

Article

Holmium Laser Enucleation of the Prostate Efficiency by Prostate Gland Size: Is There a Sweet Spot?

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Abstract: Holmium laser enucleation of the prostate (HoLEP) is one of only two AUA guideline-recommended prostate size-independent surgeries for benign prostate hyperplasia (BPH). The significant variation in gland size treated results in a wide range of enucleation and morcellation times. We sought to understand the effect of prostate size on HoLEP efficiency to better educate patients and improve operative room utilization. After IRB approval, we identified patients from 1 July 2016 to 1 January 2020 who underwent HoLEP by two endourologists. Our primary objectives were to assess the effects of increasing increments (25 g) of mean enucleated prostate tissue weight on enucleation and morcellation efficiency (g/min). One-way Kruskal–Wallis ANOVA with Dunn’s post hoc test was used, with significant $p < 0.05$. We included 675 HoLEPs with all comers mean tissue weight resected of 72.1 g (Range 1–448 g), energy used 110.00 kJ (10.73–340 kJ), enucleation time 48.6 min (5–151 min), and morcellation time 10.1 min (0.5–113 min). Average enucleation efficiency increased with increasing prostate size categories (e.g., <25 g–0.48 g/min, >325 g–3.91 g/min) (K-W ANOVA $p = 0.004$, Dunn’s post hoc $p = 0.004$). The combined average enucleation and morcellation efficiency was ≥ 5 g/min between 55 and 271 g. Inefficiency for cases <55 g was driven by enucleation, while >271 g case inefficiency was driven by morcellation. Increasing tissue weight at the time of HoLEP is associated with a linear relationship of increasing enucleation and decreasing morcellation efficiencies.

Keywords: HoLEP; BPH; surgical efficiency

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1. Introduction

Holmium laser enucleation of the prostate (HoLEP) has well proven long-term durability of both subjective and objective outcomes for patients with benign prostatic hyperplasia (BPH) [1]. Due to this durable efficacy, HoLEP is supported by both European and American Urological Association (AUA) guidelines as a size-independent first-line surgical treatment for men with moderate and severe lower urinary tract symptoms (LUTS) due to BPH [2]. Multiple studies support that HoLEP is a size-independent treatment option, as the prostate gland size itself does not significantly alter objective outcomes [3–5]. When compared with the historical gold standard, transurethral resection of the prostate (TURP), HoLEP and other enucleation techniques such as bipolar enucleation have shown superior efficacy of tissue retrieval [6]. Similar to what was observed within the kidney stone management literature, advancements in laser technology and surgical techniques now are allowing prostate enucleation techniques to improve upon both the safety profile and objective outcomes of BPH management [6,7].

Although the rate (g/min) of enucleation and morcellation are commonly reported outcomes within the HoLEP literature, particularly as a comparative outcome with other BPH surgical modalities, there is a paucity of literature specifically examining the relationship in incremental increasing prostate gland size on the efficiency of either enucleation or morcellation, which are both commonly utilized as markers for the HoLEP learning

curve [8]. Reviewing the current literature identifies large ranges in reported enucleation and morcellation efficiency rates (g/min), which appear to vary by gland size as well as how efficiency is calculated with or without incorporating energy utilized [8–10].

With continued pressure to optimize hospital and operative resources, the ability to accurately predict operative durations allows for timely interventions and maximal utilization of limited health care resources, as well as improved communication of expectations with our patients and their families. Additionally, understanding enucleation and morcellation efficiency with respect to prostate gland size can help better track trainee learning curves when learning HoLEP. For these reasons, we sought to better understand the effect of prostate size on HoLEP efficiency to better educate patients and improve operating room utilization.

2. Materials and Methods

After IRB approval, we queried our electronic medical record (EMR) and retrospective clinical registry to identify adult (>18 years old) patients who underwent HoLEP between 1 July 2016 and 1 Jan 2020 by two fellowship-trained endourologists (A.K. and T.L.) at our center. Inclusion criteria required intraoperative documentation of prostate tissue resected (grams), enucleation, morcellation, and total operative times. Preoperative patient characteristics including age, gender, BMI, comorbidities, medications, prior surgeries, and preoperative investigations were recorded. Bi- or trilobar enucleation technique depends upon the presence or absence of a median lobe and all cases utilized a bottom-up technique. Primary laser enucleation settings were 2 J and 40–50 Hz with 1 J and 20 Hz on secondary laser foot-pedal for intermittent hemostasis, as we have previously described [3]. The Piranha Wolf morcellator was used in all cases. Our primary objectives were to assess the effect of increasing increments (25 g) of prostate tissue resected on average enucleation and morcellation efficiency (g/min). Our secondary objective was to determine the effect of increasing prostate size on overall (enucleation and morcellation) efficiency.

