



# Moses Laser Enucleation of the Prostate (MoLEP): Use of Pulse Modulated Holmium Laser Technology for Prostate Enucleation

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## Abstract

**Purpose of Review** In this review, the current literature available that evaluates the use of Moses pulse-modulated holmium technology for laser enucleation of the prostate will be addressed. Topics include safety and surgical case efficiency, length of post-operative Foley catheter and hospital stay, surgical outcomes, and areas of future research.

**Recent Findings** Some early retrospective studies and select randomized control trials seek to determine if novel laser technologies can improve peri-operative outcome measures or reduce the morbidity of endoscopic enucleation of the prostate while maintaining or improving the safety profile of holmium laser enucleation of the prostate (HoLEP). Both objective and subjective outcomes of HoLEP are seen to be preserved in patients undergoing Moses laser enucleation of the prostate (MoLEP), with recent studies highlighting high rates of successful same-day catheter removal and same-day discharge in an increasingly wide range of patients.

**Summary** Initial studies focusing on Moses laser technology for prostate enucleation are promising. Further high-quality randomized controlled trials evaluating MoLEP are required to clarify the clinical impact of this laser technology on prostate enucleation outcomes as well as comparing to alternative novel benign prostate hyperplasia (BPH) treatments.

**Keywords** HoLEP · Moses · Pulse modulated · Laser technology

## Introduction

Benign prostatic hyperplasia (BPH) is a very prevalent condition in aging men which can lead to lower urinary tract symptoms (LUTS) requiring medical or surgical intervention. One in five men over 30 years old experiences LUTS from BPH which rises to 80% of men over 70 years old [1]. Endoscopic enucleation of the prostate (EEP) using holmium laser is widely endorsed by international guidelines (American Urological Association (AUA) 2021, Canadian Urological Association (CUA) 2018, European Association of Urology (EAU) 2022, and National Institute for Health

and Care Excellence (NICE) 2010) for the treatment of lower urinary tract symptoms (LUTS) due to BPH [2–5]. Holmium laser enucleation of the prostate (HoLEP) has historically been associated with an overnight stay due to the perceived need for postoperative continuous bladder irrigation (CBI) to manage hematuria and minimize catheter dysfunction or urinary retention risk. However, we know that length of stay (LOS) in the hospital is one of the main drivers of increased health care costs from the perspective of patients, insurers, and health care systems/hospitals themselves. Therefore, as the number of patients requiring intervention for BPH increases with the aging population in countries like the USA, the importance of safely reducing associated LOS while maintaining durable and comparable surgical outcomes of EEP becomes increasingly important.

The “Moses effect,” which was applied clinically to holmium lasers for the treatment of the prostate in 2017, initially separates the fluid medium using the early vapor bubble that is created [6, 7]. The Moses technology delivers the remaining energy towards the target tissue through the space created by the first pulse with less of the energy wave absorbed by the fluid medium. It is important to

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distinguish that the Moses effect occurs whenever the holmium laser is activated in a fluid medium, and it is the utilization of a subsequent Moses 1.0 technology to modulate the holmium:yttrium–aluminum–garnet (Ho:YAG) laser waveform in order to generate a pulse composite of two sub pulses with varying peak powers that is utilized by MoLEP [8]. The initial Moses 1.0 technology was further refined to utilize the high-powered 120W laser and small core Moses fibers in the 2.0 BPH version. The use of the Moses pulse modulated 2.0 BPH mode holmium laser along with the Moses D/F/L laser fibers permits the division of the laser pulse into these two peaks which have been examined in multiple bench side studies for the treatment of prostate tissue and urinary tract calculi [9–12].

These technological improvements in holmium laser energy delivery have been associated with a transition of EEP in many centers away from a predominate blunt dissection technique towards one that utilizes more laser dissection [13]. This theoretical and preclinical improvement in energy delivery may increase enucleation efficiency and hemostasis which could then allow for the transition and evaluation of shorter postoperative catheter duration and shorter length of stay after prostate enucleation in a growing cohort of eligible patients.

