Thulium versus holmium for in situ lower pole laser lithotripsy

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Introduction: *During in situ lower pole laser lithotripsy, the dependent location may result in increased challenge fragmenting stones and a risk for stone regrowth if residual fragments remain. The purpose of this study was to compare the thulium fiber laser (TFL) with the holmium laser (HL) for in situ lower pole lithotripsy.*

Materials and methods: *In a 3D printed kidney benchtop model, sixty 1 cm BegoStones were placed in the lower pole and fragmented in situ until fragments passed through a 2 x 2 mm mesh. Laser lithotripsy was performed using twelve energy, frequency and fiber size combinations and residual fragments were compared. In addition, laser fiber diameters and subsequent ureteroscope deflections and flow rates were compared between fibers.*

Results: *The TFL resulted in decreased residual fragments compared to the HL (11% vs. 17%, $p < 0.001$) and the three settings with least residual fragments were all TFL. Compared to the 150 µm TFL (265° deflection), there was a loss of 9° and 34° in the 200 µm TFL and 272 µm HL fibers, respectively. The measured fiber sizes were greater than manufacturer specified fiber size in every instance. Irrigation rates inversely correlated with fiber size.*

Conclusion: *The TFL resulted in 35% less residual stone fragments, up to 34° additional deflection, and an increased irrigation rate when compared to the HL. Optimal fragmentation settings are identified to further improve lower pole lithotripsy. The combination of reduced residual fragments, improved deflection, and better flow rates make the TFL advantageous for in situ lower pole lithotripsy.*

Key Words: kidney stone, thulium, holmium laser, laser, ureteroscopy

Introduction

Lower pole stones represent a unique challenge for lithotripsy given their dependent state, combined with the potential for an acute infundibulopelvic angle and high anatomic variability.[1] These unique challenges make ureteroscopic access to the lower pole more difficult and spontaneous passage of residual stone fragments less likely. Given the potential for residual stones to act as a nidus for future stone formation, minimizing stone fragments is of particular importance.[2] Residual fragments have been shown to increase unplanned medical visits.[3]

AUA Guidelines recommend ureteroscopy as a treatment for lower pole stones less than 2 cm in size.[4] The most common laser employed for the treatment of kidney stones has traditionally been the holmium:YAG laser (HL).[5] Stone free rates as high as 61%-79% were achieved with the HL when performing in situ ureteroscopy on lower pole stones less than 2 cm.[6,7] Due to the dependent nature of the lower pole, gravity

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impedes post-lithotripsy stone fragment clearance, and the infundibular length and variation in calyceal layout further complicate intraoperative access and postoperative stone passage.[1] Another unique challenge of treating stones in situ in the lower pole is that any removal of the laser fiber for stripping, basketing, or better visualization requires relocation of the tip of the ureteroscope to the renal pelvis prior to fiber reinsertion. This process increases operative time and risk of working channel perforation. In addition, the deflection angles required to reach the lower pole can cause ureteroscope damage due to absorption of laser energy by the working channel when the deflection angle exceeds the fiber's total internal reflection ability.[8]

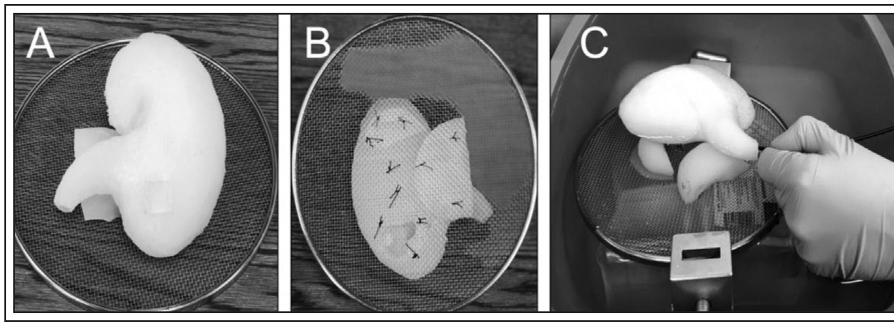

Figure 1. Benchtop model employed to test in situ lower pole laser lithotripsy. **(A)** 3D printed kidney attached to 2 x 2 mm metal mesh. **(B)** 1 cm BegoStone in the lower pole. **(C)** Ureteroscopy setup.

