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TOPIC PAPER

Assessment of the learning curves for photoselective vaporization of the prostate using GreenLight^{TM} 180-Watt-XPS laser therapy: defining the intra-operative parameters within a prospective cohort

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Abstract
Purpose To assess the learning curves for the intra-operative parameters of the GreenLight^{TM} 180-W XPS for photoselective vaporization of the prostate (PVP).
Methods A prospective study was conducted on 200 men who underwent PVP using the GreenLight^{TM} 180-W XPS over 20 months. The population was divided into four consecutive equal groups. Evolution of lasing parameters was the main endpoint to reach an average energy of 5 kJ per prostate volume and to reach a lasing time/operative time (LT/OT) ratio of 66–80 %. Changes in the IPSS and prostate volume were also evaluated 12 weeks later.
Results Total energy delivered (energy/ml of prostate) and the LT/OT ratio significantly increased over time ($p < 0.05$). Urinary function significantly improved from baseline in all groups. The first lasing parameter endpoint was reached after the 75th patient (group 1) and the second endpoint (LT/OT ratio) after the 125th patient (group 3). Only the PSA level ($p = 0.04$) and prostate volume ($p < 0.0001$) decreased significantly in the 3rd and the 4th group. Post-operative complications occurred in 20 % of patients, which were primarily Clavien–Dindo grades 1 and 2, though there were no statistical differences between the four groups ($p = 0.62$). In-hospital stay and time to catheter removal were significantly shorter in the 3rd and 4th group.
Conclusions The current study assessed the PVP learning curves within multiple intra-operative parameters. The PVP learning curves required at least 120 procedures until it met all intra-operative parameters of experts in this field.

Keywords Prostate · Laser · BPH · Learning curves · Outcomes

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Introduction

New therapies have enabled laser technologies to challenge the gold standard of transurethral resection of the prostate (TURP) for the surgical treatment of symptomatic benign prostatic hyperplasia (BPH) [1, 2]. Among them, photoselective vaporization of the prostate (PVP) using a GreenLight^{TM} laser is a minimally invasive option; in particular, its applicability has been highlighted for patients receiving anticoagulants. A recent meta-analysis that compared GreenLight^{TM} PVP and TURP in BPH patients has emphasized its safety, the lower peri-morbidity and the absence of difference in midterm functional outcomes between PVP and TURP [3].

However, learning curves for the usage of PVP have not been clearly assessed in clinical practice. Several teams have reported that it is necessary to perform between 20 [4] and 50 cases [5] to achieve a sufficient level of skill and expertise. This technology has evolved considerably from the 532-nm laser, to the GreenLight 80-W KTP-powered laser, to the latest 180-W XPS laser, which uses a MoXy side-firing fiber. However, specific data on the learning curve for the GreenLight™ PVP and its functional outcomes are still limited [6], notably for the latest 180-W XPS laser [7].

In this article, the authors have assessed the stratified learning curves for the latest generation of GreenLight™ 180-W XPS within a prospective cohort of patients managed by a single urologist with no previous experience of PVP.

Materials and methods

Study population

Data were collected prospectively during 200 consecutive procedures that used 180-W XPS laser therapy on patients with symptomatic BPH between 2011 and 2012 at a single center: age, medication, International Prostate Symptom Score (IPSS), ASA score, Charlson score, intra-operative parameter, length of hospital stay, peri-operative complications, morbidity and outcomes. The IPSS was not assessed in men with a bladder catheter. All data were collected by the attending urologists at our department. Pre-operative assessment of the patients and indications for BPH surgery included the assessment of prostate volume using transrectal ultrasound in compliance with French guidelines [8].

Patients who had a PSA value of >4 ng/ml or an abnormal finding on a digital rectal examination underwent prostate MRI and a targeted ultrasound-guided prostate biopsy before PVP [9]. The study was approved by our local ethical committee.