## Safety

As with any novel surgical technology, comparing the safety of MoLEP to the current standard is crucial. In one early study with a narrow inclusion criteria, there were no major (Clavien–Dindo  $\geq$  IIIb) 90-day complications including zero repeat surgical interventions in 30 patients undergoing MoLEP with attempted same-day catheter removal [14]. In patients undergoing HoLEP without Moses technology who were discharged on the same day as their surgery, there has been a 28% rate of re-presenting to the emergency department (ED) along with a 17.8% readmission rate within 90 day [15]. In comparison, for patients undergoing MoLEP with subsequent same-day discharge, 7.9–12% were represented to the ED within 90 days, and 1.6% were readmitted [16, 17]. Like other BPH treatments, the etiology for representation to ED after MoLEP included gross hematuria, urinary tract infection, and urinary retention [16, 17]. Other studies examining same-day discharge outcomes for the patient undergoing EEP utilizing Moses technology in the specifically large gland ( $\geq$  175 mL) prostates or in patients having  $\geq$  1 concurrent surgery have reported overall complication rates between 4.8 and 23.6% with only 1.8% high grade complications within 90 days [18]. In that series, the high-grade complication included a 74-year-old patient with preoperative indwelling foley catheter who underwent same day discharge and same day trial of void followed by

development of fever and clot retention  $>$  24 h after discharge [18]. This led to an ED presentation for urosepsis with acute kidney injury requiring temporary ( $<$  14 day) dialysis [18]. Further studies may be valuable in examining whether specific care pathways should exist for patients with indwelling preop foley catheters. Overall, a systematic review and meta-analysis recently concluded that overall 90-day complication rate for MoLEP is equivalent to HoLEP although the majority of current studies are not well-designed randomized control trials (RCTs) comparing these different laser technologies [19].

Interestingly, a study which compared three cohorts of patients who underwent prostate enucleation with Moses technology (planned inpatient admission, successful same-day discharge, and unplanned admission) found that there was no difference in postoperative complication rate between all three cohorts, further supporting same-day discharge attempts in select patients after MoLEP without portending higher complications [16].

Historical HoLEP transfusion rates have ranged from 1 to 4% [20]. The potential improvement in energy delivery to the prostate tissue throughout the duration of the enucleation could improve hemostasis and reduce the risk of transfusion. This is supported by findings from a single center, prospective, double-blind, RCT comparing MoLEP and HoLEP which found less blood loss in patients undergoing MoLEP (mean difference in hematocrit  $-$  6.3% MoLEP vs.  $-$  9.0% HoLEP,  $p=0.03$ ) [21]. However, there were no transfusions required in either cohort. The reduction in bleeding with the aid of Moses technology has also been demonstrated in another RCT that compared MoLEP and HoLEP hemostasis duration per case (4.1 min MoLEP vs. 9 min HoLEP,  $p=0.035$ ) [22].

As the cohort of patients being included in same-day discharge pathways continues to increase within the BPH literature, further well-designed prospective studies will be valuable in identifying hard clinical outcome differences (ex. transfusion rate) between MoLEP and HoLEP as a result of the reported improved hemostasis and reduced blood loss.

## Case Efficiency

EEP is one of the most efficient minimally invasive techniques for the removal of prostate tissue with one RCT finding HoLEP to be more efficient than transurethral resection of the prostate (TURP) and photo-vaporization of the prostate (PVP) (1.7 g/min vs. 1.2 g/min vs. 1.4 g/min, respectively ( $p < 0.001$ )) [23]. Within the literature, the average enucleation efficiency is commonly reported between 0.067 and 6.69 g/min and is impacted by the gland size with higher efficiency achieved in larger glands [24]. One study examining the learning curve of HoLEP over an 8-year period found

that the average initial enucleation efficiency of 0.55 g/min improved to 1.32 g/min, and there could be a potential way of tracking enucleation efficiency improvements for teaching [25]. The rate they obtained near the end of the 8-year study period is similar to results from established surgeons past their learning curve that completed cases using a combination of HoLEP & MoLEP and reported an overall average enucleation efficiency of 1.42 g/min [24]. In contrast to the increased efficiency of enucleation with larger glands, the efficiency of morcellation decreases with one study reporting an average efficiency of 8.27 g/min (range 0.5–39 g/min) [24]. With this increasing inefficiency of morcellation with very large glands, it may be increasingly valuable to save minutes on the enucleation portion of the procedure with the use of Moses technology to keep overall case duration down and maximize operating room resources. Similar to enucleation study results, case efficiency with Moses technology vs. standard holmium for prostate ablation found a similar increased efficiency with the aid of this pulse-modulated technology [26].

