The Rise and Fall of High Temperatures During Ureteroscopic Holmium Laser Lithotripsy

Running Title: Laser-Created Heat During Ureteroscopy

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Abstract:

Introduction: Temperatures over 43°C - the threshold for cellular injury – may be achieved during ureteroscopic holmium laser lithotripsy. The time to reach and subsequently clear high temperatures at variable laser power settings and irrigation pressures has not been studied.

Methods: A flexible or semirigid ureteroscope was placed within an 11/13Fr ureteral access sheath inserted into a 250mL saline bag simulating a normal caliber ureter, renal pelvis reservoir, and antegrade irrigation flow. A thermocouple was placed adjacent to a 365μm fiber fired for 45 seconds at 0.6J/6Hz, 0.8J/8Hz, 1J/10Hz, 1J/20Hz, and 0.2J/80Hz. Irrigation pressures of 200, 100, and 0mmHg were tested. Mean temperature changes were recorded with 6°C increase as a threshold for injury (as body temperature is 6° below 43°C).

Results: Semirigid scope: At 200mmHg no temperature changes >6°C were observed. At 100mmHg, changes >6° occurred with 1J/20Hz within 1 second of activation and returned to ≤6° within 1 second of cessation. At 0mmHg, changes >6° occurred with all settings; within 1 second at power ≥10W. Temperatures returned to ≤6°C within 5-10 seconds. At 0J/60Hz (35sec). Temperatures returned to ≤6°C in under 10 seconds. Flexible scope: At 200mmHg, changes >6°C occurred at 1J/10Hz (15sec), 0.2J/80Hz (3sec), and 1J/20Hz (2sec). Temperatures returned within 6° of baseline within 2 seconds. At 100mmHg, changes >6° occurred in all but 0.6J/6Hz. Temperatures returned to ≤6° in 5-10 seconds. At 0mmHg, all settings produced changes >6°C within 3 seconds, except 0.6J/6Hz (35sec). Temperatures returned to ≤6°C in under 10 seconds.

Conclusions: High temperatures were achieved in our in vitro model in as little as 1 second at common irrigation pressures and laser settings, particularly with a flexible ureteroscope and power ≥10W. However, with laser cessation, temperatures quickly returned to a safe level at each irrigation pressure.
Introduction:

The Holmium: Yttrium-Aluminum-Garnet (Ho:YAG) laser is commonly used during ureteroscopy to treat urinary stones due to its ability to fragment nearly any stone with minimal risk of injury to the ureter. Newer, high-powered lasers allow for faster fragmentation or ablation of urinary stones, but this increased power adds increased risk of injury. Due to their photothermal mechanism of lithotripsy, Ho:YAG lasers can produce significant heat, risking thermal injury to the ureter even without direct contact between the laser fiber and the ureteral wall (1-5). The threshold for cellular thermal injury, 43°C, has been shown to be exceeded using conventional, relatively low power laser settings in bench-top models of a renal calyx and a ureter (2, 5). The magnitude of heat production, and therefore the potential for injury during ureteroscopic lithotripsy, is impacted not only by laser pulse energy and frequency, but duration of laser activation and flow of irrigation (5). To date, no studies have demonstrated the relationship between heat production and the variables under direct control of the urologist: laser energy, activation time and irrigation pressure. Our aim was to determine the time required to reach and subsequently clear intraureteral temperatures over 43°C at a variety of laser and irrigation settings using both a flexible and semirigid ureteroscope in a bench-top ureteral model.

