


# Holmium laser versus thulium laser enucleation of the prostate: a matched-pair analysis from two centers

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## Abstract

**Background:** The aim of our study was to compare perioperative and functional outcomes of two different prostatic laser enucleation techniques performed in two high-volume centers: 100 W holmium laser enucleation of the prostate (HoLEP) (Lyon, France) and 110 W thulium laser enucleation of the prostate (ThuLEP) (Varese, Italy).

**Materials and Methods:** A nonrandomized, observational, retrospective and matched-pair analysis was performed on two homogeneous groups of 117 patients that underwent prostate laser enucleation in the HoLEP or ThuLEP centers between January 2015 and April 2017, following the classical 'three lobes' enucleation technique. The American Society of Anesthesiologists (ASA) score and prostate volume were the main parameters considered for matching the patients between the two groups. Patients on anticoagulant therapy, with documented detrusor hypoactivity or hyperactivity or with the finding of concurrent prostate cancer were excluded from the study. Follow up was assessed at 3, 6 and 12 months after surgery.

**Results:** Median enucleation and morcellation time was 75.5 and 11.5 min, respectively, in the HoLEP group *versus* 70.5 and 12 min, respectively, in the ThuLEP group ( $p = 0.001$  and  $0.49$ , respectively). Enucleated adenoma weight was comparable (44 g *versus* 45.6 g,  $p = 0.60$ ). Energy index (3884.63 *versus* 4137.35 J/g,  $p = 0.30$ ) and enucleation index (0.57 *versus* 0.6 g/min,  $p = 0.81$ ) were similar in the two groups. Catheterization time was comparable (1 *versus* 1 day;  $p = 0.14$ ). The International Prostate Symptom Score and Quality of Life score significantly decreased, as well as maximal urinary flow rate. Median prostate-specific antigen (PSA) drop 1 year after surgery was 2.1 ng/ml in the HoLEP group ( $-52.83\%$ ) *versus* 1.75 ng/ml in the ThuLEP group ( $-47.85\%$ ) ( $p = 0.013$ ).

**Conclusion:** Both HoLEP (100 W) and ThuLEP (110 W) relieve lower urinary tract symptoms in a comparable way with high efficacy and safety, with negligible clinical differences.

**Keywords:** endoscopic enucleation of the prostate, holmium laser enucleation of the prostate, matched-pair analysis, thulium laser enucleation of the prostate

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## Introduction

Thulium laser enucleation of the prostate (ThuLEP) and holmium laser enucleation of the prostate (HoLEP) are two endoscopic enucleation of the prostate techniques.

HoLEP is part of the usual treatment in many urological centers, and consistent literature findings

affirm its efficacy. A retrospective study by Elmansy and colleagues<sup>1</sup> reported long-term outcomes of HoLEP with a maximum follow up of 10 years (mean 62 months), reporting durable functional results with low reoperation rates. A recent meta-analysis by Cornu and colleagues<sup>2</sup> compared functional outcomes of different surgical treatments for benign prostatic hyperplasia (BPH), showing that

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HoLEP had more satisfactory outcomes than classic monopolar transurethral resection of the prostate (TURP), in terms of short-term urinary function recovery, complication rate, and hospital stay.

In 2010, Herrmann and colleagues first proposed a similar technique for prostatic adenoma enucleation using a thulium laser, called ThuLEP.<sup>3</sup> Similarly to HoLEP, a number of studies have confirmed the feasibility and efficacy of ThuLEP. A review by Barbalat and colleagues<sup>4</sup> showed that thulium laser prostatectomy represents a safe and effective procedure.

Regarding their physical properties, both lasers are ideal for endourological applications as they are completely absorbed by water, with a tissue penetration depth of 0.4 mm for holmium and of 0.25 mm for thulium laser. The main difference is that holmium has a pulsed energy, while thulium emits a continuous laser wave.<sup>5</sup>

The only comparative study in a clinical setting of HoLEP and ThuLEP is that of Zhang and colleagues<sup>6</sup> that reported a monocentric randomization of 133 patients with a maximum prostate volume of 80 ml undergoing HoLEP or ThuLEP. Adenoma enucleation was performed followed by a ‘mushroom’ monopolar electroresection of the prostate lobes, following the technique described by Hochreiter and colleagues<sup>7</sup> demonstrating their similar efficacy and safety.