In specifically large glands ( $\geq 175$  mL) undergoing EEP, 71% of which were completed with Moses technology, mean enucleation efficiency was found to be 2.34 g/min (range 1.11–4.55 g/min), and morcellation was 8.56 g/min (3.41–22.5 g/min) [18]. However, this study cohort was heterogenous and did not examine the outcomes of only those patients undergoing MoLEP. One RCT has compared MoLEP to HoLEP with case duration as a primary outcome and found increased efficiency with the use of Moses technology (1.75 vs 1.05 g/min,  $p=0.05$ ) [22].

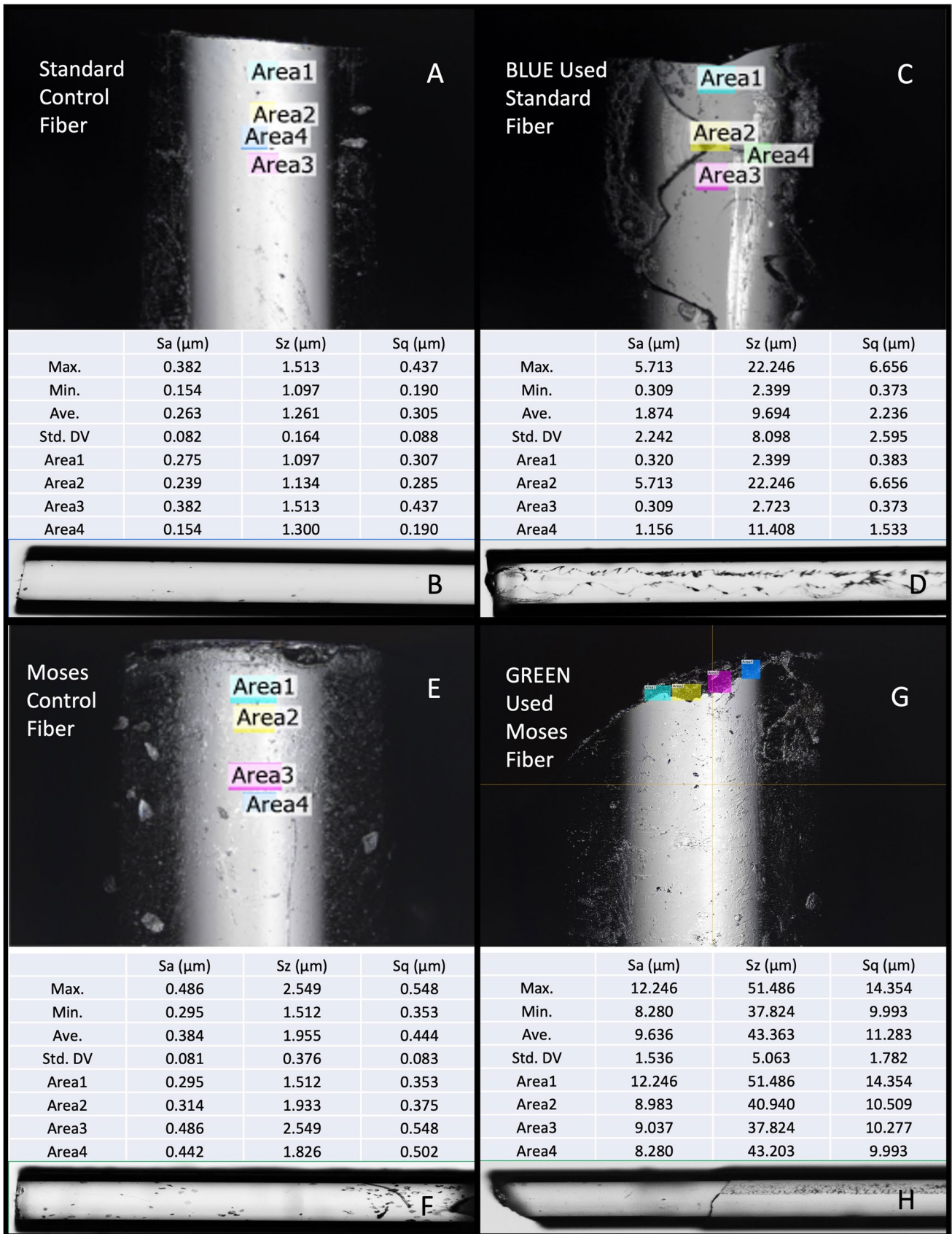
Along with improving the efficiency of the EEP procedure itself, the addition of concurrent surgeries at the time of BPH treatment can improve the health care resource utilization and minimize the need for multiple anesthetics for these patients. Increased efficiency of the prostate enucleation component of the case could provide the opportunity to safely manage other medical issues with concurrent surgery. In one study, MoLEP with  $\geq 1$  concurrent surgery was shown to be an efficient way to manage multiple patient problems without impacting outcome measures or complications [27].

