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Influence of the laser pulse shape in the treatment of stones in the upper urinary tract

Abdulmajeed Alghamdi*, **Alexander Kretschmer***, **Christian G. Stief**, **Frank Strittmatter**

Department of Urology, Ludwig-Maximilians-University (LMU), Munich, Germany

Purpose: Urinary stones can be successfully treated using a Holmium: Yttrium-Aluminum-Garnet (Ho: YAG) laser. Regarding success rates, laser pulse energy, frequency, and pulse width are well-known contributing factors. Whether the pulse shape might be a further factor influencing the laser efficiency is unclear. This study aimed to evaluate different modes of laser pulse shapes in a real-world setting.

Materials and Methods: The Dornier Medilas® H Solvo (Weßling, Germany) was used in the treatment of ureter and kidney stones. Patients were randomized into standard pulse shape (SPS) and new pulse shape groups (NPS1; ureter) and (NPS2; kidney pelvis), depending on the stone localization. The primary endpoint was laser efficiency defined as mm^3 stone destruction per overall operating time. Secondary endpoints encompassed number of stone recoveries and stone-free rate.

Results: Altogether 145 patients (24 SPS vs. 32 NPS1; 51 SPS vs. 38 NPS2) were included. No differences in sex, age, body mass index, stone localization and stone composition were found, except for preoperative stone size (133±95 [SPS] vs. 197±139 [NPS1] mm^3; p=0.023) and (348±298 [SPS] vs. 525±429 [NPS2] mm^3; p=0.042). Regarding the primary endpoint, a significant increase in laser efficiency could be detected for the NPS1 and NPS2 groups compared to the SPS groups (39.9±44.9 vs. 28.8±30.2 and 51.7±61.3 vs. 22.4±24.2 mm^3/min [mean±standard deviation]). No statistically significant differences were found for secondary endpoints and perioperative complication rates.

Conclusions: Efficiency of the Ho: YAG laser can be positively influenced by different pulse shapes. This adds the variable of individualized intraoperative decision making.

Keywords: Lasers; Operative; Pulse; Surgical procedures; Urinary calculi

INTRODUCTION

With the everchanging epidemiology of kidney stone disease due to diet and lifestyle factors, the Holmium: Yttrium-Aluminum-Garnet (Ho: YAG) laser remains the standard energy source for laser lithotripsy [1,2]. The reason for this widespread use is the marked development in endoscopic techniques allowing laser-lithotripsy in different and difficult to reach locations in the kidney. Also, the ongoing improvement in holmium laser technology, since its first published data in the mid nineteen nineties, has permitted the presence of more powerful higher watt holmium systems which consequently allow the surgeon to apply different endoscopic strategies for individualized stone management [3,4].

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Corresponding Author: Frank Strittmatter https://orcid.org/0000-0003-0237-5749
Department of Urology, Ludwig-Maximilians-University (LMU), Campus Grosshadern, Marchioninistr. 15, 81377 Munich, Germany
TEL: +49-89-4400-76723, FAX: +49-89-4400-76532, E-mail: frank.strittmatter@med.uni-muenchen.de
*These authors contributed equally to this study and should be considered co-first authors.

Laser pulse energy, frequency, and pulse width are well known contributing factors in the decision-making progress of appropriate surgical techniques for the treatment of upper urinary tract stones. Recently, it has been investigated if an innovative modification in laser pulse shape or characteristics could improve the stone fragmentation rate [5].

Dornier MedTech (Weßling, Germany) has introduced the Medilas® H Solvo laser system with innovative different pulse shape modes. Thus, the current prospective study was designed to evaluate the effect of the new pulse shapes (NPS) in this laser system in comparison with standard pulse shapes (SPS) within the scope of the real-world treatment of ureteral and renal stones.

