Am J Clin Exp Urol 2023;11(4):328-333
www.ajceu.us /ISSN:2330-1910/AJCEU0149296

Original Article

Impact of pulse duration alterable laser ureterorenoscopic lithotripsy for upper urinary tract calculi

Hideo Otsuki[1], Hironori Kojima[1], Tomohiro Hongo[1], Shunsuke Hori[1], Yukihide Matsui[1], Tomoya Yamasaki[1], Makoto Isono[1], Takeo Kosaka[2], Shinya Uehara[3], Kei Fujio[1]

[1]*Department of Urology, Abiko Toho Hospital, Abiko, Chiba 270-1166, Japan;* [2]*Department of Urology, Keio University, Shinjuku-ku, Tokyo 160-8582, Japan;* [3]*Department of Urology, Kawasaki Medical School General Medical Center, Kita-ku, Okayama 700-8505, Japan*

Received January 24, 2023; Accepted July 16, 2023; Epub August 15, 2023; Published August 30, 2023

Abstract: To assess the effectiveness of a pulse duration alterable Holmium-YAG (Ho:YAG) laser on the stone-free rate (SFR) compared to a conventional pulse duration fixed laser after ureterorenoscopic lithotripsy (URSL). The medical records from patients with upper urinary tract calculi of ≥ 9 mm and < 30 mm were retrospectively investigated. URSL using a conventional Ho:YAG Laser (group C) or a pulse duration alterable Ho:YAG system (group A) was included. In total, 228 and 188 patients were enrolled in groups C and A, respectively. A 272 μm optical core bare-ended, reusable laser fiber was used, and the laser system was set to a standard 0.8 J and 10 Hz (8 W of average power) in both groups. URSL adopts active fragmentation using an extraction approach. SF was defined as the complete absence of stone fragments on computed tomography (CT) 1-2 months after URSL. Sex, BMI, stone length, stone volume, stone density, and the number of patients with positive preoperative urine cultures were not significantly different between the groups. However, age, rate of preoperative febrile urinary tract infection (fUTI), and pre-stenting were significantly higher in group A, and the operative times and incidence of postoperative fUTI were comparable. The SFRs were 71.5% and 80.3% in groups C and A, respectively (P = 0.035). Multivariate logistic regression revealed that the use of conventional laser was associated with non-SF (odds ratio [OR] 1.090, 95% confidence interval [CI] 1.01-1.18, P = 0.040). The present study revealed the superior performance of a pulse duration alterable Ho:YAG laser on the SFR after URSL compared to a conventional pulse duration fixed laser delivery system.

Keywords: Urolithiasis, ureterorenoscopic lithotripsy, Holmium:YAG laser, pulse duration, fragment size

Introduction

The prevalence of urolithiasis has increased owing to an increase in obesity, diabetes, and dietary and lifestyle changes related to urinary tract stone formation [1]. Surgical treatment is indicated for patients without spontaneous stone passage to prevent renal function impairment or infection. Current treatment options include shockwave lithotripsy, ureterorenoscopy, and percutaneous nephrolithotomy. However, technological advances have influenced the choice of treatment options, which have recently shifted towards endourologic procedures. Ureterorenoscopic lithotripsy (URSL) is widely performed as a first-line treatment for ureteric and renal calculi up to 20 mm in diameter [2]. Advances in technology have widened the range of URSL applications in patients with large urinary tract calculi measuring > 20 mm [3-5]. We also have extensive experience with URSL in more than 2700 cases; therefore, we have safely treated patients with upper urinary tract calculi > 20 mm in size. In recent years, there has been increasing interest in examining the effectiveness of urolithiasis treatment [6-8], dusting [9, 10], and fragmentation using an extraction approach [11]. Ultimately, the choice of settings to achieve optimal stone clearance depends on the individual department or the surgeon. Furthermore, no recommendation favoring one technique or another was allowed. The choice of Holmium YAG (Ho:YAG) laser is very important to achieve a

Table 1. Difference in the performance of laser devices and URSL settings

	Conventional laser	Pulse duration alterable laser
Laser Device	VersaPulse™ (group C)	Sphinx jr.™ (group A)
Specifications		
Maximum power (W)	100	15*
Pulse length (nm)	2100	2123
Pulse duration (μs)	600 (fixed)	100~650 (variable)
Pulse modulation setting	n/a	StoneEffect™ 10~100
Range of energy (J)	0.2~3.5	0.3~2.5*
Range of frequency (Hz)	5~40	1~14*
Range of power (w)	1~100	1~15*
Laser settings		
Energy (J)	0.8	0.8
Frequency (Hz)	10	10
Average power (w)	8	8
Stone Effect	-	50
Pulse duration (μs)	600	130**
Laser fiber	SlimLine™ 272 μm	FlexiFib 272 μm
Frexible ureterorenoscope	URF-V™ (9.9 Fr)	URF-V3™ (8.4 Fr)
Ureteral access sheath	Navigator™ 12/14 Fr	Navigator™ 11/13 Fr

