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Executive Summary

Lower urinary tract symptoms commonly affect older men and are often consistent with benign prostatic hyperplasia (BPH). For over 50 years, the cornerstone of BPH treatment has been transurethral resection of the prostate (TURP). The success and diffusion of TURP is justified as long-term studies have proven that it reduces BPH symptoms and increases urinary flow. In the 1990s, a wave of new procedures surfaced as possible alternatives to TURP; one of these was laser prostatectomy. During this period, various lasers were introduced including the Neodymium:Yttrium Aluminium Garnet (Nd:YAG) laser, the Holmium (Ho):YAG laser and the frequency doubled Nd:YAG laser (also known as the potassium titanyl phosphate laser [KTP laser]). However, these efforts failed to replace TURP as the treatment of choice because too little power was applied at sub-optimal wavelengths. The recent introduction of more powerful lasers has led to a resurgence in interest in laser prostatectomy. The lasers discussed in this report include KTP lasers, lithium triborate (LBO) lasers, holmium lasers, diode lasers and thulium lasers.

In terms of safety, KTP photoselective vaporisation of the prostate (PVP) appears to be at least as safe as TURP, open prostatectomy (OP) and holmium laser ablation of the prostate (HoLAP). KTP PVP also appears to be at least as effective as TURP and OP; however, one RCT found the early functional outcomes of TURP to be superior compared with PVP. The operative time of PVP appears to be significantly longer compared with TURP and OP and significantly shorter compared with HoLAP. All studies reported a reduction in the duration of postoperative catheterisation and hospitalisation following PVP compared with TURP and OP. The newer 120W PVP procedure (LBO laser) also compared favourably with TURP.

Holmium laser enucleation of the prostate (HoLEP) appears to be at least as safe as TURP and OP and over the long-term (>2 years) HoLEP appears to achieve functional outcomes comparable with TURP. The operative time of HoLEP was found to be significantly longer than that of TURP but advantages with regards to catheterisation time and hospital stay were apparent.

The evidence available for thulium laser enucleation of the prostate (ThuLEP) and diode laser vaporisation was limited; however, both procedures appear to be safe, with no serious complications reported. Follow-up data suggests that ThuLEP may be equally effective in small and large prostates.

Overall, the more common laser prostatectomy procedures (KTP PVP and HoLEP) appear to be at least as safe and effective as TURP for the treatment of BPH. There is inadequate literature available to say the same for the less commonly used laser approaches (diode laser vaporisation and ThuLEP).

In general, laser prostatectomy using more modern lasers is a therapy that can be offered to most patients with benign prostatic hypertrophy (BPH) including those with larger glands and those recently on oral anti-coagulant therapy. Surgical times seem to be measurably longer than would be the case with standard trans-urethral resection of the prostate (TURP), although this difference may be only of the order of 10 minutes, but post procedural catheterisation times and hospital lengths of stay are shorter. Functional outcomes in the short and medium term, as determined by urinary flow rates and residual volumes seem to be equivalent for laser prostatectomy, TURP and open prostatectomy. There are some trials showing subjective evaluations by patients to be better with open prostatectomy or TURP and there is some evidence that retrograde ejaculation is more common after laser prostatectomy. Overall, it seems fair to conclude that laser prostatectomy is now non-inferior to TURP or open prostatectomy. Moreover, laser prostatectomy is less expensive because of the savings made by a reduced length of stay. Upfront costs of laser prostatectomy may be substantial given the capital costs of lasers. However, such affordability issues need to be balanced against longer term savings.

It seems reasonable to conclude that laser prostatectomy is a therapy that is a reasonable, safe and cost-effective alternative to TURP or open prostatectomy for the treatment of BPH.

Introduction

The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical, on behalf of the Medical Services Advisory Committee (MSAC), has undertaken a horizon scanning report to provide advice to the Health Policy Advisory Committee on Technology (Health PACT) on the state of play regarding the introduction and use of laser prostatectomy.

This horizon scanning report is intended for the use of health planners and policy makers. It provides an assessment of the current state of development of laser prostatectomy, its present use, overall effectiveness, and the likely impact of the new and emerging evidence on Australian practice.

This horizon scanning report is a preliminary statement of the safety, effectiveness, cost-effectiveness and ethical considerations associated with laser prostatectomy.

Background

Condition

Lower urinary tract symptoms (LUTS) commonly affect older men and are often consistent with benign prostatic hyperplasia (BPH), an enlargement of the prostate gland. BPH leads to narrowing of the lower urinary tract and places pressure on the base of the bladder (Miano et al 2008). Although not life-threatening, untreated BPH can lead to bladder and kidney disorders.

Treatment

Treatment options for BPH include watchful waiting, medical therapy (α1-adrenoreceptor antagonists and 5α-reductase inhibitors), prostatic stenting, minimally invasive treatments (e.g. transuretheral needle ablation), transuretheral resection of the prostate (TURP), and open prostatectomy (OP).

For over 50 years, the definitive treatment of BPH has been TURP. The success and diffusion of TURP is justified as long-term studies have proven that the procedure reduces BPH symptoms and increases urinary flow. In addition, TURP is less costly and has considerably lower morbidity compared to OP (Jepsen and Bruskewitz 1998). However, clinical data have also revealed that at least 15% of patients develop a complication after TURP while up to 15% of patients require re-intervention within 10 years (Mebust et al 1989, Dunsmuir et al 1996). Despite numerous attempts to modify or improve TURP, the morbidity and mortality statistics for this procedure have not changed for decades (Mulligan et al 1997).

As a result, there have been considerable efforts to develop alternatives to TURP including medical therapies and minimally invasive mechanical procedures such as urethral stents. In addition, a range of minimally-invasive thermal-based techniques have been explored, including transuretheral microwave therapy and transurethral needle ablation (Miano et al 2008).

In the 1990s, a wave of new procedures surfaced as possible alternatives to TURP; one of these was laser prostatectomy. During this period, various lasers were introduced including the Neodymium:Yttrium Aluminium Garnet (Nd:YAG) laser, the Holmium (Ho):YAG laser and the frequency doubled Nd:YAG laser (also known as the potassium titanyl phosphate laser [KTP laser]).

Each laser has a distinctive wavelength and therefore has unique tissue interaction characteristics when applied to prostatic tissue. However, these efforts failed to replace TURP as the treatment of choice because too little power was applied at sub-optimal wavelengths so, prostatic tissue could not be removed immediately, outcomes were unpredictable, and reoperation rates were high (up to 40% at 3

years) (Bachmann and Marberger 2008). However, the recent introduction of more powerful lasers has led to a resurgence in interest in laser prostatectomy.

Description of the technology

Lasers can achieve coagulation, vaporisation, incision, resection or enucleation. The laser prostatectomy procedure depends on the type of laser used and its power output, the latter determining tissue heating properties and speed of surgical effect. The lasers and techniques employed for laser prostatectomy are detailed below, including:

1. Nd:YAG
   (a) VLAP (of historical interest)
   (b) CLAP (of historical interest)
2. Ho:YAG
   (a) HoLAP
   (b) HoLRP
   (c)) HoLEP
3. KTP
4. LBO
5. Diode
6. Thulium

1. Nd:YAG laser

The Nd:YAG laser has a wavelength of 1064nm with a penetration depth from 5 to 17.5mm and can achieve coagulation or ablation/vaporisation of prostate tissue.

(a) VLAP

VLAP with the Nd:YAG laser used a side-firing probe in non-contact mode to create deep coagulative necrosis of prostatic tissue which led to prolonged tissue sloughing over 6 to 8 weeks. With the use of higher-powered units, tissue vaporisation and ablation is possible; however, coagulation often led to significant post-operative voiding symptoms as well as prolonged catheterisation. This resulted in significantly greater procedural morbidity compared with TURP despite the fact that many patients had good and durable outcomes. Eventually the higher reoperation rate to TURP and unpredictable outcomes in some patients restricted the use of VLAP (Wilson and Gilling 2005) and this technology will not be discussed in detail in this report.

(b) CLAP

Contact laser ablation of the prostate (CLAP) uses the Nd:YAG laser with a sapphire-tipped fiber that converts the laser energy to heat to create a TURP-like cavity by vaporisation and ablation. However, reoperation rates are high (~18%)

and outcomes are not always comparable to TURP. These disappointing results eventually led to CLAP's demise (Wilson and Gilling 2005) and this technology will not be discussed in detail in this report.

2. Ho:YAG

The Ho:YAG laser is a solid-state laser that works in a pulsed mode. It produces invisible light with a wavelength of 2140 nm that is rapidly absorbed by water in the tissue. Shallow penetration depth (0.4mm) causes vaporisation without deep coagulative tissue necrosis so tissue can be incised, resected, ablated/vaporised and enucleated with a clean, char-free cut as well as simultaneous coagulation of small and medium-sized blood vessels to a depth of 2-3mm (Kuntz 2007).

(a) HoLAP

Holmium laser ablation (vaporisation) of the prostate (HoLAP) was first performed in 1994 with a 60W machine. However, the considerable time required to perform this procedure led to its slow adoption and eventual demise. Recent developments and the emergence of the high powered 100W holmium laser, which shortens procedure time considerably, has led to a surge in interest in HoLAP, particularly for small and medium-sized prostates.

(b) HoLRP

Holmium laser resection of the prostate (HoLRP) involves the resection of the adenomatous tissue down to the capsule and cuts this into pieces small enough to be evacuated through the resectoscope's sheath. At the end of the procedure, all adenomatous tissue is removed leaving a prostatic cavity similar to that produced by conventional TURP with one key difference, 50% of the tissue removed is lost to vaporisation (Kuntz 2007).

(c) HoLEP

The latest evolution of holmium laser prostatectomy has been the development of a technique that involves the enucleation of entire prostatic lobes using existing surgical tissue planes. This technique, holmium laser enucleation of the prostate (HoLEP), is faster than HoLRP (Tan and Gilling 2002) and mainly addresses the rate limiting step of tissue removal from the bladder during HoLRP. The holmium laser fiber acts much like the index finger of the surgeon during an OP in shelling out the adenoma. As the most popular and deemed most promising technique utilising the holmium laser, HoLEP will be discussed here in greater detail.

3. KTP laser

The KTP laser uses an Nd:YAG laser beam passed through a KTP crystal, halving the wavelength (to 532nm), doubling the laser's frequency, and resulting in a

green light. Green light is strongly absorbed by the colour red, therefore the KTP laser is selectively absorbed by haemoglobin. With sufficient power, rapid photothermal vaporisation of intracellular tissue water occurs, also known as photoselective vaporisation of the prostate (PVP). The coagulation zone is approximately 2mm deep. However, the speed of tissue removal is limited to 0.3-0.5m/min and no tissue specimens for histological examination can be obtained.

Efforts to improve laser prostatectomy led to the production of the 60W KTP laser which demonstrated shorter mean resection times (Lee et al 2006). Soon after, the 80W KTP laser was introduced to further decrease vaporisation time. In order to preserve a thin coagulation zone while still maintaining high vaporisation efficiency, a new laser pulsing technology was integrated into the 80W system. The laser generates a continuous stream of short micro-pulses with a duration of 4.5 ms (milliseconds). Continuous bladder irrigation is necessary to cool the tissue and to provide a clear aqueous medium for laser light to transmit to target tissue without energy loss.

This report will focus on high-powered KTP lasers only, defined as lasers with power of 80W upwards.

4. LBO laser

In 2006, the 120W lithium triborate laser (LBO), also known as the Greenlight HPS™ (High Performance System) laser was introduced. This laser utilises a diode pumped Nd:YAG laser light that is emitted through an LBO instead of a KTP crystal, resulting in a higher-powered green light laser. This laser has the potential to induce more efficient tissue vaporisation for the treatment of BPH, compared with the KTP laser.

5. Diode laser

The recent introduction of a high-powered diode laser system that operates on a wavelength of 980nm has opened new possible alternatives to TURP. Due to the fact that this wavelength offers high simultaneous absorption in water and haemoglobin, it is postulated to combine high tissue ablative properties with good haemostasis (Wendt-Nordahl et al 2007). Other potential advantages over KTP and Ho:YAG laser devices include significantly lower energy consumption and the absence of a required high voltage connection, which essentially improves the mobility of the laser generator. An ex-vivo study demonstrated increased tissue ablation capacity and comparable haemostatic properties when compared to the KTP laser (Wendt-Nordahl et al 2007).

6. Thulium laser

The thulium laser is has been hailed as the potential replacement for Ho:YAG for multiple urological applications. This laser has a 200nm wavelength, similar to

the Ho:YAG, delivered as a continuous wave instead of pulsed. It retains most of the qualities of the Ho:YAG laser i.e., rapid absorption in water, short penetration depth, as well as incision and haemostatic properties (Kuntz 2007). Thulium laser enucleation of the prostate (ThuLEP) is the most common laser prostatectomy approach used for this laser type.

Clinical need and burden of disease

BPH is the most common benign tumour in aging men and is the most frequent male tumour requiring surgical intervention. Studies have shown that a histology diagnosis occurs in more than 50% of men by the age of 60, and in 90% of men by the age of 85 (Miano et al 2008).

