Guidelines on

Lasers and Technologies

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European Association of Urology

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1. INTRODUCTION

The European Association of Urology (EAU) Guidelines Office have set up a Guidelines Working Panel to analyse the scientific evidence published in the world literature on lasers in urological practice. The working panel consists of experts who, through these guidelines, present the findings of their analysis, together with recommendations for the application of laser techniques in urology. The guidelines also include information on the characteristics of lasers, which the panel believes will be very helpful to clinicians.

The aim of this document is to provide information on technical considerations and supplement the information in other EAU organ-specific guidelines, rather than be in competition.

These guidelines on the use of lasers and novel technologies in urology provide information to clinical practitioners on physical background, physiological and technical aspects, as well as present the first clinical results from these new and evolving technologies. Emphasis is given on interaction between technical tools and human tissue, surgical aspects and abilities, advantages and disadvantages of new tools, including operator convenience. In this document the panel focused on lasers, with the intention to expand further in the years to come.

The application of lasers in treating urological disorders is a swiftly developing area, with laser technology currently used for a variety of urological procedures. In some therapeutic areas, lasers have become the primary method of treatment and standard of care.

As with many other surgical or interventional procedures, there is a lack of high-quality publications. But particularly in the field of lasers, where technological advances are occurring so rapidly, many technologies will never be in use long enough for long-term study. This is obviously a challenge for anyone attempting to establish an evidence-based discussion of this topic, and the panel are very aware that these guidelines will require re-evaluating and updating within a short time frame. It must be emphasised that clinical guidelines present the best evidence available to the experts but following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences and individual circumstances of patients into account.

1.1 Safety

Safety is very important when using lasers. All intra-operative personnel should wear proper eye protection to avoid corneal or retinal damage. This is particularly important with neodymium:yttrium-aluminum-garnet (Nd:YAG) lasers, which penetrate deeply and can burn the retina faster than the blink reflex can protect it. Although holmium:YAG (Ho:YAG) lasers do not penetrate as deeply, they can cause corneal defects if aimed at the unprotected eye. For all lasers, adequate draping should be used to cover external areas, with wet towels draped over cutaneous lesions. Ideally, reflective surfaces (e.g. metal instruments) should be kept away from the field of treatment; however, if this is not possible, the field of treatment should be draped with wet drapes. Furthermore, it is very dangerous to use a laser if oxygen is in use anywhere near the operative field, as this may result in a laser fire and significant burns (1).

1.2 Methodology

The primary objective of this structured presentation of the current evidence base in this area is to assist clinicians in making informed choices regarding the use of lasers in their practice. A secondary objective was to apply EAU Guidelines methodology to this area where there is limited evidence available.

1.2.1 ***Data identification***

Structured literature searches using an expert consultant were designed for each section of this document. Searches were carried out in the Cochrane Library database of Systematic Reviews, the Cochrane Library of Controlled Clinical Trials, and Medline and Embase on the Dialog-Datastar platform. The controlled terminology of the respective databases was used and both MesH and EMTREE were analysed for relevant entry terms.

The search strategies covered the last 25 years for Medline and for Embase (1974). A total number of 436 papers were identified, of which one was a Cochrane review (laser prostatectomy for benign prostatic obstruction [BPO]) (2). A separate literature search for cost-effectiveness was carried out and yielded seven unique publications.

1.2.2 ***Publication history***

A scientific paper is now available based on this document (4). This resulted in minor changes to this published version of the Guidelines on Lasers and Technologies.

1.2.3 ***Quality assessment of the evidence***

The expert panel extracted relevant data from individual publications, the key findings of which are presented in tables throughout the document. Papers were assigned a level of evidence and recommendations have been graded following the listings in Tables 1 and 2.

Table 1: Level of evidence (LE)

Level	Type of evidence
1a	Evidence obtained from meta-analysis of randomised trials.
1b	Evidence obtained from at least one randomised trial.
2a	Evidence obtained from one well-designed controlled study without randomisation.
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study.
3	Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports.
4	Evidence obtained from expert committee reports or opinions or clinical experience of respected Authorities.

Modified from Sackett et al. (3).

Table 2: Grade of recommendation (GR)

Grade	Nature of recommendations
A	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial.
B	Based on well-conducted clinical studies, but without randomised clinical trials.
C	Made despite the absence of directly applicable clinical studies of good quality.

Modified from Sackett et al. (3).

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2. LASER-BASED TREATMENTS FOR BLADDER OUTLET OBSTRUCTION (BOO) AND BENIGN PROSTATIC ENLARGEMENT (BPE)

2.1 Introduction

Benign prostate obstruction (BPO) and enlargement (BPE) can be treated with a range of laser treatments using different laser systems and applications. The different systems produce different qualitative and quantitative effects in tissue, such as coagulation, vaporisation or resection and enucleation via incision (Table 3). Laser treatment is considered to be an alternative treatment to transurethral resection of the prostate (TURP). It must therefore achieve the same improvement in symptoms and quality of life (QoL) as TURP. It must also improve all urodynamic parameters, such as maximal urinary flow rate (Q_{max}), post-void residual urine volume (PVR) and maximal detrusor pressure (Pdetmax) with less morbidity and shorter hospitalisation than with TURP.

This section focuses on contemporary laser treatments for the management of BPE or BPO.

2.2 Physical principles of laser action

LASER is an acronym that stands for Light Amplification by Stimulated Emission of Radiation. Laser radiation is simply the directed light of a narrow bandwidth. This is synonymous to a single colour and applies to all regions of the invisible and visible electromagnetic spectrum (1).

2.2.1 ***Reflection***

When the laser beam encounters tissue, a percentage of the beam is reflected by the boundary layer and may therefore heat and damage surrounding tissue. Reflection mainly depends on the optical properties of the tissue and the irrigant surrounding it. Because reflection is not greatly affected by wavelength, it can be ignored when evaluating a laser wavelength for surgical purposes.

2.2.2 ***Scattering***

The heterogeneous composition of tissue causes an intruding laser beam to scatter. Scattering diverts part of the laser beam away from its intended direction and therefore its intended purpose. The amount of scattering depends on the size of the particles and the wavelength of the laser. Shorter wavelengths are scattered to a much higher degree than longer wavelengths, i.e. blue laser radiation is scattered more than green, green more than red, and red more than infrared.

2.2.3 ***Absorption***

Absorption is the most important process of light interaction, though it is not the only process. Intensity of the laser beam decreases exponentially as the absorbing medium increases in density. Absorbed laser radiation is converted into heat, causing a local rise in temperature. Depending on the amount of heat produced, tissue will coagulate or even vaporise. Heat is more likely to be generated next to the tissue surface than further below because of the exponential decrease in beam intensity as it passes into the tissue and the immediate action of the absorption process.

However, absorption can only occur in the presence of a chromophore. Chromophores are chemical groups capable of absorbing light at a particular frequency and thereby imparting colour to a molecule. Examples of body chromophores are melanin, blood and water. Figure 1 shows the wavelength dependence and absorption length of a laser beam. The absorption length defines the optical pathway, along which 63% of incident laser energy is absorbed.

2.2.4 ***Extinction length***

The *extinction length* defines the depth of tissue up to which 90% of the incident laser beam is absorbed and converted into heat. An extinction length is equal to 2.3 absorption lengths. Haemoglobin and water are widely used as chromophores for surgical lasers (Figure 1).

For a short time after absorption of a circular laser beam, the generated heat is confined in a cylindrical-shaped volume, which has the height of the laser beam's extinction length and the approximate diameter of the laser fibre. The density of the absorbed energy determines the effect of the laser on tissue.

It is important to match the achieved effect along the extinction length with the intended surgical effect. At the same power wattage, a laser wavelength with a long extinction length may create a deep necrosis, whereas a laser wavelength with a much shorter extinction length will produce an increase in temperature above boiling point and immediate vaporisation of tissue.

Table 3: Lasers: crystals, abbreviations, wavelength, techniques and acronyms

Active crystal	Abbreviation	Wavelength (nm)	Technique	Acronym
Holmium	Ho:YAG	2140	Holmium laser ablation	HoLAP
			Holmium laser resection of prostate	HoLRP
			Holmium laser enucleation of prostate	HoLEP
Neodym	Nd:YAG	1064	Visual laser ablation of prostate	VLAP
			Contact laser ablation of prostate	CLAP
			Interstitial laser coagulation (of prostate)	ILC
Kalium titanyl phosphate	KTP:Nd:YAG (SHG)	532	Photoselective vaporisation of prostate	PVP
Lithium borat	LBO:Nd:YAG (SHG)	532	Photoselective vaporisation	PVP
Thulium	Tm:YAG	2013	Thulium laser vaporisation of prostate	ThuVAP
			Thulium laser vaporesection of prostate	ThuVARP
			Thulium laser vapoenucleation of prostate	ThuVEP
			Thulium laser enucleation of prostate	ThuLEP
Diode lasers	-	830	Interstitial laser coagulation of prostate	ILC
		940	Vaporisation	-
		980	Vaporisation	-
		1318	Vaporisation	-
		1470	Vaporisation	-

2.3 Historical use of lasers

2.3.1 Nd:YAG laser

The Nd:YAG laser has a wavelength of 1064 nm. It has a long extinction length and penetrates tissue by approximately 4-18 mm, making it suitable for haemostasis and tissue coagulation. At that time it appeared to be ideal for the treatment of benign prostatic hypertrophy (BPH) (2). Since 1985, many Nd:YAG laser-driven transurethral treatments have been described for both BPE and BPO (3).

2.3.2 Nd:YAG laser-based techniques

Several Nd:YAG approaches have been extensively studied, including: visual laser ablation of the prostate (VLAP) (4); contact laser ablation of the prostate (CLAP) (5); interstitial laser coagulation (ILC) (6), and Nd:YAG laser hybrid techniques (7).

However, all these techniques have been superseded by the advent of newer laser-based techniques (8). As these techniques are no longer contemporary, they will not be discussed further in these guidelines. However, they are discussed in the EAU guidelines on the conservative treatment of non-neurogenic male lower urinary tract symptoms (LUTS) (9).

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3. CONTEMPORARY LASER SYSTEMS

3.1 Introduction

Following the first generation of laser-based treatments for BOO and BPE, four (groups of) laser systems are currently used:

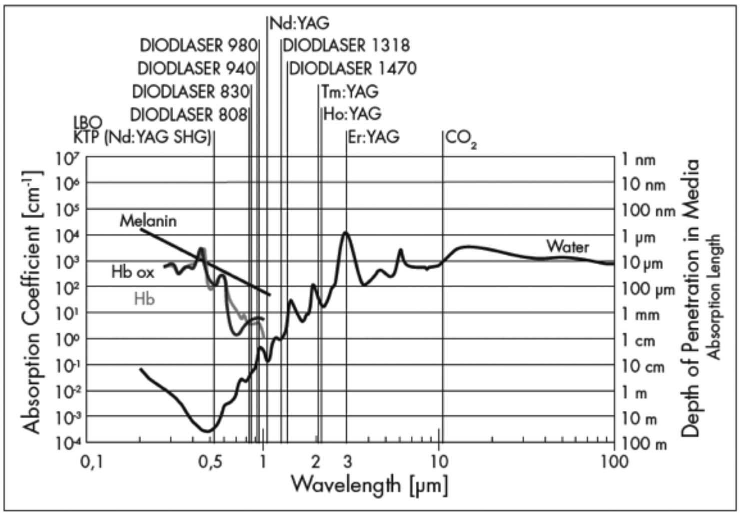
- KTP (kalium titanyl phosphate, KTP:Nd:YAG [SHG]) and LBO (lithium borat, LBO:Nd:YAG [SHG]) lasers;
- Diode lasers (various);
- Holmium (Ho):YAG (yttrium-aluminium-garnet) lasers;
- Thulium (Tm):YAG (yttrium-aluminium-garnet) lasers.

All the above-mentioned contemporary (and historical) laser therapies for the treatment of BOO and BPE use physiological sodium 0.9% solution for irrigation. This eliminates the risk of hypotonic hypervolaemic transurethral resection of the prostate (TURP) syndrome, which occurred in 1.4% of patients in large TURP reported series (1). A second advantage (that applies to all endoscopic minimal invasive therapies for the prostate) is the avoidance of secondary wound healing skin disorders, which occurred in 5.5% of the patients in a major series of open prostatectomy (OP) (2).

3.2 KTP (kalium titanyl phosphate, KTP:Nd:YAG [SHG] and LBO (lithium borat, LBO:Nd:YAG [SHG]) lasers

The KTP and LBO lasers are both derived from the Nd:YAG laser. The addition of a KTP or LBO crystal to the laser resonator converts the Nd:YAG wavelength from 1064 nm to 532 nm. This is a green wavelength, which is strongly absorbed by oxyhaemoglobin. The resultant laser has a short extinction length and penetrates vascular tissue by only a few micrometres. In red, well-circulated tissue, the density of absorbed power is high and immediately raises the tissue temperature above the boiling point (Figure 1). This causes tissue to vaporise, leaving behind a coagulated seam where the increased tissue temperature has resulted in haemostasis (3).
In this seam, haemoglobin is bleached but not vaporised. The applied laser energy must travel through the coagulated seam, where the laser beam experiences mainly scattering. The lack of absorption in coagulated tissue impairs its removal, while the scattering of the green wavelength reduces the laser beam's intensity, impairing its vaporising effect on the next tissue layer (4).

Figure 1: Wavelength of different laser types, depth of penetration in media and absorption coefficient



Er:YAG = Erbium: yttrium-aluminium-garnet laser; Ho:YAG = Holmium: yttrium aluminium garnet; KTP = potassium titanyl-phosphate; LBO = lithium triborate; Nd:YAG = Neodymium-doped: yttrium aluminium garnet; Tm:YAG = Thulium: yttrium aluminium garnet.

*3.2.1 **Physical properties***

All new lasers are extensively studied in preclinical trials in comparison with the most common vaporising laser, i.e. an 80 W KTP or 120 W LBO laser. The specific heat capacities of renal (3.89 kJ/kg/°K) and prostatic tissues (3.80 kJ/kg/°K) are almost equivalent, so making the isolated, blood-perfused, porcine kidney a very useful model for the study of laser procedures (5).

Animal models have been very useful in evaluating laser characteristics, including tissue ablation rate, efficacy of ablation in correlation to the power setting (output power efficiency), haemostatic properties, and the extent of morphological tissue necrosis. Table 4 provides a comparison of different lasers and their individual characteristics derived from a series of ex-vivo comparison studies in a porcine, perfused kidney model. The data has been given as a statistical mean or interval, according to the original publication.

3.2.1.1 Ablation capacity

The tissue ablation rate achieved with KTP and LBO lasers increases with increasing output power. In comparison to the Tm:YAG laser (70 W) KTP laser, the tissue ablation rate reached 3.99 g/10 min (80 W KTP) and 6.56 g/10 min (70 W Tm:YAG) ($p < 0.05$). When compared to TURP, both laser devices produced significantly lower rates of tissue removal (8.28 g/10 min) (6). However, the LBO laser, with its tissue ablation rate of 7.01 g/10 min laser ablation at 120 W offered a significantly higher ablation capacity compared with KTP laser at 80 W ($p < 0.005$) (7).

