *et al.* [23] compared the new HPS 120-W laser machine with TURP. There was dramatic improvement in Q$_{max}$, IPSS, and postvoid residual urine volume (PVR) and the degree of improvement was comparable in both groups during the 36-month follow-up. Intraoperative and early operative complications were in favour of GreenLight HPS, while more patients treated with laser had dysuria/urge compared with patients that had TURP (Table 3).

The International GreenLight Users (IGLU) group (formed by eight leading centres with this technology) pooled outcomes on their initial 305 patients treated with this new HPS laser with a mean follow-up of 4.2 months [19,26]. Changes in Q$_{max}$, PVR, IPSS, and prostate volume from baseline to follow-up were significant while overall, results showed comparable rates of complications with the existing 80-W GreenLight PV (Table 3). Recently, the IGLU group presented their updated 1-year prospectively pooled outcomes (*n* = 1109) [33]. The functional variables Q$_{max}$, IPSS and PVR improved significantly just after catheter removal with a re-operation rate of 1.7% after 12 months. Spaliviero *et al.* [27] treated 70 consecutive patients with the GreenLight HPS. Voiding variables were significantly improved from the first week and this was sustained during the 52-week follow-up (Table 3). The most frequent complications included postoperative clinically insignificant haematuria (78.5%), irritative symptoms (8.6%), and UTI (4.3%). In addition, no re-operation secondary to recurrent LUTS was reported at 12 months.

Durability: Long-term results of this technique are still missing. A study with a 5-year follow-up reported a durable improvement in AUA-SS and Q$_{max}$ after PVP [34]. However, that study had a very high attrition rate (85% at 5 years). Recently, Hai [25] analysed 246 patients who completed the 5-year follow-up and showed the long-term durability of GreenLight PV. Re-operation rates with the 80-W KTP laser compared with TURP have been reported; 18% vs 0% after 6 months follow-up (for large prostates), 10% vs 3.4% after 12 months and 6.7% vs 3.9% after 24 months [20,21,35]. Hai [25] reported an overall re-treatment rate of 8.9% at 5 years due to recurrent adenoma (7.7%) and bladder neck contracture (1.2%). Similarly, Ruszat *et al.* [24] reported a re-treatment rate of 14.8% due to recurrent or persisting adenoma (6.8%), bladder neck strictures (3.6%) or urethral strictures (4.4%); however, the attrition rate was again high at 5 years.

Rieken *et al.* [36] updated their long-term follow-up after GreenLight PV. After a mean follow-up of 56 months IPSS, HRQL and Q_{max} remained improved. Re-operation due to recurrent adenoma, bladder-neck sclerosis and urethral stricture was necessary in 34.2%, 5.3% and 10.5% of patients, respectively.

Diode-laser vaporization of the prostate

Currently, clinical data are available on the 980 nm (four studies) and the 1470-nm (one study) diode-laser [12–16]. These studies show promising results with significant early improvement in IPSS and Q_{max} (Table 2). The safety of the diode laser was also shown and no blood transfusion was reported. There is one comparative study between the 980 nm high-intensity diode and the 120-W LBO systems with significant and comparable improvements of subjective and objective voiding variables up to 6 months in both groups [12]. Compared with the 120-W GreenLight laser, the rate of intraoperative bleeding was significantly lower (0 vs 13%) despite anticoagulation in 51% of all patients. The most common postoperative complications were retrograde ejaculation (31.7%) and irritative symptoms/dysuria that ranged between 18% and 24%. Re-catheterization and re-operation rates were in favour of the GreenLight HPS treatment [12].

Again the main limitation of this laser procedure is the lack of long-term studies and high-quality data from RCTs.

(3) Resection or vaporesection

Laser resection represents the laser version of TURP and can be performed by both the Ho- and Tm-lasers. In this technique an end-firing fibre is used to perform bilateral bladder neck incisions and the median lobe of the prostate is then resected either as a single fragment or multiple fragments. Next, the lateral lobes are resected in multiple small prostate chips that are subsequently irrigated from the bladder. Tissue is available for histological examination.