Methods:

A digital flexible ureteroscope (Lithovue, Boston Scientific, Marlborough, MA) or a 33cm, 6.4fr semirigid ureteroscope (OES Pro, Olympus, Tokyo, Japan) was placed 15cm into a 36cm, 11/13Fr ureteral access sheath (Navigator, Boston Scientific) to simulate the ureteroscope position for a mid-ureteral stone. To simulate the reservoir effect of the renal pelvis and calyces, the proximal end of the access sheath terminated in a full 250mL saline bag (Figure 1a). Room temperature 0.9% saline irrigation was delivered via the working channel of the ureteroscope at pressures of 200mmHg, 100mmHg, and 0mmHg using a programmable fluid management device (FluidSmart, Thermedx, Cleveland, OH). Flow rate at these irrigation pressures was calculated by timed capture of irrigation exiting the distal end of the access sheath into a graduated receptacle. A wire thermocouple (Omega Engineering, Norwalk, CT) was placed within the ureteral model 3mm adjacent
and parallel to the tip of a 365μm laser fiber which was initially passed through the working channel of the ureteroscope until the tip could be seen within the ureteral model lumen using the optics of the ureteroscope (Figure 1b). A 120watt Ho:YAG laser (Pulse 120H, Lumenis, Yokneam, Israel) was used to deliver laser energy at settings of 0.6 J/6Hz, 0.8 J/8Hz, 1 J/10Hz, 1 J/20Hz, and 0.2J/80Hz for 45 seconds each. The system was allowed to equilibrate with each new irrigation pressure for 30 seconds prior to each run, with the exception of those runs with no pressure. For those runs, irrigation was delivered at 200mmHg for 30 seconds to allow the model to fill, then the irrigation arrested by a stopcock and laser firing immediately commenced. Two runs per laser energy setting, irrigation pressure, and ureteroscope type combination were completed. Mean temperature change from baseline was recorded at 1 second intervals during laser activation and for 15 seconds after cessation. 6°C above the baseline temperature was chosen as the threshold for potential ureteral injury as 43°C is 6°greater than normal body temperature of 37°C.

Results:

At an irrigation pressure of 200mmHg, none of the tested laser energy settings generated a temperature increase 6° or more over baseline using a semirigid ureteroscope (Figure 2a). Using the flexible ureteroscope, laser settings of 1J/20Hz and 0.2J/80Hz surpassed the 6° threshold within 2 seconds of activation and reached a maximum of 14° and 9.5° above baseline, respectively. 1J/10Hz also surpassed 6° above baseline after 15 seconds of continuous activation, and maximum temperature increase was 7° above baseline. After stopping laser activation, all three settings returned to below the 6° threshold within 2 seconds (Figure 2b).

At an irrigation pressure of 100mmHg in the semirigid scope, 1J/20Hz was the only laser setting to produce a temperature rise over 6°. This occurred within the first second of activation and reached a maximum of 9° above baseline. The temperature returned to near baseline levels within 2 seconds after laser cessation (Figure 2c). In the flexible scope, all laser settings other than 0.6J/6Hz produced temperature rises at least 6° over baseline. This occurred within 4 seconds of laser activation at 1J/10Hz, 0.2J/80Hz, and 1J/20Hz. At
1J/20Hz, the maximum temperature rise over baseline was 19° which required 10 seconds to return below the 6° threshold after laser cessation (Figure 2d).

With no irrigation inflow via the semirigid ureteroscope, all laser settings produced temperature rises greater than 6° over baseline. The threshold was surpassed in under 1 second at higher power settings but remained at approximately 6° over baseline for the duration of the run at 0.6J/6Hz. Settings of 0.2J/80Hz produced a maximum temperature increase over 60° after about 20 seconds of activation. Following laser cessation, temperatures dropped below the 6° threshold within 5 seconds (Figure 2e).

Using the flexible scope and 0mmHg irrigation inflow, all laser settings produced temperature rises greater than 6° over baseline with higher power settings climbing to an excess of 20° above baseline within the first 4 seconds. Settings of 0.2J/80Hz produced a maximum temperature increase over 50° after about 20 seconds of activation. Following laser cessation, temperatures dropped to or below the 6° threshold within 5 seconds (Figure 2f).

Mean irrigation flow rates at the three pressure settings for each ureteroscope are listed in Table 1.

Discussion

High-powered lasers have created new opportunities for the treatment of urinary calculi. Not only can these newer lasers deliver high energy per pulse to quickly fragment hard stones, but they can produce high frequencies that enable the urologist to “dust” a stone rather than fragment it and potentially obviate the need for basket extraction of larger fragments (6). The heat production that comes hand in hand with the photothermal mechanism of lithotripsy of the Ho:YAG laser was well described nearly two decades ago (7). However, it is only in recent years that Ho:YAG lasers with the ability to deliver high energy, high frequency, and potentially high heat have become clinically available for lithotripsy.