*Setting range only for 100 V power supply in Japan. **At StoneEffect 50 setting.

higher stone-free rate (SFR); however, few clinical articles have focused on stone-free (SF) outcomes based on different Ho:YAG laser devices. Fortunately, we had a chance to compare conventional Ho:YAG lasers with pulse duration alterable laser lithotripsy [12]; therefore, we retrospectively reviewed the results of these URSLs to investigate the superiority of these two laser devices.

Materials and methods

Inclusion and exclusion criteria

The inclusion criteria were as follows: patients who underwent initial URSLs using VersaPulse™ (Lumenis, Yokneam, Israel) between January 2017 and April 2018 (group C) or Sphinx jr.™ (Lisa Laser, Katlenburg, Germany) [12, 13] between September 2019 and March 2021 (group A), and patients with upper urinary tract calculi between 9 mm and 30 mm in size.

The exclusion criteria were as follows: patients lacking perioperative data and those without postoperative follow-up computed tomographies (CTs).

Surgical technique and management

In our department, URSLs are performed via fragmentation with extraction approach. The details of our URSL procedure have been described previously and remain unchanged [5, 14]. Briefly, the patient's ureter was inspected using a 6/7.5 Fr dual-channel semi-rigid ureteroscope (Ultra Thin™, Richard Wolf, IL, USA) under general anesthesia. Ureteral lithotripsy was performed *in situ* in patients with fixed lower ureteral stones. Mobile ureteral stones were pushed up into the renal pelvis. Through a ureteral access sheath (UAS) (Navigator HD™, BOSTON SCIENTIFIC JAPAN, 12/14 Fr in group C, 11/13 Fr in group A), a flexible ureterorenoscope (fURS) (9.9 Fr URF-V™, OLYMPUS in group C; 8.4 Fr URF-V3™, OLYMPUS in group A) was inserted. After Ho:YAG laser fragmentation, active fragment retrieval was repeated as long as graspable fragments were present using a basket catheter N-CIRCLE™ (COOK, Tokyo, Japan). The maximum laser and operation times were 90 min and 120 min, respectively. URSLs were performed by urology residents under the supervision of highly experienced specialists. In total, seven urology specialists and 23 residents participated in the study. Four specialists and 10 residents were involved in groups C, and 6 specialists and 14 residents were involved in group A. The principles of the URSL, laser performance, and URSL settings were not altered during the study period (**Table 1**).

The Sphinx jr.™ possesses a novel "StoneEffect™" feature with a range setting of 10-100%, which was mostly set at 50% (130 μs of pulse duration) [12, 13]. A 272 μm optical core bare-ended, reusable laser fiber was used with the standard settings set to 0.8 J at 10 Hz (average power of 8 W). Prophylactic antimicrobials (cefotiam) were administered within 2

Table 2. Preoperative demographic variables

	Group C	Group A	*p*-value
Number of patients	228	188	
Age (years)	59.4	63.1	0.009
Gender (M:F)	152:76	122:66	0.37
BMI	24.1	24.0	0.80
Stone Length (mm)	13.85	13.39	0.22
Stone Volume (mm^3)	1382	1299	0.49
Stone Density (HU)	909	931	0.52
Positive Urine Culture	54.8%	48.9%	0.23
Preoperative fUTI	13.2%	20.7%	0.042
Pre-Stenting	29.4%	49.5%	< 0.01
Laterality (R:L)	116:112	102:86	0.49

BMI: body mass index, fUTI: febrile urinary tract infection, HU: Hounsfield unit.

days to patients without urinary tract infections, whereas patients with a positive urine culture received antimicrobials according to bacterial susceptibility before and after URSL. A ureteral stent was routinely placed after surgery and removed within 2 weeks.

Outcome assessment

The location, number, and volume of the stones were determined using multi-slice plain CT (16-detector row CT scanner Activion 16, Toshiba, Japan). In those with multiple stones, "stone volume" was considered as the sum of all stones, and "stone length" was defined as the maximum diameter of the largest stone. Febrile urinary tract infection (fUTI) was diagnosed based on a fever of ≥ 38°C or ≥ 100.4°F in patients who tested negative for non-urinary causes, such as pneumonia, gastroenteritis, meningitis, or viral infection, or those associated with surgical invasion, as well as any evidence of lumbar back pain, lateral abdominal pain, costovertebral angle tenderness, increased perirenal fat density or hydronephrosis on CT, or pyuria or bacteriuria on urinalysis results. SF status was defined as the complete absence of stone fragments on CTs performed 1-2 months after URSL [15].