One of the key aspects of MoLEP is improved energy transmission to the target tissue at a range of distances compared to standard HoLEP. It is hypothesized that this improved energy transmission results in less potential laser fiber damage which has been observed as reduced laser fiber degradation and surgical case interruption to re-strip the laser fiber with shorter intraoperative enucleation times reported for MoLEP (Fig. 1) [22, 28, 29]. Less damage to the laser fiber tip was associated with shorter operative time for patients undergoing MoLEP compared to HoLEP in a single-center RCT [21]. A recent commentary from Corsini et al. (2022) described that the shorter time for hemostasis and case efficiency that was found during MoLEP vs. HoLEP

(8.1 vs. 10.6 min) by Nottingham et al. may not have significant clinical implications and questioned whether the mean time to hemostasis (mean difference  $-3.9$  min,  $p < 0.001$ ) could be attributed to the learning curve. However, the surgeons performing the HoLEP and MoLEP in that study were all well beyond the described learning curve within the literature (20–60 cases) [8, 29–32]. Similarly, the authors comment that the RCT from Kavoussi et al. showing shorter operative time (mean difference 25 min,  $p < 0.01$ ) and hemostasis time with MoLEP vs. HoLEP does not clearly demonstrate this finding due to potential differences in prostate sizes between groups. However, there was no statistically significant difference to support that the gland sizes were different in that study, and the hemostasis outcome remained significant on multiple linear regression [8, 21]. Conversely, when interpreting this RCT, it is important to recognize that the outcome was reported per-protocol instead of the intention to treat for which it was initially designed and that the difficulty in effectively blinding the treating surgical team to the presence or absence of Moses technology may bias the results [33]. Although there is overall limited well designed RCTs with the primary outcome of surgical efficiency, a systematic review and meta-analysis of the current literature identified mean enucleation time is shorter for MoLEP versus HoLEP (mean difference  $-7.27$  min, 95% CI:  $-11.26$  to  $-3.28$  min,  $p < 0.001$ ) [34].

## Same-Day Catheter Removal

A pilot study by Agarwal et al. (2020) examined the use of Moses holmium technology optimized for BPH with respect to same-day catheter removal [14]. In 30 select patients with a pre-operative prostate volume of 81 mL (IQR 53–114.8 mL), 90% of patients successfully voided on the day of their HoLEP without requiring re-catheterization [14]. In the 10% that failed same-day trial of void (TOV), all had the catheter successfully removed on post-operative day (POD) 1. This pilot did exclude patients with very large glands ( $> 250$  mL), cases occurring later in the day and patients with active anticoagulation. The median time from the end of surgery to the first catheter removal in this cohort was 4.9 h (IQR 3.5–6.0 h). Two of the three patients who failed same-day TOV occurred immediately after the catheter was removed, while the third failed later that evening requiring a re-presentation to the emergency department. Since that early pilot study, a recent publication examined same-day TOV and same-day discharge in specifically large gland prostates. This study found that in 55 patients with glands  $\geq 175$  mL, 71% of which utilized Moses technology, 45/55 (82%) were eligible for same-day TOV [18]. Of these 55 patients, 66% were in urinary retention at the time of surgery ( $n=32$  indwelling catheter,  $n=4$  clean