TURP is one of the most commonly performed procedures worldwide (Bouchier-Hayes 2007). The Australian Institute of Health and Welfare (AIHW) reported that TURP was performed in 43,888 patients in the fiscal year 2006/07 – 2007/08, while other closed prostatectomy procedures (e.g. cryoablation, laser ablation/excision etc.) accounted for only 6% of this number at 2543 procedures (AIHW 2010).

Stage of development

The use of lasers in a clinical setting has been explored since the 1960s although their use in urology has been limited, at least until the last decade. Currently, two lasers are considered to be key challengers to the well established TURP procedure, KTP and Ho:YAG.

Technological advancements have led to higher-powered variants of these two lasers, enabling more rapid resection or ablation/vaporization. In 2002, the 80W KTP laser was introduced and gave rise to PVP. Manufacturers have now introduced higher-powered PVP, with the most recent being the 180W GreenLight XPS system (FDA approval November, 2009). Expert clinical opinion states that the 120W LBO laser is the current standard of care due to its higher power (compared with the 80W KTP laser) and better surgical utility.

Holmium laser systems were introduced in the 1990s and have been available considerably longer than PVP laser systems. For example, the Lumenis holmium laser system received FDA clearance for surgical ablation and vaporisation in 1990, the system was not cleared until 2001 for additional indications such as ablation, vaporization, excision, incision and coagulation of soft tissue and for procedures such as HoLAP (Lumenis® 2009). Meanwhile, the Dornier Diode Laser family was FDA-approved in August 2002 (FDA 2002).

In Australia, the Therapeutics Goods Administration (TGA) has approved a range of KTP, LBO and holmium lasers (Table 1).

Table 1: TGA approved KTP, LBO and holmium lasers.

Register ID	Sponsor details/Name
KTP and LBO lasers	
139911	American Medical Systems Australia Pty Ltd - GreenLight HPS
169092	American Medical Systems Australia Pty Ltd
172515	MD Solutions Australasia Pty Ltd
93890	High Tech Laser Australia Pty Ltd
169103	American Medical Systems Australia Pty Ltd - Laser, LBO crystal
Ho:YAG lasers	
117681	High Tech Laser Australia P/L
121588	Device Technologies Australia Pty Ltd
123403	Varol Celalettin
132204	Medtel Pty Ltd
149774	Olympus Australia Pty Ltd
157508	MD Solutions Australasia Pty Ltd
160444	William A Cook Australia Pty Ltd
164007	N Stenning & Co Pty Ltd
166845	American Medical Systems Australia Pty Ltd
169527	Meditron Pty Ltd
173695	Medical Technologies Aust Pty Ltd - Quanta Ho:YAG Laser
80616	N.Stenning & Co Lasers

Practically all diode lasers within the TGA register are approved for dental, ophthalmologic and cosmetic (hair removal, skin pigmentation) procedures although use in the treatment of BPH is not described in TGA materials. At the time of writing, no thulium laser systems had been approved by the FDA or the TGA for the treatment of symptomatic BPH.

Existing comparators

For decades, surgery has been the preferred treatment for BPH. OP was the only definitive treatment until the 1930s (Holtgrewe 1998) and, although it was very effective, morbidity rates were high at ~36% (Kour 1995). OP has now been largely replaced by TURP, with the exception of the management of some patients with large prostates (>50 grams) and patients with bladder pathologies that require concurrent surgical treatment.

TURP is now the standard surgical treatment for small to medium sized prostates with BPH and is therefore the main comparator to laser prostatectomy. Alternatives developed over the past 15 years include transurethral incision of the prostate (usually for small prostates, <40 grams) and bipolar techniques (bipolar transurethral resection, vaporisation and enucleation).

The studies included in this report are presented below according to laser type:
1. 80W KTP PVP (7 studies, plus a systematic review [SR])
2. 120W LBO PVP (2 studies)
3. HoLEP (11 studies)
4. Diode laser (3 studies)
5. ThuLep (2 studies)

Introduction to the Included Studies

1. 80W KTP PVP

Eight studies were identified: an SR, four randomised controlled trials (RCTs) and three non-randomised comparative studies. (See Appendix B for study profiles.)

SR evidence

A rigorous Cochrane-modelled SR by Stafinski et al (2008) in Canada identified English-language studies available up to December 2006. Contact with eight urologists and the device manufacturer provided information on unpublished or recently completed studies. A total of 14 studies met the selection criteria (n=1376) including an RCT, a multicentre cohort study, and 12 case series. Most studies followed patients for 6 or 12 months and only one extended to 24 months. An intention to treat approach was taken and meta-analysis generated summary estimates for each outcome of interest.

RCT evidence

Of the four RCTs retrieved for inclusion, two compared PVP with TURP (Bouchier-Hayes et al 2006; Horasanli et al 2008), one compared PVP with OP (Skolarikos et al 2008) and one compared PVP with HoLAP (Elzayat et al 2009) (Table 2).

Table 2: RCTs of PVP versus a Comparator.

Authors	Year	Country	Comparator	n=	Follow-up
Bouchier-Hayes et al	2006	Australia	TURP	76	12 months
Horasanli et al	2008	Turkey	TURP	76	6 months
Skolarikos et al	2008	Greece	OP	125	18 months
Elzayat et al	2009	Canada	HoLAP	109	12 months

a) KTP PVP vs. TURP

Horasanli et al (2008) randomised (method not specified) 76 consecutive patients with prostate volume >70ml were to PVP (n=39) or TURP (n=37) from January

2005 to March 2006. Baseline data indicated no significant difference between groups. Patient outcomes were assessed at 3 and 6 months.

Bouchier-Hayes et al (2006) randomised (method not specified) patients to PVP (n=38) or TURP (n=38). Groups were well matched at baseline with regard to age and prostate volume. All operative procedures were carried out at a single centre by registrars in training or fellows who had each performed between 35 and 325 TURP procedures and <5 laser prostatectomies. This was done to alleviate expert bias and to assess the ease of mastery of the PVP procedure by the average urologist. All patients were followed up by a single investigator at 6 weeks and 68, 57, and 44 patients were followed at 3, 6, and 12 months, respectively.

b) KTP PVP vs. OP

Using random number tables, Skolarikos et al (2008) assigned patients to PVP (n=65) or OP (n=60) between March 2005 and April 2006. Groups were comparable at baseline. Blinding of the urologist responsible for assessing patient outcomes was employed. Patients were followed up to 18 months.

c) KTP PVP vs. HOLAP

Using a random number generator computer program, Elzayat et al (2009) assigned consecutive patients to PVP (n=52) or HoLAP (n=57) between March 2005 and April 2007. Baseline patient characteristics were not significantly different between groups. Allocation concealment with respect to type of laser was achieved by blinding all patients, assessing nurses and ultrasonographers. Surgeries were performed or supervised by a single surgeon who was a recognised expert in holmium laser therapy and follow-up extended to 12 months.

Note on KTP RCT evidence: The overall quality of the studies by Horasanli et al (2008) and Bouchier-Hayes et al (2006) was low, as the method of randomisation, use of allocation concealment, and calculation of minimum sample sizes were not described. As well as this, Bouchier-Hayes et al (2006) provided English-language symptom questionnaires to a large proportion on non-English speakers, which may have limited the relevance of the data collected. In contrast, the studies by Skolarikos et al (2008) and Elzayat et al (2009) used adequate randomisation methods, attempted to blind patients and/or assessors from patient allocation, and provided formal sample size calculations.

Non-randomised comparative evidence

All three studies compared PVP with TURP (Nomura et al 2009a; Ruszat et al 2008; Tugcu et al 2008) (Table 3).

Table 3: Non-randomised comparative trials of PVP versus a Comparator.

Authors	Year	Country	Comparator	n=	Follow-up
Ruszat et al	2008	Germany & Switzerland	TURP	101	24 months
Tugcu et al	2008	Turkey	TURP	210	24 months
Nomura et al	2009a	Japan	TURP	129	12 months

a) KTP PVP vs. TURP

Nomura et al (2009a) prospectively reviewed the outcomes of patients who underwent surgical treatment of BPH between March 2006 and June 2007. Based on patient choice and clinical assessment 143 patients underwent PVP and 92 patients underwent TURP; however, only 78 and 51 cases respectively were included in the final analysis of results (n=129). Both procedures were performed by two physicians with a decade's experience in performing TURP but no prior experience with PVP. The patient groups were similar except that prostate volume was significantly larger and PSA levels were significantly higher in the PVP group at baseline ($P<0.05$). Patients were followed up to 12 months.

In the study by Ruszat et al (2008), 101 consecutive patients underwent either PVP (n=64) or TURP (n=37) from December 2003 to August 2006. This trial took place in two centres; all PVP procedures were carried out at one centre by two experienced surgeons and two novices and all TURP procedures were carried out at the other centre by three surgeons who had experience with at least 200 TURP procedures prior to the trial. Patients in each group were comparable at baseline except postvoid residual volume which was significantly higher in the PVP group. Patients were followed up to 24 months.

Finally, Tugcu et al (2008) reported outcomes in 210 patients with large (>70ml) prostates who underwent PVP (n=112) or TURP (n=98) between September 2003 and June 2004. All PVP procedures were carried out at a single centre by a single surgeon after a learning curve of 30 procedures was completed, and all TURP procedures were carried out at another centre by one of two surgeons. Groups were well matched at baseline and follow-up extended to 24 months.

Particular study design faults in these studies include surgeon inexperience and unmatched patient characteristics at baseline, which may have resulted in outcomes favouring the reference test (TURP). As well, Nomura et al (2009a) allowed patients to choose the surgical intervention which may be a confounder.

2. 120W LBO PVP

Two studies were retrieved for inclusion, an RCT and a case series. (See Appendix B for study profiles.)

RCT evidence

The RCT compared LBO PVP with TURP (Al-Ansari et al 2010) (Table 4).

Table 4: RCT of LBO PVP versus a Comparator.

Authors	Year	Country	Comparator	n=	Follow-up
Al-Ansari et al	2010	Qatar	TURP	120	36 months

a) LBO PVP vs. TURP

Using computer generated random tables, Al-Ansari et al (2010) assigned symptomatic BPH patients to either high performance 120W GreenLight PVP (n=60) or TURP (n=60). Treatment groups had comparable baseline characteristics and observers were blinded to group assignment. PVP was coupled with a flexible 600μm side-firing fibre. Each procedure was performed by two urologists and patients were assessed up to 36 months post-surgery.

Case series evidence

Spaliviero et al (2008) prospectively evaluated the outcomes of 120W GreenLight PVP in 70 symptomatic BPH patients who had not responded to medical treatment. All patients were treated by a single surgeon from July 2006 to March 2008 and were assessed up to 24 weeks post-surgery.

2. HoLEP

Eight RCTs and 3 non-randomised comparative studies were included. (See Appendix B for study profiles.)

RCT evidence

Of the 8 RCTs retrieved for inclusion, 6 compared HoLEP to TURP and 2 compared HoLEP to OP (Table 5).

Table 5: RCTs of HoLEP versus a Comparator.

Authors	Year	Country	Comparator	n=	Follow-up
Montorsi et al	2004	Italy	TURP	100	12 months
Briganti et al	2006	Italy	TURP	120	24 months
Gupta et al	2006	India	TURP	150	12 months
Naspro et al	2006	Italy	OP	80	24 months
Wilson et al	2006	New Zealand	TURP	61	24 months
Ahyai et al	2007	Germany	TURP	200	36 months
Kuntz et al	2008	Germany	OP	120	60 months
Mavuduru et al	2009	India	TURP	30	9 months

a) HoLEP vs. TURP

Briganti et al (2006) randomised 120 patients with symptomatic BPH to HoLEP (n=60) or TURP (n=60). All patients were assessed preoperatively to determine suitability but no specific inclusion or exclusion criteria were provided. Groups were similar aside from transrectal ultrasound (TRUS) prostate volume which was significantly lower in the TURP group. Holmium laser energy was delivered by 360µ fiber places in a 24Fr resectoscope and enucleation was performed at 2.0 Joules and 35 Hz. All patients were assessed at 12 and 24 months

Montorsi et al (2004) examined the outcomes of 100 patients with symptomatic BPH randomised to either HoLEP (n=52) or TURP (n=48) from January 2002 to October 2002. Baseline characteristics were comparable between groups except TRUS volume which was significantly lower in the TURP group. Holmium laser energy was delivered by 360µ fibres and enucleation was performed at 2.0 Joules and 35 Hz. All patients were assessed up to 12 month post-treatment.

Mavuduru et al (2009) compared the efficacy of HoLEP versus TURP in 30 patients randomised via a computer generated random table. Excluded were patients with a previous history of prostatic or urethral surgery or documented prostate carcinoma. Groups had similar baseline characteristics. HoLEP was performed using a frequency setting of 35-40 Hz and power settings of 2 Joules. Follow-up extended to 9 months (n=27).

Using a schedule balance, Ahyai et al (2007) prospectively randomised patients with symptomatic BPH with prostate volume <100 grams to HoLEP (n=100) or TURP (n=100). Inclusion and exclusion criteria were provided and groups were comparable at baseline. HoLEP was performed at 40-50Hz, 80-100W with reusable 550µm laser fibres. Patients were assessed up to 36 months after surgery.