3.2.1.2 Bleeding rate

The KTP laser shows excellent haemostatic potential, with a bleeding rate for the 80 W KTP laser of 0.21 g/min compared with 0.16 g/min for the continuous wave (cw) 70 W Tm:YAG laser. In contrast, TURP is associated with a much higher bleeding rate of 20.14 g/min ($p < 0.05$) (6). The bleeding rate for the 120 W LBO laser was also higher at 0.65 g/min when compared to 80 W KTP with 0.21g/min, respectively ($p < 0.05$) (7).

3.2.1.3 Coagulation zone

In the porcine perfused kidney tissue ablation model, the KTP laser ($p = 0.05$) showed a 2.5-fold deeper coagulation zone (666.9 µm) than the cw Tm:YAG (264.7 µm) laser and TURP (287.1 µm). Tissue ablation resulted in a dense coagulation zone at the tissue surface (6). The corresponding depths of the coagulation zones at 120 W LBO laser and 80 W KTP laser were 835 µm and 667 µm ($p < 0.05$), respectively (7).

Table 4: Ex-vivo study on ablative capacity, haemostatic properties and coagulation zone due to tissue penetration in porcine perfused kidney model

Study	Bach et al. 2010 (8)		Heinrich et al. 2010 (7)		Wendt-Nordahl et al. 2008 (6)		
Laser Type	Tm:YAG		KTP	LBO	Tm:YAG	KTP	HF (TURP)
Wavelength (nm)	2013	2013	532	532	2013	532	
Power setting (W)	70	120	80	120	70	80	160
Tissue ablation rate (g/10 min)	9.80	16.41	3.99	7.01	6.56 ± 0.69	3.99 ± 0.48	8.28 ± 0.38
Bleeding rate (g/min)	0.11	0.15	0.21	0.65	0.16 ± 0.07	0.21 ± 0.07	20.14 ± 2.03
Coagulation zone (mm)	0.36	0.40	0.667	0.835	0.2647	0.669	0.287

KTP = kalium titanyl phosphate; LBO = lithium borate; Tm:YAG = Thulium: yttrium aluminium garnet; TURP = transurethral resection of the prostate.

*3.2.2 **Surgical technique of KTP/LBO lasers***

Both KTP and LBO lasers operate at a wavelength at which absorption in water is minimal. In the absence of a haemoglobin molecule, the extinction length increases dramatically and the beam penetrates deeply into irrigant and/or tissue. This technique is described as the photoselective vaporisation of prostate (PVP) (9). In addition, side-firing fibres are used in PVP to ensure that the surgeon has better, direct, visual control of the point at which the laser beam strikes the tissue.

Laser energy is directed towards prostatic tissue using a 70° 600 µm side-firing probe. Under direct vision, vaporisation is performed with a fibre-sweeping technique, starting at the bladder neck and continuing with the lateral lobes and the apex. The prostate gland is vaporised from inside the gland to its outer layers. This also occurs with TURP, but in contrast to TURP, no tissue remains for histopathological evaluation (10).
Since 2006, a LBO laser with a power of 120 W and collimated beam has been available (7,11).
As with all lasers, the surgeon must wear safety goggles. These goggles must include a coloured filter in the KTP/LBO laser setting.

*3.2.3 **Urodynamic results and symptom reduction***

In 1998, Malek et al. (12) showed that the 60 W KTP laser was both feasible and safe. Since then, most laser therapy trials prior to 2010 have used the 80 W KTP laser. There has been only limited data on the higher-powered 120-W LBO laser. Almost 10 years after the clinical introduction of 532-nm lasers, two randomised controlled trials (RCT) were published comparing 80 W KTP with TURP with follow-up periods up to 12 months (13,14). One of the trials compared 80 W KTP with OP (15), while the other trial compared 120 W LBO laser with TURP (16) (Table 5).

One RCT showed equivalent results to TURP (12) at 1-year follow-up, while another, non-randomised, two-centre study reported equivocal results (17). In contrast, a second RCT clearly showed that TURP resulted in greater urodynamic improvement (Q_{max}) than the KTP PVP laser (14). Another study comparing KTP PVP with OP showed equivalence in Q_{max} improvement, PVR and symptom score reduction at 18-month follow-up (15). Prostate-specific antigen (PSA), as a surrogate marker of tissue removal, decreased by 68.2% with OP and 61.2% with KTP PVP (15). However, other studies have reported much lower rates for PSA reduction using KTP PVP, including 45% reduction (18), 41.7% (19) and 37% (20).

Kalium titanyl phosphate PVP showed a higher retreatment rate in larger prostates > 80 ml within a 12 month follow-up (21). The study comparing LBO PVP treatment with TURP showed equivalence in Q_{max} improvement, PVR and symptom score reduction at 36-month follow-up (16). PVP demonstrated reduced detrusor pressure at maximum flow (Pdetqmax) (22) at 1-year follow-up. In addition, prospective, non-randomised trials have demonstrated the safety and efficiency of LBO PVP laser in patients receiving ongoing oral anticoagulation (23), in patients with retention (24), or with prostates > 80 mL (21).

In studies comparing TURP with KTP PVP, OT time was significantly shorter in prostates larger than 80 ml by 30 to 50 min (17). This difference comes down to 9 min with the LBO PVP (120 W) (16).

Table 5: KTP and LBO lasers: improvement in urodynamic parameters, symptom score and PSA reduction

Reference	Laser source (power)	Follow-up (mo)	Patients (n)	Mean prostate size (mL)	PSA reduction (%)	Change in symptoms (%)	Change in Q_{max} (mL/s) (%)	PVR change (%)	LE
Bouchier-Haydes et al. 2006 (13)	KTP PVP	12	38	42.4	n.a.	49.83	+12.1 (167)	81.63	1b
	TURP		38	33.2	n.a.	50.23	+9.2 (149)	68.90	
Horasanli et al. 2008 (14)	KTP PVP	6	39	86.1	31.8	30.68	+5.8 (157)	87.05	1b
	TURP		37	88	44.6	68.31	+13.8 (225)	73.98	
Tasci et al. 2008 (17)	KTP PVP	24	40	108.4	56.8	82.66	+13.5 (307.7)	83.69	2a
	TURP		41	104.2	78.7	83.33	+12.8 (306.4)	84.91	
Skolarikos et al. 2008 (15)	KTP PVP	18	65	93	61.2	50	+7.4 (186)	84.53	1b
	OP		60	96	68.2	59.52	+7.0 (187.5)	86.51	
Al-Ansari et al. 2010 (16)	LBO	36	60	61.8	38.4	60.29	+9.6 (239)	78.9	1b
	TURP		60	60.3	62.5	65.9	+13.6 (312.5)	80.2	

KTP = potassium titanyl-phosphate laser; LBO = lithium triborate; OP = open prostatectomy; PVP = photoselective vaporisation of the prostate; TURP = transurethral resection of the prostate.

3.2.4 Risk and complications, durability of results

3.2.4.1 Intra-operative complications

Several studies have proven the intra-operative safety of PVP with KTP and LBO lasers, including prospective studies (25-27) and RCTs in comparison to TURP (13,14,28,29) or OP (15). Furthermore, safety was demonstrated in subgroup analyses of patients with large prostates (30,31), receiving anticoagulant therapy (31,24), or in retention (31,24).

An RCT comparing 80 W KTP PVP with TURP demonstrated significantly less blood loss in KTP PVP (0.45 g/dL) versus TURP (1.46 g/dL, $p < 0.005$), resulting in a blood transfusion rate in TURP (13). Another RCT of 80 W KTP PVP compared with TURP supported these findings with a blood transfusion rate of 8.1% for TURP (14). In an RCT comparing LBO PVP to OP, the transfusion rate was 0% following KTP PVP, but 13.3% for OP (15). A total of 7.69% of patients in the KTP PVP group required intra-operative conversion to TURP for the control of bleeding, most probably due to capsule perforation (15). A study comparing LBO PVP laser therapy with TURP reported a blood transfusion rate of 20%, a capsule perforation rate of 16.7%, and a TURP syndrome of 5% for the TURP treatment arm, but none of these complications were reported for LBO PVP (16).

These findings are supported by a number of studies (not including RCTs). A major multicentre study of 500 patients comparing PVP to TURP reported an intra-operative bleeding rate in 3.6%, capsule perforation in 0.2% and conversion to TURP due to bleeding, prostate size or fibre defect in 5.2% of patients. No blood transfusions were necessary. The highest rate of intra-operative bleeding occurred in a subgroup of patients with prostates > 80 mL (5.7% of subgroup) (25). One non-RCT study of LBO PVP reported an intra-operative bleeding rate of 2.6%, capsule perforation of 1% and blood transfusion rate of 0.4% (27). In another non-RCT on LBO PVP, various subgroups of patients were compared, including patients not in retention with patients in retention, patients taking anticoagulant therapy versus patients not taking anticoagulants, and prostate size < 80 mL versus > 80 mL. Intra-operative bleeding which required conversion to TURP occurred in 1.5-3.8% (> 80 mL). Capsule perforation occurred in 0.8-1.5% of patients taking anticoagulants (31). These findings have been supported by studies from other authors in the same patient subgroups (23,24,30,32).

3.2.4.2 Early post-operative complications

An RCT that compared KTP PVP to TURP in patients with prostates > 70 mL found a significantly higher rate of urinary retention after KTP PVP (15.3 vs 2.7%, $p < 0.05$). Reinterventions were necessary in 17.6% of patients following KTP PVP versus 0% for TURP (14). Another RCT reported 0% and 16.7% clot retention in KTP PVP and TURP, respectively, while transient urinary retention with recatheterisation occurred in 5% of both groups. Urinary tract infection (UTI) occurred in 3.3% and 5% of KTP PVP and TURP, respectively, while re-admissions were necessary in 1.6% and 5%, respectively (13).

An RCT comparing KTP PVP with OP for prostatic adenomas > 80 mL showed no statistically significant difference in the incidence of post-operative complications. Prolonged dysuria was noted in 7.6% of KTP PVP and 11.6% of OP patients, while UTIs were reported in 21.5% of KTP PVP versus 27% of OP patients (15). In an RCT comparing LBO PVP with TURP, clot retention occurred in 10% of TURP-treated patients compared with none in the LBO PVP group. In the same study, dysuria within 30 days following surgery was reported in 31.7% of TURP and 93.3% of LBO PVP. In contrast, a non-RCT study on LBO PVP reported dysuria in 7.5-14.6 % in all patient subgroups (31).

The above findings are supported by the data of a major study of 500 patients (25). Following PVP using the KTP laser, haematuria was reported in 9.8%, blood transfusion in 0.4%, revision in 0.6%, acute renal failure in 0.6%, urosepsis in 0.4%, dysuria in 14.8%, transient urge incontinence in 2.4%, and UTI in 6.8% (25).

Haematuria was significantly more common in patients taking anticoagulation treatment (17.2 vs 5.4%, $p = 0.001$) (23) or with prostates > 80 mL (17.2 vs 9.8%, $p < 0.05$) (25). Patients with prostates < 40 mL had a significantly higher rate of dysuria than the overall study population (24.3 vs 14.8%, $p < 0.01$) (25).

3.2.4.3 Late complications and durability of results

The longest follow-up of an RCT in evaluating the longevity and long-term morbidity of KTP PVP and LBO PVP is the study of Al-Ansari comparing LBO PVP to TURP with a follow-up of 36 months (16). Longer follow-up of 60 months is presented by a non-randomised study of Hai. Retreatment with PVP due to recurrent adenoma occurred in 7.7% of 246 patients, three (1.2%) underwent incision of the bladder neck resulting in an overall retreatment rate of 8.9% (33).

In an RCT with a 6-month follow-up, 8.1% in the TURP group and 5.1% in the KTP PVP group underwent internal urethrotomy in response to a urethral stricture. Reintervention was required in 17.9% of patients treated with KTP PVP because coagulated tissue was significantly obstructing the bladder outlet. Retrograde ejaculation rates were similar in both groups (56.7% TURP and 49.9% KTP PVP) (14). Another RCT with a 12-month follow-up reported submeatal/urethral strictures or bladder-neck stenosis in 13.3% of TURP patients and 8.3% of KTP PVP patients (13). In an RCT of KTP PVP versus OP, and an 18-month follow-up, the reoperation rates due to urethral stricture were 3.1% versus 1.6%, bladder neck contracture (0% vs 3.3%), or need for apical resection (1.5%), with a total of 4.6% of KTP PVP and 5% OP, respectively (15). Comparing LBO PVP with TURP reported a significantly lower retreatment rate of 1.8% for LBO PVP versus 11% for TURP. Bladder neck contractures were incised in 3.6% and 7.4%, respectively.

These findings are supported by a large case series RCT for KTP PVP, with a global retreatment rate of 14.8% due to recurrent or persisting adenoma tissue (6.8%), bladder neck strictures (3.6%), or urethral strictures (4.4%) (32). The limitation of this study lies in the number of patients available at 5-year follow-up (27/500) (25). Anticoagulation and urinary retention at the time of surgery have no significant influence on the rate of long-term complications (23,24).

It is possible that KTP PVP has reduced efficacy in patients with larger prostates. According to a prospective, multicentre study, PVP efficacy was lower in patients with larger prostates and PSA levels > 6.1 ng/mL (34), but this finding has not been supported by other studies (25,30). Bladder neck strictures seem to occur more often in patients with prostate glands < 40 mL (7.8 vs 3.6%, $p < 0.05$) (25).

There is evidence from RCTs that persistent urinary stress incontinence is rare. Incontinence varies from 1.4% for KTP PVP (34) to 0.7% for LBO PVP (27).

There is limited data on sexual function following PVP. After a 24-month follow-up, overall sexual function in men undergoing KTP PVP was found to be maintained. In those IIEF-5 (International Index of Erectile Function-5) > 19, the pre-operative median value was significantly decreased from 22 to 16.7 ($p < 0.05$) (36). In an RCT of LBO PVP compared with TURP, none of the 82 patients in follow-up for 36 months presented with erectile dysfunction, and there was a comparable rate of retrograde ejaculation (PVP 49.9% vs TURP 56.7%, $p = 0.21$) (14). Another study, comparing KTP PVP and OP, reported no change in erectile function post-operatively (15). In a case series of LBO PVP, erectile function remained stable or improved in patients with mild or mild-to-moderate erectile dysfunction (37-39).

3.2.5 *Conclusions and recommendations for the use of KTP and LBO lasers*

Conclusions	**LE**
In patients with small to moderate-sized prostates, TURP remains the standard of care.	1a
KTP PVP and LBO PVP are safe and effective in the treatment of BOO and BPE in patients with a small or medium prostate gland.	1b
Over a follow-up of 3-5 years, re-treatment rates appear comparable to those with TURP.	1b (at 3 yr) 4 (at 5 yr)
KTP PVP and LBO PVP are safe and effective for patients receiving anticoagulation medication or patients in retention.	4

Recommendations	**GR**
KTP/LBO PVP is an alternative treatment for patients with BOO and BPE for small and medium glands.	A
KTP/LBO PVP can be offered as an alternative to TURP for patients with refractory urinary retention.	B
KTP/LBO PVP can be offered to patients using anticoagulant medication.	B
KTP/LBO PVP is a safe method for volume reduction in large size prostate glands.	A

BOO = bladder outlet obstruction; BPE = benign prostatic enlargement; KTP = potassium titanyl-phosphate laser; LBO = lithium triborate; PVP = photoselective vaporisation of the prostate; TURP = transurethral resection of the prostate.

