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Abstract. The thulium fiber laser (TFL) is currently being studied as an alternative to the conventional holmium:YAG (Ho:YAG) laser for lithotripsy. The diode-pumped TFL may be electronically modulated to operate with variable parameters (e.g., pulse rate, pulse duration, and duty cycle) for studying the influence of pulse train mode on stone ablation rates. The TFL under study was operated at 1908 nm, 35-mJ pulse energy, and 500- μ s pulse duration, in a train of 5 micro-pulses, with macro-pulse rates of 10 Hz, compared with conventional TFL operation at 10 to 50 Hz. TFL energy was delivered through 100- μ m-core fibers in contact with human uric acid (UA) and calcium oxalate monohydrate (COM) stones. Mass removal rates, optical coherence tomography, and light microscopy were used to analyze the ablation craters. Stone retropulsion and fiber tip degradation studies also were conducted for these laser parameters. TFL operation in micro-pulse train (MPT) mode resulted in a factor of two increase in the ablation rate of $414 \pm 94 \mu\text{g/s}$ and $122 \pm 24 \mu\text{g/s}$ for the UA and COM stones, respectively, compared to $182 \pm 69 \mu\text{g/s}$ and $60 \pm 14 \mu\text{g/s}$ with standard pulse trains delivered at 50 Hz ($P < 0.05$). Stone retropulsion remained minimal (< 2 mm after 1200 pulses) for both pulse modes. Fiber burnback was significant for both pulse modes and was higher for COM stones than UA stones. TFL operation in MPT mode results in increased stone ablation rates which, with further optimization, may approach levels comparable to Ho:YAG laser lithotripsy in the clinic. © 2012 Society of Photo-Optical Instrumentation Engineers (SPIE). [DOI: 10.1117/1.JBO.17.2.028002]

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1 Introduction

The solid-state holmium:YAG laser (Ho:YAG) is the principal laser lithotripter in clinical use. However, our research group has recently been studying the thulium fiber laser (TFL) as an alternative lithotripter.¹⁻⁵ The TFL has several potential advantages over the Ho:YAG laser. The TFL wavelength ($\lambda = 1908$ nm) more closely matches a high-temperature water absorption peak in tissue than the Ho:YAG wavelength ($\lambda = 2120$ nm),⁶ which results in a factor of four lower stone ablation threshold^{5,7} and may lead to increased stone ablation rates. The excellent TFL spatial beam profile also allows delivery of higher laser power through smaller optical fibers without risk of destroying the fiber input end.² For lithotripsy procedures that require extreme bending of the miniature ureteroscope (e.g., into the lower pole of the kidney), a smaller fiber permits greater flexibility of the instrument. The smaller fiber also permits increased irrigation through the minute working channel within the instrument,^{3,8} thus improving visibility and safety of the procedure.

Laser lithotripsy using low pulse energies (< 0.5 J) and high pulse repetition rates (> 20 Hz) has been demonstrated to be preferable to the use of high pulse energies (1 to 2 J) at low pulse rates (< 10 Hz),^{5,9,10} when stone retropulsion is a primary concern. However, this approach, while reducing stone retropulsion, may come at the expense of slower stone ablation rates,

which may be only partially compensated for by the use of higher pulse rates, thus potentially increasing operation time in the clinic.

The diode-pumped TFL has the interesting potential to more easily control and vary the pulse characteristics into packaged bursts of micro-pulse trains (MPTs) than the conventional flash-lamp-pumped Ho:YAG laser technology. Therefore, the potential of this variation in traditional pulse delivery to impact laser lithotripsy is explored in this study. More specifically, the objective of this study is to determine whether TFL delivery of MPTs may result in improved stone ablation rates, which would in turn translate into reduced operation times in the clinic. Application of bursts of short laser pulse trains previously has been shown to increase material removal for both laser processing of metals¹¹ and tissues.¹² However, in the field of urology, investigators have only recently studied a similar approach for Ho:YAG laser lithotripsy using longer pulse lengths, without significant results.¹³ In this study, application of thulium fiber laser MPTs are explored for enhanced laser lithotripsy.

