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MOSES™ Technology for Holmium Laser Enucleation of the Prostate: A Prospective Double-Blind Randomized Controlled Trial

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Abbreviations and Acronyms

BPH = benign prostatic hyperplasia

HoLEP = holmium laser enucleation of the prostate

IIEF-5 = International Index of Erectile Function 5-item version

IPSS = International Prostate Symptom Score

M-HoLEP = MOSES™ enucleation of the prostate

PSA = prostate specific antigen

QoL = quality of life

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Purpose: Holmium laser enucleation of the prostate has proven to be efficacious and safe for the treatment of benign prostatic hyperplasia. New laser technologies, such as the MOSES™ pulse laser system, improve energy delivery and may improve operative times. We sought to prospectively evaluate holmium laser enucleation of the prostate using MOSES technology in a double-blind randomized controlled trial.

Materials and Methods: This is a single-center, prospective, double-blind, randomized controlled trial comparing holmium laser enucleation of the prostate using MOSES technology to holmium laser enucleation of the prostate. Patients were randomized in a 1:1 fashion. The study was powered to evaluate for a difference in operative time. Secondary end points included enucleation, morcellation, and hemostasis times, as well as blood loss, functional outcomes and complications 6 weeks postoperatively.

Results: A total of 60 patients were analyzed without difference in preoperative characteristics in either group (holmium laser enucleation of the prostate using MOSES technology: 30/60, 50%, holmium laser enucleation of the prostate: 30/60, 50%). Shorter total operative time was seen in the holmium laser enucleation of the prostate using MOSES technology group compared to the holmium laser enucleation of the prostate group (mean: 101 vs. 126 minutes, $p < 0.01$). This difference remained significant on multiple linear regression. Additionally, the holmium laser enucleation of the prostate using MOSES technology group had shorter enucleation times (mean: 68 vs. 80 minutes, $p = 0.03$), hemostasis time (mean: 18 vs. 29 minutes, $p < 0.01$), and less blood loss (mean: −6.3 vs. −9.0%, $p = 0.03$), measured by a smaller change in hematocrit postoperatively, compared to the traditional holmium laser enucleation of the prostate. There was no difference in functional or safety outcomes at followup.

Conclusions: We report the results of a prospective, double-blind, randomized controlled trial comparing holmium laser enucleation of the prostate using MOSES technology to traditional holmium laser enucleation of the prostate. MOSES technology resulted in an improvement in operative time and a reduction in blood loss with comparable functional outcomes and complications compared to traditional holmium laser enucleation of the prostate.

Key Words: prostatic hyperplasia; lasers, solid-state

Benign prostatic hyperplasia is common with almost 50% of men having pathological changes in the prostate between 50 and 60 years old.[1] The American Urological Association Guidelines support laser enucleation of the prostate as

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a size-independent technique for treating lower urinary tract symptoms attributed to BPH.[2] The procedure has been performed using different energy sources, such as electrocautery, KTP, and thulium and holmium lasers.[3–5] Of these, multiple trials have proven that holmium laser enucleation of the prostate is efficacious, safe and durable.[6–8]

Despite this, HoLEP remains underutilized throughout the United States for multiple reasons.[9] There is a learning curve for the procedure, which may be associated with increased operative times, blood loss, and complications early in a surgeon's experience.[10] However, recent evidence suggests that advances in holmium laser technology may improve adoption of the technique.[11] An example of this is the MOSES™ laser platform developed by Lumenis (Yokneam, Israel). The laser system provides for the division of the laser pulse into 2 peaks: the first to separate water (ie bubble formation) and the second to deliver laser energy to a target.[12] The improved energy delivery is believed to increase efficiency during HoLEP and reduce operative time as well as blood loss.

A prior retrospective study showed possible advantages in operative time and hemostasis using the MOSES laser.[11] We sought to evaluate the effects of the MOSES laser on operative times for prostatic enucleation prospectively. To do so, we performed a double-blind, randomized controlled trial comparing MOSES enucleation of the prostate to traditional HoLEP.