3.2.6 *References*

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3.3 Diode lasers

3.3.1 ***General aspects***

The term diode laser refers to the method of laser beam generation.

Laser light can be generated by a resonator or a diode. The main advantages of diode lasers compared with Nd:YAG lasers are a smaller box size and a much higher wall-plug efficiency (i.e. how much of the mains supply is converted into laser power). These differences arise out of the technical principles behind the generation of laser radiation and energy. Depending on the type of laser generator, the efficiency of diode lasers is more than one order of magnitude better. Furthermore, the thermal power loss of diode lasers is much less and therefore they can be operated from a standard wall mounted power outlet.

Diode lasers in the wavelength range of 808-980 nm experience a similar absorption in water and generate a similar tissue effect to the Nd:YAG laser (1,2). Other diode lasers have wavelengths of 1318 and 1470 nm (3). The 830 nm (Indigo) diode laser has been extensively used in interstitial laser coagulation (ILC) (4).

Various types of diode lasers operating at wavelengths of 940, 980 or 1470 nm are available for the application in diode-laser prostatectomy. Currently, there are only a few studies investigating the clinical applications of diode lasers and the maximum follow-up is 1 year.

3.3.2 **Physical properties**

3.3.2.1 Ablation capacity

In the porcine perfused kidney model, the 1318 nm diode laser achieved the highest ablation rate (12.43 g/10 min, 100 W) when compared to the 1470 nm diode laser (5.27 g/10 min, 80 W), the 980 nm diode laser (8.99 g/10 min, 200 W), or the 120 W LBO laser (7.01 g/10 min, 120 W). The same result was achieved when the output power efficiency (g/W/10 min) was calculated (3). The 980 nm and 1470 nm diode lasers showed no statistical difference when compared with the LBO laser (3). The 940 nm diode laser also showed a large ablation capacity when tested in canine prostate (15.17 g/10 min) (5). In a further study, the 980 nm diode laser showed increased tissue ablation rates in the continuous-wave (cw) mode, with increasing output power levels reaching 7 g/10 min at 120 W while the KTP laser displayed a significantly lower ablation capacity. Compared with TURP, both laser devices resulted in significantly lower tissue removal (6) (Table 6).

3.3.2.2 Bleeding rate

In a perfused ex-vivo porcine kidney, the haemostatic properties, calculated by bleeding rate, of the 980 nm (0.35 g/min), the 1318 nm (0.27 g/min) and the 1470 nm (0.24 g/min) diode lasers were significantly better than for the LBO laser (0.65 g/min) (3). For the 940 nm diode laser, 60 W resulted in a bleeding rate of 0.21 g/min (5).

3.3.2.3 Coagulation zone

The 980 nm (4.62 mm), 1318 nm (4.18 mm) and the 1470 nm (1.30 mm) diode laser showed significantly deeper necrotic zones compared to the LBO laser (0.84 mm) (3). The 980 nm diode laser was shown to achieve a mean coagulation zone of 8.43 mm, 9.15 mm and 9.58 mm in a porcine, perfused kidney model at 60, 90, and 120 W output powers, respectively. Compared with 80 W KTP, the coagulation capacity in the porcine kidney model for diode lasers was 7.7 to 8.7 times deeper ($p < 0.0001$). A shift towards the pulsed emitting mode did not change these results ($p < 0.001$) (6). These results are within the range of the Nd:YAG laser (2).

In a further in-vivo study, the 1470 nm diode laser achieved a coagulation zone of 2.30 mm at 100 W (7). The diode laser had an up to 2.7 times deeper coagulation capacity than KTP ($p < 0.005$). The 940 nm diode laser was studied in a porcine perfused kidney model. The coagulation depth measured 0.86 (10 W) up to 9.54 mm (60 W). In the same study, the coagulation depth in a canine prostate model was limited to 4 mm (200 W cw mode) (7).

Table 6: Physical properties of diode laser in an ex-vivo porcine perfused kidney

Study	**Wezel et al. 2010 (3)**				**Seitz et al. 2009 (5)**			**Seitz et al. 2009 (7)**	
Laser Type	Diode			LBO	Diode	Diode	KTP	Diode	
Wavelength (nm)	1318	1470	980	532	1470	1470	532	940	940
Power setting (W)	100	80	200	120	50	100	80	200	60
Fibre confirmation	bare fibre	side fire	side fire	side fire	side fire	side fire	side fire	side fire	side fire
Animal model	ppk	ppk	ppk	ppk	ppk	bp	ppk	cp	ppk
Tissue ablation rate (g/10 min)	12.34*	5.27[§]	8.99[§]	7.0	n.a.	4.0[&]	n.a.	15.168	n.a.
Output power efficacy (g/W/10 min)	0.124	0.066[§]	0.045[§]	0.058	n.a.	[0.038; 0.042][i]	n.a.	0.07584	n.a.
Bleeding rate (g/min)	0.35[$]	0.24*	0.27*	0.65	0.17	n.a.	0.19	n.a.	0.21
Tissue necrosis (mm)	4.62*	1.3[§]	4.18*	0.84	3.39[t]	2.30[t]	1.27	4.25	n.a.

[§] Statistically not significant compared with LBO laser
* $p < 0.001$ compared to LBO laser;
[$] $p = 0.0066$ compared to LBO laser;
[&] mean [3.8-4.2];
[i] mean [0.038-0.042];
[t] statistically significant compared to KTP laser, $p < 0.001$.
bp = beagle prostate; cp = canine prostate; n.a. = not applicable.

3.3.3 *Diode laser techniques*

Diode lasers work at a wavelength at which absorption in water is low. As with KTO and LBO lasers, procedures executed with diode lasers use side-firing techniques to ensure better direct visual control of the surgeon on the point of impact of the laser beam on the tissue (1). Reported techniques are vaporising techniques (8-12). Because laser penetration levels are deeper and the coagulation zone is wider (3,7,13), some authors have suggested power should be reduced when treating the apex with the underlying sphincter region (10,11).

3.3.4 *Clinical results*

3.3.4.1 *Urodynamic parameters, symptom score reduction, PSA reduction*

Clinical data is limited to short-term follow-up (maximum follow-up 1 year) and comprises case-control studies or cohort studies (randomised cohort trials) (9-12,14). Two trials compared diode laser treatment with LBO laser systems as a standard treatment arm (9,14). The most substantial data is for the 980 nm diode laser (9-11,14).

At the end of the follow-up period, there was a significant improvement in urodynamic parameters (peak urinary flow [Q_{max}], PVR) (Table 7). There was a reduction in PSA levels, as a surrogate parameter marker for a reduction in prostatic tissue, in the range of 30% (11) and 58% (10). However, an RCT, as well as a non-RCT, did not show significant differences in improved urodynamic parameters and symptom score reduction (Table 7).

Table 7: Results of diode lasers with regard to improvement of urodynamic parameters, symptom score and PSA reduction

Reference	Laser source (power, W)	Follow-up	Patients (n)	Mean prostate size (mL)	PSA reduction (%)	Change in symptoms (%)	Change in Q_{max} (mL/s) (%)	PVR change (%)	LE
Seitz et al. 2007 (12)	1470 (50 W)	12	10	47.8	-42	-69.32	13.5 (251.68)	-88.93	3b
Chen et al. 2010 (10)	980 (200/ 150W)	6	55	66.3	-58.82	-75.62	13.7 (349.01)	-87.74	3b
Erol et al. 2009 (11)	980 (132/80 W)	6	47	51.4	-30.31	-54.99	9.4 (205.97)	-58.11	3b
Ruszat et al. 2009 (9)	980 (n.a.)	6	55	64.7	-58.13	-75.93	5.1 (147.66)	-85.55	3b
	LBO PVP		65	67.4	-45	-57.89	11.3 (191)	-80.64	
Chiang et al. 2010 (14)	980 (200 W)	12	55	66.3	-42.19	-84.26	14 (425.58)	-86.37	1b
	LBO PVP		84	60.3	-58.82	-83.08	11.2 (303.64)	-85.40	

PSA = prostate-specific antigen; Q_{max} = peak (maximal) urinary flow rate; PVR = postvoid residual urine volume; LE = level of evidence; LBO PVP = LBO photoselective vaporisation.

3.3.5 *Risk and complications, durability of results*

3.3.5.1 *Intra-operative complications*

Published available studies of 980 nm (9-11,14-17) and 1470 nm (12) diode lasers are all case series or case control series or comparative studies. The studies have indicated a high level of intra-operative safety. In the RCT, which compares the safety and efficacy of the 980 nm diode laser versus the 120 W LBO laser, the rate of intra-operative bleeding was significantly lower in the diode laser group (0% vs 13%). Anticoagulant medication was being taken by 23.6% of patients receiving diode laser treatment and 25.0% of patients in the LBO PVP group (9).

These findings are supported by a non-RCT, which found almost the same results (0% vs 11.9%). In this study (14) 52% of patients in the laser diode treatment arm and 43% in the LBP PVP treatment arm were on anticoagulant medication (14). This study is supported by preclinical studies on the novel laser energy sources, showing almost equal haemostatic potential and coagulation features to the Nd:YAG laser (6). Furthermore, one comparative non-RCT reported no capsule perforation with the 980 nm diode laser. The necessity for conversion to TURP was reported in 4% (980 nm diode) and 8% (LBO PVP) of patients (9).

3.3.5.2 Early post-operative complications
Although there is only a limited amount of data, several conclusions can still be made. The incidence of early post-operative complications reported is low. No post-operative blood transfusions occurred.

In a comparison of the 980 nm diode laser to LBO PVP, a non-RCT showed the following complications: post-operative haematuria in 20% versus 19%, transient incontinence in 14.5% versus 2.4% ($p < 0.05$), transient urgency in 34.5% versus 16.7% ($p < 0.05$), scrotal oedema 3.6% versus 0%, anal pain 3.6% versus 0%, and epididymitis 1.2% versus 9.1% (14).

A comparative study reported dysuria in 24% (980 nm diode laser) versus 18% (LBO PVP), urinary incontinence 7% versus 0% and a blood transfusion rate of 0% versus 2% (14). The recatheterisation rate was between 4.3% (11) and 20% (9).

3.3.5.3 Late complications
Diode laser vaporisation of the prostate seems to carry a high rate of late complications. In a case series, 32.1% of patients needed reoperation within a follow-up of 12 months after 980 nm diode treatment due to obstructive necrotic tissue or bladder neck stricture (15).

This finding is supported by an RCT comparing the 980 nm diode laser with LBO: 9.1% versus 3.6%, respectively, of patients required reoperation with TURP due to bladder neck obstruction; 5.5% versus 2.4% developed urethral strictures; and 1.8% versus 0% developed urethral stone formation (14).

Another study, which compared diode laser to LBO PVP found higher rates of bladder neck stricture (14.5% vs 1.6%, $p < 0.01$), higher retreatment rates (18.2% vs 1.6%, $p < 0.01$) and persistence of stress urinary incontinence (9.1% vs 0%; $p < 0.05$) (9).

However, other reports have shown only transient combined urge and stress incontinence in 4.3% of patients for 2 weeks (11). This discrepancy has been a controversial issue conducted via scientific communication within the urological community (16). A further case series has reported sloughed-off tissue in 14.5% in cystoscopic intervention and a reoperation rate with TURP in 7.3% of patients. Urinary stress incontinence remained in 1.8% of patients during a 6-month follow-up period (10). Furthermore, in 20% of patients, a repeat of TURP was necessary within a 1-year follow-up after treatment with a 1470 nm diode laser (12).

3.3.5.4 Practical considerations
In view of the available data on the use of the diode laser, it should not be a standard treatment option for BPE. The literature show a retreatment rate of up to 35%. Transitory and permanent incontinence seem to be higher than for alternative treatments. This treatment may offer a high inter-operative control of bleeding for patients on anticoagulative drugs.

3.3.5.5 Recommendation for prostate treatment with diode lasers

Recommendation	**LE**	**GR**
In patients presenting with BOO and BPE and who have bleeding disorders or are receiving anticoagulants, diode laser treatment is an alternative.	1b	C

BOO = bladder outlet obstruction; BPE = benign prostatic enlargement

3.4 Holmium (Ho:YAG) laser

3.4.1 ***General aspects***
The crystalline matrix for the holmium laser is yttrium-aluminium-garnet (YAG). In order to prevent excessive heating inside the crystal, chromium, thulium and holmium are mixed with the YAG melt from the crystal. Excitation energy is virtually handed to the holmium via a cascade from chromium over thulium. However, heat accumulation within the laser crystals restricts the holmium laser under flash lamp excitation at room temperature to pulsed operation at moderate repetition rates. Holmium laser radiation has a short extinction length in tissue due to strong absorption of the water molecule around 2140 nm (Figure 1). At this wavelength, the depth of penetration is approximately 400 μm. The density of absorbed power in irrigant and/or in tissue is high and results in an immediate increase of temperature above the boiling point.

In a typical endourological setting, the onset of vaporisation is in the irrigant next to the fibre tip, where a steam bubble is generated with each laser pulse. The diameter of the bubble depends on the energy of the laser pulse and is a few millimetres wide. The duration of this steam bubble is similar to duration of the laser pulse, which is about 500 μs (18). This duration is too short for human perception and therefore invisible.

In holmium laser enucleation of the prostate (HoLEP), the steam bubbles separate tissue layers by tearing the tissue apart (19). In soft tissue surgery, tissue vaporisation is dominated by the way in which the steam bubble tears tissue and laser radiation is absorbed in tissue. This explains the white fibrous appearance of the surgical sites during holmium laser surgery on soft tissue under irrigation. The tissue effect is rapid and haemostasis of the holmium laser is excellent.

Common pulse energy settings for holmium lasers are in the range of 2 J. Depending on the flash lamp driver technology installed, the laser pulse duration may be between 150 µs and 1 ms. About 100 µs is required for heat to diffuse out of a short cylinder established by the fibre diameter and the extinction length (thermal relaxation time). The heat generated during the absorption process accumulates during the duration of the laser pulse at the point of impact, until heat conduction levels out the temperature profile.

In laser lithotripsy, some laser radiation is absorbed inside the stone generating an immediate build-up of steam pressure, which causes fragmentation. A laser pulse duration that is shorter or of the order of the thermal relaxation time confines the absorbed energy within the above-mentioned cylinder. The shorter the laser pulse duration at a given pulse energy, the higher the pulse peak power will be and the more effective is stone fragmentation (20).

3.4.2 ***Physical properties***
General physical properties have been covered in section 3.4.1. Ho:YAG lasers have not been investigated to the extent of KTP, LBO, Tm:YAG and various diode lasers. Therefore, very limited data on these aspects are available so far.

3.4.3 ***Holmium laser techniques***
All holmium laser techniques are based on vaporisation. The energy is delivered to the prostate through an end-firing laser fibre with a diameter of about 500-600 µm. Holmium laser techniques evolved from holmium laser ablation of the prostate (HoLAP) (21) to holmium laser resecting techniques (HoLRP) (22) and, finally with the introduction of the tissue morcellator, to the holmium laser enucleation technique (HoLEP) (23). A later modification combined HoLEP with electrocautery resection of the enucleated lobe, while still attached at the bladder neck (24). As for physical characteristics, the vaporising effect of holmium laser-emitted energy is limited (15%) compared to other lasers.