Ho-laser resection of the prostate (HoLRP)

HoLRP was the first application of laser energy for excisional prostate surgery and was introduced in 1994. Since the introduction of the tissue morcellator, HoLRP has been largely superseded by the enucleation technique (HoLEP). As a result, neither new RCTs nor large case series on HoLRP have recently been reported. This technique remains relevant for re-operations and 'channel' resections for advanced prostate cancer.

Efficacy and morbidity: In a meta-analysis of clinical trials comparing HoLRP with TURP, no difference in the symptom improvement could be detected at 6 or 12 months postoperatively [37]. On the other hand, HoLRP achieved a significantly greater increase in Q_{max} compared with TURP with a weighted mean difference (WMD) of 4.8 mL/s. Detailed data are presented in Table 4 [37–41]. For morbidity, Tooher *et al.* [37] concluded that HoLRP appeared to be superior to TURP in terms of transfusion rates, duration of catheterization and hospitalization. However, that meta-analysis could not show a significant difference in rates of strictures and UTIs between HoLRP and TURP.

Durability: The study with the longest follow-up (4 years) showed that HoLRP had durable efficacy in terms Q_{max}, symptoms improvement and QOL, and these long-term results were equivalent to the TURP group [42]. In addition there was no difference in the re-operation rate between the two groups.

Tm-vaporesection of the prostate (ThuVaRP)

In prostate surgery, the 2013 nm, Tm-laser has been used for resection of the prostate with a technique similar to HoLRP. The term 'VapoResection' was coined to indicate that tissue ablation is not only achieved by resection of TUR-like tissue chips, but also by simultaneous vaporization [43]. A modification of the Ho-based technique was described by Xia *et al.* [38] who combined semi-circular and transverse incisions and created prostate segments in a tangerine-like

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TABLE 4 Studies on efficacy and morbidity of laser resection [mean values (SD)]

Study	Type	LoE	Treatment	Pts, *n*	FU, mo	bIPSS	IPSS	bQ_{max}, mL/s	Q_{max}, mL/s	DoC, days	LoS, days	Blood trans., %	Dysuria, %	Re-cath., %	Strictures, %	Re-operation, %
Tooher *et al.* [37]	Meta-analysis	1a	HoLRP		12	NA	4.2 (6.0)	NA	25.2 (11.9)	0.8 (0.5)	1.1 (0.5)	0	NA	5.0	5.0	5.0
			TURP			NA	4.3 (4.1)	NA	20.4 (8.5)	1.6 (0.7)	2.0 (0.7)	7.0	NA	8.0	7.0	8.0
Xia *et al.* [38]	RCT	1b	ThuVaRP-TT	52	12	21.9 (6.7)	3.5 (2.9)	8.0 (2.8)	23.7 (6.0)	45.7 h (25.8)	115.1 h (25.5)	0	23	0	1.9	0
			TURP	48		20.8 (5.8)	3.9 (2.7)	8.3 (3.0)	24.1 (6.4)	87.4 h (33.8)	161.1 h (33.8)	4.2	31	0	6.3	0
Szlauer *et al.* [41]	Case series	4	ThuVaRP	56	9	19.8 (5.4)	8.6 (6.5)	NA	NA	23 h (15.8)	5.0 (2.4)	3.6	NA	3.6	3.6	7.1
Bach *et al.* [40]	Case series	4	ThuVaRP	54	12	19.8	6.9	8.1	20.3	1.7	3.5	0	NA	0	0	0
Wei *et al.* [39]	Case control	3	ThuVaRP	58	12	22.6 (4.5)	3.3 (1.1)	6.5 (1.8)	21.4 (2.1)	1.8 (0.3)	3.2 (1.6)	0	26.2	10.3	1.9	0
			TURP	42		21.2 (3.7)	4.0 (1.7)	7.3 (2.4)	22.8 (1.8)	3.4 (1.9)	6.5 (2.4)	9.5	29.3	9.5	13.0	0

LoE, level of evidence; Pts, patients; FU: follow-up; mo, months; bIPSS, baseline IPSS; bQ_{max}: baseline Q_{max}; DoC, duration of catheterization; LoS, length of stay; Strictures: urethral, meatal, bladder neck; Re-operation, due to obstruction; NA: not available; trans., transfusion; Re-cath, re-catheterization.

shape. This modification is called the 'tangerine technique' (ThuVaRP-TT).