In this study, we want to further investigate the possible differences in terms of intraoperative variables, surgical complications, and outcomes between the two techniques. We herein present a matched-pair comparison between a large group of HoLEP and ThuLEP procedures in two highly experienced centers.

### Patients and methods

This observational, retrospective and matched-pair analysis was a controlled, but not randomized, study, based on the retrospective analysis of prospectively collected data of a series of patients that underwent prostate laser enucleation for symptomatic lower urinary tract symptoms (LUTS) between January 2015 and April 2017 in two different urological centers. Comparability was guaranteed by a strict analysis of clinical databases in terms of prostate volume (PV), American Society of

Anesthesiologists (ASA) score and preoperative symptomatology. To maximize the clarity and correctness of data reporting, we referred in this paper to Strengthening the Reporting of Observational Studies in Epidemiology statements reporting guidelines for observational studies.<sup>8</sup>

### Clinical setting

*HoLEP (holmium laser enucleation of the prostate) Center, Lyon, France.* HoLEP is routinely practiced in this institution by two experienced surgeons since May 2013, who performed 80 interventions each, during the first 18 months of their experience. We didn't consider for this study any patient who underwent the operation at the beginning of the surgeon's learning curve. During the study period, 200 patients underwent the procedure. According to Shah and colleagues,<sup>9</sup> a surgeon can be considered completely confident with HoLEP after 50 cases, so the two surgeons could be considered experts at the time of this analysis.

*ThuLEP (thulium laser enucleation of the prostate) Center, Varese, Italy.* ThuLEP has been practiced in this center by two expert surgeons since June 2012, with about 300 patients treated before the time considered for this study (about 150 procedures for each surgeon). As initially assessed by Bach,<sup>10</sup> the learning curve to acquire a complete surgical skill in thulium laser enucleation is relatively fast; shorter than for HoLEP. In a previous work from our study group, 30 procedures were shown as sufficient to fully achieve the skills required for the procedure.<sup>11</sup> In May 2015, an ‘en bloc’ technique was introduced by one of the surgeons (GS), although the patients treated with this new technique are not considered in the present study.<sup>12</sup>

### Surgical indication

Indications for prostatic enucleation were similar in both centers (see inclusion and exclusion criteria sections). Indication for prostatic enucleation was symptomatic BPH refractory to medical therapy. Independently from PV, patients were enrolled for surgery if they presented a maximal urinary flow rate ( $Q_{max}$ ) less than 15 ml per s, an International Prostate Symptom Score (IPSS) greater than 15 points, a history of repeated urinary tract infections or recurrent episodes of urinary retention. The IPSS questionnaire<sup>13</sup> was

administered to patients in national validated forms<sup>14,15</sup> before surgery and thereafter during follow-up controls.

Preoperative patient assessment included a physical examination with digital rectal examination, PSA assay, transrectal ecographic estimation of prostate volume, uroflowmetry, measurement of postvoid residual urine (PVR), urine analysis and urine culture. Moreover, symptomatologic questionnaires as International Prostatic Symptoms Score (IPSS) and Quality of Life (QoL) were always demanded before giving the surgical indication.

#### *Inclusion criteria*

We retrospectively identified two groups of patients: one considering all patients who underwent HoLEP in the study period and the other group that underwent ThuLEP, for which preoperative, intraoperative and postoperative data were recorded. PV and ASA score were the main preoperative variables considered for the matching procedure to identify similar patients. All patients provided signed informed consent for their inclusion in the study.

#### *Exclusion criteria*

To limit a possible result bias, we decided not to consider patients undergoing anticoagulation therapy, or with an incidental finding of prostate cancer that received successive treatment. Moreover, urodynamic evidence of a neurogenic bladder or documented detrusor hypoactivity or hyperactivity, a previous history of prostate surgery or prostate cancer were also considered excluding factors.