Surgical technique

One single senior surgeon (VM) with no previous experience of PVP performed all the procedures in accordance with the steps described previously [10]. PVP was carried out using a GreenLight™ 180-W XPS device (American Medical Systems Inc., Minnetonka, MN, USA) and a MoXy fiber inserted through the working channel of a continuous double-flow 23- or 26-Ch cystoscope with 0.9 % saline irrigation. Oral anticoagulation included coumarin derivatives and platelet aggregation inhibitors and was maintained in all cases only if the international normalized ratio was ≤2.5 as recommended previously [11]. Bridging with low molecular weight heparin was given for patients who needed an international normalized ratio of ≥2.5. All patients were discharged without a catheter after post-voiding residual volume was controlled following catheter removal.

Learning curve parameters

Standard parameters associated with transurethral prostate surgery and the prevalence of surgery-associated problems or complications were prospectively collected and measured pre-operatively. Intra-operative parameters associated with PVP surgery included lasing and operative time, total energy used and the use of the TURP loop for coagulation or resection.

To assess the learning curves, we decided from the beginning to split the patient population equally into four consecutive groups to be in line with former learning curve evaluation of laser in BPH [12]: group 1 (1–50th procedure), group 2 (51–100th procedure), group 3 (101–150th procedure) and group 4 (151–200th procedure). The learning curves were assessed using the following intra-operative criteria: operative time (min), total energy (kJ), lasing time (min)/operative time (min) (%) (LT/OT), energy/prostate volume (kJ/ml) and conversion into TURP.

Reference values for LT/OT and energy/prostate volume were defined according to those reported by experts in the literature. Thus, the aim of the surgeon was to obtain results similar to those obtained by experts in the field, which meant delivering an average energy of 5 kJ per ml of prostate volume (PV) [13] and reaching a LT/OT ratio of 66–80 % [7, 14] (shaded areas in Fig. 1).

Patients who required concomitant endoscopic treatment for a bladder stone or intra-operative conversion into TURP were excluded from the statistical analyses on the progression of the LT/OT ratio. The following post-operative parameters were recorded: length of bladder catheterization and length of hospital stay. Lastly, we recorded and graded any post-operative complications according to the modified Dindo–Clavien classification for endoscopic management of the prostate [15] and strictly in line with the most recent guidelines [16]. We focused on the early follow-up period of 12 weeks and recorded IPSS, IPSS-QOL score, Qmax (ml/s), PSA level (ng/ml), PV (ml) and percentage prostate reduction.

Statistical analyses

We designed a linear model using the variable of interest as the predicted value and the rank of the patient as the

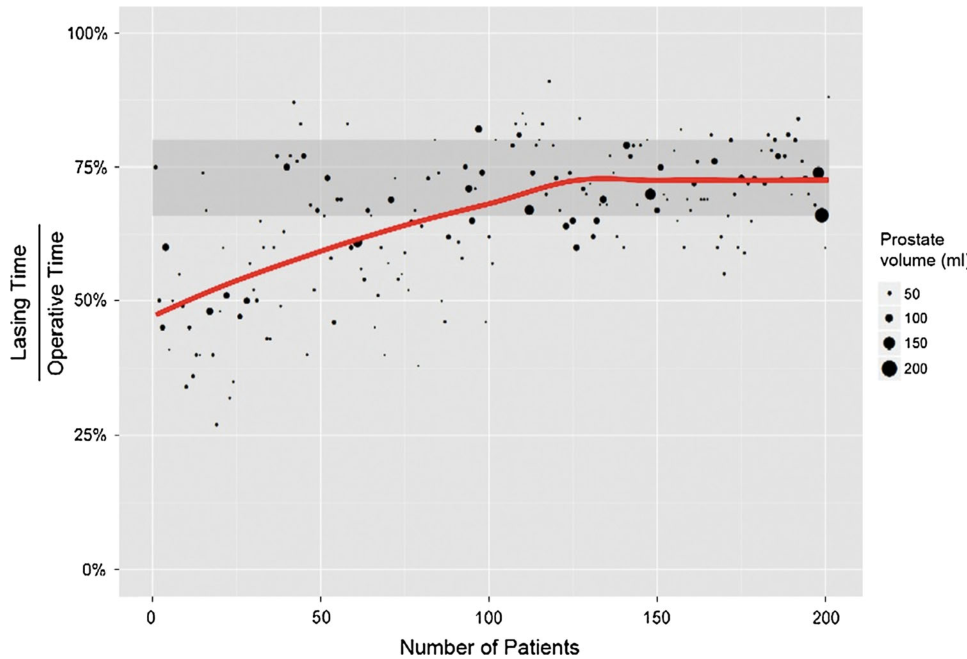

Fig. 1 Evolution of the ratio of lasing time to operative time over the time of the study. The *gray* zone *underlines* the endpoint in the learning curve of the surgeon