3.4.4 ***Holmium laser vaporisation (ablation) of the prostate (HoLAP)***
Today, HoLAP procedure is carried out using a side-firing fibre in close contact with the surface in a sweeping fashion like PVP. The energy absorbed by the water molecule means that this technique would be safe, even if performed with bare fibre. In this manner, prostatic tissue is ablated and a cavity created similar to TURP. The strong absorption of holmium laser energy by water (Figure 1) results in a sufficiently high energy density to vaporise prostatic tissue, so creating tissue ablation without deep coagulation.

There are little data on HoLAP treatment of the prostate. A single RCT has compared 60 W and 80 W HoLAP versus TURP in 36 patients (25). Q_{max} improvement was equivocal at 3, 6, and 12 months after the operation, while prostate volume was reduced by 39% (HoLAP) and 47% (TURP), respectively. However, no RCT exists for the new high-power, 100 W HoLAP versus TURP or OP. One RCT comparing 100 W HoLAP with KTP reported results from a short- and intermediate-term follow-up (Table 8). Anticoagulant medication was being taken by 12.2% of patients treated with HoLAP and 15.3% treated with TURP. No difference was found except for operation time, which was 1.5-fold greater than that for TURP (26,27).

3.4.5 ***Holmium laser resection of the prostate***
In contrast to HoLAP vaporisation, the HoLRP procedure uses vaporisation only to cut small pieces out of the prostate. This results in multiple small prostate chips falling into the bladder before being removed with a syringe at the end of the operation, similar to TURP.

Because the technological emphasis has been on HoLEP, the clinical application of HoLRP and HoLAP declined. Thus, most of the clinical data available in holmium-based literature discuss HoLEP.

The HoLRP technique is limited to small prostates. Resection time of larger prostates would take almost double the time of HoLEP, making HoLRP less suitable for treatment of BPE/BOO. One RCT compared TURP with HoLRP in 120 patients with BOO. The patients had prostates < 100 mL in volume. The study published results at three time-points in the follow-up period (28-30). Resection time was almost doubled for HoLRP when compared to TURP (42.1 versus 25.8 minutes, $p < 0.005$). The mean catheter time was significantly shorter (20.0 versus 37.2 hours, $p < 0.005$). Symptomatic and urodynamic improvement were equivalent in the two groups. However, at 12 and 18 months after the operation, HoLRP showed superior results to TURP (25.2 versus 20.4 mL/s, respectively, at 12 months, and 25.1 versus 19.2 mL/s at 18 months). The superiority of HoLRP vanished at 24 months, until the end of the study at 48 months after the operation. The Q_{max} of patients treated by HoLRP or TURP was 22.2 versus 18.5 mL/s, respectively. This data is inconclusive because it is not possible to determine whether HoLRP is better or worse than standard treatment. However, the results favoured HoLRP with regard to quality of life, hospitalisation time and catheterisation time. Patients with large median lobes and patients in urinary retention can be safely treated (31,32).

3.4.6 ***Holmium laser enucleation of the prostate***

Holmium laser enucleation of the prostate (HoLEP) is based on the same physical principle as HoLRP. However, during the HoLEP procedure, the surgical capsule of the prostate is exposed by incision and vaporisation of the periurethral prostatic tissue. After identifying the plane at the surgical capsule, the prostatic adenoma is separated from the capsule by disruption of the adenoma from the capsule, similarly to OP. Disruption is achieved by the pulsating steam bubble caused in front of the fibre by the pulsed laser energy emitting mode of Ho:YAG lasers. The introduction of HoLEP resulted in a significant improvement in the technique. The entire lobes are enucleated, moved into the bladder and morcellated (23), or fragmented with the TUR-sling at the bladder neck (mushroom technique) (24).

Several RCTs have compared HoLEP with TURP and OP, with the main findings given in Table 8.

A meta-analysis observed a tendency towards HoLEP for an improved symptom score during the entire follow-up period of up to 30 months, with larger mean changes in post-operative measurements. However, the differences in the individual studies were not statistically significant (weighted mean difference –0.82, 95% CI: –1.76-0.12; p=0.09). In the same meta-analysis, the same result was found for Q_{max} at 12-month follow-up. Compared with TURP, significantly higher Q_{max} rates were reported for HoLEP (weighted mean difference 1.48 mL/s, 95% CI: 0.58-2.40; p=0.002) (33).

In another meta-analysis, HoLEP was superior (pooled estimates) to TURP with regard to catheterisation time (17.7-31.0 h vs 43.4-57.8 h, respectively; p< 0·001), hospital stay (27.6-59.0 vs 48.3-85.5 days; p=0.001). In contrast, TURP was superior (pooled estimates of the difference) to HoLEP with regards to the duration of operation (33.1-73.8 vs 62.1-94.6 h respectively; p=0·001) (34).

Beside the evaluated RCTs, other non-RCT studies demonstrated that HoLEP has a low morbidity and is also effective in patients with urinary retention (35,36). One RCT compared changes in the urodynamic parameters of HoLEP versus TURP using computer urodynamic investigation (37). Pressure-flow studies before surgery and 6 months after the operation indicated that Pdetqmax after HoLEP (76.2 vs 20.8 cm H_2O) decreased significantly more compared to TURP (70 vs 40.7 cm H_2O; $p < 0.001$). Furthermore, the Schaefer BOO grade before and 6 months after the operation decreased significantly more after HoLEP (3.5 vs 0.2) compared to TURP (3.7 to 1.2; $p < 0.001$).

In recent years, a considerable number of studies regarding intermediate and long-term outcome of HoLEP alone in comparison to TURP or OP have been published. Gilling et al. (38) reported long-term data with a mean follow-up of 6.1 years showing that HoLEP results are durable and most patients remain satisfied. In prostates > 100 mL, HoLEP proved to be as effective as OP, regarding improvement in micturition with equally low re-operation rates at 5-year follow-up (39).

Table 8: Results of HoLAP, HoLRP and HoLEP with regard to improvement in urodynamic parameters, symptom score and PSA reduction

Ref.	Laser source/ Technique	Follow-up (mo)	Patients (n)	Mean prostate size (mL)	PSA reduction (%)	Change in symptoms (%)	Change in Q_{max} (mL/s) (%)	PVR change (%)	LE
Mottet et al. 1999 (25)	HoLAP	12	23	39	n.a.	-70	11.1 (226)	n.a.	1b
	TURP		13	34	n.a.	-80	9.6 (229)	n.a.	
Elmansy et al. 2010 (26)	HoLAP	36	46	33.1	-0.40	-71	11 (264)	-81	1b
	KTP		42	37.3	-0.28	-64	12.10 (289)	-80	
Westenberg et al. 2004 (30)	HoLRP	48	61	44.3	n.a	-76	13.6 (253)	n.a.	1b
	TURP		59	44.6	n.a.	-75	9.4 (203)	n.a.	
Kuntz et al. 2004 (40)	HoLEP	18	60	114.6	n.a.	-90	23.60 (721)	-97	1b
	TURP		60	113	n.a.	-90	24.40 (778)	-98	
Kuntz et al. 2004 (41)	HoLEP	12	100	53.5	n.a.	-92	23 (569)	-98	1b
	TURP		100	49.9	n.a.	-82	21.80 (469)	-88	
Briganti et al. 2006 (42)	HoLEP	24	60	73.30	n.a.	-83	n.a.	n.a.	1b
	TURP		60	58.20	n.a.	-83	n.a.	n.a.	
Gupta et al. 2006 (43)	HoLEP	12	18	57.9	n.a.	-78	19.20 (527)	-83	1b
	TURP		16	59.8	n.a.	-76	19.95 (487)	-77	
Naspro et al. 2006 (44)	HoLEP	24	41	113.27	n.a.	-61	11.36 (245)	n.a.	1b
	TURP		39	124.21	n.a.	-63	11.79 (242)	n.a.	
Wilson et al. 2006 (45)	HoLEP	24	31	77.8	n.a.	-77	12.6 (250)	n.a.	1b
	TURP		30	77.0	n.a.	-78	11.0 (233)	n.a	
Montorsi et al. 2008 (46)	HoLEP	12	52	70.3	n.a.	-81	16.9 (306)	n.a.	1b
	TURP		48	56.2	n.a.	-82	17.20 (326)	n.a.	
Gilling et al. 2008 (38)	HoLEP	72	71	58.5	n.a.	-67	10.9 (235)	n.a.	2a
Kuntz et al. 2008 (39)	HoLEP	60	60	114.6	n.a.	-86	20.5 (639)	-96	1b
	OP		60	113	n.a.	-86	20.8 (678)	-98	

PSA = prostate-specific antigen; Q_{max} = peak (maximal) urinary flow rate; PVR = postvoid residual urine volume; LE = level of evidence; HoLAP = holmium laser vaporisation (ablation) of the prostate; TURP = transurethral resection of prostate; n.a. = not applicable; HoLRP = holmium laser resection of the prostate; HoLEP = holmium laser enucleation of the prostate; OP = open prostatectomy.

3.4.7 *Risk and complications, durability of results*

The published literature describing Ho:YAG treatment of the prostate is dominated by discussion of HoLEP with few publications for HoLAP and very few for HoLRP. The introduction of KTP resulted in less interest in Ho:YAG as a solely vaporising laser. However, the recent availability of 100 W Ho:YAG laser devices has led to a renewed interest in HoLAP because of the popularity of vaporising using a side-fire technique (26,27).

3.4.8 *Intra-operative complications*

3.4.8.1 HoLAP

An RCT comparing HoLAP with KTP PVP reported no intra-operative bleeding in the HoLAP-treated group, while three KTP PVP-patients required intra-operative conversion to TURP electrocauterisation (27). Another RCT comparing HoLAP versus TURP did not report any intra-operative complications (25).

3.4.8.2 HoLRP

The RCTs available for HoLRP (28-30) tend to focus on the outcome for improved symptom score and urodynamic parameters. Intra-operative complications for HoLRP are not specifically displayed. In comparison, the TURP treatment arm in these studies showed a blood transfusion rate of 6.7%. Furthermore, the available case series do not focus on intra-operative complications (31,32,47).

3.4.8.3 HoLEP

The safety and low intra-operative morbidity of HoLEP has been proven in seven RCTs (40-46).

Several reviews (48) and two meta-analyses (33,34) have investigated the safety and peri-operative morbidity of HoLEP. One meta-analysis found a lower rate of blood transfusion after holmium laser enucleation (relative risk 0.27, 95% CI: 0.07-0.95; p=0.04) compared with TURP (33); a finding supported by a second meta-analysis (34). In addition, a second meta-analysis showed that HoLEP reduced catheterisation time and duration of hospital stay, although TURP resulted in a shorter total operation time (34).

In a review of studies published from 2003 until 2006, 1,847 patients were identified who had been treated with HoLEP. The blood transfusion rate was 1% and peri-operative mortality was 0.05%. A further review showed a capsular perforation rate ranging from 0.3% (49) to 10% (50). The perforations were mainly classified as small capsular lacerations and the patients' course was not affected. Superficial mucosal laceration with the morcellation device was reported ranging from 0.5% (50) to 18.2% (46). The rate of superficial ureteric orifice injury that did not require insertion of a ureteral stent or nephrostomy ranged from 1.0% (51) to 2.1% (52). The incidence of incomplete morcellation ranged from 1.9% (52) to 3.7% (54) in all cases. Cardiac adverse events were reported in up to 1.2% of patients (52).

The experience of the surgeon was the most important factor affecting the overall occurrence of complications (55,56) and intra-operative complications. In trained hands, prostate size had no statistically significant influence on complications (57). The likelihood of capsular perforations increased with smaller prostates, while injury of the ureteric orifice occurred more often during resection of large and endovesically growing median lobes (52,55).

Two meta-analyses have demonstrated that in comparison to TURP and OP, patients undergoing HoLEP have a shorter catheterisation time and hospital stay, reduced blood loss and a smaller likelihood of blood transfusions, but comparable functional outcomes (33,34).

3.4.9 *Early post-operative complications*

3.4.9.1 HoLAP

An RCT comparing HoLAP with TURP reported that 20% of patients had mild urgency or burning after catheter removal. These problems did not resolve until the first month (25). Another study, comparing HoLAP with KTP PVP, did not specifically address peri-operative complications. However, seven patients (12.2%) in the HoLAP group and six (11.5%) in the KTP PVP group required recatheterisation (26,27). Dysuria and irritative symptoms following surgery resolved before the first post-operative visit at 1 month (25).

3.4.9.2 HoLRP

An RCT comparing HoLRP to TURP has reported the rate for UTIs as 4.9% versus 8.4%, respectively. There are no other broad assessments of peri-operative complications (30).

3.4.9.3 HoLEP

Peri-operative complications within the first months after HoLEP have been assessed by several RCTs, case series, comparative studies and meta-analyses (34,41,48). In an RCT comparing HoLEP and OP for patients with prostates > 70 g, transitory urge incontinence was equally observed in 34.1% (HoLEP) and 38.6% (OP) of patients at 3 months' follow-up, whereas dysuria was significantly more frequent in the HoLEP group (68.2 vs 41.0%, $p < 0.001$) (44). In contrast, the reported rate of transitory urge incontinence showed no significant difference in a multicentre RCT comparing HoLEP and TURP. Dysuria occurred significantly more often in patients after HoLEP (58.9 vs 29.5%, $p = 0.0002$) (46). Haemorrhage requiring coagulation is reported in 0-6% (58) and clot retention in 0% (59) to 3.6% (60).

3.4.10 ***Late complications***

3.4.10.1 HoLAP

An RCT comparing HoLAP with TURP found one patient with stress urinary incontinence and one patient had opted out of the study at 6 months' follow-up. Two patients in the TURP group were treated for bladder neck contracture at 2 and 6 months by cold-knife incision. No significant difference was found in the potency and antegrade ejaculation rate between the two groups. The potency rate after 1 year was 90% for the laser group and 100% for the TURP group. The antegrade ejaculation rate was 50% in both groups (25). The retreatment rate at 7 years' follow-up was 15% (61).

An RCT comparing HoLAP versus KTP PVP found comparable complication rates at follow-up after 36 months. The overall retreatment rate was 15.8% for HoLAP and 19.3% for PVP. Urethral stricture rate was 3.5% and 5.8%, respectively. Bladder neck contracture occurred in 5.3% versus 7.7%, respectively. The re-operation was reported to be 7% for HoLAP-treated patients versus 5.8% for KTP PVP (26,27).

One patient (1.8%) with HoLAP versus two patients (3.8%) with PVP had urgency and urge incontinence that did not resolve with anticholinergic therapy at the last follow-up. There was no significant difference in post-operative complications between the two groups. The overall retreatment rate was 15.8% for HoLAP versus 19.3% for PVP.

Retrograde ejaculation of sexually active patients was reported in 36.3% of the HoLAP group compared with 43.3% of the KTP PVP group. Between the two groups, no significant difference between pre-operative and post-operative sexual function in terms of orgasmic function, sexual desire, or intercourse or overall satisfaction was reported (26).