#### *Laser equipment*

HoLEP procedures were practiced with the Lumenis Pulse 120 H laser (Lumenis, Santa Clara, CA, US) using a 1000  $\mu\text{m}$  laser fiber and a resectoscope sheath of 24 Fr.

ThuLEP procedures were performed with the Cyber TM 200 W device (Quanta System, Solbiate Olona, Varese, Italy) using an 800  $\mu\text{m}$  laser fiber and a resectoscope sheath of 27 Fr.

Morcellation was performed in both groups with the Piranha device (Richard Wolf GmbH, Knittlingen, Germany).

#### *Surgical technique*

A similar surgical technique was practiced for both HoLEP and ThuLEP. Following the initial depiction by Gilling and Fraundorfer for HoLEP<sup>16</sup> and Herrmann and colleagues for ThuLEP,<sup>3</sup> a three-lobe enucleation was performed.

The ureteral orifices were first identified and marked at short distance using coagulation. Then, the median lobe was progressively incised at 5 and 7 o'clock and enucleated following the margin of the prostatic capsule, toward the verumontanum, where an inverted-U incision was previously made. Subsequently, an upper incision at 12 o'clock separated the lateral lobes, which were enucleated by joining the lower and upper resection planes of the lateral lobes. All the enucleation was carried out while maintaining sight of the surgical capsule. The enucleation was performed by bluntly exposing the plane of the adenoma and separating it from the capsule by means of laser energy.

Laser setting was 20 W for coagulation and 100 W for enucleation in HoLEP and 60 W for coagulation and 110 W for enucleation in ThuLEP.

Morcellation was performed after completing the enucleation, by means of a long nephroscope. A double inflow maintains safe bladder distension, avoiding injuries to the bladder wall. Following surgery, all patients had a Foley catheter with continuous bladder irrigation.

#### *Immediate and long-term comparison*

Each institution progressively registered a medical database in Microsoft Excel®, recording intraoperative and follow-up variables at 3, 6 and 12 months after the intervention.

Baseline characteristics of the patients were summarized as median (interquartile range, IQR) for continuous variables and as frequencies and percentages for categorical variables. Functional outcomes were summarized both as continuous variables, as median (IQR), and as categorical variables.

These clinical databases allowed us to evaluate immediate surgical outcomes in terms of operative time, complication rate and hospital stay. Intraoperative blood loss was estimated with the calculation of hemoglobin (Hb) drop: the difference between preoperative and immediate postoperative

Hb value (calculated between 12 and 24 h after the surgery). Other important variables we measured were the energy index (energy delivered per adenoma gram ratio) and the enucleation index (gram of adenoma enucleated per enucleation time ratio). A subsequent comparison of early and late follow up was made by evaluating objective parameters (PSA reduction,  $Q_{\max}$ , PVR) and validated symptom questionnaires, such as the IPSS and the QoL index. Surgical complications were reported according to the Clavien–Dindo (CL) classification.<sup>17</sup>

### Statistical analysis

To eliminate differences in terms of preoperative variables, we created two paired groups, considering the most relevant parameters to be PV, measured in a continuous way, authorizing a maximal difference of  $\pm 10$  ml, and ASA score, grouping patients with ASA score 1 and 2 together and patients with ASA score 3 separately. We obtained 117 HoLEP–ThuLEP pairs that were matched 1:1 by propensity score analysis. Qualitative variables were evaluated with a McNemar test (for two variables) or a Cochran  $Q$  test (for more than two variables). Quantitative variables were compared using the Wilcoxon test (data not satisfying normality). All calculations were attained by the SAS software package (Version 9.4 SAS Institute Inc., Cary, NC, US).