Recently, the United States Food and Drug Administration (FDA) approved the novel thulium fiber laser (TFL) for treatment of renal and ureteral stones. The TFL has several characteristics which might prove advantageous during lower pole in situ lithotripsy including higher pulse frequency (up to 2000 Hz) and a smaller fiber caliber (150 μm).[9-11] Recently published data reviewing in vitro studies found the TFL has 1.5-4 times higher ablation rates compared to the HL.[12] However, residual fragment size in stones treated in situ in the lower pole has not been reported. The purpose of this study was to compare the effect of the TFL and HL upon fragment size, ureteroscope deflection, and irrigation flow rate during in situ lower pole lithotripsy.

Materials and methods

A kidney model was created by uploading a CT urogram onto www.embodi3d.com, which isolates the parenchyma and the collecting system from surrounding tissue. Autodesk Meshmixer editing software (Autodesk Inc., San Rafael, CA, USA) was used to further remove the unwanted surrounding tissue and Autodesk Inventor software converted the data into a 3D-printable model. A mold was 3D printed on an Ultimaker 3 three-dimensional printer (Ultimaker, Framingham, MA, USA) using polylactic acid filament and was filled with Dragon Skin Silicone (Smooth-On, Macungie, PA, USA) generating the final kidney model, Figure 1.

A window was made in the kidney model and a 2 x 2 mm metal mesh was placed under this window. The model was then submerged in a saline bath. Next, 1 cm spherical BegoStones (calcium oxalate monohydrate (COM) consistency[13]) were molded (n = 60) and individually weighed prior to hydration for 24 hours. One stone per trial was placed, un-fixed, into the lower pole of the model. These stones were then fragmented in situ by the same surgeon using an Olympus URF-P6 (Olympus America Incorporated, Center Valley, PA, USA) flexible ureteroscope with either an Olympus Soltive SuperPulsed 60W Thulium Fiber Laser or an Olympus 100W Empower Holmium Laser. Stone dusting was the treatment goal, and the stones were considered treated once all residual fragments had passed through the 2 x 2 mm mesh grid and were collected in an underlying basin. The kidney was irrigated of all debris, which was also collected. Next, all stone residue was collected from the basin, air dried for 24 hours at room temperature and weighed using an ACPro-200 scale (American Weigh Scales, Cumming, GA, USA). After over a month of further dehydration, weighing was repeated to ensure similar results.

Laser lithotripsy was performed at 20W with the following setting and fiber combinations: TFL at 1 J/20 Hz, 0.4 J/50 Hz, 0.2 J/100 Hz, 0.1 J/200 Hz for both 150 μm and 200 μm fibers; HL at 1 J/20 Hz, 0.4 J/50 Hz for both "200 Series" 272 μm ball tip and regular 272 μm fibers. Each of the 12 setting combinations was tested on five stones. An independent t-test was used to compare HL and TFL in terms of residual fragment weight. ANOVA and Tukey's HSD tests were used for statistical analysis of the setting combinations. Significance was set at $p < 0.05$.

Deflection angles of an Olympus URF-P6R ureteroscope were measured for all fiber sizes; the

150 μm and 200 μm Olympus Soltive TFL fibers and the 272 μm Olympus HL fiber. The ureteroscope with fiber inserted was maximally deflected 5 times per fiber. The resulting deflection angles were measured by digital protractor, and the mean and standard deviation was calculated for each fiber size. Mean TFL and HL deflection capabilities were compared via ANOVA followed by Tukey's HSD test.

Ureteroscopic flow rates were measured using a 1.5 meter water column connected to an Olympus URF-P6R ureteroscope fully flexed down with fibers in the working channel for a 5 minute time period. The collected fluid was weighed on an Acculab VIC-5101 digital scale (Sartorius Group, Goettingen, Germany) to determine irrigation volume (1 g = 1 mL). Rates were compared using ANOVA followed by Tukey's HSD test.

Actual fiber sizes with and without sheath were measured using UltraTech calipers (General Tools and Instruments, Secaucus, NJ, USA) for the above fibers. In addition, each fiber was imaged at 202X magnification using a Tescan Vega II LSH scanning electron microscope (Tescan, Brno, Czeck Republic).