**Fig. 1** 3D-confocal laser scanning reflection microscopy (A, C, E, G) of control fibers and representative damaged fibers of each standard and Moses fiber tips indicating damage after prostate enucleation treatments. Surface roughness parameters measured at indicated locations (areas 1–4), for each fiber (blue = standard, green = Moses technology) covering the maximum damage surface per fiber is shown with raw data below. Brightfield optical microscopy of the control and used fibers (B, D, F, H) depicted

intermittent catheterization) [18]. A comparison study of 255 MoLEP cases to 180 HoLEP cases found that there was no statistically significant association with short-term catheter reinsertion between groups [35]. However, this study had a higher than reported rate of cystoscopy clot evacuation and fulguration after EEP, as well as higher short term catheter re-insertion rates than is typically observed at a high-volume center (14% HoLEP VS. 10% MoLEP) [35].

### Length of Stay

In a pilot study using the Moses technology, the median length of stay from the time of procedure end to discharge was 2.6 h (IQR 2.1–2.9 h) for very select patients that had a successful same-day catheter removal [14]. Prior to the evaluation of MoLEP, the safety and success of same-day discharge for patients undergoing HoLEP were being evaluated by multiple studies with success rates ranging widely from 15.6–96.7% depending on eligibility criteria [15, 36–38]. The eligibility for same-day discharge in these studies was narrow with only 47/179 and 90/211 patients undergoing HoLEP meeting same-day discharge criteria [15, 36]. In one HoLEP study examining same-day discharge, patients were initially excluded if they had known prostate cancer, American Society of Anesthesiology (ASA) score > 3, prostate volume > 200 mL, age > 75 years old, the surgery ended > 1 pm, enucleation duration was > 1 h, morcellation time > 30 min, lack of care giver, and residing outside city limits [15]. Recently, published MoLEP studies have shown safe and successful same-day discharge in these patients previously felt high risk for same-day discharge including those > 75 years old, patients with > 200 mL prostate volumes, enucleation lasting > 1 h, morcellation > 30 min, surgery ending > 1 pm, and those with known prostate cancer [16, 30]. Despite these outcomes, characteristics associated with increased planned inpatient admission were found to be age, use of anticoagulation, ASA  $\geq$  3, and enucleation duration [16].

The most common reason for failed same-day discharge is a degree of hematuria in the absence of continuous bladder irrigation with one study showing higher unplanned admissions associated with a rate of post-operative bedside catheter irrigation for the degree of hematuria [16]. Another study which examined 207 patients planned for outpatient surgery