Thermal injury to tissue can occur at any temperature above 43°C (8), however the degree of injury is dependent on both temperature and time of exposure. The time of exposure for any given temperature to produce irreversible damage can be estimated; over small intervals it generally follows that for every degree above 43°, the time required for injury is
reduced by 50% (9). For example, tissue lethality requires 120 minutes of exposure at 43°C, but only 7 seconds at 53°C.

This is the first bench-top study to investigate clinically practical parameters of ureteroscope type and irrigation pressure on the rate of heat production and subsequent dissipation during Ho:YAG laser activation. Additionally, we created a unique bench-top ureteral model designed to mimic the filling of the renal pelvis and antegrade “outflow” of irrigation that is experienced clinically. We found that “traditional” low power laser lithotripsy settings such as 0.6J/6Hz and 0.8J/8Hz can produce temperature elevations equal to or in excess of 6°C within our ureteral model. However, the risk for injury at these settings under average clinical conditions is minimal. Even with moderate irrigation pressure (100mmHg) and low flow in a flexible ureteroscope, 0.8J/8Hz required at least 15 seconds of continuous activation to reach the minimum threshold for injury. Assuming the use of physiologic irrigant at 37°C and the principles described by Sapareto and Dewey (9), exposure time for injury in this scenario would be approximately 10 minutes. The use of irrigation at temperatures less than 37°C would further prolong the exposure time for any potential thermal injury. These requirements for extreme circumstances of laser activation and irrigation to create thermal injury are in agreement with several large series demonstrating the \textit{de novo} stricture rate after ureteroscopic Ho:YAG laser lithotripsy to be less than 2% (10-13). Notably, these reports utilized settings similar to the lower power settings tested here with total power output of 3.6 to 10W with rare escalations to 15W.

Higher power laser settings produce more dramatic temperature elevations. The shorter length and larger working channel of the semirigid ureteroscope results in over three-fold increased flow relative to the flexible ureteroscope, maintaining safe temperatures at all tested laser energies with irrigation pressure of 200mmHg. At moderate irrigation pressures of 100mmHg, 1J/20Hz produced high temperatures, but this was limited to a maximum of 8° above baseline, which would require roughly 30 minutes of exposure to produce injury. Using the flexible ureteroscope, high power laser fragmentation and dusting settings created temperature elevations over 6°C even with high irrigation pressure. 1J/20Hz and 0.2/80Hz created rapid temperature increases, surpassing the 6°C threshold in the first 2 seconds. However, each setting quickly plateaued at levels, which
under usual conditions, would require exposure times in excess of 5 minutes for significant injury. At moderate irrigation pressure however, 1J/20Hz reached maximum temperature elevations above baseline with the potential for thermal injury after only seconds of exposure. Fortunately, these temperatures were achieved only after 10 seconds or more of continuous laser activation.

In both ureteroscopes with no irrigation pressure, the higher power laser settings quickly created temperature elevations in excess of 20° over baseline, where there is potential for sub-second exposures to induce tissue injury. Temperature decreases to below the threshold for injury following laser cessation were delayed at least 5 seconds or more, emphasizing the safety role of irrigation during laser use. Interestingly, 0.2J/80Hz was observed to create higher maximum temperatures than 1J/20Hz in this zero irrigation pressure setting despite the 4W higher power in the latter. The etiology of this phenomenon is unclear, but suggests that increased caution regarding potential thermal injury is advised if high frequency settings are used in no or low irrigation scenarios.