Wilson et al (2006) randomised (via a balanced block randomisation schedule) 61 patients to either HoLEP (n=31) or TURP (n=30). Inclusion criteria, but no exclusion criteria, were provided. There were no significant differences between groups preoperatively. The holmium laser was set at 100W for each case. Primary outcomes were assessed up to 24 months.

From July 2002 to December 2003, Gupta et al (2006) randomised 150 patients with BPH (prostate >40 grams) who were candidates for TURP to TURP (n=50), transuretheral vapour resection (TUVRP[1]) (n=50) or HoLEP (n=50). No inclusion or exclusion criteria were reported and the method of randomisation was not provided. Groups were similar prior to surgery. HoLEP was performed with a 550µm end-firing laser fibre and a 100W holmium:YAG laser source. Power settings were 80W to 100W at 1.5 to 2 J/s and 40Hz to 50Hz. Patients were assessed up to 12 months post-surgery.

Note on HoLEP vs. TURP RCT quality: Quality was generally low, e.g., the method of randomisation was not stated in 3 studies, 3 did not provide inclusion and/or exclusion criteria, none employed blinding, and none presented sample size calculations.

b) HoLEP vs. OP

Via computer generated table, Naspro et al (2006) randomized 80 consecutive BPH patients (prostate >70 grams) to HoLEP (n=41) or OP (n=39) from March 2003 to December 2004. Inclusion and exclusion criteria were utilised and patient baseline characteristics for both groups were comparable except the OP group had a higher proportion of incidental adenocarcinoma (7.6% vs. 4.8%, p=0.02). Patients were followed up to 24 months.

Kuntz et al (2008) randomised (schedule balanced in blocks of four) 120 patients with prostates >100g.to HoLEP (n=60) or OP (n=60). Inclusion and exclusion criteria were employed and baseline characteristics between groups were comparable. Patients were assessed up to 60 months after surgery. Patients who experienced significant deterioration of micturation parameters underwent urethrocytoscopy and reoperations were performed when indicated. High-powered HoLEP was performed with the holmium laser set at 40-50Hz and 80-100W with reusable 550nm laser fibres (Lumenis Inc.). When necessary, data from earlier publications of this cohort (Kuntz and Lehrich 2002, Kuntz et al 2004) were used.

Note on HoLEP vs. OP RCT quality: Blinding was not possible in these studies due to the nature of the surgical procedures, and this can introduce assessor and patient bias. In addition, neither RCT appeared to have performed power calculations to ensure cohort sizes were adequate to detect true differences between the procedures.

Non-randomised comparative evidence

Of the three included non-randomised comparative studies, one compared HoLEP to OP (Moody and Lingeman 2001), one examined the effectiveness of HoLEP

[1] TUVRP is a modification of TURP that uses a band electrode coupled to a high electrocuting energy to achieve simultaneous resection, vaporisation and coagulation of the prostate.

for a range of prostate sizes (Humphreys et al 2008) and one compared HoLEP outcomes between two institutions (Kim et al 2005).

Moody and Lingehan (2001) compared the use of HoLEP to OP in patients with a prostate >100 grams. The investigators retrospectively examined data from 10 HoLEP cases and 10 OP cases from 1998 to 1999. The holmium laser utilised had a power of 80W, set to an energy level of 2J and 40 Hz rate, with a 550μm end-firing laser fibre. Treatment groups were comparable, at least for age and preoperative American Urological Association Symptom Score (AUA SS). Mean follow-up duration was not reported.

Humphreys et al (2008) retrospectively reviewed the records of all patients who underwent HoLEP from January 1999 to October 2006 within the authors' institution to determine the outcomes of HoLEP based on prostate size. Postoperative data points were compared at 6 months post-surgery to ensure consistency in reporting. Patients were excluded if they had a diagnosis of prostate cancer or they had no preoperative TRUS volume available. Patients were divided into three groups based on prostate size: 1) <75 grams (n=164); 2) 75 to 125 grams (n=226) and 3) >125 grams (n=117). HoLEP equipment included an 80W or 100W Ho:YAG laser and a 550μm end-firing fibre.

Finally, Kim et al (2005) retrospectively compared the efficiency of HoLEP at two institutions from January 1998 to December 2000 for all patients treated by a single surgeon at the Methodist Hospital of Indiana (United States) and the Tauranga Hospital (New Zealand). The authors achieved matches between 40 pairs of patients from each institution (match criteria were not provided).

3. Diode laser

Three case series studies reported on the use of diode laser vaporisation of the prostate in patients with BPH. The first reported outcomes of laser prostatectomy using the 50W prototype diode laser in patients with bladder outlet obstruction (BOO) (Seitz et al 2007) and the remaining two reported results using high-intensity diode lasers (Erol et al 2009; Chen et al 2010). (See Appendix B for study profiles).

Case series evidence

Seitz et al (2007) treated 10 patients with BOO with 50W diode laser between January and March 2006. Mean prostate volume was about 48 cc. Ten patients were followed up at 1 month and 8 patients were followed up at 6 and 12 months.

Erol et al (2009) studied 47 consecutive patients who underwent 80-132W diode laser prostatectomy between September 2007 and April 2008 as performed by a single surgeon. Mean preoperative prostate volume was 51 cc and follow-up extended to 6 months.

Chen et al (2010) treated 55 patients with 200W diode laser prostatectomy from December 2007 to July 2008. The physicians performing the procedures were highly experienced in KTP PVP and TURP. Mean prostate volume was 66cc. All patients were reassessed at 1 month and 44 at 6 months.

Note on study quality: All three studies reported inclusion and exclusion criteria. Methodological soundness was enhanced in the studies that enrolled consecutive patients and aimed to have all procedures performed by a single surgeon. Case series studies are more susceptible to bias than are comparative trials and RCTs but their data provide preliminary information about safety and efficacy.

4. ThuLEP

Two studies reported outcomes in the same case series population, with one study providing immediate to short-term follow-up (Bach et al 2009) and the other providing intermediate-term (>12 months) follow-up (Bach et al 2010). (See Appendix B for study profiles).

Bach et al (2009) prospectively reviewed 88 consecutive patients who underwent VapoEnucleation of the prostate with the 70W Thulium:YAG laser. Specific inclusion and exclusion criteria were used. Mean postoperative prostatic volume was 61cc. Three surgeons (with unknown proficiency in the ThuLEP) carried out the procedures at a single centre. Bach et al (2010) reported on this surgical cohort with mean follow-up 16.5 months (n=62 of the original 88).

Safety and Effectiveness

1. 80W KTP PVP

Safety

a) KTP PVP vs. TURP

There were no cases of intraoperative complications reported in association with the PVP procedure in the study by Horasanli et al (2008). Ruszat et al (2008) reported significantly more intraoperative complications in TURP patients compared with PVP patients, including bleeding (P=0.002), the need for transfusion (P=0.001) and capsule perforation (P=0.001). Tugcu et al (2008) also reported significantly more intraoperative complications associated with TURP for capsule perforation (P=0.046).

Pooled complication rates from the 12 included case series included in the SR ranged from 0% for bladder stenosis to 9.3% for mild-to-moderate dysuria. Compared with TURP, PVP complication rates were either similar or considerably lower, particularly urinary retention and clot retention. Pooled

analyses of relative risk of a complication for the two comparative studies was comparable between PVP and TURP groups with the exception of clot retention that was significantly less likely to develop in PVP. The authors concluded that PVP offers an acceptable safety profile.

The RCT enrolling men with larger prostates (Horasanli et al 2008) reported that urinary retention was significantly more common in PVP patients (15% vs. 3%; P=0.02). Boucher-Hayes et al (2006) reported more significant complications in association with TURP, mainly clot retention requiring manual bladder washouts. There were no reports of significant haematuria or dysuria in the RCT by Horasanli et al (2008); however, eight patients in both the PVP and TURP groups reported dysuria at 6 weeks follow-up in the RCT by Bouchier-Hayes et al (2006), and secondary haemorrhage necessitating recatheterisation and inpatient admission occurred in one PVP patient and three TURP patients. A significant increase in mild-to-moderate dysuria was also seen in PVP patients (n=20) in the study by Tugcu et al (2008) compared with TURP patients (n=5) (P=0.005).

Reoperation was required in 17.9% (7/39) of PVP patients in the study by Horasanli et al (2008) at 6 months follow-up due to insufficient healing of the coagulated tissue that obstructed bladder outlet, compared with 0% of TURP patients. Horasanli et al (2008) also reported the need for transfusion in 8.1% of TURP patients compared with 0% of PVP patients (P=0.001). Blood loss (measured by serum haemoglobin) on the first postoperative day was reported by Bouchier-Hayes et al (2006), with significant loss apparent in both groups of patients, although the degree of blood loss was significantly less in PVP patients (P<0.005).

b) KTP PVP vs. OP

The rate at which adverse events (AEs) occurred in patients receiving PVP versus OP at 18 months follow-up was comparable, with the exception of blood transfusion which occurred in significantly less patients in the PVP group (0%) compared with the OP group (13.3%) (P=0.002) (Skolarikos et al 2008). The most common transient AE was dysuria which affected 15% and 20% of patients, respectively. In most patients this symptom resolved spontaneously after a mean duration of 6 weeks. Prolonged dysuria resolved over a 3-month period and affected 7.6% and 11.6% of patients. Mild transient haematuria was also reported in 7 and 17 PVP and OP patients, respectively. Reoperation for urethral stricture, bladder neck contracture or persistent bladder outflow obstruction symptoms took place in 3 patients in both the PVP and OP groups (P=1.000)

c) KTP PVP vs. HoLAP

Intraoperative bleeding occurred in 5.7% (3/52) of PVP compared with 0% of HoLAP patients; however, all cases were controlled successfully with electrocauterization (Elzayat et al 2009). The rate at which complications

occurred was comparable for PVP and HoLAP, e.g., haematuria, clot retention, incontinence, infection and urethral stricture.

Effectiveness

Efficacy outcomes can be divided into three subgroups:

- Operative outcomes (length of the PVP procedure, catheterisation time)
- Functional outcomes (changes in peak urinary flow rate (Q_{max}), postvoid residual volume (V_{res}), quality of life (QoL) and sexual functioning)
- Durability of PVP, i.e., recurrence of LUTS and the need for retreatment.

Operative outcomes

a) KTP PVP vs. TURP

The SR by Stafinski et al (2008) describes average operative time for PVP between 20 and 137 minutes, with an increase in operative time correlated with prostate size, and no significant difference from the average operative time for TURP. Bouchier-Hayes et al (2006) supported this with similar operative times reported for both PVP and TURP patients. The RCT by Horasanli et al (2008) maintains that larger prostates require longer operative time, with operative time ranging from 60-110 minutes in this study, which was significantly longer than that of TURP (P=0.03). Three of the included non-randomised comparative studies reported operative time to be significantly longer in PVP patients compared with TURP patients also (Nomura et al (2009a), P<0.05; Ruszat et al (2008), P=0.001; Tugcu et al (2008), P<0.001).

The SR, two RCTs and two non-randomised comparative studies reported that PVP offered significant improvements in average catheterisation time and length of hospitalisation compared with TURP (Stafinski et al 2008; Horasanli et al 2008; Bouchier-Hayes et al 2006; Ruszat et al 2008; Tugcu et al 2008). A significant proportion of patients reported in the SR did not require postoperative catheterisation and in those that did, the average length of catheterisation ranged from 7.6 hours to 43 hours. In the same study, all but one of the included studies reported that patients were discharged from hospital less than 24 hours postoperative. Time to discharge was longer in the RCTs by Horasanli et al (2008) (1-3 days) and Bouchier-Hayes et al (2006) (1-2 days); however, this time was still significantly shorter than that of TURP (P=0.02 and P<0.001).

b) KTP PVP vs. OP

Operative time was significantly longer for PVP compared with OP (P<0.05) but PVP also showed significant improvements in average catheterisation time and length of hospitalisation (Skolarikos et al 2008).

c) KTP PVP vs. HoLAP

Elzayat et al (2009) reported significantly longer operative time for HoLAP compared with PVP (P=0.008) but length of catheterisation and hospital stay were not significantly different between groups.

Functional outcomes

a) KTP PVP vs. TURP

All 12 case series included in the SR (Stafinski et al 2008), as well as the RCTs of Horasanli et al (2008) and Bouchier-Hayes et al (2006) and the non-randomised comparative studies by Nomura et al (2009a) and Tugcu et al (2008) reported similar patterns of statistically significant improvement in functional outcomes over baseline for both PVP and TURP, including Q_{max}, V_{res} and symptom scores. The studies that also looked at improvement in QoL found consistent statically significant improvements over time in PVP and TURP patients that were comparable between study groups (Stafinski et al 2008; Bouchier-Hayes et al 2006; Nomura et al 2009a; Tugcu et al 2008). Conversely, there was a significant difference seen between the PVP and TURP groups favouring TURP, as reported by Horasanli et al (2008), with regards to subjective International Prostate Symptom Score[2] (IPSS) and objective Q_{max} and V_{res} outcomes. An improvement in Q_{max} and V_{res} favouring TURP (compared with PVP) was also seen in the study by Ruszat et al (2008); however, in this study the difference between PVP and TURP for IPSS improvement from baseline was not significant.