predictor. In this model, a significantly positive slope indicated an augmentation of the parameters over time, while a negative slope indicated a diminution of the parameter over time.

Qualitative variables are presented as their median value (inter-quartile range) and were compared using Wilcoxon's test. Qualitative variables are presented as percentages and were compared using the chi-squared test or Fisher's exact test, as appropriate. Statistical significance was defined as $p < 0.05$. All statistical analyses were performed using R 2.14.2 software, 2011.

Results

Overall, 200 men were included in this study (Table 1).

Intra-operative parameters

Median lasing and operative time were 30 (IQR 22–45) and 50 (IQR 35–67) min, respectively. Median energy applied was 231.3 (IQR 161–362.4) kJ. Median LT/OT was 66 (IQR 55–74) %. A median energy of 4.77 (IQR 3.62–5.78) kJ was applied for each 1 ml of measured prostate volume.

Operative time

There was a significant increase in the length of operative time between group 1 (median of 40 min, IQR 30–51) and group 3 (median of 43 min, IQR 35–70) ($p = 0.00039$). In addition, the following parameters increased significantly over the time of the study: prostate volume >80 ml ($p < 0.0001$) and conversion into TURP ($p < 0.0001$).

Total energy

Operative time significantly progressed from the first (median of 152.5 kJ, IQR 122.5–203.7) to the third (median of 309.5 kJ, IQR 183.5–503) group ($p = 0.00061$).

Energy/prostate volume

The ratio of joules/ml increased by a mean of 14 J/ml for every 10 patients. The cutoff of 5 kJ/ml in the J/PV (ml) ratio was not reached until the 75th patient (group 2).

Lasing time/operative time

The ratio of LT to OT increased by a mean of 1.2 % for every 10 patients. It was not linked significantly with PV ($p = 0.33$). A LT/OT ratio of 75 % was only reached by the 125th patient (group 3) (Fig. 1).

Conversion to monopolar TURP

A conversion to TURP occurred in 12 patients (6 %): Uncontrolled bleeding in eight patients or the median lobe was reversed into the bladder in four patients. The conversions to TURP were split as follows: 1, 5, 5 and 1 patient in groups 1, 2, 3 and 4, respectively, with no statistical difference between the four groups ($p = 0.074$).

Table 1 Study population characteristics

Clinical pre-operative parameters	Population: median value (inter-quartile range) or no. (%)
Age ($n = 200$)	70 (64–77)
Charlson score	4 (3–6)
ASA score	
1	13 (6.5)
2	130 (65)
3	57 (28.5)
PSA, ng/ml ($n = 188$)	2.5 (1.57–4.3)
PBx before surgery	32 (15.9)
No. PBx before surgery	169 (84.1)
IPSS ($n = 137$)*	18 (15–21)
IPSS-QOL ($n = 157$)*	4 (4–5)
Qmax, ml/s ($n = 101$)*	7 (5.325–8.85)
PVR, ml ($n = 163$)*	0 (0–140)
Bladder stone	7 (3.5)
Prostate volume, ml ($n = 200$)	50 (40–70)
Group 1	50 (40–60)
Group 2	50 (40-70)
Group 3	55 (40–90)
Group 4	50 (40–65)
No. of patients receiving	
Aspirin	54 (27)
Clopidogrel	17 (8.5)
Vitamin K antagonist	19 (9.5)
Catheterization before surgery	37 (18.5)
Past history of acute urinary retention	13 (6.5)
α-Blocker	176 (88)
5-ARI	46 (23)
Phytotherapy agents	60 (30)
Combined treatment (α-blocker + 5-ARI)	34 (17)
Past history of monopolar TURP	12 (6)