Efficacy and morbidity: Four studies reported the feasibility, efficacy and safety of ThuVaRP with a significant improvement in functional outcomes and minimal morbidity (Table 4) [38–41]. One RCT [38] and one nonrandomized controlled trial [39] compared ThuVaRP with monopolar TURP and showed equivalent short-term efficacy in terms of Q_{max}, IPSS and QOL. There were lower transfusion rates and shorter catheter and hospitalization stays in favour of laser resection, whereas there was no significant difference in the rate of retrograde ejaculation and urethral stricture [38,39]. The reported re-operation rate was 0–7.1% within a 1-year follow-up after ThuVaRP.

(4) Enucleation

Laser enucleation represents the endoscopic equivalent of simple OP and is the most technically advanced form of laser prostate surgery. The Ho-laser was the initial energy source used for the procedure using a contact bare-tip laser fibre to enter the surgical plane between the prostate adenoma and capsule and then to peel each prostatic lobe from the capsule. A tissue morcellator is required to remove tissue, which is then available for histological examination. Recent studies have reported the use of the Tm-laser for prostate enucleation.

> 'Laser enucleation represents the endoscopic equivalent of simple OP'

HoLEP

Many clinical studies have proven the efficacy and safety of HoLEP. Available systematic reviews and meta-analyses have made HoLEP the most rigorously analysed laser technique thus far.

Efficacy and morbidity: A systematic review of two RCTs and one nonrandomized comparative study concluded that HoLEP is at least as effective as TURP in relieving the symptoms of BPH [37]. Gilling *et al.* [44] performed the first meta-analysis of four RCTs comparing HoLEP and TURP. They found that urodynamic relief of obstruction (detrusor pressure at Q_{max} and Schaffer grade) was superior with HoLEP compared with TURP but only when prostate volumes were >50 g. Tan *et al.* [45] performed a meta-analysis of the available RCTs comparing HoLEP with TURP. Overall, 460 participants were randomised in the four trials, including 232 to HoLEP and 228 to TURP. At 6 and 12 months after treatment, the WMD for Q_{max} was 1.06 and 0.59 mL/s, respectively, favouring HoLEP but without reaching statistical significance [45]. Recently, in their meta-analysis of the available RCTs, Lourenco *et al.* [46] confirmed the previously described results for functional outcomes. There was a trend suggestive of greater improvement in symptoms and Q_{max} after HoLEP than TURP at 12 months. Systematic reviews and large series that have been published after these meta-analyses support the place of HoLEP as a safe and effective alternative to TURP [28,47,48]. Data from meta-analyses and the largest series are given in Table 5 [45,46,48–50].

HoLEP represents the endourological alternative to OP, as it is suitable for very large prostates. Two randomised trials comparing HoLEP to OP for large prostates reported equivalent improvements in symptoms and Q_{max} rates but significantly longer operating time for HoLEP [51,52]. In an update of their study with a follow-up of 5 years, Kuntz and Lehrich [53] reported similar durable subjective and objective improvement for both groups.

