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·论　著·

国产钬激光手术对兔肾热损伤的初步研究



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【摘要】 **目的**　探索用新西兰大白兔的新鲜离体肾脏和输尿管进行初步实验，观察国产钬激光热损伤的效果。**方法**　在手术室内（恒定温度 22℃，湿度 60%），选用国产钬 60 W 激光设备，将新西兰大白兔的新鲜离体肾脏放入已注入 50 mL 生理盐水的 50 mL 一次性使用无菌注射器内，同时将 550 μm 的钬激光光导纤维放入其中，用水银温度计测定生理盐水的温度；钬激光参数设定为频率 20 Hz，能量 2 J，激发 15 s，间歇 5 s，反复进行，分别在 2、5、7 min 测定生理盐水的温度，解剖并拍摄兔肾，进行病理学检查。**结果**　钬激光激发 2 min 时，注射器内生理盐水温度从 22℃ 升高到 38℃，兔肾皮质和髓质基本红润，病理检查提示肾皮质、髓质及输尿管均接近正常；5 min 时，注射器内生理盐水温度升至 57℃，兔肾皮质呈白色，皮质、髓质分界欠清，肾髓质色泽红润，病理检查提示皮质肾单位大部分坏死，髓质变性不明显，输尿管明显变性；7 min 时，注射器内生理盐水温度高达 78℃，肾皮质、髓质分界不清，均呈白色，皮质、髓质凝固，病理检查提示肾小球、肾小管均基本变性、坏死。**结论**　国产钬激光常用的碎石功率会产生渐增的热损伤，水温超过 50℃ 以后，将有可能对人体组织产生损伤。

【关键词】 钬激光；肾脏；输尿管；热损伤；兔

A primary research of the thermal damage of rabbit kidney by domestic holmium laser in surgery

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【Abstract】 **Objective**　To observe the effect of thermal damage in the fresh isolated kidneys of New Zealand white rabbits caused by domestic holmium laser. **Methods**　In the operation room (constant temperature 22℃, humidity 60%), Guangdong electric (POTENT) domestic holmium laser equipment was chosen. The fresh isolated kidney of New Zealand white rabbit was put into a disposable sterilized syringe with 50 mL normal saline, then the holmium laser optical fiber (550 μm) was put into it, and the temperature of normal saline was measured by a mercury thermometer. The parameters of holmium laser were setted as frequency 20 Hz, energy 2 J, stimulating time 15 seconds, intermittent time 5 seconds, which was repeated. The temperature was measured 2, 5 and 7 minutes after stimulation. Then the kidney was dissected, phtographed, haematoxylin-eosin stained, and pathologically examined. **Results**　At the 2nd minute of stimulation, the temperature of normal saline in the syringe increased from 22℃ to 38℃; the cortex and medulla of rabbit kidney were ruddy, and the cortex, medulla and ureter were almost normal in pathological section. At the 5-minute point, the temperature increased to 57℃, and the cortex turned to be white, while the medulla remained ruddy, but the demarcation between the cortex and medulla was not very clear. At the 7th minute, the temperature was 78℃, and the cortex and medulla were both white and solidification with no clear demarcation. Pathological examination showed severe degeneration and necrosis of glomerulus and renal tubule. **Conclusion**　Common power of domestic holmium laser would produce increasing thermal damage, which may cause tissue damage in the human body when the temperature increases above 50℃.

【Key words】 Holmium laser; Kidney; Ureter; Thermal damage; Rabbit

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钬激光是一种当代泌尿外科常用的激光，为脉冲式激光，工作介质为固定在钇铝石榴石晶体中的钬，波长为 2 100 nm，通过软/硬光导纤维（光纤）传送，在泌尿外科领域广泛应用，适合泌尿外科的结石、肿瘤等体腔内手术。钬激光具有以下特性：① 组织穿透度<0.5 mm，可用于精确的外科切割和止血；② 高能脉冲，常用于处理泌尿系统结石、前列腺切除、尿道或输尿管狭窄切开和膀胱肿瘤切除等。钬激光使用时约 95% 能量被周围 5 mm 的水介质吸收，方向性好，碎石效率高，是泌尿系统腔内手术理想的碎石工具，能够高效处理泌尿系统结石等[1-3]。但是随着钬激光在国内的普及，泌尿外科医生发现有些泌尿系统结石术后随诊患者出现了输尿管狭窄、粘连甚至管腔闭锁甚至肾功能受损[4]，需要后续治疗。其原因除与结石损伤、感染、手术操作等有关外，是否与术中钬激光的热效应有关？目前其相关研究较少，特别是缺乏国产钬激光设备的文献。为此，我们采用国产钬激光设备对成年新西兰大白兔的新鲜离体肾脏和输尿管进行了尝试性实验，探究钬激光手术时热效应导致的热损伤产生的不良反应。现报告如下。

1 材料与方法

1.1 材料

本研究在手术室内进行，室内恒定温度为 22℃，湿度为 60%，标准电源 220 V，频率 50 Hz。实验动物为 5 只健康新西兰大白兔，雌雄不限，年龄 6 个月，体质量 4 ~ 5 kg，由四川大学华西医学中心动物实验中心提供。采用广东普电自动化科技股份有限公司生产的钬激光治疗机（型号：POTENT-H2），最大输出功率 60 W，波长 2 100 nm，标准配置 550 μm 传导光纤。一次性使用无菌 BD 注射器，注射用生理盐水，实验室常用水银温度计。

1.2 方法

钬激光治疗机连接标准配置的 550 μm 钬激光光纤，钬激光功率参数设定为频率 20 Hz，能量 2 J 状态，保持待机。尖段光纤放入 50 mL 的一次性无菌 BD 注射器，固定在金属架上，注射器中为 50 mL 室温生理盐水；采用过量空气耳缘静脉注射处死新西兰大白兔后，立即采集肾脏并放入注射器中，保持密闭，钬激光激发 15 s，间歇 5 s，重复进行，分别在进行到 2、5、7 min 时用实验室常用的标准水银温度计在此 3 个时间点分别测定注射器内生理盐水的温度，每个时间点均取出大白兔肾脏，每个时间点重复 3 只兔，取 3 次温度的平均值。仔细观察并用普通数码相机拍摄完整兔肾脏和剖开后的肾皮质、髓质及输尿管，随后处理标本，用苏木精-伊红（hematoxylin and eosin，HE）染色，奥林巴斯显微镜不同放大倍数观察其病理切片，并拍摄分析。

2 结果

2.1 2 min 时钬激光热效应

钬激光激发 2 min 时，注射器内生理盐水温度从 22℃ 升高到 38℃。解剖兔肾脏，其皮质和髓质基本红润；病理检查提示肾脏皮质、髓质及输尿管均接近正常。见图 1。

2.2 5 min 时钬激光热效应

钬激光激发 5 min 时，注射器内生理盐水温度升至 57℃。解剖兔肾脏，其皮质部分有比较明显的变化，色泽泛白色，皮质、髓质分界欠清，肾脏的内层包括肾髓质色泽红润；病理检查提示皮质肾单位大部分坏死，髓质变性不明显，输尿管明显变性。见图 2。

2.3 7 min 钬激光热效应

钬激光激发 7 min 时，注射器内生理盐水温度高达 78℃。解剖兔肾，其内外层皮质、髓质分界不清，色泽几乎全部为白色，皮质、髓质凝固；病理检查提示肾小球、肾小管均基本变性、坏死。见图 3。

3 讨论

3.1 钬激光热效应的手术价值

钬激光属于多用途的一种临床治疗激光技术，在泌尿外科领域中应用广泛[5-6]，其优点主要包括凝固特性好、切割精确、能量易于被水介质吸收、穿透性弱、方向性好[7-8]。泌尿系统属于管道系统，针对碎石、切除、切开等操作可达到满意的效果，因此钬激光在内镜的配合下治疗泌尿外科疾病具有重要的临床价值[9]。

因为钬激光使用时约 95% 的能量被周围 5 mm 的水介质吸收，根据能量守恒原则，钬激光的能量假设完全转化成水的热能。根据比热容公式：$Q=cm\Delta t$，即 $Q=cm(t-t_1)$，其中 Q 为能量，c 为比热，m 为质量，t 为末温，t_1 为初温。而 Q=钬激光功率（W）×激发时间（s），由此可得：激发时间=$cm\Delta t$/钬激光功率。考虑到 95% 的能量被吸收的情况，水的比热在液态情况下是 4.2×10^3 J/（kg·℃），如钬激光功率为 40 W，可以算出理论上加热 10 mL 水每升高 1℃ 需要的时间为 $4.2\times10^3\times0.01/(40\times95\%)=1.11$ s，加热 50 mL 水每升高 1℃ 需要 $4.2\times10^3\times0.05/(40\times95\%)=5.53$ s[10]。考虑到实际手术

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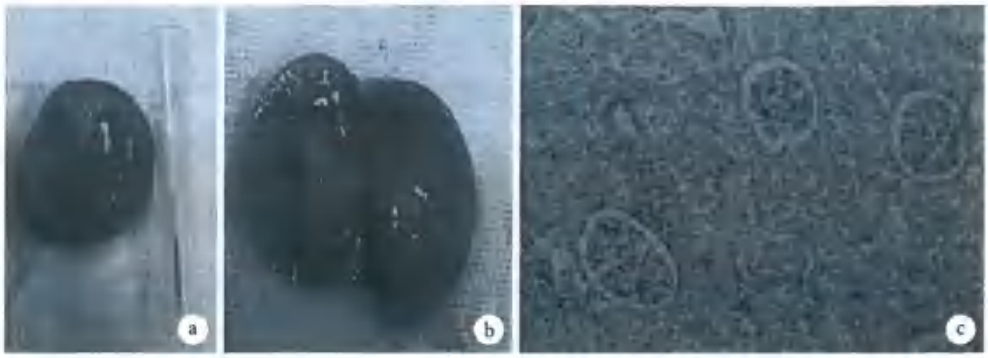


图 1　钬激光激发 2 min 时兔肾脏彩色像　a. 肾脏完整，外观基本正常；b. 剖开观察肾脏皮质、髓质基本红润；c. 病理检查示肾皮质、肾小球基本正常（HE ×200）

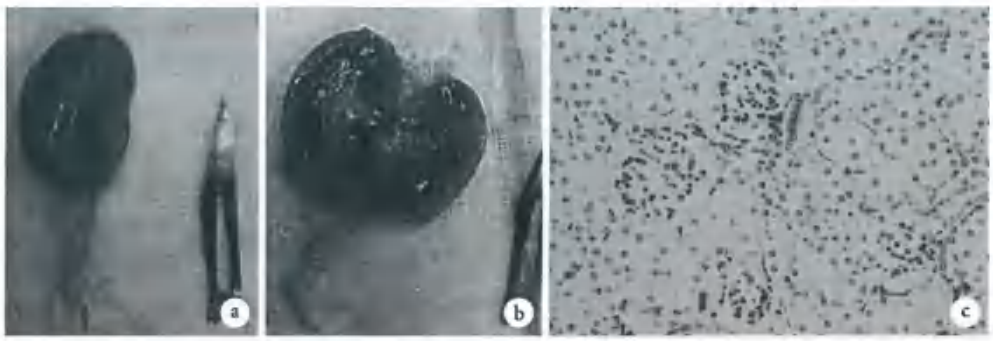


图 2　钬激光激发 5 min 时兔肾脏彩色像　a. 肾脏完整，颜色泛白；b. 剖开观察肾脏皮质、髓质分界欠清，髓质红润；c. 病理检查示皮质肾单位大部分坏死，髓质变性不明显，输尿管明显变性（HE ×400）

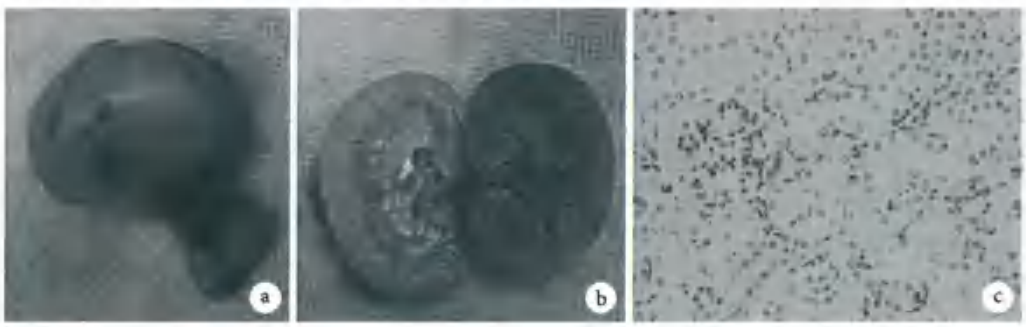


图 3　钬激光激发 7 min 时兔肾脏彩色像　a. 肾脏完整，颜色全部呈白色；b. 剖开观察肾脏皮质、髓质凝固；c. 病理检查示肾小球、肾小管均基本变性、坏死（HE ×400）

中钬激光激发环境是生理盐水混合尿液，其比热略大于水和操作过程中热量散失的具体情况后，其实和我们的实验数据结果是比较一致的[11-12]。

3.2　手术中钬激光的热损伤

泌尿系统如输尿管和肾盂内部体积一般不大，液体量有限（取决于积水程度），手术数量较多时，外科医生为快速碎石特别是上尿路结石、处理狭窄等，钬激光的功率常倾向调大[13-14]。我们前期的实验研究发现，因钬激光工作原理，常用的功率会产生明显的热效应，介质温度增高，手术室内，钬激光功率 40 W（频率 20 Hz，能量 2 J），激发 15 s，间歇 5 s，10 mL 生理盐水不到 1 min 水温将超过 50℃，可能对人体组织产生损伤作用；115 s 时水温会超过 70℃，产生的热效应会导致包括血管收缩在内的明显损伤组织[15]。钬激光常用的功率会产生热效应，随时间延长而明显增加，水温超过 50℃ 以后，可能对机体组织产生危害即损伤作用，对 50 mL 生理盐水中的兔肾、输尿管有明确损伤作用，特别是在 5、7 min 时水温分别增高至 57、78℃。况且，人体基础体温是 37℃，热量散失小于室温 22℃，提示钬激光用于肾盂和输尿管碎石术时，使用数分钟后，即可能产生积累的热损伤。而钬激光术后一些患者出现肾功能下降、泌尿管道狭窄，如输尿管狭窄、粘连甚至管腔闭锁，除结石引起的炎症和感染因素外，钬激光的热效应导致介质水温增加引起的人体组织损伤亦不可忽视[16]。

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必须承认，体外实验的钬激光介质水是静止的，实际手术时医生会持续灌注生理盐水，循环的介质可明显带走部分热量，以减少温度损伤；且根据术中情况，功率亦可调整，激发和间歇的时间也会不同。所以，体外钬激光对新鲜离体兔肾的热损伤实验并不能完全等同于人体内手术的实际情况，这有待临床医生实施钬激光碎石等手术时进一步明确。

因为工作原理，钬激光常用的碎石功率会产生渐增的热损伤，当肾盂和输尿管结石体积较大，质地较硬，预计碎石时间偏长时，应当引起临床医生注意；增加水循环，适当降低功率等是可以选择的方法。

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Caliceal Fluid Temperature During High-Power Holmium Laser Lithotripsy in an In Vivo Porcine Model

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Abstract

Introduction: With increasing use of high-power laser settings for lithotripsy, the potential exists to induce thermal tissue damage. In vitro studies have demonstrated that temperature elevation sufficient to cause thermal tissue damage can occur with certain laser and irrigation settings. The objective of this pilot study was to measure caliceal fluid temperature during high-power laser lithotripsy in an in vivo porcine model.
Methods: Four female pigs (30–35 kg) were placed under general anesthesia and positioned supine. Retrograde ureteroscopy with entry into upper or middle calices was performed. Thermocouples were placed into the calix by open exposure and puncture of the kidney or retrograde alongside the ureteroscope. A 242 μm laser fiber was positioned in the center of the calix and activated (0.5 J, 80 Hz, 40 W) for 60 seconds with high, medium, or no irrigation delivered in each trial. Finite element simulations of laser-induced heating in a renal calix were also performed.
Results: Peak temperatures of 84.8°C, 63.9°C, and 43.6°C were recorded for no, medium, and high irrigation, respectively. Mean time to reach threshold of thermal injury (t_{43} of 120 minutes) was 12.7 and 17.8 seconds for no and medium irrigation. Thermal damage thresholds were not reached in high-irrigation trials. Numerical simulations revealed similar results with peak spatial average fluid temperatures of >100°C, 58.5°C, and 37.5°C during 60 seconds of laser activation for 0.1, 15, and 40 mL/minute irrigation, respectively.
Conclusions: High-power holmium laser settings (40 W) can induce potentially injurious temperatures in the porcine in vivo model, particularly with slower irrigation rates. Characterization of thermal dose across a broader range of laser parameter settings is underway to map out the thermal safety envelope.

Keywords: holmium laser, temperature, lithotripsy, ureteroscopy, in vivo

Introduction

The introduction of high-power holmium laser systems (100–120 W) has expanded available parameter settings and ushered in a new era of ureteroscopic stone treatment. Laser lithotripsy can now be applied with higher frequency, enabling strategies of ''dusting'' and ''pop-dusting'' where stone or stone fragments are eroded to sub-millimeter particles (common parameters: 0.2–0.5 J pulse energy; 50–80 Hz frequency).[1] These new ''dusting'' strategies are effective adjuncts to traditional fragmentation laser lithotripsy and have been shown to shorten operative time.[2] In many cases, a combination of fragmentation and dusting modes of operation is necessary to treat particularly large or ''hard'' stones. A survey in 2015 revealed that 67% of endourologists commonly used some form of stone ''dusting'' technique.[3]

These laser strategies use increased power settings (up to 40 W), frequently applied as 5 to 10 second bursts of laser activation, and often with bursts applied in rapid succession. With these settings, the potential exists to overheat the caliceal fluid as demonstrated in recent bench studies.[4–7] Temperatures in bench models were seen to reach 70°C after 60 seconds of firing at 40 W laser settings,[3] generating a thermal dose that would be sufficient to damage adjacent urothelium, renal parenchyma, and/or ureter. This study was conducted to determine whether similar temperature elevation also occur in the in vivo setting. The specific objective was to measure caliceal fluid temperature during high-power laser lithotripsy in an in vivo porcine model.

Methods

After approval from the Institutional Animal Care and Use Committee, four female pigs (30–35 kg) were anesthetized,

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intubated, and positioned supine (Fig. 1A). Five kidneys were exposed with a modified subcostal incision without entering the peritoneum (Fig. 1B). A flexible cystoscope (CYF-3; Olympus) was used to insert a guidewire through the ureter into the renal pelvis. Retrograde ureteroscopy with entry into upper or interpolar renal calices was performed with a flexible ureteroscope (DUR-8 Gyrus ACMI). With visual (ureteroscope) and ultrasound guidance (GE P6 ultrasound scanner with 11L probe), a type T needle thermocouple (Physitemp) was inserted through the exposed kidney and into the targeted calix. In two kidneys, rather than surgical exposure, a wire thermocouple (Omega) was attached to the ureteroscope shaft with its tip 2 mm from the distal end and inserted retrograde into the renal collecting system with the ureteroscope (Fig. 1C). Data from one kidney were excluded as experimental protocol was not followed because of early termination of laser energy delivery when temperature exceeded 100°C.

Twenty trials were performed in seven kidneys with high (6), medium (7), and no (7) irrigation. High irrigation was established with saline contained in a pressure bag inflated to 150 mmHg and placed at 100 cm height, equivalent to 304 cm of gravity irrigation. Medium irrigation consisted of a saline bag at 100 cm height. The irrigation rate measured with a 242 lm laser fiber in the working channel and no outflow resistance was 36 to 38 and 14 to 15 mL/minute for high and medium irrigation, respectively.

During each trial, a 242 lm laser fiber (Flexiva; Boston Scientific) was introduced through the working channel of the ureteroscope with laser fiber tip positioned in the center of the calix away from the thermocouple and caliceal wall. All trials were conducted with laser energy output of 40 W (0.5 J, 80 Hz, short pulse) using a 120 W holmium laser system (pulse 120; Lumenis). Each trial was conducted for 100 seconds with continuous temperature measurement. Baseline temperature was recorded for the first 10 seconds (time 0–10 seconds) after which the laser was activated for 60 seconds (time 11–70 seconds). Temperature was then recorded for an additional 30 seconds (time 71–100 seconds).

One kidney was harvested after three trials at high, medium, and no irrigation. The kidney was bivalved and sectioned transversely through the calix where the laser had been activated to assess gross pathologic changes.

Thermal dose for each trial was calculated based on Sapareto and Dewey t_{43} equivalence calculations for each trial.[8] Using this concept, the thermal dose of any temperature curve can be converted to an equivalent time (t_{43} minutes) at a stable temperature (conventionally considered 43°C). Sapareto and Dewey found that a temperature of 43°C for 120 to 240 minutes produced thermal injury in various tissues. For the purpose of this evaluation, we consider $t_{43} = 120$ minutes to be the threshold for thermal tissue injury.

Finite element simulations were performed for high, medium, and no irrigation in COMSOL Multiphysics (COMSOL, Inc., Burlington, MA). Simulation geometry mimicking the calix consisted of an axisymmetric 6 mm diameter 50 mm long tube terminated in a hemispherical end on one side and open at the opposing end. Surrounding this lumen was a 1-mm thick wall of tissue with thermal and mechanical properties of the ureteral wall, which was further surrounded externally by tissue with properties of the kidney parenchyma. The simulation used a bioheat transfer model[9] to capture the physics of laser heat generation, diffusion, and convection, as well as blood perfusion and fluid flow because of irrigation. A steady irrigation of 40, 15, or 0.1 mL/minute (simulating high, medium, and no irrigation in the in vivo trials) was emitted from an irrigation port placed at the radial center of the fluid space, 20 mm from the end. Heat was generated as a 0.5 mm 40 W spherical source 15 mm from the end of the calix. To simulate the temporal heat profile in vivo, fluid irrigation was introduced for 20 seconds, after which the laser heating was generated for 60 seconds, then temperature was recorded for 20 seconds more. Fluid average temperature and thermal dose were calculated at each point in the field.

Data are presented as mean and standard deviation. Statistical analyses were performed using Microsoft Excel (Redmond, WA).

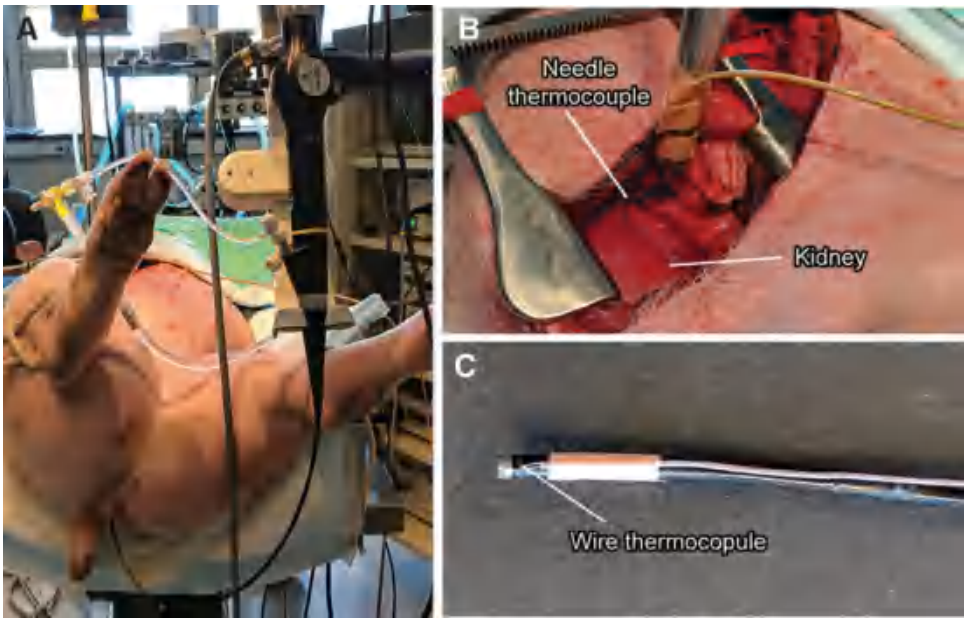


FIG. 1. Experimental setup showing (A) the pig positioned supine on the table with ureteroscope inserted to renal calix, (B) modified subcostal incision showing the exposed kidney and needle thermocouple, and (C) wire thermocouple secured to the ureteroscope.

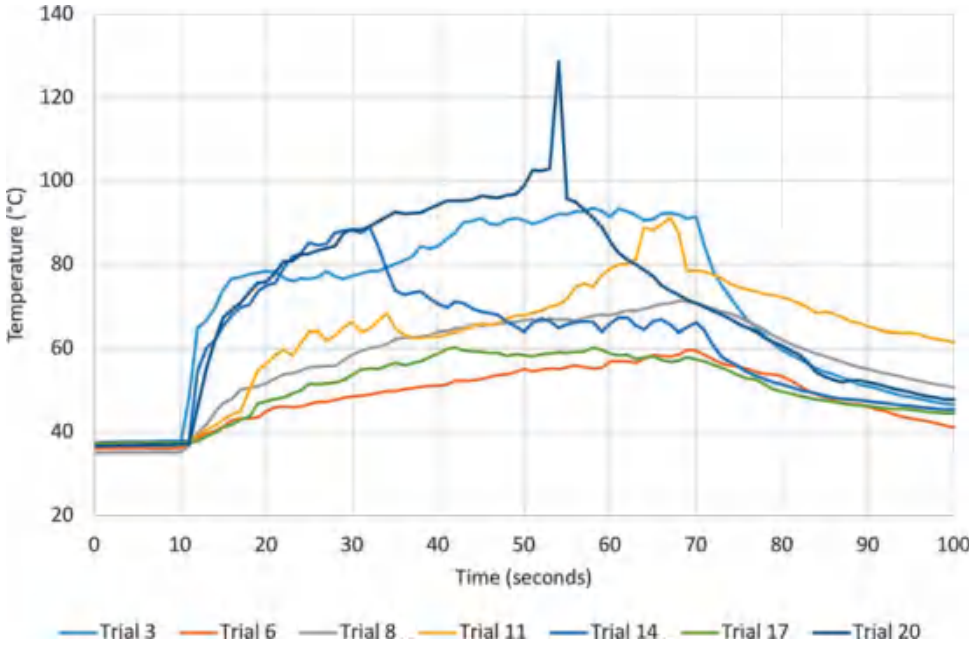


FIG. 2. Temperature recordings for all trials with no irrigation. Laser energy was applied starting at 10 seconds and ending at 70 seconds.

Results

Caliceal fluid temperature increased in all trials during laser activation (Figs. 2 and 3 and Supplementary Fig. S1; Supplementary Data are available online at www.liebertpub.com/end) with the highest temperature, 128.5°C, recorded during a trial with no irrigation. Figure 4 shows mean temperature change from baseline for each irrigation rate. After only 10 seconds of laser activation, caliceal fluid temperature reached 61.4°C, 50.1°C, and 39.2°C, corresponding to an average temperature increase of 25.4°C for no irrigation, 16.9°C for medium irrigation, and 10.6°C for high irrigation.

The thermal threshold of $t_{43} = 120$ minutes was exceeded for all trials with no irrigation and six of seven with medium irrigation (Table 1). The mean time to reach the threshold of thermal injury was 12.7 seconds (range 2–37 seconds) for no irrigation and 17.8 seconds (range 5–30 seconds) for medium irrigation. In one trial with medium irrigation and all trials with high irrigation, thermal damage thresholds were not exceeded during 60 seconds of laser activation.

Numerical simulations recorded spatial average fluid temperatures as high as >100°C, 58.5°C, and 37.5°C within 60 seconds of laser power for 0.1, 15, and 40 mL/second irrigation, respectively. Simulations did not show fluid mixing at the 0.1 mL/minute case, thus concentrating heat around

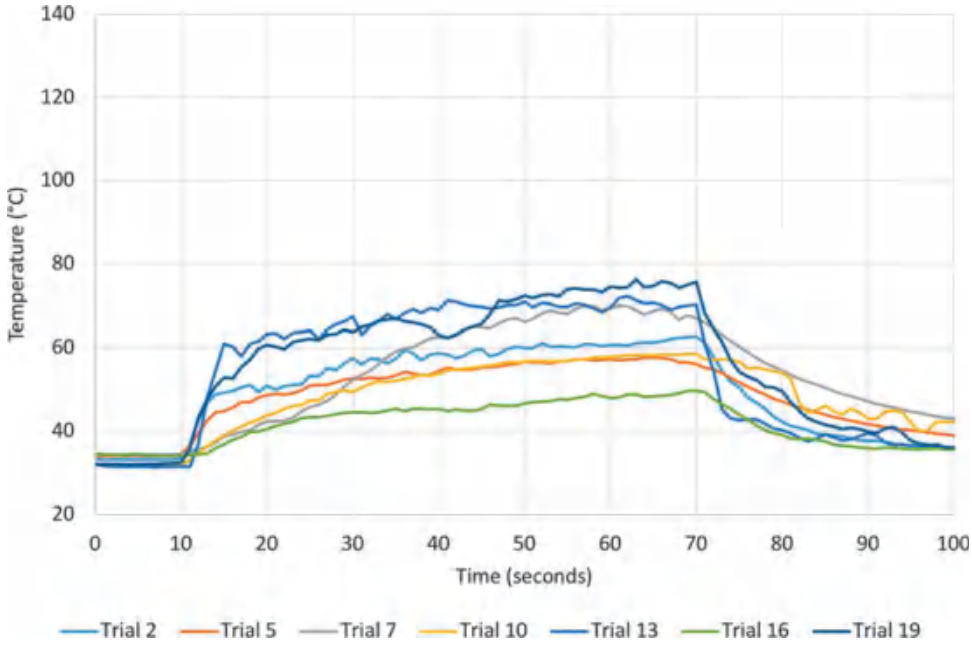


FIG. 3. Temperature recording for all trials with medium irrigation. Laser energy was applied starting at 10 seconds and ending at 70 seconds.

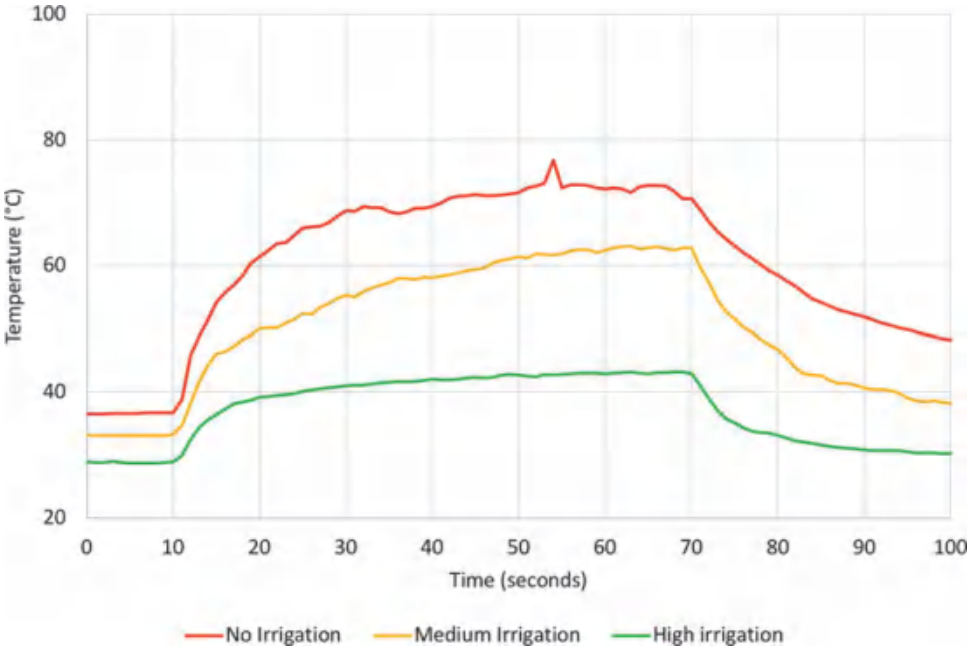


FIG. 4. Mean temperature with each irrigation rate. Laser energy was applied starting at 10 seconds and ending at 70 seconds.

the laser fiber tip. However, the fluid temperature was relatively uniform throughout the calix when irrigation was introduced. Time to onset of thermal injury based on the thermal dose anywhere in the tissue was calculated at 4.1 and 4.9 seconds for 0.1 and 15 mL/minute irrigation.

Gross pathologic tissue coagulation and injury were apparent in the one kidney harvested for gross assessment (Fig. 5). Charred (black) tissue is seen at the urothelial surface in contact with the collecting system. This is surrounded by a white zone of coagulation surrounding the margin of the calix. A concentric hyperemic (red) zone extends beyond the coagulation zone further into parenchyma. Tissue temperatures consistent with these findings were also demonstrated by numerical simulation. In the no-irrigation state, the thermal threshold boundary extended beyond the calix, urothelium, and 3 mm into the adjacent parenchyma over a length of * 14 mm (Supplementary Fig. S2 and Supplementary Video S1). In the medium irrigation state, injury was limited to a thin area (<1 mm depth) within the wall of the calix (Fig. 6 and Supplementary Video S2). Total volumetric injury in simulations was up to 2.3 cm^3 (0.1 mL/minute irrigation) and 0.28 cm^3 (15 mL/minute irrigation). No injury was produced anywhere in the field with 40 mL/minute irrigation.

Table 1. Data Recorded During All Trials with t_{43} Equivalent Calculation

Trial	Irrigation rate	Thermocouple type	Temperature after 10 seconds of laser application (°C)	Time to t_{43} 120 minutes equivalent (seconds)	Peak temperature (°C)	t_{43} Equivalent minutes
3	No	Needle	78.4	2	93.5	$>10^{13}$
6	No	Needle	45.0	37	59.7	$>10^{3}$
8	No	Needle	51.7	14	71.3	$>10^{6}$
11	No	Needle	56.3	10	91.2	$>10^{11}$
14	No	Needle	75.0	3	89.0	$>10^{11}$
17	No	Wire	47.4	21	60.3	$>10^{3}$
20	No	Wire	75.8	2	128.5	$>10^{22}$
2	Medium	Needle	51.1	17	62.7	$>10^{4}$
5	Medium	Needle	48.7	25	57.7	$>10^{3}$
7	Medium	Needle	42.4	23	70.0	$>10^{6}$
10	Medium	Needle	43.8	30	58.6	$>10^{3}$
13	Medium	Needle	63.4	5	72.3	$>10^{6}$
16	Medium	Wire	40.6	NA	49.7	19.6
19	Medium	Wire	60.8	7	76.3	$>10^{8}$
1	High	Needle	41.1	N/A	47.6	6.2
4	High	Needle	42.3	N/A	50.1	47.5
9	High	Needle	37.4	N/A	43.4	<0.1
12	High	Needle	36.8	N/A	37.9	<0.1
15	High	Wire	38.9	N/A	39.8	<0.1
18	High	Wire	38.8	N/A	42.7	0.1

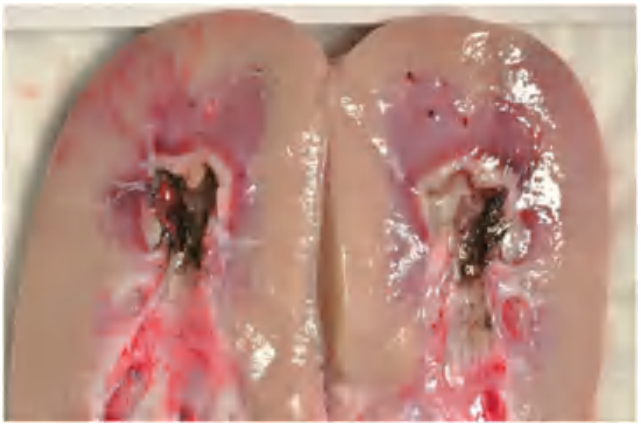


FIG. 5. Gross image of a bivalved kidney showing charred urothelium and thermal injury after three (60 seconds) trials at high, medium, and no irrigation.

Discussion

The evolution of laser lithotripsy has seen the recent introduction of high-power laser systems, borrowed from the realm of tissue ablation and prostate enucleation. Although the expanded parameter space produces many benefits—better stone comminution, smaller fragment size, and faster treatment times—the assessment of thermal safety in laser lithotripsy has lagged behind the clinical introduction of these techniques. The rationale for this study was to explore a limited portion of the parameter space at the upper end of the power range to determine whether toxic thermal dose can also be generated in the in vivo setting.

Recent in vitro bench studies assessing temperature change with holmium laser activation have concluded that high-power low-irrigation settings can lead to temperature increase sufficient to cause tissue injury.[4–7] Our group previously has shown in an in vitro bench model that temperatures can reach 50.7°C, 45.2°C, and 37.8°C after only 10 seconds of laser activation with no, medium, and high irrigation, respectively.[4] It was thought that vascular perfusion of the kidneys in the in vivo model would act as a heat sink and dampen the temperature elevations that had been measured in the in vitro bench studies.[4,10] Surprisingly, this effect was not observed and in fact, peak temperature in the no irrigation scenario was greater in the in vivo model (84.8°C) than in the in vitro model (69.8°C). This may be because of (1) less heat conduction away from the collecting system into the renal tissue and surrounding retroperitoneal structures in vivo compared with the relative ease of conduction from the test tube to the surrounding water bath in vitro and (2) the short time course of energy delivery during laser lithotripsy that likely overwhelms the heat-sink capacity of vascular perfusion.

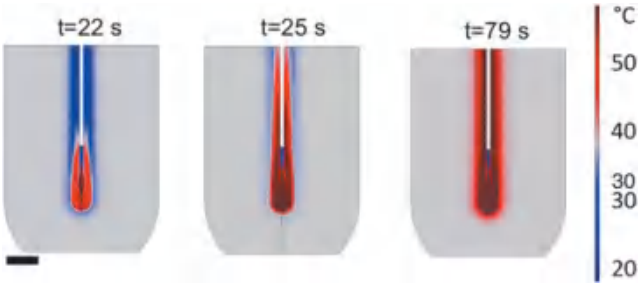


FIG. 6. Numerical simulation of temperature distribution after 2, 5, and 59 seconds of laser activation with 15 mL/minute irrigation. Room temperature irrigation fluid was introduced through a simulated ureteroscope (white tube) and started 20 seconds before laser activation. Simulated laser heating is generated by a small source 5 mm below the simulated ureteroscope, causing temperature elevation of the fluid and surrounding tissue. The scale bar is 1 cm.

Numerical simulations of laser-induced heating showed similar temperature elevations with irrigation, although the case with 0.1 mL/minute irrigation produced significantly higher temperatures than those measured in vivo. This discrepancy is likely caused by evaporation/condensation processes, as well as fluid motion and mixing that occur during laser firing and redistribute heat, but are not modeled here.

The thermal doses observed in prior in vitro studies, numerical simulations, and the in vivo results described here are capable of damage to the urothelium, kidney, and ureter potentially resulting in scarring, obstruction to the ureter or collecting system, and loss of renal function. Although tissue changes associated with thermal injury may not be apparent to urologists at the time of laser lithotripsy and likely encompass only a small fraction of the total renal tissue, no degree of irreversible thermal parenchymal tissue injury should be considered acceptable. This is particularly important for patients with multiple recurrent stones who may need many lithotripsy procedures over the course of their lifetime.

Although the experimental data presented here and in prior bench studies suggest that increased irrigation rates may be able to partially control temperature elevation,[4–7] this is often cumbersome or difficult to fully implement in the clinical setting. Furthermore, prevailing endourologic trends have been focused on decreasing intrarenal pressures to reduce infectious and hemorrhagic complications.[11–13] This can be accomplished by lowering irrigation rates although this would then increase risk of thermal injury. Alternatively, use of an access sheath during ureteroscopy has been shown to reduce intrarenal pressure and improve irrigant flow through the ureteroscope during ureteroscopy.[13] However, this is not possible in every case and often necessitates a ureteral stent afterward. This provides an opportunity and rationale for small profile active (suction) removal of collecting system fluid to maintain sufficient irrigation rates. In addition, chilled irrigation fluid may be of benefit. Another measure to minimize the effect of thermal injury is intermittent laser activation. Activating the laser for shorts periods would allow temperature to return to baseline. However, the temperature decay curves as seen in Figures 2 to 4 suggest that the needed time between laser bursts may be longer than desirable for efficient treatment. Characterization and control of the ''operator duty-cycle'' of the laser are an important area for future study.

There are several limitations to this study. First, 60 seconds of continuous laser activation is not necessarily realistic with respect to clinical practice. However, it does provide standardization for these experiments and creates a full temperature curve that also provides useful temperature data at earlier time points. This is useful for further developing computerized simulations and can be used to determine time to toxic thermal dose. Second, only one laser power setting, 40 W, was assessed, which does not allow prediction of effects at lower power

settings. Third, the calix size in which the trials were conducted was not controlled and likely contributed to some of the temperature measurement variability, although this is an expected consequence of in vivo research and clinical therapy. Finally, temperature was recorded using two methods, needle and wire thermocouple. Although one could consider this an unwanted variable in the study, it is representative of ongoing development of experimental technique, and did not appear to produce any systematic bias of the measured thermal curves.

Further research is needed to more completely explore a broader swath of the parameter space. Much of this can be done with simulation and in vitro trials as there was high concordance between the results of the previous in vitro studies and the current in vivo study. Also, investigating the effect of temperature change based on realistic laser on–off activation times, ''operator duty-cycle'' would help elucidate temperatures and thermal doses expected in actual clinical scenarios. Each of these areas of exploration is necessary to, first, define the thermal ''safety envelope'' within the parameter space provided by high-power laser lithotripsy systems and, second, develop thermal mitigation tools and techniques that enhance laser lithotripsy efficiency while maintaining thermal safety.

In conclusion, delivery of high-power (40 W) holmium laser energy can induce potentially injurious temperature elevations in the porcine in vivo model, particularly with lower irrigation rates. Further characterization of thermal dose across a broader range of laser parameter settings is underway to map out the thermal safety envelope. This will provide a baseline from which techniques and tools to control and mitigate thermal effects during holmium laser lithotripsy can be developed.

Acknowledgment

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Author Disclosure Statement

KRG is a consultant for Boston Scientific and Lumenis.