### Results

From January 2015 to January 2017, data from 117 patients who underwent HoLEP were compared with those of 117 similar patients who underwent ThuLEP in the same period. Patient baseline characteristics are listed in Table 1. Age, PV (also its subcategories), ASA score, preoperative functional variables (such as IPSS score, QoL index and  $Q_{\max}$ ), as expected, were not significantly different. Median PSA value was slightly higher, even if nonsignificantly, in the HoLEP group. The number of patients on indwelling catheterization was greater in the ThuLEP group.

### Intraoperative values comparison

All perioperative parameters are presented in Table 2. Median time required for enucleation and morcellation was 75.5 (58–104 IQR) and 11.5 (8–16 IQR) min, respectively, in the HoLEP group, versus 70.5 (58.0–87.3 IQR) and 12 (9.5–14.5 IQR) min, respectively, in the ThuLEP group ( $p = 0.0011$  and  $0.450$ , respectively).

Overall mean operation time was 90 (70–129 IQR) min for HoLEP and 82.25 (69–97 IQR) min for ThuLEP. This shows a shorter enucleation time in favor of ThuLEP.

Median weight of the resected adenoma was similar in the two groups (44 versus 45.6 g,  $p = 0.60$ ).

The energy index (energy delivered per adenoma gram ratio) was slightly lower in the HoLEP group, although the difference was not statistically significant (3884.63 versus 4137.35 J/g,  $p = 0.30$ ), and similarly for the enucleation index (grams of adenoma enucleated per enucleation time ratio) (0.57 versus 0.6 g/min,  $p = 0.81$ ).

Morcellation was carried out with the same instrument and technique, and we did not find any significant difference between the two groups, even in terms of impaired vision due to bleeding.

Intraoperative complication rate (see Table 3) and transfusion rate were also similar: 5.7% versus 7.1% and 3.2% versus 2.5%, respectively. Median hemoglobin drop after surgery was similarly comparable (0.9 versus 0.5 g/dl,  $p = 0.36$ ).

### Hospitalization and short-term complications

All patients had bladder catheterization with continuous bladder irrigation, which was continued over a similar median length of time between the two groups (1 versus 1 day,  $p = 0.14$ ). Patients were promptly discharged after verifying correct voiding, without significant PVR.

A total of 47.8% of patients in the HoLEP group and 53% in the ThuLEP group were discharged on postoperative day (POD) 1 ( $p = 0.43$ ); 38.4% versus 35.0% on POD 2 ( $p = 0.58$ ); 9.5% versus 5.2% on POD 3 ( $p = 0.20$ ); 3.4% versus 4.27% on POD 4 ( $p = 0.73$ ); 0.85% versus 2.56% on POD 5 or 6 ( $p = 0.31$ ).

Immediately after surgery, 11 patients (9.4%) in the HoLEP group and 13 (11.1%) in the ThuLEP group presented with postoperative complications. Of these, the most common were Clavien grade II complications, mostly hemorrhagic, which were conservatively managed with prolonged bladder catheterization. Only two were Clavien grade IIIb, requiring a reintervention (one in the HoLEP group because of incomplete morcellation and one in the ThuLEP group for bipolar

**Table 1.** Preoperative characteristics of the patients considered in the study.

		HoLEP ( <i>n</i> = 117)	ThuLEP ( <i>n</i> = 117)	<i>p</i> value
Age, years (range)		71 (66–75)	70 (65–75)	0.587
Age in classes	<60 years, <i>n</i> (%)	10 (8.6)	9 (7.8)	0.745
	60–70 years, <i>n</i> (%)	45 (38.8)	50 (43.1)	0.468
	>70 yrs, <i>n</i> (%)	61 (52.6)	57 (49.1)	0.602
ASA score		2 (1–2)	2 (1–2)	0.430
ASA score in classes, <i>n</i> (%)	1 + 2	103 (88)	103 (88)	0.392
	3	14 (12)	14 (12)	0.500
Prostatic volume, ml (range)		75 (60–100)	75 (60–95)	0.715
Prostatic volume in classes, ml (%)	<60	37 (31.6)	40 (34.2)	0.676
	60–80	32 (27.4)	29 (24.8)	0.655
	80–100	27 (23.1)	28 (23.9)	0.877
	100–120	13 (11.1)	10 (8.5)	0.510
	>120	8 (6.8)	10 (8.5)	0.623
Indwelling catheterization <i>n</i> (%)		31 (26.7)	47 (40.5)	<b>0.026</b>
IPSS (range)		21 (17.5–25.5)	20 (18.25–24)	0.548
QoL (range)		5 (4–5)	5 (5–6)	0.492
PSA ng/ml (range)		5.48 (3.135–8.4)	3.8 (2.92–5.5)	0.463
$Q_{\max}$ ml/s (range)		7 (5.0–9.4)	7 (6–9)	0.172
PVR ml(range)		103.5 (58.5–200)	90 (20–100)	0.135
Preoperative Hb (range)		14.05 (13.6–15.3)	13.5 (12.5–14.1)	0.086