Statistical analyses

We analyzed the collected data of the patients using Student's t-test and Binomial Logistic Regression Analysis with SPSS version 25.0 (IBM Corp., Armonk, NY, USA). To estimate the association between laser devices and SF outcomes, we used a multivariate logistic regression model. We selected confounders such as age, sex, body mass index (BMI), preoperative fUTI, pre-stenting, stone length, stone density, stone volume, UAS, operative time, postoperative fUTI, and laser device types from the candidates based on previously published studies [16-18]. All confounders were divided into two groups, and the cutoff was calculated from the average as follows: age > 61.1 years, BMI > 24.03 kg/m^2, stone density > 919.3 HU, stone length > 13.6 mm, a large stone volume > 1344 mm^3, and operation time > 69.1 min. We analyzed the data collected from the patients, and statistical significance was set at $P < 0.05$.

Ethics statement

This study was conducted after obtaining approval from the Institutional Review Board (no. 201909). Written informed consent was obtained from each patient prior to surgery.

Results

Preoperative characteristics

The preoperative demographic variables are listed in **Table 2**. The sex, BMI, stone length, stone volume, stone density, stone laterality, and prevalence of preoperative positive urine culture were not significantly different between the two groups. However, the rate of pre-stenting was significantly higher in group A than in group C (49.5% vs 29.4%, respectively, $P < 0.01$). The age and incidence of preoperative fUTIs were also significantly higher in group A.

Operative outcome and statistical analysis

A comparison of the operative results is shown in **Table 3**. The operative time and incidence of fUTI did not differ between the groups. Regarding surgical complications, all postoperative fUTIs were classified as Clavien-Dindo grade 2. The use of a pulse duration-alterable laser contributed to a better SFR: 71.8% in group C and 80.3% in group A ($P = 0.035$). Multivariate logistic regression analysis (**Table 4**) indicated that the use of conventional lasers was associated with non-SF outcomes (odds ratio [OR] 1.090, 95% confidence interval [CI] 1.01-1.18, $P = 0.040$).

Table 3. Postoperative demographic variables

	Group C	Group A	*p*-value
Procedure (rigid:flexible)	29:199	24:164	0.23
Operative Time (min)	67.1	71.4	0.14
Emitted laser energy (kj)	4.67	4.70	0.97
Stone composition			
Calcium oxalate	196	144	
Calcium phosphate	4	15	
Uric acid	7	7	
Struvite	10	15	
Other	11	7	
Postoperative fUTI	10.5%	12.8%	0.46
Stone free rate	71.5%	80.3%	0.035

fUTI: febrile urinary tract infection.

Table 4. Multivariate analysis for non-stone free outcomes

	OR	95% CI	*p*-value
Use of conventional laser	1.090	1.01-1.18	0.040
Male sex	1.041	0.95-1.14	0.372
Old age (> 61.1 y.o.)	1.059	0.97-1.15	0.188
High body mass index (> 24.03)	1.015	0.94-1.10	0.713
Preoperative fUTI	1.009	0.89-1.14	0.889
Non pre-stenting	1.025	0.93-1.13	0.608
Stone Length (> 13.6 mm)	1.045	0.94-1.16	0.416
Large stone volume (> 1344 mm^3)	1.275	1.13-1.44	< 0.001
Hard stone (> 919.3 HU)	1.025	0.95-1.11	0.543
No use of UAS	1.073	0.93-1.24	0.329
Operative Time (> 69.1 min)	1.005	0.91-1.11	0.921
Postoperative fUTI	1.121	0.99-1.27	0.079

CI: confidence interval, OR: odds ratio, fUTI: febrile utinary tract infection, HU: Hounsfield unit, UAS: ureteral access sheath.

Discussion

The present study revealed for the first time that the use of Sphinx jr.™ was associated with a higher likelihood of SF outcomes than the use of conventional laser devices.

The performance of the laser systems plays an important role in the effectiveness and success of URSLs. It is difficult to evaluate the performance of laser lithotripters for small stones because laser lithotripsy does not take a long time for patients with small stone burdens. To investigate the efficiency of the laser lithotripter, the present study was set up with a limit of 9 mm-30 mm stone size.