3.4.10.2 HoLRP

One RCT reported no difference between HoLRP and TURP in terms of urodynamic parameters, potency, continence, symptoms scores and major morbidity at 48 months. Complication rates were comparable. Persisting *de novo* urine leakage was reported to be 3.3% in the HoLRP group versus 1.7% in the TURP group. The overall retreatment rate was 8.2% for HoLRP versus 11.8% for TURP and 1.7% in the TURP arm needed artificial sphincter implantation. Urethral stricture rate was 9.8% versus 10.1%, respectively. Bladder neck incision for bladder neck contracture occurred in 4.9% versus 5.1%, respectively (30). Pre-operatively 50% of HoLRP versus 70% of TURP were potent, at the 4-year follow-up 53% of HoLRP versus 60% of TURP had sufficient erection for intercourse. A decrease in erectile quality was reported in 8% of the HoLRP and 17% of the TURP groups. However, 10% of the HoLRP group and 7% of the TURP group reported an improvement of erections (30).

3.4.10.3 HoLEP

In a meta-analysis, no statistically significant differences were noted between HoLEP and TURP for urethral stricture (2.6 versus 4.4%; $p = 0.944$), stress incontinence (1.5 versus 1.5%; $p = 0.980$), blood transfusion (0 versus 2.2%; $p = 0.14$) and reintervention (4.3 versus 8.8%; $p = 0.059$). No obvious publication bias was noted ($p = 0.170$, Egger's test) (34).

A further meta-analysis evaluated the risk of erectile dysfunction after HOLEP compared to standard treatment. Erectile dysfunction rates showed were similar to TURP (33). In the same meta-analysis the rate of strictures during follow-up after holmium laser enucleation was similar to those after transurethral resection (33).

Numerous trials involving the long-term outcome of HoLEP have been published and have confirmed the long-term and significant improvement in voiding parameters and the low complication rate. In a 6-year follow-up analysis of 38 patients treated with HoLEP, urge incontinence was reported in three of 38 (7.9%) patients, mixed incontinence in 10.5% and stress incontinence in 2.6%. Re-operation was necessary in 1.4% after 5 years and one patient (1.4%) underwent urethrotomy at 6 months (38,61).

Comparable long-term results were reported from other studies with a re-operation rate of 4.2% due to residual adenoma, urethral strictures (1.7%), meatal stenosis (0.8%) and bladder neck contracture (0.8%), resulting in a 5-year surgical retreatment rate of 8%. The earlier group of patients showed a higher retreatment rate (8 vs 1.4%) (62). Another study observed a re-operation rate of 2.7% during a 36-month follow-up. In the group of patients with prostates < 50 mL, the incidences of urethral stenosis and bladder neck contracture were significantly higher (63).

Re-operation rates in a RCT comparing HoLEP with TURP were comparable at 3-year follow-up with a rate of 7.2 and 6.6%, respectively (64). These data are confirmed by other prospective trials comparing HoLEP to TURP (43). In an RCT comparing HoLEP versus OP, the re-operation rate at 5-year follow-up was 5% for HoLEP and 6.7% for OP-treated patients (39).

Studies focussing on sexual function after HoLEP are rare. Due to retrograde ejaculation HoLEP and TURP significantly lowered the IIEF orgasmic function domain in one RCT. Similar results were observed in the comparison of HoLEP and OP, with no significant reduction of erectile function compared with baseline (39). Patients after HoLEP and TURP reported retrograde ejaculation in 75% and 62%, respectively (45,61).

3.4.11 ***Practical considerations***
Although the literature has mainly focused on HoLEP, both HoLAP and HoLRP are suitable alternatives for vaporising (HoLAP) or resecting (HoLRP) approaches in the treatment of BOO and BPE. One issue for both techniques that needs to be considered is the longer ablation or resection time. HoLEP is the most studied novel minimal therapy approach and is a real alternative to TURP for medium- and large-sized prostates for OP. However, the excellent early results obtained with HoLEP, as the prototype for transurethral laser enucleation, have not been matched by the wider use of this technique.

3.4.12 ***Recommendations for holmium (Ho:YAG) laser treatment***

Recommendations	LE	GR
HoLAP can be offered to patients with BOO or BPE with small- to medium-sized prostates.	1b	A
HoLRP can be offered to patients with BOO or BPE with small- to medium-sized glands.	1b	A
HoLEP can be offered to any patient with BOO and BPE.	1a	A
HoLEP can be offered to patients in chronic urinary retention.	2b	B
HoLEP can be offered to patients on anticoagulant or antiplatelet medication.	2b	B

BOO = bladder outlet obstruction; BPE = benign prostatic enlargement

3.4.13 ***References***

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3.5 Thulium:yttrium-aluminium-garnet (Tm:YAG) laser

Laser energy is emitted at a wavelength of about 2000 nm in a continuous-wave fashion (1-4). In contrast to the flash-lamp excitation of the holmium laser, thulium ions are directly excited by high-power laser diodes. Although a thulium laser has the same absorption characteristics as a holmium laser in water and tissue, it has superior properties in soft tissue surgery because of the continuous-wave output. Due to the slightly shorter wavelength, the depth of penetration is decreased to 250 μm. The wavelength is close to the absorption peak of water and, together with the short penetration depth, this results in a high-energy density leading to rapid vaporisation of water and tissue. Instead of the tearing action on tissue caused by the pulsed emission of Ho:YAG, the continuous-wave output of Tm:YAG allows smooth incision and vaporisation of tissue with excellent haemostasis. The ubiquity of the water molecule as the target chromophore provides constant conditions for the laser tissue chromophore and therefore tissue interaction. Water retains its absorption properties when heated by the laser beam up to the boiling point, which marks the onset of tissue vaporisation.

The tissue left behind after each laser pass is covered by a coagulated seam of tissue, which provides haemostasis. It still contains sufficient water for efficient absorption of the following laser pass. Thus the laser tissue effect remains unchanged and effective throughout the entire surgical procedure. In contrast to the pulsed emission mode of Ho:YAG, the continuous emission does not allow lithotripsy.

3.5.1 ***Physical properties***

To date, one clinical paper has reported data on vaporisation efficacy using the Tm:YAG 2013 nm (2 μm) continuous-wave (cw) laser. There is one publication each for the 70 W and 120 W Tm:YAG 2-μm cw laser devices in an identical, experimental, organ perfused, porcine kidney model.

3.5.1.1 Ablation capacity

The tissue ablation rate increases with increasing output power. In comparison to the KTP laser, the tissue ablation rate reached (mean) 6.56 g/10 min (70 W Tm:YAG) and 3.99 g/10 min (80 W KTP) ($p > 0.05$). When compared to TURP, both laser devices produced significantly lower rates of tissue removal (8.28 g/10min) (5).

The ablative potential of Thu:YAG lasers was confirmed in a further study. At 70 W, 3.03 g/10 min were ablated using the 550 μm bare fibre. At 120 W, the amount of ablated tissue increased to 16.41 g/10 min using the 550 μm bare fibre. These rates were reduced when using a larger fibre core diameter (800 μm), as energy density is a function of core diameter (6).

3.5.1.2 Bleeding rate

The thulium laser has good haemostatic potential. In the same model, the bleeding rate for the cw 70 W thulium laser reached 0.16 ± 0.07 g/min, compared to 0.21 ± 0.07 g/min for the 80 W KTP laser. In contrast, TURP showed a significantly increased bleeding rate of 20.14 g/min ($p < 0.05$) (5). The results were unaffected by increasing the energy output and core diameter (6).

3.5.1.3 Coagulation zone

In the kidney perfused tissue ablation model, cw thulium showed the shallowest coagulation depth. Histological examination revealed that tissue ablation resulted in a dense coagulation zone at the tissue surface. The corresponding depth of the coagulation zone was 264.7 ± 41.3 μm for the cw thulium laser, which is almost as deep as that achieved with TURP (287.1 ± 27.5 μm), but less than the 2.5-fold deeper coagulation zone (0.6669 mm) of the KTP laser ($p < 0.05$) (Table 4) (5). With increased power output and increased fibre diameter, the extent of coagulation and the necrotic tissue zone remained stable (6).

Tissue ablation increased with increasing power and was superior to that achieved with the 80 W KTP laser. Furthermore, the bleeding rate was for the cw 70 W thulium laser reached 0.16 ± 0.07 g/min, compared to 0.21 ± 0.07 g/min for the 80 W KTP laser, though considerably lower than with monopolar TURP (5). In contrast to the 120 W LBO laser (7), the bleeding rate remained stable for the 120 W Tm:YAG laser with an increase in ablation rate. In addition, the study demonstrated shallow penetration and an energy-independent zone of tissue necrosis of 0.4 mm (6).

3.5.2 ***Thulium laser techniques***

Four different technical approaches have been described so far:
1) Tm:YAG vaporisation of the prostate (ThuVAP);
2) Tm:YAG vaporesection (ThuVARP);
3) Tm:YAG vapoenucleation (ThuVEP);
4) Tm:YAG laser enucleation of the prostate (ThuLEP) (8).

As the data from prospective RCTs are very sparse, these techniques cannot be assessed to levels of evidence. But, a number of studies, including two RCTs and one non-RCT have been published so far. The evidence of these studies will be discussed below.

3.5.2.1 Thulium laser vaporisation of the prostate

ThuVaR is a solely vaporising technique. Because the beam is fully absorbed in water, there is no necessity for side-fire application, as with KTP or LBO. A multicentre, non-randomised, case series study has reported clinical data of pure vaporisation of the prostate in 99 patients with small prostates (< 35 mL). As the results are presented alongside the results for patients with larger prostates (> 35 mL), the clinical data cannot be separated. The improvement of urodynamic parameters in the whole group of patients (n = 200) shows clinically efficient vaporisation or vaporesection in 12 months of follow-up (Table 9). These findings reflect the results of two preclinical trials in an organ-perfused model investigating the physical properties of Tm:YAG.

In comparison with a KTP laser, the 70 W Tm:YAG laser showed a larger ablation capacity, reduced bleeding rate and shallower coagulation zone (5). The 70 W Tm:YAG and the novel 120 W KTP showed a similar bleeding rate and coagulation properties (6), in contrast to 120 W LBO, which showed a higher bleeding rate and slight increase in coagulation zone (7). Higher energy resulted in a marked increase of ablation capacity in both Tm:YAG and LBO lasers (Table 4).

Twelve patients on anticoagulant drugs have been treated safely with ThuVAP/ThuVARP (9). The operation time was between 25 and 140 minutes, with catheterisation for 16 hours and no transfusion required (10). No urethral stricture or bladder neck sclerosis was reported. However, seven patients received insufficient vaporisation and required retreatment, while four patients had urinary retention after catheter removal. Six per cent of ThuVAP patients demonstrated irritative voiding symptoms post-operatively, which resolved after 1-3 months.

3.5.2.2 Thulium laser resection of the prostate (ThuVARP)

ThuVARP is a technique that resects the prostate in TUR-like tissue chips. Although Tm:YAG is similar to the Ho:YAG with regard to its shallow tissue and water penetration and haemostasis, vaporisation capacity is significantly increased by the cw emitting mode. Therefore, tissue ablation is not only achieved by resection, but also by simultaneous vaporisation.

The largest number of thulium-associated publications have been published on ThuVARP. One RCT, one non-randomised controlled study and three prospective studies have been published since 2007. In total, 730 patients have been included in these trials, which have all been reported in peer-reviewed journals.

One RCT (11) and one non-RCT (12) compared ThuVARP with monopolar TURP. The two procedures showed similar clinical outcomes and an improvement in urodynamic parameters with reduced morbidity. The Tm:YAG-treated patient group showed reduced bleeding with lower transfusion rates and shorter catheter and hospitalisation times compared to the TURP-treated patient group (11,12). All other studies (13-16) showed clinical and urodynamic results in the range of the above studies with durable improvement in voiding function (Table 9), up to an 18-month follow-up. Post-operative PSA levels as a surrogate parameter for volume reduction declined by 56% (16) and 69.4% (15).

3.5.2.3 Thulium laser vapoenucleation of the prostate (ThuVEP)

The evolution in Tm:YAG prostate surgery has virtually followed the same path as for Ho:YAG surgery. ThuVEP was introduced in 2008 for patients with larger prostates (10). Published data in peer-reviewed journals is sparse (1-3,17,18).

The clinical efficacy of ThuVEP versus HoLEP was studied in one prospective RCT (17) and ThuVEP alone was studied in three prospective non-RCTs (1,2,18). Efficient tissue reduction and consistent improvement in clinical symptoms was observed within the follow-up period of up to 18 months (1,2,18). Blood loss was reduced in the Tm:YAG group, when compared to HoLEP, with equi-effective de-obstruction within a short follow-up interval of 3 months (17). In patients with refractory urinary retention (RUR), no differences with regards to improvement of urodynamic parameters and peri-operative complications were recorded, except for a higher rate of UTIs (15.5 vs 4.6) in patients with RUR (4). ThuVEP was safely applied to 96 high-risk patients, of whom 16 were on anticoagulant drugs. Within the whole study group, six patients developed UTI, three of whom required either post-operative transfusion or second-look surgery due to clot retention, or had insufficient voiding function (13). Post-operative PSA levels, as a surrogate parameter for volume reduction, declined by 56.1 (11) to 69.4% (10) for ThuVARP and 88% for ThuVEP (18).

3.5.2.4 Thulium laser enucleation of the prostate (ThuLEP)

ThuLEP is a transurethral technique with widely blunt dissection of the adenoma, such as OP. Permanent incisions are made at the apex and the bladder neck, the nutrifying vessels from the peripheral to the transition zone are punctiformly coagulated, leaving the capsule widely untouched. Except for a description of the technique, no clinical data has been reported so far (19).

Table 9: Results of ThuVAP, ThuVARP, ThuVEP for improvement in urodynamic parameters

Trial	Laser source/ Technique	Follow-up (mo)	N	Mean prostate size (mL)	PSA reduction (%)	Change in symptoms (%)	Change in Q_{max} (mL/s) (%)	PVR change (%)	LE
Mattioli et al. 2008 (9)	ThuVAP	12	99	45*	n.a.	-67*	14.8 (289)*	-88.9*	4
	ThuVARP		101						
Xia et al. 2008 (11)	ThuVARP	12	52	59.2	n.a.	-84	15.7 (296)	-94.4	1b
	TURP		48	55.1	n.a.	-81	15.8 (290)	-92.8	
Fu et al. 2009 (15)	ThuVARP	12	58	49.8	n.a.	-85.4	14.9 (329)	-84.3	2b
	TURP		42	48.2	n.a.	-81.1	15.5 (312)	-84.8	
Bach et al. 2007 (13) 2009 (14)	ThuVARP	18	54	30.3	n.a.	-67	12.8 (258)	-86	2b
Fu et al. 2009 (15)	ThuVARP	12	72	65.8	-69.4	-72.6	15.1 (364)	-65.7	2b
Szlauer et al. 2009 (16)	ThuVARP	9	56	50.0	-56.1	-56	13.8 (270)	-62.4	2b
Shao et al. 2009 (17)	ThuVEP	6	52	40.3	- 40.8	-70	14.9 (350)	- 80	1b
	HoLEP		46	37.3	- 35.7	-60	15.5 (330)	- 80	
Bach et al. 2009 (10) 2010 (1)	ThuVEP	18	88	61.3	n.a.	-63	15.7 (664)	-72.4	2b
Bach et al. 2011 (18)	ThuVEP	12	90	108.59	- 88	-79.7	18.7 (326)	-90.8	2b

* for both groups.

PSA = prostate specific antigen; PVR = postvoid residual urine volume; LE = level of evidence; ThuVAP = thulium laser vaporisation of the prostate; ThuVARP = Tm:YAG vaporesection; ThuVEP = Tm:YAG vapoenucleation; TURP = transurethral resection of the prostate.