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活体猪模型高功率钬激光碎石术中肾盏液温度

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摘要

引言：随着高功率激光碎石技术的广泛应用，热损伤风险日益凸显。体外实验表明，某些激光参数和冲洗条件足以引发组织热损伤。本研究旨在通过活体猪模型，测量高功率激光碎石术中肾盏液温度变化。

实验方法：将四头体重30-35公斤的母猪置于全身麻醉下仰卧位，通过逆行输尿管镜术进入上盏或中盏进行操作。采用开放式暴露技术将热电偶置入肾盏，同时对肾脏进行穿刺或沿输尿管镜逆行穿刺。将242μm激光光纤置于肾盏中心，以0.5J（80Hz，40W）功率持续60秒进行激光治疗，每次试验分别采用高流量、中流量或无冲洗三种模式。此外，还对肾盏内激光诱导的热效应进行了有限元模拟分析。

结果：无灌注、中等灌注和高灌注组的峰值温度分别为84.8°C、63.9°C和43.6°C。达到热损伤阈值（$_{43}$ 120分钟）的平均时间，无灌注组为12.7秒，中等灌注组为17.8秒，而高灌注组未达到该阈值。数值模拟结果表明，在60秒激光激活期间，0.1、15和40毫升/分钟灌注组的峰值空间平均流体温度分别超过100°C、58.5°C和37.5°C。

结论：高功率钬激光（40W）在猪体内模型中可能引发损伤性温度，尤其在低速冲洗时更为明显。目前正通过研究不同激光参数下的热剂量分布，以确定热安全范围。

关键词：钬激光，温度，碎石术，输尿管镜，体内

引言

高功率钬激光系统（100 ~ 120 W）的引入扩大了可用参数设置，开启了输尿管镜治疗结石的新时代。如今激光碎石术可实现更高频率操作，开创了“粉尘碎石”和“爆破碎石”等创新模式——通过将结石或碎石侵蚀成亚毫米级颗粒（常规参数：0.2-0.5焦耳脉冲能量；50-80赫兹频率）。[1]这些新型“粉尘碎石”技术作为传统碎石激光的高效辅助手段，已被证实能显著缩短手术时间。[2]对于体积较大或“顽固”结石，往往需要碎石与粉尘碎石两种模式联合应用。2015年一项调查显示，67%的泌尿外科医生常规采用某种形式的结石“粉尘碎石”技术。[3]

这类激光治疗方案通常采用功率设置提升（最高可达40瓦），以5至10秒的激光脉冲形式施加，且常以快速连续脉冲模式进行。正如近期实验室研究显示，这种操作方式可能导致盏状体液体过热。实验模型数据显示，当以40瓦功率设置持续照射60秒后，[4–7]温度可升至70摄氏度，[3]产生的热剂量足以损伤邻近的尿路上皮、肾实质和/或输尿管。本研究旨在验证体内环境是否同样会发生类似温度升高现象，具体目标是在活体猪模型中测量高功率激光碎石术期间盏状体液体的温度变化。

方法

经机构动物护理与使用委员会批准后，对四头体重30-35公斤的母猪实施麻醉，

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[4] Applied Physics Laboratory, University of Washington, Seattle, Washington.
A video demonstrating this technique is available online at www.liebertpub.com/end

经气管插管后采取仰卧位（图1A）。采用改良肋下切口暴露五个肾脏，切口未进入腹膜（图1B）。使用柔性膀胱镜（CYF-3型；奥林巴斯）将导丝经输尿管插入肾盂。通过柔性输尿管镜（DUR-8 Gyrus ACMI）进行逆行输尿管镜检查，进入上极或极间肾盏。在输尿管镜直视引导和超声引导（GE P6超声扫描仪配11L探头）下，将Physitemp型T型针式热电偶经暴露肾脏插入靶向肾盏。对于两个肾脏，未采用手术暴露方式，而是将Omega品牌导丝热电偶固定于输尿管镜杆体，其尖端距远端2毫米处，随输尿管镜逆行插入肾集合系统（图1C）。由于实验方案未按要求执行——当温度超过100℃时提前终止激光能量输送，故排除了其中一个肾脏的数据。

本研究在7个肾脏模型中进行了20次灌注试验，分别采用高灌注（6次）、中灌注（7次）和无灌注（7次）三种模式。高灌注采用充气至150毫米汞柱的压力袋，将生理盐水置于100厘米高度，相当于304厘米重力灌注。中灌注则使用100厘米高度的生理盐水袋。通过242μm激光光纤在工作通道测量的灌注速率（无流出阻力）显示：高灌注组为36-38毫升/分钟，中灌注组为14-15毫升/分钟。

每次实验中，医生会通过输尿管镜的工作通道插入一根242μm激光光纤（Flexiva；波士顿科学公司），将光纤尖端置于杯状结构中心，远离热电偶和杯状壁。所有实验均采用120瓦钬激光系统（脉冲120；Lumenis）进行，激光能量输出为40瓦（0.5焦耳，80赫兹，短脉冲）。每次实验持续100秒，期间持续监测温度。实验开始时记录基线温度（0-10秒），随后启动激光器持续60秒（11-70秒），最后再记录30秒温度数据（71-100秒）。

在高、中、无灌注三种条件下进行三次试验后，取下一只肾脏。将肾脏对半切开，沿激光激活的杯状部位横向切片，以观察肉眼可见的病理变化。

每个试验的热剂量均根据Sapareto与Dewey的热$_{43}$等效计算方法进行计算。[8]基于这一理论，任何温度曲线的热剂量均可转换为在恒定温度（通常设定为43℃）下等效的时间（$_{43}$分钟）。Sapareto和Dewey的研究表明，当温度维持在43℃持续120至240分钟时，可导致多种组织产生热损伤。在本次评估中，我们将$_{43}$t=120分钟作为组织热损伤的判定阈值。

我们使用COMSOL多物理场软件（COMSOL公司，美国马萨诸塞州伯灵顿市）对高、中、无灌注三种条件下的有限元模拟进行了建模。模拟装置采用轴对称结构：一根直径6毫米、长50毫米的管状结构，一端封闭形成半球形，另一端保持开放。管腔外包裹着1毫米厚的组织壁，其热力学和力学特性与输尿管壁一致，外围则覆盖着具有肾实质特性的组织层。该模拟采用生物传热模型[9]来模拟激光热能的产生、扩散与对流过程，同时考虑灌注液引起的血液灌注和流体流动。通过位于流体空间径向中心、距管端20毫米处的灌注端口，以40毫升/分钟、15毫升/分钟或0.1毫升/分钟的速率持续注入液体（对应体内试验中的高、中、无灌注条件）。热源则由位于管端15毫米处的0.5毫米直径40瓦球形热源产生。为模拟体内温度变化曲线，首先进行20秒液体冲洗，随后启动激光加热持续60秒，最后再记录20秒温度数据。在照射区域各点分别计算液体平均温度和热剂量。

数据以均值和标准差的形式呈现。统计分析使用Microsoft Excel（华盛顿州雷德蒙德）进行。

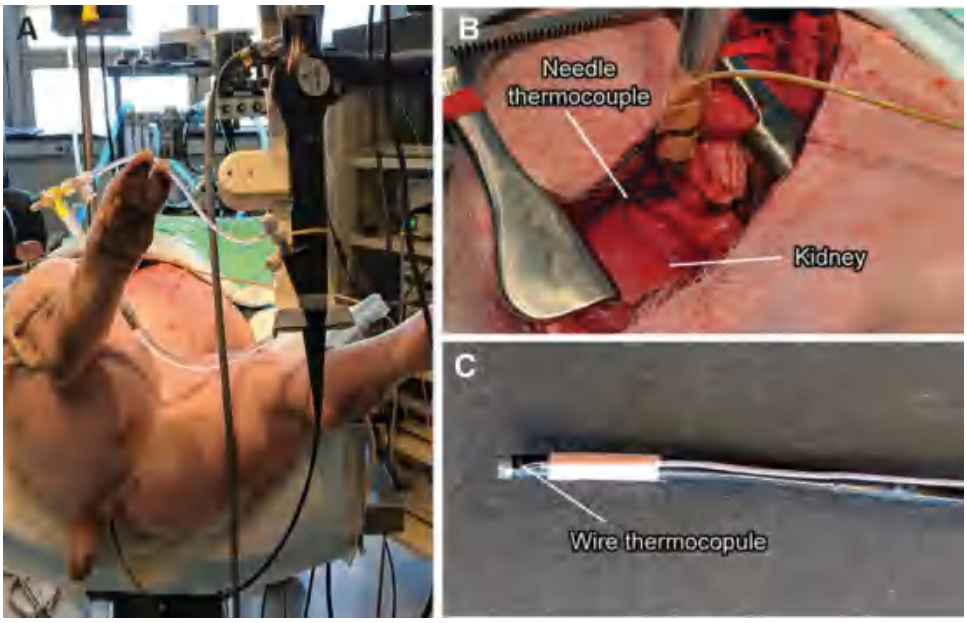


图1.实验装置示意图：(A)猪仰卧于实验台，输尿管镜插入肾盏；(B)改良肋下切口暴露肾脏及针式热电偶；(C)金属丝热电偶固定于输尿管镜。

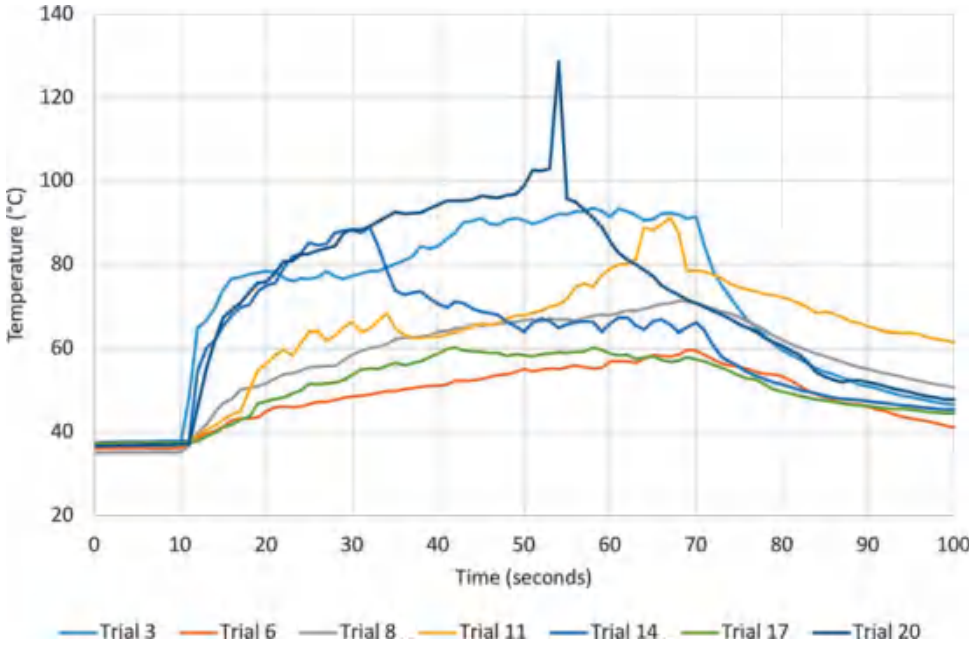


图2.未进行灌注时所有试验的温度记录。激光能量从10秒开始施加，持续至70秒。

结果

在所有实验中，激光激活期间晶状体房水温度均有所上升（图2、图3及补充图S1；补充数据可在线获取于www.liebertpub.com/end），其中未进行灌注的实验记录到最高温度128.5°C。图4展示了各灌注速率下相对于基线的平均温度变化。仅需10秒激光激活，晶状体房水温度分别达到61.4°C、50.1°C和39.2°C，对应未灌注组平均温度升高25.4°C、中等灌注组16.9°C、高灌注组10.6°C。

所有无灌注试验及七项中等灌注试验中的六项均超过t_{43}=120分钟的热损伤阈值（见表1）。无灌注组达到热损伤阈值的平均时间为12.7秒（范围2-37秒），中等灌注组为17.8秒（范围5-30秒）。在一项中等灌注试验及所有高灌注试验中，激光激活60秒内均未超过热损伤阈值。

数值模拟显示，在0.1毫升/秒、15毫升/秒和40毫升/秒三种灌注速率下，激光功率作用60秒内，空间平均流体温度分别达到100°C以上、58.5°C和37.5°C。其中0.1毫升/分钟的模拟结果未出现流体混合现象，从而将热量集中在

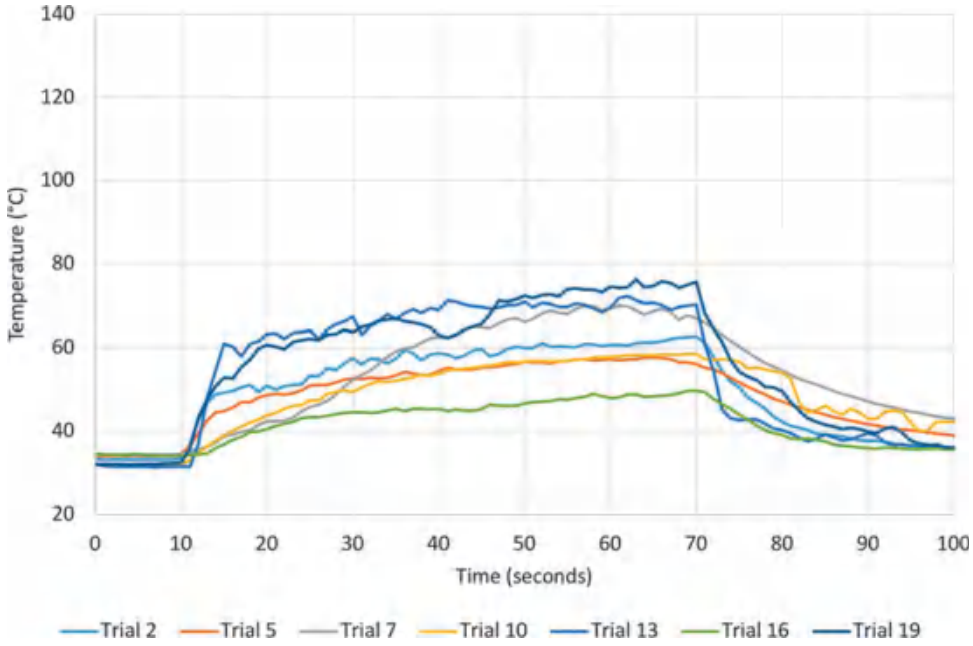


图3.中等灌溉条件下所有试验的温度记录。激光能量从10秒开始施加，持续至70秒。

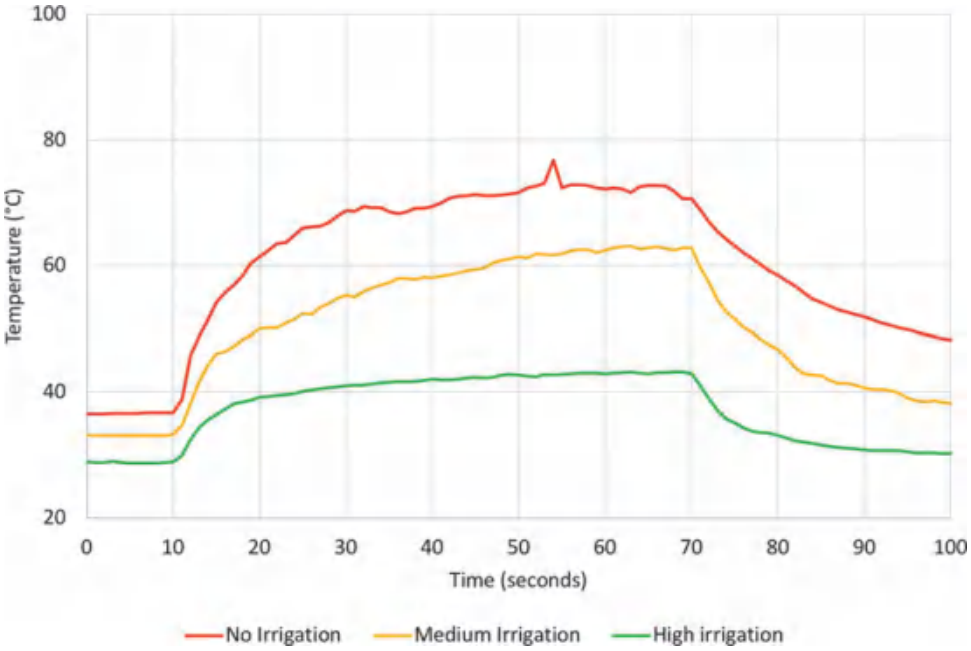


图4.不同灌水速率下的平均温度。激光能量从10秒开始施加，持续至70秒。

激光光纤尖端周围。然而，当引入灌注时，整个杯状结构内的液体温度分布相对均匀。根据组织中任意位置的热剂量计算得出，热损伤发生时间在0.1毫升/分钟和15毫升/分钟灌注条件下分别为4.1秒和4.9秒。

在用于大体评估的单个肾脏中，肉眼可见明显的组织凝固和损伤（图5）。尿路上皮表面与集合管系统接触处可见焦黑（黑色）组织，其周围环绕着一个白色凝固区，该凝固区围绕着杯状突的边缘。向心性充血（红色）区超出凝血区进一步延伸至软组织.

数值模拟结果也证实了与这些发现一致的组织温度.在无灌注状态下，热损伤阈值边界延伸至距杯状结构、尿路上皮及邻近实质组织3毫米处，总长度约14毫米（补充图S2及补充视频S1）。在中等灌注状态下，损伤仅局限于杯状结构壁内薄层区域（深度不足1毫米）（图6及补充视频S2）。模拟结果显示，灌注量达2.3立方厘米^3（0.1毫升/分钟）时损伤最严重，^{3}（15毫升/分钟）时损伤达0.28立方厘米。而40毫升/分钟的灌注量则未在任何区域引发损伤。

表1.使用t_{43}等效计算法记录的所有试验数据

试验	灌溉比率	热电偶类型	激光应用10秒后的温度（℃）	至t_{43} 120分钟的时间（秒）	最高温度（℃）	t_{43} 等效分钟
3	无	针	78.4	2	93.5	$>10^{13}$
6	无	针	45.0	37	59.7	$>10^{3}$
8	无	针	51.7	14	71.3	$>10^{6}$
11	无	针	56.3	10	91.2	$>10^{11}$
14	无	针	75.0	3	89.0	$>10^{11}$
17	无	线	47.4	21	60.3	$>10^{3}$
20	无	线	75.8	2	128.5	$>10^{22}$
2	中等	针	51.1	17	62.7	$>10^{4}$
5	中等	针	48.7	25	57.7	$>10^{3}$
7	中等	针	42.4	23	70.0	$>10^{6}$
10	中等	针	43.8	30	58.6	$>10^{3}$
13	中等	针	63.4	5	72.3	$>10^{6}$
16	中等	线	40.6	NA	49.7	19.6
19	中等	线	60.8	7	76.3	$>10^{8}$
1	高	针	41.1	N/A	47.6	6.2
4	高	针	42.3	N/A	50.1	47.5
9	高	针	37.4	N/A	43.4	<0.1
12	高	针	36.8	N/A	37.9	<0.1
15	高	线	38.9	N/A	39.8	<0.1
18	高	线	38.8	N/A	42.7	0.1

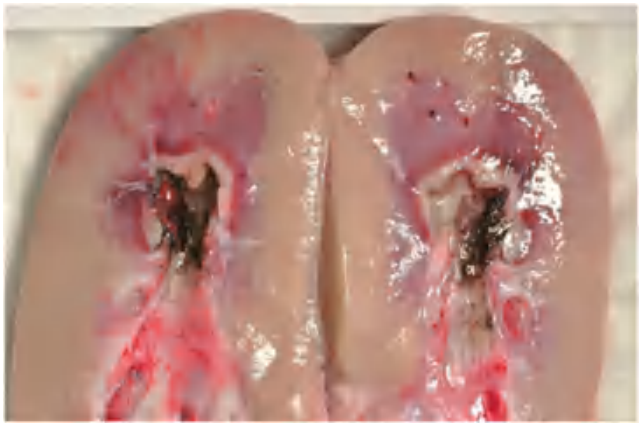


图5.双瓣肾的宏观图像显示：在高、中、无冲洗三种条件下各进行三次（每次60秒）冲洗试验后，尿路上皮出现焦化现象并伴有热损伤。

讨论

激光碎石技术的发展历程中，近期引入了高功率激光系统，这些系统借鉴自组织消融和前列腺剜除术领域。尽管扩展的参数空间带来了诸多优势——结石粉碎效果更佳、碎石颗粒更小、治疗时间更短——但激光碎石的热安全性评估却滞后于这些技术的临床应用。本研究旨在探索功率范围上限端的参数空间中一小部分区域，以确定在体内环境中是否也会产生毒性热剂量。

近期体外实验研究表明，钬激光激活过程中温度变化表明，高功率低灌注模式可能导致组织损伤所需的温度升高。[4–7]我们团队此前在体外模型中发现，仅需10秒激光激活，在无灌注、中等灌注和高灌注条件下，温度分别可升至50.7℃、45.2℃和37.8℃。[4]在体内模型中，肾脏的血管灌注被认为可以起到散热器的作用，并抑制体外实验中测量到的温度升高。

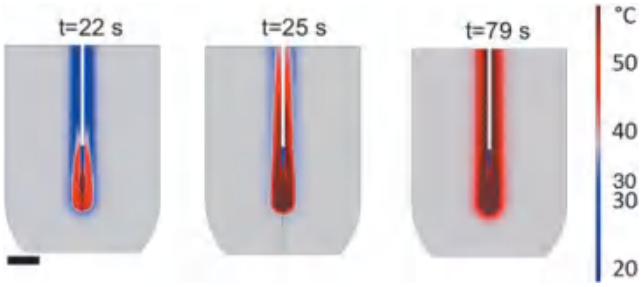


图6展示了激光激活2秒、5秒及59秒后温度分布的数值模拟结果，实验采用15毫升/分钟的灌注流速。实验中，研究人员通过模拟输尿管镜（白色管状结构）注入室温灌注液，并在激光激活前20秒启动。模拟激光加热由输尿管镜下方5毫米处的小型光源产生，可使灌注液及周围组织温度升高。图中比例尺为1厘米。

[4,10]出人意料的是，这种效应并未出现。实际上，在无灌注条件下，体内模型的峰值温度（84.8℃）反而高于体外模型（69.8℃）。这可能源于两个原因：(1)与体外试管到水浴槽的热传导相对容易相比，体内收集系统向肾组织及周围腹膜后结构的热量传导效率较低；(2)激光碎石术中能量输送时间较短，可能无法完全满足血管灌注的散热需求。

激光加热的数值模拟显示，与灌注处理相比温度升高幅度相似，但0.1毫升/分钟的灌注方案测得温度明显高于体内实验值。这种差异可能源于蒸发/凝结过程，以及激光照射时产生的流体运动与混合导致的热量再分布——这些因素虽未被纳入模型，但可能影响了温度分布。

既往体外研究、数值模拟及本文所述体内实验中观察到的热剂量，足以对尿路上皮、肾脏及输尿管造成损伤，可能引发瘢痕形成、输尿管或集合系统梗阻，甚至导致肾功能衰竭。尽管在激光碎石术实施时，泌尿科医生可能尚未察觉与热损伤相关的组织改变，且这些损伤可能仅涉及肾脏组织的一小部分，但任何程度的不可逆热性实质组织损伤都不应被视作可接受。对于需要终身接受多次碎石治疗的多发性复发性结石患者而言，这一点尤为重要。

尽管本研究及既往实验数据表明，提高冲洗液流速可能部分控制温度升高，但[4–7]这种方法在临床操作中往往难以全面实施且流程繁琐。当前泌尿系统治疗趋势主要聚焦于降低肾内压以减少感染和出血并发症。[11–13]虽然降低冲洗液流速可实现该目标，但会增加热损伤风险。另一种方法是在输尿管镜检查时使用通道鞘，这能有效降低肾内压并改善冲洗液在内镜中的流动。[13]不过这种方法并非适用于所有情况，且常需术后置入输尿管支架。这为采用小型主动（负压）引流系统液体提供了合理依据。此外，使用冰镇冲洗液可能带来额外益处。另一种减轻热损伤的措施是采用间歇性激光激活技术。若采用短时脉冲激光，可使温度恢复至基线水平。但图2至图4所示的温度衰减曲线表明，激光脉冲间隔时间可能过长，不利于治疗效率。未来研究的重点应放在激光器‘操作员占空比’的特性分析与调控上。

本研究存在若干局限性。首先，60秒的连续激光激活在临床实践中未必现实，但该设置为实验提供了标准化条件，并生成完整的温度曲线，同时在早期时间点获取了有价值的温度数据，这对后续计算机模拟开发具有重要价值，也可用于确定热毒剂量的产生时间。其次，我们只评估了一个激光功率设置，40W，这无法预测较低功率设置的效果。

第三，实验所用的杯状结构尺寸未作控制，这可能是导致温度测量存在波动的原因之一，不过这种情况在体内研究和临床治疗中本就属于正常现象。最后，温度记录采用了针式和线式两种热电偶方法。虽然这种双方法并用可能被视为研究中的干扰因素，但实属实验技术发展过程中的常规操作，且并未对测得的热曲线产生系统性偏差。

要更全面地探索参数空间的更广范围，仍需开展更多研究。由于前期体外研究结果与本次体内研究高度吻合，大部分工作可通过模拟和体外试验完成。此外，基于实际激光开关时间（即“操作员工作周期”）研究温度变化的影响，有助于明确临床场景中预期的温度和热剂量。这些研究方向的探索具有双重意义：首先，需要在高功率激光碎石系统参数空间内界定热“安全边界”；其次，开发既能提升碎石效率又确保热安全的热缓解工具与技术。

综上所述，在猪体内模型中施加高功率（40W）钬激光能量时，特别是在较低冲洗速率条件下，可能会引发潜在的损伤性温度升高。目前正通过更广泛的激光参数设置对热剂量进行深入研究，以绘制热安全边界图。这将为开发控制和缓解钬激光碎石术热效应的技术工具提供基础数据。

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作者声明

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Simulation of Laser Lithotripsy-Induced Heating in the Urinary Tract

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Abstract

Purpose: Holmium laser lithotripsy is a common modality used to fragment urinary stones during ureteroscopy. Laser energy deposited during activation produces heat and potentially causes thermal bioeffects. We aimed to characterize laser-induced heating through a computational simulation.

Materials and Methods: A finite-element model was developed and used to estimate temperature in the urinary tract. Axisymmetric models of laser lithotripsy in a renal calyx, the renal pelvis, and proximal ureter were created. Heat generation by laser and heat transfer were simulated under different laser powers between 5 and 40 W. Irrigation fluid flow was introduced at rates between 0 and 40 mL/min. The model was validated by comparison with previous in vitro temperature data in a test tube, then used to calculate heating and thermal dose in the three tissue models.

Results: Simulated temperature rises agreed well with most in vitro experimental measurements. In tissue models, temperature rises depended strongly on laser power and irrigation rate, and to a lesser extent on location. Injurious temperatures were reached for 5–40 W laser power without irrigation, >10 W with 5 mL/min irrigation, 40 W with 15 mL/min irrigation, and were not found at 40 mL/min irrigation. Tissue injury volumes up to 2.3 cm^3 were calculated from thermal dose.

Conclusions: The results suggest a numerical model can accurately simulate the thermal profile of laser lithotripsy. Laser heating is strongly dependent on parameters and may cause a substantial temperature rise in the fluid in the urinary tract and surrounding tissue under clinically relevant conditions.

Keywords: laser lithotripsy, urinary stone, ureteroscopy

Introduction

Urinary tract stones are commonly treated by three procedures: shockwave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy. SWL and URS are used in >90% of cases.[1] Although SWL is at present the only truly noninvasive intervention, its use has been declining in favor of URS,[1] which has become more effective with improvements to the technology.[2] SWL has not seen such advances in efficacy, although several emerging technologies may eventually improve it.[3–5]

URS for stone treatment is performed almost exclusively using laser lithotripsy, where a fiber-optic Holmium:YAG laser generates pulses with sufficient energy to produce stone disintegration.[6] This instrument operates in different modes to produce either fragments to be removed through basket, or dust that will expel spontaneously from the urinary tract.

In recent years, laser parameters with higher power have been advocated to increase efficiency. However, most of the energy deposited by the laser ultimately converts to heat. In vitro and in vivo studies have suggested that laser lithotripsy may produce substantial heat during procedures through repeated laser pulsing.[7–11] In conjunction with fluid irrigation, it is not clear how heat dissipation evolves during URS.

We propose that the thermal profile of laser lithotripsy can be evaluated through computational simulations in conjunction with physical experiments. Such models can complement experimental data and allow systematic investigation of clinical and biological factors affecting heating. In this study, we first compare our simulation with in vitro experiments[7] to validate its accuracy. We then simulate several cases of laser lithotripsy to evaluate the fluid and tissue temperature distribution and parameters controlling heating.

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Materials and Methods

Experiment

The experimental setup and tests are fully described in a separate article.[7] In brief, the setup consisted of a water tank filled with 14 L of 37°C deionized water, with a submerged 10 mm diameter glass test tube simulating a human calyx and positioned with the opening 1 cm above the bath surface. A lithotripsy laser system (pulse 120; Lumenis, San Jose, CA) was used with the laser fiber passed through the working channel of an ureteroscope. The fiber was positioned 15 mm from the bottom of the tube and the ureteroscope was held 20 mm from the bottom. A thermocouple was held 5 mm from the bottom * 2 mm lateral from the position of the laser to record temperature.

Room temperature irrigation was introduced for 20 seconds before laser activation. Different laser parameters were used in each trial, with pulse energies and pulse repetition frequencies of 0.5 J × 10 Hz (5 W), 1.0 J × 10 Hz or 0.5 J × 20 Hz (10 W), 1.0 J × 20 Hz or 0.5 J × 40 Hz (20 W), 1.0 J × 40 Hz or 0.5 J × 80 Hz (40 W), and irrigation flow of 0, 15, or 40 mL/min for 60 seconds. The laser was then deactivated and irrigation was continued for 20 seconds.

Numerical simulation

Numerical simulations were performed on a workstation computer in COMSOL Multiphysics finite-element modeling software (COMSOL, Burlington, MA). The numerical model included heat transfer components of diffusion, convection, and sourcing. Fluid was modeled to include laminar flow, and heat-induced convection and mixing. An axisymmetric model was used to minimize calculation time.

The experimental setup from the previous section was first simulated for model validation. The test tube was surrounded by water, approximating the large water bath in experiments. The tube was 10 mm diameter and 55 mm length (volume 8.1 mL) with 1 mm wall thickness (Fig. 1), with an open continuous flow boundary condition (fluid flows out of the tube during irrigation). The laser was modeled as a 0.5 mm diameter heat source in the center of the test tube 15 mm above the bottom surface. Laser radiation force was modeled as a volume force in the fluid. A 1 mm diameter tube was positioned 5 mm above the laser source as an irrigation inlet. Irrigation was introduced at 22°C with rates between 0 and 40 mL/min. Fluid velocities and temperature were calculated for all spatial points in the model. The average temperature within the entire test tube volume was also calculated.

For simulations of in vivo cases, we modeled three simplified scenarios in the proximal ureter, the renal pelvis, and a renal calyx. All material parameters are included in Table 1. Most physical dimensions applied here are approximated from literature measurements captured by urography, CT, or MRI,[12–14] although these vary substantially between individuals. Cooling effects from blood perfusion were modeled in the tissues. The three models were axisymmetric to reduce computational complexity (Fig. 1).

(1) The calyx was modeled as a 6 mm diameter by 5 cm length tube (volume 2.7 mL) with 1 mm collecting system wall that terminated 15 mm from the laser similar to the geometry of the test tube. The wall was surrounded by kidney parenchyma.
(2) The renal pelvis was modeled as a 2 cm diameter spherical fluid-filled chamber with 6 mm diameter tube extending for 7.5 cm from one side to simulate the ureter (volume 8.7 mL). The urinary tract was lined with a 1 mm wall. The laser and irrigation were positioned at the orifice between the ureter and pelvis. Kidney tissue surrounded the collecting system and ureter wall.
(3) The ureter model was simulated in the same geometric model as the renal pelvis, but the laser was placed 4.5 cm from the opening of the collecting space and the irrigation placed 5 mm distal to the laser.

The thermal dose was calculated to estimate the extent of tissue damage. Thermal dose is a common metric based on empirical data that combines temperature and exposure time of a tissue to estimate when tissue is considered nonviable:

$$TD_{43} = \int_0^\infty R^{43-T} dt. \quad (1)$$

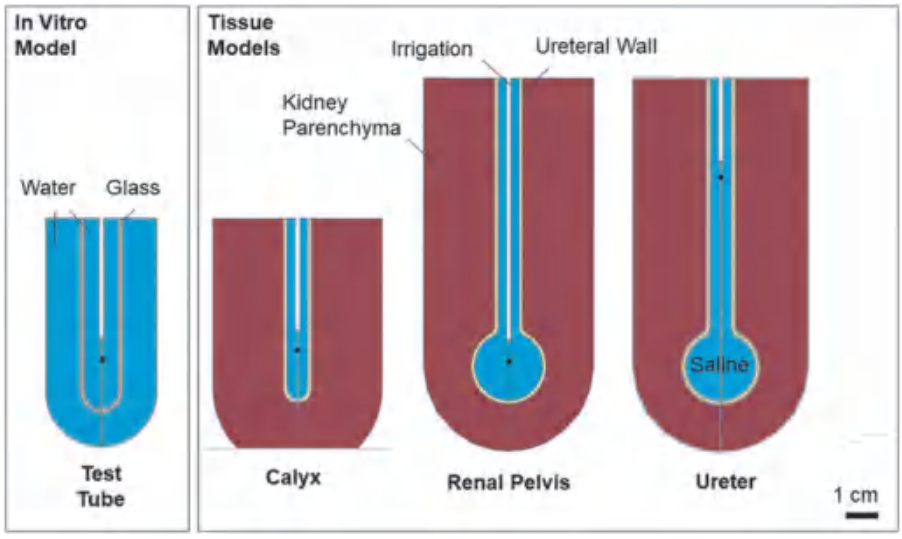


FIG. 1. Model geometry for the in vitro test tube simulations (left), as well as the calyx (center left), renal pelvis (center right), and ureter (right) simulations. An irrigation tube is inserted at the center axis of each model, with the heat source represented below it as a black circle. Material areas are separated by color.

Table 1. Material and Tissue Parameters Used for Simulations of In Vitro and In Vivo Conditions

	Density (kg/m^3)	Specific heat capacity (J/kg$K)	Thermal conductivity (W/m$K)	Perfusion rate (L/min$kg)
Water	998	4184	0.608	—
Glass	2230	750	0.800	—
Urine	1023	4178	0.560	—
Blood	1049	3617	0.517	—
Urinary tract wall	1101	3306	0.462	0.19
Kidney parenchyma	1049	3587	0.527	3.80

In Equation 1, T is temperature, t is time, R is a factor (0.25 for $T < 43°C$ and 0.5 for $T \geq 43°C$), and TD_{43} is the thermal dose, in cumulative equivalent minutes held at 43°C. Tissue is considered denatured for $TD_{43} > 240$ minutes.[15,16] Thermal dose is a strongly nonlinear function of temperature; it takes 240 minutes to render tissue nonviable at 43°C, but only * 15 seconds at 53°C.

Laser powers (calculated from pulse energy and rate) between 5 and 40 W were considered at irrigation rates of 0, 5, 15, and 40 mL/min in each model.

Results

In vitro simulation and validation

Without irrigation, heat accumulated around the laser and radiated in a nearly symmetric manner, with temperature increasing until termination of laser pulsing. With irrigation, heat was carried with the fluid toward the distal surface of the test tube, which impacted and then displaced toward the tube opening, causing mixing of the fluid and a more uniform temperature throughout the tube. Heat dissipated after laser cessation.

Quantitatively, thermocouple temperature (10 mm distal and 2 mm lateral from laser fiber) reached >100°C at 0 mL/min irrigation in simulation, whereas the volume-averaged temperature in the tube reached up to 68°C at the highest laser power of 40 W in both experiment and simulation (Table 2). Peak temperatures in experiments were nearly identical with parameters of the same power regardless of pulse setting or frequency. Temperatures >100°C are unlikely in the fluid for even a short duration because of boiling that is not captured in these simulations. Instead, the volume-averaged temperature in the test tube gave more reasonable estimates of temperature rise expected in well-mixed fluid. Without irrigation, a significant discrepancy exists between experimental measurements and those in simulation, particularly in cases where boiling is predicted. Simulations and experiments without irrigation agree well provided fluid mixing is introduced (Fig. 2). This is demonstrated by simulations where we artificially increased the radiation force of the laser on the fluid, causing enhanced mixing. This change does not cause a significant difference with irrigation that causes mixing naturally.

Table 2. Maximum Temperatures Reached in Experiment and Simulation

Irrigation (mL/min)	Power (W)	Experiment TC (°C)	Simulation TC (°C)	Simulation average (°C)
0	5	47	85	46
	10	52	104	50
	20	56	100	57
	40	68	244	68
15	5	30	28	28
	10	34	32	32
	20	42	42	40
	40	50	60	56
40	20	30	30	30
	40	37	37	37

TC = thermocouple temperature.

With 15 and 40 mL/min irrigation, temperature rises were reduced. However, temperatures >43°C occurred with 15 mL/min irrigation at 40 W laser power. At 40 mL/min of irrigation, temperature never reached >37°C under any condition. Temperature elevation in simulations compared favorably with experiments, with a maximum difference of 6°C rise (Fig. 2 and Table 2).

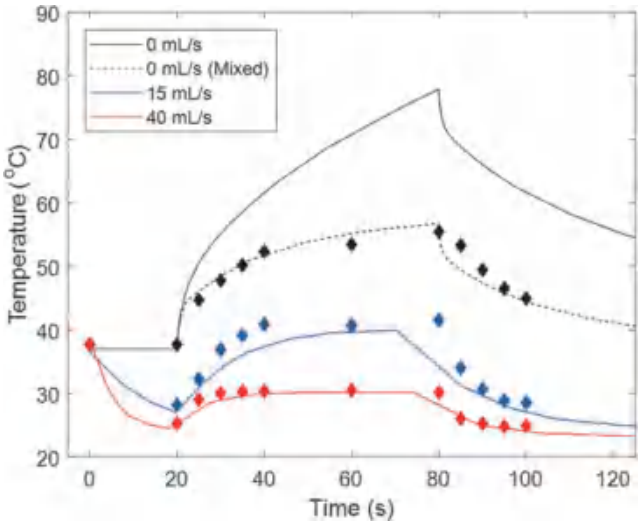


FIG. 2. Temporal thermal profiles measured by thermocouple (points) and simulated volume-averaged fluid temperature (lines) in the test tube for 20 W laser power at different irrigation rates. Curves follow an initial steep rise with initiation of laser firing at 20 seconds, but approach an asymptotic value, particularly at 15 and 40 mL/min irrigation levels. The simulation overpredicts temperature rise for no irrigation because of absence of fluid mixing the simulation. Artificially forcing this mixing produces better agreement (dashed line).

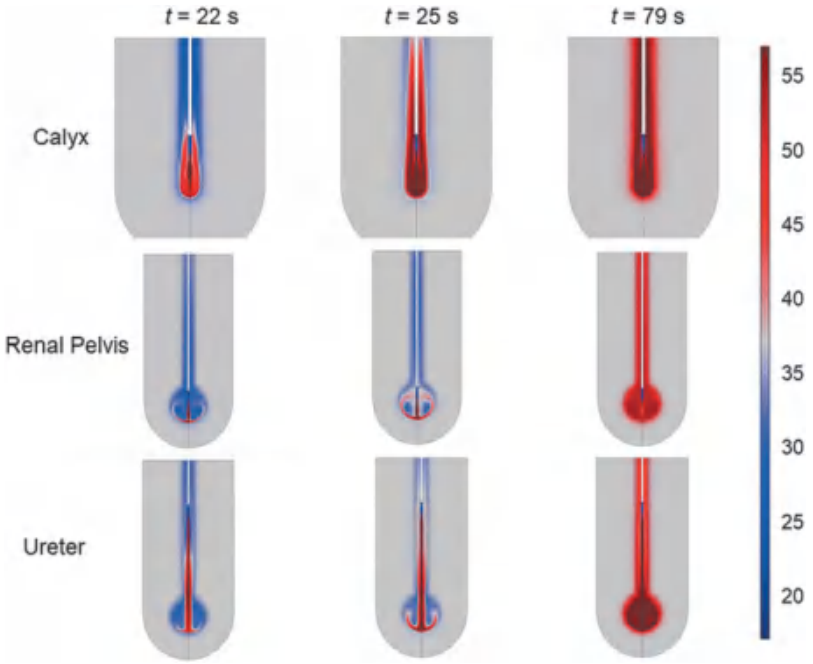


FIG. 3. Example images of heat deposition in the calyx (top row), renal pelvis (center row), and ureter (bottom row) models at three time points with laser power of 40 W and irrigation rate of 15 mL/min. The color bar indicates temperature (°C).

Simulation of heating in caliceal fluid and tissue

Simulations of heating in the urinary tract showed similar trends to those in vitro. Without irrigation, heat deposited around the laser fiber, causing tissue to receive thermal doses sufficient to cause irreversible damage. With irrigation, heat was distributed over larger regions. In all three locations, irrigation carried the heat retrograde and impinged on the distal surface of the collecting system before deflecting anterograde, after which the fluid temperature reached a more uniform value by mixing. Significant temperature rises and injury could occur far from the fiber (Fig. 3). For instance, with high irrigation and laser power, heat deposited in the ureter caused injury at the distal surface of the renal pelvis 6.5 cm away from the laser. In severe cases, injury was predicted in both the collecting system wall and the kidney parenchyma.

Without irrigation, volume-averaged fluid temperatures of 44°C to >100°C were achieved (Fig. 4). Temperatures in the calyx were greater than the other two locations for the same laser power. Irrigation at 5 mL/min resulted in fluid temperatures between 36.5°C and 99.6°C, depending on the power and location. Peak tissue temperatures were ≥46°C, sufficient to cause thermal bioeffects for ≥10 W laser power. Peak temperatures for 15 and 40 mL/min irrigation ranged from 37.2°C to 79°C and 37.0°C to 40.5°C, respectively. Thus, irrigation could almost entirely mitigate heating.

Injury volumes calculated based on a thermal dose for 43°C > 240 minutes varied strongly with laser power and irrigation rate, and less so with location. Injury occurred for the following conditions regardless of location: ≥5 W power at 0 mL/min irrigation, ≥10 W power at 5 mL/min, and 40 W power at 15 mL/min. No thermal injury was produced at 40 mL/min. Injury to the parenchyma was generated only with irrigation ≤5 mL/min. Injury volumes up to 2.35 cm^3 occurred (Fig. 5). The laser activation time required to initiate injury reduced with increasing laser power. The time to initial injury with irrigation was <1–21 seconds (Fig. 6). Certain

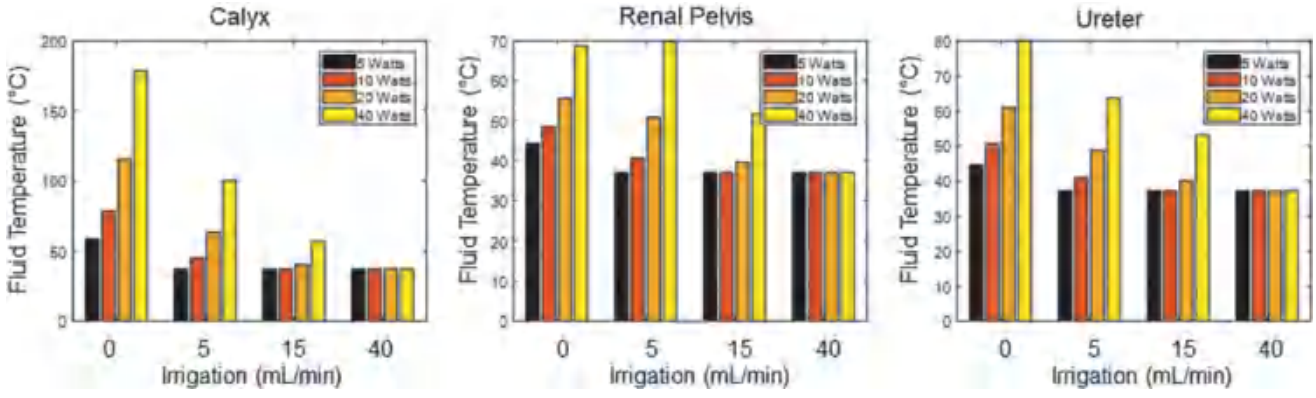


FIG. 4. Bar plots displaying volume-averaged temperature of urine reached within 60 seconds of laser pulsing under different parameters in a calyx (left), renal pelvis (center), and ureter (right).