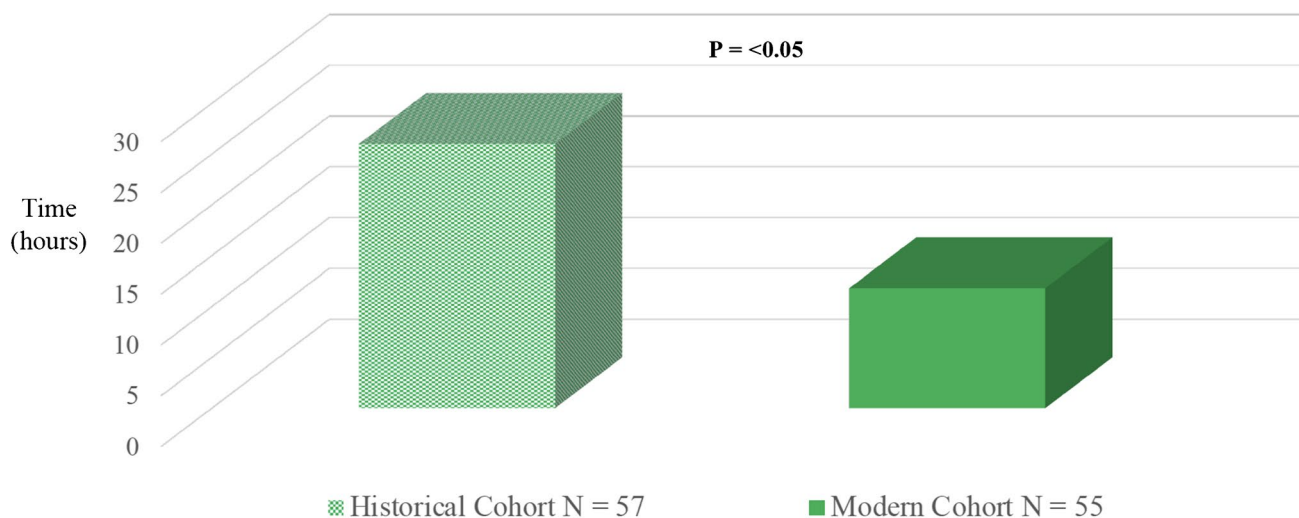
identified that the use of Moses technology resulted in a higher rate of same-day discharge success [16]. Historical outcomes for patients undergoing HoLEP found that gland size affected the success of same-day discharge, while recent publications which include MoLEP found high all-comer rates (70%) of same-day discharge success even in these very large prostates ( $\geq$  175 mL) [15, 16, 18]. The same-day discharge success in specifically large gland prostates undergoing MoLEP that were planned for same-day discharge pathway was 84% [18]. When comparing LOS in very large glands at a single high-volume center with the use of Moses technology compared to historical large gland HoLEP LOS, there was a significant reduction in LOS (Fig. 2). The findings described above are supported by a shorter LOS in patients undergoing MoLEP vs. HoLEP in the systematic review and meta-analysis comparing 214 MoLEP cases to 267 HoLEP cases (mean difference – 0.3 d).

### Anti-Coagulant/Anti-Platelet Medications

In a small single-center study examining 50 consecutive patients who use anti-coagulant or anti-platelet medications > ASA 81 mg daily and underwent MoLEP with an average gland size of 75.5 mL (range 10–215 mL), successful same-day discharge occurred in 32/37 (86.5%) of eligible patients. Additionally, 29/33 (87.9%) patients with planned same-day catheter removal were successful in this complex cohort of patients [13]. None of these patients required urologic surgery within 90 days, and only 6% were re-admitted [13]. Of note, 62% were able to hold their perioperative medication resulting in a heterogeneous patient cohort, and to date, there is no well-designed RCT examining MoLEP vs HoLEP outcomes in patients that continued all anticoagulation/antiplatelet medications throughout the operative period.

### Post-Operative Outcomes

The median American Urological Association (AUA) symptom score (AUASS) post-MoLEP was significantly reduced from 18 (IQR 13–29) to 5 (IQR 2–5) with a quality of life (QOL) score improving from 4 (IQR 3.5–5.5) to 1 (IQR 0–2) [14]. These validated symptom outcomes were also demonstrated in specifically large prostates undergoing MoLEP with AUASS improvements at 3 month follow up (22.3 vs. 6.7,  $p < 0.05$ ) [18]. Looking at objective outcome measures, post-MoLEP median post-void residual (PVR) was reduced from 82 mL (IQR 30–132 mL) to 16 mL (IQR 8–37 mL) [14]. Post-MoLEP prostate-specific antigen (PSA) was reduced to 0.7 ng/mL (IQR 0.36–1.0) in one study while a second showed PSA reduction from 8.58 to 0.87 ng/mL



**Fig. 2** Comparison of mean length of stay for patients assessed to have very large glands ( $\geq 175$  mL) undergoing prostate enucleation in a historical cohort (without Moses technology) and a modern cohort (with Moses technology)

comparable to that reported in the HoLEP literature [14, 18]. Any degree of transient urinary incontinence post-MoLEP occurred in 37.5% of patients, which decreased to 6.3% at 3 months follow up [14]. Long term follow up studies are required to compare LUTS and urinary incontinence outcomes head to head between MoLEP and HoLEP. Qmax improvements have also been demonstrated with MoLEP (preop 8.8 mL/s vs. 20.4 mL/s postop,  $p < 0.05$ ) [18]. These results are comparable to long term  $\geq 10$  year follow up studies of HoLEP which reported postoperative Qmax rates of 16 mL/s [13–23], PVR 10 mL (5–15 mL), International Prostate Symptom Score (IPSS) 5 [1–7] and postop PSA of 0.7 ng/mL (0.4–1.4 ng/mL) [20].