3.5.3 ***Risk and complications, durability of results***

Several case series studies and two RCTs (11,17) have proven the intra-operative safety of Tm:YAG surgery of the prostate, as well as in subgroups of patients with large prostates (1,10), on anticoagulation therapy (3,9), or in retention (2).

3.5.3.1 Intra-operative complications

The rate of intra-operative complications occurring during ThuVARP or ThuVEP is low. There is no report on the occurrence of TURP syndrome. Intra- or early post-operative bleeding was reported in 3.4% of patients undergoing enucleation of the prostate and the rate of blood transfusions varied from 0% (17) to 2.2% (2) for ThuVEP. Transfusions are not reported during or after vaporesection of the prostate, whereas in a level 1b, prospective, randomised trial, blood transfusion was necessary in 4% (11) and 9.5% (12), respectively with TURP, while TURP syndrome occurred in 2.1% of patients (11).

3.5.3.2 Early post-operative complications

In the early post-operative course after ThuVEP, symptomatic UTI occurred in 6.8% (10), in 2.2% a second-look procedure during hospitalisation was necessary. In 1.1% of patients recatheterisation was necessary (10). Comparing the complications of patients with pre-operative urinary retention and indwelling catheter prior to enucleation of the prostate with catheter-naïve patients, a significantly higher rate of post-operative haematuria (3.1% vs 1.4%) and UTI (15.4% vs 4.2%) was observed in patients with pre-operative urinary retention (2).

The 3.9% rate of UTIs after ThuVARP was significantly lower than the 8.3% UTI rate after TURP (11), while similar UTI rates (6.9% vs 7.1%) were reported by another study.

Transitory early urge incontinence occurred less often than after TURP (23.1 vs 31.3%) (11). No difference was seen in the occurrence of mild-to-moderate dysuria for ThuVARP in 8.6% versus 7.1% for TURP, respectively. Irritative symptoms occurred in 26.2% and 29.3%, respectively (12).

3.5.3.3 Late complications and retreatment rate

In the current literature, data with a follow-up of 18 months after ThuVARP and ThuVEP are available. Within the 18 months follow-up after ThuVARP, no re-operation or recatheterisations occurred (14). *De novo* erectile dysfunction was not reported. A total of 55% of patients reported retrograde ejaculation after ThuVARP compared to 65% after TURP (11). Another study did not show a significant difference for retrograde ejacuation (44.2% vs 44.7%) (12). No bladder neck stricture occurred. Occurrence of urethral stricture was significantly lower in TuVARP, when compared to TURP (1.9% vs 6.5%, respectively) (11,12).

Within a follow-up of 18 months after ThuVEP, 2.2% of patients needed retreatment using ThuVARP. One patient (1.1%) required transient recatheterisation, while one patient developed a urethral stricture, requiring urethrotomia interna (1%) (1).

Transient recatheterisation was necessary in 5.6% of patients with an indwelling catheter prior to enucleation. The re-operation rate showed no difference between patients with and without an indwelling catheter prior to enucleation (2.8 vs 3.1%) within a 12-month follow-up period (14).

Despite the encouraging results, a follow-up period of 18 months is a relatively short time upon which to make final conclusions.

3.5.4 ***Conclusions and recommendations for use of Thulium:YAG lasers***

Conclusions	**LE**
ThuVARP showed equivalent effectivity when compared to TURP in one RCT and one non-randomised prospective controlled trial with small and medium volume glands. Tm:YAG treated patient showed shorter catheterisation time and shorter hospitalisation time. Adverse events were significantly lower than in TURP (intra-operative and post-operative bleeding).	1b
Currently, only one RCT with a short follow-up has compared ThuVEP to HoLEP. Nevertheless, three prospective cohort studies with a follow-up of 18 months demonstrated efficacy for ThUVEP, as well as low perioperative complications and retreatment rates.	1b
Study data are awaited comparing ThuVEP and ThuLEP to HoLEP. HoLEP is the most extensively studied transurethral enucleation technique to date and long-term anatomical data are of particular interest.	4

Recommendations	LE	GR
ThuVARP is an alternative to TURP for small- and medium-sized prostates.	1b	A
ThuVARP and ThuVEP are suitable for patients at risk of bleeding or taking anticoagulant medication.	2b	C
ThuVEP can be offered as an alternative to TURP, to HoLEP and OP for large size prostates.	1b, 2b	B

3.5.5 ***References***

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4. APPLICATION OF LASER DEVICES FOR THE TREATMENT OF BLADDER CANCER PATHOLOGIES

4.1 Introduction

The use of laser devices in urology was first reported by Staehler et al. in 1978 (1) who described the successful destruction of urinary bladder tumours with a Nd:YAG-laser.

There are only retrospective analyses concerning laser ablation of bladder cancer, mostly single-institution studies with small patient numbers. In 2001, there were the first reports of bladder tumours being resected en bloc using the holmium laser (2), while in 2008, there was the first report of a bladder malignancy being resected by thulium laser (3).

4.2 Clinical application and results

Although various lasers have been used to treat bladder tumours, there has been no prospective comparison of the different devices (4). Some studies have compared TUR of the bladder (TURB) with laser treatment in non-controlled, retrospective analyses (5-7). Most studies compared laser therapy to standard TURB procedures. No indwelling catheter was used. Some studies reported carrying out the procedure under local anaesthesia in an ambulant setting (8-11). Although there have been some reports of adjacent bowel injury when using lasers with a deep penetration, the bladder wall remained intact (12,13). Major studies are represented in Table 10. The use of lasers to treat bladder tumours in non-muscle invasive disease has the major drawback of a lack of tissue for histopathological evaluation if only laser vaporisation is used.

Total complication rates were reported ranging from as low as 5.1% up to 43%. Data regarding the morbidity and complications of TURB describe the rate of UTIs as up to 24%, bleeding (2.8-8%), haemorrhage requiring transfusion (0.9-13%) and bladder perforation (1.3-5%) (14-18). The use of holmium laser for en bloc resections may help to evaluate pathological stage and grades in primary bladder tumours for evaluating the pathological stage and grade (8,10,19). At this time, there are not enough data to predict progression rates, but based on currently available data, recurrence rates after holmium laser application in bladder cancer appear similar, or lower, compared with TURB (11). The effect of lower scattering leading to a decrease in local and out-of-field recurrence rates is under debate (20). Overall recurrence rates, however, seem to be comparable to TURB.

According to current data, the optimal indication for laser excision of a bladder tumour is a relatively small tumour located at the trigonum, lateral bladder wall, or bladder neck. It has been suggested that the oncological outcome following laser treatment is comparable to TUR. However, at present, there are no larger studies able to provide reliable long-term equivalence.

In experienced hands, laser treatment of bladder pathologies, e.g. tumours, diverticles, and ureteroceles, provides an alternative to conventional TUR surgery in well-selected patients.

Table 10: Applications of laser devices for the treatment of bladder cancer pathologies

Ref.	Study design	LE	Patients (n)	Surgical technique	Operation time (min)	Compli-cations	Follow-up (mo)	Recurrence (%)		
								Local	Out of field	Overall
Ho:YAG (holmium) laser										
Das et al. 1998 (5)	Prospective	3	23	Photoablation + biopsy	18.6	1 recatherisation	n.a.	n.a.	n.a.	n.a.
Saito 2001 (2)	Retrospective	3	35	En bloc + biopsy	n.a.	None	n.a.	n.a.	n.a.	n.a.
Soler-Martinez et al. 2007 (19)	Prospective	3	36	Biopsy + photoablation	14 (5-17)	None	3, 6, 12	n.a.	n.a.	14, 22, 25
Zhu et al. 2008 (10)	Prospective	2b	101	En bloc	30.7 (±16.1)	1 perforated bladder	34 (18, 43)	n.a.	n.a.	n.a.
Xishuang et al. 2010 (11)	Prospective	2b	64	En bloc	16.5 (±3.8)	1 urethral stricture	24	n.a.	n.a.	LR 15 IR 34.6 HR 31.7
Zhong et al. 2010 (21)	Retrospective	3	25	En bloc	21.5 (±12.5)	None	12, 24	n.a.	n.a.	12.5, 26, 6
Tm:YAG (thulium) laser										
Gao et al. 2008 (3)	Prospective	3	32	En bloc	25 (15-35)	None	3, 6, 12	3, 7, 11	6, 17, 21	9, 22, 28
Zhong et al. 2010 (21)	Retrospective	3	34	En bloc	29.1 (±16.5)	None	12, 24	n.a.	n.a.	17.6, 29.9
Yang et al. 2009 (7)	Prospective	3	9	En bloc	8.7 (7-15)	1 perforated bladder	7.5 (6-9)	0	n.a.	-

LE = level of evidence; n.a. = not applicable; LR = low-risk; IR = intermediate-risk; HR = high-risk.

4.3 Conclusions and recommendation for laser treatment of bladder cancer

Conclusions	LE
The use of lasers is feasible for resection, coagulation and enucleation of non-muscle invasive bladder tumours.	3
Transurethral resection of the bladder remains the gold standard.	1a
In laser coagulation of tumours, no tissue for pathological staging is obtained.	
Long-term recurrence and progression rates are unknown for this novel technique.	
Currently, no data are available to indicate superiority of one device over another in bladder pathology.	
Complications are generally directly related to the laser's wavelength (penetration depth) and surgical technique.	

Recommendation	GR
Laser treatment for bladder cancer should only be used in a clinical trial setting or for patients who, due to co-morbidities or other complications, are not fit for conventional treatment.	C

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5. APPLICATIONS OF LASERS IN LAPAROSCOPY/ ENDOSCOPY

5.1 Laser-assisted partial nephrectomy

5.1.1 ***Introduction***

The need for hilar clamping in case of laparoscopic partial nephrectomy (PN) is currently necessary to create a bloodless field for renal excision. However, hilar clamping increases the complexity of the operation because of the time constraint and the significant risk for increased times of warm renal ischaemia and subsequent post-operative compromise of renal function. Laser technology presents a promising alternative to achieve tumour excision, pelvicaliceal water tightness and renal haemostasis in a time-sensitive manner, with or without hilar occlusion.

5.1.2 ***Clinical application and results***

Several experimental studies have demonstrated the efficiency of laser-assisted PN in various experimental set-ups. However, to date only eight small series concerning clinically tested laser-assisted PN have been published, of which only two series were performed laparoscopically (one conventional and one robotic) (Table 11) (1-8) (LE: 3). Consequently, the evidence is considered poor and further investigation is necessary in order to establish the method as a routine alternative for nephron-sparing surgery.

Early experience with laser technology in renal surgery can be traced back to 1982. Preliminary results with the use of carbon dioxide laser for renal ablation were promising, demonstrating a reduction in blood loss, shortening of operative time and preserving of functional integrity in remaining renal tissue (1,2). In 1986, the first series of PN without the need for hilar clamping was reported. Malloy et al. employed the Nd:YAG laser in the treatment of three elderly patients with renal cell carcinoma in a solitary kidney. The Nd:YAG laser was used together with standard open surgical techniques for tumour extraction. No occlusion of the renal artery was needed and the oncological outcome was considered perfect in all three cases (3) (LE: 3).

Initial experience with the use of contact Nd:YAG laser resection in PN was first described in 1993. In a series of six resections, surgeons occluded the renal artery to ensure good intra-operative haemostasis. Cutting properties of the laser were considered more accurate, while energy levels could be reduced causing less damage to the remaining parenchyma. Oncological outcome was considered perfect (4) (LE: 3). Additionally, the combination of both the KTP laser (for cutting) and the YAG laser (for coagulation of large vessels) allowed fast removal of kidney tissue, with minimal blood loss and minimal loss of renal parenchyma in as small a series of three paediatric cases of bilateral Wilms’ tumours (5).

The safety and feasibility of laser PN without the need for hilar occlusion was further supported in another small series of patients treated in an open fashion. A total of five patients with renal tumours up to 3.8 cm in size were subjected to open PN. A 2.0-μm cw laser (RevoLix) by LISA laser, which is a diode-pumped solid-state laser emitting a wavelength of 2013 nm and penetrating tissue to a depth of about 0.5 mm was used. In all cases, no peri-operative haemorrhage was noted and no sutures or other means of haemostasis were needed. No post-operative massive bleeding or significant creatinine level alteration were noted. In accordance with the authors, efficient and safe vascular coagulation was possible up to a vessel diameter of 1.5 mm. The laser technique should only be used in peripheral renal tumours (6) (LE: 3).

Successful accomplishment of laparoscopic PN (LPN) without the need for hilar occlusion in three human cases using the Ho:YAG laser was first reported in 2002. The indications for LPN were a complicated renal cyst and a 2.5-cm renal-cell carcinoma in two adult patients and a non-functioning lower pole in a duplicated collecting system in an 8-year-old child. Energy settings used were 2 J/pulse at 60 pulses/sec and 0.8 J/pulse at 40 pulses/sec. Despite the fact that haemostasis was considered adequate, fibrin glue was applied in two cases and oxidised cellulose in one case to reinforce the tissue against delayed bleeding. No complications were encountered and all patients left the hospital within 3 days.

The two major disadvantages of the technique were increased smoke accumulation during laser activation and significant splashing of blood onto the camera lens during resection, which occasionally impaired visibility (7) (LE: 3).

More recently, preliminary experience with laser robotic PN without hilar clamping was reported in two patients. KTP laser robotic PN was performed with a purpose-built, prototype, robotic, laser delivery instrument. A Greenlight HPS® laser unit was used at settings up to 50 W. In one patient, hilar clamping was necessitated during the procedure because of bleeding from a large central segmental vessel. The depth of thermal injury was estimated to be approximately 1 mm. No major complications were reported (8) (LE: 3).

Table 11: Clinical experience with laser-assisted partial nephrectomy

Reference	Patients (n)	Treatment	Laser beam	Hilar clamping	Comments or adverse effects	LE
Barzilay et al. 1982 (1)	4	Partial nephrectomy (n=3), bivalving of kidney (n=1)	CO_2 laser beam	Yes	Open	3
Rosemberg 1985 (2)	3	Partial nephrectomy	CO_2 laser beam	Yes	Open	3
Malloy et al. 1986 (3)	3	Partial nephrectomy	Nd:YAG laser	No	Open	3
Korhonen et al. 1993 (4)	5	Partial nephrectomy	Nd:YAG laser	Yes	Open	3
Merguerian et al. 1994 (5)	3	Partial nephrectomy	Nd:YAG laser and KTP laser	Yes	Open	3
Gruschwitz et al. 2008 (6)	5	Partial nephrectomy	2.0-μm continuous wave laser	No	Open	3
Lotan et al. 2002 (7)	3	Partial nephrectomy	Ho:YAG laser	No	Laparoscopic/ smoke accumulation and splashing of blood on camera	3
Hodgson et al. 2008 (8)	2	Partial nephrectomy	KTP laser	No	Robotic/hilar clamping was necessitated in one occasion	3

Ho:YAG = Holmium: yttrium aluminium garnet; KTP = potassium titanyl-phosphate laser; Nd:YAG = neodymium-doped yttrium aluminium garnet.