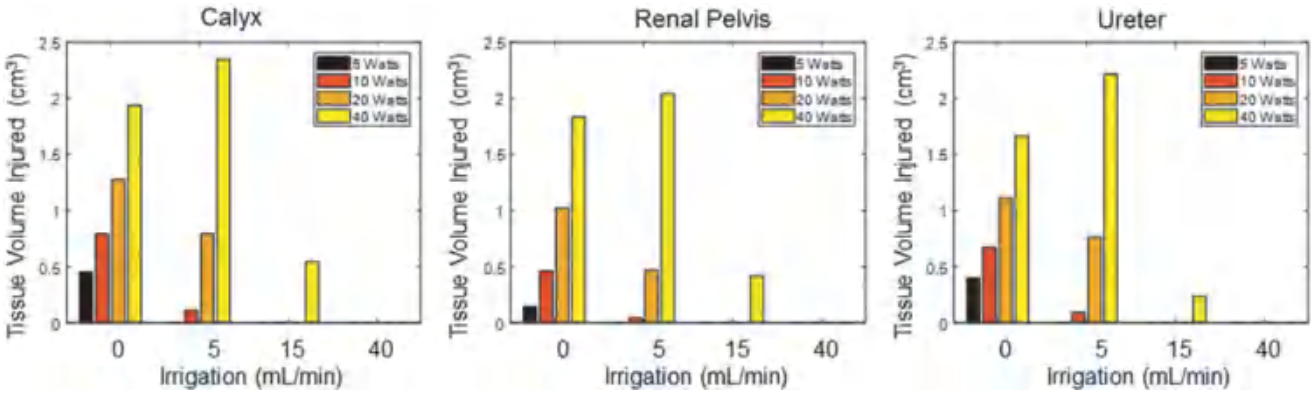


FIG. 5. Calculated volume of tissue injury (in cm^3) after simulation under different parameters in the calyx (left), renal pelvis (center), and ureter (right). No bar is shown for situations where volume was $<1\,mm^3$.

simulations with irrigation produced almost immediate tissue injury because of a localized jet of hot fluid carried to the surface.

Discussion

Holmium laser lithotripsy is the dominant instrumentation for disintegrating stones during URS. It is powerful enough to fracture nearly any stone type and the parameters allow control between fragmentation and dusting. Dusting is associated with shorter treatment times and fewer risks to the ureter,[17] and often uses more rapid pulsing and higher laser power, although trends in parameters vary between practices and across different parts of the world.[18] With introduction of new lasers using higher powers,[19] the potential for new bioeffects exists. The range of parameters modeled in this study are consistent with those used in commercial instruments.[19,20]

Light at the wavelength of a holmium laser is absorbed over a very short distance.[21] As a result, the water directly in front of the tip is boiled, producing a vaporous cavity between the fiber and stone. The remaining light energy of the pulse reaches the stone and causes disintegration through a photothermal effect.[21] After the pulse, the vapor cloud condenses back into liquid. Thus, the energy from the laser is transformed into two effects: creation of new surfaces in the stone and heating. The estimated mechanical energy expended to turn a stone into fragments is small. For instance, a 1 cm diameter sphere of gypsum cement (a common stone model) turned into 1 mm fragments would increase the surface area by a factor of * 10, necessitating * 50–100 mJ of energy. This is less than the typical energy of one pulse. Therefore, it can be assumed most of the energy is converted to heat. In this study, the total energy deposition ranged from 300 to 2400 J over 60 seconds. This energy is sufficient to heat an entire 150 cm^3 adult kidney by roughly 0.5–3.8°C. These estimates indicate that laser lithotripsy has the potential to cause a substantial temperature rise within a small volume.

This study demonstrates that laser lithotripsy heating can be numerically modeled. In vitro, both point and average fluid temperature in simulation agreed well with temperatures recorded in experiment with irrigation. However, simulated temperatures displayed larger discrepancies with measured data in the absence of irrigation. These data suggest absence of fluid mixing in the simulation as the likely reason. In practice, the growth and collapse of the boiling bubble stirs the fluid, likely producing dispersion of heat and more uniform temperature throughout the liquid.

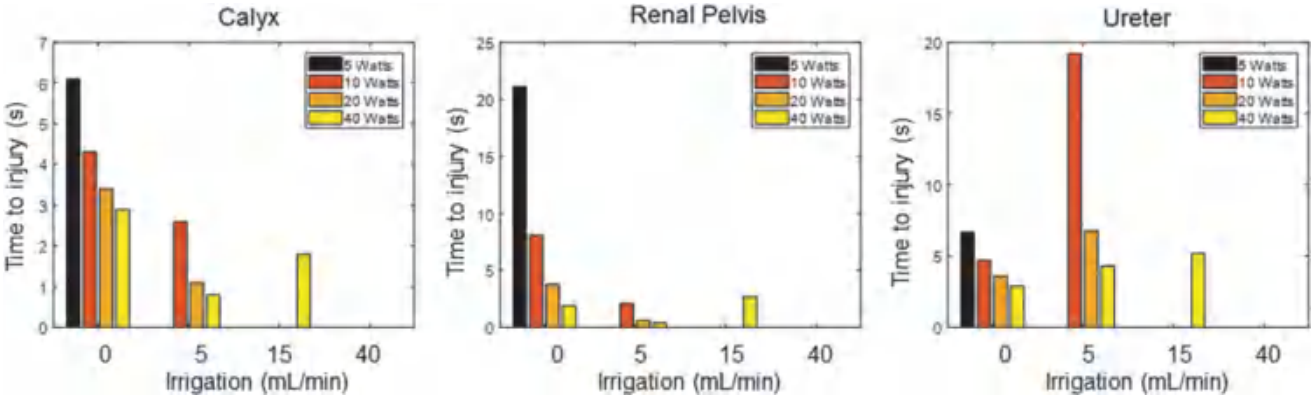


FIG. 6. Time to initiate injury (threshold 1 mm^3) under different pulsing and irrigation in the calyx (left), renal pelvis (center), and ureter (right). No bar is shown for situations where injury did not occur.

In simulated tissue, further complexity of heating was revealed. Without irrigation, even 5 W laser power deposited for <30 seconds could cause thermal injury. At maximum power in the calyx model without irrigation, injury to the wall and surrounding parenchyma was predicted over a 2 cm length around the fiber tip. With 5 mL/min irrigation, the damage was extended to >5 cm of the collecting space wall, but with minimal parenchymal injury. Irrigation sometimes reduced time to initiate injury, as the fluid transported hot liquid to the tissue faster than natural convection. Kidney parenchyma is highly perfused compared with other tissues that produced some protective effect, evident as a short pause in the onset of thermal injury at the boundary. Blood perfusion was insufficient to stop heating entirely, and in the most severe scenarios injury to >1 cm^3 of parenchyma occurred (* 0.5% of an adult's functional renal volume[22]).

Although these results highlight the strong possibility of thermal injury during laser lithotripsy, the limitations of the model prevent drawing quantitative conclusions, and further data in vivo are needed to confirm these effects. The axisymmetric model is computationally efficient, but does not capture the complex flow and heat distribution in actual anatomy. In addition, this study did not capture variations in dimensions of the urinary tract that can be substantial between patients. However, our axisymmetric model also compared favorably with recent in vivo temperature data.[11] In addition, the presence of a stone could alter local heating around the laser fiber, but certain modes such as ''pop-dusting'' primarily deposit energy into the fluid. Aldoukhi and colleagues found in vitro with slow motion analysis that only 17.5% of pulses struck fragments with 0.5 J × 80 Hz parameters mimicking pop-dusting.[23] The fluid physics should include boiling and condensation to simulate added fluid motion and improve accuracy. Under moderate irrigation, the model gave a good approximation of the temperature expected during laser lithotripsy. Such models may provide valuable information to help define guidelines for safe parameters during laser lithotripsy.

Conclusions

We established a numerical model of heat generated during laser lithotripsy, which suggested that laser heating can cause significant temperature rises in the collecting system fluid and surrounding tissue. The temperature rises varied substantially with laser parameters, irrigation, and duration of pulsing. Under severe conditions, both the urinary tract and kidney parenchyma could reach temperatures sufficient to cause irreversible thermal injury. These findings may be clinically relevant particularly in light of trends toward high-power laser usage for treating stones.

Acknowledgment

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Author Disclosure Statement

Adam Maxwell has equity and consulting arrangements with SonoMotion, Inc. No other competing financial interests exist.

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Abbreviations Used
SWL = shockwave lithotripsy
URS = ureteroscopy

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激光碎石术所致尿路加热的模拟

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摘要

目的：钬激光碎石术是输尿管镜检查中常用的碎石方法。激光激活时释放的能量会产生热量，可能引发热生物效应。本研究通过计算模拟，旨在表征激光诱导的加热效应。

材料与方法：本研究采用有限元模型对泌尿系统温度进行估算。构建了肾盏、肾盂及近端输尿管的轴对称激光碎石模型，模拟不同激光功率（5-40瓦）下的热能生成与热传导过程。通过0-40毫升/分钟的冲洗液流量进行模拟。模型通过与试管实验的体外温度数据对比验证后，用于计算三种组织模型的加热量及热剂量。

实验结果：模拟温度升高的数据与大多数体外实验测量结果高度吻合。在组织模型中，温度升高主要受激光功率和冲洗速率影响，受位置因素影响较小。在无冲洗条件下，5-40瓦激光功率可达到损伤温度；使用5毫升/分钟冲洗时超过10瓦，40瓦功率配合15毫升/分钟冲洗时达到损伤温度，而40毫升/分钟冲洗则未检测到损伤温度。根据热剂量计算得出，组织损伤体积最大可达2.3立方厘米^3。

结论：研究结果表明，数值模型能精确模拟激光碎石术的热分布。激光加热效果与参数密切相关，在临床相关条件下，可能导致尿路及周围组织内的液体温度显著升高。

关键词：激光碎石术，尿路结石，输尿管镜检查

引言

尿路结石常用三种治疗方法：冲击波碎石术（SWL）、输尿管镜（URS）和经皮肾镜取石术（pcnl）。90%的病例采用SWL和URS。[1]虽然目前SWL是唯一一种真正的无创干预措施，但URS的应用越来越少，随着技术的改进，URS变得更加有效。[2]尽管一些新兴技术可能最终会改善SWL的疗效，但SWL在疗效方面还没有看到这样的进步。[3-5]

结石的URS治疗几乎完全采用激光碎石术，由光纤钬激光产生具有足够能量的脉冲，使结石碎裂。[6]该仪器以不同模式运行，以产生通过碎石篮清除的碎石或从尿路自发排出的碎石粉尘。

近年来，医学界提倡采用功率更高的激光参数以提升治疗效率。但值得注意的是，激光沉积的大部分能量最终都会转化为热量。体外和体内研究均表明，激光碎石术在操作过程中因反复激光脉冲作用会产生大量热量。[7–11]当配合液体冲洗使用时，目前尚不明确尿路结石碎石术（URS）过程中热量的消散机制。

我们提出，可以通过结合物理实验的计算机模拟来评估激光碎石术的热分布特征。这类模型不仅能补充实验数据，还能系统研究影响加热效果的临床和生物因素。本研究首先通过体外实验对比验证模拟结果的准确性[7]，随后模拟多个激光碎石术病例，评估流体与组织的温度分布规律及控制加热的关键参数。

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材料和方法

实验

实验装置与测试方法详见另一篇独立论文。[7]简而言之，实验装置包含一个装有14升37°C去离子水的水槽，其中放置一根直径10毫米的浸没式玻璃试管，模拟人体肾盏结构，开口位置距水槽表面1厘米。采用Lumenis公司（美国加州圣何塞）生产的脉冲120型碎石激光系统，将激光光纤穿过输尿管镜的工作通道。光纤定位在试管底部下方15毫米处，输尿管镜保持在底部下方20毫米位置。温度记录采用热电偶，安装在距底部5毫米处，横向偏离激光器约2毫米的位置。

在激光激活前，先进行20秒室温冲洗。每次实验采用不同激光参数：脉冲能量与脉冲重复频率分别为0.5焦耳×10赫兹（5瓦）、1.0焦耳×10赫兹或0.5焦耳×20赫兹（10瓦）、1.0焦耳×20赫兹或0.5焦耳×40赫兹（20瓦）、1.0焦耳×40赫兹或0.5焦耳×80赫兹（40瓦），同时冲洗流量设置为0、15或40毫升/分钟，持续60秒。随后关闭激光，继续冲洗20秒。

数值模拟

数值模拟在工作站计算机上使用COMSOL Multiphysics有限元建模软件（COMSOL公司，美国马萨诸塞州伯灵顿）完成。该数值模型包含扩散、对流和热源三种传热方式。流体模型采用层流状态，同时考虑热致对流与混合效应。为缩短计算时间，采用轴对称模型进行建模。

为验证模型准确性，我们首先对前一节的实验装置进行了模拟。实验管被水包围，模拟了实验中使用的大型水浴环境。该试管直径10毫米、长度55毫米（体积8.1毫升），壁厚1毫米（见图1），采用开放连续流边界条件（在灌注过程中液体会从试管流出）。激光器被建模为位于试管底部上方15毫米处的热源，直径0.5毫米。激光辐射力模拟为流体中的体积力。将直径1毫米的管子置于激光源上方5毫米处作为灌注入口。灌注液在22°C下以0至40毫升/分钟的速率注入。计算了模型中所有空间点的流体速度和温度，并测定了整个试管体积内的平均温度。

在模拟体内病例时，我们构建了近端输尿管、肾盂和肾盏三个简化模型。所有材料参数详见表1。本文采用的大部分物理参数均基于尿路造影、CT或MRI等影像学检查的文献测量数据进行估算，[12–14]虽然这些参数在个体间存在显著差异。我们通过组织建模模拟了血液灌注引发的冷却效应。为降低计算复杂度，三个模型均采用轴对称结构（见图1）。

(1) 将花萼建模为直径6毫米、长度5厘米的试管（体积2.7毫升），其收集系统壁厚1毫米，末端距离激光源15毫米，几何结构与试管相同。管壁周围环绕着肾实质。
(2) 肾盂被建模为一个直径2厘米的球形充液腔室，其中包含一根直径6毫米的导管，该导管从一侧延伸7.5厘米以模拟输尿管（体积8.7毫升）。尿路内壁采用1毫米厚的衬垫。激光和灌注装置被安置在输尿管与肾盂之间的开口处。肾脏组织环绕着收集系统和输尿管壁。
(3) 输尿管模型采用与肾盂相同的几何模型进行模拟，但激光器被放置在不同位置。
收集空间开口处距4.5厘米，灌注装置位于激光器远端5毫米处。

为评估组织损伤程度，我们计算了热剂量。热剂量是基于实测数据的常用指标，通过结合温度和组织暴露时间，判断组织何时失去活性。

$$TD_{43} = \int_0^{\infty} R^{43-T} dt. \quad (1)$$

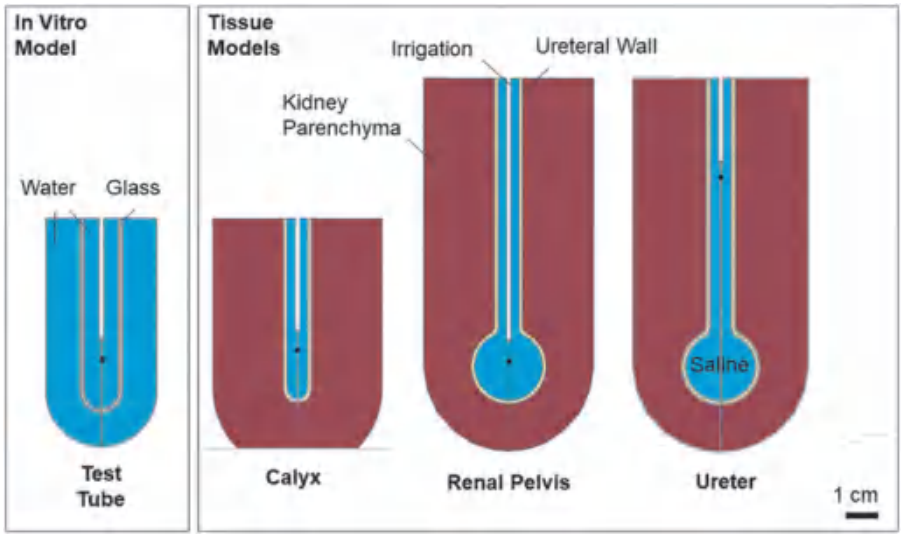


图1展示了体外试管模拟（左）的模型几何结构，以及花萼（左中）、肾盂（右中）和输尿管（右）的模拟模型。每个模型的中心轴线上都插入了灌注管，其下方用黑色圆圈表示热源。不同材料区域通过颜色区分。

表1.体外和体内条件模拟所用材料和组织参数

	密度（kg/m ^{3}）	比热容（J/kg.K）	导热系数 (W/m$K)	灌注率 (L/min$kg)
水	998	4184	0.608	—
玻璃	2230	750	0.800	—
尿液	1023	4178	0.560	—
血	1049	3617	0.517	—
尿路壁	1101	3306	0.462	0.19
肾实质	1049	3587	0.527	3.80

在公式1中，T表示温度，t表示时间，R是一个系数（T <43 ° C时为0.25，T≥43 $_{43}$ oC时为0.5），TD $_{43}$是热剂量，以43oC下保持的累积当量分钟表示。当TD $_{43}$>240分钟时，组织被认为是变性的。[15,16]热剂量是温度的强非线性函数；在43oC下需要240分钟才能使组织失去活性，但在53oC下只需约15秒。

各模型在0、5、15和40毫升/分钟四种灌注速率下，分别采用5至40瓦的激光功率（基于脉冲能量与频率计算得出）。

结果

体外模拟和验证

未进行灌注时，激光器周围积聚的热量以近乎对称的方式辐射，温度持续升高直至激光脉冲停止。灌注时，热量随液体流向试管远端表面，该表面接触后推动液体向开口处流动，使液体混合并使试管内温度分布更加均匀。激光停止后，热量随即散逸。

定量分析显示，在模拟实验中，当以0毫升/分钟的流速进行冲洗时，热电偶测得的温度（位于激光光纤远端10毫米处和侧方2毫米处）均超过100°C。而实验与模拟结果均表明，当激光功率达到40瓦峰值时，管内体积平均温度最高可达68 °C（见表2）。值得注意的是，实验中不同脉冲设置和频率条件下，相同功率参数下的峰值温度基本一致。由于在这些模拟中没有捕捉到沸腾，因此即使在很短的时间内，

表2.实验和模拟中达到的最高温度

灌溉 （毫升/分钟）	权力 (W)	实验 泰语 （°C）	模拟 泰语 （°C）	模拟 平均的 （°C）
0	5	47	85	46
	10	52	104	50
	20	56	100	57
	40	68	244	68
15	5	30	28	28
	10	34	32	32
	20	42	42	40
	40	50	60	56
40	20	30	30	30
	40	37	37	37

TC=热电偶温度。

流体中的>100℃也不太可能。相比之下，试管中的体积平均温度更能合理预测充分混合流体的温度上升情况。在未进行冲洗的情况下，实验测量值与模拟结果存在显著差异，特别是在预测沸腾的案例中。但若引入流体混合，模拟与实验结果则高度吻合（图2）。通过模拟实验可以验证这一点：当人为增强激光对流体的辐射作用力时，混合效果得到显著提升。这种人为干预与自然混合的冲洗方式相比，并未产生显著差异。

当采用15毫升/分钟和40毫升/分钟两种灌注速率时，温度升幅均有所降低。但当灌注速率为15毫升/分钟且激光功率为40瓦时，温度仍会超过43°C。而采用40毫升/分钟灌注速率时，无论何种条件，温度均未超过37°C。模拟结果与实验数据吻合良好，两者温差最大仅为6°C（见图2和表2）。

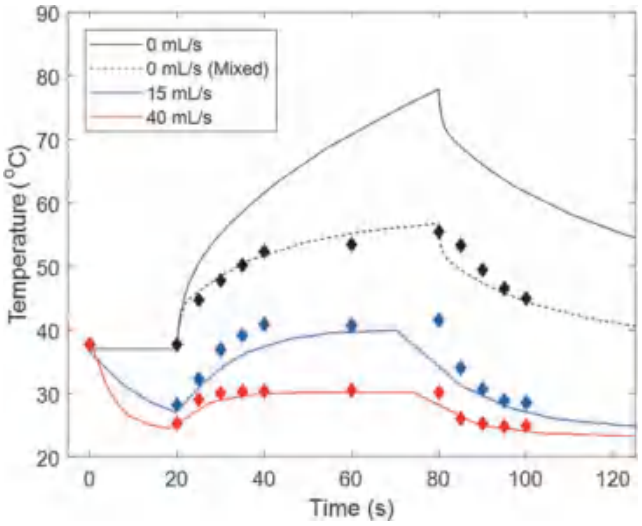


图2展示了在20瓦激光功率下，不同灌注速率时试管内热电偶测得的温度随时间变化曲线（点）与模拟的体积平均流体温度曲线（线）。曲线在20秒激光启动时呈现初始陡峭上升趋势，但随后逐渐趋近渐近值，尤其在15毫升/分钟和40毫升/分钟灌注速率下表现明显。由于模拟中未考虑流体混合效应，导致温度上升值被高估。通过人为强制流体混合后，模拟结果与实验数据吻合度显著提升（虚线）。

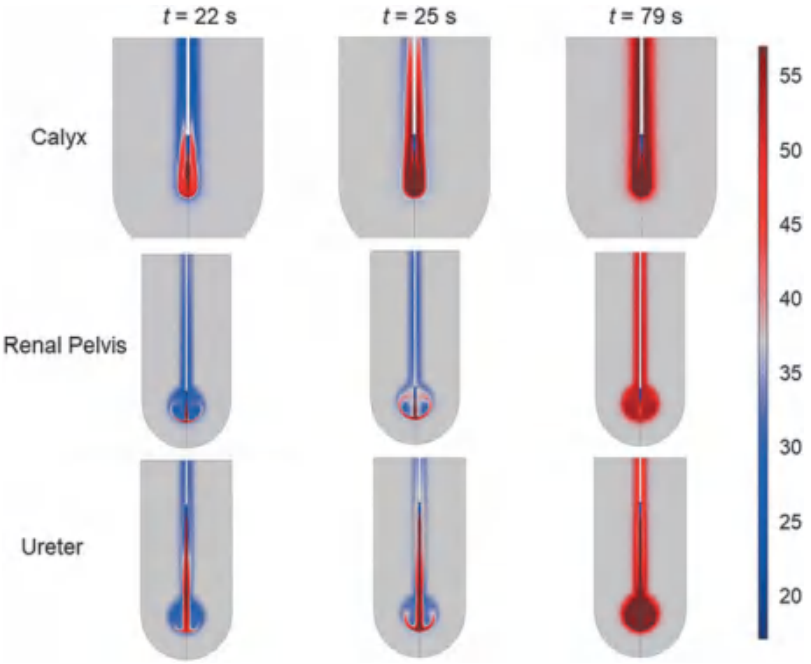


图3展示了在40瓦激光功率和15毫升/分钟灌注速率下，三个时间点时花萼（上排）、肾盂（中排）和输尿管（下排）模型的热沉积示例图像。色标表示温度（℃）。

杯状体液和组织中的加热模拟

尿路加热模拟实验显示，其趋势与体外实验结果相似。在未进行冲洗的情况下，热量会聚集在激光光纤周围，导致组织承受足以造成不可逆损伤的热剂量。而通过冲洗操作，热量分布范围显著扩大。在三个实验位置中，冲洗均使热量呈逆向流动，先作用于收集系统的远端表面，随后转向正向流动，通过混合作用使液体温度趋于均匀。值得注意的是，即使远离光纤的位置也可能出现显著温度升高和损伤（图3）。例如，当冲洗强度和激光功率较高时，输尿管中的热量沉积会在距激光源6.5厘米的肾盂远端表面引发损伤。在严重病例中，收集系统壁和肾实质均可能出现损伤。

未进行灌溉时，测得体积平均流体温度介于44°C至100°C以上（图4）。相同激光功率下肾盏内的温度高于其他两个位置。当以5毫升/分钟的流速进行冲洗时，液体温度会根据功率和位置不同，介于36.5°C至99.6°C之间。当激光功率≥10瓦时，组织温度峰值≥46°C，足以引发热生物效应。以15毫升/分钟和40毫升/分钟流速冲洗时，温度峰值分别在37.2°C至79°C和37.0°C至40.5°C之间波动。由此可见，冲洗几乎能完全抑制组织加热现象。

基于43°C热剂量计算的损伤体积在240分钟内会随着激光功率和冲洗速率发生显著变化，而与损伤部位的差异较小。无论位置如何，以下条件均会产生损伤：功率≥5瓦且冲洗速率为0毫升/分钟、功率≥10瓦且冲洗速率为5毫升/分钟、功率40瓦且冲洗速率为15毫升/分钟。当冲洗速率为40毫升/分钟时未产生热损伤。仅当冲洗速率为5毫升/分钟或更低时才会对实质组织造成损伤。损伤体积最大可达2.35立方厘米^3（图5）。随着激光功率的增加，引发损伤所需的激光激活时间逐渐缩短。使用冲洗模式时，初始损伤发生时间通常在1-21秒之间（图6）。在某些

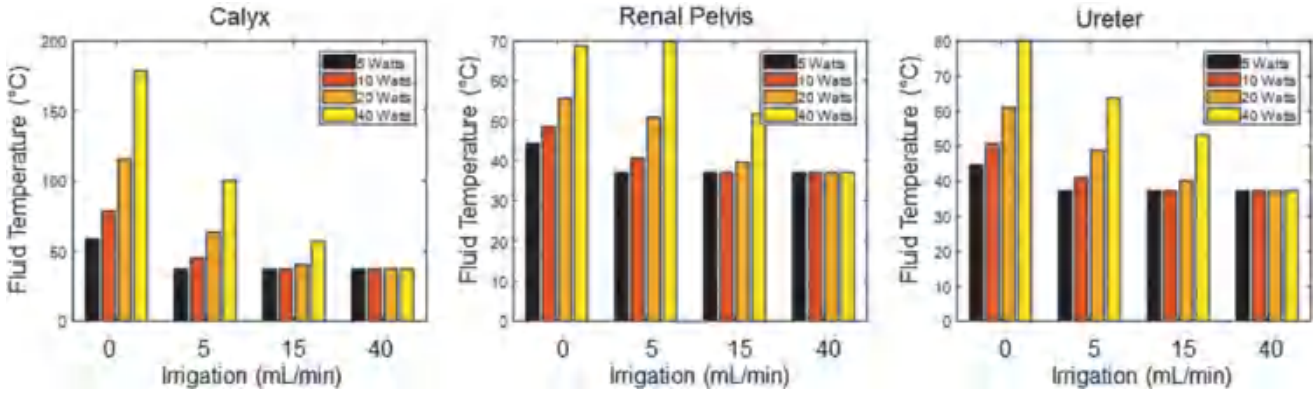


图4.条形图展示了不同参数下，膀胱（左）、肾盂（中）和输尿管（右）在激光脉冲60秒内达到的尿液体积平均温度。

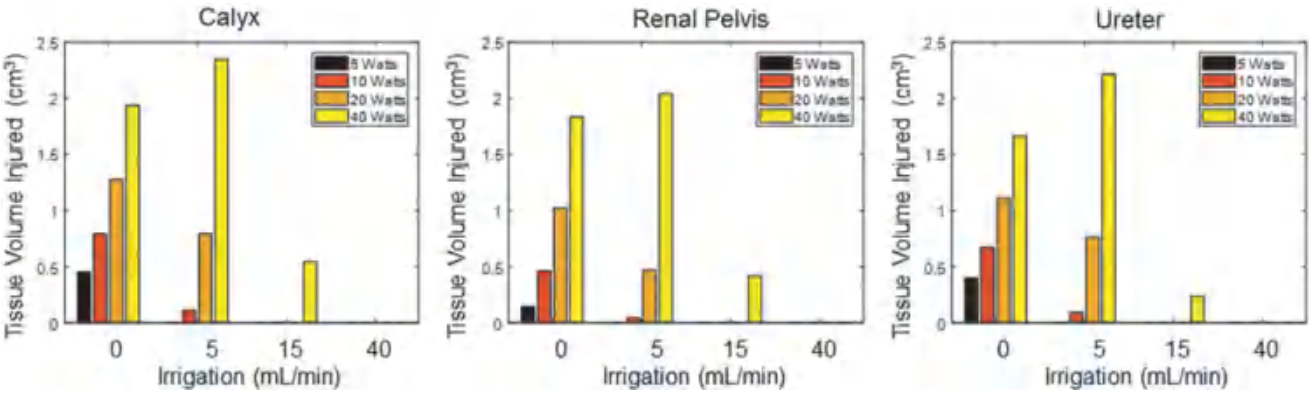


图5.在肾盏（左）、肾盂（中）和输尿管（右）中，不同参数模拟后计算的组织损伤体积（单位：cm^3）。对于体积<1 mm的情况，未显示条形图[3]。

模拟中，由于局部的热流体喷射到地表，几乎立即造成了组织损伤。

讨论

钬激光碎石术是经尿道碎石术中粉碎结石的主要器械。其能量足以粉碎几乎所有类型的结石，参数设置可精准调控碎石程度与粉尘生成。粉尘生成技术能缩短治疗时间并降低输尿管风险，[17]通常采用更快的脉冲频率和更高功率的激光，不过不同医疗机构及地区间的参数趋势存在差异。[18]随着高功率新型激光器的问世，[19]该技术在生物效应方面展现出新潜力。本研究建立的参数模型范围与市售器械的实际使用参数保持一致。[19，20]

钬激光的光波在极短距离内即可被完全吸收。[21]这使得光纤尖端正前方的水体瞬间沸腾，在光纤与结石之间形成蒸汽空腔。脉冲剩余的光能抵达结石后，通过光热效应引发碎裂。脉冲结束后，蒸汽云会[21]冷凝固化。

激光能量转化为两种效应：在结石内部形成新表面和产生热量。将结石破碎所需的机械能估算值其实很小。以直径1厘米的石膏水泥球（常见结石模型）为例，若将其破碎成1毫米碎片，表面积将增加约10倍，仅需消耗约50-100毫焦耳能量。这还不到单次脉冲能量的十分之一，因此可推断大部分能量转化为热能。本研究显示，60秒内总能量沉积量在300至2400焦耳之间，足以使整个150厘米^{3}成人肾脏温度升高0.5-3.8摄氏度。这些数据表明，激光碎石术能在小体积内引发显著温度升高。研究表明，激光碎石术的热效应可通过数值模拟实现。体外实验中，模拟的点温度和平均流体温度与灌注实验记录值吻合良好，但在无灌注条件下，模拟温度与实测数据存在较大偏差。这些数据表明，模拟中缺乏流体混合可能是主要原因。实际上，沸腾气泡的生长和坍塌会搅动液体，很可能产生热量的分散，并在整个液体中产生更均匀的温度。

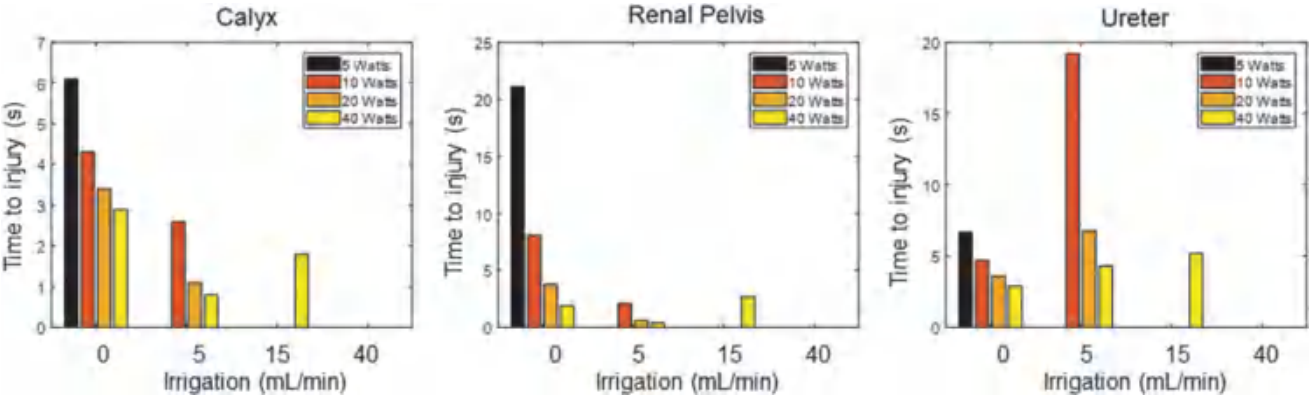


图6.肾盏（左）、肾盂（中）、输尿管（右）在不同脉冲和灌注条件下的损伤起始时间（阈值1mm^3）。未显示损伤未发生情况的柱状图。

在模拟组织中，加热的进一步复杂性被揭示出来。在没有灌注的情况下，即使5瓦激光功率沉积时间不足30秒也可能导致热损伤。在花萼模型中，即使在最大功率且无灌注的情况下，纤维尖端周围2厘米长度的壁和周围实质组织仍会受到损伤。当使用5毫升/分钟的灌注时，损伤范围扩展至收集空间壁超过5厘米，但实质组织损伤最小。灌注有时会缩短损伤发生的时间，因为液体将热液输送到组织的速度比自然对流更快。与其他组织相比，肾脏实质灌注量极高，这产生了一定的保护作用，表现为边界处热损伤开始时间的短暂延迟。血液灌注量不足以完全阻止加热，在最严重的情况下，超过1厘米^{3}的实质组织会受损（约占成人功能性肾体积的0.5%[22]）。

尽管这些结果表明激光碎石术中存在显著热损伤风险，但模型的局限性使得无法得出定量结论，仍需更多体内实验数据来验证这些效应。轴对称模型虽然计算效率高，但无法模拟真实解剖结构中复杂的流体流动和热量分布。此外，本研究未考虑患者间可能存在的显著差异性尿路尺寸。不过，我们的轴对称模型与近期体内温度数据的对比结果仍具说服力。[11]此外，结石的存在可能改变激光光纤周围的局部加热情况，但某些模式（如“爆粉效应”）主要将能量沉积在液体中。Aldoukhi团队通过慢动作分析发现，仅17.5%的脉冲在模拟爆粉效应的0.5J×80Hz参数下击中碎石。[23]为提高模拟精度，流体力学模型应包含沸腾和凝结过程以模拟额外流体运动。在中等冲洗条件下，该模型对激光碎石术中预期温度的预测效果良好。这类模型能提供重要参考，为制定激光碎石术的安全参数指南提供依据。

结论

我们建立了激光碎石过程中产生的热量数值模型，结果显示激光加热会导致收集系统液体及周围组织温度显著升高。温度变化与激光参数、冲洗方式及脉冲持续时间密切相关。在极端条件下，尿路和肾脏实质组织的温度可能达到不可逆热损伤的程度。这些发现具有临床意义，特别是在当前治疗结石普遍采用高功率激光的趋势下。

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作者声明

Adam Maxwell与SonoMotion，Inc.存在股权及咨询服务协议，不存在其他竞争性财务利益。

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使用的缩写SWL=冲击波碎石术；URS=输尿管镜

·综述·

泌尿系结石钬激光碎石热效应研究进展

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【摘要】 钬激光碎石术以其碎石效果可靠、对组织损伤较小的优势而被广泛应用于泌尿系结石的微创治疗。但输尿管结石钬激光碎石术后常合并输尿管狭窄、粘连等并发症,其原因除输尿管黏膜局部病变、合并感染之外,一定程度上与钬激光的热效应有关。钬激光热效应的常见影响因素包括:钬激光脉冲能量和频率、脉宽模式、光纤直径、灌注速度、灌注液的温度、碎石模式等,现就钬激光碎石术热效应的研究进展作一综述。

【关键词】 尿路结石;碎石术,激光;激光,固体;钬

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泌尿系结石是我国常见的泌尿外科疾病[1]。泌尿系结石的治疗除传统的切开取石外,还有体外冲击波碎石术(extracorporeal shock wave lithotripsy, ESWL)、钬激光碎石术(holmium laser lithotripsy, HLL)、超声碎石术(ultrasound lithotripsy, USL)、气压弹道碎石术(pneumatic lithotripsy, PL)等。钬激光碎石术因其可观的临床碎石效率以及可与经皮肾镜、输尿管硬镜、输尿管软镜等设备配合使用等突出优势,在泌尿系结石腔内治疗中得以广泛应用[2]。

1 钬激光的特点

钬激光具有以下特点:① 高能脉冲式激光,可以击碎各种成分的泌尿系结石;② 对结石冲击力小,可以有效减少碎石过程中的结石后移效应;③ 组织穿透深度较浅,不易引起输尿管或膀胱穿孔[3]。钬激光吸收峰与水接近,其释放的能量95%可被周围水介质吸收[2],进而转化为水分子的热能,使周围环境中的水温升高,对周围组织产生明显的热效应。

2 钬激光的碎石机制及热效应原理

目前认为钬激光碎石机制主要有光热机制(photothermal decomposition)和光机械机制(photomechanical mechanisms)[4-5];Sperrin 等[6]研究测量了光纤尖端不同距离处的冲击波压力,当脉冲能量为 2 J 时,在光纤尖端 4 mm 处的压力为 510 MPa,该压力水平足以击碎结石。光热机制是指钬激光光纤尖端的水介质吸收能量后温度升高发生汽化形成微气泡,大量微气泡形成传递激光能量的汽化通道,结石吸收激光能量后温度急速升高,高温使结石发生热分解,最终消融结石[5]。这种由微气泡形成的汽化通道被称之为“摩西效应”[7]。Chan 等[8]利用高速摄像设备拍摄钬激光碎石的过程发现在激光作用于结石约 50 us 时,结石表面便出现碎裂迹象,而此时微气泡尚未形成,因此并没有冲击波产生。同时他们研究发现当光纤与结石表面平行时,结石表面受到的冲击波压力最强,但此时却没有结石碎裂。Cecchetti 等[9]研究发现在能量设置为 1.5 J 时,光纤尖端 2 mm 处的温度为750℃,当频率升高为 30 Hz 时,温度达到 1400℃以上,它们认为这些微气泡其实便是等离子气泡,只有等离子气泡破碎产生的热效应才能达到如此高温。这些均是光热机制的有力证据。Finley 等[10]认为钬激光的碎石机制与钬激光的能量和脉宽呈正相关,脉宽越长,光热机制作用就越明显,钬激光脉宽相对较长,因此,光热机制在钬激光碎石过程中发挥主要作用,而光机械机制则起到冲散结石碎片的作用。

3 钬激光热效应对细胞的影响

Bettaieb 等[11]研究显示 43℃可引起细胞钙稳态的破坏,继而导致蛋白质变性,在此环境中 120 min 会导致细胞死亡,Molina 等[12]研究证明时间和温度对细胞损伤具有共同作用,温度每升高 1℃,造成相同细胞损伤所需的时间便减少一半,当温度达到 56℃时,细胞在 1 s 内即可死亡。钬激光碎石时能量密度相对较高,灌注液和周围组织的温度迅速升高[13],Wollin 等[14]在体外使用 200 μm 的光纤,分别测量 0.2 J×50 Hz、0.6 J×6 Hz、0.8 J×8 Hz、1.0 J×10 Hz、1.0 J×20 Hz 等五组能量设置组合在无灌注条件下 60 s 内的温度变化,发现五组的最高温度均超过 43℃,0.8 J×8 Hz、1.0 J×10 Hz 组的最高温度超过 60℃,1.0 J×20 Hz 组的最高温度甚至超过 100℃,由此可见钬激光热效应所致的高温远超细胞所能承受的极限温度,无疑会对细胞造成严重影响。

4 钬激光热效应与输尿管狭窄

临床研究发现钬激光碎石术后常出现输尿管狭窄、闭锁等并发症[15],输尿管狭窄的主要原因有:①合并感染;②结石长期炎症刺激引起的输尿管局部黏膜病变;③碎石过程中因操作视野不清导致的管壁组织直接损伤;④由于结石完全梗阻,镜端水流不畅,长时间钬激光碎石,局部易致高温,对

输尿管黏膜、肌层甚至浆膜层造成热灼伤,损伤局部呈凝固样坏死,组织修复后形成病理性瘢痕组织,最终导致输尿管狭窄甚至闭锁[15-17]。由此可见,钬激光的热效应是引起输尿管狭窄的重要因素,然而,钬激光热效应的高低尚与诸多因素相关。

5 钬激光热效应的影响因素

钬激光热效应的影响因素包括:脉冲能量和频率、脉宽模式、光纤直径、灌注速度、灌注液温度以及碎石模式等。

5.1 脉冲能量和频率对钬激光热效应的影响

Aldoukhi 等[18]用热电偶测量了 0.5 J×10 Hz、1.0 J×10 Hz、1.0 J×20 Hz、1.0 J×40 Hz 等 4 组能量设置组合在无灌注时钬激光连续激发 60 s 内的温度变化。结果显示 4 组的最高温度分别为 45.2℃、50.1℃、55.6℃、70.3℃,0.5 J×10 Hz 与 1.0 J×10 Hz 组数据表明脉冲频率不变时,钬激光的热效应随着脉冲能量增加呈现增强趋势;1.0 J×10 Hz、1.0 J×20 Hz、1.0 J×40 Hz 等三组数据表明脉冲能量不变时,钬激光热效应随脉冲频率增加呈现增强趋势。Wollin 等[14]监测了 0.2 J×50 Hz 组与 1.0 J×10 Hz 组在无灌注时钬激光连续激发 60 s 内的温度变化,发现 1.0 J×10 Hz 组的灌注液温度明显高于 0.2 J×50 Hz 组。可见,脉冲能量对钬激光的热效应影响更明显。Kallidonis 等[19]通过体外实验测量了在灌注开放时钬激光功率为 5 W、10 W、20 W 时灌注液的温度,发现随着功率增大,灌注液的温度也随着升高。

5.2 脉宽模式对钬激光热效应的影响

随着碎石设备的发展,最新的钬激光能量平台可以选择不同的脉宽进行碎石。Yoshida 等[20]研究了不同脉宽对钬激光热效应的影响,与初始温度相比,150 us、300 us、450 us、600 us、800 us 组灌注液温度分别升高了 1.2℃、1.3℃、1.4℃、1.9℃、2.4℃,这说明在钬激光脉冲能量、频率等一致的情况下,增加脉宽会使钬激光热效应增加。钬激光释放热量所需要的时间约为 100 us,而钬激光的脉冲宽度为 150~1000 us,脉宽越长,脉冲持续时间内释放的热量就越多,钬激光的热效应就越显著[10,21]。

5.3 光纤直径与灌注速度对钬激光热效应的影响

Buttice 等[22]研究表明在无灌注时,272 μm 光纤比 200 μm 光纤热效应更明显,能量组合为 0.5 J×20 Hz 时,两组的最高温度均超过 45℃,但 272 μm 光纤比 200 μm 光纤温度升高更快。而当灌注开放时,两种直径的光纤对灌注液温度影响无明显差异。可见在无灌注时,减小光纤直径可以降低钬激光的热效应。Wollin 等[14]测量了 0.2 J×50 Hz、0.6 J×6 Hz、0.8 J×8 Hz、1.0 J×10 Hz、1.0 J×20 Hz 组在灌注速度为 0、50、100 mL/min 时钬激光连续激发 60 s 内的温度变化,发现灌注速度为 0 mL/min 时,五组最高温度均超过 43℃,灌注速度为 50 mL/min 时,仅有 1 J×20 Hz 组的最高温度超过 43℃,当灌注速度为 100 mL/min 时,五组的最高温度均未超过 43℃。可见,增加灌注速度,可以降低钬激光的热效应。随着钬激光使用功率不断增大,充足顺畅的腔内灌注是降低钬激光热效应的有效措施,灌注不足时,即便功率很低也会对周围组织产生明显热效应。输尿管软镜碎石时,灌注液和钬激光光纤使用共同的通道,根据泊肃叶定律,灌注流量与灌注通道半径的四次方成正比,因此,光纤直径的轻微改变即可引起灌注流量的巨大变化。有研究表明使用大直径的钬激光光纤,会降低软镜的灌注流量,使灌注液的温度升高,对周围组织产生明显热效应,同时会降低软镜的弯曲度及手术视野的清晰度,增加手术时间[23-24]。

5.4 灌注液温度对钬激光热效应影响

由于常温生理盐水可能会引起术后低体温、寒战、低氧血症等不良反应,因此在腔镜手术中常使用 36.5℃生理盐水作为灌注液[25]。而在钬激光碎石术中,为了降低钬激光的热效应,常选择常温生理盐水作为灌注液。Buttice 等[22]对比研究 20℃和 36.5℃生理盐水作为灌注液的安全性,结果显示在无灌注时,二者最高温度均超到 45℃,36.5℃的灌注液组用时更短,温度升高更快;而在灌注开放时,二者温度均未超过 45℃。研究表明在无灌注时,钬激光在不同温度的灌注液中均会产生明显的热效应,灌注液的温度越高则钬激光热效应越明显;而在灌注开放时,使用 20℃和 36.5℃的生理盐水作为灌注液均是安全的,同时 36.5℃灌注液可以减少术后低体温等不良反应。

5.5 碎石模式对钬激光热效应的影响

目前,钬激光热效应研究多为体外试验,这些试验均是在钬激光空激发的条件下测量温度,并未对比研究结石在腔内碎石模式下对于钬激光热效应的影响。钬激光碎石时,钬激光的能量转化为灌注液的热能和碎石的动能。因此,在碎石条件下,结石吸收了部分钬激光的能量,这有助于降低钬激光热效应[21]。此外,持续碎石模式模式和间断碎石模式也会影响钬激光的热效应。Aldoukhi 等[18]测量了在灌注速度为 14~15 mL/min 时,0.5 J×10 Hz、1.0 J×10 Hz、0.5 J×20 Hz、1.0 J× 20 Hz、0.5 J×40 Hz、1.0 J×40 Hz、0.5 J×80 Hz 等能量设置组合在钬激光持续激发 60 s 及停止之后 20 s 内灌注液的温度变化,发现灌注液温度在钬激光激发前 20 s 内快速升高,之后达到平台期,在钬激光停止工作后 5 s 内灌注液温度快速下降,10 s 时温度基本恢复至正常温度,因此钬激光持续激发时间少于 20 s,间歇时间长于 5 s,有助于降低钬激光的热效应。钬激光碎石中不可避免的一个问题是结石的后移效应,结石后移时,寻找结石、光纤尖端与结石的重新接触等均会使钬激光短暂停止工作,这些也有助于降低钬激光的热效应。输尿管本身的弹性扩张、血管分布、血液流动、尿液的连续产生等均可能对钬激光热效应产生影响[22]。此外,光纤尖端的保护涂层、光纤的修剪方式、弯曲程度等也可能会影响钬激光的热效应。

6 小结

综上所述,钬激光热效应受钬激光脉冲能量和频率、脉宽模式、灌注速率、灌注液温度、光纤直径以及碎石模式等诸多因素的影响:增加脉冲能量和频率可以使钬激光的热效应

明显增强,增加灌注速度可以降低钬激光热效应,但应避免肾内压过高;减少脉宽可以降低钬激光热效应;在无灌注时,小直径光纤可以降低钬激光的热效应,但可能会增加光纤的损耗;在灌注开放的条件下,36.5℃的灌注液可能是安全的,同时可以减少术后低体温等并发症;间断的碎石模式及结石对能量的吸收也有助于降低钬激光的热效应。目前,钬激光热效应研究尚缺乏多因素的系统体外试验以及在体动物实验,尚需要进一步研究。

利益冲突 所有作者均声明不存在利益冲突

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UROLOGY - ORIGINAL PAPER

Temperature profiles of calyceal irrigation fluids during flexible ureteroscopic Ho:YAG laser lithotripsy

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Abstract

Purpose To evaluate calyceal irrigation fluid temperature changes during flexible ureteroscopic Ho:YAG laser lithotripsy.