Statistical analysis was performed using IBM SPSS software (Version 25, Armonk, NY, USA). Continuous variables were expressed as mean and range, while proportions were used for categorical variables. Enucleation and morcellation efficiency were defined as grams of intraoperative enucleated and morcellated prostate tissue per minute. A combined enucleation and morcellation overall efficiency score was calculated as the average of the two rates with a threshold target value of >5 g/min set. The HoLEP efficiency score (HES) and enucleation time–energy efficiency (ETEE) were calculated as previously described [11,12]. One-way Kruskal–Wallis ANOVA with Dunn’s post hoc test was used, with significance $p < 0.05$.

3. Results

3.1. Overall Cohort Characteristics

Between 1 July 2016 and 1 January 2020, 675 HoLEPs were performed, meeting inclusion criteria. All come average (mean) prostate tissue weight resected was 72.1 g (range of 1.0–448.0 g), energy used 110.00 KJ (range of 10.73–340.00 kJ), enucleation time 48.5 min (range of 5.0–151.0 min), and morcellation time 10.1 min (range of 0.5–113 min) (Table 1).

3.2. Enucleation Efficiency

Overall average enucleation efficiency was 1.42 g/min (range of 0.067–6.69 g/min). Average enucleation efficiency increased with increasing prostate size categories (Ex. <25 g–0.48 g/min, >325 g–3.91 g/min) (K-W ANOVA $p < 0.001$, Dunn’s post hoc $p < 0.001$). Figure 1 depicts the relationship between interval (25 g) increasing prostate size by intraoperative weight on both enucleation efficiency and morcellation efficiency. Prostate enucleation efficiency did not differ significantly by prostate morphology (Bilobar vs. Trilobar) ($p = 0.053$), presence of preoperative UTI ($p = 0.96$), use of 5-ARi ($p = 0.16$), or antiplatelet medications ($p = 0.58$).

Table 1. Overall patient characteristics.

Characteristic	Value (Range)
Total patients	675
Average age (years)	71.1 (33.1–95.7)
Average ASA score	II (I–IV)
Preoperative prostate Size (mL)	111.2 (14.0–672.0)
BMI (kg/m ²)	28.6 (18.1–72.7)
Average enucleation time (min)	48.5 (5.0–151.0)
Average morcellation time (min)	10.1 (0.5–113.0)
Average energy (kJ)	110.00 (10.73–340.00)
Average intraoperative tissue weight (g)	72.1 (1.0–448.0 g)
	N (% of Total)
History of preop urinary retention	435 (64.4)
History of preop prostate cancer	21 (3.1)
History of preop utis	97 (14.4)
History of preop prostatitis	42 (6.3)
History of diabetes	76 (11.2)
Preop alpha blocker use	519 (77.0)
Preop 5-ARi use	221 (32.9)
Preop antiplatelet/anticoagulation medication	133 (19.8)
- Antiplatelet	56 (8.3)
Previous BPH surgery	48 (7.1)
Prostate morphology	
- Bilobar	179 (26.5)
- Trilobar	496 (73.5)

ASA—American Society of Anesthesiology; BMI—body mass index; UTI—urinary tract infection; 5-ARi—5-alpha reductase inhibitor.