Bold numbers represent statistical significance. Values are expressed in median (interquartile range, IQR) or in percentage. Quantitative variables are compared with the Wilcoxon test and qualitative variables with the McNemar test (for two variables) or Cochran Q test (for more than two variables). ASA score, American Society of Anesthesiologists classification; Hb, hemoglobin; IPSS, International Prostate Symptom Score; PSA, prostate-specific antigen; PVR, postvoid residual urine;  $Q_{\max}$ , maximum urinary flow rate; QoL, Quality of Life Index.

hemostatic coagulation). Table 3 summarizes the complications that occurred in the two groups.

#### Follow-up data

All patients considered in the study underwent a complete follow up at 3, 6 and 12 months after surgery. Table 4 summarizes the main parameters evaluated in the study. Symptom resolution is well represented by the clear median IPSS score improvement at 3 months, that is 6 (3–9 IQR) for HoLEP and 4 (1–8 IQR) ( $p = 0.0581$ ) for

ThuLEP. Similarly, mean IPSS was 3.5 (2–7 IQR) versus 4 (1–7 IQR) ( $p = 0.9899$ ) at 6 months and 5 (2–7 IQR) versus 3.5 (0–6 IQR) ( $p = 0.058$ ) at 12 months.

ThuLEP showed better, but not significant, early IPSS and  $Q_{\max}$  parameters at the 3-month follow up ( $p = 0.0581$  and 0.2371, respectively), while at 6 months, values were comparable. The late follow up (12 months) showed a similar trend to the 3-month one ( $p = 0.0580$  and 0.8715, respectively).

**Table 2.** Intraoperative characteristics and outcomes of the two match-paired patient groups.

	HoLEP (n = 117)	ThuLEP (n = 117)	p value
Total surgical time, min (range)	90 (70–129)	82.25 (69–97)	<b>0.0003</b>
Enucleation time, min (range)	75.5 (58–104)	70.5 (58–87.3)	<b>0.0011</b>
Morcellation time, min (range)	11.5 (8–16)	12 (9.5–14.5)	0.497
Delivered energy, J (range)	157930 (124,627.5– 213,070)	161430 (122,960– 206,577.5)	0.948
Enucleated adenoma weight, g (range)	44 (30–62)	45.6 (31.5–62.7)	0.598
Enucleation index, g/min (range)	0.57 (0.39–0.75)	0.6 (0.37–0.78)	0.812
Energy index, J/g (range)	3884.63 (2979.7–5414.5)	4137.35 (2753.9–6184.8)	0.301
Morcellation index, g/min (range)	3.6 (2.38–5.28)	3.52 (2.64–5.0)	0.952
Hemoglobin drop, g/dl (range)	0.9 (0.3–1.67)	0.5 (0.3–1.1)	0.363
Catheterization, days (range)	1 (1–2)	1 (1–2)	0.142
Hospital discharge, days (range)	2 (1–2)	1 (1–2)	0.068

Bold numbers represent statistical significance. Results are expressed as median (interquartile range, IQR). Data are herein compared with the Wilcoxon test (non-independent quantitative variables).  
HoLEP, holmium laser enucleation of the prostate; ThuLEP, thulium laser enucleation of the prostate.