Methods Between May 2019 and January 2020, patients with kidney stones undergoing flexible ureteroscopic Ho:YAG laser lithotripsy were enrolled. A K-type thermocouple was applied for intraoperative temperature measurement. Laser was activated at different power (1 J/20 Hz and 0.5 J/20 Hz) and irrigation (0 ml/min, 15 ml/min and 30 ml/min) settings, temperature–time curve was drawn and time needed to reach 43 °C without irrigation was documented.

Results Thirty-two patients were enrolled in our study. The temperature–time curve revealed a quick temperature increase followed by a plateau. With 15 ml/min or 30 ml/min irrigation, 43 °C was not reached after 60 s laser activation at both 1 J/20 Hz and 0.5 J/20 Hz. At the power setting of 1 J/20 Hz and irrigation flow rate of 15 ml/min, the temperature rise was significantly higher than other groups. Without irrigation, the time needed to reach 43 °C at 1 J/20 Hz was significantly shorter than that at 0.5 J/20 Hz (8.84 ± 1.41 s vs. 13.71 ± 1.53 s).

Conclusion Ho:YAG laser lithotripsy can induce significant temperature rise in calyceal fluid. With sufficient irrigation, temperatures can be limited so that a toxic thermal dose is not reached, when irrigation is closed, the temperature increased sharply and reached 43 °C in a few seconds.

Keywords Ho:YAG laser · Ureteroscopy · Lithotripsy · Temperature · Thermal injury

Abbreviations

SWL	Shockwave lithotripsy
URS	Ureteroscopy
PCNL	Percutaneous nephrolithotomy
RIRS	Retrograde intrarenal surgeries
Ho:YAG	Holmium:yttrium aluminum garnet
SD	Standard deviation
ANOVA	Analysis of variance
BMI	Body mass index
CEM_{43}	Cumulative equivalent minutes at 43 °C

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Background

The incidence of urolithiasis is increasing worldwide [1]. Currently, shockwave lithotripsy (SWL), ureteroscopy (URS) and percutaneous nephrolithotomy (PCNL) constitute the mainstream procedures. It is reported that retrograde intrarenal surgeries (RIRS) including semi-rigid and flexible ureteroscopy have encountered a drastic growth in the past few years [2].

Holmium:yttrium aluminum garnet (Ho:YAG) laser is recognized as the optimum standard for URS and flexible nephroscopy due to its effectiveness in all stone types irrespective of compositions [3]. In contrast to short-pulsed duration lasers, whose fragmentation mechanism relies on photoacoustic effect with little risk of thermal injuries, Ho:YAG laser is long-pulsed duration laser with the fragmentation mechanism of photothermal effect, which may cause significant temperature rise of surrounding fluids while activated [4, 5]. Recent years, thulium fiber laser (TFL) has been used as a promising novel laser technology and may become the standard of care in lithotripsy [6]. Although superiority of TFL over Ho:YAG has been widely

recognized, the thermal effect of TFL is still inevitable [7]. With the evolvement of laser technology and the application of high-power laser system, lithotripsy becomes more effective; meanwhile, the latent risk of thermal injuries increases as well.

Several studies were carried out concerning irrigation fluids temperature changes during laser activation [6–17]. Among these studies, most were performed using in-vitro models, only Wang et al. [17] presented us with intraoperative ureteral irrigation fluids temperature data. The real intraoperative calyceal thermal profile remains unrevealed. The aim of this study is to evaluate calyceal irrigation fluid temperature changes during flexible ureteroscopic holmium laser lithotripsy at different laser and irrigation settings.

Methods

From May 2019 to January 2020, patients undergoing flexible ureteroscopic Ho:YAG laser lithotripsy in our center were enrolled into our study. Inclusion criteria were: (1) patients diagnosed with kidney stones, with/without ureter stones, (2) the longest diameter of the stone was less than 2 cm, (3) pelvis dilation measured by type-B ultrasound was no more than 3 cm. Patients with congenital kidney/ureter malformations or ureter stricture were excluded.

Our temperature measurement system consists of a KAIPUSEN WRNT-01K-type wire thermocouple (Suma, Taizhou, Zhejiang, China) and a Fluke 53 IIB thermometer (Fluke, Everett, WA, USA). To measure calyceal temperature during operation, a thermocouple was attached to the Storz fiberoptic flexible ureteroscope 11278A1 (Karl Storz, Tuttlingen, Baden-Württemberg, Germany) with its tip 5 mm from the distal end (Fig. 1) and was inserted into the collecting system together with the flexible ureteroscope through a 12/14 Fr single lumen ureteral access sheath (Cook, Bloomington, IN, USA).

Saline irrigation (preheated to 37 °C to reduce hypothermia risk) was delivered using YDJ-111 pumping system (Yida, Hangzhou, Zhejiang, China) at flow rate of 0, 15 ml/min and 30 ml/min measured with a 200 µm laser fiber in the working channel of the flexible ureteroscope. Lithotripsy was performed using HANS-H75 holmium laser system (CureStar, Hefei, Anhui, China) with a 200 µm laser fiber (Lumenis, Yokneam, Israel). The following energy and Frequency settings were explored: 0.5 J/20 Hz and 1 J/20 Hz.

The laser was held above the stone and activated for 60 s in the calices with an irrigation flow of 15 ml/min or 30 ml/min and temperature changes were documented every 5 s. Then, the laser was activated without irrigation and the time needed to reach 43 °C was recorded. During the whole procedure, laser activation was paused when temperature reached 43 °C to avoid potential damage to the kidney.

Data is presented as mean ± standard deviation (SD). For group comparisons, Student's *t* test or one-way analysis of variance (ANOVA) followed by Tukey's test was used. All statistical analyses were performed using GraphPad Prism

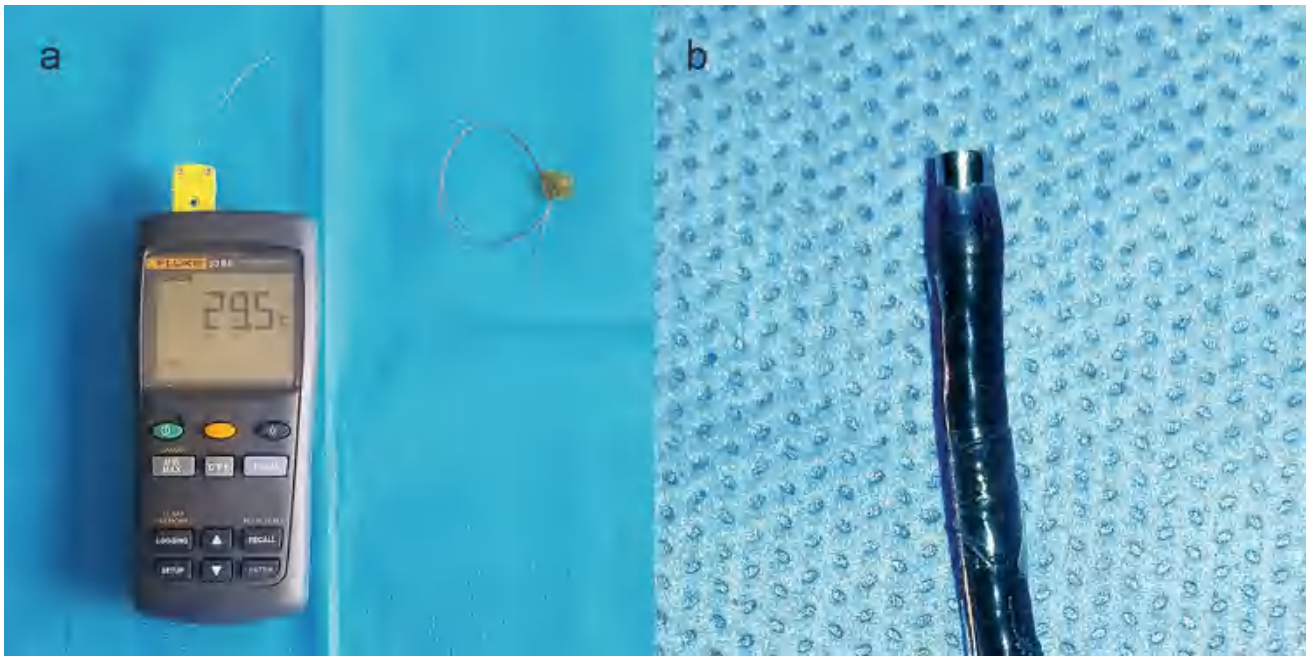


Fig. 1 Setup of temperature measurement system. **a** K-type wire thermocouple connected to thermometer. **b** Thermocouple secured to flexible ureteroscope

8 (GraphPad Software, San Diego, CA, USA). $P < 0.05$ was considered statistically significant.

Results

In all, 32 patients were included into our study, including 20 males and 12 females. The mean age was 41.9 ± 9.2 years. The mean body mass index (BMI) was 22.3 ± 2.4 kg/m^2. Of all the 32 patients, 24 patients solely had kidney stones, while 8 patients had both kidney and ipsilateral ureter stones. The mean pyelic dilation was 8.1 ± 5.1 mm.

For all laser power and irrigation settings (except 0 ml/min), the calyceal fluid temperature increased drastically during the first 10 s of laser activation, then after 20 s, the temperature curve reached a plateau (Fig. 2a). With sufficient irrigation, none of these groups reached a temperature of 43 °C after 60 s laser activation.

The highest temperature rise after 60 s laser activation was observed in 1 J/20 Hz, 15 ml/min group, while the lowest in 0.5 J/20 Hz, 30 ml/min group (4.91 ± 0.58 vs. 1.50 ± 0.44, $P < 0.01$). With the same laser power setting, the temperature rise was significantly higher in groups with lower irrigation flow rate (1 J/20 Hz, 15 ml/min vs. 1 J/20 Hz, 30 ml/min: 4.91 ± 0.58 vs. 2.34 ± 0.25, $P < 0.01$. 0.5 J/20 Hz, 15 ml/min vs. 0.5 J/20 Hz, 30 ml/min: 2.17 ± 0.30 vs. 1.50 ± 0.44, $P < 0.01$). With the same irrigation flow rate, the temperature rise was significantly higher in groups with higher laser power setting (1 J/20 Hz, 15 ml/min vs. 0.5 J/20 Hz, 15 ml/min: 4.91 ± 0.58 vs. 2.17 ± 0.40, $P < 0.01$. 1 J/20 Hz, 30 ml/min vs. 0.5 J/20 Hz, 30 ml/min: 2.34 ± 0.25 vs. 1.50 ± 0.44, $P < 0.01$). (Fig. 2b).

With no irrigation (0 ml/min), the time needed for a temperature rise from baseline to 43 °C with a laser power setting of 1 J/20 Hz was significantly shorter than that with 0.5 J/20 Hz (8.84 ± 1.41 s vs. 13.71 ± 1.53 s, $P < 0.01$) (Fig. 3).

Discussion

Ho:YAG laser has become the most widely used intracoporeal lithotripter since its incorporation into urological practice in the 1990s [16]. With a wavelength of 2100 nm, Ho:YAG laser belongs to the mid-infrared light spectrum, and is readily absorbed by water [18]. At a pulse duration longer than 10 µs, photothermal effect is predominantly produced, as pulse duration exceeds 200 µs, photoacoustic effect is negligible [19]. The pulse duration of Ho:YAG laser is 250 µs, suggesting its mechanism of action is mainly

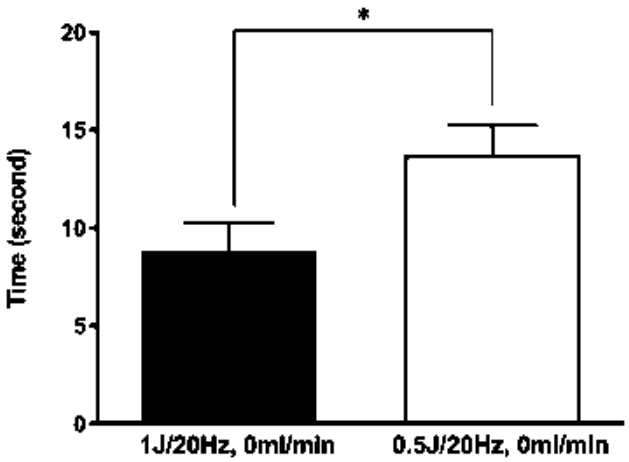


Fig. 3 Time needed to reach 43 °C at different power settings without irrigation. *$p < 0.01$

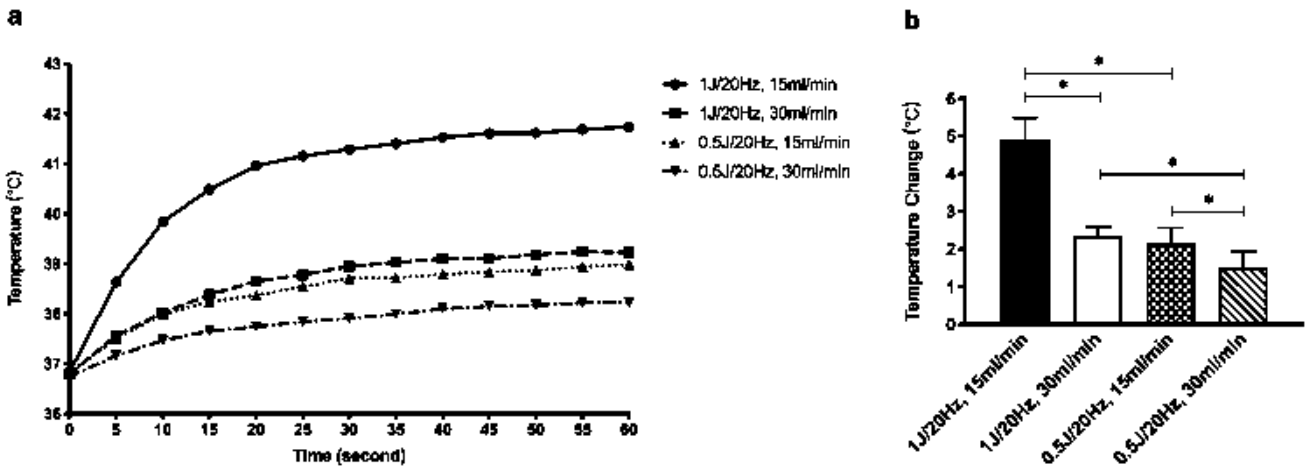


Fig. 2 Temperature profiles during Ho:YAG laser activation. **a** Temperature–time curve at various power and irrigation settings. **b** Mean temperature changes after 60-s laser activation. *$p < 0.01$

photothermal effect [4]. It is reported that direct absorption of the laser energy by stones and chemical decomposition of stones constitute the main process of Ho:YAG lithotripsy [20]. During this process, heat would not be exclusively limited to the stone; meanwhile, the surrounding fluid in the collecting system would experience significant temperature rise, resulting in thermal damages to tissues.

It is not only the peak temperature reached during a procedure, but also the exposure time contributes to the thermal cytotoxic effect. Sapareto and Dewey [21] developed an equation to assess the thermal dose calculated as an exposure time at a reference temperature of 43 °C. This equation is also known as cumulative equivalent minutes at 43 °C (CEM_{43}), which is described mathematically as: $CEM_{43} = \Sigma \Delta t \cdot R^{(43-T)}$ ($R = 0.5$ for $T > 43$ °C, $R = 0.25$ for $T < 43$ °C). Sapareto and Dewey stated a "break" temperature of 43 °C was arbitrarily chosen as a best estimate from all available data. Actually, thermal response differs between tissues and species. Animal experiments demonstrated that $CEM_{43} = 11.2$ min was a safe thermal dose for bladder, while $CEM_{43} > 80$ min led to significant damage, and for kidney, $CEM_{43} < 20$ min resulted in minor damage, while $CEM_{43} > 70$ min caused significant damage [22]. Currently, there is no accurate data regarding the safe thermal dose for human kidney and ureter. In our study, a cut-off temperature of 43 °C was used as the endpoint of laser activation simply referring published studies, since no better threshold was available.

Several studies were published concerning intra-pelvis temperature changes during Ho:YAG laser activation, most of them were in-vitro model studies [7–14], only 1 in-vivo porcine study [15], no human study on this subject was published. Although these experiments maximally reflected RIRS, it is not the real situation, clinical measurements are needed to verify the results. To the best of our knowledge, this is the first intraoperative study concerning calyceal irrigation temperature profiles.

During 60-s laser activation, the calyceal fluid experienced a quick temperature increase followed by a plateau. This phenomenon coincides with previous in-vitro studies [9, 11, 13]. The temperature change should be constant according to the thermodynamic formula $Q = cm\Delta T$; however, in this experimental setting, irrigation circulation might be a rational explanation. At the beginning, the outflow of the irrigation is mainly pelvis fluid, which has not been heated by laser activation. When heated fluid is drained and heat loss equals heat generation, a plateau is reached.

It is reported that perfusion-mediated tissue cooling reduces coagulation necrosis during radiofrequency ablation [23]. Thus, it is hypothesized that this might mitigate temperature rise during lithotripsy [11]. However, a porcine study conducted by Aldoukhi et al. [15] revealed that without irrigation the peak temperature reached was greater in the in-vivo model than that in the in-vitro model. In our study, the two no-irrigation groups all reached 43 °C in several seconds, while with sufficient irrigation, the threshold temperature was never reached. Besides, for groups with the same laser power, significantly higher temperature was observed with lower irrigation flow rate. Taken together, these results indicated that perfusion-mediated tissue cooling effect plays minor role in dampening temperature rise compared to irrigation.

In our daily practice, we usually use pumping system while performing ureteroscopy to maintain a constant irrigation. It should be kept in mind that the irrigation flow would decrease or even fall to zero in the case of a bad outflow. It is important to ensure that the sheath is placed in ureteropelvic junction to obtain a fluent fluid outflow. In addition, the operating channel diameter of the ureteroscope also influences the irrigation flow. As a result, the actual flow rate might differ from the setting value. In some circumstances, for example, the stone moves back and forth with the impact of the irrigation flow, it is difficult to focus the stone with the laser tip, a common maneuver to handle this situation is to temporarily suspend the irrigation flow. However, this procedure should be done with caution, noticing the fact that 1 J/20 Hz with no irrigation caused a drastic temperature increase to 43 °C in 8.84 s and 0.5 J/20 Hz with no irrigation 13.71 s. Therefore, the continuous activation of the laser should not exceed the time limit and enough intervals with sufficient irrigation should be left to allow heat dispersion.

Certain limitations exist in our study. First, the number of patients included in our study is small. This may lead to bias when estimating population means. Second, due to our laser equipment, only two power settings were assessed, while 'dusting' and high-power settings were not evaluated. Third, the size of the wire thermocouple, although is only 0.1 mm in diameter, would impact the outflow of the irrigation fluid when compared to real-world practice; however, it is inevitable in such experimental settings. Forth, stone composition analysis was not carried out, thus the impacts of composition on the temperature profile were not evaluated in the current study. Fifth, we did not assess the thermal effect of TLF during lithotripsy; however, we established a way to test intrarenal temperatures that can be applied to various laser types. Further large-scale, more detailed sub-group study was needed to address this issue.

Conclusions

In conclusion, Ho:YAG laser lithotripsy can induce significant temperature rise in calyceal fluid. With sufficient irrigation, the temperature can be limited to a safe range below 43 °C, when irrigation is closed, the temperature increased sharply and reached 43 °C in a few seconds.

Author contributions Conception and design: JT and XA; Collection and assembly of data: YW, ZJ, YG and WF; Analysis and interpretation of data: JT, YW and ZJ; Drafting of the manuscript: JT and ZJ; Revision of the manuscript: XA; Supervision: XA. All authors read and approved the final manuscript.

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Data availability The data used and analyzed in the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethics approval The study was conducted in accordance to the principles of Declaration of Helsinki. Approval was granted by the Ethics Committee of The Seventh Medical Center of Chinese PLA General Hospital.

Consent to participate Informed consent was obtained from all individual participants included in the study.

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泌尿外科-原始论文

柔性输尿管镜下Ho：YAG激光碎石术中肾盏灌注液的温度分布

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摘要

目的：评估在输尿管软镜下Ho：YAG激光碎石术过程中膀胱输尿管冲洗液温度的变化。
方法 2019年5月至2020年1月期间，接受柔性输尿管镜Ho：YAG治疗的肾结石患者研究纳入了激光碎石术患者。术中采用K型热电偶进行温度测量。激光以不同功率（1 J/20 Hz和0.5 J/20 Hz）和灌洗设置（0 ml/min、15 ml/min和30 ml/min）激活，绘制温度-时间曲线，并记录无灌洗时达到43°C所需的时间。
结果 本研究共纳入32例患者。温度-时间曲线显示温度迅速升高随后进入平台期。在15 ml/min或30 ml/min的灌注条件下，无论采用1 J/20 Hz还是0.5 J/20 Hz的功率设置，激光激活60秒后均未达到43°C。在1 J/20 Hz的功率设置和15 ml/min的灌注流速下，温度升高的幅度显著高于其他组。未进行灌注时，达到43°C所需时间在1 J/20 Hz组显著短于0.5 J/20 Hz组（8.84±1.41秒vs.13.71±1.53秒）。
结论 Ho：YAG激光碎石术可引起盏状液温度显著升高。在充分冲洗的情况下，通过控制温度可避免产生毒性热剂量。当关闭灌溉系统时，温度会急剧上升，几秒内即可达到43°C。

关键词 钬：YAG激光·输尿管镜检查·碎石术·温度·热损伤

缩写

SWL	冲击波碎石术
URS	输尿管镜检查术
PCNL	经皮肾镜取石术
RIRS	逆行性肾内手术
Ho:YAG	钬钇铝石榴石
SD	标准偏差
ANOVA	差异分析
BMI	体重指数
CEM_{43}	43°C下的累积等效分钟数

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背景

全球范围内尿路结石发病率持续攀升[1]。目前，冲击波碎石术（SWL）、输尿管镜（URS）和经皮肾镜取石术（PCNL）是主流治疗手段。近年来，包括半刚性输尿管镜和柔性输尿管镜在内的逆行性肾内手术（RIRS）应用量呈现爆发式增长[2]。

钬酸钇铝石榴石（Ho：YAG）激光因其对各类结石（无论成分如何）均具有显著疗效，被公认为上尿路结石碎石术和软性肾镜术的最优标准[3]。与短脉冲激光器依赖光声效应碎石、热损伤风险较低不同，Ho：YAG激光采用光热效应碎石机制，工作时会产生显著的周围液体温度升高[4，5]。近年来，铥光纤激光器（TFL）作为新型激光技术崭露头角，有望成为碎石术的标准治疗方案[6]。虽然TFL较Ho:YAG的优越性已得到广泛认可，

但TFL的热效应仍不可避免[7]。随着激光技术的发展和高功率激光系统的应用，碎石术变得越来越有效，但同时，潜在的热损伤风险也增加了。

多项研究探讨了激光激活过程中灌注液温度变化[6–17]。其中多数研究采用体外模型，仅Wang等人[17] 本研究提供了术中输尿管冲洗液的温度数据，但术中输尿管盏的热分布特征仍未明确。本研究旨在评估在不同激光参数和冲洗设置下，输尿管镜钬激光碎石术过程中输尿管盏冲洗液温度的变化情况。

方法

2019年5月至2020年1月期间，本中心接受柔性输尿管镜钬：钇铝石榴石激光碎石术的患者被纳入研究。纳入标准包括：(1)确诊为肾结石患者，无论是否合并输尿管结石；(2)结石最长直径小于2厘米；(3)经B型超声测量的盆腔扩张不超过3厘米。先天性肾/输尿管畸形或输尿管狭窄的患者被排除在外。

本温度测量系统由凯普森WRNT-01K型金属丝热电偶（中国浙江台州苏玛公司）和福禄克53 IIB温度计（美国华盛顿州埃弗里特市福禄克公司）组成。

为测量手术过程中膀胱壶腹温度，将热电偶连接至Storz光纤柔性输尿管镜11278A1型（德国巴登-符腾堡州图特林根市卡尔·斯托尔茨公司），热电偶尖端距远端5毫米处（图1），随后通过12/14 Fr单腔输尿管套管（美国印第安纳州布鲁明顿市库克公司）与输尿管镜一同插入收集系统。

使用YDJ-111泵送系统（Yida，杭州，浙江，中国）以0、15 ml/min和30 ml/min的流速进行盐水灌洗（预热至37°C以降低低体温风险），并使用200μm激光光纤在柔性输尿管镜的工作通道中测量。碎石术采用Hans-H75钬激光系统（CureStar，合肥，安徽，中国）配合200μm激光光纤（Lumenis，约克奈姆，以色列）完成。探索了以下能量和频率设置：
0.5 J/20 Hz和1 J/20 Hz。

将激光器置于结石上方并激活60秒，使用15 ml/min或30 ml/min的灌注流速，每5秒记录一次温度变化。随后，在不进行灌注的情况下激活激光器，并记录达到43°C所需的时间。在整个过程中，当温度达到43°C时暂停激光激活，以避免对肾脏造成潜在损伤。

数据以均值±标准差（SD）表示。进行组间比较时，采用*t检验*或单因素方差分析（ANOVA）后接Tukey检验。使用GraphPad Prism8 （GraphPad Software, San Diego， CA， USA）进行所有统计分析。

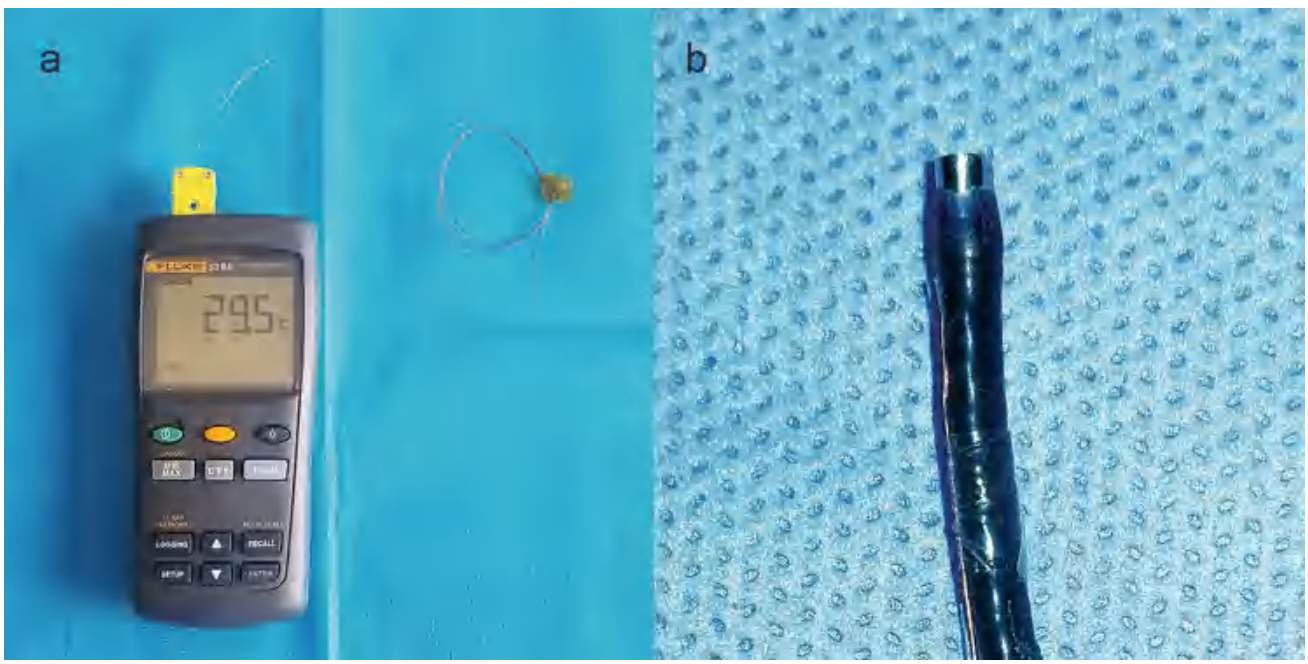


图1温度测量系统设置。**a** K型金属丝热电偶连接到温度计。**b**热电偶固定在输尿管镜上

P<0.05视为具有统计学意义。

结果

本研究共纳入32例患者，其中男性20例，女性12例。平均年龄为41.9±9.2岁。平均体重指数（BMI）为22.3±2.4 kg/m ^{2}。在所有32例患者中，24例仅患有肾结石，而8例同时患有肾结石和同侧输尿管结石。平均肾盂扩张为8.1±5.1毫米。

对于所有激光功率和灌洗设置（0ml/min除外），在激光激活的前10s内，肾盏液温度急剧上升，然后在20s后，温度曲线达到平台期（图2 a）。在充分灌洗的情况下，这些组在60s激光激活后均未达到43°C的温度。

在60秒激光激活后，1 J/20 Hz、15 ml/min组的温度升高最高，而0.5 J/20 Hz、30 ml/min组的温度升高最低（4.91±0.58 vs.1.50±0.44，*P*<0.01）。在相同的激光功率设置下，较低冲洗流速组的温度升高显著更高（1 J/20 Hz、15 ml/min vs.1 J/20 Hz、30 ml/min：4.91±0.58 vs.2.34±0.25，*P*<0.01；0.5 J/20 Hz、15 ml/min vs.0.5 J/20 Hz、30 ml/min：2.17±0.30 vs.1.50±0.44，*P*<0.01）。在相同的冲洗流速下，较高激光功率设置组的温度升高显著更高（1 J/20 Hz、15 ml/min vs.0.5 J/20 Hz、15 ml/min：4.91±0.58 vs.2.17±0.40，*P*<0.01；1 J/20 Hz、30 ml/min vs.0.5 J/20 Hz、30 ml/min：2.34 ±0.25vs.1.50±0.44，*P*<0.01）。（图2 b）。

在无灌注（0 ml/min）条件下，当激光功率设置为1 J/20 Hz时，温度从基线升至43°C所需时间显著短于0.5 J/20 Hz组（8.84±1.41秒vs.13.71±1.53秒，P<0.01）（图3）。

讨论

Ho：YAG激光自20世纪90年代引入泌尿外科领域以来，已成为应用最广泛的腔内碎石器[16]。该激光波长2100纳米，属于中红外光谱，能被水分子高效吸收[18]。当脉冲持续时间超过10 μ s时，主要产生光热效应；若超过200 μ s，光声效应则可忽略不计[19]。Ho：YAG激光的脉冲持续时间设定为250 μ s，其作用机制主要为

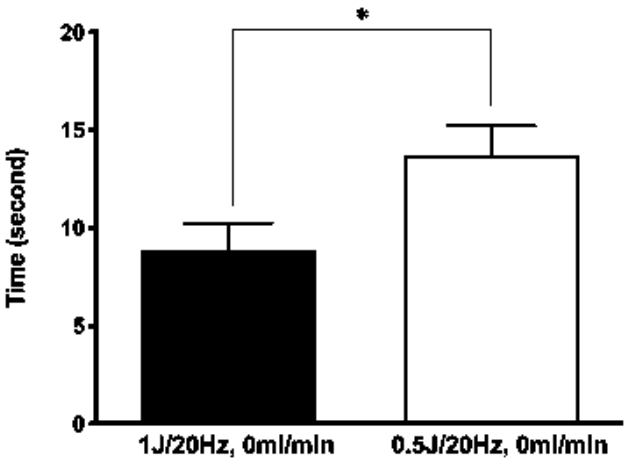


图3不灌溉时不同功率设置下达到43°C所需时间。*p<0.01

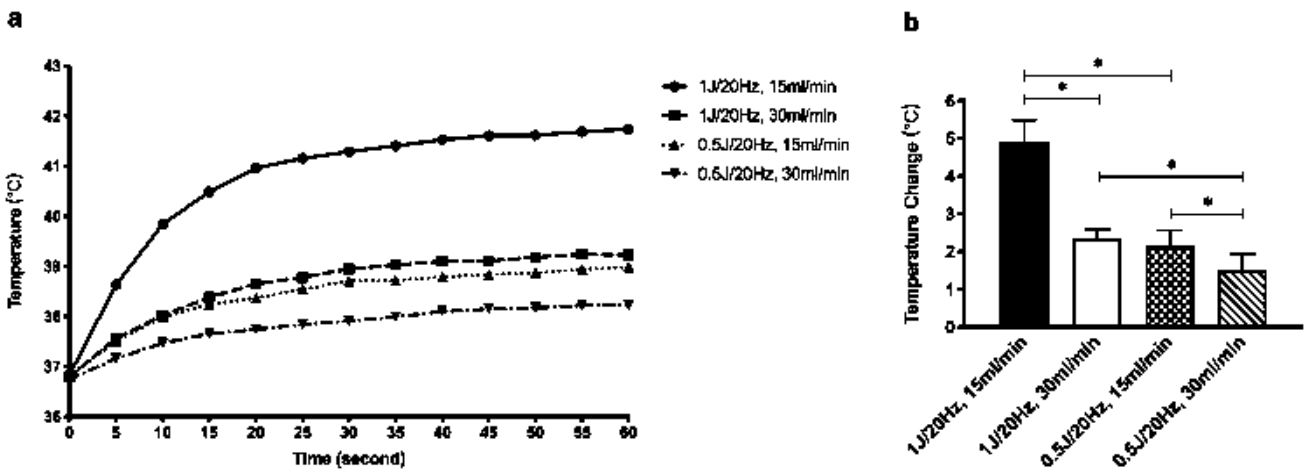


图2 Ho：YAG激光激活过程中的温度曲线。**a**不同功率和灌注设置下的温度-时间曲线。**b** 60s激光激活后的平均温度变化。*p<0.01

光热效应[4]。研究表明，钬钇铝石榴石（Ho：YAG）碎石术的主要作用机制是结石对激光能量的直接吸收及其化学分解[20]。在此过程中，热量不仅会积聚在结石内部，收集系统中的周围液体也会因温度急剧升高而产生热损伤。

热细胞毒性效应不仅取决于操作过程中的峰值温度，暴露时间同样起着关键作用。萨帕雷托和杜威[21]提出了一套热剂量评估公式，该公式以43°C为基准温度计算暴露时间。这个公式在业内被称为$43^{\circ}C$累积当量分钟（CEM_{43}），其数学表达式为：$CEM_{43}=\Sigma\ \Delta t\cdot R^{(43-T)}$（当$T>43^{\circ}C$时$R=0.5$，$T<43^{\circ}C</43^{\circ}C>$时$R=0.25$）。研究者指出，43°C这个“临界温度”是根据现有数据综合推算得出的最佳参考值。但需要强调的是，不同组织和物种的热反应存在显著差异。动物实验表明，$CEM_{43}=11$。2分钟是膀胱的安全热剂量，而超过43分钟$_{80分钟}$会导致显著损伤；对于肾脏，43分钟$_{43分钟}<20分钟</20分钟>$会造成轻微损伤，而$_{超过70分钟}$则会导致显著损伤[22]。目前，关于人类肾脏和输尿管的安全热剂量尚无确切数据。在本研究中，我们参考已发表的研究，将43°C作为激光激活的临界温度，由于缺乏更好的阈值可供参考。

已有数项研究探讨了Ho：YAG激光激活过程中骨盆腔内温度变化，其中大部分为体外模型研究[7–14]，仅有一项活体猪研究[15]，尚未见针对人类的同类研究。尽管这些实验最大程度地模拟了RIRS，但并不能反映真实临床情况，仍需通过临床测量来验证研究结果。据我们所知，这是首项关于输尿管膀胱冲洗温度曲线的术中研究。

在60秒激光激活过程中，盏状体液体会经历快速升温后进入平台期。这一现象与先前的体外研究[9，11，13]结果一致。根据热力学公式$Q=cm\Delta T$，温度变化本应保持恒定；但在本实验条件下，灌注循环可能是合理的解释。初始阶段，流出的主要是未被激光激活加热的盆腔液。当受热液体排出且热损失等于产热量时，系统便进入平台期。

研究表明，灌注介导的组织冷却可降低射频消融术中的凝固性坏死[23]。因此推测该机制可能缓解碎石术中的温度升高[11]。但Aldoukhi等学者在猪模型中开展的研究[15] 研究发现，在没有灌洗的情况下，体内模型的峰值温度要高于体外模型，体内模型的降温效果更为显著。本研究发现，两组无灌注组在数秒内均达到43°C的临界温度，而充分灌注组则始终未达此温度阈值。此外，在相同激光功率条件下，灌注流速越低，组织温度升幅越大。综合实验结果表明，相较于灌注作用，灌注介导的组织冷却效应在抑制温度升高方面所起的作用相对次要。

在日常操作中，我们通常采用泵送系统进行输尿管镜检查以维持恒定灌洗。需要注意的是，若出液不畅，灌洗流量会逐渐减少甚至完全中断。为确保液体顺畅排出，必须将鞘管置入输尿管肾盂连接处。此外，输尿管镜的操作通道直径也会影响灌洗流量，导致实际流量与设定值存在偏差。例如当结石因灌洗冲击产生往复运动时，激光头难以准确定位，此时常见的应对措施是暂时停止灌洗。但需谨慎操作，需特别注意：1焦耳/20赫兹无灌洗条件下8.84秒内温度骤升至43℃，0.5焦耳/20赫兹无灌洗条件下温度升至13.71秒。因此，激光持续激活时间不应超过设定阈值，需留出充足灌洗间隔以确保热量充分散逸。

本研究存在若干局限性。首先，纳入研究的患者数量较少，可能导致人群均值估算存在偏差。其次，由于使用激光设备，仅评估了两种功率设置，而未对“粉尘”模式和高功率模式进行测试。第三，虽然导丝热电偶直径仅为0.1毫米，但与临床实际操作相比仍会影响冲洗液的流出量，不过在实验条件下这是不可避免的。第四，未进行结石成分分析，因此本研究未能评估成分对温度分布的影响。第五，未评估碎石术中TLF的热效应，但建立了适用于多种激光类型的肾内温度检测方法。针对这一问题，需要开展更大规模、更详细的亚组研究。

结论

综上所述，Ho：YAG激光碎石术可引起盏状液温升。充分冲洗时，温度可控制在43℃以下的安全范围内；当关闭冲洗时，温度急剧上升，几秒钟内即可达到43℃。

作者贡献研究设计：JT和XA；数据收集与整理：YW、ZJ、YG和WF；数据分析与解读：JT、YW和ZJ；论文撰写：JT和ZJ；论文修订：XA；项目指导：XA。所有作者均审阅并同意最终稿件。

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利益冲突作者声明无利益冲突。

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参与同意所有研究受试者均签署了知情同意书。

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A Simulated Model for Fluid and Tissue Heating During Pediatric Laser Lithotripsy

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Summary

Background: Laser lithotripsy (LL) is a common modality for treatment of children and adolescents with nephrolithiasis. Recent introduction of higher-powered lasers may result in more efficacious “dusting” of urinary calculi. However, *in vivo* animal studies and computational simulations have demonstrated rapid and sustained rise of fluid temperatures with LL, possibly resulting in irreversible tissue damage. How fluid and tissue heating during LL vary with pediatric urinary tract development, however, is unknown. We hypothesize that kidneys of younger children will be more susceptible to changes in fluid temperature and therefore tissue damage than those of older children.