*5.1.3 **Conclusions about laser-assisted partial nephrectomy***

Conclusions	LE
Current data on nephron-sparing surgery using laser energy as an ablative method remain inconclusive.	3
Preliminary results indicate that laser-assisted laparoscopic PN without the need for hilar clamping is feasible.	3
No major complication has been reported in humans.	3
Laser-assisted PN is a promising alternative in renal surgery, which is worth further evaluation in clinical trials.	3

5.2 Laser-assisted laparoscopic nerve-sparing radical prostatectomy (LNSRP)

Experimental and preliminary clinical data have highlighted promising future applications of laser technology in LNSRP (Table 12). After examining the suitability of the technique in an experimental set-up of RP in dogs, Gianduzzo et al. performed a 532 nm KTP laser robotic NSRP in 10 patients using the AuraXP laser unit, delivering 12W through a 300-μm Endostat® fibre. The ability of KTP laser to be selectively absorbed by haemoglobin allows fine dissection, haemostasis and minimal tissue injury at the same time. However, in the current series, additional haemostasis using diathermy, suture or clips was required on several occasions for each case. Complications were one urine leak and one drain-site infection. Long-term potency outcomes were not demonstrated.

This is the first clinical evaluation of KTP laser as an ablative method in NSRP (9) (LE: 3). In accordance with the author, the main disadvantage of the technique is the requirement for a filter for the KTP green light emission to prevent interference with the camera system, and the wearing of tinted safety glasses, both of which significantly detract from the laparoscopic view. Experimental data on dogs verify that the ability of KTP laser to preserve cavernous nerve function is comparable to the athermal techniques (sharp dissection and clip placement) (10). However, further clinical assessment is needed to determine the value of this technique.

Promising results in matters of LNSRP using Nd:YAG laser dissection have been reported as well. In a preliminary feasibility study enrolling five patients with clinically localised adenocarcinoma of the prostate neurovascular bundle (NVB) preservation was evaluated. The 1064 nm Nd:YAG laser was used and a cw mode applied in direct tissue contact at a 8W power setting was suggested as the appropriate setup for most of the cases. Minimal blood loss, rapid dissection and minimal adjacent tissue injury estimated to be at 687μm (mean) were noted. As the NVBs were excised at the end of the operation for histological analysis, erectile functional data could not be assessed, which is a limitation of the current study (9)
(LE 3).

Table 12: Clinical experience with laser-assisted laparoscopic nerve-sparing radical prostatectomy

References	Patients (n)	Treatment	Laser beam	Comments or adverse effects	LE
Gianduzzo et al. 2007 (9)	5	LNSRP	1064 nm Nd:YAG laser	Laparoscopic	3

LNSRP = Laser-assisted laparoscopic nerve-sparing radical prostatectomy; Nd:YAG = neodymium-doped yttrium aluminium garnet.

5.2.1 ***Conclusions about laser-assisted laparoscopic nerve-sparing radical prostatectomy***

Conclusions	LE
Data are sparse and safe conclusions cannot be drawn yet.	
Preliminary results indicate that laser-assisted LNSRP is feasible and could possibly enhance neuro-vascular bundle preservation.	3
Laser-assisted LNSRP remains experimental.	3

6. RENAL TUMOUR LASER INTERSTITIAL ABLATION

The current consensus for small renal tumours supports thermal coagulation as an alternative treatment option, but only in selected cases of patients with co-morbidities that make them unsuitable candidates for partial nephrectomy (11).

Clinical experience with renal tumour laser interstitial ablation is still limited (Table 13). Renal magnetic resonance imaging (MRI)-guided percutaneous laser thermal ablation (LTA) was first introduced by de Jode and used in a preliminary feasibility study, treating three patients with inoperable renal tumours using a Nd:YAG laser delivered percutaneously to the renal tumour through a water-cooled interstitial fibre. Using MRI, laser placement was guided and treatment monitored in real time. Tissue necrosis within the targeted tissue was confirmed (12) (LE: 3).

Dick et al. evaluated the safety and feasibility of the technique in a series of nine patients with inoperable renal tumours. The operation took place under local sedation and opiate analgesia alone in 6 out of 9 patients, with the rest under general anaesthesia. A water-cooled 600 μm interstitial fibre was used to deliver 1064 μm Nd:YAG laser energy to the tumour. Laser energy was applied at 25 W for 10-30 minutes per treatment session. In all patients, the percentage enhancement of the tumour significantly decreased after LTA at the mean follow-up period of 16.9 months after the procedure. No subsequent infiltration of tumour into surrounding structures, e.g. peripheral fat and the renal vein, was noted. Reported complications were two cases of peripheral haematoma (resolving with conservative management) and one case of bradycardia (responded rapidly to atropine) (13) (LE: 3).

Table 13: Clinical experience with renal tumour laser interstitial ablation is still limited

Reference	Patients (n)	Disease	Laser beam	Comments	LE
de Jode et al. 1999 (12)	3	Inoperable renal tumours	Nd:YAG laser	Percutaneously or MRI-guided	3
Dick et al. 2002 (13)	9	Inoperable renal tumours	Nd:YAG laser	Percutaneously or MRI-guided	3

6.1 Conclusions and recommendation for laser treatment of small renal masses

Conclusions	LE
Data are poor and safe conclusions cannot be drawn yet regarding oncological outcome and safety.	4
Renal tumour interstitial laser ablation remains experimental.	4

Recommendation	GR
Laser-assisted laparoscopic PN, laser-assisted LNSRP and renal tumour laser interstitial coagulation are still experimental and should only be used in a clinical trial setting.	C

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7. RETROGRADE LASER ENDOURETEROTOMY

7.1 Introduction

Endoureterotomy is often first-line treatment for benign ureteral strictures. Since its introduction in 1997, retrograde laser endoureterotomy has become a popular tool for this procedure (1). Publications concerning the approach are based on retrospective analysis, i.e. single-institution studies resulting in levels 3 and 4 evidence (1-12) (Table 14).

7.2 Clinical application and results

Success rates of laser endoureterotomy are not uniformly evident. Large variations in success rates between published literature most probably arise because benign ureteral strictures are comprised of several different entities, each possibly responding differently to laser endoureterotomy (6). Nevertheless, large retrospective studies are lacking to elucidate which strictures respond well and which do not (LE: 4).
Non-ischaemic (e.g. iatrogenic) benign ureteral strictures after calculi management or abdominal surgery are reported to respond well to laser endoureterotomy, with a reported success rate between 68.4% and 91% (LE: 3). Stricture length is probably the most important predictor of outcome. Long ureteric strictures (> 2 cm) tend to be associated with poorer success rates (LE: 3). Stricture duration, ipsilateral renal function, stone impaction and stricture localisation (upper, middle or lower) have been also suggested to affect the outcome, though published results are controversial (LE: 3). Patients with ureteroenteric and malignant strictures do not respond well to laser endoureterotomy. Success rates in these cases are reported to be less than 60% (LE: 3).

The outcome of retrograde laser endoureterotomy compared to open surgical revision is slightly inferior (LE: 2b). However, due to the minimally invasive nature of the technique, laser endoureterotomy is associated with less morbidity and should be considered a first-line treatment option (LE: 3). When compared with other well-substantiated, endourological methods (e.g. hot-wire balloon catheter, endoincision with electrocautery or cold knife), laser endoureterotomy has been reported to have the same or superior long-term results (9). However, currently, there are no larger studies available presenting reliable long-term equivalence.

Holmium:YAG laser appears the only well tested-treatment modality (LE: 4). Currently, other laser energy sources are under evaluation which should still be considered experimental.

Since large studies are lacking and long-term studies are rare, the median time to failure has not yet been elucidated. Stricture recurrence as long as 18 months post-operatively has been reported. Yet, recurrence is most likely to be evident within the first 3 months (LE: 3). Balloon dilation after laser incision and post-operative placement of a ureteral stent for 4 weeks to 6 months are common practices that appear to aid long-term effectiveness (LE: 4). However, there remains a lack of studies comparing treatment failure with or without balloon dilation and post-operative ureteral stenting.

Table 14: Clinical experience with retrograde laser endoureterotomy

Reference	Patients (n)	Disease	Success rate	Mean follow-up (mo)	Comments
Lin et al. 2009 (2)	19	Benign ureteral strictures	52.6%	40.2	Stricture length and severity of hydronephrosis correlated with successful outcome
Gnessin et al. 2009 (3)	35	Benign ureteral strictures	82% sympto-matic, 78.7% radiographic	27	Success rate was higher for nonischaemic strictures (100% vs 64.7%, p = 0.027). Most failures occur < 9 months after surgery
Fu et al. 2009 (4)	18	Benign ureteral strictures, 6 cases complicated with ureteral calculus	88.8%	10.7	Post-operatively, an ortho-paedic ureteral stent was left in place for 3-6 months
Corcoran et al. 2009 (5)	9	Benign ureteral strictures (20% idiopathic, 80% after calculi management or abdominal sur-gery)	85%	25.2	Laser urethrotomy was fol-lowed by balloon dilation in most cases
Gdor et al. 2008 (6)	13	Ureteral strictures associated with ureteral calculi (impacted ureteral calculi in 4)	62%	21	In case of impacted ureteral calculi, success rate was 56%. Without a history of impacted calculi, success rate was 75%
Hibi et al. 2007 (7)	20		80%	60.5	All failures occurred within 18 months
Lane et al. 2006 (8)	19	Non-obliterative iatrogenic ureteral strictures	68.4%	36	Failure was uniformly evident within the first 3 months
Razdan et al. 2005 (9)	17	Ureteral strictures of varying causes		40.8	
Kourambas et al. 2001 (10)	7	Ureteral strictures	91%	3	
Singal et al. 1997 (1)	22	Ureteral stric-tures from a variety of causes and including ure-teroenteric anas-tomoses	76%	9	Failure was uniformly evident within the first 3 months
Watterson et al. 2002 (11)	23	Ureterointestinal strictures	56%	36	Some recurrences 16 months or longer postoperatively
Laven et al. 2001 (12)	19	Ureterointestinal strictures	57%	20.5	

7.3 Conclusions and recommendations for retrograde laser endoureterotomy

Conclusions	LE
Retrograde laser endoureterotomy is a feasible and safe treatment option for ureteral strictures.	3
Open surgical revision remains the gold standard.	1a
Ureteral strictures of different aetiologies appear to respond differently to treatment.	2b
In selected cases, success rate can reach 90%.	3
Ureteroenteric anastomosis strictures respond poorly to laser endoureterotomy.	3
Late stricture recurrence should be expected as long as 18 months post-operatively.	3

Recommendations	GR
Retrograde endoureterotomy should be considered a first-line treatment option for ureteral strictures.	C
Longer follow-up is needed.	C

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8. RETROGRADE LASER ENDOPYELOTOMY FOR URETEROPELVIC JUNCTION OBSTRUCTION (UPJO)

8.1 Introduction

Initial experience with laser endopyelotomy for the treatment of ureteropelvic junction obstruction (UPJO) can be traced back to the early 1990s (1). Since then, laser retrograde endopyelotomy has been a well-established method for the treatment of primary or secondary ureteropelvic junction (UPJ) strictures. Publications concerning retrograde laser endopyelotomy are mostly based on retrospective analysis, i.e. single-institution studies resulting in level 3 and 4 evidence data (Table 15) (2-19).

8.2 Clinical application and results

The optimal indication for laser endopyelotomy is a short (< 2 cm) UPJO of intrinsic aetiology in the absence of a very large pelvis, high insertion of the ureter, renal split function below 20%, and ipsilateral renal calculi (LE: 4). When particular inclusion criteria are selected, success rates are reported to be around 80% or even higher in more selected cases in the hands of an experienced urologist (LE: 4). Inferior success rates have been reported in cases of extrinsic cause of UPJO and severe hydronephrosis and in poor renal function (16,17).

The outcome of retrograde laser endopyelotomy compared to open pyeloplasty is slightly inferior (LE: 2b). However, due to the minimally invasive nature of the technique, laser endopyelotomy is associated with minimum blood loss, reduced hospital stay and less post-operative pain and should be one of the first-line treatment options (7) (LE: 2b). In addition, a failed endopyelotomy is not a contraindication for secondary open or laparoscopic pyeloplasty. When compared with other well-substantiated, endourological methods (e.g. hotwire balloon catheter, endoincision with electrocautery or cold knife), laser endopyelotomy is reported to have a similar or higher success rate and a lower rate of complications (8) (LE: 3). However, there are as yet no larger studies to provide reliable long-term equivalence.

The Ho:YAG laser appears to be the only well-tested treatment modality (LE: 4), with other laser energy sources under evaluation and still experimental. Complication rates associated with retrograde laser endopyelotomy have been reported as 12.5%, although the complications referred to are usually minor. More serious measures, such as conversion to open surgery, rarely need to be taken (LE: 3).

Despite the fact that long-term studies are rare, the median time to failure is reported to be as high as 7.7 months post-operatively (6). Post-operative placement of ureteral catheters, such as JJ stents for several weeks, is a common practice, despite the lack of studies comparing treatment failure with or without post-operative ureteral stenting.

Table 15: Clinical experience with retrograde laser endopyelotomy for ureteropelvic junction obstruction

Reference	Patients (n)	Disease	Success rate	Mean follow- up (mo)	Comments
Acher et al. 2009 (2)	15	Failed pyeloplasty	100%	6	No complications reported
Stilling et al. 2009 (3)	44	Primary (n=37) and secondary (n=7) UPJO	Symptom relief complete 66%; improved 23%	27.5	Strict inclusion criteria
Savoie et al. 2009 (4)	27	Primary (n=16) and secondary (n=11) UPJO	70%	35	Median time to failure: 2.7 months
Braga et al. 2007 (5)	10	Failed pyeloplasty in children	60% radiographic relief	47	Age < 4 years and narrowed ureteral segment greater than 10 mm were associated with a poor outcome

Doo et al. 2007 (6)	47	UPJO	67.5%	37.3	Median time to failure: 7.7 months
Rassweiler et al. 2007 (7)	113	Extrinsic as well as intrinsic UPJO	72.6% (85.7% intrinsic vs 51.4% extrinsic)	63 months	Complication rate of 5.3%
Ponsky et al. 2006 (8)	37	Primary and secondary UPJO	74.2%	75.6	No major complications reported
Geavlete et al. 2007 (9)	30	Failed pyeloplasty (n=17); failed endopyelotomy (n=13)	83.3% (at 18 months)	31	
el-Nahas et al. 2006 (10)	20	Primary and secondary UPJO	85%	29.9	10% complication rate
Minervini at al. 2005 (11)	30	UPJO	80% (at 10 months)	24	12.5% complication rate
Seveso et al. 2005 (12)	16	Primary (n=10) and secondary (n=6) UPJO	81%	18	One case of intra-operative haemorrhage
Matin et al. 2003 (13)	46	Primary (n=40) and secondary (n=6) UPJO	65.4% symptomatic and 73.1% radiographic	23.2	No intra-operative complications; 11.1% post-operative complications
Hibi et al. 2002 (14)	5	UPJO	80%	12.8	
Giddens et al. 2000 (15)	23	Primary and secondary UPJO	83%	10	Repeat laser incision successful in 50% of primary failures
Biyani et al. 2000 (16)	22	Primary (n=16) and secondary (n=4) UPJO	75%	34	Success rate tends to be poor in patients with poor renal function
Renner et al. 1998 (17)	34	Primary (n=27) and secondary (n=7) UPJO	85%	18	Minor complications in 15%
Conlin et al. 1998 (18)	21	UPJO	81%	12	
Biyani et al. 1997 (19)	8	Primary (n=5) and secondary (n=3) UPJO	87.5%	12.4	

UPJO = ureteropelvic junction obstruction.