Previous studies have shown the risks of non-SF outcomes as large stone sizes, female sex, preoperative fUTIs, and non-pre-stenting [16-18]. A large stone burden is often difficult and requires considerably more time and energy for fragmentation during URSL [19]. The significant difference in SFR between the 2 groups reflects the difference in the performance of the lithotripter. Multivariate analysis also revealed an association between non-SF outcomes, large stone volume, and the use of a pulse-duration-fixed Ho:YAG laser.

The excellent performance of the laser was due to less retropulsion, leading to the superior SFR in group A. Retropulsion is an important factor influencing fragmentation efficiency [20]. Stone retropulsion prevents rapid and effective fragmentation; therefore, a laser with less retropulsion is desirable [21]. Patients in group A underwent URSLs under more difficult situations performed by inexperienced residents with a narrower UAS than those in group C. However, the operative time and incidence of postoperative fUTIs were comparable. The sphinx laser with 50% of the StoneEffect feature induced less retropulsion, finer powderization, and consequently contributed to a higher SFR.

Fragments after the conventional Ho:YAG lithotripsy using VersaPulse™ left in the urinary tract after fragment extraction looked like "sand"; however, it looked like "powder" after lithotripsy using the Sphinx jr.™ laser. We measured the size of the fragments with a microscope; the main fragments were submillimeter-sized in group C. On the other hand, it was less than 50 μm in group A. The fragment size was significantly smaller in patients who underwent URSLs by Sphinx jr.™ Medium pulse duration laser generated by Sphinx jr.™ can pulverize stone fragments effectively at the "StoneEffect 50%" setting. The Lumenis laser also emits a middle-duration pulse, making it difficult to fragment stones thoroughly into pieces because of strong retropulsion. Powderization of fragments less than

50 μm might also contribute to promoting natural stone passage and attaining a higher SFR.

The definition of "stone-free" outcomes differs depending on the institution or study [15]. Routine CT evaluation of residual fragments after URSLs is associated with issues related to medical expenses and radiation exposure. The most sensitive imaging modality for this purpose is CT. Low-dose non-contrast CT has superior sensitivity (97%) and specificity (95%) compared to that of ultrasound (11-93% and 82-100%, respectively) and plain kidney, ureter, and bladder radiographs (45-58% and 69-77%, respectively) [22]. To assess SF outcomes strictly, we adopted routine non-contrast CT for the evaluation of residual fragments following URSLs.

The present study had some limitations: its non-randomized, retrospective design, no overlap period of URSLs, and differences in URSL devices, settings, and operators. The URSs and laser fragmentations were performed by resident urologists who were regularly replaced, and the number of URSLs experiences for each resident in group A was smaller than that in group C. Considering that the diameter of the UAS was smaller in group C, the essential difficulty of URSL in group A was not lower than that in group C. The present study indicated that the performance and quality of the laser device contributed to the effective stone passage and superior SFRs.

Conclusions

The SFR in URSL-targeted patients with upper urinary tract calculi of between 9 mm and 30 mm in size, was higher in the pulse duration alterable laser group (80.3%) than in the conventional pulse duration fixed laser group (71.5%) ($P = 0.035$). The clinical implication of the present study is the finding that the use of a pulse duration alterable laser can contribute to higher SFRs after URSLs. A pulse duration alterable laser during URSL is desirable for better stone clearance.

Acknowledgements

The authors would like to thank Takashi Yoshioka for the statistical assistance and modification of the manuscript.

Disclosure of conflict of interest

None.

Address correspondence to: Hideo Otsuki, Department of Urology, Abiko Toho Hospital, 1851-1, Abiko, Chiba 270-1166, Japan. Tel: +81-4-7182-8166; E-mail: hideotsuki2004@hotmail.com

References

[1] Scales CD Jr, Smith AC, Hanley JM and Saigal CS; Urologic Diseases in America Project. Prevalence of kidney stones in the United States. Eur Urol 2012; 62: 160-165.

[2] Türk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M and Knoll T. EAU guidelines on interventional treatment for urolithiasis. Eur Urol 2016; 69: 475-82.

[3] Hyams ES, Munver R, Bird VG, Uberoi J and Shah O. Flexible ureterorenoscopy and holmium laser lithotripsy for the management of renal stone burdens that measure 2 to 3 cm: a multi-institutional experience. J Endourol 2010; 24: 1583-1588.

[4] Huang JS, Xie J, Huang XJ, Yuan Q, Jiang HT and Xiao KF. Flexible ureteroscopy and laser lithotripsy for renal stones 2 cm or greater: a single institutional experience. Medicine (Baltimore) 2020; 99: e22704.