Methods: Computational simulations were developed for LL in children utilizing COMSOL Multiphysics finite-element modeling software. Simulation parameters were varied, including the child’s age (3, 8, and 12 years), flow of irrigation fluid (gravity − 5 mL/min or continuous pressure flow − 40 mL/min), treatment location (renal pelvis, ureter, calyx), and power settings (5W–40W). Using a simplified axisymmetric geometry to represent the collecting space, the model accounted for heat transfer via diffusion, convection, perfusion, and heat sourcing as well as tissue properties and blood flow of the urothelium and renal parenchyma. Laminar and heat-induced convection flow were simulated, assuming room-temperature ureteroscopic irrigation. Renal size was varied by age, based on normative values. The maximum fluid temperature after 60 seconds of simulated

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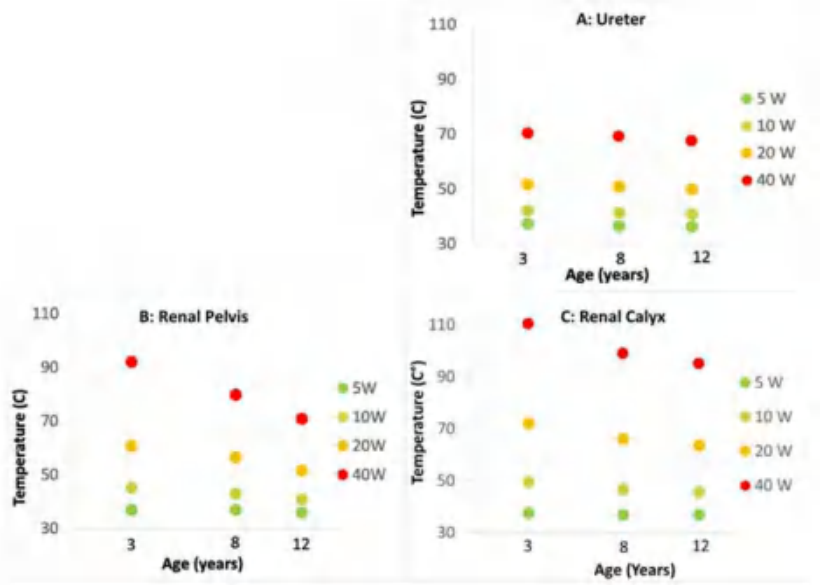
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LL was captured. Thermal dose was calculated using the t_{43} equivalence of 240 minutes as a threshold for tissue damage, as was tissue volume at risk for irreversible cellular damage.

Results: Simulation with gravity flow irrigation revealed generation of thermal doses sufficient to cause tissue injury for all ages at 20W and 40W power settings. Higher temperatures were seen in younger ages across all power settings. Temperature increases were dampened with intermittent laser activity and continuous pressure flow irrigation..

Conclusions: Smaller renal size is more susceptible to thermal changes induced by LL. However, power settings equal to or greater than 20 W can result in temperatures high enough for tissue damage at any age. Continuous pressure flow and intermittent laser activity may mitigate the potential thermal damage from high power LL.

Graphical Abstract



Summary Figure: Max temperature (°C) at 5 mL/min flow in the ureter (A), renal pelvis (B), and renal calyx (C)

Keywords

holmium laser; temperature; lithotripsy; ureteroscopy; pediatrics

Introduction:

Ureteroscopy is the most common modality for treatment of upper tract urinary calculi in the pediatric population.[1, 2] Benefits of ureteroscopic lithotripsy include direct visualization of the calculus, which can then be fragmented and removed or treated to sub-clinical fragments with higher-powered “dusting” or “pop-dusting” techniques.[3] Additionally, the holmium laser delivers energy directly to the calculus, as opposed to shock wave lithotripsy which transmits across the renal parenchyma. [4] Thus, laser lithotripsy is believed to place

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the kidney at low risk for direct injury, provided direct contact to the urothelium is avoided during treatment.

However, recent *in vitro*, *in vivo*, and simulation studies have shown dramatic rises in intra-renal temperature during laser lithotripsy.[5, 6] The mechanism for this rapid temperature rise is based in the physical characteristics of the holmium energy source. The 2100 nm wavelength of the holmium laser is readily absorbed by water, resulting in local vaporization and creation of vapor bubbles.[7] While this bubble creation is important to the mechanism of lithotripsy, the by-product of this absorption is heat generation in adjacent fluid, stone, or tissue, which results in a temperature rise that could place the renal tissues at risk for thermal injury.[8] Importantly, this fluid absorption occurs even during treatment of the stone itself, a phenomenon which is the basis for the MOSES™ laser system. [9] As such, fluid heating from the application of the holmium laser would be expected to occur even while the stone itself is being treated.

The thermal effect of laser lithotripsy has yet to be characterized across the range of renal sizes naturally occurring during normal renal growth during childhood and adolescence. As ureteroscopic laser lithotripsy becomes more common in even the youngest patient populations, it is important to assess the impact of this technology within smaller intraluminal spaces, where heat dissipation may be restricted. We created a computational model for thermal energy dissipation during laser lithotripsy based on prior *in vitro* studies, simulating clinical scenarios varying by age-adjusted renal size, laser energy settings, and irrigation flow. We hypothesized that the model would show kidneys of younger children to be more susceptible to changes in fluid temperature and therefore tissue damage than those of older children and that this modeled effect could be mitigated by fluid irrigation and intermittent laser activity.

Methods

This study is not human research; no institutional review board approval was necessary.

Model Assumptions

We utilized COMSOL Multiphysics finite-element modeling software (COMSOL, Burlington, MA) to develop computational simulations for laser lithotripsy in children. The model uses a simplified axisymmetric geometry to represent the ureter, renal pelvis, and renal calyx. The model simulates bioheat transfer through physical interactions including diffusion, convection, perfusion, and heat sourcing as well as tissue properties and blood flow of the urothelium and renal parenchyma. This simulation has been previously validated against *in vitro* and *in vivo* experiments.[5, 10] Laminar, heat-induced convective flow are simulated by the model, assuming room-temperature irrigation through the working channel of a ureteroscope. Thermal properties of the holmium laser and urothelial tissue were acquired from literature data and included in Table 1.

Model Variables

Age-based renal size (3, 8, 12 years), irrigation flow rates (0, 5, 40 mL/min), anatomic location of lithotripsy (renal pelvis, ureter, calyx), and holmium laser energy settings (5 –

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40W) were adjusted between simulations. The renal pelvis was shaped in simulation as a spherical fluid-filled chamber with cylindrical tube extending from one side to model the ureter. The urinary tract was lined with a 1-mm wall of urothelium. Kidney parenchymal tissue surrounded the collecting system and ureter wall. For renal pelvic calculi, the laser and irrigation were modeled to be located at the ureteropelvic junction. For ureteral calculi, the model was simulated in the same geometric configuration as the renal pelvis. However, for the ureteral simulation, the laser location was modeled 3.5 cm distal to the ureteropelvic junction and the irrigation source modeled 5 mm distal to the laser. The calyx was modeled as a cylinder with a thin urothelial wall which terminated with a hemispherical end rather than a larger spherical end as was modeled in the renal pelvis simulation.

To account for changes in renal size with age, physical dimensions for kidneys were approximated from published literature measurements in children and adults captured by urography, ultrasound, CT or MRI.[11–13]. The renal length-age relationship is relatively linear for children 3 years of age or greater. Accordingly, dimensions of the ureter, renal pelvis, and renal calyx were linearly scaled using adult measured dimensions as a reference. (Supplemental Table).[12, 14, 15]

Simulation of Laser Lithotripsy

The simulation was initiated at standard body temperature of 37°C, with room-temperature (22° C) irrigation introduced for 20 seconds prior to continuous lithotripsy. Laser activation was continued for 60 seconds followed by an additional 40 seconds of room-temperature irrigation. Intra-luminal and tissue temperature were recorded throughout the model every tenth of a second at each spatial location within the model.

Prior *in vitro* work has established irrigation flow rates of 5 mL/min to be equivalent to 40 cm H_2O (i.e. a saline bag elevated to 40 cm above the patient flowing by gravity) and 40 mL/min to be equivalent to 300 cm H_2O (i.e. a pressurized irrigation bag) which was simulated in a continuous (as opposed to intermittent) fashion.[16] Holmium laser settings were chosen to represent a range of typical settings for laser lithotripsy, including higher energy settings to represent “dusting” and “pop-dusting” energy ranges.

Acknowledging that continuous firing of the laser for a full 60 seconds is unrealistic in clinical care, simulations to reflect more realistic treatment parameters were also undertaken. The pattern of laser activation during lithotripsy has been termed the “operator duty cycle” and reflects a ratio of the time for laser activation on the stone and the time the laser is at rest throughout the treatment course. Aldoukhi et al prospectively measured the operator duty cycle for the highest laser activation to be 72%, indicating that over a 60 second period of time, the laser would be activated for 43 seconds.[17] Anticipating some variation on operator duty cycle across surgeons, we chose a more conservative operator duty cycle for 50% over a 60 second period with a 5 seconds “on”/5 seconds “off” pattern of laser activity to assess the impact of intermittent laser firing on thermal energy distributions during laser lithotripsy.[18] This cycle was modeled using the 3 year old, 5 mL/min, 40W power settings to demonstrate the impact of operator duty cycle on situations with the greatest potential for thermal injury.

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Estimation of Thermal Injury

Thermal dose was calculated using the t_{43} equivalence as a metric for tissue damage, which is commonly used for tissue viability in evaluation of hyperthermal or ablative effects.[19, 20] This metric provides a comparative equivalency for tissues exposed to varying temperature for differing lengths of time. The time interval to tissue injury based on thermal dose is reduced by half for each degree increase in temperature.[21] For example, kidney parenchyma is estimated to show initial signs of injury when elevated to 43°C for between 20 to 70 minutes, but would require only ~1 – 4 seconds at 53 °C.[22] For this study, we chose a conservative thermal dose threshold of t_{43} = 240 minutes, above which most tissues are considered to undergo irreversible thermal injury.[19] Based on this definition, tissue volume at risk for irreversible cellular damage was also calculated. Maximum temperature and thermal dose were approximated in the geometric models of the collecting system, as shown by example in Supplemental Figure.

Results:

Using a model assuming 5 mL/min of room temperature irrigation, maximum temperatures were predicted to be consistently higher with higher power settings. This trend was observed irrespective of location of treatment or patient age. Maximum temperature did not vary substantially across age groups within the ureteral location. For instance, at 40W power settings and 5 mL/min of irrigation, maximum temperatures were calculated to be 70.4° C for age 3 and 67.7° C for age 12 (Table 2). However, for both renal pelvis and calyceal locations, maximum temperature trended higher in the smaller kidneys within the model, especially at higher power settings. Within the calyx at 40W power settings and 5 mL/min of irrigation, maximum temperatures were calculated to be 110.5° C for age 3 and 95.1° C for age 12. Notably, treatment within renal pelvis and calyceal locations consistently displayed higher maximum temperatures as compared to the ureter. Maximum temperatures in the renal pelvis and calyces varied by age and laser settings, with the largest variation noted in the younger age group and highest power settings.

Thermal dose also varied in a similar fashion to maximum temperature for clinically-modified parameters within the model. Higher thermal dose was noted in renal pelvis and calyx, younger age groups, and higher power settings. When utilizing a t_{43} of greater than 240 minutes as a threshold to consider tissue at risk, all parameters with gravity flow (5 mL/min irrigation) and power settings ≥ 20W resulted in thermal dose substantial enough to result in tissue damage (Table 2). Additionally, with 10W power settings within the renal calyx for the 3 and 8 year old models, the thermal dose was estimated to cross the threshold capable of inducing thermal injury. The calculated volume of tissue injury followed similar trends. The largest lesion volumes were noted in the 3 and 8 year old renal pelvis models at 40W, estimated at 2.71 cm^3 and 2.72 cm^3 respectively (Table 2).

When pressurized irrigation at 40 mL/min was introduced into the model, the heating effects of laser lithotripsy were predicted to be mitigated across all power settings, locations, and age ranges. For the renal pelvis and calyx, these predicted effects were more pronounced than the ureter, with maximum temperatures not exceeding 37 °C even at 40W, reducing maximum predicted temperature by up to 73° C as compared to the model with gravity flow

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irrigation. Using pressurized irrigation, none of the simulated situations resulted in maximum predicted temperatures greater than 37° C. (Figure 1)

A 50% operator duty cycle also demonstrated mitigation of overall thermal parameters. Maximum temperature during intermittent laser activation was 63.5° C and oscillated in a saw-like pattern with nadir temperature of 54.1 °C until treatment cessation. Temperatures greater than 60 °C were noted after 25 seconds of intermittent laser activation. Calculated tissue at risk for intermittent laser activity was 1.2 cm^3, which represents a 54% reduction in potential lesion volume as compared to continuous laser activity.(Figure 2)

Discussion

Herein we present a computational simulation modeling the effects and implications of fluid heat transfer during laser lithotripsy within the pediatric urinary tract. Our findings have several key themes. First, irrespective of location or patient age, higher power settings result in incrementally higher maximum temperatures, thereby exposing surrounding tissue to potential thermal damage. Second, while patient age appears to minimally impact the heat transfer within the ureter, there can be a substantial increase in maximum temperature and corresponding thermal dose to both the renal pelvis and calyx with younger age ranges in the model. This insight could have important implications as advanced dusting techniques and higher-powered laser models permeate the pediatric landscape.[23] Assessment of multiple mitigation strategies revealed opportunities to minimize risk of thermal damage even during settings which pose the greatest potential for thermal injury. Using pressurized room temperature irrigation appears to mitigate all thermal effects and throughout our models resulted in theoretically safe temperature profiles even at the highest power settings. Furthermore, models of an intermittent laser activation pattern, reflective of typical clinical practice, showed reduced maximum temperature exposure, though overall thermal parameters were not diminished to the degree of pressurized irrigation. As focus has shifted recently within the endourologic community to decreasing intra-renal pressure during ureteroscopy, defining the appropriate balance between pressurized flow and intra-renal pressure will be an important aspect of future study.

The introduction of higher-powered laser technology into the surgical marketplace has reinvigorated interest in the thermal exposure from these instruments within the renal collecting system. Recent *in vitro* and *in vivo* studies have revealed the risks of unchecked fluid heating during high-powered laser lithotripsy as well as the potential mitigating effects of pressurized irrigation on thermal parameters.[5, 6] Our study adds to this literature by demonstrating the influence of age and therefore renal size on thermal profiles during laser lithotripsy. Assessment of differential thermal effects throughout the urinary tract and within varying age ranges will be important for defining optimal treatment settings across age ranges. Interestingly, while greater thermal dose was noted in younger age ranges and different locations, the overall volume of tissue at risk did not necessarily increase in our model in a similar linear fashion. In fact, while the renal calyx model had the highest estimated thermal dose exposures across all parameters, the calculated volume of tissue damage associated with each of these models was less than the corresponding model in the renal pelvis. One potential reason for this result is the smaller overall surface area for tissue

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considered at-risk within the smaller renal collecting system (for younger ages) or within a smaller portion of the renal collection system (for the renal calyx models). Conversely, however, it should be noted that a greater proportion of renal tissue (as indicated by percentage of volume at risk) may be exposed to higher thermal dose in younger patients. The variability in thermal dose based on treatment location is also notable within our study. The ureter was consistently exposed to lower thermal dose across age and power settings as compared to the renal pelvis and calyceal models. This effect could be due to heat diffusion along the ureter within the model.

Our study has several limitations worth discussing. First, these results represent computational modeling, as direct measurement of heating effects and subsequent tissue damage would be difficult if not impossible to replicate during actual laser lithotripsy. However, these models are based off of detailed information gained from *in vivo* and *in vitro* simulations, and thus are consistent with and validated by empiric observations. Additionally, those prior studies showed higher, rather than lower, renal temperatures in the *in vivo* settings.[5] One further consideration in our modeling is the maximum temperatures in extreme situations, such as the smallest renal model where temperatures exceeded 100° C. Our models do not simulate evaporation or condensation processes. As a result, additional heat beyond 100° C increases the temperature of the fluid via conservation of energy principles. While this would not reflect a typical situation a 1 atmosphere, qualitatively this likely does not influence results as thermal damage simulated just prior to the temperature reaching 100° C remains substantial. Our primary models simulate a full 60 seconds of continuous laser firing, which is not representative of a typical clinical scenario. However, *in vitro* studies suggest that optimal popcorn-dusting parameters include *total* laser firing time of 4 minutes.[24] Using an operator duty cycle of 50%, we demonstrated mitigation of thermal parameters. As such, focus on duration of firing and rest during treatment may additionally improve the safety envelope during laser lithotripsy. However, even with intermittent activity maximum temperatures surpassed 60 °C, resulting in an estimated volume of tissue at risk of greater than 1 cm^3. As cooling of the collecting system between laser activation depends upon the duration of rest periods, the collecting system fluid may not reach baseline temperatures during laser inactivation. Because thermal injury is a product of both intensity and duration of thermal energy exposure, this concept should be kept in mind during treatment. Lastly, current patterns of treatment for laser lithotripsy within the pediatric population are not well defined. Due to the relative infrequent nature of pediatric stone disease, as compared to adults, pediatric centers may not routinely perform a volume of ureteroscopy which warrants purchase of higher-powered laser lithotripters. However, given the close collaboration between pediatric and adult urologists especially at academic medical centers as well as the increased interest in dusting within all age groups, it is likely that dissemination of this technology to the pediatric realm is quickly forthcoming. [3, 23]

These limitations notwithstanding, our work has several important implications. Our prime objective was to select clinical scenarios that warrant further investigation with higher-fidelity simulations when indicated. To this end, we have identified several important situations wherein tissue may be at risk during laser lithotripsy. Acknowledging the limitations of our computational model, a logical next step would be to investigate these

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specific scenarios with *in vitro* experiments in tissue phantoms of varying sizes. Future work will need to focus on efforts to mitigate thermal effects, such as utilization of pressurized irrigation. Within the pediatric population, striking the balance between flow and pressure is even more challenging, as ureteral access sheaths are not without risk and may be challenging to place in the smallest of kidneys (i.e. those at highest risk for potential thermal injury).[27, 28] Finally, in identifying the importance of various power settings on thermal exposure, it will be important to further define practice patterns for pediatric laser lithotripsy. This information could help to guide further simulation and education regarding optimal laser settings within the pediatric population, especially as newer technologies such as "Moses" technology and thulium lasers enter the marketplace.[16, 26]

In conclusion, we have simulated the thermal conditions of the renal and ureteral collecting systems during laser lithotripsy in children. Power settings greater than 20W in any location or age-range pose a risk of thermally-induced tissue damage at low-flow irrigation. Additionally, younger and therefore smaller kidneys appear to be at higher risk of exposure to maximum temperatures during laser lithotripsy, which could translate into a higher risk of thermal damage. Finally, pressurized irrigation appears to mitigate these heating effects, thereby introducing at least one mechanism to reduce the risk of thermal damage. Ultimately, future studies are needed to validate these simulations in *in vitro* or *in vivo* situations as well as to explore current practices of surgeons who treat children with nephrolithiasis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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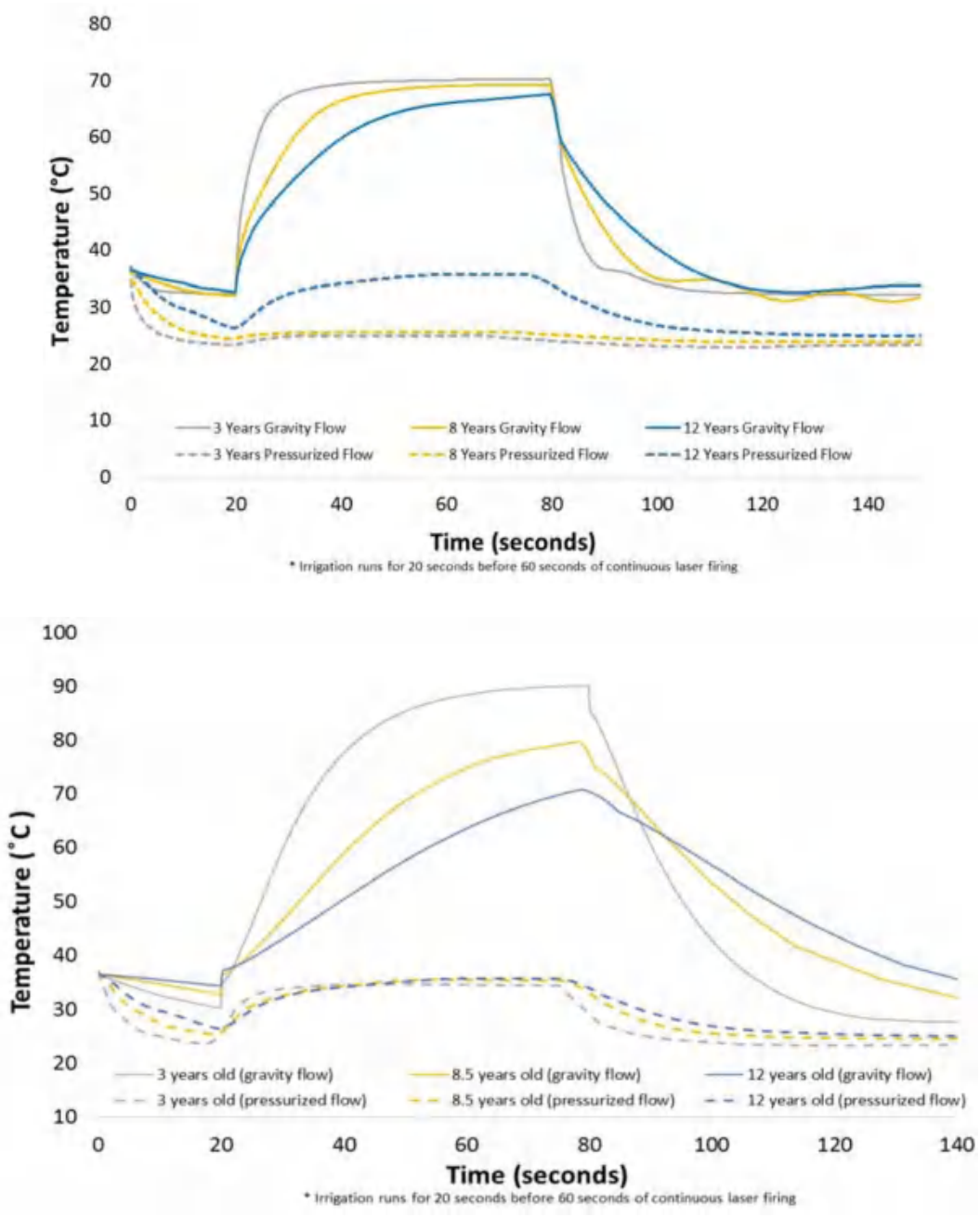


Figure 1:

Temperature Curves at 5 mL/min (gravity flow) and 40 mL/min pressurized flow within the ureter (A) and renal pelvis (B)

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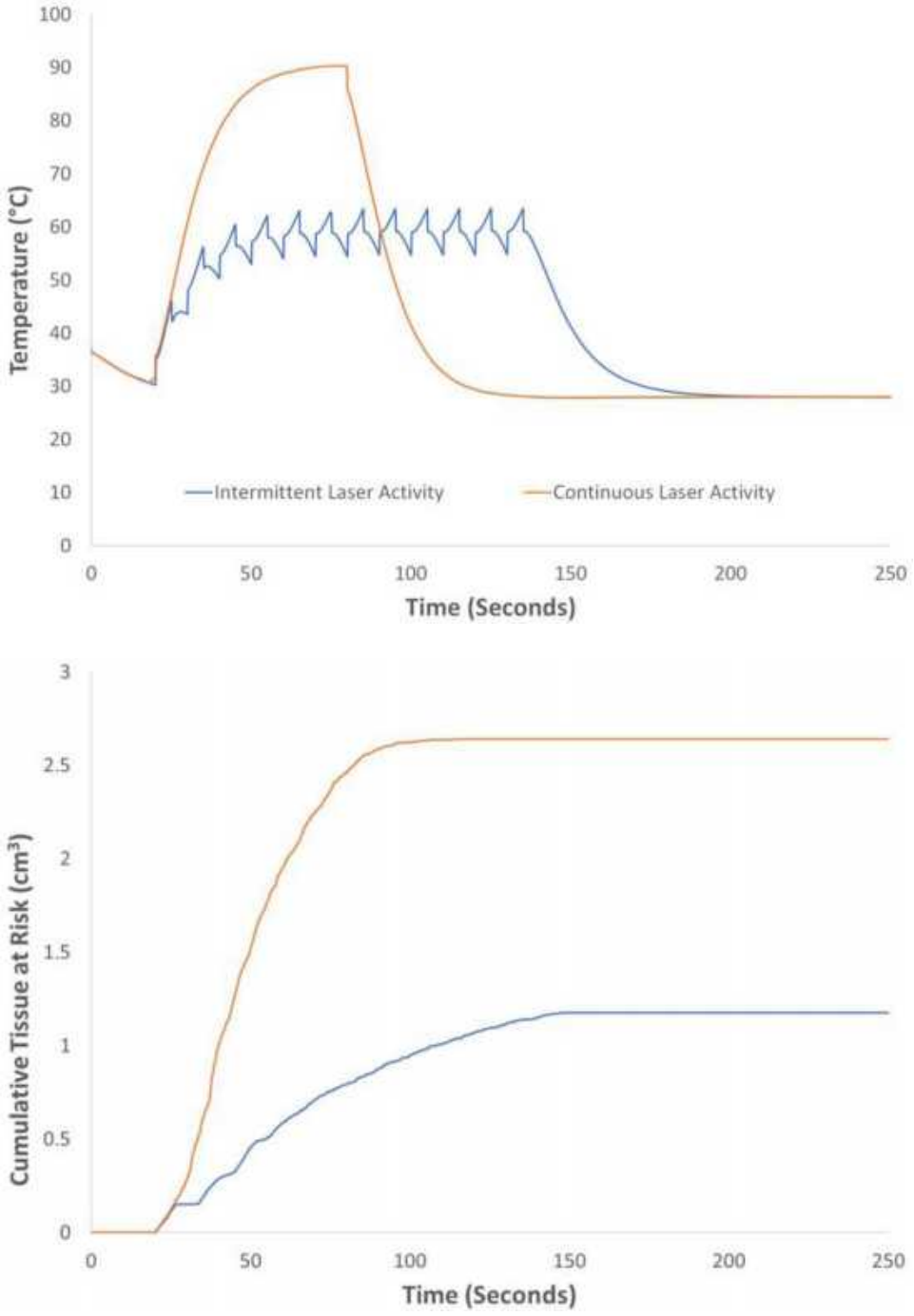


Figure 2:

Temperature (A) and thermal dose (B) within the renal collecting system for intermittent and continuous laser activity (3 year old, 40 W, 5 mL/min Gravity Flow, renal calyx)

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Table 1:

Material and tissue parameters used for simulations of in vitro and in vivo conditions.

	Density (kg/m^3)	Specific Heat Capacity (J/kg-K)	Thermal Conductivity (W/m-K)	Perfusion Rate (L/min-kg)
Water	998	4184	0.608	-
Glass	2230	750	0.800	-
Urine	1023	4178	0.560	-
Blood	1049	3617	0.517	-
Urinary Tract Wall	1101	3306	0.462	0.19
Kidney Parenchyma	1049	3587	0.527	3.80

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Table 2:

Thermal dose and tissue at risk (indicated by “Lesion Volume”) for the model across ages, power settings and treatment location, assuming treatment with gravity flow (5 mL/sec)

Ureter						
	Thermal Dose (t43)			Lesion Volume (cm3)		
Power (W)	**3 years**	**8 years**	**12 years**	**3 years**	**8 years**	**12 years**
5	1.1	0.7	0.6	0.0	0.0	0.0
10	26.5	14.3	8.1	0.2	0.1	0.1
20	19148.1	8566.8	3352.4	0.8	0.8	0.7
40	6.4×10^{9}	2.5×10^{9}	3.9×10^{8}	1.8	2.3	2.6
Renal Pelvis						
	Thermal Dose (t43)			Lesion Volume (cm3)		
Power (W)	**3 years**	**8 years**	**12 years**	**3 years**	**8 years**	**12 years**
5	0.5	0.5	0.5	0.0	0.0	0.0
10	86.2	16.5	5.4	0.1	0.1	0.1
20	4.8×10^{6}	1.1×10^{6}	4196.1	1.0	0.7	0.6
40	7.2×10^{15}	9.7×10^{11}	1.9×10^{9}	2.7	2.7	2.5
Renal Calyx						
	Thermal Dose (t43)			Lesion Volume (cm3)		
Power (W)	**3 years**	**8 years**	**12 years**	**3 years**	**8 years**	**12 years**
5	1.2	0.4	0.3	0.0	0.0	0.0
10	4163.7	609.5	235.2	0.2	0.2	0.1
20	2.2×10^{10}	3.7×10^{8}	5.2×10^{7}	0.8	0.9	0.9
40	6.1×10^{21}	2.4×10^{18}	1.1×10^{17}	1.6	2.0	2.2

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小儿激光碎石术中液体和组织加热的模拟模型

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摘要

背景：激光碎石术（LL）是治疗儿童及青少年肾结石的常用方法。近年来高功率激光的引入可能使尿路结石的“粉碎”效果更佳。然而，*体内*动物实验和计算机模拟研究表明，LL过程中液体温度会迅速且持续升高，可能导致不可逆的组织损伤。但目前尚不清楚LL过程中液体与组织的加热情况如何随儿童泌尿系统发育阶段变化。我们推测，相较于年龄较大的儿童，年幼儿童的肾脏对液体温度变化更为敏感，因此更容易发生组织损伤。

方法：利用COMSOL Multiphysics有限元建模软件为儿童LL开发了计算模拟。模拟参数包括儿童年龄（3岁、8岁和12岁）、灌注液流量（重力流——5 mL/min或连续压力流——40 mL/min）、治疗部位（肾盂、输尿管、肾盏）以及功率设置（5W—40W）。本模型采用简化的轴对称几何结构来模拟收集空间，全面考虑了尿路上皮和肾实质的热传导（扩散、对流、灌注）及热源特性，同时模拟了组织属性与血流状态。在模拟尿道镜灌洗时，我们分别建立了层流与热致对流两种流动模式。根据年龄差异采用标准值调整肾脏尺寸，采集模拟LL 60 s后的最高流体温度。

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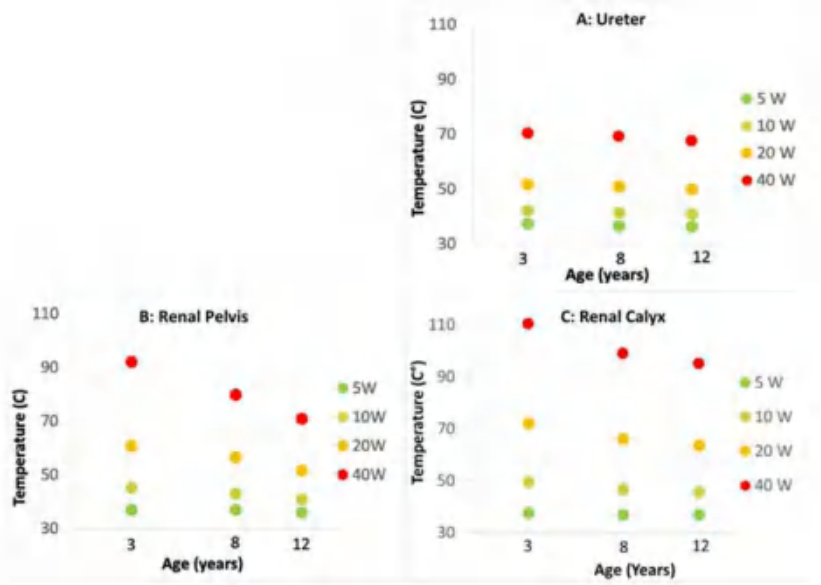
热剂量的计算采用240分钟的t_{43}等效作为组织损伤的阈值，组织体积风险为不可逆的细胞损伤。

结果：采用重力流灌注进行的模拟显示，在20W和40W功率设置下，所有年龄段均会产生足以造成组织损伤的热剂量。在所有功率设置下，年轻组的温度更高。间歇性激光活动和持续压力流灌注可抑制温度升高。

结论：肾脏体积越小，越容易受到LL引起的热变化的影响。
然而，功率设置达到或超过20瓦时，任何年龄段的使用者都可能因温度过高而造成组织损伤。

采用持续压力气流配合间歇性激光照射，可有效降低高功率激光治疗引发的热损伤风险。

图形摘要



总结图：输尿管(A)、肾盂(B)和肾盏(C)在5 mL/min流速下的最高温度（℃）

关键词

钬激光；温度；碎石术；输尿管镜检查；儿科

简介：

输尿管镜检查是治疗儿童上尿路结石最常用的方法。[1,2]输尿管镜碎石术的优势在于能直接观察结石，通过碎石技术将其粉碎取出，或采用高能“粉尘碎石术”或“爆破碎石术”处理成亚临床碎石。[3]此外，钬激光可直接向结石输送能量，而冲击波碎石术的能量需穿透肾实质才能作用。[4]因此，如果在治疗期间避免与尿路上皮直接接触，

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激光碎石术被认为可以降低肾脏的直接损伤风险。

然而，近期*体外*、*体内*及模拟研究显示，激光碎石术过程中肾内温度会出现急剧上升。[5,6]这种快速升温的机制源于钬激光能量源的物理特性。钬激光2100纳米的波长能被水分子高效吸收，引发局部汽化并形成气泡。[7]虽然气泡形成是碎石机制的关键，但这种吸收过程会产生热效应，使周围液体、结石或组织温度升高，可能对肾组织造成热损伤风险。[8]值得注意的是，这种液体吸收现象甚至发生在结石治疗过程中——这正是摩西™激光系统的核心原理。[9]因此，即使在结石治疗期间，钬激光产生的液体加热效应仍将持续存在。

目前，针对儿童及青少年正常肾脏发育过程中自然出现的各种肾体积范围，激光碎石术的热效应尚未得到充分研究。随着输尿管镜激光碎石术在更年轻患者群体中的应用日益普遍，评估该技术在较小管腔空间（热耗散受限区域）的影响变得尤为重要。我们基于既往*体外*研究，建立了激光碎石术热能耗散的计算模型，模拟了不同年龄调整肾体积、激光能量设置及冲洗流量的临床场景。研究假设表明：相较于年龄较大的儿童，年幼儿童肾脏对液体温度变化的敏感性更高，因此更容易发生组织损伤；而通过液体冲洗和间歇性激光操作，可有效缓解这种模型预测的热效应。

方法

本研究不属于人体研究，因此无需获得机构审查委员会的批准。

模型假设

我们采用COMSOL Multiphysics有限元建模软件（COMSOL公司，美国马萨诸塞州伯灵顿市）对儿童激光碎石术进行计算模拟。该模型采用简化的轴对称几何结构来模拟输尿管、肾盂和肾盏。模型通过扩散、对流、灌注及热源等物理相互作用，结合尿路上皮和肾实质的组织特性与血流特性，对生物热传递进行模拟。该模拟方法已通过*体外*和*体内*实验验证[5,10]。模型模拟了层流与热诱导对流现象，假设输尿管镜工作通道采用室温冲洗液。钬激光与尿路上皮组织的热学参数均来自文献数据，并列于表1中。

模型变量

基于年龄的肾脏大小（3、8、12岁）、冲洗流量（0、5、40 mL/min）、碎石术的解剖位置（肾盂、输尿管、肾盏）以及钬激光能量设置（5—

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40 w）进行模拟。肾脏盂腔在模拟中被设计为球形充液腔室，其中延伸出的圆柱形管状结构用于模拟输尿管。尿路内壁覆盖着1毫米厚的尿路上皮层，肾实质组织环绕着集合系统和输尿管壁。针对肾盂结石的模拟，激光和灌洗装置被设定在输尿管-肾盂连接处。对于输尿管结石的模拟，模型采用了与肾盂相同的几何构型，但输尿管模拟中激光位置被设定在连接处远端3.5厘米处，灌洗源则位于激光远端5毫米处。盏状结构被建模为带有薄尿路上皮壁的圆柱体，其末端采用半球形而非肾盂模拟中采用的较大球形结构。

为反映肾脏随年龄增长的体积变化，研究人员通过尿路造影、超声、CT或MRI等影像学技术，参考已发表文献中儿童和成人的测量数据，对肾脏的物理尺寸进行估算[11-13]。对于3岁及以上儿童，肾脏长度与年龄呈相对线性关系。因此，输尿管、肾盂和肾盏的尺寸均采用成人测量数据作为参考，进行线性比例换算。
（补充表）。[12,14,15]

激光碎石术模拟

模拟实验在标准体温37°C条件下启动，连续碎石术前先进行20秒室温（22°C）冲洗。激光激活持续60秒后，再进行40秒室温冲洗。整个模型运行期间，每0.1秒在不同空间位置记录一次管腔内温度和组织温度数据。

先前*体外*研究已确定5 mL/min的灌洗流速相当于40厘米H_2O（即盐水袋通过重力提升至患者上方40厘米处流动），而40 mL/min则相当于300厘米H_2O（即加压灌洗袋），后者以连续（而非间歇）方式模拟。[16]钬激光设置选择代表激光碎石术的典型参数范围，包括更高能量设置以模拟“粉尘”和“爆破粉尘”能量区间。

鉴于在临床护理中持续发射激光60秒是不现实的，我们还进行了模拟以反映更真实的治疗参数。碎石术期间的激光激活模式被称为“操作员工作周期”，反映了激光在结石上激活的时间与整个治疗过程中激光处于休息状态的时间之比。Aldoukhi等人前瞻性地测量了最高激光激活率的操作员工作周期为72%，表明在60秒的时间内，激光将被激活43秒。[17]考虑到不同外科医生的操作员工作周期可能存在一些差异，我们选择了一个更为保守的60秒周期内50%的操作员工作周期，采用5秒“开”/5秒“关”的激光活动模式，以评估间歇性激光发射对激光碎石术期间热能分布的影响。[18]该周期使用3年、5 mL/min、40W的功率设置进行建模，以展示操作员工作周期对热损伤风险最高情况的影响。

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热损伤估计

热剂量的计算采用温度43等效性作为组织损伤的评估指标，该指标在热疗或消融效应的组织存活率评估中被广泛使用。[19,20]该指标能为不同温度和持续时间下暴露的组织提供可比性评估。根据热剂量理论，温度每升高1摄氏度，组织损伤所需时间就会缩短一半。[21]例如，当肾脏实质温度升至43°C时，预计会出现初始损伤迹象，持续时间介于20至70分钟，但在53°C条件下仅需约1-4秒即可完成[22]。本研究采用保守的热剂量阈值标准，设定t_{43}=240分钟为临界值，超过此时间大多数组织将遭受不可逆的热损伤[19]。根据该定义，我们还计算了存在不可逆细胞损伤风险的组织体积。如补充图示例所示，收集系统的几何模型中对最高温度和热剂量进行了估算。

结果

使用假设5毫升/分钟室温灌洗的模型，预测最大温度会随着功率设置的提高而持续升高。这一趋势与治疗位置或患者年龄无关。在输尿管位置，不同年龄组的最大温度差异不大。例如，在40瓦功率设置和5毫升/分钟灌洗条件下，3岁组的最大温度计算为70.4°C，12岁组为67.7°C（表2）。然而，对于肾盂和盏部位置，模型中较小肾脏的最大温度趋势更高，尤其是在较高功率设置下。在盏部位置，40瓦功率设置和5毫升/分钟灌洗条件下，3岁组的最大温度计算为110.5°C，12岁组为95.1°C。值得注意的是，与输尿管相比，肾盂和盏部位置的治疗始终显示出更高的最大温度。肾盂和盏部的最大温度随年龄和激光设置而变化，其中年轻年龄组和最高功率设置下的变化最为显著。

热剂量的变化模式与模型中临床调整参数的最大温度变化相似。在肾盂和肾盏、年轻患者群体以及高功率设置条件下，热剂量较高。当采用超过240分钟的t43作为组织风险的阈值时，所有采用重力流（5 mL/min冲洗）且功率设置≥20W的参数均导致热剂量足以造成组织损伤（表2）。此外，对于3岁和8岁模型，当肾盏功率设置为10W时，热剂量估计已超过可能引发热损伤的阈值。计算出的组织损伤体积呈现相似趋势。在40W功率下，3岁和8岁肾盂模型的病变体积最大，分别估计为2.71 cm^3 3和2.72 cm^3 3（表2）。

当在模型中引入40 mL/min的加压灌注时，预测激光碎石术的加热效应在所有功率设置、位置和年龄范围内都会减轻。对于肾盂和肾盏，这些预测效应比输尿管更为显著，即使在40W时，最高温度也不会超过37°C，与重力流灌溉模型相比，最大预测温度降低高达73℃。

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采用加压灌溉时，所有模拟情况下的预测最高温度均未超过37°C（图1）。

50%的运行周期也显示出整体热参数的缓解。
间歇性激光治疗期间最高温度达到63.5°C，温度呈现锯齿状波动，最低温度为54.1°C，直至治疗终止。间歇性激光激活25秒后，温度超过60°C的情况被记录。计算得出间歇性激光活动风险组织面积为1.2平方厘米^3，相较于连续激光活动，潜在病灶体积减少54%。（图2）

讨论

本研究通过计算模拟，系统分析了激光碎石术在儿童泌尿系统中流体热传递的效应与影响。研究结果揭示了三个核心发现：首先，无论结石位置或患者年龄如何，功率设置越高，最高温度随之升高，从而增加周围组织遭受热损伤的风险。其次，虽然患者年龄对输尿管热传递的影响微乎其微，但在模型中发现，随着年龄增长，肾盂和肾盏的最高温度及相应热剂量显著增加。这一发现具有重要临床意义，因为当前儿科领域正广泛采用先进的碎石技术和高功率激光设备[23]。通过评估多种防护策略，我们发现即使在热损伤风险最高的功率设置下，也能有效降低热损伤风险。研究显示，采用常温加压冲洗技术可全面缓解热效应，在所有模型中即使在最高功率设置下，仍能形成理论上安全的温度分布曲线。
此外，模拟间歇性激光激活模式的临床模型显示，虽然整体热参数未降低到加压冲洗的程度，但最大温度暴露时间有所减少。随着泌尿内镜领域近期研究重点转向输尿管镜检查期间降低肾内压力，如何在加压流量与肾内压力之间找到最佳平衡点，将成为未来研究的重要方向。

高功率激光技术在手术领域的应用，重新引发了学界对这类器械在肾集合系统中热效应的关注。近期*体外*和*体内*研究揭示了高功率激光碎石术中液体无序加热的风险，以及加压冲洗对热参数的潜在缓解作用。[5,6]本研究通过揭示年龄（进而影响肾脏大小）对激光碎石术热分布的影响，为相关文献提供了新视角。评估不同年龄段及泌尿道各部位的热效应差异，将有助于制定适合各年龄段的最佳治疗方案。值得注意的是，尽管年轻患者群体和不同部位的热剂量有所增加，但我们的模型显示，风险组织的总体体积并未呈现线性增长趋势。事实上，虽然肾盏模型在所有参数中估计的热剂量暴露量最高，但与肾盂模型相比，各模型计算出的组织损伤体积均较小。出现这一结果的一个可能原因是，在较小的肾集合系统（对于较年轻的患者）