Results

Prior to treatment, stones weighed 1.00 g ± 0.02 g with no significant difference ($p = 0.78$) between stones used in TFL vs. HL arms. TFL lithotripsy resulted in fewer residual stone fragments compared to the HL, with a mean fragment weight of 110 mg ± 50 mg vs. 170 mg ± 50 mg, respectively. This corresponds to 11% ± 5% vs. 17% ± 5% of initial stone weight, a relative reduction of 35%, $p < 0.001$, Figure 2. Re-weighing fragments after over one month of drying gave similar results.

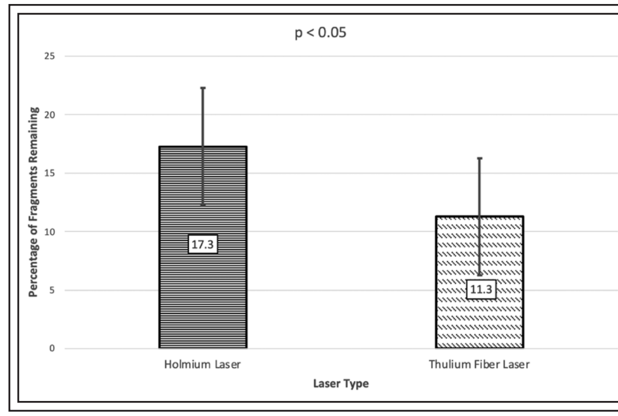

Figure 2. Comparison of mean percentage of remaining BegoStone fragment weight after lasering with either holmium laser or thulium fiber laser.

Three power/frequency/fiber combinations, Table 1, resulted in significantly less residual stone fragments. These settings were all TFL and included

TABLE 1. **Laser type and setting combinations used in this study**

Laser settings			
100 W Olympus Empower holmium laser			
Fiber size	**Pulse rate**	**Pulse energy**	**Power**
"200 Series"			
272 µm ball tip	20 Hz	1.0 J	20 W
	50 Hz	0.4 J	20 W
272 µm	20 Hz	1.0 J	20 W
	50 Hz	0.4 J	20 W
60 W Olympus Soltive SuperPulsed thulium fiber laser			
Fiber size	**Pulse rate**	**Pulse energy**	**Power**
150 µm	20 Hz	1.0 J	20 W
	50 Hz	0.4 J	20 W
	100 Hz	0.2 J	20 W
	200 Hz	0.1 J	20 W
200 µm	20 Hz	1.0 J	20 W
	50 Hz	0.4 J	20 W
	100 Hz	0.2 J	20 W
	200 Hz	0.1 J	20 W

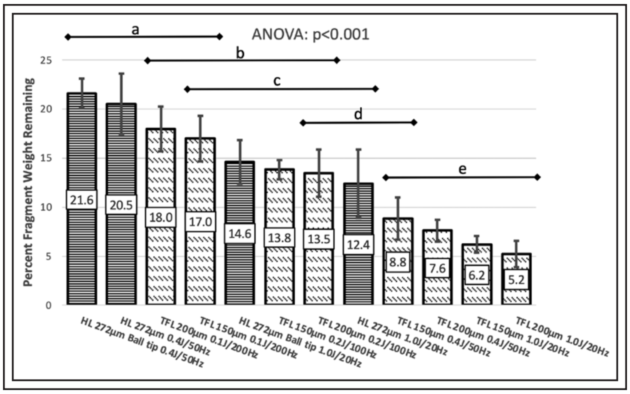

Figure 3. Residual fragment mean percentage using different fiber/power/frequency settings for holmium laser (HL) and thulium fiber laser (TFL). Letters **a, b, c, d,** and **e** represent statistically similar treatment groups.