In the SR, the cases series that examined changes in sexual function, PSA levels and prostate volume from baseline to post-procedure found no significant differences between groups undergoing PVP or TURP. The same was reported of sexual function in the RCT by Horasanli et al (2008); however, decreases in PSA level and prostate volume were significantly greater in patients following TURP compared with PVP ($P<0.05$). Nomura et al (2009a) observed the same trends at 6 months follow-up ($P<0.05$).

b) KTP PVP vs. OP

Skolarikos et al (2008) found significant postoperative improvement in IPSS, IPSS-QoL, Q_{max} and V_{res} for patients undergoing either PVP or OP. Of these four outcomes, only IPSS-QoL was statically superior in one group (OP) and the remaining three outcomes were comparable between groups. Reductions in both PSA and prostate volume were significantly larger in the OP group, whereas sexual function did not change from baseline or differ between the groups.

[2] IPSS is an 8 question written screening tool regarding urinary symptoms (7 questions) and quality of life (1 question), where each question is assigned points from 0 to 5. The total score can therefore range from 0 to 35, where scores from 0-7 indicate mild symptoms, scores from 8-19 indicate moderate symptoms and scores from 20-35 indicate severe symptoms.

c) KTP PVP vs. HoLAP

Elzayat et al (2009) reported significant improvements in voiding parameters (Q_{max}, V_{res}), IPSS and QoL following PVP and HoLAP. Both groups experienced a marginal improvement in sexual function (not significant) and similar significant reductions in PSA and prostate volume (P<0.05).

Durability of PVP

a) KTP PVP vs. TURP

Reoperation rates in the SR (Stafinski et al 2008) and the non-randomised comparative study by Ruszat et al (2008) did not vary significantly between groups. In studies reporting 12-month follow-up, 0% to 7.5% of PVP patients required reoperation. Bouchier-Hayes et al (2006) also reported the need for TURP for persistent obstructive symptoms in two PVP patients, noting residual tissue (both patients were among the first 10 to undergo PVP, highlighting surgeon learning curve as a possible explanation).

b) KTP PVP vs. HoLAP

Need for reoperation to remove residual adenoma was not significantly different between groups (Elzayat et al 2009). In the PVP group one patient required reoperation at 2 months follow-up and in the HoLAP group two patients required reoperation at 10 and 12 months.

2. 120W LBO PVP

Safety

Al-Ansari et al (2010) documented 12 cases (20%) of blood transfusion during surgery in the TURP group versus 0% for the 120W PVP group (P=0.0001). In addition, the incidence of capsule perforation was significantly higher for TURP (16.7% vs. 0%; p=0.0001). Assessment of early (<30 days) postoperative complications revealed that TURP patients experienced a higher rate of clot retention (10% vs. 0%; p=0.01). However, the 120W PVP group had a higher rate of dysuria/urge (93.3% vs. 31.7%; p=0.001). Late postoperative complications (≤3 years) were more common in PVP patients, with 11% requiring reoperation (all had volume >80ml) compared to 1.8% for TURP patients (P=0.04). No patients in either group developed urethral stricture or urinary incontinence. There were no complications that affected erectile function in the 82 patients who were potent prior to surgery.

Spaliviero et al (2008) stated that 2 patients (9.5%) required temporary (< 24 hours) re-catheterisation for urinary retention of unknown aetiology 3 weeks after

120W PVP. There were no incidences of bladder neck contracture, urethral strictures or urinary incontinence up to 24 weeks post-surgery.

Effectiveness

In the Al-Ansari et al (2010), there were no significant reductions in haemoglobin and serum sodium levels in the PVP group post-procedure but significant decreases were seen in the TURP group. Mean operative time was longer for PVP relative to TURP (89 vs. 80 mins; $p<0.01$) but catheterisation time was shorter for PVP patients (1.4 vs. 2.7 days; $p<0.0001$). Functional outcomes (Q_{max}, IPSS and V_{res} urine) improved considerably and similarly after both treatments. Both PSA level and prostate volume decreased after 120W PVP and TURP for all follow-up timepoints. However, the percentage decrease in PSA levels as well as prostate volume was significantly greater for TURP patients.

Spaliviero et al (2008) reported findings based on whether patients were discharged with or without a catheter. At 4 weeks, mean QoL scores decreased from 4.5 to 0.4 for the catheter-free (C-) group and from 4.0 to 0.9 for the catheter (C+) group ($P<0.001$ for both). In terms of functional outcomes, Q_{max} increased significantly from 10 to 24ml/s for the C- group and from 8 to 21ml/s for the C+ group. The increase in Q_{max} was actually significantly higher for the C- group at the 1 and 4-week assessment timepoints ($P=0.01$ and $p=0.001$, respectively). Nevertheless, both groups had comparable results in all the subsequent assessments. Mean V_{res} did not decrease significantly for both C+ and C- groups.

Clinical studies refining the use of PVP in different patient populations

Six non-randomised comparative studies comparing the use of PVP in different patient populations were also eligible for inclusion in this report. Of these studies, two compared outcomes of PVP in patients with varying prostate volumes (Nomura et al 2009b; Pfitzenmaier et al 2008), one assessed the outcomes of PVP in patients with or without oral anticoagulation therapy (OAT) (Ruszat et al 2007), and the remaining studies assessed the affect of urinary retention (Ruszat et al 2006), detrusor muscle overactivity (Cho et al 2010) and preoperative catheterisation for bladder management (Kavoussi et al 2008). The findings of these studies form the basis of a brief discussion below.

Performance of PVP in large versus small prostates

Nomura et al (2009b) reported outcomes in the same patient population reported in their previous study and compared only those patients who underwent PVP in regards to their prostate volume. Group 1 consisted of patients with prostate volumes < $40cm^3$ (n=25), Group 2 of prostate volume 40-$80cm^3$ (n=53) and Group 3 of prostate volume >$80cm^3$ (n=24). Results from this study indicated that PVP is safe and effective in treating BPH irrespective of prostate size. There were no significant differences in the number of AE that occurred between groups and as expected total operative time and the efficacy of vaporisation (gram/min and

gram/kJ) increased with prostate volume. Similar findings in regards to functional outcomes were obtained in the study by Pfitzenmaier et al (2008) who compared patients with prostate volume ≥80ml with patients with prostate volume <80ml. However, reoperation rate was significantly higher in patients with larger prostates (23.1%) compared with smaller prostates (10.4%) (P=0.09).

Performance of PVP in high-risk patient groups

OAT is a contraindication to TURP, due to the high-risk of surgical bleeding complications. Ruszat et al (2007) sought to determine the feasibility, safety and efficacy of PVP in patients on OAT (n=116) by comparing them with patients receiving PVP who were not on OAT (n=92). Operative time, haemoglobin level and IPSS were comparable between groups and there were no bleeding complications necessitating transfusion.

Performance of PVP in patients with urinary storage symptoms

Cho et al (2010) compared 39 patients with detrusor overactivity (DO) with 110 patients with normal detrusor activity. Both patient groups experienced a significant reduction in storage and voiding symptoms following PVP. In particular patients with DO might show more improvement in storage symptoms than those without DO. Ruszat et al (2006) investigated the affect of refractory urinary retention secondary to BPH in patients undergoing PVP (n=70) by comparing their outcomes with those without urinary retention (n=113). This study was included in the Stafinski et al (2008) SR but was selected to be included separately here so that the affect of urinary retention could be reported more clearly. Postoperative urinary retention and complication rates were comparable between these two groups; therefore, PVP seems to be safe and effective for the treatment of patients with refractory urinary retention caused by prostatic enlargement.

Kavoussi et al (2008) separated patients into three groups based on patients' pre-operative status: catheter free (n=86), indwelling catheter (n=8), and clean intermittent catheterisation (n=11). Sexual function was maintained in patients who were catheter free or required intermittent catheterisation, and was improved in patients with indwelling catheters. However, there was no significant change in sexual function in patients who had mild or no erectile dysfunction preoperatively.

3. HoLEP

Safety

a) HoLEP vs. TURP

At 24 months follow-up, Wilson et al (2006) reported that in the HoLEP group (n=31) 6 patients had experienced AEs (5 recatheterisation and 1 urethral stricture). This compared favourably with the TURP group (n=30) in which 13 patients experienced AEs (1 blood transfusion, 4 catheterisations, 2 reoperations,

2 urinary tract infections, 3 urethral strictures and 1 death 15 months post-surgery). No statistical tests were performed.

Mavuduru et al (2009) reported total AEs to be comparable for both study arms (40% vs. 27%; p=0.4). Similarly, Ahyai et al (2007) noted that at 3 years post-surgery, the incidence of urethral stricture, bladder neck contracture and BPH recurrence was comparable between groups.

Montorsi et al (2004) did not observe a difference with regards to preoperative and postoperative serum haemoglobin or blood loss between groups but acute urinary retention rate was higher after HoLEP compared to TURP (5.3% vs. 2.2%) (statistical significance unclear). However, HoLEP patients had more occurrences of bladder mucosal injury (18% vs. 0%; p=0.001) and dysuria (59% vs. 30%; p=0.0002). At 12 months post-procedure, urethral strictures were more common in TURP patients (7.4% vs. 1.7%) but statistical significance is unclear.

For patients with prostate size >40 grams, Gupta et al (2006) noted that HoLEP resulted in less blood loss than did TURP (41 ml vs. 141 ml; p<0.001); however, transient dysuria was more common for HoLEP patients (10% vs. 2%; p<0.03). Rates between groups did not differ for recatheterisation, fever, hyponatraemia, capsular perforation, bladder mucosal injury, death, stricture and incontinence.

Three RCTs reported on sexual function outcomes after HoLEP (Briganti et al 2006, Montorsi et al 2004, Wilson et al 2006).

- Briganti et al (2006) focused specifically on sexual function after HoLEP relative to TURP. About half the enrolled patients (63 of 120) reported various degrees of erectile dysfunction before surgery. Results showed no significant difference in erectile function at 12 and 24 months, but significant deterioration in International Index of Erectile Function[3] (IIEF) orgasmic function domain score in both groups due to retrograde ejaculation.

- Montorsi et al (2004) noted no significant change between study arms in erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction between groups at 6 and 12 months although ejaculatory function worsened due to retrograde ejaculation.

- Wilson et al (2006) reported 2 patients (3.9%) with improved potency and two others (3.9%) with deterioration after treatment. At 24 months, two patients in each treatment group had new onset of erectile dysfunction compared to baseline. Retrograde ejaculation was more common in HoLEP patients (12/16, 75%) compared to TURP patients (8/13; 62%) but statistical significance was not reported.

[3] IIEF is an 5 question written screening tool regarding erectile function, where each question is assigned points from 1 to 5. The total score can therefore range from 5 to 25, where a score of 5 indicates suboptimal erectile function and a score of 25 indicates normal erectile function.

b) HoLEP vs. OP

Naspro et al (2006) noted that blood loss and the need for transfusions were lower for HoLEP patients versus OP. Data on postoperative irritative symptoms at 3 months revealed that dysuria was the most common symptom in both groups, particularly HoLEP patients (68% vs. 41%; p<0.001). In addition, bladder mucosal injury occurred in 3 HoLEP patients (7.3%) compared with 0 for OP (P<0.001). At 12-months follow-up, dysuria persisted in 11% and 9% of HoLEP and OP patients, respectively (P=0.02). Stricture incidence was comparable between groups 1 and 2 years post-treatment.

Kuntz and Lehrich (2002) (n=120) noted that at short-term follow-up, urge incontinence was reported by 2 HoLEP (3%) and 5 OP (8%) patients (no P-value reported), but this resolved completely within 1 month for all HoLEP patients and within 3 months for all OP patients. Moderate to severe incontinence developed in 5 HoLEP (8%) and 6 OP (10%) patients. Late complications for this cohort at 5 years were reported in Kuntz et al (2008) at which point reports of strictures, bladder neck contractures, and reoperation rates were similar between groups, although 38% of the patients were lost to follow-up.

The early retrospective comparative study by Moody and Lingeman (2001) (n=20; patients received surgery in 1998 and 1999) noted that 4 HoLEP patients developed stress urinary incontinence (short-term and self-limited), one patient suffered from prostatic perforation and another had neurogenic bladder dysfunction. Meanwhile, the OP group had one case of stress incontinence after surgery, one case of urge incontinence, and two cases of bladder neck contracture. In terms of erectile function post-surgery, Naspro et al (2006) noted that there was no significant reduction in IIEF scores throughout follow-up when compared to baseline values in HoLEP or OP patients.

Effectiveness

a) HoLEP vs. TURP

Operative outcomes

Montorsi et al (2004) reported that time in the operating room was higher for the HoLEP group at 74 versus 57 minutes (P<0.05), although more tissue was removed (36 vs. 25 grams; P<0.05) for this group, catheterisation time was shorter (31 vs. 54 hours) as was hospital stay (59 vs. 86 hours; p<0.001).