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或较小的肾集合系统（对于肾盏模型）中，被认为有风险的组织的总体表面积较小。但值得注意的是，年轻患者中更大比例的肾组织（以风险体积百分比衡量）可能暴露于更高热剂量。本研究中，不同治疗部位的热剂量差异显著。与肾盂和盏状模型相比，输尿管在不同年龄组和功率设置下始终暴露于较低热剂量。这种现象可能源于模型中输尿管的热扩散效应。

本研究存在若干值得探讨的局限性。首先，这些结果基于计算机模拟，因为在实际激光碎石术中，直接测量加热效应及后续组织损伤将难以甚至无法复现。然而，这些模型是基于从体内和体外模拟中获得的详细信息，因此与经验观察结果一致，并得到经验观察结果的验证。此外，先前研究显示体内肾脏温度呈现升高趋势而非下降[5]。我们在建模时还需考虑极端情况下的最高温度，例如最小肾脏模型中温度超过100°C的情况。由于模型未模拟蒸发或凝结过程，当温度突破100°C后，根据能量守恒原理，额外热量会持续提升液体温度。虽然这不符合标准大气压下的典型场景，但定性分析表明这不会显著影响结果——因为在温度达到100°C前模拟的热损伤仍相当严重。我们的基础模型模拟了60秒连续激光照射，这与临床常规操作存在差异。不过*体外*研究表明，最佳爆米花碎石参数应设置为*总*激光照射时间4分钟[24]。通过设定50%的设备工作周期，我们成功降低了热参数。因此，在激光碎石治疗中适当延长照射时间并安排休息，可能进一步提升操作安全性。然而，即便在间歇性活动时最高温度超过60°C，导致处于风险中的组织体积估计仍超过1平方厘米^3。由于收集系统在激光激活之间的冷却时间取决于休息时段的长短，其冷却液可能无法在激光停用时恢复至基线温度。鉴于热损伤既与热能强度相关又与暴露时长相关，治疗过程中需牢记这一原理。最后需要指出的是，目前针对儿童群体的激光碎石治疗方案尚未明确。由于儿童泌尿系统结石发病率相对成人较低，儿科中心可能不会常规开展输尿管镜检查，因此无需购置高功率激光碎石仪。不过，鉴于儿科与成人泌尿科医生在学术医疗中心的密切合作，以及各年龄段人群对膀胱冲洗技术日益增长的关注，这项技术向儿科领域的推广很可能很快就会实现。[3,23]

尽管存在这些局限性，我们的研究仍具有重要启示。本研究的核心目标是筛选出需要通过高保真模拟进行深入探究的临床场景。为此，我们识别出激光碎石术中可能危及组织的若干关键情况。考虑到我们计算模型的局限性，合乎逻辑的下一步

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将是在不同大小的组织体模中进行体外实验，研究这些特定场景。未来研究需重点探索缓解热效应的解决方案，例如采用加压冲洗技术。在儿科患者群体中，流量与压力的平衡控制更具挑战性——输尿管套管存在潜在风险，且在最小肾脏（即最易发生热损伤的部位）置入时操作难度较大。[27,28]最后，在明确不同功率设置对热暴露影响的关键作用时，需进一步规范儿科激光碎石术的操作规范。这些信息将有助于指导针对儿科患者的模拟训练和教育工作，特别是在“摩西”技术（Moses）和铥激光等新型设备进入临床应用阶段时，为优化激光参数提供科学依据。[16,26]

综上所述，我们通过模拟儿童激光碎石术中肾盂输尿管集合系统的热环境发现：当功率超过20瓦时，无论手术部位或患者年龄，均可能在低流量冲洗条件下引发热损伤。此外，由于肾脏体积较小，年轻患者在激光碎石术中更容易暴露于高温环境，从而增加热损伤风险。而加压冲洗技术能有效缓解这种热效应，至少为降低热损伤风险提供了新的解决方案。

最终，需要未来的研究来验证这些模拟在*体外*或*体内*的情况，并探索治疗肾结石儿童的外科医生的当前做法。

补充材料

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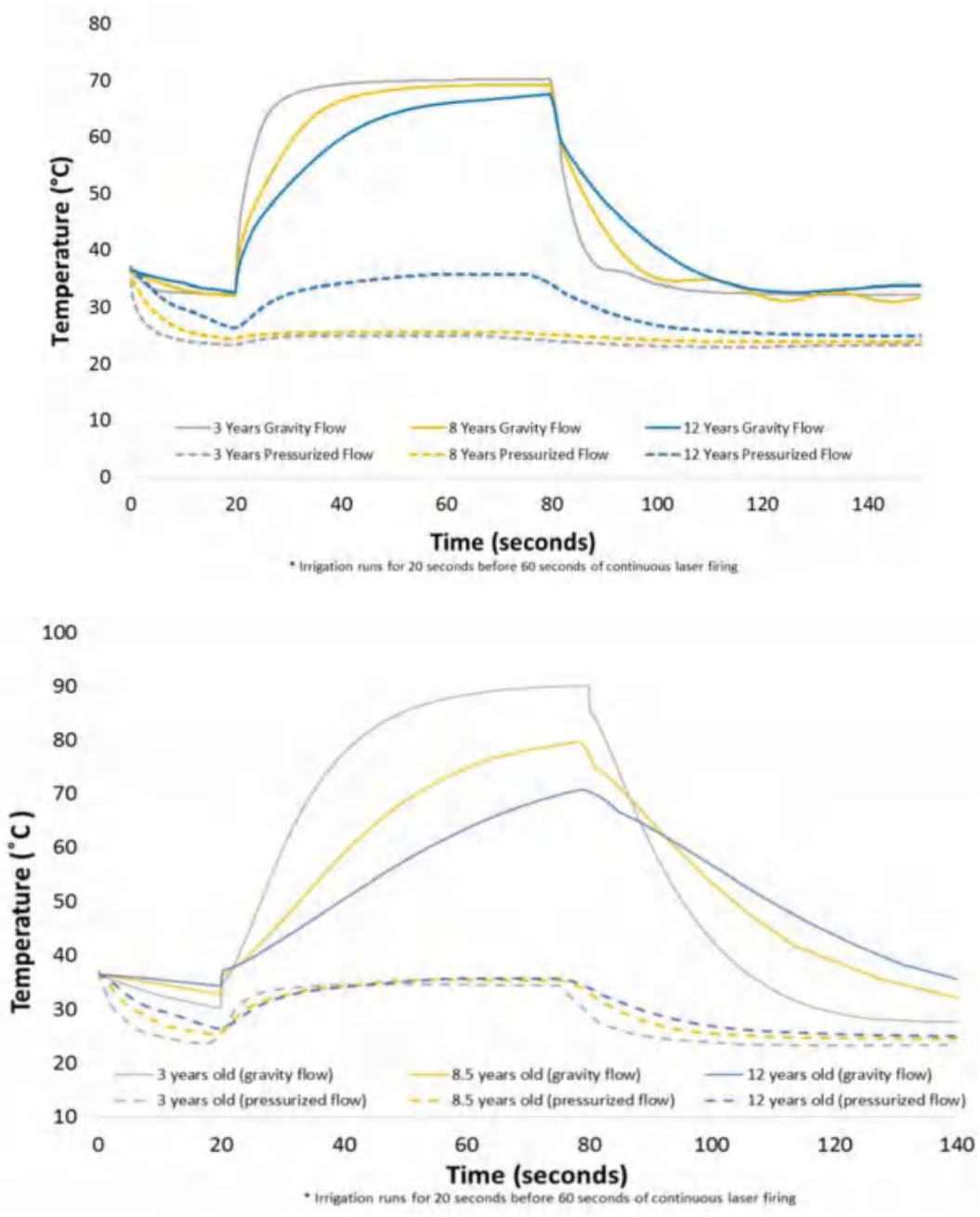


图1：

输尿管(A)和肾盂(B)在5 mL/min（重力流）和40 mL/min加压流下的温度曲线

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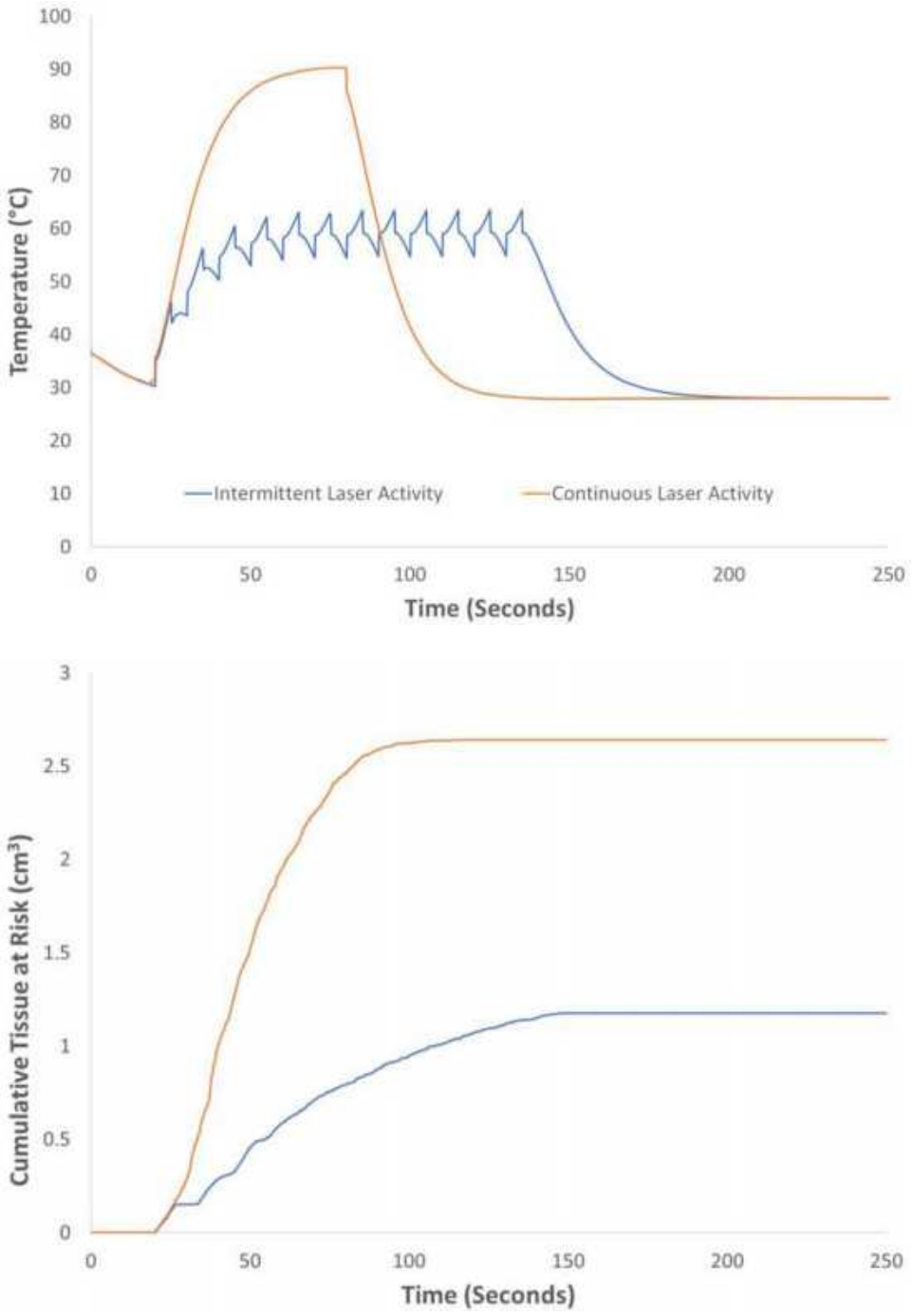


图2：

肾集合系统内温度(A)和热剂量(B)在间歇性和连续性激光活动中的变化（3岁，40 W，5 mL/min重力流，肾盏）

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表1：

用于体外和体内条件模拟的材料与组织参数。

	密度（kg/m 3）	比热容（J/kgK）	导热系数（W/m K)	灌注率（L/min-kg）
水	998	4184	0.608	-
玻璃	2230	750	0.800	-
尿液	1023	4178	0.560	-
血	1049	3617	0.517	-
尿路壁	1101	3306	0.462	0.19
肾实质	1049	3587	0.527	3.80

作者手稿

表2：

该模型在不同年龄、功率设置及治疗位置下的热剂量与组织风险（以“病灶体积”表示），假设采用重力流速（5毫升/秒）进行治疗

输尿管						
	剂量（t43）			病灶体积（cm3）		
功率(W)	3年	8年	12年	3 年	8 年	12 年
5	1.1	0.7	0.6	0.0	0.0	0.0
10	26.5	14.3	8.1	0.2	0.1	0.1
20	19148.1	8566.8	3352.4	0.8	0.8	0.7
40	6.4×10^{9}	2.5×10^{9}	3.9×10^{8}	1.8	2.3	2.6
肾盂						
	热剂量（t 43）			病灶体积（cm3）		
功率(W)	3年	8年	12年	3 年	8 年	12 年
5	0.5	0.5	0.5	0.0	0.0	0.0
10	86.2	16.5	5.4	0.1	0.1	0.1
20	4.8×10^{6}	1.1×10^{6}	4196.1	1.0	0.7	0.6
40	7.2×10^{15}	9.7×10^{11}	1.9×10^{9}	2.7	2.7	2.5
肾盏						
	热剂量（t 43）			病灶体积（cm3）		
功率(W)	3年	8年	12年	3年	8 年	12 年
5	1.2	0.4	0.3	0.0	0.0	0.0
10	4163.7	609.5	235.2	0.2	0.2	0.1
20	2.2×10^{10}	3.7×10^{8}	5.2×10^{7}	0.8	0.9	0.9
40	6.1×10^{21}	2.4×10^{18}	1.1×10^{17}	1.6	2.0	2.2

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RESEARCH ARTICLE Open Access

Thermal effect of holmium laser during ureteroscopic lithotripsy

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Abstract

Background: Holmium laser lithotripsy is the most common technique for the management of ureteral stone. Studies founded that holmium laser firing can produce heat which will cause thermal injury towards ureter. The aim of our current study is to explore factors affecting thermal effect of holmium laser during ureteroscopic lithotripsy.

Methods: An in vitro experimental model is design to simulate the ureteroscopic lithotripsy procedure. Different laser power settings (10w (0.5JX20Hz, 1.0 JX10Hz), 20w (1.0 JX20Hz, 2.0 JX10Hz), 30w (1.5JX20Hz, 3.0 JX10Hz)) with various firing time (3 s, 5 s, 10s) and irrigation flow rates(10 ml/min, 15 ml/min, 20 ml/min and 30 ml/min) were employed in the experiment. The temperature around the laser tip was recorded by thermometer.

Results: The temperature in the "ureter" rises significantly with the increasing laser power, prolonging firing time and reducing irrigation flow. The highest regional temperature is 78.0 °C at the experimental set-up, and the lowest temperature is 23.5 °C. Higher frequency setting produces more heat at the same power. Laser power < =10w, irrigation flow> = 30 ml/min and "high-energy with low-frequency" can permit a safe working temperature.

Conclusion: We clarify that the thermal effect of holmium laser is related with both laser working parameters and irrigation flow. The proper setting is the key factor to ensure the safety during ureteroscopic holmium laser lithotripsy.

Keywords: Holmium laser, Thermal effect, Lithotripsy

Background

Ureteral calculus is a common urological entity which is usually managed by ureteroscopic lithotripsy. The Holmium:YTTRIUM-ALUMINUM-GARNET (Ho:YAG) laser is the most efficient and versatile modality for ureteroscopic management of ureteral calculus [1]. Holmium laser's safety profile has been previously shown to be favorable compared to other lithotrites, since the 2100-nm wavelength of the Ho:YAG laser permits rapid absorption in water and thereby limits the depth of penetration and surrounding tissue injury. However, with the widely application of Ho:YAG laser, complications entailed by ureteroscopy such as ureteral stricture become common. It is reported that post-ureteroscopy ureteral stricture can be as high as 1–4% [2]. The potential cause of stricture is more likely to be the direct thermal injury towards the ureteral wall rather than acoustic or photonic energy [3]. Laser energy can produce heat and potentially cause thermal bioeffects [4–7]. In our current study, we aim to characterize the relationship between working parameter and intra-ureteral temperatures during ureteroscopic holmium lithotripsy.

Methods

An in vitro model mimicking ureteroscopic laser lithotripsy was established to assess the temperature changes during laser discharge. A segment of ligated F20 rubber tube was used to simulating human ureter with stone impaction. The lithotripsy laser system was used with the 200um laser fiber passed through the working channel of a F8/9.8 ureteroscope (Fig. 1). Raykeen Holmium laser (Raykeen, Shanghai, China) was applied in the

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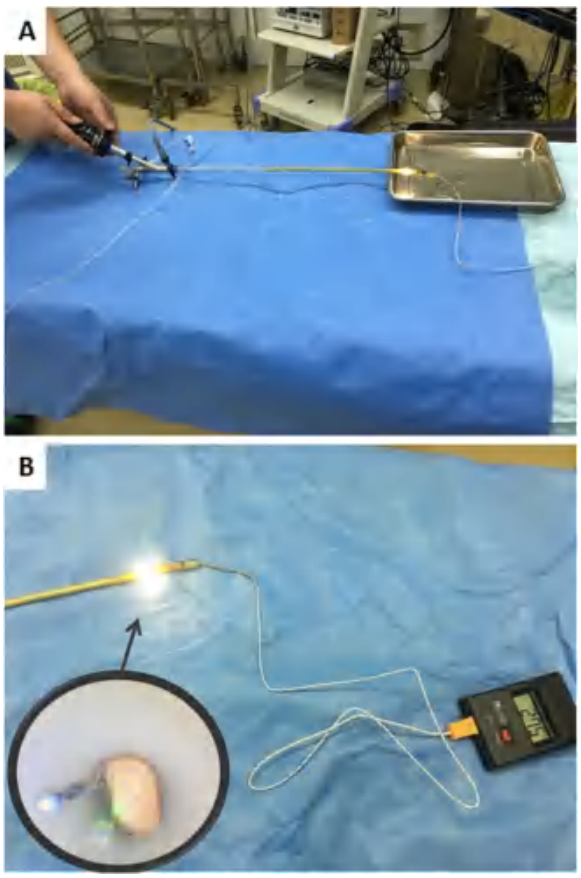


Fig. 1 a A simulated ureteroscopic laser lithotripsy procedure was established within a rubber tube. b Regional temperature was recorded by thermocouple

experiment with the various power settings commonly used in clinical practice. Energy settings were 0.5, 1.0, 1.5 and 2.0 J. Frequency settings of 10 and 20 Hz were tested at different energy settings. Laser firing time was 3 s, 5 s and 10s. The relevant irrigation flow rates of 10 ml/min, 15 ml/min, 20 ml/min and 30 ml/min were employed by infusion pump at room temperature. A thermocouple was held 5 mm from the bottom and approximately 2 mm lateral from the position of the laser tip to record temperature. The temperature for each power and irrigation setting combination was recorded five times, and means were calculated for statistical comparison in different setup.

Results

Heat accumulated around the laser fiber tip. The temperature data was summarized in Table 1. The temperature rises with the increasing laser power and firing time. Adequate irrigation flow can carry the heat away. The peak temperature, 78.0 °C, occurred with continuous laser firing for 10s at the power setting of 1.5JX20Hz and irrigation flow rate 10 ml/min. While the lowest temperature, 25.3 °C, was captured after continuous laser firing for 3 s at the power setting of 1.0 JX10Hz and irrigation flow rate 30 ml/min.

For the power setting of 10w, the temperature remains more stable irrespective of laser firing time or irrigation flow rate. When the power reaches 20w, the temperatures rapidly rise if irrigation is insufficient. Adequate irrigation or shorter laser firing time will be required to restrict the temperature. Figure 2 depicts temperature tracings for trials with different laser settings at 4 different irrigation flow rates. Another interesting finding is that for the same power setting, the “high-energy with low-frequency” parameter generates less thermal effect. The mean temperature difference is more evident when the irrigation is insufficient.

Discussion

Holmium laser is the most powerful energy tool for stone fragmentation during ureteroscopic lithotripsy [8]. Even though it is regarded as a minimally invasive surgical approach, it still brings troublesome complication, such as ureteral stricture [9]. Ureteral stricture is one of common complication post ureteroscopic surgery, especially for the impacted ureteral stone [9]. Previously, mechanical injury is considered as the main cause for ureteral stricture. However, more and more evidence indicates ureteral stricture can also occur even without mechanical injury. The issue of the intra-opertative holmium laser thermal effect has gradually gained attention

Table 1 Regional temperature changes with different laser working models and irrigation flow rates

Power	Flow rates	10 ml/min			15 ml/min			20 ml/min			30 ml/min		
	Firing Time	3 s	5 s	10s	3 s	5 s	10s	3 s	5 s	10s	3 s	5 s	10s
10w	0.5 J,20HZ	32.0	34.9	34.3	29.6	28.4	32.0	29.7	30.8	31.4	28.2	28.0	28.7
	1.0 J,10HZ	30.6	31.9	30.8	29.0	29.6	30.3	28.8	28.6	29.8	25.3	26.1	26.4
20w	1.0 J,20HZ	56.3	65.2	73.5	42.2	54.6	56.2	37.9	39.4	39.5	35.4	36.5	36.1
	2.0 J,10HZ	45.3	47.3	55.0	36.5	40.4	48.9	34.0	34.3	35.5	31.8	31.4	32.1
30w	1.5 J,20HZ	63.1	67.3	78.0	55.6	58.2	59.9	44.7	48.2	52.3	34.5	37.4	38.8
	3.0 J,10HZ	55.8	57.5	55.5	39.7	47.9	51.8	37.5	40.5	41.9	30.7	32.9	34.9

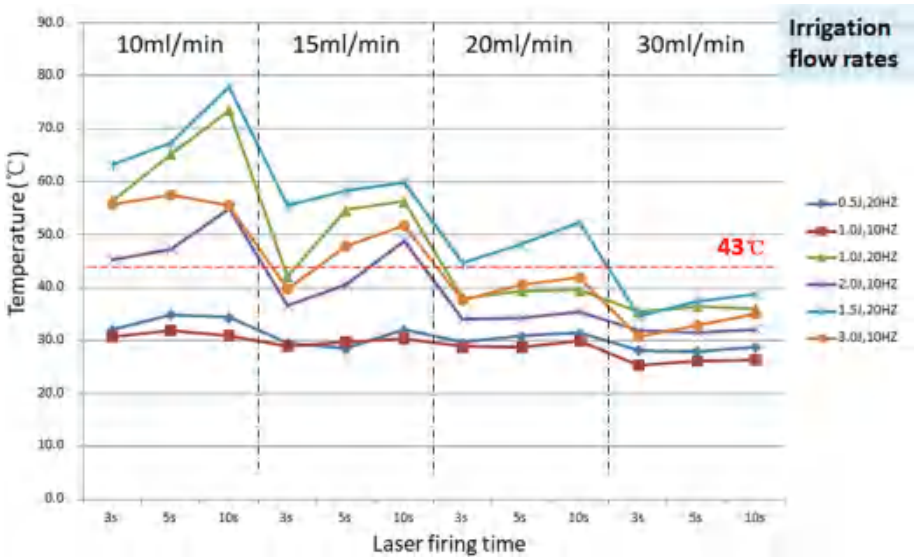


Fig. 2 Temperature curve of different laser power setting

[3, 10]. Thermal effect stemmed from holmium laser is considered the hidden etiology for ureteral stricture.

The holmium laser is a long-wavelength pulsed laser, which can transform the energy into optomechanical/photoacoustic and photothermal effect during calculi fragmentation [11, 12]. The estimated mechanical effect to turn a stone into fragments is small. Most of energy will turn into the thermal effect boiling the fluid around the laser tip. Numerous studies have confirmed that significant temperature rise can occur around the fiber. Once, the temperature exceeds the "threshold" (43 °C), it can lead to cell damage, protein coagulation and tissue injury [13], which subsequentially progresses to scar formation and ureteral stricture. According to the relationship of the tissue thermal damage and temperature, for every 1 °C exceeds the threshold temperature, the time required to cause damage to the same number of cells will decrease by half [14]. Therefore, when the temperature reaches 56 °C, it takes only 1 s to cause thermal damage to the tissue. So, the thermal injury towards ureter will be easily neglected during lithotripsy procedure.

In our current study, we established an in vitro model to evaluate the thermal effect of holmium laser and the protection effect of fluid irrigation during ureteroscopic laser lithotripsy. According to our model, the temperature rise causing by laser firing depends on the laser power, working time and fluid irrigation. Higher power laser can increase temperature much more quickly. The 20w laser setting can increase the temperature as high as 73.5 °C if irrigation is insufficient. Meanwhile, the high-frequency dusting model of holmium laser is much more efficient in heat production. Fluid irrigation plays an important role in regional heat dispersion. The flow rate up to 20 ml/min seems to be the optimal requirement during the laser lithotripsy while considering the intra-renal pelvis pressure and stone retropulsion at the same time. When the flow rate reaches 30 ml/min, the temperature can not surpass the threshold.

Thus, we provide several feasible suggestions to prevent thermal injury during endoscopic laser lithotripsy, especially for impacted ureteral calculi. First, lithotripsy is advised start with low power setting. Generally, low power setting is sufficient to fragment majority of calculi. We recommend that the power setting should not exceed 20w for most devices. Second, apply "high-frequency" setting with more caution. Previous study have showed that dusting maneuver with higher frequency can acquire better stone free rates for renal calculi [15]. Even though the dusting maneuver is more time-consuming and will produce more heat, the renal pelvis can disperse the heat quickly because of its larger space comparing with ureter. So, try to avoid the "high-frequency" laser parameter for stone dusting in the ureter. Third, ensure the fluid irrigation during the procedure. Irrigation flow should be sufficient to clear field of view and cool down the regional temperature. Using a smaller caliber ureteroscope accompanied with fine laser fiber can facilitate a better fluid irrigation and counter-flow. Last, for the impacted calculi, in-situ lithotripsy will be clumsy [9]. It can impair the fluid irrigation by blocking fluid circulation and cause the direct injury towards the ureter mucosa at the impacted site. So, we suggest displace the calculi to proximal portion of ureter prior to calculi fragmentation, since the dilated ureter will provide much more space for fluid irrigation and have less chance of direct injury by the laser fiber.

Conclusion

In conclusion, we found that laser heating can cause significant temperature rise in the ureter with various laser parameters and duration of pulsing. Laser can cause irreversible thermal injury towards ureter. Thus, during clinical application of laser lithotripsy technique, caution should be taken.

Abbreviations

Holmium: YTTRIUM-ALUMINUM-GARNET; Ho: YAG

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Not applicable.

Authors' contributions

HL designed the study and conducted the experiment. BH, JC, CW and ZZ performed the experiment and collect the data. LL drafted original manuscript. YY reviewed and edited the manuscript. XL summarized the data. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.
All authors have read the paper and agree that it can be published.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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钬激光治疗过程中的热效应输尿管镜碎石术

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Hui Liang*, Lijian Liang, Yin Yu, Bin Huang, Jia'nan Chen, Chaoguo Wang, Zhangguo Zhu and Xiaozhong Liang

摘要

背景：钬激光碎石术是治疗输尿管结石最常用的技术。研究表明，钬激光发射产生的热量会对输尿管造成热损伤。本研究旨在探讨影响钬激光在输尿管镜碎石术中热效应的因素。

方法：设计体外实验模型以模拟输尿管镜碎石术过程。实验采用不同激光功率设置（10W（0.5JX20Hz，1.0JX10Hz）、20W（1.0JX20Hz，2.0JX10Hz）、30W（1.5JX20Hz，3.0JX10Hz））与不同发射时间（3秒、5秒、10秒）及灌注流速（10 ml/min、15 ml/min、20 ml/min和30 ml/min）进行实验。使用温度计记录激光尖端周围的温度。

结果：随着激光功率的增加，“输尿管”内的温度显著上升，延长了放电时间并减少了灌注流量。实验装置中最高的区域温度为78.0°C，最低温度为23.5°C。在相同功率下，更高频率设置会产生更多热量。激光功率≤10w，灌注流量≥30 ml/min，且“高能低频”可允许安全的工作温度。

结论：本研究表明，钬激光的热效应与工作参数及冲洗流量密切相关。合理设置参数是确保输尿管镜钬激光碎石术安全性的关键。

关键词：钬激光，热效应，碎石术

背景

输尿管结石是泌尿系统常见病症，通常采用输尿管镜碎石术进行治疗。钬酸钇铝石榴石（Ho：YAG）激光因其高效性和多功能性，成为输尿管镜碎石术中最优选择[1]。研究表明，相较于其他碎石技术，钬酸钇铝石榴石激光具有更佳的安全性——其2100纳米波长的光波能快速被水体吸收，从而有效控制碎石深度，减少对周围组织的损伤。然而随着Ho：YAG激光应用的普及，输尿管镜检查引发的并发症（如输尿管狭窄）也日益常见。临床数据显示，输尿管镜术后输尿管狭窄的发生率可达1%-4%[2]。该狭窄的潜在成因更可能是输尿管壁受到的直接热损伤，而非声波或光能作用[3]。激光能量会产生热量，可能引发热生物效应[4-7]。本研究旨在探讨输尿管镜钬激光碎石术过程中工作参数与输尿管内温度之间的关联性。

方法

为评估激光碎石过程中温度变化，研究人员建立了一种模拟输尿管镜激光碎石术的体外模型。实验采用结扎的F20橡胶管段模拟结石阻塞的人体输尿管，通过F8/9.8型输尿管镜的工作通道导入200微米激光光纤（图1），应用Raykeen钬激光（上海Raykeen，中国），

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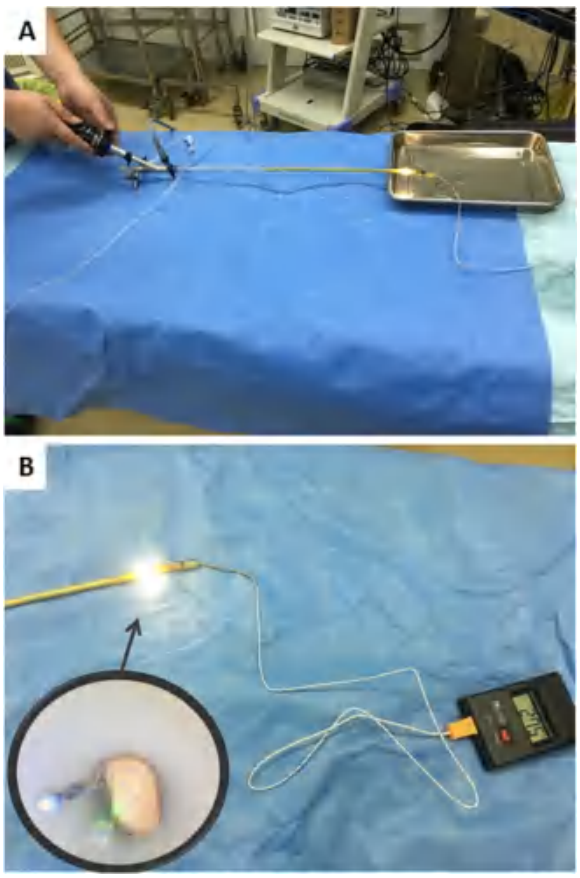


图1 a在橡胶管内建立模拟输尿管镜激光碎石术操作。b通过热电偶记录局部温度。

在临床常用的各种功率设置下进行实验。能量设置分别为0.5、1.0、1.5、2.0 J。在不同能量设置下测试了10赫兹和20赫兹的频率设置。激光发射时间为3秒、5秒和10秒。使用室温下的输液泵，采用10 ml/min、15 ml/min、20 ml/min和30 ml/min的相关灌注流速。温度计距离底部5毫米，距离激光尖端位置约2毫米处记录温度。每个动力和灌水设置组合记录5次温度，计算平均值，进行不同设置下的统计比较。

结果

激光光纤尖端周围积聚了热量。温度数据汇总于表1中。温度随激光功率和照射时间的增加而上升。充足的灌注流量可以带走热量。在功率设置为1.5JX20Hz、灌注流速为10 ml/min的情况下，连续激光照射10秒时达到峰值温度78.0°C。而在功率设置为1.0 JX10Hz、灌注流速为30 ml/min的情况下，连续激光照射3秒后测得最低温度25.3°C。

当功率设定为10瓦时，无论激光脉冲持续时间或冲洗流量如何变化，温度都能保持稳定。但当功率提升至20瓦时，若冲洗水量不足，温度会急剧上升。此时需要增加冲洗水量或缩短激光脉冲时间来控制温度。图2展示了不同功率设置下，在四种不同冲洗流量条件下的温度变化曲线。另一个有趣发现是：在相同功率设置下，“高能量低频”参数产生的热效应较弱。当冲洗水量不足时，平均温差会更加明显。

讨论

钬激光是输尿管镜碎石术[8]中粉碎结石最强大的能量工具。尽管该技术被视为微创手术方式，但仍存在输尿管狭窄[9]等棘手并发症。输尿管狭窄是输尿管镜术后常见的并发症，尤其在输尿管结石嵌顿的情况下更为突出[9]。过去学界普遍认为机械性损伤是导致输尿管狭窄的主要原因，但越来越多的证据表明，即使没有机械性损伤，输尿管狭窄也可能发生。术中钬激光热效应这一问题正逐渐引起学界关注。

表1不同激光工作模式与灌注流速下的区域温度变化

权力	流速	10 ml/min			15 ml/min			20 ml/min			30 ml/min		
	发射时间	3 s	5 s	10s	3 s	5 s	10s	3 s	5 s	10s	3 s	5 s	10s
10w	0.5 J,20HZ	32.0	34.9	34.3	29.6	28.4	32.0	29.7	30.8	31.4	28.2	28.0	28.7
	1.0 J,10HZ	30.6	31.9	30.8	29.0	29.6	30.3	28.8	28.6	29.8	25.3	26.1	26.4
20w	1.0 J,20HZ	56.3	65.2	73.5	42.2	54.6	56.2	37.9	39.4	39.5	35.4	36.5	36.1
	2.0 J,10HZ	45.3	47.3	55.0	36.5	40.4	48.9	34.0	34.3	35.5	31.8	31.4	32.1
30w	1.5 J,20HZ	63.1	67.3	78.0	55.6	58.2	59.9	44.7	48.2	52.3	34.5	37.4	38.8
	3.0 J,10HZ	55.8	57.5	55.5	39.7	47.9	51.8	37.5	40.5	41.9	30.7	32.9	34.9

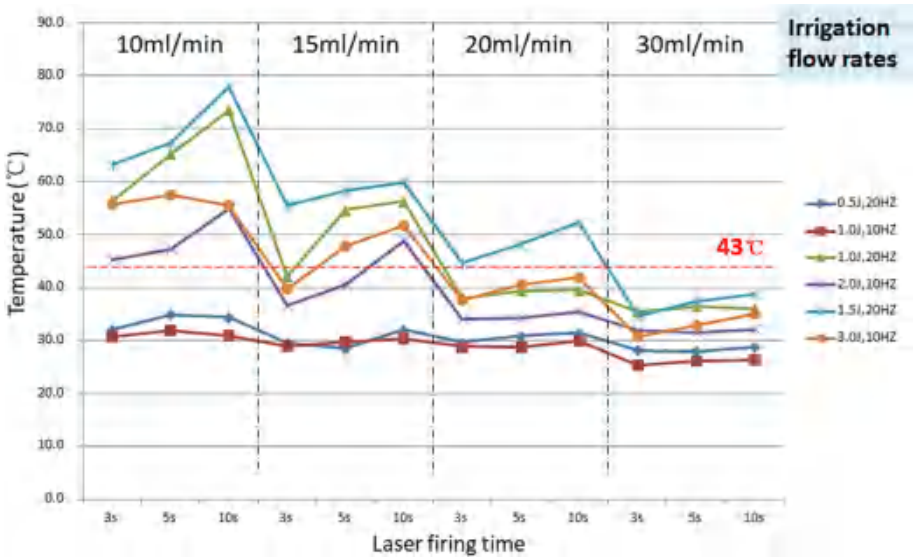


图2不同激光功率设置的温度曲线

[3，10]。钬激光热效应被认为是输尿管狭窄的潜在病因。钬激光是一种长波长脉冲激光，在碎石过程中可将能量转化为光机械/光声效应和光热效应[11，12]。虽然机械碎石效果微弱，但大部分能量会转化为热效应，使激光尖端周围的液体沸腾。大量研究证实，光纤周围会出现显著温度升高。当温度超过“临界值”（43℃）时，会导致细胞损伤、蛋白质凝固及组织损伤[13]，进而引发瘢痕形成和输尿管狭窄。根据组织热损伤与温度的关系，温度每超过临界值1℃，损伤相同数量细胞所需时间就会缩短一半[14]。因此，当温度达到56℃时，仅需1秒即可对组织造成热损伤。这意味着在碎石术过程中，输尿管的热损伤很容易被忽视。

在我们当前的研究中，我们建立了一个体外模型来评估钬激光的热效应以及输液冲洗在输尿管镜激光碎石术中的保护作用。根据我们的模型，激光发射引起的温度上升取决于激光功率、工作时间和输液冲洗。功率更高的激光可以更快地提高温度。如果冲洗不足，20瓦的激光设置可以使温度高达73.5°C。同时，钬激光的高频喷尘模型在产热方面效率更高。输液冲洗在区域热扩散中起着重要作用。在同时考虑肾盂内压力和结石排出的情况下，20 ml/min是激光碎石术的最佳流量要求。当流速达到30 ml/min时，温度不能超过阈值。

因此，我们针对内窥镜激光碎石术（特别是处理梗阻性输尿管结石时）提出几项切实可行的预防热损伤建议。首先，建议从低功率模式开始碎石。通常低功率足以粉碎大多数结石，我们建议多数设备的功率设置不应超过20瓦。其次，高频模式操作需格外谨慎。既往研究表明，采用高频碎石技术可获得更高的肾结石无结石率[15]。尽管高频碎石耗时更长且产热更多，但由于肾盂空间较大，散热效率优于输尿管，因此建议避免在输尿管碎石时使用高频激光参数。第三，术中需确保充分冲洗。冲洗流量应足够清除视野并降低局部温度。使用口径较小的输尿管镜配合细光纤激光器，可更有效地实现冲洗和逆流冲洗。最后，对于结石嵌顿的情况，原位碎石术操作难度较大[9]。该技术可能因阻断液体循环而影响冲洗效果，同时在结石嵌顿部位直接损伤输尿管黏膜。因此，我们建议在碎石前先将结石移位至输尿管近端，因为扩张后的输尿管能为液体冲洗提供更充足的空间，同时降低激光光纤直接损伤的风险。

结论

综上所述，我们发现不同激光参数和脉冲持续时间的激光加热可导致输尿管温度显著升高，激光可对输尿管造成不可逆的热损伤，因此在临床应用激光碎石术时应谨慎。

缩写

钬：钇铝石榴石；Ho：YAG

致谢

不适用。

作者的贡献

HL负责研究设计与实验实施，BH、JC、CW和ZZ共同完成实验操作与数据采集，LL撰写初稿，YY参与审阅修订，XL负责数据汇总，全体作者审阅并最终确认稿件。

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本研究使用的数据集可通过合理申请向通讯作者获取。

所有作者均已阅读论文，并同意发表。

伦理审查和参与同意

不适用。

同意发表

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竞争利益

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激光腔内碎石术后并发输尿管狭窄的预防研究进展

秦鹏飞[1] 黄挺[2] 方立[2] 程跃[2△]

［摘要］ 激光技术的广泛应用极大提高了泌尿外科腔内碎石的手术效率，而其术后出现的输尿管狭窄是一种非常危险的并发症，一旦发生便难以处理。目前认为术中机械损伤和热损伤是其主要成因，尤其是激光热损伤，近年来引起了学者们的重点关注。本文就激光腔内碎石术后并发输尿管狭窄的发生机制、危险因素及预防策略的研究进展作一综述。

［关键词］ 激光；碎石术；输尿管狭窄；热损伤；预防
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Research progress on the prevention of ureteral stricture after laser lithotripsy

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Abstract The wide application of laser technology has greatly improved the efficiency of lithotripsy in urology. However, postoperative ureteral stricture is a very dangerous complication which is difficult to deal with once it occurs. Currently, it is believed that mechanical damage and thermal damage are the main causes, especially laser thermal damage, which has attracted the attention of scholars in recent years. In this paper, the pathogenesis, risk factors and prevention strategies of ureteral stricture after laser lithotripsy are reviewed.