Our results add to the existing data on the thermal properties of Ho:YAG laser lithotripsy. Using a glass test tube submerged in a 37°C bath as a calyceal model, Hein et al (4) demonstrated temperatures as high as 68°C when using high power laser settings of up to 100W without irrigation. In a similar bench-top set-up, Aldoukhi et al (2) demonstrated maximum temperatures of 69.8°C without irrigation and 40W of laser energy. They went on to further test their findings in vivo using pigs and found peak temperatures 15°C higher than in their bench-top model and observed tissue charring of the calyx and renal parenchyma on gross pathologic exam (1). Prior to this, the heat-sink effect of the highly vascular renal parenchyma was hypothesized to be protective against the generation of high temperatures. As the authors suggest, it is likely that the heat generated by high power Ho:YAG lasers accumulates quickly and overwhelms any heat sink effect of the renal parenchyma. Reduced irrigant flow in vivo likely contributed to the observed higher temperatures relative to their bench-top model.

The potential for urinary system injury is likely worse in the ureter relative to a renal calyx as there is less surrounding vasculature to provide any possible heat-sink, the narrow
lumen reduces the flow of irrigation, and increases the risk of circumferential injury and subsequent stricture formation. This has been illustrated by Molina et al (14), who demonstrated thermal spread of at least 1cm from the tip of a 365μm laser fired at 10 watts for just 3 seconds in a sheep ureter. Additionally, it is tempting to limit or stop irrigation during ureteroscopic lithotripsy to decrease stone migration proximally up the ureter and away from the laser. Our group has previously demonstrated that high power laser settings can create high temperatures in a bench top model and that judicious use of irrigation can mitigate heat production (5). The current study builds off this work by employing an improved ureteral model which is more representative in caliber (11/13fr versus 15fr), includes a ureteroscope for delivery of irrigation and obstruction of its outflow, and adds a small volume reservoir to mimic the natural filling of the renal pelvis and antegrade flow of fluid observed clinically. Additionally, in the current study we emphasize irrigation pressure rather than flow as pressure is the variable directly manipulated by the operating urologist during ureteroscopy.

Although smaller diameter fibers are often used during ureteroscopy, we chose to use a 365μm fiber as its larger diameter restricts the flow of irrigation via the ureteroscope more than a small 200μm or 272μm fiber (15) and thus provides the most conservative extrapolation to clinical scenarios. However, if the urologist decreases the flow of irrigation to reduce stone movement or urinary system pressure, the size of the fiber is less significant. Additionally, 365μm or larger fibers are the referenced fiber size in many reports on the safety of ureteroscopic laser lithotripsy (10-13). For some centers there may even be an incentive to use larger fibers as they are more durable (16) and thus may represent a cost savings relative to smaller fibers. Although there is controversy over whether larger fibers create more or less heat than smaller fibers, what differences exist between fiber sizes appear relatively subtle relative to the impact of irrigation. Hein et al (4) tested 272μm and 940μm laser fibers in a test tube model and found the smaller fiber generated higher temperatures, though no statistical analysis of the difference is reported and the measured energy output for each fiber did not appear equivalent. Buttice et al (3) observed more rapid temperature elevation during laser activation in a kidney model using a 272μm compared to a 200μm fiber, however maximum temperature was not different
between the 2 fibers. Importantly, any difference between the fibers was lost when continuous irrigation was applied.

Previous work on this subject both at our center and others have suggested increased irrigation and avoidance of prolonged laser activation as mitigating strategies to address high-power laser generated heat. Stone retropulsion and increased renal pressures leading to increased rates of post-operative infectious complications limit irrigation as a solitary solution. Our results support limiting activation time provided there is some irrigation present. If irrigation is held, even a few seconds of lasing can create high temperatures when power is over 10W. Limiting activation time by using short bursts of laser energy may not be adequate as a single strategy either. Our results suggest somewhat long intervals, 3-5 seconds of cessation, may be required to clear high temperatures. More significantly, multiple short exposures to elevated temperatures have been shown to be injurious to tissues when the interval between exposures is brief as the case may be during ureteroscopic laser lithotripsy (17). Based on these results, if laser power over 10W is to be used in the ureter, we suggest a combination strategy of 1) at least moderate irrigation, 2) limiting laser activation to 3-4 second bursts with 3-4 second pauses between to allow temperature normalization and 3) consideration of reversion to lower power settings if a prolonged procedure is expected. Finally, the use of cooled or non-warmed irrigation can also be considered to add an additional margin of safety.