MATERIALS AND METHODS

1. Inclusion, exclusion criteria, study procedures

The present study protocol was reviewed and approved by the Institutional Review Board of the Ludwig-Maximilians-University, Munich (approval number: 703-15). Informed consent was obtained by all subjects when they were enrolled. Patients with a single ureteral or renal calculus who were admitted to our tertiary care department were included in the study. All patients were treated by two well-experienced surgeons (both more than one thousand stone treatments via ureterorenoscopy in the past). For the treatment of ureter stones, semirigid- and for kidney stones, flexible ureteroscopes of the same type were used. Operations were performed under comparable conditions and assisted by two colleagues with the same experience.

The participants were evaluated by a thorough clinical history, serum creatinine, bleeding profile, and urine analysis before the procedure. Routine prophylactic antibiotics were administered preoperatively. Patients with positive urine analysis received appropriate antibiotic agents based on urine culture and sensitivity. In the case of an infection, urine analysis was repeated, and operation was performed only if urine analysis was negative for infection. Additional patient data obtained included: age, sex, and body mass index. Exclusion criteria encompassed multiple ureteral and multiple renal stones or stones in the ureter and kidney at the same time. Renal anomalies e.g., pelvic junction obstruction, malrotation or narrow goblet neck kidney, uncontrolled coagulopathy, pregnancy, aged <18 years, and unwillingness to sign the informed consent were also excluded from randomization. Randomization was performed by using a sealed envelope. The stone size was calculated based on a mandatory preoperative low-dose computed tomography scan by the formula: $\pi \times L \times W \times H \times 0.167$, as described before [6]. Stone size measurement was performed by the same auditor without having information about the randomization process. Operating time was defined as the time between beginning with the laser procedure until the removal of the last stone fragment. The stone-free rate was defined as no stones left in the upper urinary tract or stones <1 mm.

2. Laser pulse shapes

The HO: YAG Medilas® H Solvo device was used with a single-use 275 µm fiber for flexible ureterorenoscopy or a single-use 600 µm fiber for semirigid ureterorenoscopy (SingleFlex®; both from Dornier MedTech, Weßling, Germany). Patients were randomly assigned into the SPS group or the NPS1 and NPS2 groups, depending on the stone localization (NPS1=ureter; NPS2=kidney pelvis). The difference between the pulse shapes is in ramping up the power of the laser pulse. The pulse shapes NPS1 and NPS2 used in this study provide pulses with differences in the power at the beginning of the laser pulse and different pulse durations compared to the standard pulse shape. The pulse shape NPS1 has a lower power at the beginning of the pulse while pulse shape NPS2 has a higher power at the beginning of the pulse. NPS1 has a similar (full width half max [FWHM] is equal, full width [FW] longer), NPS2 a shorter pulse duration than SPS. The laser pulse shapes are demonstrated in Fig. 1. The pulse beam profiles were recorded with an oscilloscope (Oscilloscope TDS 2,012,100 MhZ; Tektronix Inc., Beavereton, OR, USA). The pulse durations are listed in Table 1. To minimize the impact of additional laser pulse parameters a fixed frequency of 10 Hz and energy of 1.5 J were used in all groups.

3. Statistical analysis

Primary endpoint encompassed laser efficiency (LE) defined as stone disintegration in mm^3 based on operating time. The aim was to perform stone-treatment until the defined stone-free rate was achieved. Secondary endpoints included operating time, number of stone recovery procedures, laser time, and stone-free rate.

Categorial data were analyzed by Fisher's exact test and chi-square test. For continuous data, the Mann–Whitney U test was performed whenever indicated. All p-values <0.05 were considered statistically significant.

RESULTS

1. Patients characteristics

In total, 145 patients met the inclusion criteria and were included in the current study. Briefly, there were no signifi-