The meta-analysis by Tan *et al.* [45] provided significant information on perioperative variables and AEs. There were no statistically significant differences between pooled estimates between HoLEP and TURP for urethral stricture (2.6% vs 4.4%), blood transfusion (0% vs 2.2%) and re-intervention (4.3% vs 8.8%). However, the overall complication rate was 8.1% (19/232) in the HoLEP group and 16.2% (37/228) in the TURP group, with a statistically significant difference in the pooled estimates. Pooled data suggest that catheterization time, hospital stay and blood loss were significantly lower in the HoLEP group compared with TURP. In an extensive review of publications between 2003 and 2006, Kuntz pooled the

TABLE 5 Studies on efficacy and morbidity of laser enucleation [mean values (SD)]

Study	Type	LoE	Treatment	Pts, *n*	FU, mo	bIPSS	IPSS	bQ_{max}, mL/s	Q_{max}, mL/s	DoC, days	LoS, days	Blood trans., %	Dysuria, %	Re-cath., %	Strictures, %	Re-operation, %
Tan *et al.* [45]	Meta-analysis	1a	HoLEP	232	12	NA	NA	NA	0.59*	17.7–31.0 h	27.6–59.0 h	0	NA	NA	2.6	4.3
			TURP	228		NA	NA	NA		43.4–57.8 h	48.3–85.5 h	2.2	NA	NA	4.4	8.8
Lourenco *et al.* [46]	Meta-analysis	1a	HoLEP	293	12	NA	−0.82*	NA	1.48*	NA	−1.05*	0.27†	NA	0.71†	NA	0.68†
			TURP	287		NA		NA		NA						
Krambeck *et al.* [48]	Case studies	4	HoLEP	1065	>12	20.3	5.3	8.4	22.7	19.1 h	32.0 h	NA	NA	2.8	3.8	0.1
Bach *et al.* [49,50]	Case studies	4	ThuVEP	88	12	18.4 (7.0)	6.8 (4.0)	3.5 (4.7)	23.3 (10.3)	2.1 (1.1)	NA	2.2	27	2.2	1.1	2.2

*LoE, level of evidence; Pts, patients; FU: follow-up; mo, months; bIPSS, baseline IPSS; bQ_{max}: baseline Q_{max}; DoC, duration of catheterization; LoS, length of stay; Strictures: urethral, meatal, bladder neck; Re-operation, due to obstruction; NA: not available; trans., transfusion; Re-cath, re-catheterization. *WMD (HoLEP–TURP); †Relative risk.*

results of large case series (in total 1847 patients) and showed low complication rates including perioperative mortality (0.05%), transfusion (1%), UTI (2.3%), urethral stricture/bladder-neck contracture (3.2%), and re-operation (2.8%) [54]. In addition, RCTs indicated that HoLEP was better than OP for blood loss, catheterization and hospitalization time [51,52].

The impact on erectile dysfunction and retrograde ejaculation is very similar between HoLEP and TURP/OP [52,55]. The overall EF did not decrease from baseline in either group while three quarters of sexually active patients had retrograde ejaculation after HoLEP.

Durability: Recently Naspro *et al.* [28] evaluated medium and long-term durability of HoLEP by pooling the data from all the available studies with a follow-up of ≥2 years. In all, 607 patients with a mean follow-up of 43.5 months were analysed and showed the durability of functional results, with a mean Q_{max} of 21.9 mL/s and a mean (range) re-operation rate of 4.3% (0–14.1). Similarly, the studies with the longest follow-up (>5 years) showed that both subjective and objective improvement remained sustained whereas the re-operation rate ranged from 1.4% to 4.3% [56,57].

Thulium enucleation

Enucleation of the prostatic adenoma can be performed using the Tm : YAG laser. The initial technique involved enucleation of the median and the lateral lobes combined with vaporization similar to HoLEP and the term 'Tm : YAG VapoEnucleation of the prostate (ThuVEP)' was coined for this types of Tm : YAG laser-based prostatectomy [43]. Recently, a modification of the VapoEnucleation, the 'Tm-laser enucleation of the prostate (ThuLEP)' was introduced by Herrmann *et al.* [58]. Unlike ThuVEP and HoLEP, ThuLEP employs apical incision of the prostatic tissue down to the surgical capsule using the Tm-laser and blunt enucleation with the sheath of the resectoscope. A morcellator is required in both techniques for the removal of the prostatic tissue.