Similarly, Mavuduru et al (2009) reported that operative time was significantly longer for HoLEP relative to TURP (53 vs. 43 mins; p<0.01) although in this study the weight of the resected gland was lower for HoLEP patients (7 vs. 20 gram; p<0.001). Kuntz et al (2004a) reported similar resection weights between treatment groups but noted lower postoperative catheterisation time and hospital stay for HoLEP versus TURP patients.

Gupta et al (2006) also noted longer operative time required for HoLEP versus TURP although mean blood loss, nursing contact time and catheter duration were significantly lower for the former.

Functional outcomes

Assessments at 1, 6 and 12 months post-surgery by Montorsi et al (2004) did not reveal any statistically significant differences between HoLEP and TURP patients in terms of I-PSS, QoL or uroflowmetry.

Wilson et al (2006) reported no significant between-group differences for SS, QoL and Q_{max} from 6 months to 24 months. PSA levels decreased by 87% in the HoLEP group and 65% in the TURP group but there were no significant differences in V_{res}. The HoLEP group achieved significantly greater improvements in TRUS volume, $PdetQ_{max}$[4] and Schaffer Grade at 6 months follow-up when compared to the TURP group ($P<0.05$ each).

At 3 months post-surgery, Mavuduru et al (2009) (n=30) documented significant and comparable improvements in IPSS scores for both HoLEP and TURP groups, as well as significant improvements in V_{res} volumes. At 9 months follow-up, IPSS, V_{res}, uroflow, incontinence and stricture were comparable between groups.

Up to 3 years post-surgery, Ahyai et al (2007) noted that both HoLEP and TURP resulted in significant and comparable improvements over baseline in AUA SS, Q_{max} and V_{res} volume.

Gupta et al (2006) found that all three patient groups (HoLEP, TURP and TUVRP) experienced similar statistically significant improvements in Q_{max}, IPSS and V_{res} 6 months and at 1 year post-treatment.

b) HoLEP vs. OP

Operative outcomes

Naspro et al (2006) reported catheterisation time (1.5 vs. 4.1 days) and hospital stay (2.7 vs. 5.4 days) were significantly shorter for HoLEP versus OP patients although operative time for HoLEP was significantly longer 72 vs. 58 mins. In contrast, the small retrospective review by Moody and Lingemann (2001) found comparable operative times and resected prostate weights.

Functional outcomes

One to 5-year follow-up data presented by Kuntz et al (2008) on patients with prostates >100 grams demonstrated that both HoLEP and OP resulted in

[4] PdetQmax: Mean detrusor pressure at maximum flow rate.

significant improvements in AUA SS, Q_{max} and V_{res} volume over baseline although changes were similar between groups.

Similarly, Naspro et al (2006) highlighted that from 3 to 24 months, both urodynamic and uroflowmetry data significantly improved over baseline for both HoLEP and OP patients starting from 3 to 24 months, as did $PdetQ_{max}$ and Schafer grade although there were no significant differences between treatment groups.

In another cohort of patients with prostates >100 grams, the retrospective review by Moody and Lingeman (2001) demonstrated that postoperative AUA SS significantly improved for both HoLEP and OP ($P<0.004$ each) although both treatments had comparable outcomes.

The effect of prostate size on HoLEP and reproducibility of the procedure

Humphreys et al (2008) retrospectively compared HoLEP outcomes in three groups of patients who were categorized by prostate size (<75 grams, 75 to 125 grams and >125 grams). Enucleation time increased between group1 and group 2, but not between group 2 and group 3. Efficiency in gram tissue per minute increased significantly as prostate size increased. All 3 groups achieved comparable improvements in AUA SS, Q_{max} and PSA, indicating that prostate size had no influence on functional outcomes after HoLEP.

When patient outcomes between two institutions that perform HoLEP were compared in a retrospective review, Kim et al (2005) reported that the mean weight of tissue retrieved was comparable (Indiana 27 gram; New Zealand 23 gram). In Indiana, mean enucleation time was significantly longer (48 mins vs. 29 mins), although the mean rates of enucleation were comparable (0.58 vs. 0.71 gram/min). Efficiency increased as prostate gland size increased in both institutions.

4. Diode laser

Safety

All three studies (Seitz et al 2007; Erol et al 2009; Chen et al 2010) reported no serious intraoperative complications or postoperative haematuria. Two patients in Seitz et al (2007), and two in Erol et al (2009) required re-catheterisation for urinary retention and in the former, the two patients were not satisfied with their outcomes and underwent TURP within 2 months. Chen et al (2010) reported 10 patients with transient dysuria and two of these men experienced acute urinary retention, resolved by removal of sloughed tissue via TURP. In addition, two more patients underwent TURP due to insufficient vaporisation or regrowth of prostatic tissue, making the total need for reoperation rate 7%. The most common complications encountered in Erol et al (2009) were mild-moderate irritative symptoms (n=11, 23%) which resolved within the first two weeks of follow-up.

Erol et al (2009) reported retrograde ejaculation in 13 of 41 patients (32%) and 2 patients had temporary combined urge and stress incontinence which resolved within 2 weeks. A late bleeding complication (requiring hospitalisation) attributed to bicycle riding was encountered in one patient at 4 weeks follow-up. Transient urge and stress incontinence was also reported by Chen et al (2010) in 8 (15%) and 1 (2%) of patients but all responded to medication. Additional complications in this study included urethral stricture (n=2, 4%), epididymitis (n=4, 7%) and mild scrotal oedema (n=2, 4%).

Effectiveness

Erol et al (2009) reported mean operative time of 53 (standard deviation [SD] 13) minutes. Lengths of hospital stay were 4.7 (SD 2.3) days in Seitz et al (2007) and 2.8 (SD 1.8) days in Chen et al (2010). Table 6 below summarises the changes seen in functional effectiveness outcomes following diode laser prostatectomy.

Table 6: Effectiveness outcomes following diode laser therapy.

	Effectiveness outcome (mean [SD])				
	Baseline	1 month	3 months	6 months	12 months
Seitz et al (2007)					
PSA (ng/ml)	3.8 (2.31)	-	-	2.64 (1.51) P=0.236	-
IPSS	16.3 (2.24)	12.8 (2.7) P<0.05	-	5.3 (1.4) P<0.001	5.0 (1.6) P<0.001
QoL	3.3 (0.56)	2.3 (0.6) P<0.01	-	1.0 (1.1) P<0.001	0.875 (0.9) P<0.001
Q_{max} (ml/s)	8.9 (2.9)	18.2 (5.0) P<0.01	-	23.2 (4.8) P<0.001	22.4 (4.3) P<0.001
V_{res} (ml)	243 (241.6)	81 (61.8) P<0.05	-	22.5 (9.7) P<0.001	26.9 (15) P<0.001
Erol et al (2009)					
Prostate volume (cc)	51.04 (24.14)	-	32.06 (11.37) P=0.0001	31.06 (10.12) P=0.0001	-
PSA (ng/ml)	2.54 (1.43)	-	1.85 (1.13) P=0.0001	1.77 (1.03) P=0.0001	-
IPSS	21.93 (4.88)	-	10.31 (3.79) P=0.0001	9.87 (3.19) P=0.0001	-
QoL	4.19 (0.85)	-	2.82 (1.16) P=0.0001	2.15 (1.10) P=0.0001	-
IIEF	17.42 (8.86)	-	17.74 (8.64) P=0.554	17.21 (8.72) P=0.550	-
Q_{max} (ml/s)	8.87 (2.18)	-	17.51 (4.09) P=0.0001	18.27 (3.92) P=0.0001	-
V_{res} (ml)	115.28 (103.64)	-	45.34 (27.87) P=0.0001	48.28 (29.27) P=0.0001	-
Chan et al (2010)					
Prostate volume (ml)	66.3 (30.3)	-	-	31.7 (16.3) P<0.001	-
PSA (ng/ml)	5.1 (3.5)	-	-	2.1 (2.0) P<0.001	-
IPSS	20.1 (5.2)	7.3 (5.7) P<0.001	-	4.9 (5.2) P<0.001	-
QoL	5.1 (0.8)	2.7 (1.3) P<0.001	-	2.2 (1.3) P<0.001	-
Q_{max} (ml/s)	5.5 (5.4)	15.5 (4.7) P<0.001	-	19.2 (7.9) P<0.001	-
V_{res} (ml)	173.3 (157.5)	42.9 (49.4) P<0.001	-	21.2 (23.9) P<0.001	-

In general, prostate volume and PSA levels were reduced from baseline. IPSS, QoL, Q_{max} and V_{res} were significantly improved in all studies from baseline to immediately postoperative follow-up. These improvements were maintained to the longest point of follow-up (12 months), reported in the study by Seitz et al (2007). Erectile function was unchanged in all patients reported to be sexually active at baseline in Erol et al (2009). Note that no comparative studies were available for diode laser therapy.

5. ThuLEP

Safety

Twelve of 88 patients (14%) in the single ThuLEP case series experienced complications including intra- or post-operative bleeding in 5 (2 required transfusion), urinary tract infection in 6, and reoperation in 3 (Bach et al 2010). Due to 2 deaths and 15 patients lost to follow-up, only 62 patients (70%) were available for 12-month evaluation.

Effectiveness

Total operative time (including cystoscopy, enucleation and morcellation) was 72 minutes (SD 27 minutes; range 35-144 minutes) and laser time was 32 minutes (SD 10 minutes; range 16-59 minutes). The mean duration of catheterisation was 2 days. Patient discharge generally occurred after catheter removal, and three patients were discharged with suprapubic tubes in place. Pathological assessment revealed four patients with incidental adenocarcinoma of the prostate (Bach et al 2009, Bach et al 2010).

Statistically significant improvements in functional outcomes including Q_{max} and V_{res} were apparent from baseline to the time of discharge and to intermediate-term follow-up. IPSS and QoL also improved significantly from baseline to intermediate-term follow-up. Table 7 below summarises the improvements seen in functional outcomes following ThuLEP.

Table 7: Summary of effectiveness outcomes reported following ThuLEP.

Outcome	Baseline n=88	Discharge n=88	P value[a]	Follow-up n=62	P value[b]
Q_{max} (ml/s)	3.5 (SD 4.7)	19.8 (SD 11.6)	<0.001	23.26 (SD 10.33)	<0.001
V_{res} (ml)	121.4 (SD 339.9)	22.4 (SD 32.7)	0.03	33.49 (SD 47.01)	<0.05
IPSS (points)	18.4 (SD 7)	NR	NA	6.8 (SD 3.96)	<0.005
QoL (points)	4.6 (SD 1.1)	NR	NA	1.45 (SD 1.12)	<0.001

[a] baseline to discharge.
[b] baseline to follow-up.

During intermediate follow-up patients were asked about their symptoms and 27% (17/62) complained about mild storage symptoms, such as postoperative urgency or frequency. Most patients experienced complete remission from LUTS within 1 month of surgery; however, four patients required anticholinergic treatment due to persistent symptoms at 3 months follow-up.

Clinical studies refining the use of thulium lasers

In addition to these findings, the case series studies by Bach et al (2009 and 2010) provided a brief analysis of ThuLEP in large versus small prostates. These data, discussed briefly below, assist in the preliminary refinement of thulium lasers in regards to the patient population who would benefit most from the procedure.

Results were analysed based on prostate volume with large prostates ≥60cc and small prostates <60cc. As expected operative time and laser time were significantly reduced in patients with smaller prostates (P=0.002 and P=0.014); however, there were no significant differences seen between the groups in regards to IPSS, QoL, Q_{max} and V_{res}. Similarly, complications were not significantly different between groups.

Other Issues

Patient duplication among 80W KTP PVP studies likely occurred in Ruszat et al 2006, Ruszat et al 2007 and Ruszat et al 2008. Only Ruszat et al (2008) was included in the main safety and effectiveness analysis with the others providing preliminary data on patients using OAT or with urinary retention (Ruszat et al 2006; Ruszat et al 2007).

A new generation of KTP laser was announced in May 2010. This device is proposed to supersede the current KTP model (GreenLight HPS®) by offering enhanced treatment efficiency with extended fiber longevity and improved coagulation capabilities (The Medical News 2010). The new (180W) GreenLight Xcelerated Performance System (XPS) ^{TM} is purported to have a similar safety profile to GreenLight HPS® and to achieve the same results in half the time. Peer-reviewed literature regarding this new device has not yet become available.

Cost Analysis

Most patients without bothersome BPH symptoms undergo watchful waiting in including lifestyle changes, regular examinations and testing and possibly pharmacotherapy (Black et al 2006). When surgery is indicated, cost effectiveness is impacted by the cost of operative equipment, operative length, and length of hospitalisation. Most of the lasers included in this report described early catheter removal (compared with the gold standard surgical procedures), which is usually associated with earlier mobilisation, shorter hospital stay, and reduced hospitalisation (Bachmann et al 2005).

Conversely, one study published in 2005 and conducted in a Turkish hospital found laser prostatectomy (type not specified) to be the most costly way of treating BPH from a hospital perspective compared with TURP and OP, in regards to cost per improvement in prostate symptom score and quality of life index (Agirbas et al 2005).