METHODS

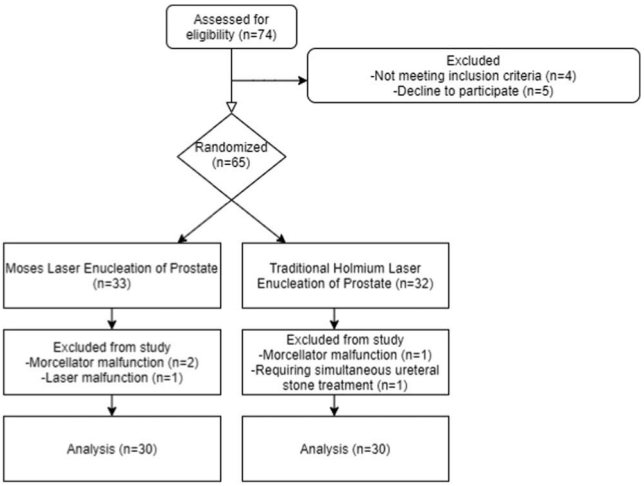
Study Design and Participants

We performed a prospective, double-blind, randomized controlled trial comparing MOSES laser technology to traditional holmium laser settings for enucleation of the prostate (ClinicalTrials.gov, NCT 04263987). Included patients were men older than 45 years of age with a prostate size greater than 80 cc as measured by transrectal ultrasound, magnetic resonance imaging, or computerized tomography, moderate or severe symptoms indicated by International Prostate Symptom Score, undergoing prostate enucleation for surgical treatment.

Men were excluded if they had a history of prostate cancer, concomitant bladder or upper tract stone disease requiring treatment at the time of their procedure, acute urinary tract infection, or urethral stricture disease. All anticoagulation and antiplatelet medications were held perioperatively. All participants provided written informed consent and the study was approved by the local institutional review board (IRB No. 182310). All observed adverse events were recorded for the study duration and reported per institutional protocol.

Randomization and Surgical Procedure

Patients were assigned at random in a 1:1 ratio to M-HoLEP or HoLEP and blinded to their assignment. Randomization was performed through a web-based system and assignments were concealed in envelopes. At the start of each case, a laser technician would open the envelope and activate either MOSES or traditional settings without informing the operating surgeon of the setting being used. The Lumenis 120H dual pedal laser unit, as well as a MOSES 550 μm laser fiber, were used for every case. This fiber can be used in both MOSES and traditional settings, allowing for the blinding of the operating surgeon. During the case, the surgeon was asked to try and identify whether or not MOSES settings were activated.



Flow diagram of study

The laser system was routinely used at an energy of 2J and frequency between 20 and 40 Hz. Prostatic enucleation was performed via a 2-lobe, bottom-up technique in all cases by a single surgeon. Complete hemostasis was achieved after enucleation. Normal saline was routinely used as the irrigation fluid and intravenous fluids were managed by the anesthesia team. Morcellation was performed with the Wolf (Sunrise, Florida) PIRANHA morcellator at a frequency between 500 and 1,500 rpms.

A 22F 3-way catheter was placed at the end of the procedure for continuous bladder irrigation. All patients were admitted postoperatively and monitored in-house. On postoperative day 1, patients had a blood draw for hematocrit. Patients underwent a voiding trial prior to or within 1 week after discharge. All patients had a followup appointment scheduled for 6 weeks postoperatively. Patients and providers were blinded to randomization assignment until after the 6-week followup visit.

Study Outcomes

The primary study outcome was change in total operative time. Secondary outcomes included enucleation, morcellation and hemostasis times, as well as blood loss measured by change in hematocrit. Intraoperative intravenous fluid volume and total laser energy used were also recorded. Further outcomes included complications (based on the Clavien-Dindo Classification), length of stay and catheterization time, as well as 6-week postoperative changes in prostate specific antigen, noninvasive uroflow measurements, and symptoms evaluated using IPSS, IPSS Quality of Life, and the International Index of Erectile Function 5-item version scores.[13]

Table 1. *Preoperative patient information*

	MOSES	Standard HoLEP
No. pts	30	30
Mean±SD yrs age	70.1± 8.2	68.6 ± 6.1
Mean±SD kg/m^2 body mass index	28.6± 4.1	29.9 ± 5.2
No. diabetes mellitus history (%)	5 (17)	9 (30)
No. hypertension history (%)	22 (71)	15 (50)
Mean±SD Charlson comorbidity index	2.5± 1.3	2.75± 1.2
No. pt on anticoagulation/antiplatelet prior to surgery (%)	10 (33)	9 (30)
No. preop retention requiring indwelling or intermittent catheterization (%)	10 (33)	8 (27)
No. prior prostatic surgery (%)	4 (13)	2 (7)
Mean±SD IPSS score	19.5± 7.4	18.3 ± 8.1
Mean±SD IPSS QoL score	4.2±0.89	3.7 ± 1.1
Mean±SD IIEF-5 score	11.3± 6.8	10.1 ± 7.6
Mean±SD cc/s preop flow rate*	7.9± 4.6	7.5 ± 5.7
Mean±SD % preop voiding efficiency*	58.9±34.2	47.6 ±37.5
Mean±SD preop hematocrit	44.0± 4.4	45.1 ± 3.2
Mean±SD preop ng/ml PSA	6.1± 2.6	5.6 ± 2.5
Mean±SD preop gm prostate size estimation	131 ± 41	153 ± 58

* Preoperative flow rate or voiding efficiency was not calculated for patients managed with indwelling catheter or on intermittent catheterization regimen (calculated in 13 MOSES patients and 14 traditional HoLEP patients).