2 Methods

2.1 Stone Sample Preparation

Human uric acid (UA) and calcium oxalate monohydrate (COM) urinary stone samples with purity greater than 95% were obtained from two stone analysis laboratories (Louis C. Herring & Co, Orlando, FL and Labcorp, Oklahoma City,

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OK) and the Carolinas Medical Center (clinic of P. Irby) and used for the ablation rate and fiber burnback studies. The stones were immersed in a saline bath and kept fixed in place during the lithotripsy experiments.

2.2 Laser Parameters

An experimental thulium fiber laser (TLR 110-1908, IPG Photonics, Inc., Oxford, MA) was externally modulated with a function generator (Model DS345, Stanford Research Systems, Sunnyvale, CA) to operate in pulsed mode with a wavelength of 1908 nm, pulse energy of 35 mJ, 500- μ s pulse duration, and pulse rates of 10 to 50 Hz. The 1908 nm wavelength was chosen because it is a major TFL emission line that very closely matches a high-temperature water absorption peak in tissue at 1910 nm, thus providing a factor of four lower ablation threshold than the Ho:YAG laser wavelength at 2120 nm, for UA and COM stones. A pulse energy of 35 mJ was used for all of the studies because it was the maximum output pulse energy achievable from the TFL and optical fiber used in these studies for a 500- μ s pulse duration. This pulse duration was chosen because it is similar to the 350 to 700 μ s macro-pulse lengths currently used with the Ho:YAG laser in the clinic. The laser energy was delivered through a 100- μ m-core, low-OH silica optical fiber (AFS105/125Y, Thorlabs, Newton, NJ) for all of these studies. This fiber has a smaller core diameter and was not sterilized, but otherwise it is of similar composition to the fibers used in the clinic with the Ho:YAG laser.

The TFL was operated at 1908 nm, 35-mJ pulse energies, and 500- μ s pulse duration, in a train of five micro-pulses,

and macro-pulse rates of 10 Hz (Fig. 1). The ablation results from this MPT were directly compared with conventional macro-pulse TFL operation at 10, 30, and 50 Hz. The urinary stone samples were dried by heating them to 60 °C for 30 min and then cooled to room temperature in a container filled with desiccant before and after each experiment. Stone mass loss was measured using an analytical balance (AB54-S, Mettler-Toledo, Switzerland), and mass loss rates were calculated by dividing this value by the total number of pulses and total irradiation time.

2.3 Optical Imaging of Ablation Craters

Imaging of the urinary stone ablation craters after thulium fiber laser lithotripsy was performed using a light microscope (FS70, Mitutoyo America, Aurora, IL) to observe the ablation crater dimensions at the stone surface. Optical Coherence Tomography (OCT) of the stone samples also was performed to image the cross-sectional profile of the ablation crater. An endoscopic OCT system (Niris, Imalux, Cleveland, OH) with 7-Fr probe was used for the studies, providing images of 2.0 mm width by 1.6 mm depth, with an axial resolution of 11 μ m and a lateral resolution of 25 μ m in tissue.

2.4 Fiber Tip Degradation Studies

For each group of laser parameters, each stone sample received a total of 6000 pulses corresponding to a total energy of 210 J. Fiber tip burnback during lithotripsy was quantified, simply by placing markers on the fiber and then measuring under