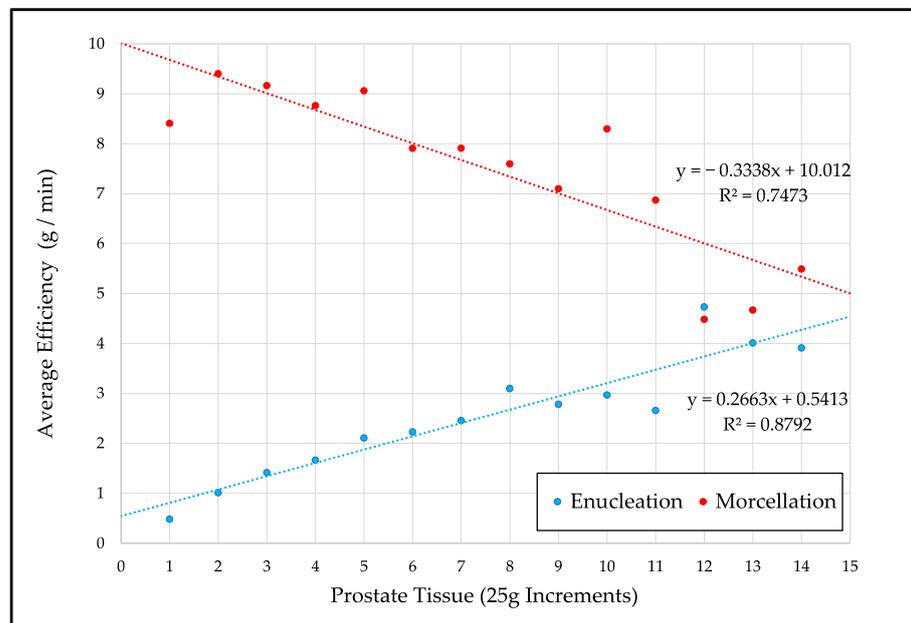


Figure 1. Trend of enucleation (blue) and morcellation (red) efficiency (g/min) displayed by increasing 25 g interval intraoperative prostate gland tissue weight. Linear relationship trendline (dotted) with equation and R-squared values displayed.

3.3. Morcellation Efficiency

Overall average morcellation efficiency was 8.27 g/min (range of 0.5–39 g/min). Average morcellation efficiency decreased with increasing prostate size (e.g., <25 g = 8.41 g/min, >325 g = 5.49 g/min) (K-W ANOVA $p = 0.004$, Dunn’s post hoc $p = 0.004$) (Figure 1). Mor-

cellation efficiency did not differ by prostate morphology (Bilobar 7.93 g/min vs. Trilobar 8.39 g/min, $p = 0.32$), preoperative history of UTI ($p = 0.34$), use of 5-ARi ($p = 0.72$), or antiplatelet agents ($p = 0.18$).

3.4. Overall Operative Efficiency

Combined average enucleation and morcellation efficiency was ≥ 5 g/min between 55.0 and 271.0 g of intraoperative prostate weight (Figure 2). There was significantly increased overall efficiency (enucleation and morcellation) within the 55.0–271.0 g intraoperative tissue weight range (5.28 g/min), compared with cases with <55.0 g ($p = 0.019$) and cases >271.0 g ($p = 0.0095$). There was no significant difference in overall efficiency between <55.0 g versus >271.0 g intraoperative tissue weight cohorts (4.84 g/min vs. 4.54 g/min, $p = 0.27$). Inefficiency for cases <55 g was driven by enucleation, while >271 g case inefficiency was driven by morcellation. The overall average HES score was 94.8 (Range 5–247). Overall ETEE was 0.014 ± 0.012 .