Efficacy and morbidity: There are very few studies on ThuVEP and only one on ThuLEP that show the feasibility and clinical efficacy

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of the techniques [49,50,58,59]. Only in one study is the follow-up > 12 months, therefore data on durability are lacking at the moment [50]. In general, there is a significant improvement in IPSS, Q_{max} and PVR after ThuVEP (Table 5). Morbidity of ThuVEP is minimal with postoperative bleeding, rate of blood transfusions, and symptomatic UTI said to occur in 3.4%, 2.2%, and 6.8% of the patients, respectively. Bach *et al.* [59] evaluated 208 patients (65 in retention) who underwent Tm-prostatectomy (including resection or enucleation). At discharge Q_{max} was improved in both groups (with and without retention) and PVR was similar. Complications occurred more frequently in the retention group, but they were mostly minor and re-intervention was needed in 3% of the patients.

There is only a feasibility study on ThuLEP [58]. No clinical results were provided with the exception of preliminary data on PSA level decrease (80% on average) 4 weeks after ThuLEP suggestive of complete prostatic tissue removal. In addition, it was speculated that bleeding complications and the need for blood transfusions are unlikely to occur with ThuLEP due to the visual coagulation of vessels.

It is obvious that more studies including RCTs are required to evaluate enucleation of the prostate using the Tm : YAG laser.

COMPARISON BETWEEN DIFFERENT LASERS

Because of the lack of direct, head-to-head comparative studies and that the available lasers are at different points in their clinical maturation comparisons are difficult to make. HoLEP and PVP are the most studied options and currently dominate the arena of laser treatment of LUTS associated with BPH. Therefore, our comparison will focus on HoLEP and PVP. As efficacy and morbidity were extensively reviewed above, fields of indirect comparison will include specific subgroup of patients, learning curve and cost.

SPECIFIC CONDITIONS

Anticoagulated men with medical comorbidities

Studies of the Greenlight PV have indicated that the procedure seems to be safe and beneficial for high-risk patients. A study evaluated 66 men with an ASA score of ≥3, with 26 of them under ongoing oral anticoagulant therapy (OAT) and three with a severe bleeding disorder [60]. No blood transfusions were required. Efficacy results showed a durable improvement in both Q_{max} and IPSS. Sandhu *et al.* [61] reported the results of the 80-W GreenLight laser in 24 men receiving various forms of OAT including warfarin (eight patients), and platelet aggregation inhibitors (PAis). Only men on warfarin discontinued the drug 2 days before surgery and restarted it the day after. Overall, all patients underwent vaporization of the prostate safely without any thromboembolic or bleeding AEs. Ruszat *et al.* [62] evaluated the safety of GreenLight PV in the largest series of men with serious comorbidities on coumadin or PAis. There were no thromboembolic or bleeding complications, no blood transfusions were required and only the rate of transient postoperative bladder irrigation was significantly higher in patients on OAT (17.2%) compared with the control group that underwent GreenLight PV without taking anticoagulants (5.4%) [62].

> ‘more studies including RCTs are required to evaluate enucleation of the prostate using the Tm : YAG laser’

Recent data on the GreenLight HPS also showed that patients on or not on OAT had significant and comparable improvements [19]. The postoperative complication rate was low and similar to the control group without any blood transfusion requirement [26].

Similarly, HoLEP has been successfully performed in patients who are normally considered unfit for a TURP, including those with significant comorbidities, such as coagulopathy, anticoagulant dependency, and significant anaemia [63]. Blood transfusion was required in seven patients (8%), including one who had stopped OAT, five on low-molecular-weight heparin substitution, and one who was on full anticoagulation. In addition, platelet transfusion was required in one patient who did not stop clopidogrel. Another study compared the results of HoLEP between 39 patients who were on OAT (13 on coumadin and 25 on aspirin) at the time of their surgery, and 37 who were controls [64]. No transfusions were required in any of their 76 patients and there was no statistical difference in bleeding complication rates between the coumadin, aspirin, and control groups.

An excellent review of laser treatment for patients on OAT concluded that laser prostatectomy seems to decrease the risk of bleeding in patients taking PAis or coumarin derivatives [65].