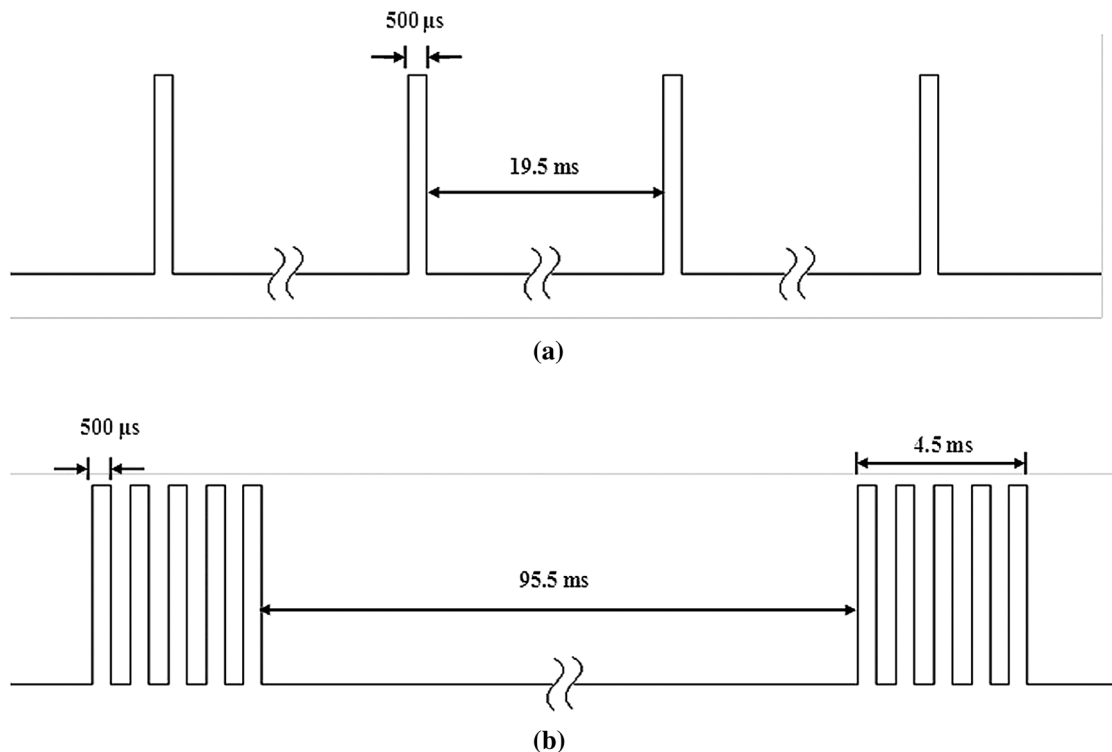


Fig. 1 Diagram comparing thulium fiber laser pulse delivery modes. (a) Standard pulse mode consisting of 500 μ s pulse length and a pulse repetition rate of 50 Hz and (b) Micro-pulse train (MPT) mode consisting of a packet of five standard 500 μ s long pulses, with an overall pulse rate of 10 Hz. Each configuration (a, b) delivers the same total number of pulses (50) per second and the same total energy to the urinary stone. Each individual pulse delivers 35 mJ to the stone.

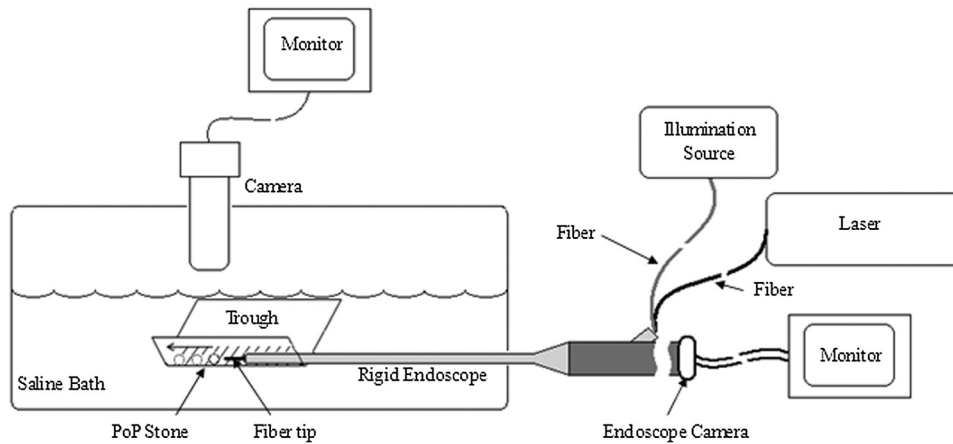


Fig. 2 Diagram of experimental setup for measuring stone retropulsion distances during thulium fiber laser lithotripsy. Plaster-of-Paris (PoP) stone phantoms were used as a stone model to provide a reproducible sample in terms of mass, shape, and surface smoothness for the studies. A rigid ureteroscope attached to a light source, camera, and monitor was used to accurately position the optical fiber tip so it was perpendicular to, centered on, and in contact with the stone prior to irradiation.

magnification the loss in length at the distal fiber tip, to the nearest 100 μm , after the lithotripsy procedure was completed.