A retrospective comparison of MoLEP and HoLEP found subjective postop IPSS, IPSS QOL, Michigan Incontinence Severity Index (MISI) bother and Sexual Health Inventory in Men (SHIM) at 3 months follow up were not different between groups (all  $p > 0.05$ ) [30]. When comparing objective measures, they again found no difference in postop uroflow metrics (ex. Qmax) and PVR between groups [30]. One systematic review and meta-analysis found that mean PVR was lower in the MoLEP outcomes vs. HoLEP, while mean Qmax favored HoLEP although both cohorts saw significant improvement compared to pre-intervention flow rates [34].

## Discussion

Overall, MoLEP has been shown to preserve objective and subjective outcomes seen with HoLEP with many studies seeking to reduce patient perioperative morbidity by expanding inclusion criteria of patients eligible for concurrent surgery at the time of HoLEP, same-day catheter removal and

same-day discharge. The safety of these changes to patient care has been demonstrated to be equal to that of HoLEP. There is some evidence to support increased enucleation efficiency and improved hemostasis with MoLEP, although further well-designed prospective RCTs may better clarify the clinical implications of these improvements.

Further studies will be beneficial to examine the impact Moses technology has on the learning curve of EEP compared to HoLEP. A double-blinded, randomized study of patients undergoing EEP treated 27 patients with half of the enucleation done with MoLEP and the other half done with HoLEP [22]. In trainees, the MoLEP cohort had shorter hemostasis laser time and non-validated subjective evaluation of case videos by 2 reviewers reported better incision sharpness, fiber control, tissue separation, hemostasis, and visibility compared to HoLEP [22]. Further studies are required to examine if the improved hemostasis and visualizing translates into a clinically significant impact on the learning curve.

A single publication has examined the cost of HoLEP vs MoLEP at a single center in the USA. Of 312 men undergoing EEP (192-MoLEP, 120-HoLEP), MoLEP resulted in hospital cost savings of \$840.00 for the initial surgical episode ( $p = 0.030$ ), and when accounting for ED representation rates, which were higher in the MoLEP group, that savings was lower at \$747.00/case ( $p = 0.057$ ) [39]. Further studies are needed to explore the generalizability of these findings to other centers and other health systems outside the USA.

At the time of this review, there are a few studies examining MoLEP outcomes registered with ClinicalTrials.gov. One study is a double blinded, prospective RCT examining MoLEP vs. HoLEP with a primary outcome of 24-h postoperative hemoglobin change (NCT04648176). Other

studies seek to compare MoLEP to alternative laser EEP (ex. Thulium fiber laser) with the primary outcome of LOS (NCT04807296 & NCT05240001). Finally, there is an RCT of MoLEP patients with and without the addition of intra-operative tranexamic acid examining the primary outcome of same-day discharge success.

## Conclusion

The current literature on MoLEP highlights comparable objective and subjective postoperative outcomes to HoLEP with similar complication rates, although there are few well-designed prospective RCTs evaluating MoLEP versus HoLEP or alternative minimally invasive BPH treatments. Some MoLEP studies have sought to improve EEP care by reducing catheter duration, increasing eligible and successful same-day discharge rates, improve surgical case efficiency and the ability to safely complete concurrent surgeries at the time of MoLEP. Despite these valuable and encouraging studies, there remain multiple areas for future research to best understand the widespread clinical impact of MoLEP on BPH surgical training and patient care.

## Declarations

**Conflict of Interest** Mark Assmus declares that he has no conflict of interest.

Amy Krambeck is a consultant for Boston Scientific, Lumenis, Ambu, Storz, Virtusoso Surgical and is on the data safety monitoring board for Sonomotion and Uriprene.

**Human and Animal Rights and Informed Consent** All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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