Patients in retention

Historically patients in retention are considered to be associated with a higher complication rate and sometimes a poorer outcome in terms of voiding parameters.

A study comparing the outcome of 70 men with refractory retention and 113 patients without retention was conducted [66]. All patients in the retention group were able to void spontaneously 1 month after treatment with the 80-W GreenLight laser and PVR was significantly reduced by 74.8% at discharge and 82.7% at the 12-month follow-up. Transient retention requiring catheterization occurred in 12.9% of the patients. Overall, functional results and perioperative complications were similar in the two groups over an observational period of 24 months. In the series of patients in retention treated with the 120-W laser, the IGLU group found that patients in retention achieved similar functional results with the control group with the exception of Q_{max}, while the most frequent complication was dysuria (11.1%) and transient retention requiring re-catheterization (4.8%) [19].

HoLEP has proved its short-term efficacy in patients with urinary retention. In a study with 169 patients, only three (1.8%) failed to void after treatment [67]. Catheter time and hospital stay (1.6 and 1.7 days, respectively) was comparable to previously reported results from patients without retention. Similarly, Peterson *et al.* [68] studied 154 patients in retention. All patients were able to void postoperatively and remained catheter free at follow-up to 1 year, although only 22% of the original patients were evaluated at 1 year. The mean catheterization and hospitalization times were 22.5 h and 33.7 h, respectively.

All these studies reported short-term results and it should be underlined that long-term results for this group of patients are extremely limited.

LEARNING CURVE

HoLEP has been criticized for having a steep learning curve that hinders its widespread application. Endpoints of the learning curve include increase in operative and morcellation efficiency, decrease in operative duration, intraoperative complications, conversion rates, improved patient outcomes and comfort with the procedure. Seki *et al.* [69] based on the volume of tissue enucleated per minute, suggested a learning curve of at least 50 procedures. Shah *et al.* [70] showed that an inexperienced endourologist could perform the procedure with reasonable efficiency after ≈50 cases with an outcome comparable to that of expert surgeons. El-Hakim and Elhilali [71] reported the experience of a senior resident's in learning this procedure. The resident performed on average 85% of the operation during the first 15 cases, but he was able to complete the next 12 cases. The resident became adept with the HoLEP technique after a mean of 20 patients. It was concluded that HoLEP requires more training than TURP. Training programmes and proctoring are critical for most urologists and shortens the learning curve. It was correctly indicated that new HoLEP practitioners who do not have the patient load to maintain regular operative frequency will have a longer learning curve and experience more complications [72].

> 'It seems that 30–50 procedures are required for most users to achieve sufficient competence'

KTP- or LBO-laser vaporization is considered to be a more urologist-friendly procedure, but no study to date has correctly investigated the learning curve. Pioneers of the technique suggest that new practitioners should start with small prostates and only after 10–20 cases should they pass to larger prostates (>50 mL) [73]. It is also strongly recommended that even experienced urologists should attend a formal training course and to have an experienced mentor present at their first cases. It seems that 30–50 procedures are required for most users to achieve sufficient competence [73]. A retrospective evaluation of the learning curve of GreenLight-laser vaporization was performed [74]. A significant correlation was not evident between the learning curve and the functional outcomes, the total incidence and AEs or blood loss following GreenLight PV. The new 120-W HPS and 180-W XPs need comparable technical knowledge to the 80-W PVP, but it remains to be seen whether they require a longer learning curve due to the higher energy application.

COST

The introduction of new technology in healthcare is sometimes charged as one of the major causes of escalating costs due to the purchase of the capital equipment and treatment failure in terms of efficacy, morbidity, and durability.

Despite the high cost of the equipment and fibres, studies have shown that GreenLight PV was less expensive compared with TURP due to the difference in hospital stay, duration of catheterization, and complication rates. In Australia the cost for GreenLight PV and TURP was AU$3368 vs AU$4291, respectively, and in USA $4266 vs $5097 [20,75].