Specific cost analysis studies were identified for 80W KTP PVP and HoLEP:

80W KTP PVP

Alivizatos and Skolarikos (2008) reported that a study in Switzerland compared 105 patients treated with high-powered KTP laser or TURP and found similar hospital costs for the two procedures.[5] Operating room and postoperative nursing costs were higher for TURP whereas the costs of disposables (including laser fibers) were higher for PVP.

An Australian RCT published in 2006 also compared patients treated with PVP and TURP (from January 2004) and found the mean cost per operative day-case to be significantly less for PVP (AU$3,368) compared with TURP (AU$4,292) ($P<0.0005$) due to reduced hospital stay and catheterisation duration (Bouchier-Hayes et al 2006). Similarly, Goh et al (2010) reported the hospital costs (direct and indirect, excluding physician fees) of PVP to be significantly lower than those of TURP, primarily due to decreased hospitalisation time and complication rate.

Another study performed an economic analysis of five alternative interventions to treat symptomatic BPH including PVP, interstitial laser coagulation of the prostate (ILC), TURP, transurethral microwave thermotherapy of the prostate (TUMT) and transurethral radiofrequency needle ablation of the prostate (TUNA) (Stovsky et al 2006). Costs were estimated from a payer perspective and included

[5] The studies that were referenced as reporting these outcomes did not include the figures reported by Alivizatos and Skolarikos (2008); therefore perhaps Alivizatos and Skolarikos (2008) obtained this information from the authors of the cited studies directly.

costs of initial treatment, follow-up care, AEs and re-treatment. The expected cost per patient at 6, 12 and 24 months was lowest for PVP, followed by ILC and then TURP. Table 8 below summarises the expected cost per patient for all five procedures.

Table 8: Expected cost per patient.

Procedure	Expected cost*		
	6 months	12 months	24 months
PVP	$3,020	$3,214	$3,589
ILC	$3,573	$3,965	$4,754
TURP	$4,030	$4,331	$4,927
TUMT[a]	$4,388	$4,810	$5,549
TUNA	$4,457	$5,089	$6,179

*2005 US$

[a] average cost across three devices used to deliver TUMT.

The cost savings associated with PVP were attributed to lower rates of AEs and need for reoperation, with 70-94% of PVP costs attributed to the initial procedural intervention, which is consistent with the findings of other studies.

HoLEP

One study comparing the cost effectiveness of HoLEP with OP in patients undergoing surgery for the treatment of BPH in large prostates found HoLEP to be associated with a significant hospital net cost saving (about 10%) compared with OP (Salonia et al 2006). This study reported the total perioperative cost of HoLEP per patient at US$2,919 compared with US$3,556 per patient for OP. As is the case for PVP, the largest cost for HoLEP was equipment-related (approximately double that of OP); however, this was offset by considerably reduced costs associated with hospital stay (HoLEP US$936 vs. OP US$1,895).

Similarly, Tan and Gilling (2003) reported significant costs associated with the initial purchase of a 100W holmium laser unit (US$140,000); however, the authors of this study believed the cost benefits of HoLEP would be seen over the medium to long-term due to reductions in length of hospital stay, peri-operative morbidity and reoperation rates.

Ethical Considerations

Informed Consent

Patients undergoing treatment for symptomatic BPH should be aware of the risks associated with laser prostatectomy procedures as well as the advantages of these techniques. In particular, the latest developments in laser prostatectomy such as ThuLEP and the Diode laser should be approached with caution as the available evidence on the safety, effectiveness and durability of these procedures remains limited.

Access Issues

Laser prostatectomy required the use of technically complex equipment and specific expertise. The costs associated with the use of the laser generators and fibres are likely to be prohibitive as well. These procedures are therefore likely to be practiced at specialist hospitals with the necessary infrastructure. As a result, laser prostatectomy will likely be limited to major metropolitan areas, at least in the near future.

Training and Accreditation

Training

There appears to be a learning curve associated with laser prostatectomy. Specific literature in regards to learning curve and training for PVP and HoLEP were identified:

80W KTP PVP

One study examined the effect of physician experience on the risk of AEs and complications (Bouchier-Hayes 2007). In this study, physicians were experienced in performing TURP and had each completed less than five laser prostatectomies. Despite this, results demonstrated no difference in complication rates as the number of procedures undertaken increased. This lead Stafinski et al (2008) to conclude in their SR that PVP appears to involve a shorter learning curve relative to other laser approaches to treat BPH; therefore, surgeons may be able to adopt this technology more readily than others.

HoLEP

One study addressed the training requirements of HoLEP and found that following 20-30 procedures under supervision, a training surgeon could expect to achieve outcomes similar to that of a more experienced surgeon (El Hakim and

Elhilali 2002). Another study reported that, in their experience, prostates between 40 and 50g are anecdotally the best size for trainees to begin mastery of the HoLEP procedure; the same study reported that trainees who were new to both HoLEP and TURP tended to find HoLEP easier to learn due decreased bleeding, improved visibility and the intuitive nature of dissecting along a surgical plane (Tan and Gilling 2003).

Clinical Guidelines

Andrology Australia together with Monash University and the Australian Department of Health and Aging produced a Clinical Summary Guideline in 2007 for prostate disease, BPH and prostatitis (Andrology Australia 2010). This guideline states that surgical therapy for BPH is indicted in patients with severe or high impact symptoms.

The type of surgery indicated depends on the preoperative characteristics of BPH, as seen in Table 9. These guidelines also state that laser ablation or resection of BPH is available in specific surgical centres and that laser surgery is regarded as equivalent to TURP in regards to efficacy.

Table 9: Surgical therapy for BPH (Andrology Australia 2010).

Prostate	Type of surgery indicated
30-80ml	TURP
<30ml and without middle lobe	Transurethral incision of the prostate (TUIP)
>80ml	OP or TURP

It is important to note that according to these Australian guidelines prostates that are eligible for OP (>80ml) are not usually eligible for laser prostatectomy, so that, although this report includes studies comparing laser with OP, it is an inappropriate comparator in Australian context.

The National Institute of Clinical Excellence (NICE) in the United Kingdom (UK) released specific Interventional Procedure Guidance for holmium laser prostatectomy, including HoLEP, (NICE 2003) and KTP laser vaporisation of the prostate for BPH (NICE 2005). These guidance documents state that the current evidence on the safety and efficacy of both procedures (short-term efficacy in the case of KTP PVP) appears to be adequate to support their use, provided normal arrangements are in place for consent, audit and clinical governance. They also state that clinicians undertaking holmium laser prostatectomy or KTP PVP require specialist training. The British Association of Urological Surgeons has agreed to produce training standards (unable to locate).

Limitations of the Assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon scanning forms an integral component of health technology assessment; however, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level, leaving the technology under investigation obsolete and replaced.

A horizon scanning report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost-effectiveness of a technology.

In the context of a rapidly evolving technology, a horizon scanning report is a 'state of play' assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of laser prostatectomy for the treatment of BPH, its present and potential uses in the Australian public health system, and future implications.

Search Strategy used for the Report

The sources utilised in this assessment are listed in Table 10. The medical literature was searched to identify relevant studies up to 10 March 2010 in English only, using the search terms outlined in Table 11. In addition to this, major international health technology assessment databases and clinical trial registers were searched.

Table 10: Literature sources utilised in assessment.

Source	Location
Electronic databases	
AustHealth	University of Adelaide library
Australian Medical Index	University of Adelaide library
CINAHL	University of Adelaide library
Cochrane Library – including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Databese, the NHS Economic Evaluation Database	University of Adelaide library
Current Contents	University of Adelaide library
Embase	Personal subscription
Pre-Medline and Medline	University of Adelaide library
PyscINFO	Personal subscription
RACS electronic library	Personal subscription
Internet	
Blue Cross and Blue Shield Association's Technology Evaluation Center	http://www.bcbs.com/tec/
Canadian Agency for Drugs and Technologies in Health	http://www.cadth.ca
Current Controlled Trials metaRegister	http://www.controlled-trials.com/
EuroScan	http://www.euroscan.bham.ac.uk/
Health Technology Assessment International	http://www.htai.org/
International Network for agencies for Health Technology Assessment	http://www.inahta.org

Medicines and Healthcare products Regulatory Agency (UK)	http://www.mhra.gov.uk/
US Food and Drug Administration, Center for Devices and Radiological Health	http://www.fda.gov/cdrh/index.html
US Food and Drug Administration, Manufacturer and User Facility Device Experience Database	http://www.fda.gov/cdrh/maude.html
UK National Research Register	http://www.nrr.nhs.uk/
Websites of specialty organisations	http://www.andrologyaustralia.org/

Table 11: Search terms utilised.

Search terms
Text words Prostatic hyperplasia, benign prostatic hyperplasia, prostatectom*, prostatic hyperplasia surger*, laser surger*, photoselective vaporisation, holmium yttrium aluminum garnet laser*, ho yag laser*, potassium titanyl phosphate laser*, lithium triborate laser*, semiconductor diode laser*, thulium laser* **Limits** English, human

* is a truncation character that retrieves all possible suffix variations of the root word; for example, surg* retrieves surgery, surgical, surgeon, etc.

Availability and Level of Evidence

A total of 32 studies were retrieved for inclusion in this horizon scanning report. Given the various laser types reported, specific study numbers in regards to their level of evidence is presented in tabular form below. The profiles of the included studies are summarised in Appendix B.

Table 12: Included studies.

Level of evidence	**Laser type (number of studies)**				
	KTP PVP	**LBO PVP**	**HoLEP**	**Diode**	**ThuLEP**
Level I	1	0	0	0	0
Level II	4	1	8	0	0
Level III	9	0	3	0	0
Level IV	0	1	0	3	2
TOTAL	14	2	11	3	2

List of ongoing clinical trials on laser prostatectomy:

Source	ID	Title	Laser/ comparator	Study design	Estimated completion date
Australian New Zealand Clinical Trials Registry	ACTRN1261-0000518066	A randomized trial comparing Transurethral resection of the prostate (TURP) with 120W photoselective vapourization of the prostate (PVP) in men with lower urinary tract symptoms.	120W KTP PVP/TURP	RCT	NR*
Clinicaltrials.gov	NCT00908427	Impact of 80 W KTP Laser Vaporization Prostatectomy on Severity of Obstruction in benign prostatic hyperplasia.	80W KTP PVP/TURP	Non-randomised comparative	Completed September 2007
	NCT00465101	A Long-Term Study Examining the Treatment of Benign Prostatic Hyperplasia With Photoselective Vaporization (PVP)	120W KTP/TURP	Non-randomised comparative	April 2015
	NCT00527371	Photoselective Vaporization of the Prostate Compared to Transurethral Resection of the Prostate for the Treatment of Benign Hyperplasia of the Prostate (PVP)	120W KTP PVP/TURP	Non-randomised comparative	December 2012
	NCT01043588	TRP Versus Photo Selective Vaporization for Obstructive benign prostatic hyperplasia Management (REVAPRO)	80W KTP PVP/TURP	RCT	December 2010
	NCT00877669	Efficacy Study of HoLEP and TURP on LUTS Secondary to BPH	HoLEP/TURP	RCT	October 2010
	NCT00364585	A Prospective Evaluation of the GreenLight Model 120 Laser	120W KTP PVP	Case series	Completed April 2007
UK Trials	ISRCTN14776501	Transurethral High Power (80W) Potassium-Titanyl-Phosphase (KTP) Laser Vapourisation of the Prostate Compared with Holmium Laser Ablation of the Prostate: A Single Centre Randomised Controlled Trial in Patients with Obst. Benign prostatic hyperplasia.	80W KTP PVP/HoLAP	RCT	Completed 1/5/2007

*anticipated date of first participant enrolment 1 September 2010.

Conclusions

High-quality literature was retrieved for inclusion, including an SR and a number of RCTs. Lasers that are used more commonly for the treatment of BPH (such as KTP lasers and holmium lasers) comprise the largest proportion of the evidence.

PVP versus TURP, OP or HoLAP

In terms of safety, the SR comparing KTP PVP with TURP reported similar AE and complication rates. Two RCTs compared PVP with TURP, and both found PVP to offer an advantage over TURP in terms of intraoperative and preoperative safety. All three non-randomised comparative studies comparing PVP and TURP found complication rates to be similar. RCTs comparing PVP with OP and HoLAP, respectively, reported comparable safety outcomes.

In terms of efficacy, functional outcomes including Q_{max}, V_{res}, IPSS and QoL were similar for PVP and TURP in five of the six studies that compared the two procedures (1 SR, 1 RCT, and 3 non-randomised comparative studies). The remaining study, an RCT, found early functional outcomes to be superior for TURP compared with PVP. The RCT comparing PVP with OP also reported similar functional outcome improvements between the two procedures.

In the studies that compared operative time, PVP was reported as being significantly longer compared with TURP or OP. The RCT comparing PVP with HoLAP found HoLAP operative time to be significantly longer than that of PVP. However, all studies reported a reduction in durations of catheterisation and hospitalisation following PVP compared with TURP or OP. Catheterisation and hospitalisation duration was comparable following PVP and HoLAP.

Prostate size does not appear to affect the safety or efficacy of PVP; however, larger prostate volume may be associated with longer procedural time and a higher risk of residual adenoma and need for reoperation. Because PVP is associated with fewer bleeding complications, it may also be a viable alternative to TURP, particularly in patients on OAT where TURP is contraindicated.