[5] Otsuki H, Yoshioka T, Shimizu T, Nakanishi Y, Fujio K, Murao W, Uehara S, Kikuchi H and Fujio K. Calcium phosphate composition affects ureteroscopic laser lithotripsy. Acta Med Okayama 2016; 70: 25-29.

[6] Matlaga BR, Chew B, Eisner B, Humphreys M, Knudsen B, Krambeck A, Lange D, Lipkin M, Miller NL, Monga M, Pais V, Sur RL and Shah O. Ureteroscopic laser lithotripsy: a review of dusting vs fragmentation with extraction. J Endourol 2018; 32: 1-6.

[7] Wenzel M, Bultitude M and Salem J. Dusting, fragmenting, popcorning or dustmenting? Curr Opin Urol 2019; 29: 108-112.

[8] El-Nahas AR, Almousawi S, Alqattan Y, Alqadri IM, Al-Shaiji TF and Al-Terki A. Dusting versus fragmentation for renal stones during flexible ureteroscopy. Arab J Urol 2019; 17: 138-142.

[9] Peretti D, Dalmasso E, Biancolini R, Pecoraro A, Ambruosi C, Venzano F, Fiori C, Porpiglia F and Maugeri O. Flexible ureteroscopy using a 120-w holmium laser: the low-energy/high-frequency approach. Arch Esp Urol 2021; 74: 343-349.

[10] Aldoukhi AH, Roberts WW, Hall TL and Ghani KR. Holmium laser lithotripsy in the new stone age: dust or bust? Front Surg 2017; 4: 57.

[11] Humphreys MR, Shah OD, Monga M, Chang YH, Krambeck AE, Sur RL, Miller NL, Knudsen

BE, Eisner BH, Matlaga BR and Chew BH. Dusting versus basketing during ureteroscopy-which technique is more efficacious? A prospective multicenter trial from the EDGE research consortium. J Urol 2018; 199: 1272-1276.
[12] LISA Laser Products GmbH, https://www.promedltd.com/wp-content/uploads/2020/03/036006071WMSphinxJrBrochure_en.pdf.
[13] Netsch C, Knipper S, Tiburtius C and Gross AJ. Systematic evaluation of a holmium:yttrium-aluminum-garnet laser lithotripsy device with variable pulse peak power and pulse duration. Asian J Urol 2014; 1: 60-65.
[14] Yoshioka T, Otsuki H, Uehara S, Shimizu T, Murao W, Fujio K, Fujio K, Wada K, Araki M and Nasu Y. Effectiveness and safety of ureteroscopic holmium laser lithotripsy for upper urinary tract calculi in elderly patients. Acta Med Okayama 2016; 70: 159-166.
[15] Deters LA, Jumper CM, Steinberg PL and Pais VM Jr. Evaluating the definition of "stone free status" in contemporary urologic literature. Clin Nephrol 2011; 76: 354-357.
[16] Erbin A, Tepeler A, Buldu I, Ozdemir H, Tosun M and Binbay M. External comparison of recent predictive nomograms for stone-free rate using retrograde flexible ureteroscopy with laser lithotripsy. J Endourol 2016; 30: 1180-1184.
[17] Hori S, Otsuki H, Fujio K, Kobayashi H, Nagao K, Nakajima K and Mitsui Y. Novel prediction scoring system for simple assessment of stone-free status after flexible ureteroscopy lithotripsy: T.O.HO. score. Int J Urol 2020; 27: 742-747.
[18] Richard F, Marguin J, Frontczak A, Barkatz J, Balssa L, Bernardini S, Chabannes E, Guichard G, Bittard H and Kleinclauss F. Evaluation and comparison of scoring systems for predicting stone-free status after flexible ureteroscopy for renal and ureteral stones. PLoS One 2020; 15: e0237068.
[19] Takazawa R, Kitayama S and Tsujii T. Appropriate kidney stone size for ureteroscopic lithotripsy: when to switch to a percutaneous approach. World J Nephrol 2015; 4: 111-117.
[20] Lee H, Ryan RT, Teichman JM, Kim J, Choi B, Arakeri NV and Welch AJ. Stone retropulsion during holmium:YAG lithotripsy. J Urol 2003; 169: 881-885.
[21] Bader MJ, Pongratz T, Khoder W, Stief CG, Herrmann T, Nagele U and Sroka R. Impact of pulse duration on Ho:YAG laser lithotripsy: fragmentation and dusting performance. World J Urol 2015; 33: 471-477.
[22] Lipkin ME and Preminger GM. Imaging techniques for stone disease and methods for reducing radiation exposure. Urol Clin North Am 2013; 40: 47-57.