A small number of patients reported urinary incontinence after the operation (2.13% of total): two in the HoLEP group and three in the ThuLEP group. This was in three cases a transitory urge incontinence, treated with anticholinergic drugs and resolved by the 6-month follow up, and in two cases a minimal stress incontinence that was managed with physical rehabilitation therapy that didn't require any protection at the 3-months follow up.

Median PSA drop after the operation was 2.1 ng/ml in the HoLEP group (–52.83%) versus 1.75 ng/ml in the ThuLEP group (–47.85%). The Wilcoxon test was performed to compare the PSA drop between the two techniques, showing a more effective PSA drop for HoLEP ( $p = 0.013$ ).

### Discussion

During the last decade, growing interest in BPH surgical treatment has focused on endoscopic prostate laser enucleation techniques, which is recognized to be more effective than classical monopolar TURP or open prostatectomy (OP) and to have lower complication rates and blood loss.<sup>18,19</sup> More specifically, laser enucleation of the prostate is an 'endoscopic prostatic adenomectomy,' mimicking the results of OP but achieving

these endoscopically. Moreover, laser properties permit a more precise and complete tissue coagulation than classic electrical coagulation used in mono- or bipolar TURP.

The first depiction of HoLEP was made about 20 years ago<sup>16</sup> and today, this technique is recognized as the gold standard for BPH surgical treatment worldwide, proposed as a first-line treatment in the European Association of Urology (EAU) and American Urology Association (AUA) guidelines. A recent paper by Vincent and Gilling states that 'HoLEP has come of age,' as a plethora of works have demonstrated its feasibility, efficacy, safety, durability and cost effectiveness.<sup>20</sup>

Much of the existing literature shows that ThuLEP can achieve similar results to HoLEP, with the same efficacy and safety. This is also stated in the latest version of EAU guidelines on treatment of non-neurogenic male LUTS (level of evidence 1b grade A).<sup>21</sup> However, there is still a lack of studies performing a direct comparison between two similar patient populations treated with these two laser techniques.

In this retrospective matched-pair analysis, we compared surgical and functional results of

**Table 3.** Early and late surgical complications occurring in our holmium, and thulium, laser enucleation of the prostate series.

Complications	Description	HoLEP ( <i>n</i> = 117)	ThuLEP ( <i>n</i> = 117)	<i>p</i> value
Intraoperative, <i>n</i> (%)	Necessity of mono(bi)polar coagulation	1 (0.85)	2 (1.71)	0.561
	Incomplete morcellation (CL IIIb)	2 (1.71)	2 (1.71)	1
	Incomplete enucleation (CL IIIb)	2 (1.71)	1 (0.85)	0.561
	Laser machine breaking	1 (0.85)	0	–
Perioperative, <i>n</i> (%)	Massive hematuria (CL II)	2 (1.71)	1 (0.85)	0.561
	Need of transfusion (CL II)	1 (0.85)	1 (0.85)	1
Late (>1 month), <i>n</i> (%)	Bladder neck sclerosis	3 (2.56)	2 (1.71)	0.651
	External urethral meatus stenosis	7 (5.98)	3 (2.56)	0.196
	Chronic urinary retention	3 (2.56)	3 (2.56)	1
	Urinary infection	4 (3.42)	5 (4.27)	0.734
Total <i>n</i> (%)		26 (22.2)	20 (17.09)	0.323

Results are reported numerically and with the corresponding Clavien grade.<sup>17</sup>  
 CL, Clavien–Dindo classification grade; HoLEP, holmium laser enucleation of the prostate; ThuLEP, thulium laser enucleation of the prostate.

prostatic enucleation performed by HoLEP 100 W and ThuLEP 110 W. Although ThuLEP appeared to be faster in terms of operative and enucleation time, the two techniques were similar in terms of intraoperative efficacy, showing a similar energy index and enucleation index ( $p = 0.3$  and  $0.81$ , respectively). The energy index is not different even if the laser emission power settings are not equal for the two enucleations techniques and the laser wave properties are different (pulsed for holmium and continuous for thulium). Hemoglobin loss was also similar, showing an analogous hemostatic capacity between the two lasers. Complication rate was comparable, and the incidence of complications was very low with both techniques (overall  $5.7\%$  versus  $4.27\%$ ).