The newer 120W PVP procedure (LBO laser) compared favourably to TURP. One RCT revealed that TURP patients required more blood transfusions and experienced more capsule perforations, as well as clot retentions. However, 120W PVP patients had significantly higher reoperation rates. The included studies reported that patients who underwent 120W PVP achieved significant functional improvements that were comparable to TURP although decreases in PSA and prostate volume were greater for TURP patients. There is some indication that the 120W PVP procedure takes significantly longer than TURP, however the absolute difference was only 9 minutes and may have little affect on real-world experience.

HoLEP versus TURP or OP

When HoLEP was compared to TURP, most RCTs indicated that HoLEP has a comparable safety profile. However, there were some specific instances where HoLEP patients fared worse, specifically for bladder mucosal injuries and dysuria. The incidence of erectile dysfunction appears to be similar to TURP; however, HoLEP patients tended to be more susceptible to retrograde ejaculation after surgery. Relative to OP, HoLEP patients had significantly less blood loss but had comparably higher incidence of dysuria. One RCT demonstrated that the incidence of reoperations were similar while 2 RCTs noted that bladder neck contractures and urethral strictures were comparable between HoLEP and OP.

Five RCTs demonstrated that over the long-term (>2 years) HoLEP achieves comparable functional outcomes to TURP. However, there is some evidence from two RCTs that HoLEP patients achieved better results, at least in the early stages after treatment.

Compared to OP, all three included studies demonstrated that HoLEP patients had comparable outcomes to OP patients. One study highlighted that prostate size has no influence on functional outcomes while another study reported that the efficiency of HoLEP actually increased as the gland size increased, suggesting that HoLEP is an effective treatment for larger prostates.

In terms of operative outcomes, all studies comparing HoLEP to TURP found that HoLEP required a significantly longer operative time but conferred advantages with regards to catheterisation time and hospital stay. One RCT indicated that operative time for HoLEP is significantly longer relative to OP, but this was refuted in another RCT that found operative times to be comparable.

ThuLEP

The evidence available on ThuLEP was limited to a case series studies (n=88) which reported that 14% of patients experienced mostly minor, transient complications after ThuLEP (urinary tract infection, intra/post-operative bleeding). Reoperation rates were 2% to 3%. Follow-up data on the same cohort suggest that ThuLEP is effective. There is some preliminary evidence that ThuLEP is equally effective in small and large prostates. Nevertheless, additional comparative studies are necessary to examine its effectiveness relative to TURP and determine its long-term durability.

Diode laser vaporization

Diode laser vaporisation appears to be safe, with no serious complications in the three case series studies selected for inclusion. However, the incidence of retrograde ejaculation appears to be quite high (31%), at least in one study. The overall evidence suggests that diode laser vaporisation leads to significant

reduction in prostate volume and PSA levels. Functional outcomes appear promising but no comparative trials were available .

Overall, the more common laser prostatectomy procedures (KTP PVP and HoLEP) appear to be at least as safe and effective as TURP for the treatment of BPH. There is inadequate literature available to say the same for the less commonly used laser approaches (diode laser vaporisation and ThuLEP).

Appendix A: Levels of Evidence

Designation of levels of evidence according to type of research question

Level	Intervention [§]	Diagnosis [**]	Prognosis	Aetiology [†††]	Screening
I [*]	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, [§§] among consecutive patients with a defined clinical presentation [††]	A prospective cohort study [***]	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, [§§] among non-consecutive patients with a defined clinical presentation[††]	All or none [§§§]	All or none [§§§]	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial [†] Cohort study Case-control study Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: Non-randomised, experimental trial Cohort study Case-control study
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study [‡] Interrupted time series without a parallel control group	Diagnostic case-control study [††]	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: Historical control study Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard) [‡‡]	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Tablenotes

* A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence.

§ Definitions of these study designs are provided on pages 7-8 *How to use the evidence: assessment and application of scientific evidence* (NHMRC 2000b*)*.

† This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (i.e. utilise A vs. B and B vs. C, to determine A vs. C).

‡ Comparing single arm studies i.e. case series from two studies.

** The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes. See *MSAC (2004) Guidelines for the assessment of diagnostic technologies*. Available at: www.msac.gov.au .

§§ The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study. See Whiting P, Rutjes AWS, Reitsma JB, Bossuyt PMM, Kleijnen J. The development of QADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Medical Research Methodology*, 2003, 3: 25.

†† Well-designed population based case-control studies (e.g. population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. These types of studies should be considered as Level II evidence. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias because the spectrum of study participants will not be representative of patients seen in practice.

‡‡ Studies of diagnostic yield provide the yield of diseased patients, as determined by an index test, without confirmation of accuracy by a reference standard. These may be the only alternative when there is no reliable reference standard.

*** At study inception the cohort is either non-diseased or all at the same stage of the disease.

§§§ All or none of the people with the risk factor(s) experience the outcome. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

††† If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'Intervention' hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (i.e. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'Aetiology' hierarchy of evidence should be utilised.

Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question e.g. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence etc.

Hierarchies adapted and modified from: NHMRC 1999; Lijmer et al 1999; Phillips et al 2001; Bandolier editorial 1999)

Appendix B: Profiles of studies

Study	Location	Study design	Study population	Outcomes assessed
Stafinski et al (2008)	Alberta, Canada	Systematic review Pseudo-Level I intervention evidence*	1 RCT, 1 cohort study, 12 case series PVP: 1376 TURP: 75 *Inclusion criteria* Patients diagnosed with moderate-severe LUTS attributable to BPH who require surgical intervention (including 80W KTP PVP or TURP). *Exclusion criteria* Diagnosis of prostate cancer, PVP with 40W or 60W KTP lasers.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, operative time, length of hospitalisation, length of catheterisation, blood transfusion, complications.
Horasanli et al (2008)	Istanbul, Turkey	RCT Level II intervention evidence	TURP: 37 PVP: 39 *Inclusion criteria* Prostate volume 70-100mL. Maximum urinary flow rate <15mL/sec or postvoid residual volume >150mL in conjunction with IPSS >7. *Exclusion criteria* Neurogenic bladder disorder, urethral strictures, postvoid residual volume >400mL, history of adenocarcinoma of the prostate or any previous prostatic, bladder neck, or urethral surgery.	Q_{max}, V_{res}, IPSS, IIEF, reduction in prostate volume, PSA level, operative time, length of hospitalisation, length of catheterisation, complications.
Skolarikos et al (2008)	Athens, Greece	RCT Level II intervention evidence	PVP: 65 OP: 60 *Inclusion criteria* Age >50 years, lower urinary tract symptoms due to benign prostate enlargement, prostate volume on TRUS >80cc, IPSS >12, medical therapy failure, no a-blockers during the last month, no 5a reductase over the last three months, postvoid residue <150mL, peak urinary flow rate <12mL/sec, able to complete QOL, IPSS and IIEf-5 questionnaires, operated on within 4 weeks of randomisation, able to give fully informed consent. *Exclusion criteria* Neurogenic bladder, history of adenocarcinoma of the prostate, urethral stricture, any previous prostatic, bladder neck or urethral surgery, urethral catheter at baseline, history of bladder cancer, indwelling urethral catheter.	Q_{max}, V_{res}, IPSS, IIEF, QoL, reduction in prostate volume, PSA, operative time, length of hospitalisation, length of catheterisation, complications.

Bouchier-Hayes et al (2006)	Melbourne, Australia	RCT Level II intervention evidence	TURP: 38 PVP: 38 *Inclusion criteria* Age >50 years, referred by family physician for LUTS, flow rate ≤15mL/sec, IPSS ≥12, gland 15-85cm^3 on TRUS, obstructed on A-G nomogram, able to complete QoL, Bother Score and BSFQ questionnaires, able to give fully informed consent. *Exclusion criteria* Neurogenic bladder, known or suspected prostate cancer, chronic retention, taking a-blocker or herbal medication believed active in prostate, permanently on anticoagulant, taking finasteride or dutasteride.	Q_{max}, V_{res}, IPSS, QoL, bother score, operative time, length of hospitalisation, length of catheterisation, complications, cost.
Elzayat et al (2009)	Cairo, Egypt	RCT Level II intervention evidence	HoLAP: 57 PVP: 52 *Inclusion criteria* Ability to give informed consent, having LUTS secondary to BPH with an IPSS ≥9, total prostate volume ≤60cc, TRUS biopsy performed when necessary, Qmax <15mL/sec. *Exclusion criteria* Previously diagnosed with prostate cancer, urethral strictures or neurogenic bladder, IPSS <9, Qmax ≥15mL/sec, prostate volume >60cc, previous urethral or prostate surgery	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, PSA, operative time, laser time, length of hospitalisation, length of catheterisation, complications.
Nomura et al (2009a)	Fukuoka, Japan	Non-randomised comparative trial Level III-1 intervention evidence	PVP: 143 TURP: 92 *Inclusion criteria* Past history of acute urinary retention and severe subjective symptom, or reluctance to continue drug therapies *Exclusion criteria* Neurogenic lower urinary tract dysfunction, age <50 years, total IPSS <8 and/or QOL score <3, PV <20mL, urethral indwelling catheter	Q_{max}, V_{res}, IPSS, QoL, bladder capacity, detrusor overactivity, operative time, length of hospitalisation, length of catheterisation, blood transfusion, complications.
Tugcu et al (2008)	Istanbul, Turkey	Non-randomised comparative trial Level III-1 intervention evidence	PVP: 112 TURP: 98 *Inclusion criteria* Moderate to severe LUTS (IPSS>8), failed previous medical therapy, Q_{max} <10ml/s, prostate volume <70ml on transrectal ultrasonography. *Exclusion criteria* Patients with preoperative PSA >4ng/ml, V_{res} >400ml, use of an indwelling catheter, urethral stricture, bladder stone, prostatic malignancy, or neurogenic bladder disease.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, PSA, operative time, length of hospitalisation, length of catheterisation, complications.
Ruszat et al (2008)	Basel, Switzerland	Non-randomised comparative trial Level III-1 intervention evidence	PVP: 64 TURP: 37 *Inclusion criteria* Q_{max} ≤15ml/s or transvesically measured V_{res} >100ml in conjunction with the IPSS >7. *Exclusion criteria* Known neurogenic bladder disorder (e.g. detrusor instability or hyperreflexia), urethral stricture or a V_{res} >400ml. patients with a history of acute or repeated urinary retention or with the necessity of an indwelling catheter were excluded.	Q_{max}, V_{res}, IPSS, QoL, bother score, reduction in prostate volume, PSA level, operative time, intraoperative irrigation volume, length of hospitalisation, length of catheterisation, complications.

Nomura et al (2009b)	Fukuoka, Japan	Non-randomised comparative trial Level III-1 intervention evidence	PVP, prostate < 40cm^3: 25 PVP, prostate 40-80cm^3: 53 PVP, prostate ≥80cm^3: 24 *Inclusion criteria* Completion of preoperative evaluation and postoperative analysis at 12 months *Exclusion criteria* Patients aged under 50 years, total IPSS <8 and/or QoL index <3 at baseline and prostate size <20ml before operation.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, PSA level, length of hospitalisation, length of catheterisation, complications.
Pfitzenmaier et al (2008)	Heidelberg, Germany	Non-randomised comparative trial Level III-1 intervention evidence	PVP, prostate <80ml: 134 PVP, ≥80ml: 39 *Inclusion criteria* Patients with prostates of all sizes, with special attention to those ≥80ml, Q_{max} <15ml/s or V_{res} >50ml or IPSS ≥8. *Exclusion criteria* Patients with catheter in situ for acute urinary retention.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, length of hospitalisation, length of catheterisation, complications.
Cho et al (2009)	Seoul, Korea	Non-randomised comparative trial Level III-1 intervention evidence	PVP with detrusor overactivity: 39 PVP with normal detrusor activity: 110 *Inclusion criteria* Patient age older than 50 years and presence of moderate or severe LUTS (IPSS >8) or Qmax value < 10 mL/s. *Exclusion criteria* 5-alpha-reductase inhibitor use, presence of an indwelling urinary catheter, previous prostate surgery, urethral stricture, prostate malignancy, and neurogenic bladder disease.	V_{res}, IPSS, QoL, detrusor overactivity, reduction in prostate volume, PSA level, length of hospitalisation, length of catheterisation, complications.
Ruszat et al (2007)	Basel, Switzerland; Munich, Germany	Non-randomised comparative trial Level III-1 intervention evidence	PVP with anticoagulation drugs: 116 PVP without anticoagulation drugs: 92 *Inclusion criteria* Q_{max} ≤15ml/s or transvesically measured V_{res} >100ml in conjunction with the IPSS >7. *Exclusion criteria* Known neurogenic bladder disorder (e.g. detrusor instability or hyperreflexia), urethral stricture or a V_{res} >400ml. patients with a history of acute or repeated urinary retention or with the necessity of an indwelling catheter were excluded.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, PSA level, operative time, length of hospitalisation, length of catheterisation, complications.
Ruszat et al (2006)	Basel, Switzerland; Munich, Germany	Non-randomised comparative trial Level III-1 intervention evidence	PVP with urinary retention: 70 PVP without urinary retention: 113 *Inclusion criteria* Refractory urinary retention, indwelling catheter. For those patients without urinary retention inclusion criteria included V_{res} >100ml and/or Q_{max} ≤15ml/s in combination with an IPSS >7. *Exclusion criteria* Patients with diagnosis of prostate cancer.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, PSA level, operative time, length of hospitalisation, length of catheterisation, complications.
Kavoussi et al (2008)	Texas, USA	Non-randomised comparative trial Level III-1 intervention evidence	PVP without catheter: 86 PVP with intermittent catheter: 11 PVP with indwelling catheter: 8 *Inclusion criteria* All patients who were candidates for surgical intervention for BPH. *Exclusion criteria* Patients requiring tissue for possible cancer diagnosis.	Sexual function measured by Sexual Health Inventory for Men (SHIM) questionnaire.