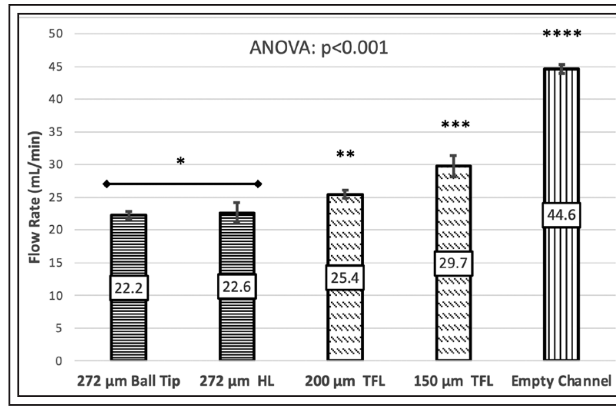

Figure 5. Irrigation flow rates through a flexible ureteroscope in the flexed position with various laser fibers in the working channel. Asterisks denote significant differences ($p < 0.05$). Horizontal line indicates statically similar results. HL = holmium Laser; TFL = thulium fiber laser.

the 200 μm 1.0 J/20 Hz and 0.4 J/50 Hz, and 150 μm 1.0 J/20 Hz; in addition, the TFL 150 μm 0.4 J/50 Hz was statistically similar to these three, but also statistically similar to two other settings, Figure 3.

Mean deflection angles were 265° ± 3° and 256° ± 4° for the TFL 150 μm and 200 μm fibers, respectively. The 272 μm HL fiber resulted in a mean deflection of 231° ± 3°. The results for the measurement of each fiber size by both a scanning electron microscope, Figure 4, and digital calipers can be seen in Table 2. As measured by microscopy, actual fiber sizes were an average of 27%

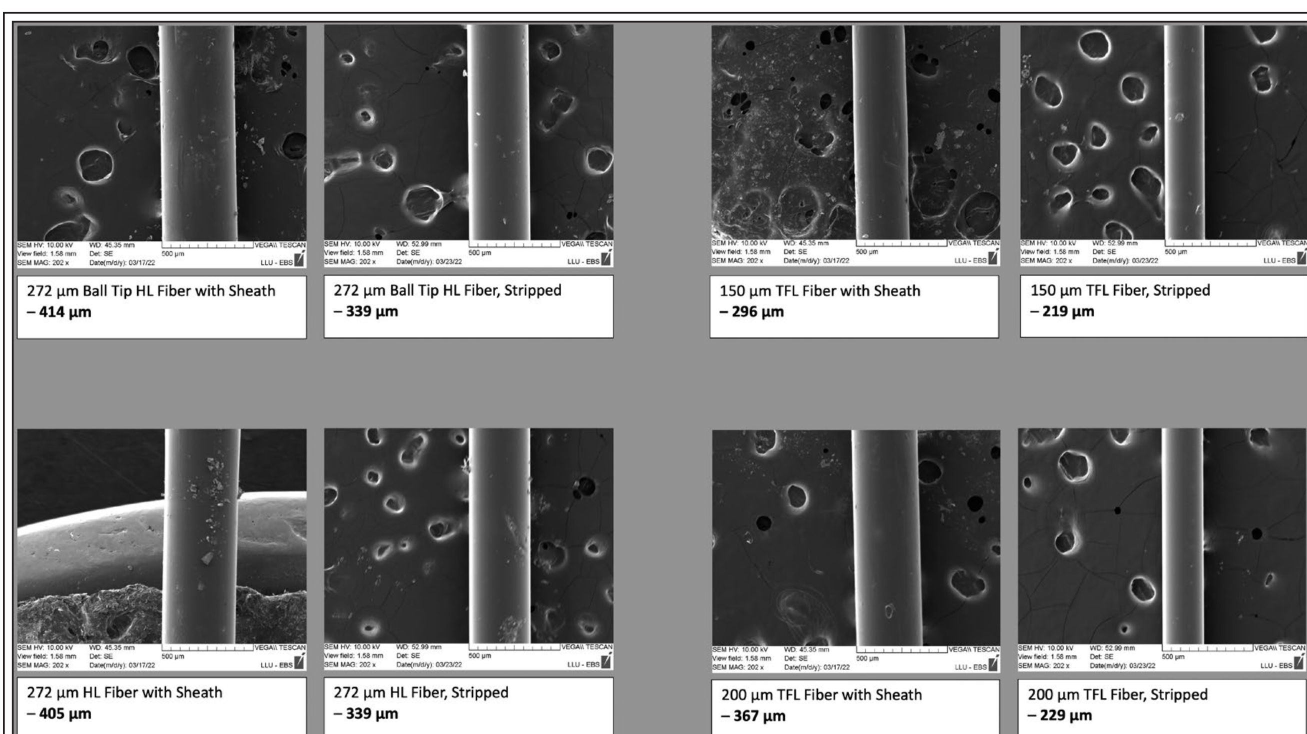

Figure 4. Laser fiber diameters as measured using scanning electron microscopy at 202X magnification for holmium laser (HL) fibers and thulium fiber laser (TFL) fibers.