2.5 Stone Phantom Retropulsion Studies

Laser energy was delivered through 100- μm -core optical fibers in contact mode with 6-mm-diameter Plaster-of-Paris (PoP) stone phantoms, submerged in a saline bath. Spherical PoP stone phantoms having approximately the same size (6 mm diameter) and density as urinary stones were created using a mold and then used for the stone retropulsion studies as a model for providing more reproducible results than the irregularly shaped human stone samples. A rigid ureteroscope (9.5-Fr ID, Karl Storz, Germany) attached to a light source (X7000, Stryker Endoscopy, San Jose, CA), camera (1188HD, Stryker), and monitor was used to accurately position the optical fiber tip so that it was perpendicular to, centered on, and in contact with the PoP stone phantom prior to irradiation (Fig. 2). Stone retropulsion distance was measured for each set of laser parameters, for a fixed total number of pulses (1200) and total energy (42 J) delivered to the stone.

2.6 Data Analysis

Stone ablation mass loss, fiber burnback, and stone retropulsion were reported as a mean \pm the standard deviation (S.D.). A minimum of five samples were tested for each data set. A T-test was performed to determine statistical significance between MPT and standard (50 Hz) pulse train data sets for each study (ablation mass loss, fiber burnback, and stone retropulsion). A value of $P < 0.05$ was determined to be statistically significant.

3 Results

3.1 Stone Ablation Rates

The stone ablation rates ($\mu\text{g/s}$) for thulium fiber laser lithotripsy are provided in Table 1, as a function of stone type and pulse delivery mode. As anticipated, stone mass removal increases as the pulse rate is increased from 10 to 50 Hz for the standard pulse mode. However, TFL operation in MPT mode resulted in a factor of two increase in the stone mass removal rate of

$414 \pm 94 \mu\text{g/s}$ and $122 \pm 24 \mu\text{g/s}$ for the UA and COM stones, respectively, compared to $182 \pm 69 \mu\text{g/s}$ and $60 \pm 14 \mu\text{g/s}$ with individual pulses delivered at 50 Hz, for the same number of pulses delivered (UA: $P = 0.00006$; COM: $P = 0.00009$). Optical coherence tomography cross-sectional images and light microscopy of the surface show larger stone ablation crater dimensions for MPT mode versus the standard pulse train, for both the UA and COM stone samples (Figs. 3 and 4).

3.2 Fiber Tip Degradation Studies

Degradation to the fiber tip also was quantified during the ablation studies as a function of stone type and pulse delivery mode, simply by measuring the amount of fiber burnback that occurred during lithotripsy (Table 2). Fiber burnback was significantly higher for COM stones than UA stones and increased with pulse rate. The MPT mode produced less burnback than the 50 Hz standard pulse train (UA: $P = 0.01$; COM: $P = 0.04$).

Table 1 Mean ablation rates ($\mu\text{g/s}$) for thulium fiber laser lithotripsy as a function of stone type and pulse delivery mode.^a

Pulse train	UA	COM
Standard pulse:		
10 Hz	51 ± 13	18 ± 2
30 Hz	117 ± 31	41 ± 12
50 Hz	182 ± 69	60 ± 14
Micro-pulse train:		
5 pulse packet at 10 Hz	414 ± 94	122 ± 24

^aThe pulse energy was 35 mJ, pulse duration was 500 μs , fiber diameter was 100 μm , and total number of pulses was 6,000. $N \geq 5$ samples for each data set.