Key words laser; lithotripsy; ureteral stricture; thermal damage; prevention

激光技术目前已广泛应用于泌尿外科各类腔内碎石术式中[1]，其中钬激光（Holmium：YAG laser）是临床较为主流的选择。伴随着较高的碎石效率与清石率[2]，激光腔内碎石术后并发输尿管狭窄的发生率也在逐渐增长，有国外文献报道其发生率可达 2.95%[3]，国内研究也出现过 4.09%的术后高狭窄率[4]，这引起了学者们的广泛关注。输尿管狭窄会导致不同程度肾积水，且被发现时往往已伴有肾功能的损害，属于较严重的并发症。因此，术后高狭窄率背后的原因以及如何减少此类并发症的发生是学者们研究聚焦的方向。本文就激光腔内碎石术后并发输尿管狭窄的可能发生机制、相关危险因素及相应预防策略作一综述，为临床医师们解决这类问题提供一些思路。

1 术后输尿管狭窄的可能发生机制

1.1 机械性损伤-炎症纤维化

传统研究中，更多关注点往往在机械性因素于术后输尿管狭窄中的作用。包括术前结石长期嵌顿产生的黏膜慢性损伤[5]，术中腔镜、激光光纤、导引鞘等对输尿管黏膜的机械性牵拉和刮擦，激光对黏膜的直接击打作用以及术后残留结石碎块的损伤等[6]。机械性损伤会破坏输尿管组织造成局部缺血和炎症反应，黏膜上皮细胞出现肥大、增生和水肿并进一步导致纤维化-管腔狭小的发生[7]。然而，Fam 等[8]通过一项前瞻性研究得出输尿管黏膜的机械性损伤及炎症反应其实是可逆的，尚不能认为其是导致输尿管狭窄的危险因素。

1.2 激光热效应损伤

近些年越来越多的学者开始关注到激光的热效应在术后输尿管狭窄形成中的作用。钬激光的工作原理是利用光-热效应（photothermal）和光-机械效应（photomechanical）进行熔石、碎石[9]。虽然钬激光的碎石范围只有 0.5～1.0 mm，但由于其波长（2120 nm）与水的最大吸收峰（1940 nm）非常接近[10]，大部分能量会被激光纤维头周围的液体吸收从而产生热效应[11]。已有研究表明，人体组织的热损伤阈值大约为 43℃，在该温度下输尿管组织已开始发生蛋白质凝固变性，异常的转录、翻译及 DNA 复制，引起细胞凋亡，进而产生病理性瘢痕组织并引起输尿管狭窄[12-14]。若在 43℃下暴露 120 min，则直接可致细胞组织发生不可逆性的坏死。且每超过阈值温度 1℃，对相同数量的细胞造成损伤所需的时间将减少一半[15]。在 Winship 等[12]的体外模型实验中，常规灌注流量及钬激光

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设置下(尤其在输尿管软镜下且钬激光功率≥10 W时),钬激光头端附近液体的温度可在 1 s 内达到热损伤阈值。这提示热效应也是激光腔内碎石术后输尿管狭窄形成的重要机制。

2 输尿管狭窄形成的主要危险因素

2.1 嵌顿性结石

长时间嵌顿的结石,其周围输尿管黏膜往往水肿严重且常伴息肉形成,这使管腔操作空间变小从而间接增大术中激光对黏膜直接损伤的机会[8]。且这类患者输尿管黏膜受到慢性炎症刺激更持久,组织增生和纤维化严重。Darwish 等[16]认为,嵌顿的结石因堵塞管腔而使术中灌注液的循环减弱,可导致结石周围的压力和温度升高,这加重了对输尿管的损害。

2.2 大负荷结石

结石负荷大的患者常伴有输尿管梗阻与肾积水,尤其高位结石,这类病例碎石难度大[4],手术时间久。Sorokin 等[17]通过对 10 年来病例的回顾性研究得出:结石体积对手术时间的影响最大,并且结石体积每增加 100 mm^3,手术碎石时间约增加 2 min。这就意味着,术中激光热效应对输尿管黏膜的损伤也随之增加。

2.3 灌注不足

灌注液的循环引流可有效带走激光产生的多余热量,在灌注量相对不足的情况下,术中输尿管腔内、肾盂内很快出现高温[12],输尿管壁受到热损伤,引起其术后纤维化狭窄的出现。Wollin 等[18]测量了 0.2 J×50 Hz、0.6 J×6 Hz、0.8 J×8 Hz、1.0 J×10 Hz、1.0 J×20 Hz 5 组分别在灌注量为 0、50、100 mL/min 时钬激光持续激活 60 s 内的水温变化,结果显示灌注量为 0 时,5 组最高温度均超过热损伤阈值(43℃),灌注量为 50 mL/min 时,仅有 1.0 J×20 Hz 组的最高温度到阈值,当灌注量达 100 mL/min 时,5 组的最高温度均未超过阈值。这表明,要想在术中防止热损伤的发生,对灌注量的要求可能会非常高。

2.4 术中危险操作

缺乏经验的术者往往操作不熟练,除了会发生牵拉刮擦输尿管、反复进退镜等机械性伤害外[4],还会出现因激光纤维定位不精准而对黏膜造成直接破坏、单次长时间持续激活激光碎石产生高温热损伤等现象,这些不当操作也是导致术后并发症不可忽视的因素[19]。

3 术后输尿管狭窄的预防策略

近年来国内外学者进行了大量的随机对照试验、回顾性分析以及体外/体内模型研究,旨在寻找出有效的手段以解决激光腔内碎石术后输尿管狭窄的问题。相比于以往着眼于输尿管狭窄形成后的治疗方式,今天的学者们则把更多的目光聚焦在并发症出现之前的预防策略上,力求降低该并发症的发生率。

3.1 术式的选择

以往指南建议,对于直径≥2 cm 的结石更推荐行 PCNL 治疗[1]。然而,设备仪器的改进包括镜径的缩小、镜体偏转力的加强,光学成像的优化以及一次性器材的应用,尤其是输尿管镜通道鞘(ureteral access sheath,UAS)的应用与改良十分有效地保护了输尿管黏膜免受重复的机械性损伤并且改善了灌注液的引流[20],这些都导致越来越多的术者在处理 2 cm 以上大结石时尝试选择 URL/FURL[21]。已有系统综述报道,对于≥2 cm 的结石,目前 RIRS 的清石率可达到达 91%[22]。但陈珂宇等[23]研究发现,输尿管镜/软镜在治疗大结石(直径≥2 cm)时,激光持续激活时间可从几秒延长达几十秒,热效应显著。同时,在实际操作中灌流率其实并不恒定且往往低于设定值,击打高位结石时为防止结石被冲回肾盂,如果调低灌注量甚至会有零灌注的情况出现,这更使局部温度短时间内骤增至安全临界点[24-25]。而在 PCNL 术中,由于鞘的直径较大,使灌注液回水通畅,且体积稍大的结石也能被直接取出,避免了长时间的钬激光激活,碎石过程中局部热效应控制较好。因此,对于直径≥2 cm 的结石,尤其是高位结石,PCNL 在术中温度控制及对术后输尿管狭窄的预防中,较 URL/FURL 仍具有一定理论优势[23]。

另外,对于术前评估结石情况复杂合并危险因素的病例(如长期嵌顿结石、大负荷结石、合并感染)[26],为减少因手法不娴熟导致的不当操作如在术野不清的情况下盲目碎石、单次长时间激活激光等,缩短输尿管在危险因素下的暴露时间,降低术后输尿管狭窄发生率,更推荐由高年资的医生施行手术。

3.2 激光参数的设置

合理的激光参数即能量和频率设置是非常重要的,Liang 等[27]建立了体外模型来模拟输尿管镜碎石的过程,他们认为碎石应首先从低功率设置开始,对大多数设备来说功率设置不应超过 20 W,因为此功率已能处理绝大部分的结石。他们的实验中,在 1.0 J×20 Hz 的功率设置配合 10 mL/min 的灌流量下,连续激活钬激光仅 3 s,即可使周围水温达到 56.3℃之高,这已经远高于热损伤阈值[12-13]。另外,在同样的功率设置下,比如 1.0 J×20 Hz 与 2.0 J×10 Hz 均为 20 W,但前者测得的水温在任何时间点都明显高于后者,这表明高频低能模式可能比高能低频模式的热效应更显著。而在清石率上,Li 等[28]的研究认为低能高频设置与高能低频设置的表现相似。因此,尽量避免在输尿管中使用相对高频模式碎石可能更有助于预防术

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后管腔狭窄的发生。

3.3　灌注液的引流

在腔内手术中，灌注液除了能清晰视野、冲回碎石外，还能吸收大部分激光热量，所以灌注量对术后并发症的预防也至关重要。前文提到 Wollin 等[18]的对照试验表明，要想在术中做到杜绝热损伤的发生，适当增加灌注即能有效缓冲激光的热效应。然而，盲目要求高灌注量可能会导致肾盂内压过高而增加术后感染的风险。所以，在灌注量问题上如何平衡热损伤的风险与肾盂高压的风险值得学者们进一步的探究。目前，负压吸引工作鞘(negative pressure ureteral access sheath)的应用已为解决此问题提供了一个可行的角度。例如，邓小林等[29]研发了一种可监测肾盂内压的输尿管软镜负压吸引鞘，吸引口与负压泵相连，持续抽吸灌注液，实现腔内“降压”的同时还能“降温”。因传统 URL/FURL 术中液体流出通道较小较长，灌注液循环受阻，致输尿管腔内散热效果不佳；又无高效的排石方法，主要通过高压灌注回流和手动钳取，花费了大量取石时间[30]。而使用负压吸引鞘后，灌注量就可适当增大，在高循环流速下，击碎的结石连同多余的热量被快速排出体外[31]，既阻止了热量的累积又节省了部分取石时间以缩短输尿管壁在危险因素下的暴露时间，这对管壁损伤乃至术后狭窄的预防有积极作用。相似的，Fang 等[32]也着眼于灌注液的引流问题，他们在体外猪肾模型中模拟钬激光碎石术以对比不同“镜鞘比”下的肾盂内压及灌注液流速。镜鞘比越小，即镜的外径与鞘内通道直径之比越小，镜与鞘之间的出水通道越大，会加速灌注液的引流，所以适当减小镜鞘比理论上可保护肾脏及输尿管免受高压、高温的损害。最终得出镜鞘比≤0.75 是较为安全的。目前，他们仅对镜鞘比与肾盂内压的关系研究作了报道，而镜鞘比对钬激光热效应的影响仍有待更进一步的探究。

3.4　灌注液的选择

有学者提出应用低温灌注液的想法，试图用低于生理温度(36.5℃)的灌注液来吸收更多热量以保护肾脏及输尿管[25]。然而，Butticè 等[24]的研究表明常温盐水(24.5℃)与 36.5℃盐水在相同钬激光设置及灌注量下的散热能力差异无统计学意义，但常温盐水会降低人体核心温度反而会引起低体温、寒战、低氧血症等并发症。所以，实际操作中仍然更推荐使用接近生理温度的盐水。

3.5　激光碎石方法

对于较大结石，尤其是嵌顿性结石，碎石方法尤为重要。刘为池等[4]报道了击碎结石边缘发现输尿管黏膜损伤的经验。叶照华等[33]认为长期嵌顿的大结石周围输尿管黏膜往往水肿严重，管壁黏膜与结石贴合紧密，甚至存在黏膜下结石，故此时采用“钻孔法”从结石中部开始击打比“周边蚕食法”会更安全稳妥[34]。结石周边与管壁黏膜相接触的部分应夹离管壁后，再行碎石[33]。也有学者[27]建议先将嵌顿结石朝输尿管近端移动后再行碎石以获得更大的操作空间，但仍需进一步实验验证。Dretler 等[6]有报道，激光碎石术后遗留的残余草酸钙结石容易定植于输尿管壁上引发异物巨细胞反应生成异物肉芽肿最终堵塞管腔使之狭窄。对此，我国学者提出的“粉末化碎石”[34]概念有一定的理论指导意义，即在术中将结石粉碎至＜2 mm的碎片，此等大小的结石能在术后顺利排出体外而不会残留形成石街。术者可以 200 μm 钬激光光纤为参照，将结石粉碎至其直径的 10 倍以下(即 2 mm)，减少残余结石的沉积定植。

另外，手术中术者为了提高碎石效率，激光处于持续激活状态的情况时常发生，Aldoukhi 等[25]进行了体内猪肾模型实验，结果表明相邻两次钬激光激活所需要的间隔时间实际应大于有效碎石时间，即采取“间歇性激活”能有效减少热效应的产生。可以预见，“操作者占空比(operator duty-cycle)”将会是未来研究的一个重要方向。

3.6　双 J 管的留置

钬激光碎石术后常规留置双 J 管引流，但术后双 J 管的留置一直是较富争论的话题，Ozyer 等[35]通过回顾性分析发现在同侧输尿管内留置两根双 J 管的引流效果更佳。这与刘杰等[36]的报道相符，他们认为单根双 J 管在一些狭小输尿管中会像“塞子”一样堵塞管腔，尿液只能从引流管管腔流出，一旦管腔堵塞则形成无效引流。而两根双 J 管之间可相互支撑，使尿液从双管的间隙中也可流出，减少尿外渗，降低输尿管瘢痕发生率，且两根双 J 管间的相对运动可减少粘连的形成[37]。因此，对于存在较严重输尿管损伤(包括机械性损伤和热损伤)可能性的患者，术后留置两根双 J 管是一种可尝试的选择。关于双 J 管的留置时间问题，刘为池等[4]的经验是对术中存在明显黏膜损伤的患者，应适当延长留置时间至 8～12 周。然而，叶照华等[33]的研究并未发现延长双 J 管留置时间为输尿管狭窄的保护因素，相反，他们认为留置超过 4 周者输尿管狭窄率会更高。另外，Assimos 等[38]通过一项多中心前瞻性研究发现，术前留置双 J 管可明显提高肾结石手术清石率并减少并发症的发生，这可能与通道鞘置入成功率的提高使输尿管损伤减少有关[39]。

3.7　药物预防

有学者研究发现，血管紧张素转换酶抑制剂(ACE-I)如卡托普利可通过降低表皮生长因子(EGF)、纤维蛋白原、Ⅰ型胶原蛋白 a2(Col Ⅰa2)

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等的表达以抑制纤维化瘢痕的形成，也可应用于预防激光腔内碎石术后并发输尿管狭窄[40]，但目前该理论仍需进一步研究验证。

4 总结与展望

激光腔内碎石术因其微创、安全、清石效率高等众多优点，已成为泌尿系结石的主流治疗手段。但由于其存在对输尿管壁的机械性损伤和热损伤，术后并发输尿管狭窄的问题正逐渐得到关注。目前，对其预防的重点主要在激光设置、灌注问题以及碎石方法上。部分危险因素如嵌顿、大负荷结石仍无法从根源上去除，并且对于术中持续存在的激光热损伤，依然缺乏切实可靠的术中监测手段及保护措施。这是一项复杂但具有意义的任务，有待之后的学者继续探索，以期进一步提高激光腔内碎石术的安全性及减少术后输尿管狭窄并发症的发生率。

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Incidence of Ureteric strictures Following Ureteroscopic Laser Lithotripsy: Holmium:YAG Versus Thulium Fiber Laser

ABSTRACT

Objective: We aimed to compare the incidence of ureteric strictures between holmium:yttrium aluminum garnet and thulium fiber laser following ureteroscopic laser lithotripsy. In the present era of miniaturization of endourologic armamentarium and better optics, how safe are lasers to fire inside ureter?

Materials and Methods: It is a prospective comparative study over a period of 2 years that included patients who underwent ureteroscopic laser lithotripsy for ureteric stones. Patients were randomly divided into 2 groups: group A underwent holmium:yttrium aluminum garnet laser lithotripsy and group B underwent thulium fiber laser lithotripsy.

Results: A total of 478 patients were analyzed after excluding patients not willing to participate and patients lost to follow-up. Two hundred forty patients underwent holmium:yttrium aluminum garnet laser lithotripsy (group A) and 238 patients underwent thulium fiber laser lithotripsy (group B). The demographic data of 2 groups were comparable. The mean age of patients in group A and group B was 36.5 ± 12.52 years and 38.62 ± 10.71 years, respectively. The mean operative time in group A and group B was 47 ± 15 and 36 ± 13 minutes, respectively, while the mean laser time in group A and group B was 13.5 ± 45 minutes and 9.25 ± 3.2 minutes, respectively. Four (1.67%) patients in group A and 11 (4.62%) patients in group B developed ureteric strictures during follow-up, and the difference was statistically significant ($P < .001$). The mean length of stricture was 2.67 ± 1.27 cm in group A and 4.42 ± 2.2 cm in group B, and the difference was statistically significant.

Conclusion: Thulium fiber laser, projected as safe laser previously, has a higher incidence of ureteric strictures compared to holmium:yttrium aluminum garnet laser when used for ureteroscopic laser lithotripsy.

Keywords: Holmium, YAG laser, thulium fiber laser, ureteric strictures, ureteroscopy, ureteroureterostomy

Introduction

Ureteric stones presenting as acute flank pain is a common cause of emergency department visits, and a large number of patients require definitive treatment in the form of ureteroscopic lithotripsy. Ureteroscopic lithotripsy by lasers or pneumatic lithotripters allows fragmentation of larger stones and subsequent clearance. Lasers have outclassed pneumatic lithotriptors in the management of ureteric strictures, with less retropulsion and better fragmentation o all types of stones.[1]

Holmium:yttrium aluminum garnet (Ho:YAG) laser, being an efficient lithotripter and compatible with both flexible and rigid uretroscopes, has been considered as the gold standard for ureteroscopic lithotripsy.[2] Because of some inherent flaws in the Ho:YAG laser, thulium

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fiber laser (TFL) was introduced into the armamentarium of laser lithotripters to overcome these deficiencies. As a lithotripter, TFL outclasses the Ho:YAG laser in many aspects as follows: it uses fine fibers to deliver energy with core diameter as low as 50 µm; it is possible to operate TFL at modest pulse energy as low as 0.025 J; (3) it has a peak operating frequency up to 2000 Hz; (4) it has a pulsed infrared energy emission at a wavelength of 1940 nm that has a 4-fold absorption coefficient compared to the Ho:YAG laser and therefore has low threshold for lithotripsy and tissue ablation.[3] Comparative studies have suggested faster stone ablation rates (1.5-4 times) in favor of TFL.[4] With the use of Ho:YAG laser lithotripsy through small-size uretroscopes, the incidence of ureteric strictures was reduced compared to the use of rigid lithotripters through larger-sized uretroscopes.

Thermal effect of lasers on ureteric mucosa leads to mucosal ablation and subsequent ureteric stricture formation in many cases. Thulium fiber laser has a low depth of penetration and has been projected as safe laser for intracorporeal lithotripsy. However, studies have shown that rise in ureteric temperature was 9°C-12°C higher for TFL than the Ho:YAG laser when operated at higher frequency and slow irrigation flow, leading to increased thermal stress to the surrounding tissues.[5] In the present study, we compared the incidence of ureteric strictures between TFL and Ho:YAG laser when used for ureteroscopic lithotripsy.

Materials and Methods

This is a 2-year prospective comparative study, carried at our institute from January 2020 to December 2021. This study includes all the cases of ureteric stones that underwent ureteroscopic laser lithotripsy. Patients with ureteric stones were evaluated with computed tomography (CT) urography and subsequently planned for ureteroscopic laser lithotripsy. Patients were randomized to undergo lithotripsy with the Ho:YAG laser (Lumenis pulse 100H Ho laser, group A) or TFL (IPG photonics 50/500-QCW, group B). Written informed consent was taken from the patients, and ethical committee clearance was obtained to carry out this study. The study has been approved by Ethical committee of Sher-i-Kashmir Institute of Medical Sciences Srinagar Jammu and Kashmir India. Approval number is IEC/Skims protocol #231E/2020. Patients with past history of extracorporeal shockwave lithotripsy, ureteroscopy, or open surgery done on the ureter were excluded from study. Also, patients with past history of genitourinary strictures, endometriosis, retroperitoneal fibrosis, or pyonephrosis were also excluded from the study.

Ureteroscopy was done under spinal anesthesia using 6/7.5 Fr semi-rigid ureteroscope with normal saline irrigation by continuous and pulsatile irrigation bulb. The steps of the procedure were same except the type of laser used in 2 groups. In both groups 200 µm fiber was used to deliver laser energy. Lithotripsy was started with 0.4 J and 8 Hz in both the groups and gradually increased if disintegration was ineffective. After lithotripsy, larger stone fragments were removed with a forceps and a double J (DJ) stent was deployed at the end of the procedure. Stone clearance and placement of DJ stent was confirmed with fluoroscopy. A follow-up x-ray kidney ureters and bladder (KUB) was done after 2 weeks to look for any residual fragments. The DJ stent was removed 4 weeks after the procedure. An ultrasound examination of the abdomen was done 6 weeks after stent removal to look for any residual hydronephrosis. Patients with fever, flank pain, increase in hydroureteronephrosis, or obstructive uropathy underwent CT urography to identify any stricture. Patients with pyonephrosis or urosepsis underwent percutaneous nephrostomy tube placement. The length and site of stricture was estimated by CT urography (Figure 1), table retrograde pyelography (Figure 2), and antegrade pyelography (Figure 3). All those patients with ureteric strictures underwent Tc^{99m} diethylenetriamine pentaacetate (DTPA) scan to quantify renal function. Patients with ureteric strictures underwent endoureterotomy, ureteroureterostomy (Figure 4), ureteroneocystostomy, Boari flap reconstruction, or nephrectomy depending on the length of stricture, site of stricture, and salvageability of renal function. Patients treated for ureteric strictures were followed at 3 months post-surgery with Tc^{99m} DTPA

MAIN POINTS

- *Thulium fiber laser has low threshold for lithotripsy and tissue ablation compared to holmium:yttrium aluminum garnet (Ho:YAG) laser.*
- *Although the optical penetration depth of thulium fiber laser (TFL) is less compared to the Ho:YAG laser, the TFL energy is absorbed 16 000 times more than the Ho:YAG laser after passing 1 mm depth of tissue, reflecting into severe tissue ablation associated with TFL.*
- *Thulium fiber laser has a higher incidence of ureteric strictures compared to the Ho:YAG laser when used for ureteroscopic laser lithotripsy.*
- *Thulium fiber laser should be used cautiously inside the ureter with low energy at lower frequency setting with continuous irrigation.*



Figure 1. Computed tomography urography: reconstructed image showing right-sided hydroureteronephrosis due to upper ureteric stricture.

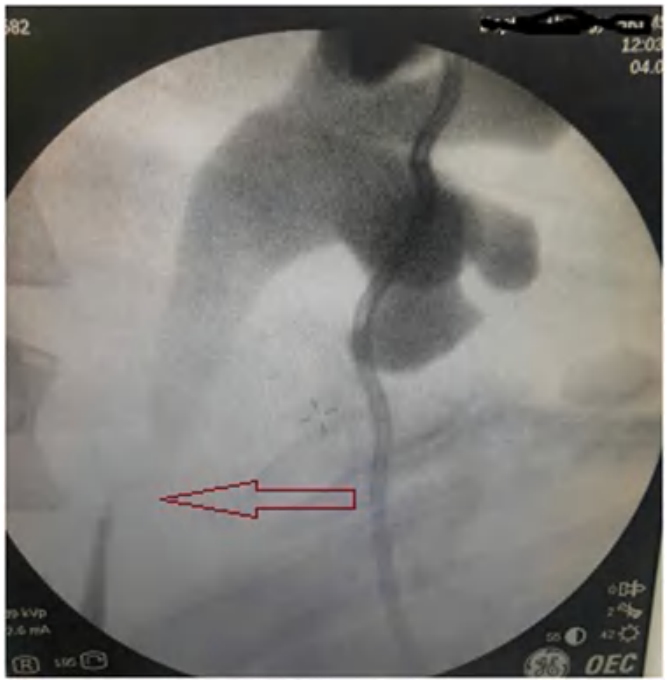


Figure 2. Antegrade and retrograde pyelography delineating the length of stricture (red arrow).

scan and CT urography. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 22.0. (IBM SPSS Corp.; Armonk, NY, USA). The qualitative data are presented as numbers and percentages, while the quantitative data are presented as mean (SD). The normal distribution of quantitative data was assessed by



Figure 3. Left antegrade pyelography showing complete cutoff in the upper ureter.

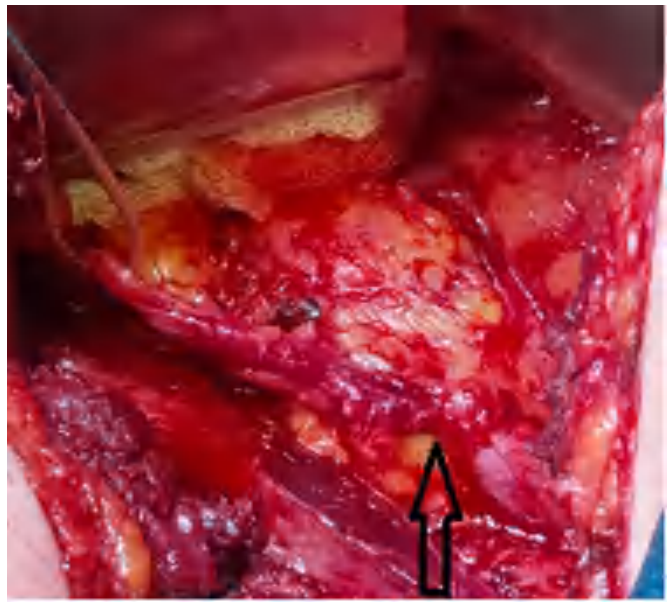


Figure 4. Intraoperative picture of the upper ureteric stricture (black arrow).

an independent sample *t*-test. Comparison of qualitative variables between the groups was done using the chi-square test. Statistical significance of any parameter was defined as *P*-value <.05.

Results

Between January 2020 and December 2021, 540 patients with ureteric calculi were planned for ureteroscopic laser lithotripsy. Out of these 21 declined to participate and a further 30 patients were excluded as they did not qualify to participate in the study. The remaining 489 patients were randomly divided into 2 groups: group A (246 patients) who underwent Ho:YAG laser lithotripsy and group B (243 patients) who underwent TFL lithotripsy. During the study, 6 patients from group A and 5 patients from group B lost to follow-up. Figure 5 shows the stages of our study in a Consolidated Standards of Reporting Trials diagram.

The demographic profile of our study groups is shown in Table 1, and there was no statistically significant difference between the 2 groups. The percentage of females in group A and group B was 36.25% and 35.29%, respectively. The average age of patients in group A and group B was 36.5 ± 12.52 years and 38.62 ± 10.71 years, respectively, and the difference was not statistically significant ($P = .45$). The average waiting period to undergo procedure is 7.5 ± 1.5 days and 8 ± 2.5 days in group A and group B, respectively, and the difference was not statistically significant. The average stone size in group A was 8.9 ± 3.5 mm and that in group B was 9.1 ± 3.2 mm ($P = .25$). Stone density was 922 ± 241 hounsfield unit (HU) and 918 ± 235 HU in group A and group B, respectively ($P = .82$). The stone parameters of 2 groups were comparable. The percentage of stones in the upper ureter (above crossing of iliac vessels) was 40% and 39% in group A and group B, respectively ($P = .21$).

The intraoperative parameters of the 2 groups are shown in Table 2. The mean operative time in group A and group B was 47 ± 15 and 36 ± 13 minutes, respectively, and the difference was

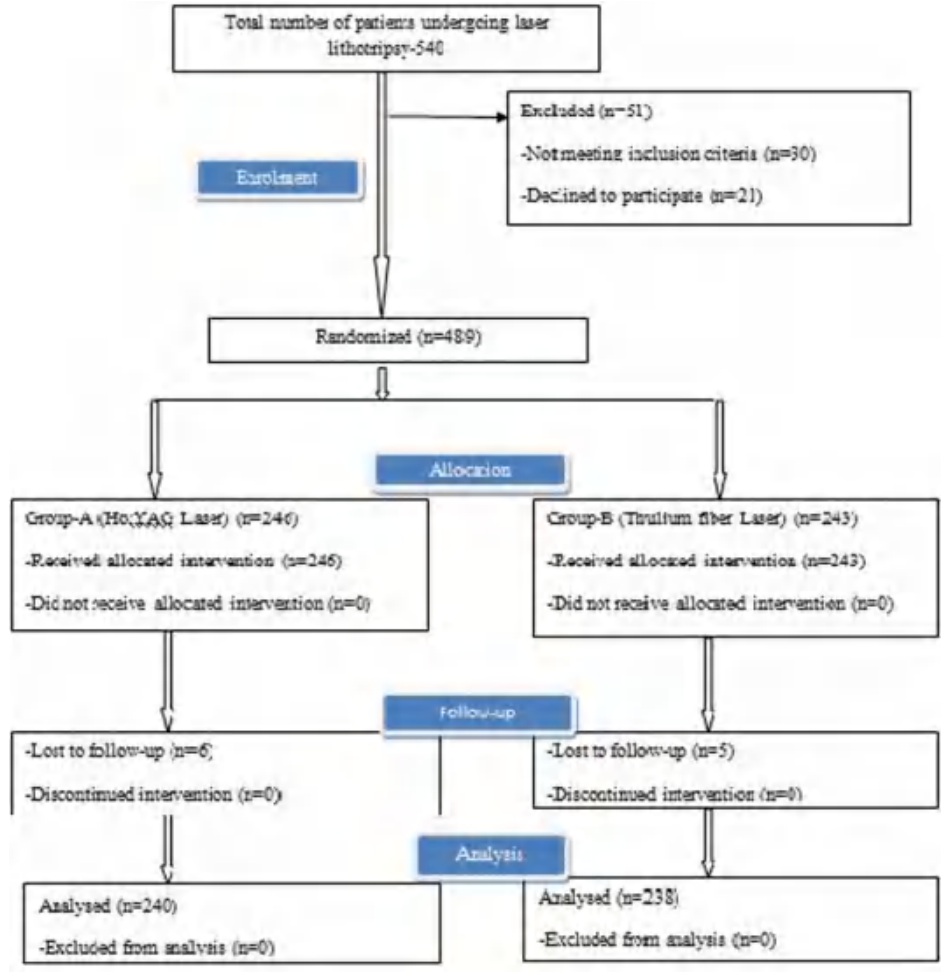


Figure 5. Stages of our study in a Consolidated Standards of Reporting Trials diagram.

statistically significant ($P < .05$). The mean laser time in group A was 13.5 ± 4.5 minutes and that in group B it was 9.25 ± 3.2 minutes. The difference in the laser time was statistically significant ($P < .001$). Forty-eight percent of patients in group A and 37% of cases in group B required augmentation in frequency and energy to achieve the desirable fragmentation after starting with low-energy setting, and the difference was significant ($P < .05$). The average laser energy spent in group A and group B was 4.4 ± 1.2 and 3.12 ± 1.3 kJ/case, respectively, and the difference was not statistically significant ($P < .23$). Fifteen percent of patients in group A and 13.02% of patients in group B had adverse events recorded intraoperatively that included bleeding impairing vision (10% in group A and 8.82% in group B), visible mucosal ablation (8.75% in group A and 7.56% in group B), and ureteric perforation (1.25% in group A and 0.84% in group B). The difference was not statistically significant ($P < .42$).

Table 1. Demographic Profile of Patients

Demographic Profile	Group A (Ho:YAG), n = 240	Group B (TFL), n = 238	*P*
Age in years (mean ± SD)	36.5 ± 12.52	38.62 ± 10.71	.45
Sex (male/female)	153/87	154/84	.28
Stone size in mm (mean ± SD)	8.9 ± 3.5	9.1 ± 3.2	.25
Stone density in HU (mean ± SD)	922 ± 241	918 ± 235	.82
Location of stone in percent (upper ureter/lower ureter)	40/60	39/61	.21

Ho, holmium; TFL, thulium fiber laser; YAG, yttrium aluminum garnet.

The incidence of postoperative ureteric strictures following ureteroscopic laser lithotripsy is shown in Table 3. Four (1.67%) patients in group A and 11 (4.62%) patients in group B developed ureteric strictures during follow-up, and the difference was statistically significant ($P < .001$). Majority of patients with strictures presented with flank pain and fever (75% in group A and 82% in group B). Asymptomatic progressive hydronephrosis was reported in 1 patient of group A and 2 patients of group B. The mean time of presentation following removal of DJ stent was 41 ± 19 days in group A and 39 ± 17 days in group B, and the difference was not significant ($P < .45$). Percutaneous nephrostomy tube placement was required to drain pyonephrosis and control sepsis in 3 patients of group A and 9 patients of group B. Strictures were predominantly located in the upper ureter in both the groups (75% in group A and 78% in group B). The mean length of stricture documented on CT urography/antegrade or retrograde pyelography was 2.67 ± 1.27 cm in group A and 4.42 ± 2.2 cm in group B, and the difference was statistically significant ($P < .001$).

Table 2. Intraoperative Parameters of the 2 Study Groups

Intraoperative Parameters	Group A (Ho:YAG), n = 240	Group B (TFL), n = 238	*P*
Operative time in minutes (mean ± SD)	47 ± 15	36 ± 13	.05
Laser time in minutes (mean ± SD)	13.5 ± 4.5	9.25 ± 3.2	.001
Laser energy spent in kJ/case (mean ± SD)	4.4 ± 1.2	3.12 ± 1.3	.23
Adverse events recorded (%)	15%	13.02%	.42
–Bleeding impairing vision	10%	8.82%	
–Visible mucosal ablation	8.75%	7.56%	
–Ureteric perforation	1.25%	0.84%	

Ho, holmium; TFL, thulium fiber laser; YAG, yttrium aluminum garnet.

Laser endoureterotomy was done to treat small passable strictures. One patient in each group had strictures amenable to laser endoureterotomy. Two patients in group A and 5 patients in group B required ureteroureterostomy to restore continuity of ureter. Short-segment lower ureteric strictures, 1 in group A and 2 in group B, required ureteroneocystostomy. One patient in group B with long-segment lower ureteric stricture required Boari flap reconstruction. Two patients in group B required nephrectomy for non-functional kidney; however, no nephrectomy was reported in group A.

Discussion

Ureteroscopic lithotripsy is considered as the gold standard treatment for ureteric stones. Conventional lithotripsy by pneumatic lithotripters had the problem of poor fragmentation of harder stones and retropulsion. Introduction of laser lithotripters has allowed the use of small-size uretroscopes, better vision because of good flow of irrigation fluid through ureteroscope, efficient fragmentation, and less retropulsion, thus reducing the operative time and the incidence of ureteric strictures.[6] Holmium:YAG laser became the gold standard in laser lithotripsy with its ability to fragment all kinds of stones and a better safety profile. Safety was attributed to its limited tissue penetration and high absorption coefficient in water, thus reducing the collateral damage.[7]

Table 3. Comparison of Ureteric Strictures in 2 Study Groups

Ureteric Strictures Following Procedure	Group A (Ho:YAG), n = 240	Group B (TFL), n = 238	*P*
Incidence of ureteric strictures, n (%)	4 (1.67%)	11 (4.62%)	.001
Presenting symptom, n (%)			.22
–Fever and pain	3 (75%)	9 (82%)	
–Asymptomatic progressive hydronephrosis	1 (25%)	2 (18%)	
Time of presentation following the removal of DJ stent, in days (mean ± SD)	41 ± 19	39 ± 17	.45.
Percutaneous nephrostomy tube placed, n (%)	3 (75%)	9 (81.81%)	.42
Location of stricture, n (%)			.35
–Upper ureter	3 (75%)	8 (72.72%)	
–Lower ureter	1 (25)	3 (27.27%)	
Mean length of stricture in cm (mean ± SD)	2.67 ± 1.27	4.42 ± 2.2	.001
Procedures done for ureteric strictures			
–Laser endoureterotomy	1	1	
–Ureteroureterostomy	2	5	
–Ureteroneocystostomy	1	2	
–Boari flap reconstruction	0	1	
–Nephrectomy	0	2	

DJ, double J; Ho, holmium; TFL, thulium fiber laser; YAG, yttrium aluminum garnet.

There are some flaws associated with the Ho:YAG laser generator. The generator requires an adequate cooling system that contributes to its large size. High-power Ho:YAG generator employs numerous crystal cavities to integrate the overall power output. These architectural anomalies result in an output beam that is multimodal and nonuniform with hotspots. This type of laser beam is difficult to precisely focus onto a small target and therefore demands the use of thicker optical fiber with a core diameter of 200 µm or larger.[8] The architecture of the Ho:YAG generator makes it susceptible to external shocks, leading to the misalignment of reflecting mirrors within the crystal cavity causing enduring damage to the generator and the optical fiber. These limitations paved the way for TFL into intracorporeal lithotripsy. The TFL uses a thin (10-20 µm core diameter) and long silica fiber doped with thulium ions. Multiple diodes are used to excite thulium ions. The final output beam has a wavelength of 1940 nm that can be operated in continuous or pulsed mode. The diode laser used for laser pumping has an emission spectrum that precisely matches the thulium ion absorption line. There is less heat dissipation and a potential to operate at high-power setting (>50 W) and higher frequencies (up to 2000 Hz). It uses small-sized fans for forced air cooling, reducing the size of the machine.[9]

Thulium fiber laser is an efficient lithotripter with 2 times faster fragmentation and 4 times superior dusting compared to the Ho:YAG laser. Schembri et al[10] reported that TFL attains high ablation rates and surpasses Ho:YAG laser over a range of different settings and ablation modes. The ability of TFL to operate at low pulse energy reduces retropulsion and need of ancillary procedures for residual stones. In our study, the mean operative time and mean laser time were less in the TFL group compared to the Ho:YAG laser group, and the difference was statistically significant. Besides efficient lithotripsy, better vision and less retropulsion by TFL may be the reason for less operative time compared to the Ho:YAG laser. The mean laser energy spent in lithotripsy did not differ in the 2 groups. Stone factors like density, composition, and size of the stone determine the mean laser energy spent during the procedure, and these factors were comparable in the 2 groups.

There is a significant variability about the ureteric stricture rate following ureteroscopic lithotripsy reported in the literature, with incidence ranging from 0.30% to 23.81%. Adiyat et al[11] and Li et al reported a stricture rate of 1.4% and 2.95%, respectively, following Ho:YAG laser lithotripsy, and the results are comparable with our study. The incidence of ureteric strictures in our study was reported to be higher in the TFL group as compared to the Ho:YAG laser group, and the difference was statistically significant. The TFL used for the procedure in our study was IPG photonics 50/500-QCW TFL. The TFL beam has a wavelength of 1940 nm, which is equivalent to the near-infrared absorption peak of water at 22°C. The absorption coefficient of the TFL is 14 mm^{-1}, which corresponds to the optical penetration depth of 0.077 mm in water and is much less than that of the Ho:YAG laser having an optical penetration depth of 0.4 mm.[12] These features

should add to the safety profile of the TFL, but what is the reason for clustering of stricture cases in our study that is predominantly related to TFL use? The answer needs to be dug out.

The intensity of the laser beam diminishes while travelling through a medium because of absorption, and the rate of decay in intensity is determined by the absorption coefficient of the material α. According to Beer–Lambert law, the intensity of laser beam diminishes exponentially with the depth as it travels through the medium.[13]

$I_z = I_0 e^{-\alpha z}$

where I_z is the intensity after penetrating the depth z, z is the depth penetrated, e ($e = 2.7182$) is the Euler's number, and α is the absorption coefficient of the material α.

According to this mathematical equation, the energy of a laser beam will decay by a factor of e (2.71828) while traversing each successive optical penetration depth of that medium. The energy of the Ho:YAG laser beam will be reduced to 37% of its energy at origin after travelling through a medium for a distance corresponding to its optical penetration depth. For TFL, energy will reduce to 1.7% of its energy at source after travelling the distance equivalent to the optical penetration depth of that medium. Practically after traversing 1 mm depth of water, the Ho:YAG laser pulse will possess about 4% of its energy at source, while the TFL beam will have a mere intensity of 0.00024% left with it after travelling the same distance. No doubt, the optical penetration depth of TFL is less compared to the Ho:YAG laser. Because of the logarithmical pattern of laser energy absorption in the tissue, the TFL energy is absorbed 16 000 times more than the Ho:YAG laser after travelling 1 mm depth. This high absorption coefficient reflects in low threshold for tissue ablation and more tissue damage in favor of TFL. The TFL has a natural "moses" potential attributed to its uniform pulse energy.[14] The depth traversed is again augmented by the "Moses" effect. The TFL pulse has a low threshold for tissue ablation and vapor channel initiation because of its high water absorption coefficient that translates into worse tissue damage in the ureter during laser lithotripsy.[15]

Another factor suggested for more stricture rate is the high temperature generated during TFL laser lithotripsy. Ureteric temperatures have exceeded physiological limits after TFL use at high-energy setting and low irrigation rate.[16] Lack of ureteric access sheath and poor return of irrigation fluid in rigid ureteroscopy are the obvious reasons for raised intrauretric temperature. The threshold temperature for cellular damage being 43°C is crossed within the first 1 second of laser use in the absence of adequate irrigation. Surgical factors increasing the chance of thermal ureteric injury are low irrigation flow, higher laser energy setting, and instrument use without access sheath.[17] Liang et al[18] reported a marked rise in the ureteric temperature at higher frequency compared to lower frequency setting at equal power. So these might be contributing factors to the high stricture rate in the TFL group. Tokas et al[19] studied the effect of rise in the intrauretric temperature during laser lithotripsy and its effect on the course of healing. At higher energy settings, TFL causes a marked rise in intrauretric temperature and worse tissue damage reflecting into dense scars on subsequent healing. They proposed brief on/off laser activation intervals, cold continuous irrigation, and use of access sheaths for better irrigation to maintain physiological intrauretric temperature.

The average length of stricture in our study was 2.67 ± 1.27 cm in the Ho:YAG group and 4.42 ± 2.2 cm in the TFL group. Larger stricture length in the TFL group can be attributed to low threshold for tissue ablation and more pronounced rise in the intrauretric temperature. Small-length upper ureteric strictures are well managed by ureteroureterostomy with excellent results.[20] Two patients in group A and 5 patients in group B needed ureteroureterostomy to restore the continuity of ureter. Laser endoureterotomy has a success rate of 62% for small-length ureteric strictures.[21] One patient in each group underwent laser endoureterotomy with successful outcome. Small-segment lower ureteric strictures are amenable to ureteroneocystostomy, while long-segment lower ureteric strictures require Boari flap reconstruction.[22] One patient in the Ho:YAG group and 2 in the TFL group required ureteroneocystostomy, while 1 patient in the TFL group required Boari flap reconstruction for long-segment lower ureteric stricture. Non-salvageable renal function with pyonephrosis was managed by nephrectomy in the TFL group.

Conclusion

There is a higher incidence of ureteric strictures following the use of TFL for ureteroscopic lithotripsy. Although projected as a safe laser, TFL should be used cautiously inside the ureter especially at higher power/frequency settings. Low energy at low frequency setting with continuous irrigation can reduce the incidence of ureteric strictures in TFL lithotripsy.