Power and Statistical Analysis

Power analysis was performed for sample size estimation based on prior reports from the literature, which previously estimated a 20% improvement in operative time when performing M-HoLEP.[11] A sample size of 60 subjects had greater than 80% power to detect this change with $\alpha=0.05$. Continuous and categorical variables were compared using the Student T-test (2-tailed) and Fisher exact test, respectively. Multiple linear regression was performed to evaluate for the effect of the MOSES technique on operative time controlling for age, Charlson comorbidity index, change in hematocrit, and the amount of prostatic tissue enucleated. All testing was performed with $p<0.05$ as significant. All analyses were conducted in Stata 14.2 (StataCorp, College Station, Texas).

RESULTS

A total of 74 patients at our institution were evaluated for possible enrollment in the study in a 12-month period (July 2019 to July 2020). Excluding 9 preoperatively for not meeting inclusion criteria or declining to participate in the study, 65 patients were randomized. Two patients in the M-HoLEP group were excluded due to morcellator malfunction and laser malfunction. One patient was excluded in the HoLEP group due to morcellator malfunction, while another was excluded due to requiring concomitant ureteral stone treatment at time of surgery. Thus, 60 patients were analyzed (see figure). Baseline characteristics were equal between the groups (table 1). Specifically, there was no difference in age, comorbidities, IPSS scores, preoperative hematocrit, or measured prostate size between groups.

On univariate analysis, total operative time significantly favored the M-HoLEP group compared to the HoLEP group (101 vs. 126 minutes, $p<0.01$). Specifically, enucleation (68 vs. 80 minutes, $p=0.03$) and hemostasis (18 vs. 29 minutes, $p<0.01$) times were significantly improved in the M-HoLEP group compared to HoLEP group, but morcellation times were not significantly different. Additionally, change in hematocrit was significantly less for the M-HoLEP group compared to the HoLEP group (−6.4 vs. −9.0, $p=0.03$). There were no blood transfusions in either group. Furthermore, there was no difference in intraoperative energy utilization, estimated blood loss, prostate tissue removed or total intravenous fluid volume (table 2). Postoperatively, there was no difference in catheterization time, length of hospitalization time, change in PSA, noninvasive uroflow measurements, change in IPSS or IPSS QoL score, nor complication rate (table 3). IIEF-5 scores were obtained in a subset of patients (21) but showed no difference between groups. The surgeon was only able to accurately determine whether or not MOSES settings were activated in 42% of cases.

There were 3 complications in the M-HoLEP group and 4 in the HoLEP group (all grade I or II). In the M-HoLEP group, 2 patients had cystitis postoperatively requiring antibiotics and 1 patient had urinary retention requiring temporary catheter replacement. Only 1 of these patients was in retention preoperatively. In the HoLEP group, 2 patients had cystitis requiring antibiotics, 1 patient had retention requiring temporary catheter replacement, and 1 patient returned to the emergency department

Table 2. *Perioperative outcomes*

	MOSES	Standard HoLEP	p Value
No. pts	30	30	
Mean±SD mins total operative time (IQR)	101 ±30 (84—131)	126 ±22 (106—145)	<0.01
Mean±SD mins enucleation time (IQR)	68 ±20 (54—85)	80 ±19 (65—95)	0.03
Mean±SD mins morcellation time (IQR)	14 ±10 (7—21)	16 ±10 (9—20)	0.27
Mean±SD mins hemostasis time (IQR)	19 ± 8 (11—23)	29 ±15 (20—31)	<0.01
Mean±SD change in hematocrit	−6.4± 4.1	−9.0± 4.6	0.03
Mean±SD days length of hospital stay	1.1± 0.64	1.2± 0.61	0.20
Mean±SD days length of catheterization	1.2± 0.63	1.1± 0.50	0.79
Mean±SD kJ energy used	130 ± 47	143 ±27	0.23
Mean±SD cc estimated blood loss	115 ± 34	133 ±60	0.15
Mean±SD gm prostate tissue removed	65 ± 29	76 ±28	0.15