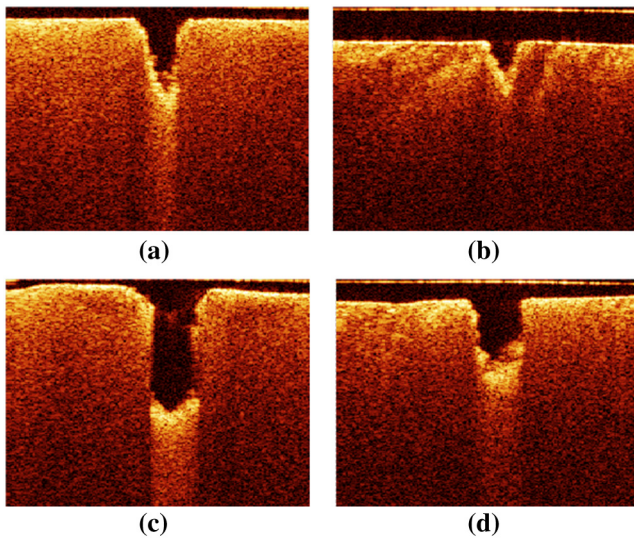


Fig. 3 Representative optical coherence tomography images of uric acid (UA) and calcium oxalate monohydrate (COM) stone samples after thulium fiber laser lithotripsy. The first row of images shows cross-sectional (width \times depth) ablation craters using standard pulse mode (500 μ s pulses at 50 Hz) for a total of 50 pulses delivered to the stone sample: (a) UA stone and (b) COM stone. The second row of images shows ablation craters for a micro-pulse train (MPT) consisting of a packet of five 500 μ s pulses, with an overall pulse rate of 10 Hz, also for a total of 50 laser pulses delivered to the stone sample: (c) UA stone and (d) COM stone. The MPT (bottom row) produces larger ablation craters than the standard pulse (top row) for both UA and COM stone types. Scale of images (2 mm width \times 1.6 mm depth).

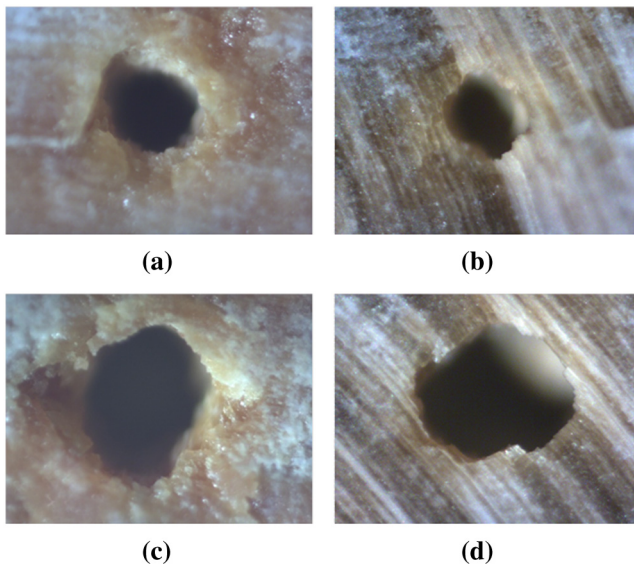


Fig. 4 Representative light microscopy images of uric acid (UA) and calcium oxalate monohydrate (COM) stone samples after thulium fiber laser lithotripsy. The first row of images shows ablation craters using standard pulse mode (500 μ s pulses at 50 Hz) for a total of 50 pulses delivered to the stone sample: (a) UA stone and (b) COM stone. The second row of images shows ablation craters for a micro-pulse train (MPT) consisting of a packet of five 500 μ s pulses, with an overall pulse rate of 10 Hz, also for a total of 50 laser pulses delivered to the stone sample: (c) UA stone and (d) COM stone. The MPT (bottom row) produces larger ablation craters than the standard pulse (top row) for both UA and COM stone types. Scale of images (700 μ m width \times 500 μ m height).

Table 2 Fiber burnback (mm) for thulium fiber laser lithotripsy as a function of stone type and pulse delivery mode.^a

Pulse train	UA	COM
Standard pulse:		
10 Hz	0.9 \pm 0.8	1.3 \pm 0.4
30 Hz	1.1 \pm 0.7	2.0 \pm 0.4
50 Hz	1.0 \pm 0.7	3.4 \pm 0.5
Micro-pulse train:		
5 pulse packet at 10 Hz	0.3 \pm 0.4	2.9 \pm 0.4

^aThe pulse energy was 35 mJ, pulse duration was 500 μ s, fiber diameter was 100 μ m, and total number of pulses was 6,000. $N \geq 5$ samples for each data set.

Table 3 Retropulsion distance (mm) of Plaster of Paris stone phantoms for thulium fiber laser lithotripsy as a function of pulse profile.^a

Pulse profile	Retropulsion
Standard pulse:	
50 Hz	0.6 \pm 0.4
Micro-pulse train:	
5 pulse packet at 10 Hz	1.3 \pm 0.8

^aThe pulse energy was 35 mJ, pulse duration was 500 μ s, fiber diameter was 100 μ m, and total number of pulses was 1,200. $N = 10$ samples for each data set.