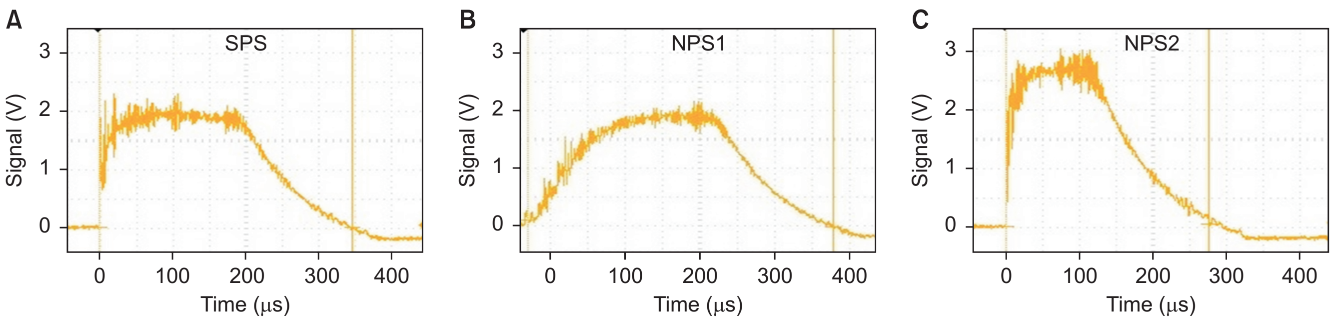

Fig. 1. With courtesy of Dornier MedTech: Laser beam profile for the pulse shapes (A) standard pulse shape (SPS), (B) new pulse shape 1 (NPS1), (C) new pulse shape 2 (NPS2).

Table 1. With courtesy of Dornier MedTech: pulse durations (unit: µs)

Pulse shape (1.5 J/10 Hz)	SPS	NPS1	NPS2
Full width (FW)	340	400	270
Full width half max (FWHM)	260	260	160

SPS, standard pulse shape; NPS, new pulse shape.

cant differences regarding the subgroup distribution, except for the stone size (133±95 [SPS] vs. 197±139 [NPS1] mm^3; p=0.023) and (348±298 [SPS] vs. 525±429 [NPS2] mm^3; p=0.042). Patients characteristics are summarized in Table 2 for ureter and Table 3 for kidney stones.

2. Outcomes in ureteric stones

In the subgroup analysis of patients with a ureter stone, SPS vs. NPS1, no statistical significant effects in number of stone removal procedures (3.5±1.7 [SPS] vs. 4.0±2.9 [NPS1]; p=0.583), laser time (41.7±63.7 [SPS] vs. 40.0±39.4 s [NPS1]; p=0.380) and stone free rate (83% [SPS] vs. 87% [NPS1]; p=0.568), were found. In addition, there was no statistical difference in mean operating time SPS (10.6±12.0 min) compared to NPS1 (9.3±9.9 min); p=0.387.

Regarding the primary endpoint, the laser efficiency (mm^3/operating time [min]; mean±standard deviation [SD]) was significantly higher in the NPS1 group compared to the SPS group (39.9±44.9 vs. 28.8±30.2; p=0.017). The results are summarized in Table 4.

3. Outcomes in renal pelvis stones

In patients with a single stone in the renal pelvis, no statistically significant effects in number of stone removal procedures (10.2±8.4 [SPS] vs. 8.3±6.9 [NPS2]; p=0.467), laser time (114.6±126.3 [SPS] vs. 91.6±130.5 s [NPS2]; p=0.256) and stone-free rate (82% [SPS] vs. 84% [NPS1]; p=0.571), were found. Regarding the mean operating time, there was a statistical trend favoring the NPS2 group, but not significant (21.7±17.2 [SPS] vs. 17.9±18.7 [NPS2] min; p=0.090).

Taking the primary endpoint into account, the laser efficiency (mm^3/operating time [min]; mean±SD) was significantly higher in the NPS2 group compared to the SPS group [51.7±61.3 vs. 22.4±24.2; p<0.001]. The results are summarized in Table 5.