Table 3. *6-Week postoperative outcomes*

	MOSES	Standard HoLEP	p Value
No. pts	30	30	
Mean±SD ng/ml change in PSA	−4.5 ± 2.8	−4.3 ± 3.5	0.84
Mean±SD % change in PSA	−82 ±15	−83 ±19	0.86
Mean±SD L total intravenous fluid vol	2.1 ± 1.1	1.2 ± 0.43	0.78
Mean±SD change in IPSS	−11.9 ± 9.3	−11.5 ± 9.8	0.55
Mean±SD change in IPSS QoL	−2.80 ± 1.7	−2.79± 1.84	0.98
Mean±SD change in IIEF-5*	−1.4 ± 0.76	1.0 ± 0.31	0.91
Mean±SD % change in voiding efficiency	37 ±45	21 ±50	0.10
No. complication rate (%)	3 (10)	4 (13)	0.69

* IIEF-5 scores were obtained on 21 patients (MOSES = 16, Standard = 5).

for a syncopal episode and required intravenous fluids. All patients requiring catheter for retention passed subsequent voiding trials.

A multiple linear regression was performed to predict operative time based on use of MOSES technology as well as age, Charlson comorbidity index, change in hematocrit, and total size of the prostate enucleated. Total operative time decreased with use of MOSES technology (−17.4, $p < 0.01$; table 4).

DISCUSSION

This is the first prospective study evaluating MOSES laser technology compared to traditional holmium laser for prostate enucleation in the setting of lower urinary tract symptoms attributed to BPH. We found an improvement in total operative time, enucleation time and hemostasis time when performing M-HoLEP compared to HoLEP. The improved energy delivery of the technology likely leads to more effective tissue ablation and hemostasis during enucleation, improving visibility and allowing the surgeon to operate efficiently. Though blood loss and the amount of prostate tissue removed could confound our findings, multiple linear regression analysis maintained a significant improvement in operative time while controlling for age, Charlson comorbidity index, change in hematocrit and amount of prostate tissue removed. Of note, operative time also independently correlated with prostate size on linear regression analysis. Morcellation times were unchanged, as there was no difference in the amount of tissue being removed between groups. The decrease in operative time may be advantageous from a cost perspective as has been seen in prior studies evaluating the MOSES laser for stone treatment.[14] However, a more robust analysis is required to determine the cost benefit of MOSES technology for prostatic enucleation.

Functional outcomes, hospitalization and catheterization times, as well as complications were no different between groups, suggesting safety and efficacy of the MOSES settings compared to traditional HoLEP. We also found an improvement in blood loss measured by change in hematocrit. Though hematocrit can be impacted by volume status (both from intravenous and irrigation fluids intraoperatively), this outcome is a clinically relevant laboratory value used routinely to assess for bleeding and to determine the need for blood transfusion. Notably, there were no transfusions in either group. Though other studies have shown an average transfusion rate of 2%−7% for HoLEP, it is likely that surgical experience is associated with transfusion risk, which would be low at a high volume institution.[15–17] We believe that improvements in hemostasis with the MOSES technology may be integral to performing the procedure in an outpatient setting.[16]

A prior retrospective study showed similar improvements to our findings following prostatic enucleation when using the MOSES laser technology. Large et al compared 3 groups categorized by fiber used during prostatic enucleation (MOSES 550 μm, Slimline 550 μm, and Slimline 1,000 μm).[11] They found an improvement in change in hemoglobin when using MOSES technology as well as a 3.9-minute decrease in time to achieve hemostasis. These advantages are facilitated by novel laser optimization technology.[18] The wavelength of the holmium laser (2,100 nm) is highly absorbed in water, leading to microbubble formation and the attenuation of energy as it approaches the target.[19] By modulating the laser pulse into 2 peaks, bubble formation is carefully controlled to allow for increased energy delivery to a target.[20] In vitro studies have shown this effect leading to 10% more laser radiation to a target as well as transmission of the energy over longer distances.[19]

Table 4. *Multiple linear regression analysis of factors affecting total operative time*

	Coefficients (standard error)	p Value
M-HoLEP (binary data)	−17.4 (−30—−4.7)	<0.01
Age	0.58 (−0.52—1.67)	0.30
Charlson comorbidity index	−0.79 (−7.6—6.0)	0.82
Change in hematocrit	0.65 (−0.87—2.2)	0.40
Prostate tissue removed	0.51 (0.28—0.74)	<0.01

$p < 0.05$ was considered statistically significant.

To our knowledge, this study is the first prospective, double-blind, randomized controlled trial to evaluate MOSES technology for prostatic enucleation. There are some limitations to our study. This is a single institutional study with a short followup of 6 weeks. As such, long-term effects or complications cannot be assessed. As a high volume HoLEP center, conclusions related to wider applicability of the technology could be limited. Additionally, the long-term effects of the MOSES settings cannot be evaluated by our study. Anticoagulation or antiplatelet agents were held perioperatively, prohibiting the assessment of the technology for patients on these medications.