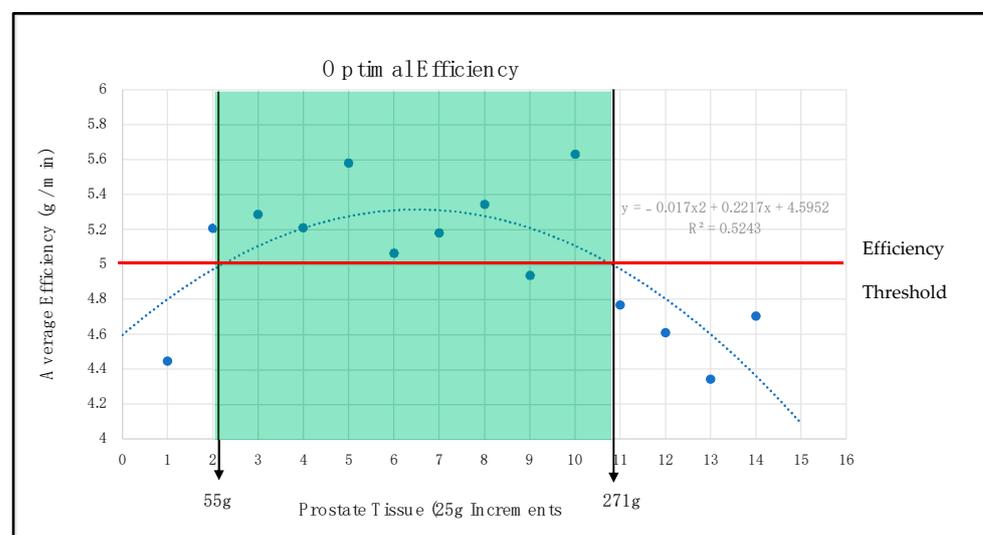


Figure 2. Optimal combined average enucleation and morcellation efficiency (defined as >5 g/min) range by increasing 25 g prostate tissue increments. Polynomial line of best fit (dotted).

4. Discussion

Historically, HoLEP has been associated with a steep surgical learning curve [9]. The efficiency of enucleation and morcellation rates during HoLEP has previously been predominately examined as surrogate markers for operative experience during training or to compare variations in surgical technique [11,13]. One study examining HoLEPs performed over an 8-year period of training identified initial enucleation efficiency rates of 0.55 g/min, which improved to 1.32 g/min during the last 5 years of the study period [9]. A retrospective study of 1816 men undergoing HoLEP reported average enucleation and morcellation times within four prostate volume quartiles (20–57 mL, 58–80 mL, 81–105 mL, 106–280 mL) and found that increasing gland size was associated with increased total time ($p < 0.001$); however, the relationship of the increase and rate were not further examined [14]. In our study, we highlight that increasing increments of 25 g intraoperative tissue at the time of HoLEP is associated with increasing enucleation efficiency and concurrent decreasing morcellation efficiency. The combined overall average efficiency (average of enucleation and morcellation) reaches a threshold of >5 g/min between 55 and 271 g of prostate tissue, with inefficiencies driven by enucleation <55 g and morcellation >271 g.

One group recently examined operative characteristics in specifically 200–299 mL glands versus ≥ 300 mL prostate glands undergoing HoLEP [8]. Overall, they reported that the mean total operative time (171 vs. 182 min) and mean enucleation time (77 vs. 83 min) were not different between cohorts [8]. In support of our study's findings, they found

that enucleation efficiency was greater for glands ≥ 300 mL compared with 200–299 mL glands (2.6 mL/min vs. 2.0 mL/min, $p = 0.04$). Although they did not describe morcellation efficiency outcomes, they indeed highlighted that average morcellation time in the ≥ 300 mL prostate gland cohort was longer than the 200–299 mL cohort ($p = 0.021$), further supporting the morcellation efficiency trend we observed.

A single surgeon series of 135 patients that underwent an en bloc “no-touch” technique HoLEP with preop transrectal ultrasound (TRUS) volume assessments of <50 mL, 50–80 mL, and >80 mL reported enucleation efficiency rates by gland size [13]. Apart from increasing gland size, they found that a history of prior urinary tract infection (UTI) and history of antiplatelet agents affected enucleation time. One significant difference between this study and our current study is that the two high-volume surgeons in our study have already reached the plateau of their HoLEP efficiency, with baseline enucleation rates (>1.4 g/min), significantly higher than the efficiency presented in other smaller series such as Lin et al. (2020) reported (0.5 g/min) [13]. Additionally, the overall average and range of prostate gland size within their study were significantly lower. In our study, we did not detect that prior UTI history of antiplatelet medication independently affected either enucleation or morcellation efficiency.

Previous studies have shown that 5-ARI use affects the ratio of glandular to stromal prostatic tissue, with a hypothesized increase in the difficulty of enucleation due to the increased fibrous tissue [15]. However, similar to published outcomes examining the effect of 5-ARI use on enucleation efficiency, we did not detect that this medication class significantly affected either enucleation or morcellation efficiency [13]. In addition, 5-ARI use has been hypothesized to reduce intraoperative bleeding during prostate surgery; however, the significant improvement in hemostasis obtained with HoLEP, compared with alternative treatments (Turp, open simple prostatectomy), resulted in no significant difference in bleeding between patients undergoing HoLEP with or without preoperative 5-ARI [16]. Additionally, we found that trilobar versus bilobar prostate morphology did not independently affect enucleation or morcellation efficiency, which supports the findings reported in a series of 304 patients [17]. Overall, it is evident that advances within BPH surgical technology, including improvements in lasers and morcellators, have improved the safety and outcomes of management compared with historical treatments (e.g., open simple prostatectomy) [7,18]. This trend mirrors what was observed within the urinary tract calculi treatment realm with increasing utilization of retrograde ureteroscopic management of stones due to significant technologic advancements [7].