ThuLEP is known to have a sort of ‘eschar-like’ effect on the surface of the incised tissue owing to its physical properties, which contrasts with the ‘scar-free’ quality of HoLEP tissue. This aspect

has led some researchers to speculate about a relationship with the longer operative time in ThuLEP due to a worse visualization of the capsule in comparison with HoLEP.<sup>6</sup>

Findings of this study contradict this, as capsular identification appeared to be easy and did not have a negative impact on operative time. Enucleation, unlike vapoenucleation (ThuVEP), has a limited escharing effect on the tissue that is only present where adhesions between the lobes and the capsule that are tensioned with the aid of resectoscope’s beak, are incised. Moreover, we registered a shorter enucleation time in the ThuLEP group, maybe owing to the easier enucleation achieved by the thulium laser, which has an intrinsic vaporization effect during enucleation and a continuous wave mode. A recent work by Ketan and colleagues on a series of 236 patients who underwent ThuLEP also showed an enucleation time comparable to that in our ThuLEP group, with similar functional results.<sup>22</sup>

**Table 4.** Follow up on early and late functional results in the two groups at 3, 6 and 12 months after surgery.

	HoLEP (n = 117)	ThuLEP (n = 117)	p value
3-month follow up			
IPSS (range)	6 (3–9)	4 (1–8)	0.0581
QoL(range)	1 (0–2)	1 (0–2)	0.442
$Q_{max}$ , ml/s (range)	20 (14.3–28)	19 (12.5–25)	0.2371
PVR, ml (range)	40 (0–71)	17 (0–59)	0.2094
6-month follow up			
IPSS (range)	3.5 (2–7)	4 (1–7)	0.9899
QoL(range)	1 (0–1)	0 (0–1)	0.087
$Q_{max}$ , ml/s (range)	26 (14–29)	20.3 (15–25)	0.1273
PVR, ml (range)	27 (0–73)	10 (0–41)	0.0633
12-month follow up			
IPSS (range)	5 (2–7)	3.5 (0–6)	0.0580
QoL(range)	1 (0–1)	0 (0–1)	0.164
$Q_{max}$ , ml/s (range)	23 (16–29)	22 (16–25)	0.8715
PVR, ml (range)	22.5 (0–54)	8.5 (0–30)	0.3429
PSA drop (%)	-52.83	-47.85	<b>0.013</b>
<p>Bold numbers represent statistical significance. Results are expressed in median (interquartile range, IQR). Data analysis was performed with the Wilcoxon test (non-independent quantitative variables). The PSA drop was calculated with the Wilcoxon test.</p> <p>HoLEP, holmium laser enucleation of the prostate; ThuLEP, thulium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; PSA, prostate-specific antigen; PVR, postvoid residual urine; <math>Q_{max}</math>, maximum urinary flow rate; QoL, Quality of Life Index.</p>			

Unlike holmium laser, for which only enucleation procedures have been described, several techniques have been proposed for thulium laser prostatectomy that could generate some confusion to novice surgeons facing this surgery. These peculiarities are fully discussed in a work by Bach and colleagues.<sup>23</sup> This systematic review analyzes all the different kinds of thulium: yttrium aluminum garnet (YAG) prostatectomy techniques described in the literature, including vaporization (ThuVaP), vaporessection (ThuVaRP), vapoenucleation (ThuVEP), and pure enucleation (ThuLEP), proposing a recognized and precise nomenclature for each intervention and analyzing the clinical studies presented in literature. Pure vaporization is only suitable for small prostates (<30 ml) and, like TURP, ThuVaRP can be purposed only for moderate-size prostates. Alternatively, enucleation techniques are practicable at any PV. Among the enucleation

techniques, ThuVEP exploits tissue vaporization to achieve prostate incision and enucleation; ThuLEP, after the initial incision of the prostatic tissue down to the surgical capsule, follows the plane of the surgical capsule by bluntly putting in tension the adenoma attachments with the sheath of the resectoscope, a technique that is more like HoLEP.