TABLE 2. **Actual fiber sizes as measured with scanning electron microscope and digital calipers**

Fiber sizes Manufacturer specified size Fiber type	Scanning electron microscope With sheath (μm)	 Stripped (μm)	Calipers With sheath (μm)	 Stripped (μm)
272 μm HL ball tip	414	339	410	340
272 μm HL	405	339	410	350
200 μm TFL	367	229	360	230
150 μm TFL	296	219	280	200

HL = holmium laser; TFL = thulium fiber laser

greater than reported by the manufacturer. Irrigation flow rates were inversely proportional to fiber size, Figure 5, and there was a relative difference of 24% between the 150 μm TFL and the 272 μm HL.

Discussion

Thorough lithotripsy with a goal of minimizing residual stone fragments is particularly important in the lower pole, given its dependent nature, acute infundibulopelvic angle, and potential for anatomic variability. These factors often combine to reduce the efficacy of in situ lithotripsy, especially in situations where basketing and movement of a stone to a different calyx is not performed. Ureteroscopic laser lithotripsy is currently the most common treatment option for ≤ 1 cm lower pole stones in the United States.[14] The HL is well described in the literature, but given the challenges of the lower pole, stone free rates as low as 50% have been reported.[15] However, recent FDA approval of the novel TFL provides urologists an alternative tool with potential advantages for lower pole lithotripsy. These include lower ablation thresholds for a given stone density, an increased frequency and power parameter range, less retropulsion and higher energy density.[16] Similarly, a recently published review article concluded these factors could provide significant advantages in the clinical setting.[17] Furthermore, the TFL would appear to be specifically advantageous in the lower pole, given the difficulties noted above, but this has yet to be completely characterized. Our study was designed to perform a direct comparison between the TFL and HL in the lower pole using a benchtop model to eliminate variability and patient specific factors that would occur in the clinical setting.

In this study, the TFL achieved better fragmentation than the HL, decreasing the weight of residual fragments by 35%. As previously shown, stone passage rate is linearly related to stone size, with stones ≤ 2 mm (the maximal size of the fragments in our study) having a 98% chance of spontaneously passing.[18] Therefore, the TFL's increased ability to dust stones will result in less fragments that would require passage.

Various strategies have been employed to tackle the challenges of lower pole stones. For example, a basket can be used to reposition a stone to the upper pole prior to fragmentation. Likewise, a modified ultrasound device has had some success in moving stones out of the lower pole.[19] Percussion, diuresis and inversion therapy have been utilized in the adjuvant setting after lower pole lithotripsy.[20] Even rollercoaster riding has shown promise in facilitating lower pole stone passage.[21] Given its ability to minimize residual fragments, the TFL emerges as a desirable and cost-effective option for in situ lower pole stone management.

Optimal settings for in situ lower pole fragmentation of COM stones with the TFL have not been comprehensively reported. Previous research has suggested that generally increasing pulse rate and energy on the TFL results in increased ablation, theoretically due to an increased wattage. However, with progressive increases in pulse rate, ablation rates begin to plateau and stone retropulsion becomes significant, thereby inhibiting efficient fragmentation in the clinical setting.[10] With this in mind multiple laser settings were tested. The TFL 200 μm fiber at 0.4 J/50 Hz and 1.0 J/20 Hz, and 150 μm fiber at 1.0 J/20 Hz resulted in less residual stone burden than the other fiber size and power setting combinations tested. Using these settings, stones were reduced to 5.2%-7.6% of original weight, less than all HL power and frequency settings tested. This knowledge can aid in achieving optimal fragmentation, and this study provides preliminary evidence for setting selection during in situ lower pole laser lithotripsy.