Kim et al. (2018) showed that energy consumption decreases as the surgeon’s enucleation technique develops [11]. Calculating our study enucleation time–energy efficiency outcome, as described by Kim et al., further supports that the two surgeons in our study were operating at an efficiency rate beyond the described learning curve. They found a rate of 0.013 ± 0.005 after 100 HoLEPs once the learning curve had been surpassed. Within our study, all comers’ average ETEE was comparable at 0.014 ± 0.012 . As regards our morcellation efficiency rates, they were comparable to a study examining oscillating versus reciprocating morcellators, which found that staff-alone morcellation efficiency for all comers (average 69 g, range 17–224 g) was 9.8 g/min (versus our overall rate of 8.27 g/min) [19].

In an effort to standardize reporting of the learning curve surgical efficiency, one group developed the HoLEP efficiency score (HES), which they reported demonstrated the most reflective single value of enucleation efficiency [12]. The median HES in their study for the staff surgeon was 82.8 min kJ/g, which is the enucleation speed \times laser energy/removed tissue weight. A lower HES score is associated with higher efficiency and a surgeon performing HoLEP further along the learning curve with trainees, obtaining average scores >170 within the first 40 HoLEP cases of the learning curve [12]. The HES score for all comers within our study was <95 . As an additional novel marker of surgical technique, we described an overall efficiency (mean average of enucleation efficiency and morcellation efficiency) with a threshold set to >5 g/min. Statistical comparison of

the overall efficiency for patients with intraoperative tissue weight below and above the intersecting thresholds (Figure 2) highlighted that there may be a maximally efficient size range (55–271 g) where the balance of enucleation and morcellation is optimized during HoLEP. When comparing our tissue removal efficiency outcomes with alternative BPH surgical techniques, we support findings that HoLEP removed prostate tissue, at a rate higher than reported photovaporization (PVP) or TURP techniques [18]. One randomized control trial comparing tissue removal efficiency between HoLEP, TURP, and PVP found that HoLEP was the most effective (1.7 g/min vs. 1.4 g/min (PVP) and 1.2 g/min (TURP), $p < 0.001$).

One limitation to our study is that the retrospective study design prevented us from accurately detecting to what extent surgical trainees were involved within the surgical cases. However, overall enucleation efficiency, morcellation efficiency, ETEE, and HES scores all suggest that the HoLEP cases included within our study were being performed at a rate beyond previously reported learning curve rates, and the two primary surgeons included were well past the literature-defined learning curve case count of 20–60 independent HoLEPs. Although our cohort is heterogeneous and may include portions of the enucleation or morcellation being performed by endourology fellow or resident trainees, we present a real-world description of trends in enucleation and morcellation efficiency with increasing prostate sizes. One important area for further research would be to correlate preoperative prostate size estimates to the intraoperative weights and HoLEP surgical times in order to create a predictive surgical duration model, which could better guide operative resource utilization.

5. Conclusions

Increasing prostate tissue weight resected at the time of HoLEP is associated with a linear relationship of increasing efficiency of enucleation with concurrent decreasing efficiency of morcellation. As prostate gland size increases beyond 100 g, the enucleation efficiency of HoLEP is higher than reported alternative BPH techniques such as PVP and TURP. A threshold combined enucleation and morcellation efficiency >5 g/min was reached between 55 and 271 g of intraoperative tissue weight.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of Indiana University (#10492, 17 February 2021).

Informed Consent Statement: Patient consent was waived due to the temporal retrospective nature of the study design in which all human subjects had already completed all care and follow-up, and the study had no impact on their urologic care.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available for patient confidentiality.

Conflicts of Interest: Amy Krambeck is a consultant for Boston Scientific, Ambu, Wolf, Virtuoso, and Lumenis. Amy Krambeck is on the data safety monitoring board for Sonomotion. Tim Large is a consultant for Boston Scientific and Lumenis. Mark Assmus has no conflict of interests to declare.

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