PSA prostate-specific antigen, *PBx* prostate biopsy, *IPSS* International Prostate Symptom Score, *Qmax* maximum flow rate, *PVR* post-voiding residual (urine), *5-ARI* 5a-reductase inhibitor

* Not measurable in catheterized patients. *TURP* transurethral resection of the prostate

Length of hospital stay

The length of bladder catheterization decreased significantly over time: In group 1, the catheter removal was done at day 1 ($n = 29$; 58 %) or at day 2 or after ($n = 21$; 42 %) versus day 1 ($n = 43$; 86 %) or day 2 or after ($n = 7$; 14 %) in group 4 ($p = 0.003$).

The length of hospital stay was significantly shorter over the period of the study: In group 1, discharge was observed before post-operative day 2 in 22 patients (44 %) versus 34 patients (68 %) in group 4 ($p = 0.002$).

Post-operative complications

Immediate post-operative complications occurred in 40 patients (20 %). According to the Clavien classification, they were listed as follows: group 1 [grade I ($n = 1$), grade II ($n = 6$), grade 3b ($n = 1$)]; group 2 [grade I ($n = 6$), grade II ($n = 4$)]; group 3 [grade I ($n = 8$), grade II ($n = 2$), grade 3b ($n = 1$)]; and group 4 [grade I ($n = 1$), grade II ($n = 9$), grade 3b ($n = 1$)]. We found no statistical difference between the four groups ($p = 0.62$). No statistically significant relationship was found between the ASA score ($p = 0.31$) or the Charlson score (0.77) and the number of complications. Unplanned readmission occurred in 19 patients (9.5 %) within the 12 weeks of follow-up because of acute urinary retention ($n = 5$), clot retention ($n = 1$), meatal stenosis ($n = 3$), urethral stricture ($n = 3$), urinary tract infection ($n = 2$), urinary urge or stress incontinence ($n = 5$), with no statistical difference between the four groups ($p = 0.94$).

Functional outcomes

Functional outcomes at 12 weeks are provided in Table 2. Statistically significant improvements were noted in all parameters from the baseline up to 12 weeks post-operatively. However, a decrease in PSA level ($p = 0.04$) and PV ($p < 0.0001$) was more significant in groups 3 and 4.

Discussion

GreenLight™ PVP appears to be a simple procedure, which requires no particular skill [17]. However, its learning curve needs to be assessed like any other surgical procedure, as a surrogate of surgical quality [16]. The learning curves for holmium laser enucleation of the prostate (HOLEP) have been assessed [18]. To date, only one retrospective study has evaluated the learning curves for PVP using the former 80-W generation of lasers [19]. In view of the lack of data for the GreenLight™ 180-W XPS, we have attempted to provide appropriate data.

Our results showed that there was a steady increase in all intra-operative parameters of vaporization between the 1st and 125th patient. This finding agrees with the intra-operative parameter recognized by experts in the field of 5 kJ/ml of prostate [13] and a 66–80 % ratio of LT/OT [7, 14]. We have also confirmed a previous statement regarding the significant increase in the duration of vaporization and the total energy delivered between the 1st and last of the 74 procedures performed by two operators without experience of PVP [19]. Several experts emphasize the need to start PVP in the presence of a proctor in early learning curves [4, 5]. Nevertheless, the recent validation

Table 2 Functional outcomes after a follow-up of 12 weeks after PVP in 200 patients