Our study's evidence of decreased fragment weight compliments previous research which shows more complete fragmentation with the TFL when compared to the HL.[22,23] While these research studies looked specifically at the fragmentation rate, our study demonstrates decreased residual fragments, specifically in an in situ lower pole model. Recent clinical studies suggest a possible improvement in stone free rates when the TFL is used, highlighting the impact of improved fragmentation when using the TFL.[24,25] The increased fragmentation may be due to the proximity of the TFL's wavelength (1940 nm) to water's peak absorption wavelength, which optimizes the thermomechanical function of laser lithotripsy.[10,23,26] Hardy et al has shown the thermomechanical mechanism of the TFL plays a significant role in stone fragmentation. They hypothesized the energy absorbed by water within the stone rapidly expands the water, causing direct fragmentation. Consistent with their hypothesis, the fragmentation effect doesn't occur when the stones are lasered in air.[27] This further emphasizes the benefit of utilizing a laser whose wavelength optimally aligns with water's peak absorption.

The alignment of the TFL's wavelength with water's peak absorption may be useful for fragmentation but may also cause secondary heat generation that may affect urothelial tissue in the immediate vicinity. Heat generation was noted during experimental stage testing of the TFL, where temperatures during ureteral lithotripsy were shown to be higher than those generated by the HL.[28] A benchtop study by Belle et al examined the potential for thermal damage to the ureter and reported supraphysiologic temperatures which could lead to ureteral damage during sustained lasering with high power and lower irrigation flow rates.[29]

Increased irrigation and increased scope deflection are important when working in the lower pole. Introduction of a laser fiber into the ureteroscope may reduce both irrigation flow rate and deflection.[30] A recent study by Uzan et al highlights how the mechanics of the TFL allows for a much smaller laser core with resulting smaller fiber, which helps maintain total internal reflection and decreases the energy leaked into the fiber sheath. These factors were shown to translate to fewer fiber fractures when compared to the HL.[31] Building on this, our study demonstrated that ureteroscopic deflectability is greater with the smaller TFL. The difference in deflection between the larger 272 µm HL fiber and the smaller 150 µm TFL was shown to be 34°. This can lead to a clinical advantage as improved deflection has been shown to translate to decreased post-procedure stone burden, especially with infundibulopelvic angles < 30°.[32]

Direct measurement of HL and TFL fibers showed them to be larger than the size stated on the packaging. Even the central fiber core was larger than the manufacturer's reported fiber size, Figure 4. However, the size including the sheath is what occupies the working channel volume within the ureteroscope and is likely more important for determining irrigation flow rates. Our study confirmed increased fiber size led to decreased irrigation rates. The combination between the better deflection and irrigation could prove particularly useful when treating lower poles stones in situ. The increased irrigation afforded by smaller TFL fibers could irrigate fragments out of the lower pole and mitigate the increased temperatures seen with the TFL.

There are some limitations with our study. The first limitation of the study is its benchtop nature which does not completely replicate all aspects of an actual patient. However, use of a benchtop kidney model allowed for control of variables and increased standardization across the trials, which is important when comparing multiple laser/fiber/setting combinations. The second limitation of this study was the use of BegoStones constructed to mimic COM stone characteristics. This stone consistency may not clarify optimal settings for all stones encountered in urologic surgery, but it is the most common stone type. The third limitation of this study is that all trials were performed by a single surgeon, which limits any assessment for surgeon related factors, but is necessary to allow direct comparison of the laser/fiber settings. Finally, the nature of the study made blinding of the surgeon unfeasible. Even though the surgeon was not blinded, all trials were performed using identical technique and equipment. Despite these limitations, this study better characterizes use of the TFL for in situ lower pole lithotripsy.

Conclusion

This study shows that use of the TFL results in less residual stone, better ureteroscope deflection and improved irrigation compared to the HL. Furthermore, the TFL settings of 1.0 J/20 Hz and 0.4 J/50 Hz were identified as optimal settings to reduce residual stone fragments during in situ lower pole lithotripsy of COM stones. Further human clinical trials should be performed to demonstrate the reproducibility of our findings. □

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