Al-Ansari et al (2010)	Mansoura, Egypt	RCT Level II intervention evidence	120W LBO PVP: 60 TURP: 60 *Inclusion criteria* Patients with moderate to severe LUTS, IPSS >16, failure of precious medical treatment with a washout period of at least 2 weeks, Q_{max} <15ml/s, V_{res} <100ml, prostate volume <100ml. *Exclusion criteria* Patients on permanent anticoagulants, those with urethral strictures, bladder stone, neurogenic bladder, diagnosed/suspected prostate cancer.	Q_{max}, V_{res}, IPSS, reduction in prostate volume, PSA, operative time, length of hospitalisation, length of catheterisation, complications.
Spaliviero et al (2008)	Oklahoma, USA	Case series study Level IV intervention evidence	120W LBO PVP: 70 *Inclusion criteria* Persistent moderate to severe LUTS despite medical therapy, obstruction on pressure-flow studies, gross haematuria of prostatic origin, bladder stones, urinary tract infections. *Exclusion criteria* Prostate adenocarcinoma, urethral stricture, bladder tumours, urinary retention, diabetes mellitus, bladder dysfunction due to neurologic disease.	Q_{max}, V_{res}, IPSS, QoL, ejaculation function, reduction in prostate volume, PSA, operative time, length of hospitalisation, length of catheterisation, complications.
Briganti et al (2006)	Bergamo, Italy	RCT Level II intervention evidence	HoLEP: 60 TURP: 60 *Inclusion criteria* NR *Exclusion criteria* NR	QoL, IIEF-5, IPSS, PSA, reduction in prostate volume.
Montorsi et al (2004)	Bergamo, Italy	RCT Level II intervention evidence	HoLEP: 52 TURP: 48 *Inclusion criteria* Patients younger than 75 years of age, peak urinary flow rate <15ml/s, V_{res} < 100cc, medical therapy failure, transrectal ultrasound adenoma volume less than 100 gram, urodynamic obstruction (> grade 2). *Exclusion criteria* Neurogenic bladder, diagnosis of prostate cancer, previous prostate, bladder neck or urethral surgery.	IPSS, QoL, IIEF-5, reduction in prostate volume, PSA, operative time, catheterisation time, hospitalisation time, complications.
Wilson et al (2006)	Tauranga & Christchurch, New Zealand	RCT Level II intervention evidence	HoLEP:31 TURP: 30 *Inclusion criteria* Prostate volume 40-200 gram, Qmax ≤15ml/s, symptom score ≥8, Vres <400ml, urodynamics Schaffer grade ≥2. *Exclusion criteria* Prostatic carcinoma, catheterised patients and those with history of previous urethral or prostatic surgery.	AUA symptom score, QoL, Qmax, Vres, reduction in prostate volume, continence, potency, complications.

Mavuduru et al (2009)	Chandigarh, India	RCT Level II intervention evidence	HoLEP: 15 TURP: 15 *Inclusion criteria* NR *Exclusion criteria* History of previous prostatic or urethral surgery, documented cases of prostatic carcinoma.	Operative time, amount of prostate excised, blood transfusion, incidence of TURP syndrome, complications, total volume of irrigation fluid needed, catheterisation duration, hospitalisation duration, IPSS, histopathology, uroflowmetry, Vres, stricture urethra, urine culture.
Kuntz et al (2004); Ahyai et al (2007)	Hamburg & Berlin, Germany	RCT Level II intervention evidence	HoLEP: 100 TURP: 100 *Inclusion criteria* American Urological Association symptom score ≥12, Qmax ≤ 12ml/s, Vres ≥50ml, Schaffer grade ≥2 in pressure flow studies, prostate volume < 100cc. *Exclusion criteria* Previous prostate or urethral surgery, voiding disorder not related to BPH, prostate carcinoma.	AUA symptom score, Qmax, Vres, complications, incontinence and erectile dysfunction.
Gupta et al (2006)	New Delhi, India	RCT Level II intervention evidence	HoLEP:50 TURP: 50 Transurethral vapour resection of the prostate: 5o *Inclusion criteria* NR *Exclusion criteria* Previous history of prostatic and urethral surgery, neurovesical dysfunction, carcinoma of the prostate.	Operative duration, blood loss, resected tissue weight, nursing contact time, duration of catheterisation, complications, IPSS, Qmax, Vres.
Kuntz et al (2008); Kuntz et al (2004); Kuntz et al (2002)	Berlin & Hamburg, Germany	RCT Level II intervention evidence	HoLEP: 60 OP: 60 *Inclusion criteria* AUA score ≥8, Qmax 12ml/s or less, Vres ≥50ml, Schafer grade ≥2, total prostate volume ≥100ccm. *Exclusion criteria* Previous prostate or urethral surgery and non-BPH-related voiding disorder.	AUA symptom score, Qmax, Vres, complications, reduction in prostate volume, detrusor pressure at peak flow, Schafer grade.
Naspro et al (2006)	Milan, Italy	RCT Level II intervention evidence	HoLEP: 41 OP: 39 *Inclusion criteria* Patients with BPH-related obstructed voiding symptoms with prostate volume >70g who had not responded to pharmacologic therapy. Vres <150ml, Qmax <15ml/s, Schafer grade >2. *Exclusion criteria* Neurogenic bladder, history of adenocarcinoma of the prostate, or any previous prostatic, bladder neck, or urethral surgery.	PSA, Vres, IPSS, QoL, IIEF-5, operative time, quantity of tissue removed, catheterisation time, hospitalisation time, blood transfusion, complications.

Moody et al (2001)	Indiana, USA	Non-randomised comparative trial Level III-2 intervention evidence	HoLEP: 10 OP: 10 *Inclusion criteria* Urinary retention, failed medical therapy, high V_{res}, bladder calculi, bladder diverticula, azotemia. *Exclusion criteria* NR	Symptom scores, operating time, changes in preoperative and postoperative serum haemoglobin and sodium, resected prostatic weight, pathological diagnosis, length of stay, complications.
Kim et al (2005)	Indiana, USA; Tauranga, New Zealand	Non-randomised comparative trial Level III- 1 intervention evidence	HoLEP USA: 40 HoLEP NZ: 40 *Inclusion criteria* NR *Exclusion criteria* NR	Amount of prostatic tissue removed, enucleation time, morcellation time, HoLEP efficiency rate.
Humphreys et al (2008)	Arizona, Tennessee, Indiana, USA	Non-randomised comparative trial Level III- 2 intervention evidence	HoLEP, prostate <75 gram: 164 HoLEP, prostate 75-125 gram: 226 HoLEP, prostate >125 gram: 117 *Inclusion criteria* NR *Exclusion criteria* Diagnosis of prostate cancer or no preoperative volume was available.	Resected prostatic weight, pathological diagnosis, duration of hospitalization and catheterization, enucleation and morcellation time, complications, symptom score, PSA and Q_{max}.
Chen et al (2010)	Kaohsiung, Taiwan	Case series study Level IV intervention evidence	200W diode laser: 55 *Inclusion criteria* Patients with moderate-severe urinary symptoms, as indicated by Q_{max} ≤15ml/s and IPSS ≥10. *Exclusion criteria* Patients with neurogenic bladder, prostate cancer, prostate volume ≤25ml or those who had previously undergone urethral surgery.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, PSA, laser time, length of hospitalisation, complications.
Erol et al (2009)	Duzce, Turkey	Case series study Level IV intervention evidence	80-132W diode laser: 47 *Inclusion criteria* Q_{max} ≤12ml/s, V_{res} ≥150ml, IPSS ≥12, QoL ≥ 3. *Exclusion criteria* Patient with a history of neurogenic voiding dysfunction, chronic prostatitis, prostate and/or bladder cancer.	Q_{max}, V_{res}, IPSS, QoL, IIEF-5, prostate volume, PSA level, operative time, complications.
Seitz et al (2007)	Basel, Switzerland; Munich, Germany	Case series study Level IV intervention evidence	50W diode laser: 10 *Inclusion criteria* Moderate to severe urinary symptoms, as determined by IPSS score ≥8 and Q_{max} <15ml/s with or without V_{res}, in patients who were judged to be high-risk owing to oral antiplatelets therapy and severe cardiopulmonary comorbidities. *Exclusion criteria* Urethral stricture, previous prostatic surgery, prostate cancer, and obvious manifested neurogenic bladder dysfunction.	Q_{max}, V_{res}, IPSS, QoL, reduction in prostate volume, PSA, laser time, length of hospitalisation, length of catheterisation, complications.

Bach et al (2009); Bach et al (2010)	Hamburg, Germany	Case series study Level IV intervention evidence	ThuLEP: 88 *Inclusion criteria* Refractory urinary obstruction, indwelling catheter, symptomatic LUTS, Q_{max} <15ml/s and IPSS >7. *Exclusion criteria* Patients with urodynamically diagnosed neurogenic bladder or known cancer of the prostate.	Q_{max}, V_{res}, IPSS, IIEF, QoL, reduction in prostate volume, PSA, operative time, length of catheterisation, complications.

Appendix C: HTA internet sites

AUSTRALIA

- Centre for Clinical Effectiveness, Monash University
  http://www.med.monash.edu.au/healthservices/cce/evidence/

- Health Economics Unit, Monash University
  http://chpe.buseco.monash.edu.au

AUSTRIA

- Institute of Technology Assessment / HTA unit
  http://www.oeaw.ac.at/ita/welcome.htm

CANADA

- Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/en/

- Alberta Heritage Foundation for Medical Research (AHFMR)
  http://www.ahfmr.ab.ca/publications.html

- Canadian Coordinating Office for Health Technology Assessment (CCOHTA)
  http://www.cadth.ca/index.php/en/

- Canadian Health Economics Research Association (CHERA/ACRES) – Cabot database http://www.mycabot.ca

- Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org

- Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca

- Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm

- Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca

DENMARK

- Danish Institute for Health Technology Assessment (DIHTA) http://www.dihta.dk/publikationer/index_uk.asp

- Danish Institute for Health Services Research (DSI) http://www.dsi.dk/engelsk.html

FINLAND

- Finnish Office for Health Technology Assessment (FINOHTA) http://finohta.stakes.fi/FI/index.htm

FRANCE

- L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES)

  http://www.anaes.fr/

GERMANY

- German Institute for Medical Documentation and Information (DIMDI) / HTA

  http://www.dimdi.de/dynamic/en/

THE NETHERLANDS

- Health Council of the Netherlands Gezondheidsraad
  http://www.gr.nl/adviezen.php

NEW ZEALAND

- New Zealand Health Technology Assessment (NZHTA)
  http://nzhta.chmeds.ac.nz/

NORWAY

- Norwegian Centre for Health Technology Assessment (SMM)
  http://www.kunnskapssenteret.no/

SPAIN

- Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud "Carlos III" / Health Technology Assessment Agency (AETS)
  http://www.isciii.es/htdocs/investigacion/Agencia_quees.jsp

- Catalan Agency for Health Technology Assessment (CAHTA)
  http://www.aatrm.net/html/en/dir394/index.html

SWEDEN

- Swedish Council on Technology Assessment in Health Care (SBU)
  http://www.sbu.se/www/index.asp

- Center for Medical Health Technology Assessment
  http://www.cmt.liu.se/

SWITZERLAND

- Swiss Network on Health Technology Assessment (SNHTA)
  http://www.snhta.ch/

UNITED KINGDOM

- NHS Quality Improvement Scotland
  http://www.nhshealthquality.org

- National Health Service Health Technology Assessment (UK) / National Coordinating Centre for health Technology Assessment (NCCHTA)
  http://www.hta.nhsweb.nhs.uk/

- University of York NHS Centre for Reviews and Dissemination (NHS CRD)
  http://www.your.ac.uk/inst/crd/

- National Institute for Clinical Excellence (NICE)
  http://www.nice.org.uk/

UNITED STATES

- Agency for Healthcare Research and Quality (AHRQ)
  http://www.ahrq.gov/clinic/techix.htm

- Harvard School of Public Health – Cost-Utility Analysis Registry
  http://www.tufts-nemc.org/cearegistry/index.html

- U.S. Blue Cross / Blue Shield Association Technology Evaluation Center (TEC)
  http://www.bcbs.com/tec/index.html

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