Regardless, our results suggest the efficiency, safety and effectiveness of MOSES laser technology for prostate enucleation in the treatment of BPH. Further multi-institutional studies, as well as more rigorous cost analysis across multiple institutions, are necessary.

CONCLUSIONS

We report the results of a prospective, double-blind randomized controlled trial comparing M-HoLEP and HoLEP. M-HoLEP improves operative time and hemostasis, with similar functional and safety outcomes compared to traditional HoLEP.

REFERENCES

1. Berry SJ, Coffey DS, Walsh PC et al: The development of human benign prostatic hyperplasia with age. J Urol 1984; **132:** 474.
2. Yin L, Teng J, Huang C et al: Holmium laser enucleation of the prostate versus transurethral resection of the prostate: a systematic review and meta-analysis of randomized controlled trials. J Endourol 2013; **27:** 604.
3. Pirola GM, Saredi G, Codas-Duarte R et al: Holmium laser versus thulium laser enucleation of the prostate: a matched-pair analysis from two centers. Ther Adv Urol 2018; **10:** 223.
4. Elshal AM, Elkoushy MA, El-Nahas A et al: GreenLight laser (XPS) photoselective vapoenucleation versus holmium laser enucleation of the prostate for the treatment of symptomatic benign prostatic hyperplasia: a randomized controlled study. J Urol 2015; **193:** 927.
5. Boeri L, Capogrosso P, Ventimiglia E et al: Clinical comparison of holmium laser enucleation of the prostate (HoLEP) and bipolar transurethral enucleation of the prostate (BTUEP) in patients under either anticoagulation or antiplatelet therapy. Eur Urol Suppl 2019;**181:** e1924.
6. Humphreys MR, Miller NL, Handa SH et al: Holmium laser enucleation of the prostate—outcomes independent of prostate size? J Urol 2008; **180:** 2431.
7. Montorsi F, Naspro R, Salonia A et al: Holmium laser enucleation versus transurethral resection of the prostate: results from a 2-center, prospective, randomized trial in patients with obstructive benign prostatic hyperplasia. J Urol 2004; **172:** 1926.
8. Krambeck AE, Handa SE and Lingeman JE: Experience with more than 1,000 holmium laser prostate enucleations for benign prostatic hyperplasia. J Urol 2010; **183:** 1105.
9. Robles J, Pais VM and Miller N: Mind the gaps: adoption and underutilization of holmium laser enucleation of the prostate (HoLEP) in the United States from 2008-2014. J Endourol 2020; **34:** 770.
10. Peyronnet B, Robert G, Comat V et al: Learning curves and perioperative outcomes after endoscopic enucleation of the prostate: a comparison between GreenLight 532-nm and holmium lasers. World J Urol 2017; **35:** 973.
11. Large T, Nottingham C, Stoughton C et al: Comparative study of holmium laser enucleation of the prostate with MOSES enabled pulsed laser modulation. Urology 2020; **136:** 196.
12. Ibrahim A, Badaan S, Elhilali MM et al: MOSES technology in a stone simulator. Can Urol Assoc J 2018; **12:** 127.
13. Mitropoulos D, Artibani W, Biyani CS et al: Validation of the Clavien-Dindo grading system in urology by the European Association of Urology Guidelines ad hoc panel. Eur Urol Focus 2018; **4:** 608.
14. Stern KL and Monga M: The MOSES holmium system—time is money. Can J Urol 2018; **25:** 9313.
15. Romero-Otero J, Garcia-Gonzalez L, Garcia-Gomez B et al: Factors influencing intraoperative blood loss in patients undergoing holmium laser enucleation of the prostate (HoLEP) for benign prostatic hyperplasia: a large multicenter analysis. Urology 2019; **132:** 177.
16. Elzayat EA, Habib EI and Elhilali MM: Holmium laser enucleation of the prostate: a size-independent new "gold standard". Urology, suppl., 2005; **66:** 108.
17. Martin AD, Nunez RN and Humphreys MR: Bleeding after holmium laser enucleation of the prostate: lessons learned the hard way. BJU Int 2011; **107:** 433.
18. Vincent MW and Gilling PJ: HoLEP has come of age. World J Urol 2015; **33:** 487.
19. Ventimiglia E and Traxer O: What is MOSES effect: a historical perspective. J Endourol 2019; **33:** 353.
20. Fried NM and Irby PB: Advances in laser technology and fibre-optic delivery systems in lithotripsy. Nat Rev Urol 2018; **15:** 563.