The clinical outcomes and the cost characteristics of PVP, microwave thermotherapy, transurethral needle ablation, ILC and TURP were compared from a payer perspective in an economic simulation model [76]. The model included costs of initial treatment, follow-up care, AEs and re-treatment, and the patients were followed for 2 years after the initial intervention. The estimated cost was lower for PVP than for any other procedural option at any interval studied [76].

Salonia *et al.* [77] addressed the cost issue in a study of 63 patients randomized to undergo either HoLEP or OP. The cost of a HoLEP was significantly lower than the cost of an OP (a 9.6% net cost saving) mainly due to the shorter hospital stay. The authors did not include in the analysis the cost related to the initial purchase of the machine.

Recently, cost-effectiveness of surgical treatments for the management of BPH was assessed using a Markov model reflecting

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likely care pathways [78]. When all treatment strategies were compared against TURP alone as a common comparator, it was estimated that HoLEP is more cost-effective than a single TURP but less effective than a strategy involving repeat TURP if necessary. On the other hand, GreenLight PV is less effective and more costly than TURP. It was concluded that overall TURP remains both clinically effective and cost-effective.

However, the cost effectiveness of all techniques depends on the existence of long-term data, costs of complications, and the different reimbursement systems in different countries. Therefore, it is difficult to draw solid conclusions applicable to every country.

CONCLUSIONS

During the last decade, the development of laser therapy from coagulation to vaporization, resection and enucleation has been dramatic. Into this frame, coagulation-based techniques (i.e. ILC and VLAP) have been abandoned completely, while HoLAP and HoLRP were the forerunners of many of the applications used today (such as photoselective vaporization, diode applications and Tm-vaporesection) but they have paid the price of the development of HoLEP. The short-term efficacy of the emerging laser treatments (including diode and Tm-prostatectomy) has been suggested by low quality studies.

More than ever, TURP is being challenged by HoLEP and GreenLight PV, which both represent valid clinical alternatives. Current evidence supports the conclusion that HoLEP offers favourable and durable outcomes for any prostate size with low early and late morbidity. GreenLight laser prostatectomy has achieved a higher level of acceptance, although long-term results from high quality studies are still awaited.

The present review has also documented the need for better quality data to increase the level of evidence for each laser treatment.

CONFLICT OF INTEREST

Oliver Reich received a speaker's honoraria from AMS and Olympus; Claus G. Roehrborn is a study investigator for AMS; Peter J. Gilling is a meeting participant for Lumenis Inc.

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Correspondence: Stavros Gravas, Department of Urology, University of Thessaly, Larissa, Greece.
e-mail: sgravas2002@yahoo.com

Abbreviations: **AE**, adverse event; **AUA-SS**, AUA-symptom score; **EF**, erectile function; **HoLAP**, Ho-laser ablation of the prostate; **HoLEP**, holmium laser enucleation of the prostate; **HoLRP**, Ho-laser resection of the prostate; **IGLU**, International GreenLight Users group; **ILC**, interstitial laser coagulation; **IPSS**, International Prostate Symptom Score; **LBO**, lithium triborate; **OAT**, oral anticoagulation therapy; **OP**, open prostatectomy; **PVP**, photoselective vaporization of the prostate; **PAi**, platelet aggregation inhibitor; **PVR**, postvoid residual urine volume; $\mathbf{Q_{max}}$, maximum urinary flow rate; **QOL**, quality of life; **RCT**, randomized clinical trial; **ThuVaRP(-TT)**, Tm-vaporesection of the prostate ('tangerine technique'); **ThuLEP**, Tm-laser enucleation of the prostate; **ThuVEP**, Tm : YAG VapoEnucleation of the prostate; **TUR**, transurethral resection; **VLAP**, visual laser ablation of the prostate; **WMD**, weighted mean difference; **(Ho)(KTP)(Nd)(Tm) : YAG**, (holmium) (potassium titanyl phosphate) (neodymium) (thulium) : yttrium aluminium garnet.