3.3 Stone Phantom Retropulsion Studies

Plaster-of-Paris stone phantoms were used to study stone retropulsion as a function of stone type and pulse delivery mode (Table 3). The retropulsion distance measured after delivery of 1200 pulses was greater for the MPT (1.3 \pm 0.8 mm) than for the standard pulse train (0.6 \pm 0.4 mm) ($P = 0.007$). However, retropulsion for both pulse modes was considered to be minimal, based on criteria that will be discussed below.

4 Discussion

4.1 Stone Ablation Rates

For the laser pulse lengths used in this study, on the microsecond timescale, laser lithotripsy is primarily based on a photothermal mechanism.¹⁴ Water is the dominant absorber at the infrared TFL wavelength used in this study, and the bound water in the urinary stone and the surrounding fluid environment in the urinary tract contribute significantly to laser ablation efficiency. In general, ablation of the stone is achieved by rapid superheating of the water and surrounding stone material to ablative temperatures through the absorbed laser energy. This is balanced by the diffusion of the thermal energy or heat into the surrounding stone material. Thus, there is no reason to believe that a standard pulse mode inherently results in optimal transfer of the laser energy into the ablative process.

Alternative pulse mode schemes may produce higher ablation efficiencies, resulting in more rapid stone removal.

In this study, TFL lithotripsy in MPT mode resulted in a factor of two increase in ablation rates compared to standard pulse mode for both UA and COM stones, for the same pulse rate (50 Hz) and total number of pulses (6000) delivered to the stones. One possible explanation for this result is that the standard pulse train at 50 Hz produces very little thermal buildup in the stone sample in between pulses, while the MPT mode produces a rapid, stacked pulse sequence resulting in thermal buildup within the stone sample and enhanced stone ablation, but also sufficient cooling between MPTs to avoid excessive stone charring. Any attempt to increase TFL ablation mass loss by simply increasing the TFL pulse energy and pulse length using the standard pulse mode is not feasible because it produces excessive charring of the stone, accelerated fiber burnback, and increased stone retropulsion, as observed during previous studies.^{4,5}

It is possible that further exploration of the interaction between laser pulse length, duty cycle, and pulse repetition rate parameters for both the individual micro-pulses and the macro-pulse envelope of the MPT mode could result in an even greater improvement in the ablation rate. However, for this preliminary study, we were limited to operation at a 1:1 duty cycle (On: 500 μ s / Off: 500 μ s) for the micro-pulse sequence and to individual micro-pulse energies of equal magnitudes (35 mJ). With improved flexibility in pulse generation and modulation of the laser, variation of these parameters also may play an important role in optimization of TFL stone ablation rates.

Furthermore, it should be noted that TFL technology is currently limited to operation in short-pulse mode (e.g., nanosecond pulse lengths) or CW mode with the option of external modulation, as used in this study. Thus, pulse lengths are either too short or too long for direct comparison with the Ho:YAG laser lithotripter, which has pulse lengths on the order of 350 to 700 μ s. Therefore, the objective of this preliminary study was to determine whether stone ablation mass loss could be increased by using custom MPTs within the limitations of external modulation for pulsed mode of operation from a CW TFL laser.

The TFL was limited to operation with a maximum pulse energy of 35 mJ for the 500- μ s pulse duration used in these studies. The TFL pulse energy may appear significantly lower than typical minimum Ho:YAG laser pulse energy settings of \sim 400 mJ provided by clinical laser systems used with 200- μ m-core fibers. However, the 100- μ m-core fibers used in these TFL lithotripsy studies compensated for the low pulse energy by providing an energy density more comparable with Ho:YAG laser lithotripsy. For example, the radiant exposure for TFL lithotripsy was \sim 446 J/cm², compared with the Ho:YAG radiant exposure of \sim 1273 J/cm² in the clinic. When the (factor of four) lower stone ablation threshold for the TFL compared to the Ho:YAG laser is also factored in, the 35 mJ pulse energy delivered through a 100- μ m-core fiber translates into a comparable range of parameters for TFL lithotripsy to that of the Ho:YAG laser. The radiant exposures used in this study are also well above the TFL ablation thresholds previously measured for UA (6.5 J/cm²) and COM stones (20.8 J/cm²),^{5,7} which is required for efficient and rapid lithotripsy.