Table 2. Patient characteristics of 56 patients with ureter stones

Characteristic	SPS	NPS1	p-value
Patients (n)	24	32	
Sex (%)			0.501
Male	75.0	84.4	
Female	25.0	15.6	
Body mass index (kg/m^2)	26.1±3.8	26.3±3.9	0.513
Stone size (mm^3)	133±95	197±139	0.023
Mixed stones (%)	64.7	53.3	0.548
Stone composition (%)			0.386
COM	58.8	80.0	
COD	17.6	10.0	
CA	11.8	3.3	
UA	5.9	6.7	
Others	5.9	0.0	

Values are presented as number only or mean±standard deviation.
SPS, standard pulse shape; NPS1, new pulse shape 1; COM, calcium oxalate monohydrate; COD, calcium oxalate dehydrate; CA, carbonate apatite; UA, urinary acid.

DISCUSSION

The Ho: YAG laser remains the most effective lithotripsy system, since its first published experience as an energy source for lithotripsy in the nineties [3].

Because of its efficiency in treating all stone types, the actual guidelines still strongly recommend the use of Ho: YAG laser and consider it still as the gold standard for semirigid as well as for flexible ureterorenoscopy in the treatment of stones in the upper urinary tract [2,7].

However, there is still room for improvement regarding its ablative efficiency and hence procedure time. To choose the appropriate method, the surgeon needs to modify some

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Table 3. Patient characteristics of 89 patients with kidney stones

Characteristic	SPS	NPS2	p-value
Patients (n)	51	38	
Sex (%)			0.496
Male	66.7	73.7	
Female	33.3	23.3	
Body mass index (kg/m^2)	28.9±6.5	27.6±8.5	0.070
Stone localization (%)			0.135
Lower pole	56.9	39.5	
Upper and middle pole	43.1	60.5	
Stone size (mm^3)	348±298	525±429	0.042
Mixed stones (%)	47.7	48.6	1.000
Stone composition (%)			0.098
COM	40.9	65.7	
COD	11.4	11.4	
CA	22.7	8.6	
UA	25.0	11.4	
Others	0.0	2.9	

Values are presented as number only or mean±standard deviation.
SPS, standard pulse shape; NPS2, new pulse shape 2; COM, calcium oxalate monohydrate; COD, calcium oxalate dehydrate; CA, carbonate apatite; UA, urinary acid.

Table 4. Primary and secondary endpoints comparing SPS and NPS1 in patients with ureter stones

	SPS	NPS1	p-value
Number of stone recovery	3.5±1.7	4.0±2.9	0.583
Laser time (s)	41.7±63.7	40.0±39.4	0.380
Operating time (min)	10.6±12.0	9.3±9.9	0.387
Stone free rate (%)	83	87	0.568
Laser efficiency (mm^3/operating time [min])	28.8±30.2	39.9±44.9	0.017

Values are presented as mean±standard deviation or number only.
SPS, standard pulse shape; NPS1, new pulse shape 1.

adjustable pulse settings of the available laser systems. Even with remarkable development in laser technology within the last decade, leading towards more powerful Ho: YAG lithotripters, the surgeon still has the limitation of manually adjusting pulse energy, pulse frequency, and pulse width to achieve the desired results [8].

In the fragmentation setting, the urologist should work with a low pulse frequency and high pulse energy [9]. On the other hand, the availability of high-power systems achieving higher frequency settings with low energy has resulted in the development of dusting techniques [10]. The "popcorn" effect, which is mainly used as the last step in the lithotripsy session after fragmenting or dusting the stones, requires usually moderate to high energy and frequency [11].

Pulse width is considered as an additional adjustable parameter, which can affect laser fragmentation efficiency

Table 5. Primary and secondary endpoints comparing SPS and NPS2 in patients with kidney stones

	SPS	NPS2	p-value
Number of stone recovery	10.2±8.4	8.3±6.9	0.467
Laser time (s)	114.6±126.3	91.6±130.5	0.256
Operating time (min)	21.7±17.2	17.9±18.7	0.090
Stone free rate (%)	82	84	0.571
Laser efficiency (mm^3/operating time [min])	22.4±24.2	51.7±61.3	<0.001

Values are presented as mean±standard deviation or number only.
SPS, standard pulse shape; NPS2, new pulse shape 2.

and stone retropulsion rate [12,13]. Hereby, it has been demonstrated that pulse width is inversely correlated with its ablative features [14], and shorter pulse duration induce more rapid bubble expansion and collapse than longer pulse duration and correlate inversely with the retropulsion [15]. The picture of the pulse shape in [15] shows much higher power for shorter pulses than for longer pulses during the time of bubble expansion. We could suggest the speed of bubble expansion/collapse, and hence the retropulsion is depending on the power at the beginning of the pulse.