8.3 Conclusions and recommendations for laser treatment for UPJO

Conclusions	**LE**
Retrograde laser endopyelotomy is a feasible and safe treatment option for the treatment of UPJO.	3
Open or laparoscopic pyeloplasty remains the gold standard.	1a
In selected cases, success rate can reach 90%.	2b
Treatment morbidity is minimal and major complications are rare.	3
Treatment failure may occur up to 1 year post-operatively.	3

Recommendations	GR
Retrograde laser endopyelotomy could be one of the first-line treatment options.	C
Follow-up should be prolonged for at least 1 year post-operatively.	C
Open or laparoscopic pyeloplasty remain options in cases in which minimally invasive measures fail.	C
Ensure identification of crossing vessels which is of particular relevance in reducing bleeding complications.	B
Ureteric stent placement before the procedure is an option that may affect the post-operative success rate.	C

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9. TRANSURETHRAL LASER URETHROTOMY

9.1 Introduction

The introduction of transurethral laser urethrotomy using the Nd:YAG laser can be traced back to 1979 (1). Since then, laser urethrotomy has become a common urological practice worldwide in the management of urethral strictures. Publications concerning this approach are based on retrospective analysis, i.e. single-institution studies leading to level 3 or 4 evidence data (2-19) (Table 16).

9.2 Clinical application and results

Success rates of laser urethrotomy for urethral strictures are reported to be as high as 100% in selected cases (LE: 3). Short segment urethral strictures tend to respond excellently to this treatment modality (LE: 3). However, long (> 1.5 cm) or recurrent urethral strictures are reported to demonstrate inferior results (LE: 3). Periodic urethral dilatation is usually enough for the management of treatment failure (LE: 3).

The types of lasers tested on laser urethrotomy are the Nd:YAG, the KTP, the argon, the Ho:YAG and the diode laser. No superiority of one type of lasers has been demonstrated (LE: 3). There is a lack of large multicentre studies comparing the success rate of laser endourethrotomy with conventional optical urethrotomy. Currently, the midterm effectiveness of both treatment options is considered equal (LE: 3). However, in a randomised control study comparing the effectiveness of Nd:YAG laser with conventional cold-knife optical urethrotomy in the treatment of varying length urethral strictures (0.3-2.4 cm), laser treatment significantly decreased the probability of therapeutic failure and recurrence of strictures (20) (LE: 3).

Table 16: Clinical experience with transurethral laser urethrotomy

Reference	Patients (n)	Disease	Success rate %	Mean follow-up (mo)	Comments
Guo et al. 2010 (2)	238	Urethral strictures	81.9%	6	2-micron thulium laser
Guo et al. 2008 (3)	192	Urethral strictures (n = 179) or atresia (n = 13)	81.7%	6	2 micron thulium laser
Xiao et al. 2008 (4)	34	Urethral strictures	94.7%	3-18	Holmium laser: 4 received urethral dilation and 2 underwent a second holmium laser urethrotomy

Eltahawy et al. 2008 (5)	24	Anastomotic stenosis following radical prostatectomy, 79% recurrent-resistant to other treatment modalities	83%	24	Holmium laser + steroid injection
Futao et al. 2006 (6)	28	Paediatric patients with urethral strictures (n=25) and urethral atresias (n=3)	89.3%	(2-48)	Ho:YAG
Hossain et al. 2004 (7)	30	Short segment anterior urethral structure	90%	6	Ho:YAG
Dogra et al. 2004 (8)	29	Urethral stricture (< 2.5 cm)	65.51% excellent, 31.03% acceptable	15	Ho:YAG
Gürdal et al. 2003 (9)	21	Recurrent benign urethral strictures 5-20 mm in length	52%	24	Nd:YAG
Dogra et al. 2003 (10)	61	Obliterative post-traumatic urethral strictures in children	100%	24	Nd-YAG
Matsuoka et al. 2002 (11)	31	Ureteral stricture of varying lengths	74%		Ho:YAG
Dogra et al. 2002 (12)	65	Post-traumatic urethral strictures	95.3%	9-44	Nd- YAG
Kamal 2001 (13)	22	Urethral strictures (8 recurrent)	54% (78.5% in non recurrent strictures)	26.7	Diode laser
Schmidlin et al. 1997 (14)	20	Anterior urethral strictures	81%	6	KTP
Becker et al. 1995 (15)	900	Urethral strictures (most iatrogenic)	30%	15.2	Argon
Faerber et al. 1994 (16)	12	Paediatric urethral strictures	83%	12	Nd-YAG
Turek et al. 1992 (17)	37	Benign urethral strictures	59% complete, 20.5% partial success	9.7	KTP
Vicente et al. 1990 (18)	15	Benign urethral strictures	73.3%	12	Cold knife + Nd:YAG laser
Bloiso et al. 1988 (19)	115	31 short strictures 36 bladder neck 48 complicated	96.7% (short strictures); 100% (bladder neck); 22.91% (complicated)	10 (short strictures); 7 (bladder neck); 14 (complicated)	Nd:YAG

Ho:YAG = Holmium: yttrium aluminium garnet; KTP = potassium titanyl-phosphate laser; Nd:YAG = neodymium-doped yttrium aluminium garnet

9.3 Conclusions and recommendation for transurethral laser urethrotomy

Conclusions	**LE**
Transurethral laser urethrotomy is a feasible and safe treatment option for the treatment of urethral strictures.	3
Cold-knife optical urethrotomy remains the gold standard.	1a
Success rates as high as 100% are reported in selected cases	3
Treatment morbidity is minimal and major complications are rare.	3

Recommendation	GR
Transurethral laser urethrotomy could be one of the first-line treatment options for benign urethral strictures.	C

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10. LASER CLINICAL APLICATIONS IN UPPER URINARY TRACT STONES AND TUMOURS

10.1 Introduction

The entire upper urinary tract can be accessed and explored with flexible endoscopes (1-3). Miniaturisation especially with laser fibres became an armamentarium in the endourological field. In Ho:YAG lasers, energy is delivered most commonly in a pulsatile manner, using a thermomechanical action. Absorption depth in tissue is about 1-2 mm, as long as it is used in a water-based medium. This specific light energy provides good homeostasis when used in a pulsed mode of 250-millisecond duration and at low pulse rate. At higher pulse rates, it may also be used for incisions. The frequency-doubled, double-pulse Nd:YAG (FREDDY) laser is a short-pulsed, double-frequency solid-state laser with wavelengths of 532 and 1064 nm. Although FREDDY laser is effective for lithotripsy, it is does not have a soft-tissue application (e.g. tumours). The erbium (Er:YAG) laser may be superior to the Ho:YAG laser for precise ablation of strictures with minimal peripheral thermal damage and for more efficient laser lithotripsy (4). Er:YAG laser cuts urethral and ureteral tissues more precisely than Ho:YAG laser and produces less peripheral thermal damage. With any laser, all intra-operative personnel should wear proper eye protection to avoid corneal or retinal damage. This is especially true with Nd:YAG (FREDDY), which penetrates deeply and can burn the retina faster than the blink reflex can protect it. Ho:YAG does not penetrate as deeply, but it may cause corneal defects if aimed at the unprotected eye.
An adequate draping should be used around external areas. Wet towels should be draped around cutaneous lesions. Reflective surfaces (e.g., metal instruments) should be kept away from the field if possible and, if not possible, should be draped with wet drapes. Furthermore, using laser where oxygen is in use anywhere near the operative field is dangerous. This can result in a laser fire and cause significant burns.

10.2 Upper urinary tract stones

Endoscopic intracorporeal laser lithotripsy is widely used as a treatment for upper urinary tract stones (5-7). Lasers are ideally suited for retrograde intra-renal surgery or percutaneous approach (8).

Flexible quartz fibres deliver laser energy to fragment all types of stones. That energy is delivered in a pulsatile fashion through low-water density quartz fibres. In water, a vaporisation bubble surrounds the fibre tip. This bubble actually destabilises stones, creating fine dust and small fragments. Accurate fibre contact against a calculus is the primary safety factor. Successful stone fragmentation is achieved in on average > 90% of cases (6). Stone fragmentation with Ho:YAG laser further minimises ureteral wall trauma; provided that, the distance between the tip of the fibre and ureter is > 1 mm. the risk of ureteral perforation during laser lithotripsy is negligible since the depth of thermal injury is 0.5 to 1 mm. Ho:YAG laser is fully absorbed within the first few millimetres of tissue; therefore, when applied in water or saline irrigant, minimal risk of surrounding thermal injury exists as compared to Nd:YAG (9,10). Ho:YAG has a minimal fragment migration and retrograde propulsion when low settings compared to Nd:YAG (9).

Hard stones in difficult locations (e.g., lower pole caliceal calculi, stone bearing caliceal stone) can be treated using a thin, 150 to 200-μm, that is easily deflected.

Moreover, the type of eye protection used for Ho:YAG does not affect colour perception. Nd:YAG laser combines of solid and dye lasers. In vitro studies (11), have compared Ho:YAG lasers across several parameters relating to stone treatment; fragmentation was significantly better with Nd:YAG laser than with Ho:YAG laser. Nevertheless, in 2006, a study reported Nd:YAG laser provided suspect fragmentation of calcium oxalate monohydrate stones and ineffective fragmentation of cystine stones (12). In addition to that, stone retropulsion was significantly greater (9,11,13). Alexandrite laser has been used, it is safe and effective, although it is rarely used in recent clinical practice (14).

All of the initial laser lithotrities (pulsed dye, Q-switched YAG and alexandrite) fragmented stones through the generation of a shock wave. Those waves disrupt the stone along fracture lines.

The Holmium laser works through a photo-thermal mechanism, which involves the direct absorption of the laser energy by the stone. The absence of strong wave in Holmium laser avoids the retropulsion phenomenon (15). Nevertheless, it is still strong enough to create stone dust and thereby facilitate stone fragmentation with smaller fragments than those produced by pulsed lasers or other devices. Residual fragments place patients at higher risk for recurrent stone formation or growth (16). Holmium laser energy is absorbed by all stone compositions; this laser can be used to fragment all stone types (17). Cyanide production was reported as a side effect of uric acid stones fragmentation (18).

10.2.1 ***Conclusions***

	LE
Pulsed lasers are an effective and safe treatment for UUT stones, using endoscopes.	2a
Lasers present a safe option for fragmenting stones in the upper urinary tract.	1b

10.3 Upper urinary tract urothelial tumours

The aim of the conservative management of upper tract urothelial tumours (UUT-UT) is to preserve renal function (19-21). This may be considered imperative or absolutely indicated in patients with a solitary anatomic kidney, solitary functioning kidney or limited renal function.

The development of sophisticated endourologic techniques for the treatment of benign urologic disease has translated to the treatment of malignant neoplasms, with the use of flexible ureteroscope and laser ablation becoming common place in urologic practice (19-23). Further, the cancer-control efficacy of this management approach has been established (20,21).

Even though nephro-ureterectomy is the gold standard; the current literature supports the use of lasers in patients with UUT-UT; however, meticulous and long-term follow up is needed (23,25). Ho:YAG and Nd:YAG lasers are presently the most commonly used lasers. The laser combining of both is convenient and effective but Ho:YAG can be used alone, preferentially with the variable pulse duration. Nd:YAG laser energy is used to coagulate with a thermal effect that extends deeper than other lasers. Holmium is more precise, with less of a coagulative effect. Laser therapy for tumour ablation is safe in patients with bleeding diathesis (25). In contrast to tumour ablation (Holmium/Thulium), in case of tumour vaporisation no pathology specimen will be available (Nd:YAG/Holmium/Thulium). Therefore multiple prior biopsy samples to determine depth of invasion should be obtained. Appropriate staging of the tumour (CT/biopsy) is important to allow selection of patients for nephron-sparing surgery. There are reports on percutaneous laser treatment of TCC of the kidney and this technique has been recognised in urological practice (26-28).

A true drawback with the Nd:YAG laser is that the area of destruction is deep and not fully visualised. Within the renal pelvis, the energy choice depends mainly upon the size of the lesion. Larger vascular tumours (> 1 cm) can be coagulated initially with the Nd:YAG and then ablated and cleared with the Holmium when a combination laser is available. Lower Holmium energy tends to maximise the coagulative effect and minimise the risk of bleeding (e.g. 0.5 to 0.6 joules and 5 hertz). The stricture rate in larger series has ranged from 5% to 13.7% (29). Because of the miniaturisation of instruments and development of laser fibres, the incidence of stricture rate is considered lower. Moreover, the stricture rate is considered lower due to minimal fibrotic reaction after laser use in comparison with electrocautery devices. To avoid urothelial damage and possible stricture, all endoscopic laser modalities should be used under direct vision, through the working channel of an endoscope.

10.4 Conclusion and recommendations for laser treatment of UUT urothelial tumours

Conclusion	**LE**
Nephro-ureterectomy is still the gold standard for UUT urothelial tumours.	1a

Recommendations	**GR**
Laser ablation of small low-grade upper tract transitional cell carcinoma with close follow-up can be a safe alternative treatment to nephroureterectomy in patients with normal contralateral kidneys.	B
Endoscopic conservative treatment can be the preferred treatment in high-risk patients, as well as those with bilateral disease, solitary kidney or reduced renal function.	C

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11. ABBREVIATIONS USED IN THE TEXT

(This list is not comprehensive for the most common abbreviations)

BPE	benign prostatic enlargement
BOO	bladder outlet obstruction
BPO	benign prostatic obstruction
CW	continuous wave
EAU	European Association of Urology
Er:YAG	erbium: yttrium-aluminium-garnet
GR	grade of recommendation
HoLAP	Holmium laser ablation of the prostate
HoLEP	Holmium laser enucleation of the prostate
HoLRP	Holmium laser resection of the prostate
Ho:YAG	Holmium: yttrium-aluminium-garnet
IIEF-5	international index of erectile function (abbreviated version)
KTP	kalium titanyl phosphate
LBO	lithium triborate
LE	level of evidence
LNSRP	laser-assisted laparoscopic nerve-sparing radical prostatectomy
LPN	laparoscopic partial nephrectomy
LTA	laser thermal ablation
MRI	magnetic resonance imaging
Nd:YAG	neodymium-doped: yttrium-aluminium-garnet
Nd:YAG (FREDDY)	frequency-doubled, double-pulse
Nd:YAG (LBO)	lithium triborate modulated Nd:YAG
NVB	prostate neurovascular bundle
OP	open prostatectomy
PN	partial nephrectomy
PSA	prostate specific antigen
PVP	photoselective vaporisation of the prostate
PVR	postvoid residual urine
Q_{max}	urinary peak flow
QoL	Quality of Life
Tm:YAG	thulium:yttrium-aluminium-garnet
ThuVAP	Tm:YAG Vaporisation of the prostate
ThuVARP	Tm:YAG Vaporesection
ThuVEP	Tm:YAG Vapoenucleation
ThuLEP	Tm:YAG laser enucleation of the prostate
TUR	transurethral resection
TURB	TUR of the bladder
TURP	TUR of the prostate
UPJO	ureteropelvic junction obstruction
UTI	urinary tract infection

Conflict of interest

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