Parameters	Baseline	Group 1	Group 2	Group 3	Group 14	*p* value
IPSS* ($n = 137$)	18 (15–21)*	−14 (−15–11)	−13 (−16.7–10)	−13 (−16–11)	−11.5 (−16–8.5)	NS
IPSS-QOL* ($n = 145$)	4 (4–5)*	−3 (−2–4)	−4 (−2–4)	−3 (−2–4)	−3 (−2–4)	NS
Qmax (ml/s)* ($n = 94$)	7 (5.3–8.8)	+8.5 (6–12.3)	+9 (7–12)	+7 (3.7–10.7)	+8 (6–12)	NS
PVR (ml)* ($n = 191$)	0 (0–140)*	10 (0–150)	0 (0–100)	0 (0–100)	14 (0–110)	NS
PSA (ng/ml) ($n = 188$)	2.5 (1.5–4.3)	−0.8 (−1.5–0.5)	−1.3 (−2.3–0.4)	−1.6 (−3.1–0.7)	−1.55 (−2.4–0.7)	0.04
PSA reduction (%)		−36.8 (−54.5–23.8)	−47.4 (−61.2 –24.8)	−66.7 (−77.6–55)	−63.8 (−76.4–3.3)	0.00015
Prostate volume (ml) ($n = 191$)	50 (40–70)	−20 (−25.2–14.7)	−26.5 (−36.5–16.5)	−32 (−53.7–22.2)	−30 (−40–20.5)	<0.0001
Prostate volume reduction (%)		35.4 (26.2–46.2)	50 (43.5–59.5)	61 (50–71.4)	60 (50–66.7)	<0.0001

IPSS International Prostate Symptom Score, *Qmax* maximum flow rate, *PVR* post-voiding residual (urine), *QOL* quality of life, *PSA* prostate-specific antigen

* Not measurable in catheterized patients

of a dedicated GreenLight stimulator appears to be a good way to overcome learning curves, which also enhances the patient's safety [20].

We also show that there was an improvement in the early functional outcomes between baseline parameters and early data after PVP in all cases; this agrees with a previous publication from Bachmann et al. [13] who also used a 180-W XPS GreenLight laser. Similar to Seki et al. [19], we also found that short-term functional outcomes were not improved by the parallel improvement in the surgeon's experience. We have demonstrated that GreenLight PVP led to a significant improvement in the subjective and objective voiding parameters in all men included herein.

In our study, 50 and 100 PVP procedures were conducted before there was a decrease in baseline PV of 50 and 60 %, respectively. The decrease in PV became significantly greater after 100 procedures had been completed with respect to a higher amount of total energy and energy/ml of prostate delivered. In this study, the analysis of the relationship between the peri-operative results and the number of surgical cases has demonstrated that vaporization time and total applied laser energy, as well as the weight of vaporized tissue, were increased as the surgeon's experience increased. This suggests that the surgeon spent more time performing vaporization while they gained experience with the procedure. Similar to the enucleation technique using the holmium laser [18], for which there is a clear learning curve, the efficacy of vaporization significantly increased as experience increased with PVP.

Zorn et al. [4] reported that up to 20 interventions were needed on smaller-sized prostates (<40 ml) in order to understand the prostate tissue–laser interaction and to gain experience in the management of intra-operative bleeding. Gomez Sancha et al. [5] advocated that experience with TURP cannot be transposed to PVP, and it would be necessary to achieve between 30 and 50 interventions to overcome the learning curve.

Our 6 % rate of intra-operative conversion into TURP was low and similar to those reported in the literature (1.8–8 %) [13, 21]; in addition, there was a trend toward attenuation of conversion over time. The number of conversions was higher in large PV, but there was no statistical significance until group 3 was reached.

Our post-operative complication rate was comparable to those reported in the literature, both in terms of retention and in terms of macroscopic hematuria [3]. As Seki et al. [19] have reported, we also found that the rate of complications was not statistically linked with the learning curve.

Regarding the duration of bladder catheterization, our results were similar to those reported by Seki et al. [19] regardless of the learning period.

Considering the rate of reoperation for recurrence of adenomatous obstruction, our follow-up period was too short to provide a reoperation rate [21].

In agreement with Reich et al., we believe that the learning curves for PVP are not as simple as some expert TURP surgeons have reported [22, 23]. Learning without training or proctoring could lead to harmful complications and could discredit the technique. It needs to be kept in mind that any kind of urologic laser is a very powerful and potentially dangerous tool that has to be handled with care [17].

Conclusion

In our experience, the PVP learning curves for GreenLight™ 180-W XPS required at least 120 procedures to be conducted to overcome the main intra-operative parameter and to agree with recognized experts in this field. A long-term functional outcome analysis of these first 200 patients would refine the learning phase.

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