With innovative Laser-modifications like the "burst lithotripsy" or the recently developed Moses technology, there is an effort to improve the efficiency of the laser in stretching the pulse.

One burst in the "burst lithotripsy" consists of three laser pulses (all pulses with different energies) to increase the pulse length. First *in vitro* data have shown to be more ablative than conventional lithotripsy [5]. With the recently developed Moses technology, *in vitro* experiments showed more ablative effects with reduced retropulsion but still with no significant difference in total laser or procedural times *in vivo* [16,17].

Regarding the laser pulse shapes used in the current study, based on the findings from Kang et al. [15] one can easily expect that the shorter pulse of NPS2 leads to a higher treatment efficiency in NPS2 group compared to SPS-group because retropulsion should have a lower impact on the operating time in the renal pelvis than in the ureter when fragments can migrate back into the renal pelvis.

Based on [15] for the NPS1 group we would expect similar or slightly lower treatment efficiency compared to SPS group because pulse duration is similar (FWHM) or longer (FW).

We assume the lower power of pulse shape NPS1 at the beginning of the pulse leads to less retropulsion while a similar power (peak power) does not reduce the ablation efficiency compared to the SPS group. Therefore we suppose that less retropulsion in the ureter leads to the surprising and significantly higher efficiency in the NPS1 subgroup of this study.

In the current study, we standardized the pulse energy and frequency to specifically test for the effect of pulse shape and therefore making it the only variable pulse feature between the two subgroups. Hence, the goal was to compare the effect of new pulse shapes in the NPS1 and NPS2 compared to the standard SPS subgroup. To eliminate potential stone size-related confounders, we defined laser efficiency as follows: mm^3 stone destruction per operating time per minute. Hereby, we observed significantly increased laser efficiency for NPS1 and NPS2 compared to SPS. The significant differences in stone size between the groups might be a limitation in the study, nevertheless, the measurement based on the preoperative computed tomography scans was performed by an independent investigator.

The findings of the current study provide insights about the laser pulse shape highlighting it as an important adjustable laser feature that can improve the efficiency of laser lithotripsy. The combination of more than one of the known surgical techniques (fragmenting, dusting, or popcorn) is now the current trend in laser lithotripsy [18]. Thus, with the availability of another adjustable pulse feature in a laser system there will be versatile combination options, ultimately resulting in a positive difference in procedural time.

CONCLUSIONS

Our findings highlight that different pulse shapes might influence the disintegration of stones in the upper urinary tract. The efficiency of HO: YAG lasers can be improved by laser pulse shapes as provided by the Dornier Medilas® H Solvo laser. Thus, with the availability of such shapes, the surgeon has the advantage of an additional pulse variable, ultimately affecting the planning of the respective lithotripsy session.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Abdulmajeed Alghamdi, Alexander Kretschmer, and Frank Strittmatter. Data acquisition: Abdulmajeed Alghamdi, Alexander Kretschmer, and Frank Strittmatter. Statistical analysis: Alexander Kretschmer and Frank Strittmatter. Data analysis interpretation: Abdulmajeed Alghamdi, Alexander Kretschmer, and Frank Strittmatter. Drafting of the manuscript: Abdulmajeed Alghamdi, Alexander Kretschmer, and Frank Strittmatter. Critical revision of the manuscript: Alexander Kretschmer, Frank Strittmatter, and Christian G. Stief. Obtaining funding: none. Administrative, technical, or material support: Frank Strittmatter and Christian G. Stief. Supervision: Christian G. Stief. Approval of the final manuscript: Alexander Kretschmer, Frank Strittmatter, and Christian G. Stief.

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