Finally, previous reports have shown that the beam profile emitted from a small-diameter fiber (e.g., 100- μ m-core) may

produce a different irradiance along its optical axis than the beam profile from a larger, multimode fiber (e.g., 200- μ m-core) because of the presence of higher order mixed modes.¹⁵ Normally, the spatial beam profile would need to be considered in any comparisons using different fiber diameters. However, during laser lithotripsy, the fiber tip is in constant contact with the stone, and the fiber tip experiences rapid degradation from ablative stone fragments. As a result, the spatial beam profile out of the fiber is constantly changing and difficult to quantify. Nevertheless, in summary, the radiant exposures used in this preliminary TFL lithotripsy study are well above previously reported UA and COM stone ablation thresholds.

4.2 Fiber Tip Degradation Studies

The relatively large amount of fiber burnback experienced in all of these studies is most likely due to the delicate nature of the 100- μ m-core fiber tip, despite the pulse energy being kept low. Smaller optical fiber tips previously have been shown to experience greater burnback for both the TFL and Ho:YAG lasers during lithotripsy.^{3,16} For a given set of laser parameters, fiber burnback also was consistently less for UA stones than for COM stones, presumably due to the softer composition and smoother surface of the UA stones. On the contrary, the COM stones exhibited a more irregular surface that increased the probability of the fiber tip becoming lodged and damaged in the stone crevices.

The phenomenon of fiber burnback should be put into proper perspective. It previously was stated that the initial spatial beam profile at the distal end of the fiber tip during Ho:YAG laser lithotripsy is usually destroyed due to impact of ablative stone fragments early in the lithotripsy procedure, since the fiber is in contact mode with the stone. Additionally, the sterile clinical fibers are typically designated as disposable, single-use fibers. However, a high amount of fiber burnback during an individual lithotripsy procedure may be clinically significant. For example, if bleeding (although rare) occurs during laser lithotripsy, continuous irrigation is necessary to keep the visual field clear. However, if the surgeon has to pause frequently to recleave a damaged fiber tip, blood clots can form quickly and vision may become obscured, in turn leading to increased operative times and potentially lower stone-free rates.

4.3 Stone Phantom Retropulsion Studies

Stone retropulsion is a major side effect of laser lithotripsy because it results in the urologist wasting significant operative time chasing the stone within the urinary tract, effectively reducing the stone ablation efficiency in the process. Less retropulsion, therefore, would be a desirable feature of a laser lithotripter. In this study, stone retropulsion remained minimal (less than 2 mm after 1200 pulses) for both pulse modes. The amount of stone retropulsion that would be considered acceptable in a clinical study is not easy to quantify. However, for the purposes of this study and previous studies,⁵ minimal retropulsion was defined to be a retropulsion distance of less than 2 mm. This value is based in part on the observation that the fiber-tip-to-stone surface working distance needs to be relatively short, requiring near-contact working conditions, for efficient stone vaporization during laser lithotripsy. Otherwise, large gaps in the fiber-to-stone working distance result in significant absorption of the laser radiation by the intervening water layer and a corresponding decrease in ablation efficiency.

The weak retropulsion effects observed in this study may be explained by both the low pulse energy (35 mJ) and the small optical fiber diameter (100 μm) used in these experiments. Previous Ho:YAG laser lithotripsy retropulsion studies also have reported that the use of lower pulse energies, longer pulse durations, higher pulse rates, and smaller optical fiber diameters is the optimal combination of laser parameters for minimizing stone retropulsion.^{17–22} The TFL technology is ideally suited for operation with this combination of laser parameters.

5 Conclusions

Thulium fiber laser operation in MPT mode results in a factor of two increase in the ablation rate compared with standard pulse mode for uric acid and COM urinary stones, with minimal stone retropulsion. With further optimization, thulium fiber laser ablation rates may approach values comparable to holmium:YAG ablation rates in the clinic.

Acknowledgments

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