There are several limitations to recognize in this work. First, we report our results as temperature changes from baseline and acknowledge that a temperature elevation of 6°C will not equate to an intraureteral temperature of 43°C \textit{in vivo} except under a perfect set of circumstances. Intraureteral temperature is a complex result of the starting temperature of the irrigation, its flow rate, and any heating or cooling that may occur from contact with the patient’s tissues. The use of continuous versus pulsed irrigation may additionally have unique impacts on laser-induced heating. Second, we recognize that the use of high-power laser settings during ureteroscopy is rare in contrast to their use in the bladder or the renal pelvis. However, as discussed above, newer lasers are not only more powerful, but they can generate high frequency. A relatively low pulse energy combined with a very high frequency results in the delivery of a large amount of power. As low pulse
energy, high frequency stone ablation, or “dusting,” of stones continues to gain popularity, there may be urologists who use settings with power over 10W in the ureter to try to avoid opening expensive disposable equipment such as a basket. The addition of new endoscopic technology, such as robotic-assisted ureteroscopy, may also increase the urologist’s confidence regarding aim and ability to maintain contact with the stone such that dusting within the ureter becomes more attractive. Additionally, our model does not incorporate a stone. Lithotripsy implies the presence of a stone and as the intended target of laser energy, the stone material will absorb laser energy that would otherwise contribute to heat production. Lee et al (18) demonstrated that the force of ejected fragments from the stone surface is the primary contributor to stone retropulsion during lithotripsy and thus by the law of conservation of momentum, some laser energy must be converted to this mechanical energy, rather than heat. However, given the impact of irrigation flow demonstrated here and by others (1-3, 5) the limitation of flow by stone material may create a counterintuitive increase in laser-related heat production. Indeed, the presence of stone material has been demonstrated in another bench-top study to increase laser-generated heat by up to 12% (4). Further study with stone material of varying size and composition is required. Finally, this is an in vitro bench-top study. Further study is needed in vivo to better demonstrate temperature generation, dissipation, and actual thermal tissue injury.

Conclusions

Temperatures over the threshold for cellular injury were achieved in our in vitro model in as little as 1 second at common irrigation pressures, particularly when using a flexible ureteroscope and laser settings ≥10W. These high temperatures returned to a safe level within 5 seconds at each irrigation pressure. Judicious use of irrigation, limited activation time, and adequate time between laser activations may decrease the risk of thermal injury if high energy laser lithotripsy is pursued in the ureter.

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**Author Disclosure Statement:**

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References


Abbreviations used:

**Ho: YAG**: Holmium: Yttrium-Aluminum-Garnet
**Table 1:** Measured irrigation flow rates at various pressures applied through flexible and semirigid ureteroscopes with 365μm laser fiber in the working channel.

<table>
<thead>
<tr>
<th>Scope/Pressure</th>
<th>200mmHg</th>
<th>100mmHg</th>
<th>0mmHg</th>
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<tbody>
<tr>
<td>Semirigid</td>
<td>90.3mL/min</td>
<td>49.6mL/min</td>
<td>7.1mL/min</td>
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<tr>
<td>Flexible</td>
<td>24.7mL/min</td>
<td>13.1mL/min</td>
<td>4.6mL/min</td>
</tr>
</tbody>
</table>
**Figure 1:** (A) Bench-top model experimental set up. (B) Intraluminal view using ureteroscope optics with the thermometer and laser fiber tips in view.
Figure 2: Mean temperatures produced during Ho:YAG laser firing in a ureteral model at various laser settings, irrigation pressures, and ureteroscope types. Semirigid ureteroscope irrigation pressures of (a) 200mmHg, (c) 100mmHg, (e) 0mmHg. Flexible ureteroscope irrigation pressures of (b) 200mmHg, (d) 100mmHg, (f) 0mmHg. Horizontal bars denote temperature change of >6°C from baseline, which correlates to >43°C, the threshold for tissue injury, if irrigation is normal body temperature of 37°C. Vertical bars denote the end of 45sec of continuous lasing.