Our early and late follow-up results show clear improvement in the IPSS after surgery, that is, about five to sixfold lower already at 3-month follow up. The size independence of ThuLEP and HoLEP is also demonstrated by the important number of prostates with volume >100 ml reported in this study (21 versus 20 cases, see Table 1). This is in contrast to the study by Zhang and colleagues<sup>6</sup> where prostate volumes were lower than 80 ml and supports the efficacy of these techniques for large-volume prostates.



Completeness of adenoma resection was confirmed by the significant PSA drop, which was 2.1 ng/ml in the HoLEP group ( $-52.83\%$ ) versus 1.75 ng/ml in the ThuLEP group ( $-47.85\%$ ). The possible impact of these laser prostatic surgeries on erectile function has not been evaluated, even if several papers show that neither HoLEP<sup>24</sup> nor ThuLEP<sup>25</sup> have a negative impact on it.

As HoLEP and ThuLEP do not appear to show significant differences, the discrepancy in the amount of literature between these two laser techniques can still generate some doubts. The first depiction of HoLEP was made in 1998 by Gilling and Fraundorfer,<sup>16</sup> while ThuLEP was first proposed more than 10 years later, in 2010.<sup>3</sup> Therefore, this ‘outcome equivalence’ is only being demonstrated now. This statement was also one of the main points of a recent paper by Gilling,<sup>26</sup> who recognized that we should refer to these procedures as ‘laser enucleation techniques,’ irrespectively of the type of laser used, as clinical outcomes appear to be similar.

Similarities between holmium and thulium laser enucleation are also found in a recent randomized single-center trial by Netsch and colleagues<sup>27</sup> that compares early outcomes of ThuVEP and HoLEP. Despite a shorter enucleation time and efficiency in ThuVEP ( $p \leq 0.04$  and  $\leq 0.005$ , respectively), authors didn’t find any difference in postoperative outcomes and complications.

According to our analysis and existing literature, both HoLEP and ThuLEP can be proposed for BPH surgical treatment, independently of PV, patient symptoms or preoperative PSA status. As a different learning process is required to achieve complete mastery of the technique, the choice of technique should be oriented toward one of the two lasers, except in high-volume centers where a consistent number of procedures can be performed with each laser. One advantage of holmium laser to be considered is its setting versatility, allowing both prostate enucleation and urinary stones lithotripsy to be performed with the same device. Surgeon’s preference and laser availability are therefore the main factors in choosing one laser over the other. As the instrument setting requirements are not different, a common operative protocol can be adopted for this kind of surgery, as well as a common hospitalization protocol. A 1-day hospitalization period could be the goal for prostate laser surgery. This

objective can only be reached in centers with experienced surgeons and this protocol should be discussed throughout multicentric studies.

This work presents some limitations: firstly, its retrospective and unblinded nature. Moreover, the ThuLEP procedures were performed in Italy and the HoLEP procedures in France, so the impact of the different healthcare systems is difficult to ascertain. Furthermore, the ThuLEP surgeons were more experienced than the HoLEP surgeons, and it may be this that has resulted in the ThuLEP operation times being shorter. Finally, it was not possible to determine a comparison between erectile and sexual function after surgery and the same for urinary irritative symptoms.

However, even without the power of a randomized prospective trial, we believe that a matched-pair comparison study design is an effective method to select patients with comparable preoperative characteristics.

## Conclusion

Our comparison of HoLEP and ThuLEP has demonstrated the efficacy, safety and effectiveness of the two techniques for the treatment of symptomatic BPH. Results show that there are no significant clinical differences in the intraoperative and follow-up data between the two techniques, and they have equal efficacy for all adenoma volumes, with minimal complication rates and blood loss.

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## Conflict of interest statement

The authors declare that there is no conflict of interest.

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