Ethics Committee Approval: *Ethical committee approval was received from the Ethical committee of Sher-i-Kashmir Institute of Medical Sciences Srinagar Jammu and Kashmir India (Approval number: IEC/Skims protocol #231E/2020).*

Informed Consent: *Written informed consent was obtained from patients who participated in this study.*

Peer-review: *Externally peer-reviewed.*

Author Contributions: *Concept – S.A.P.; Design – M.S.W.; Supervision – A.H.; Resources – S.A.M.; Materials – A.R.K.; Data Collection and/or Processing – S.A.P.; Analysis and/or Interpretation – A.H.; Literature Search – S.M.; Writing Manuscript – A.R.K.; Critical Review – M.S.W.*

Declaration of Interests: *The authors declare that they have no competing interest.*

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输尿管镜激光碎石术后输尿管狭窄的发生率：钬YAG激光与铥光纤激光

摘要

目的：本研究旨在比较钬：钇铝石榴石激光与铥光纤激光在输尿管镜激光碎石术后输尿管狭窄的发生率。在当前内镜器械小型化和光学性能提升的时代，输尿管内发射激光的安全性如何？

材料与方法：本研究为前瞻性对比研究，为期2年，纳入接受输尿管镜激光碎石术治疗输尿管结石的患者。患者随机分为两组：A组采用钬：钇铝石榴石激光碎石术，B组采用铥光纤激光碎石术。

结果：经过剔除不参与研究的患者和失访患者后，共纳入478例患者进行分析。其中240例接受钬：钇铝石榴石激光碎石术（A组），238例接受铥光纤激光碎石术（B组）。两组患者人口学资料基本一致。A组和B组患者的平均年龄分别为36.5±12.52岁和38.62±10.71岁。两组平均手术时间分别为47±15分钟和36±13分钟，激光治疗时间分别为13.5±45分钟和9.25±3.2分钟。随访期间，A组有4例（1.67%）患者出现输尿管狭窄，B组有11例（4.62%）患者出现，两组差异具有统计学意义（P <.001）。A组狭窄平均长度为2.67±1.27厘米，B组为4.42±2.2厘米，两组差异同样具有统计学意义。

结论：在输尿管镜激光碎石术中，铥光纤激光器与钬：钇铝石榴石激光器相比，发生输尿管狭窄的几率更高，而此前认为铥光纤激光器是安全的。

关键词：钽、YAG激光、铥光纤激光、输尿管狭窄、输尿管镜、输尿管尿道造口术

介绍

输尿管结石急性发作引发的剧烈腰痛是急诊科常见病例，多数患者需通过输尿管镜碎石术进行根治。该手术采用激光或气压式碎石器，能有效粉碎大块结石并完成碎石排石。在治疗输尿管狭窄方面，激光碎石技术已超越传统气压式碎石器，其回弹力更小，对各类结石的碎石效果更佳。[1]

钬酸钇铝石榴石（Ho：YAG）激光作为高效碎石器，可与软硬式输尿管镜兼容，一直被视为输尿管镜碎石术的金标准。[2]但由于钬酸钇铝石榴石激光器本身存在一些缺陷，铥

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为弥补传统激光碎石仪的不足，光纤激光（TFL）被引入临床应用。作为新型碎石设备，TFL在多个方面超越了钬：钇铝石榴石（Ho：YAG）激光器：其核心直径低至50μm的细光纤即可实现高效能量传输；可采用低至0.025焦耳的脉冲能量进行操作；(3)工作频率峰值可达2000赫兹；(4)其脉冲红外能量波长为1940纳米，吸收系数是Ho：YAG激光器的四倍，因此在碎石和组织消融方面具有更低的阈值。[3]比较研究表明，TFL的结石消融速度比Ho：YAG激光器快1.5-4倍。[4]通过小型尿道镜进行Ho：YAG激光碎石术时，相较于使用大型尿道镜配合刚性碎石器，输尿管狭窄的发生率显著降低。

激光对输尿管黏膜的热效应常导致黏膜消融及继发性狭窄。铥光纤激光器因其穿透深度较浅，曾被视为内镜碎石术的安全选择。但研究表明，当采用高频操作和低流量冲洗时，铥光纤激光器使输尿管温度升高幅度比钬：钇铝石榴石激光器高出9-12℃，从而对周围组织产生更大的热应力。[5]本研究通过对比输尿管镜碎石术中使用TFL和钬：钇铝石榴石激光器的输尿管狭窄发生率，探讨不同激光器的临床差异。

材料和方法

本研究为一项为期两年的前瞻性对比研究，于2020年1月至2021年12月在本院开展。研究纳入所有接受输尿管镜激光碎石术治疗的输尿管结石病例。患者经计算机断层扫描（CT）尿路造影评估后，计划接受输尿管镜激光碎石术治疗。患者随机分组接受Ho：YAG激光（Lumenis脉冲100H Ho激光，A组）或TFL激光（IPG photonics 50/500-QCW，B组）碎石治疗。所有患者均签署书面知情同意书，本研究已获得印度查谟和克什米尔地区斯利那加舍尔-克什米尔医学科学研究所伦理委员会批准，批准号为IEC/Skims协议#231E/2020。研究对象既往曾接受过体外冲击波碎石术、输尿管镜检查或开放手术治疗的患者

要点

- *与钬铝石榴石（Ho：YAG）激光相比，铥光纤激光在碎石和组织消融方面具有更低的阈值。*
- *虽然铥光纤激光（TFL）的光穿透深度比Ho：YAG激光低，但当穿透1毫米组织深度后，TFL能量被吸收的量是Ho：YAG激光的16 000 倍，这导致TFL出现严重的组织烧蚀。*
- *在输尿管镜激光碎石术中，铥光纤激光器引发输尿管狭窄的风险高于钬：钇铝石榴石激光器。*
- *使用铥光纤激光治疗输尿管时，应采用低能量、低频设置，并配合持续冲洗，操作需格外谨慎。*

本研究排除了输尿管患者，同时排除了有泌尿生殖道狭窄、子宫内膜异位症、腹膜后纤维化或肾盂肾炎病史的患者。

输尿管镜检查在脊髓麻醉下进行，采用6/7.5 Fr半刚性输尿管镜，通过连续灌注和脉冲灌注球进行生理盐水冲洗。两组手术步骤相同，仅激光类型不同。两组均使用200 μ m光纤传输激光能量。碎石术初始能量为0.4焦耳、频率8赫兹，若碎石效果不佳则逐步增加能量。碎石后用镊子取出较大结石碎块，并在手术结束时置入双J型支架。通过X光透视确认结石清除及支架置入情况。术后2周进行肾输尿管膀胱造影（KUB）复查残留碎石。双J支架于术后4周取出，取出支架6周后进行腹部超声检查，观察是否残留肾积水。发热、腰痛、输尿管肾积水加重或梗阻性尿路病变患者需行CT尿路造影检查狭窄情况。出现肾脓肿或尿脓毒症的患者需行经皮肾造瘘管置入术。通过CT尿路造影（图1）、平卧位逆行肾盂造影（图2）和直立位肾盂造影（图3）评估输尿管狭窄的长度和部位。所有输尿管狭窄患者均接受$^{锝-99}$乙二胺五乙酸（DTPA）显像扫描以量化肾功能。根据狭窄长度、部位及肾功能可挽救性，患者将接受输尿管内切开术、输尿管吻合术（图4）、输尿管肾造瘘术、博亚里瓣修复术或肾切除术。术后3个月通过$^{锝-99}$DTPA对接受治疗的输尿管狭窄患者进行随访。



图1.计算机断层扫描尿路造影：重建图像显示因上尿路狭窄导致的右侧输尿管肾积水。

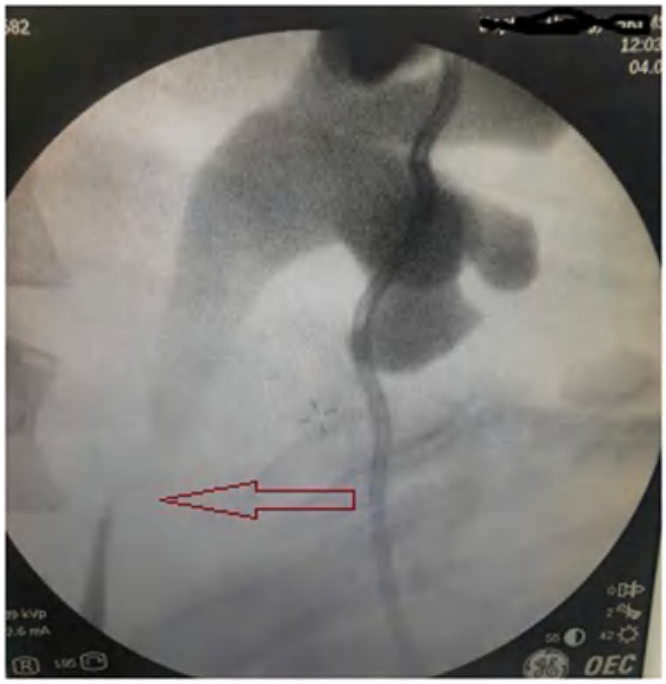


图2.前向与逆行肾盂造影显示狭窄部位长度（红色箭头）。

采用扫描和CT尿路造影进行检查。统计分析使用社会科学统计软件包（SPSS）22.0版（IBM SPSS公司，美国纽约州阿蒙克市）完成。定性数据以数量和百分比呈现，定量数据则以均值（标准差）表示。通过统计学方法评估了定量数据的正态分布情况。



图3.左侧顺行肾盂造影显示上尿路完全闭塞。

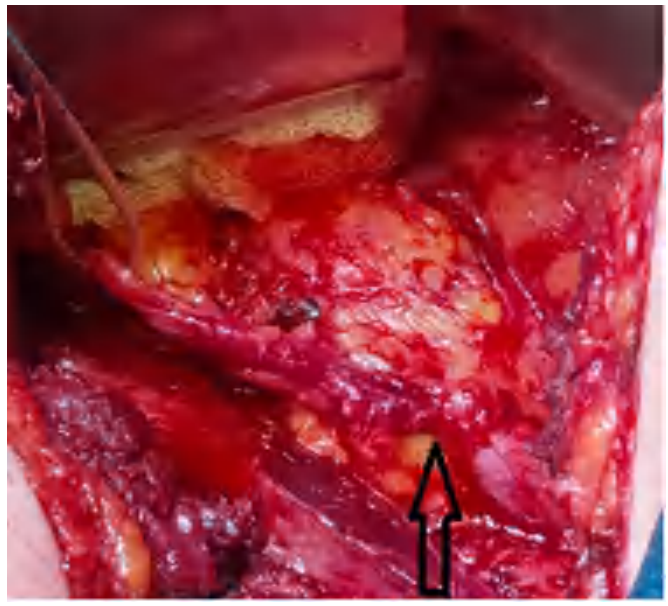


图4.上尿路狭窄术中影像（黑色箭头所示）。

采用独立样本*t*检验。使用卡方检验比较组间定性变量。任何参数的统计学显著性定义为*P*值<.05。

结果

2020年1月至2021年12月期间，共有540名输尿管结石患者计划接受输尿管镜激光碎石术。其中21人拒绝参与研究，另有30名患者因不符合研究条件被排除。剩余489名患者被随机分为两组：A组（246人）接受Ho：YAG激光碎石术，B组（243人）接受TFL碎石术。研究期间，A组6人和B组5人失访。图5以《临床试验报告统一标准》图表形式展示了本研究的实施阶段。

我们研究组的人口学特征详见表1，两组间未发现统计学显著差异。A组和B组女性比例分别为36.25%和35.29%。两组患者的平均年龄分别为36.5±12.52岁和38.62±10.71岁，差异无统计学意义（*P*=0.45）。两组患者接受手术前的平均等待时间分别为7.5±1.5天和8±2.5天，差异同样无统计学意义。A组结石平均大小为8.9±3.5毫米，B组为9.1±3.2毫米（*P*=0.25）。两组结石密度分别为922±241亨氏单位（HU）和918±235 HU（*P*=0.82），结石参数两组基本一致。两组患者输尿管上段（髂血管交叉以上）结石占比分别为40%和39%（*P*=0.21）。

两组术中参数见表2，A组与B组平均手术时间分别为47±15分钟和36±13分钟，差异无统计学意义

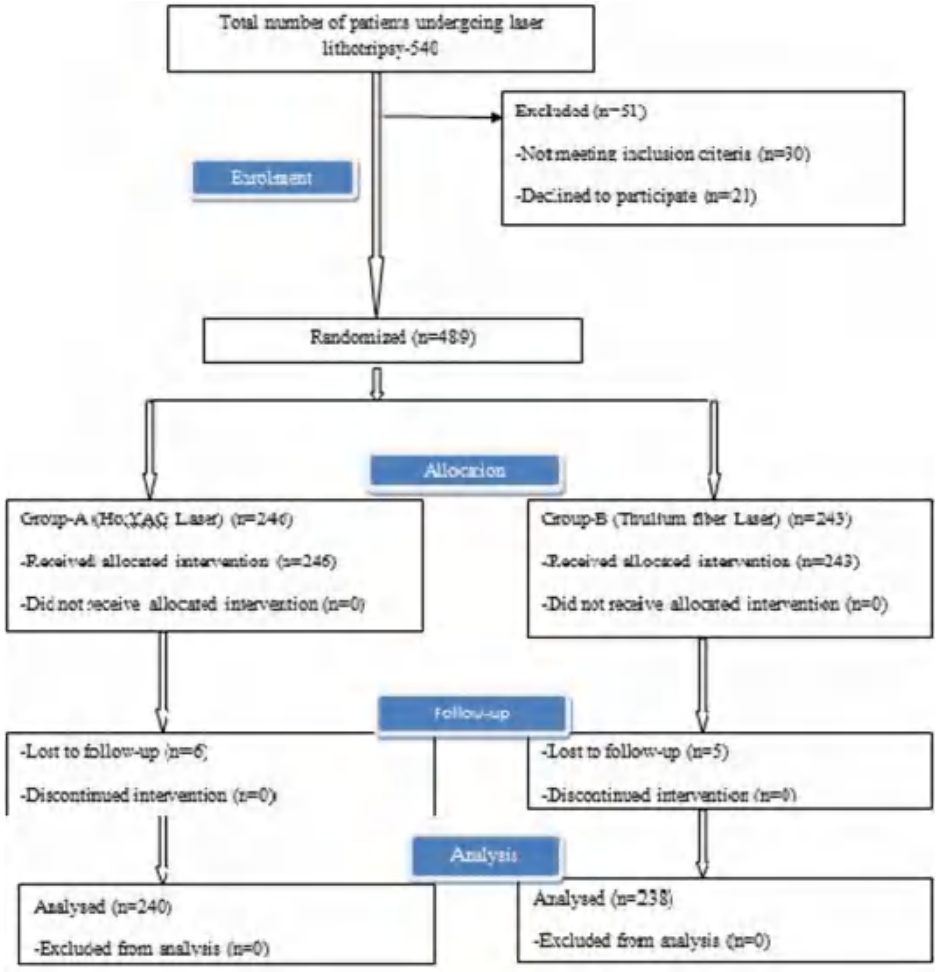


图5.本研究在《临床试验报告统一标准》（CONSORT）框架中的各阶段示意图。

统计学显著性（*P*<0.05）。A组平均激光治疗时间为13.5±4.5分钟，B组为9.25±3.2分钟，两组差异具有统计学显著性（*P*<0.001）。A组48%的患者和B组37%的病例在初始低能量设置下仍需通过频率和能量增强才能达到理想的碎石效果，两组差异具有统计学显著性（*P*<0.05）。A组和B组每例平均激光能量消耗分别为4.4±1.2kJ和3.12±1.3kJ，差异无统计学显著性（*P*<0.23）。A组15%的患者和B组13.02%的患者出现不良事件记录。

表1.患者人口统计学特征

人口统计学资料	A组（Ho：YAG），n=240	B组（TFL），n=238	*P*
年龄（岁，平均值±SD）	36.5 ± 12.52	38.62 ± 10.71	.45
性别（男/女）	153/87	154/84	.28
石块尺寸（mm，平均值±标准差）	8.9 ± 3.5	9.1 ± 3.2	.25
HU中的结石密度（平均值±标准差）	922 ± 241	918 ± 235	.82
结石位置百分比（上输尿管/下输尿管）	40/60	39/61	.21

Ho，钬；TFL，铥光纤激光器；YAG，钇铝石榴石。

术中包括影响视力的出血（A组10%，B组8.82%）、可见的粘膜消融（A组8.75%，B组7.56%）和输尿管穿孔（A组1.25%，B组0.84%）。差异无统计学意义（*P*<.42）。

表3显示了输尿管镜激光碎石术后输尿管狭窄的发生率。A组4例（1.67%）患者和B组11例（4.62%）患者在随访期间出现输尿管狭窄，差异具有统计学意义（*P*<0.001）。多数狭窄患者表现为腰痛和发热（A组75%，B组82%）。A组1例、B组2例患者报告出现无症状进行性肾积水。A组患者取出DJ支架后平均就诊时间为41±19天，B组为39±17天，差异无统计学意义（*P*<0.45）。A组3例、B组9例患者需经皮肾造瘘引流脓肾和控制脓毒症。两组狭窄部位主要位于输尿管上段（A组75%，B组78%）。CT尿路造影/顺行或逆行肾盂造影显示的狭窄平均长度分别为A组2.67±1.27厘米、B组4.42±2.00厘米。B组为2 cm，差异具有统计学意义（*P*<.001）。

表2.2组研究的术中参数

术中参数	A组（Ho：YAG），n=240	B组（TFL），n=238	*P*
手术时间（分钟，平均值±SD）	47 ± 15	36 ± 13	.05
激光时间（分钟，平均值±SD）	13.5 ± 4.5	9.25 ± 3.2	.001
每例激光能量消耗（kJ，平均值±标准差）	4.4 ± 1.2	3.12 ± 1.3	.23
记录的不良事件（%）	15%	13.02%	.42
-出血影响视力	10%	8.82%	
–可见粘膜消融	8.75%	7.56%	
输尿管穿孔	1.25%	0.84%	

Ho，钬；TFL，铥光纤激光器；YAG，钇铝石榴石。

为治疗可经尿道通过的小型狭窄，我们采用激光输尿管内切术。A组和B组各有一例适合进行激光输尿管内切术的狭窄病例。A组有2例、B组有5例患者需要通过输尿管尿路吻合术来恢复输尿管连续性。A组1例、B组2例短节段下尿路狭窄患者需行输尿管肾囊吻合术。B组1例长节段下尿路狭窄患者需进行博阿里瓣重建术。B组2例因肾功能不全需行肾切除术，而A组未报告此类病例。

讨论

输尿管镜碎石术是治疗输尿管结石的金标准疗法。传统气压碎石器存在碎石效果差、结石易反冲等缺陷。随着激光碎石器的问世，不仅可使用更小型的输尿管镜，还能通过优化的碎石流获得更清晰的视野。

表3.2个研究组输尿管狭窄的比较

术后输尿管狭窄	A组（Ho：YAG），n=240	B组（TFL），n=238	*P*
输尿管狭窄发生率，n（%）	4 (1.67%)	11 (4.62%)	.001
首发症状，n（%）			.22
发烧和疼痛	3 (75%)	9 (82%)	
–无症状进行性肾积水	1 (25%)	2 (18%)	
取出DJ支架后症状出现的时间（天，平均值±标准差）	41 ± 19	39 ± 17	.45.
置入经皮肾造瘘管，n（%）	3 (75%)	9 (81.81%)	.42
狭窄部位，n（%）			.35
–上输尿管	3 (75%)	8 (72.72%)	
–下输尿管	1 (25)	3 (27.27%)	
狭窄平均长度（cm，平均值±SD）	2.67 ± 1.27	4.42 ± 2.2	.001
为以下对象执行的流程			
输尿管狭窄			
–激光内镜下子宫内膜切除术	1	1	
–Ureteroureterostomy	2	5	
–Ureteroneocystostomy	1	2	
-髋臼唇重建术	0	1	
-肾切除术	0	2	

DJ，双J；Ho，钬；TFL，铥光纤激光器；YAG，钇铝石榴石。

通过输尿管镜进行碎石时，该技术能有效碎石且反冲力较小，从而缩短手术时间并降低输尿管狭窄的发生率。[6]钇铝石榴石（Holmium：YAG）激光因其能碎裂各类结石且安全性更高，已成为激光碎石术的金标准。其安全性源于组织穿透深度有限且在水中吸收系数高，从而减少附带损伤。[7]

钬：钇铝石榴石（Ho：YAG）激光器存在若干缺陷。该设备需要配备完善的冷却系统，这也导致其体积较大。高功率Ho：YAG激光器采用多个晶体腔来整合整体功率输出，这种结构缺陷会导致输出光束呈现多模态且分布不均，形成热点区域。此类激光束难以精确聚焦于小目标，因此需要使用芯径200μm或更大的粗光纤。[8]该激光器的结构使其容易受到外部冲击影响，可能导致晶体腔内反射镜错位，进而对激光器和光纤造成永久性损伤。这些局限性促使了铥光纤（TFL）在体内碎石术中的应用。TFL采用掺铥离子的纤细（10-20μm芯径）长硅光纤，通过多个二极管激发铥离子。最终输出光束波长为1940 nm，可实现连续或脉冲工作模式。用于激光泵浦的二极管激光器具有与铥离子吸收线精确匹配的发射光谱。它具有较少的热量散发，且具有在高功率设置（>50W）和更高频率（高达2000Hz）下运行的潜力。它使用小型风扇进行强制空气冷却，从而减小了机器的尺寸。[9]

铥光纤激光器是一种高效的碎石设备，其碎石速度比钬：钇铝石榴石（Ho：YAG）激光器快两倍，碎石粉尘量更是高出四倍。Schembri等学者[10]研究表明，TFL在不同参数设置和碎石模式下均能实现高消融效率，性能超越Ho：YAG激光器。TFL采用低脉冲能量工作模式，有效减少了碎石后反冲现象，也无需额外处理残留结石。本研究数据显示，TFL组的平均手术时间和激光治疗时间均显著短于Ho：YAG组，且差异具有统计学意义。除高效碎石外，TFL更佳的视野清晰度和更低反冲率可能是缩短手术时间的关键因素。两组在碎石过程中平均激光能量消耗无显著差异。结石的密度、成分及大小等特性决定了术中平均激光能量消耗，而这些参数在两组间具有可比性。

文献报道的输尿管镜碎石术后输尿管狭窄发生率差异显著，其发生率范围介于0.30%至23.81%之间。Adiyat等[11]和Li等分别报道Ho：YAG激光碎石术后狭窄发生率为1.4%和2.95%，与本研究结果具有可比性。本研究中TFL组的输尿管狭窄发生率较Ho：YAG激光组显著升高，且差异具有统计学意义。本研究采用的TFL设备为IPG光子学50/500-QCW TFL，其波长1940nm与22℃水体近红外吸收峰波长一致。TFL的吸收系数为14mm $^{-1}$，对应水体中光穿透深度0.077mm，远低于Ho：YAG激光0.4mm的光穿透深度。[12]这些特性表明

应有助于完善TFL的安全性特征，但本研究中狭窄病例的聚集现象主要与TFL使用相关，其成因尚需进一步探究。

激光束在介质中传播时，由于吸收作用，其强度会逐渐衰减，衰减的快慢由材料的吸收系数决定 α。根据比尔-朗伯定律，激光束的强度会随着在介质中传播的深度增加呈指数衰减。[13]

$$I_z = I_0 e^{-\alpha z}$$

其中z是穿透深度后的强度，z是穿透深度，

根据这个数学方程，激光束的能量在穿透介质的每个连续光学穿透深度时会衰减e（2.71828）倍。当Ho：YAG激光束穿过相当于其光学穿透深度的介质后，其能量将降至初始值的37%。而TFL激光在相同穿透深度下，能量仅剩1.7%。实际应用中，Ho：YAG激光脉冲在水下1毫米深度后，能量仅剩约4%；而TFL光束在相同深度后，强度仅剩0.00024%。显然，TFL的光学穿透深度远低于Ho：YAG激光。由于激光能量在组织中的吸收呈现对数衰减特性，TFL在1毫米深度后被吸收的能量是Ho：YAG的16 000倍。这种高吸收系数使得TFL在组织消融方面具有更低的阈值和更强的组织损伤效果。TFL脉冲因其均匀的能量分布而具有天然的“摩西效应”特性。[14]这种效应能显著增强其穿透深度。由于TFL脉冲具有高吸水系数，其组织消融阈值和气道形成阈值较低，这使得在输尿管激光碎石术中对组织的损伤程度更严重。[15]

TFL激光碎石术中产生的高温是导致狭窄率升高的另一个潜在因素。当使用高能量设置和低冲洗速率时，输尿管温度会超过生理极限。[16]无输尿管套管且刚性输尿管镜冲洗液回流不良，是导致输尿管内温度升高的主要原因。若未充分冲洗，在激光使用最初1秒内温度就会突破43℃的细胞损伤临界值。增加热性输尿管损伤风险的手术因素包括：冲洗流量不足、激光能量设置过高以及未使用套管进行器械操作。[17] Liang等[18]研究者发现，在功率相同的情况下，高频设置会导致输尿管温度显著升高。这些因素可能是TFL组狭窄率较高的促成因素。Tokas等[19]研究者则探讨了输尿管内温度升高对激光碎石术愈合进程的影响。当能量设置较高时，TFL会导致尿道内温度显著升高，造成更严重的组织损伤，愈合后会形成致密瘢痕。为此，研究者建议采用短时激光开关模式、持续冷冲洗，并使用导管鞘辅助冲洗，以维持尿道内生理温度。

本研究显示，Ho：YAG组的平均狭窄长度为2.67±1.27厘米，TFL组则为4.42±2.2厘米。TFL组狭窄长度更大的原因在于组织消融阈值较低，且尿道内温度升高更为显著。对于短段上尿路狭窄，输尿管吻合术能取得良好疗效。A组有2例、B组有5例患者需通过输尿管吻合术恢复尿路通畅。激光输尿管吻合术对短段尿路狭窄的成功率为62%，[21]两组各有1例患者接受该术式并获得成功。[22]短段下尿路狭窄可采用输尿管膀胱吻合术，而长段下尿路狭窄需进行博阿里瓣重建。Ho：YAG组有1例、TFL组有2例患者需行输尿管膀胱吻合术，TFL组另1例因长段下尿路狭窄需采用博阿里瓣重建。对于伴有肾盂肾炎的不可逆肾功能衰竭，TFL组采取肾切除术进行治疗。

结论

在输尿管镜碎石术中使用TFL激光时，输尿管狭窄的发生率较高。尽管TFL被视作安全激光，但在输尿管内操作时仍需谨慎，尤其在高功率/高频设置下。采用低能量、低频设置并配合持续冲洗，可有效降低经尿道碎石术中输尿管狭窄的发生率。

伦理委员会批准：*已获得印度查谟和克什米尔斯利那加尔谢尔-克什米尔医学科学研究所伦理委员会的批准（批准编号：IEC/Skims方案编号231E/2020）。*

知情同意：*从参与本研究的患者处获得书面知情同意。*

同行评审：*外部同行评审。*

作者贡献：*概念——S.A.P.；设计——M.S.W.；监督——A.H.；资源——S.A.M.；材料——A.R.K.；数据收集和/或处理——S.A.P.；分析和/或解释——A.H.；文献检索——S.M.；撰写论文——A.R.K.；批判性审查——M.S.W.*

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TOPIC PAPER

The heat is on: the impact of excessive temperature increments on complications of laser treatment for ureteral and renal stones

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Abstract

Objective Technological advancements in the field of urology have led to a paradigm shift in the management of urolithiasis towards minimally invasive endourological interventions, namely ureteroscopy and percutaneous nephrolithotomy. However, concerns regarding the potential for thermal injury during laser lithotripsy have arisen, as studies have indicated that the threshold for cellular thermal injury (43 °C) can be exceeded, even with conventional low-power laser settings. This review aims to identify the factors that contribute to temperature increments during laser treatment using current laser systems and evaluate their impact on patient outcomes.

Materials and methods To select studies for inclusion, a search was performed on online databases including PubMed and Google Scholar. Keywords such as 'temperature' or 'heat' were combined with 'lithotripsy', 'nephrolithotomy', 'ureteroscopy', or 'retrograde intrarenal surgery', both individually and in various combinations.

Results Various strategies have been proposed to mitigate temperature rise, such as reducing laser energy or frequency, shortening the duration of laser activation, increasing the irrigation fluid flow rate, and using room temperature or chilled water for irrigation. It is important to note that higher irrigation fluid flow rates should be approached cautiously due to potential increases in intrarenal pressure and associated infectious complications. The utilization of a ureteral access sheath (UAS) may offer benefits by facilitating irrigation fluid outflow, thereby reducing intrapelvic pressure and intrarenal fluid temperature.

Conclusion Achieving a balance between laser power, duration of laser activation, and irrigation fluid rate and temperature appears to be crucial for urologists to minimize excessive temperature rise.

Keywords Urolithiasis · Endourology · Thermal Injury · Laser Lithotripsy

Introduction

Urolithiasis is a commonly encountered urological disorder, with a prevalence estimated to be between 1 and 15%. The occurrence of urolithiasis varies globally and has shown a steady rise over the past decades [1]. Medical management has proven to be insufficient for most cases of urinary stones, with surgical intervention being the primary method of treatment for symptomatic patients. While open lithotomy was once the preferred surgical approach, technological advancements have shifted the standard of care to minimally invasive endourological interventions, such as ureteroscopy and percutaneous nephrolithotomy. Shock wave lithotripsy is also considered a viable option for treating upper urinary tract stones [2].

The use of laser technology in urology dates back to Pearsons et al.'s initial experiment, where they demonstrated the effects of laser on a dog's bladder. Mulvany et al. subsequently conducted research on urinary stone fragmentation using a ruby crystal laser. However, the ruby laser proved ineffective in urology, as it produced excessive heat and vaporized stones. Over time, pulsed-wave lasers, such as Nd: YAG (FREDDY) and holmium:yttrium–aluminum-garnet (Ho: YAG), were introduced and have since become very important armamentarium in urology [3].

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The threshold for cellular thermal injury is known to be 43° C and has been observed to be exceeded, even with conventional low-power laser settings, in models of renal calices and ureters. Factors such as the duration of laser activation, the quantity of irrigation fluid used, and the laser pulse energy and frequency can all contribute to cumulative heat production and, consequently, potential tissue injury during lithotripsy [4].

Through this review, we seek to identify the factors that contribute to temperature increments during laser treatment using current laser systems and evaluate their impact on patient outcomes. By doing so, we hope to develop strategies to mitigate these situations and minimize the risk of complications associated with laser treatment for urolithiasis.

Materials and methods

For our study selection, we conducted online searches through PubMed and Google Scholar with no time restrictions, using keywords such as 'temperature' or 'heat' in combination with 'lithotripsy', 'nephrolithotomy', 'ureteroscopy', or 'retrograde intrarenal surgery', both alone and in combination. We also scanned the references in all included studies to identify any additional sources of information that could be relevant to our investigation. To ensure the consistency of our findings, we restricted the language of the eligible studies to English. All current studies related to temperature rise during lithotripsy with consistent results and studies related to prevent temperature rise were included the study. Reviews of the related topics were excluded from the study. Author and year of the studies, part of urinary system assessed for temperature rise, models for the experiments, type of laser, laser fiber size, laser settings, duration of activation of laser, irrigation fluid flow rate, and temperature status were recorded.

Literature review

Type of laser and temperature

In another study, Molina et al. [2] investigated the temperature profiles of two laser systems, the 120 W Ho: YAG (model P120, Lumenis Ltd., Israel) and the 60 W SPTF (SOLTIVETM, Olympus, MA), during ureteral lithotripsy using an ex vivo porcine kidney and ureter model. The irrigation was conducted with saline at room temperature (27 °C) using a manual pumping system. The authors reported that both laser systems' temperature profiles remained below the threshold for potential cellular injury (43 °C) during the experiments. Moreover, at dusting settings (0.3 J, 70 Hz, Long Pulse), the Ho: YAG laser's median temperature increase was higher than that of the SPTF laser (40.6 °C vs. 35.8 °C, respectively, $p = 0.064$).

Belle et al. [6] investigated the temperature differences between thulium fiber laser (TFL) and Ho: YAG lasers during ureteral stone lithotripsy. TFL was found to produce the highest temperature at all laser settings of 3.6 W, 10 W, and 30 W compared to the 30 W Medilas H Solvo HL (Dornier, Munich, Germany) and 100 W Empower HL (Olympus, MA) lasers. There was no significant difference between the TFL (40.93 °C) and the Empower HL (41.17 °C, $p > 0.05$) at 20 W. At 30 W, the TFL produced a significantly high maximum temperature of 44.37 °C and exceeded the threshold.

Hardy et al. [10] compared the effects of Ho: YAG and TFL on temperatures in an in vitro ureteral model. They used Ho: YAG laser at 600 mJ, 350 µs, 6 Hz, and TFL at 35 mJ, 500 µs, 150–500 Hz settings. Saline irrigation flow rates were 22.7 ml/min for TFL and 13.7 ml/min for Holmium laser. They found a mean peak irrigation fluid temperature of 24 ± 1 °C for Holmium and 33 ± 3 °C, 33 ± 7 °C, and 39 ± 6 °C for TFL at pulse rates of 150, 300, and 500 Hz, respectively. The researchers concluded that to avoid excessive thermal rise and provide a sufficient safety margin, TFL lithotripsy should be performed with pulse rates under 500 Hz and/or with increased irrigation rates.

In another experimental study, Sierra et al. [15] compared the safety of Ho: YAG and TFL in an in vivo porcine model and in vitro ureteral model. The temperature reached 40.2 °C with TFL and 41 °C with Ho: YAG laser at max 20W power with gradually decreased irrigation (40 cmH_2O continuous).

Similarly, Taratkin et al. [16] investigated the temperature profile between Ho: YAG laser and a novel TFL during laser lithotripsy in an in vitro model. The researchers reported that both lasers yielded similar temperature increases, and the amount of energy used was equivalent to the amount of heat introduced into the system. Temperature increase at 20W without irrigation was 10.9 ± 0.5 °C for Ho: YAG and 11.0 ± 0.5 °C for super-pulsed TFL.

Laser settings, irrigation flow rate and temperature

In their study, Wollin et al. [1] examined the impact of laser settings and irrigation flow rates on ureteral temperature during ureterolithotripsy in an in vitro setting. Specifically, they utilized a 200 µm laser with varying pulse energies and frequencies (0.2 J/50 Hz, 0.6 J/6 Hz, 0.8 J/8 Hz, 1 J/10 Hz, and 1 J/20 Hz) for a duration of 60 s within a tubing system that allowed for specified room temperature flow rates (100, 50, and 0 mL/minute). Their findings indicated that at an irrigation rate of 100 mL/min, only the highest laser setting (1 J/20 Hz) produced a maximum temperature of 30.7C, which was deemed clinically insignificant. However, with no irrigation fluid flow, all maximum temperatures exceeded the

threshold for cellular thermal injury (43 °C). Furthermore, at the highest laser setting (1 J/20 Hz) with no irrigation, the maximum temperature exceeded 100 °C in their study [1].

Molina et al. [3] investigated the temperature profile of Ho: YAG laser lithotripsy in the urinary tract of Ovis Aries (sheep) with and without irrigation. They reported that the temperature rise was significantly higher in the intact ureteral model without irrigation compared to with irrigation, with temperatures of 49.5 ± 2.3 °C versus 37.4 ± 2.5 °C, respectively.

Aldoukhi et al. [5] investigated the caliceal fluid temperature during high-power Ho: YAG lithotripsy in an in vitro porcine model. They used the Ho: YAG laser at a 0.5 J × 80 Hz = 40 W setting with high, medium, or no irrigation. The peak temperatures for no, medium, and high irrigation were 84.8 °C, 63.9 °C, and 43.6 °C, respectively.

Hein et al. [11] utilized an in vitro model to simulate the renal pelvis and assess the changes in temperature during Ho: YAG lithotripsy. The results indicated that without irrigation, laser application led to a rapid temperature rise of up to Δ28 K, increasing to 68 °C at 100 W. However, higher irrigation rates resulted in a lower temperature increase. At the highest irrigation rates of 100 ml/min and the highest laser power setting (100 W), the temperature increased by only 5 K.

Teng et al. [17] conducted a study to assess the changes in irrigation fluid temperature in renal calyces during Ho: YAG lithotripsy using flexible URS in a real-life scenario. The authors found that at a power setting of 1 J/20 Hz and an irrigation flow rate of 15 ml/min, the temperature rise was significantly higher than other groups. Moreover, the temperature increase was significantly higher in groups with lower irrigation flow rates at the same laser settings. The time required to reach a temperature of 43 °C at 1 J/20 Hz was significantly shorter than that at 0.5 J/20 Hz when there was no irrigation.

In another study, Winship et al. [19] investigated the temperature rise in a benchtop ureteral model using both flexible and semi-rigid ureteroscopes with Ho: YAG laser. Laser energy was delivered at various settings, and with irrigation at 100 mm Hg using the semi-rigid scope, 1 J/20 Hz was the only laser setting to produce a temperature rise over 6 °C. The temperature returned to close to baseline levels within 2 s after laser cessation.

Aldoukhi et al. [4] investigated the effect of pedal activation on fluid temperature and thermal profiles in an in vitro experimental caliceal model using the Ho: YAG laser (pulse120; Lumenis). They reported that longer pedal activation times led to higher peak temperatures and thermal effects. The thermal injury threshold (43 °C) was reached in 9 s when 40 W was applied at 50% operator duty cycle (ODC = lasing time/lithotripsy time) with laser activation patterns of 30 s on/off and 15 s on/off.

Wriedt et al. [20] evaluated tissue heating with magnetic resonance imaging in an ex vivo porcine kidney model using different lithotripsy parameters. The authors reported that an irrigation rate of at least 70 ml/min is necessary to avoid exceeding 120 min CEM_{43} when using a laser application of 30 W for 10 s. Additionally, they observed a focal temperature rise on the calyx wall in experiments with human stones, which they attributed to non-elimination of heated fragmented stone pieces from the surgical area in the kidney.

Pelvicalyceal volume and temperature

Khajeh et al. [13] studied the relationship between pelvicalyceal volume and temperature rise during Ho: YAG laser lithotripsy. The findings showed that the temperature elevation and thermal dose from laser activation were inversely related to the fluid volume in each model and the irrigation rate. The safe temperatures below the threshold of tissue injury were obtained at an irrigation rate of 40 mL/min during 1 min of continuous laser activation in all models [13].

Types of pulse modulation and temperature

In a study by Peteinaris et al. [14], the effects of the newly introduced Holmium pulse modulation system MOSES were compared with conventional pulse delivery technology on irrigation fluid temperature (IFT) during flexible ureteroscopy in a live-anesthetized porcine model. The study considered the threshold for a dangerous IFT as 54 °C. The results revealed that both the MOSES and conventional laser activation at 60 W led to a significant temperature rise, exceeding the safety threshold of 54 °C in approximately 10 s and reaching a hazardous temperature of 66.4 °C in 18 s under gravity irrigation. However, the IFT did not exceed 54 °C at any settings with manual pump irrigation.

Winship et al. [18] investigated the effect of pulse type of Ho: YAG (short pulse (SP), long pulse (LP), MOSES contact (Mc), MOSES distance (MD)) on irrigation fluid in an experimental ureteral model. The authors reported that LP produced the greatest temperature change from baseline at a 1 J/20 Hz setting, and thermal dose exceeded the injury threshold for all pulse types in < 3 s of activation at the same setting.

Formula to suggest temperature rise

In a separate study, Hein et al. [12] examined the thermal effects of Ho: YAG laser during retrograde intrarenal surgery and percutaneous nephrolithotomy in an ex vivo porcine kidney model. The researchers suggested a formula to calculate temperature changes with irrigation rates higher than 30 ml/min: ΔT = 15 K × (power [W]/ irrigation [ml/min]) based on their results.

Lastly, Williams et al. [21] developed a mathematical model to predict laser-induced temperature alterations in a kidney during lithotripsy. The model was based on renal volume, irrigation flow rate, irrigation fluid temperature, and laser power. The researchers cautioned clinicians to use room temperature irrigation fluids for irrigation and avoid extensive laser usage. They also suggested altering the irrigation fluid rate by adjusting the inflow (i.e., pressured irrigation fluid) or outflow (i.e., usage of UAS).

Possible preventive measures for temperature rise

In their study, Dau et al. [7] investigated the effect of chilled irrigation on caliceal fluid temperature and time to reach the thermal injury threshold in an in vitro model. The experiments utilized a 120 W Ho:YAG laser (pulse120; Lumenis, CA) at a 0.5 J · 80 Hz (40 W) setting in short pulse mode for 60 s. The thermal injury threshold was reached in 28 s with room temperature (19 °C) irrigation and in 33 s with chilled irrigation (1 °C) with a flow rate of 8 mL/min. With 12 mL/min irrigation, the threshold was reached in 46 s with room temperature irrigation, but it was not reached with chilled irrigation. In another study, they evaluated and compared the thermal effects of chilled irrigation (4 °C–1 °C), room temperature (RT) (20 °C–1 °C), and warm (WM) irrigation (37 °C–1 °C) during ureteroscopy with laser activation in an in vivo porcine model. The researchers concluded that irrigation with chilled saline during ureteroscopic laser lithotripsy decelerates temperature rise, decreases peak temperature, and lengthens the time to thermal injury compared with irrigation with room temperature or warm saline solutions [7].

In their study, Gallegos et al. [8] reported that using a ureteral access sheath (UAS) provides lower intrarenal temperatures regardless of laser configuration and irrigation solution height. The rise in temperature obtained per minute with an irrigation height of 50 cm H_2O, an energy of 1 J, and a frequency of 15 Hz was higher when UAS was not utilized (5.8 °C versus 3.8 °C) [8]. Similarly, Noureldin et al. [9] investigated the effects of irrigation rates and UAS size on intrarenal temperature during flexible ureteroscopy in a live-anesthetized porcine model. They found that fURS under gravity irrigation (the fluid bag at 1 m over the operation table) without UAS was associated with hazardous intrarenal temperatures (54 °C) even at a laser power as low as 20 W for as short as 20 s of laser activation. With pump irrigation, if the laser was activated at the highest power setting (60 W) for 60 s, the intrarenal temperature remained on the safe side, even without the use of UAS [9] (Table 1).

Discussion

Numerous studies have been conducted on temperature changes during laser lithotripsy using various experimental models and lasers. There are several factors that may contribute to temperature rise, including the type of laser, laser settings (high power, high frequency), irrigation fluid rate, laser activation time, amount of fluid in the space, and stone particles collecting heat during lithotripsy. The two main lasers currently used in endoscopic lithotripsy are Ho: YAG and Thulium lasers, and each laser system has undergone several modifications over the years. The power of these lasers has increased significantly, and the most recent innovations in lasers for lithotripsy include pulse modulation using MOSES technology for Ho: YAG and pulsed Thulium YAG lasers, as well as Thulium fiber lasers.

Increased power leads to higher temperature rise, and clinicians must balance multiple variables to avoid adverse effects. To mitigate temperature rise, modifications such as decreasing the laser energy or frequency, decreasing the duration of laser activation, increasing the irrigation fluid flow rate, and using room temperature or chilled water for irrigation may be considered.

While higher irrigation fluid flow rates may be an option to decrease temperature rise, the increased intrarenal pressure and related infectious complications must be taken into consideration. Pyelo-venous reflux may occur when the intrapelvic renal pressure exceeds 30–35 mmHg [22], so when increasing the flow rate or heightening the irrigation fluid bag, this phenomenon must be considered. Ureteral access sheath (UAS) use may facilitate irrigation fluid outflow and decrease not only intrapelvic pressure but also intrarenal fluid temperature [9], but UAS use may also cause complications like ureteral damage and stricture. Using novel pressure-controlled suctioning UAS may overcome this issue [23], but further studies are warranted to determine its utility.

Laser settings and lasing time are the primary determinants of heat production, and the total energy created is calculated based on the formula "Total energy = pulse energy x frequency." Thus, special care must be given to the lasing time, particularly under low irrigation rates, when working with high pulse energy and/or frequency.

The fluid volume at the lased area is also related to increased temperature. With the same applied energy, less fluid will be heated more quickly. Therefore, excessive temperature rise must be kept in mind when using the laser in a relatively small space such as a renal calyx or ureter.

In addition to the aforementioned issues, the initial temperature of the irrigation fluid is another factor that can contribute to temperature rise during laser lithotripsy.

Table 1 Descriptives and significant results of studies on effect of lasers on intrarenal temperatures

Author and year	Assessed area	Model for the experiments	Laser type	Fiber size	Laser settings	Duration of laser activation	Irrigation fluid flow rate	Maximum temperature
Molina WR, 2021	Ureter	Ex vivo porcine ureter-kidney	Ho:YAG laser (model P120, Lumenis Ltd., Israel)	200 µm	Dusting: 0.3 J, 70 Hz, Long Pulse. Fragmentation: 0.8 J, 8 Hz, Short Pulse	5 s	Manual pumping system	Median temperature at fragmentation: 30.0 °C for Ho: YAG, 33.3 °C for SPTFL, $p=0.004$ Median temperature dusting: 40.6 °C for Ho: YAG vs 35.8 °C for SPTFL, $p=0.064$
			Super-pulsed Thulium Fiber (SPTFL) (SOLTIVE ™, Olympus, MA)		Dusting: 0.1 J, 200 Hz, SP Fragmentation: 0.8 J, 8 Hz, Short Pulse (SP) and			
Molina WR, 2015	Ureter	Ex vivo sheep ureter model	Ho:YAG laser (Dornier Medilas, Kennesaw, GA)	365 µm	10W = 1 J × 10 Hz	3 s	8 mL/s	Temperatures obtained: 37.4 °C with irrigation and 49.5 °C without irrigation The thermal spread along the external ureter wall: 0.9 ± 0.1 cm with irrigation and 1.1 ± 0.1 cm without irrigation
Aldoukhi AH, 2021	Kidney	Human and in vitro calyceal model	Ho: YAG (pulse 120; Lumenis, CA)	242 µm	1200 J for 60 s in five different patterns: 0.5 J·80 Hz (40 W) at 50% ODC (30 s on/30 s off), 0.5 J · 80 Hz (40 W) at 50% ODC (15 s on/15 s off · 2), 0.5 J · 80 Hz (40 W) at 50% ODC (10 s on/10 s off · 3), 0.5 J · 80 Hz (40 W) at 50% ODC (5 s on/5 s off · 6), 0.5 J · 40 Hz (20 W) at 100% ODC	ODC(Operator duty cycle) = lasing time/lithotripsy time	Peristaltic pump (Masterflex; Cole Parmer, IL) at 8 mL/min	$t_{43}=120$ equivalent minutes, was reached after 9 s when the laser was activated at 40 W with 30 s on/off and 15 s on/off patterns

Table 1 (continued)

Author and year	Assessed area	Model for the experiments	Laser type	Fiber size	Laser settings	Duration of laser activation	Irrigation fluid flow rate	Maximum temperature
Aldoukhi AH, 2018	Kidney	In vivo porcine	Ho: YAG (pulse 120; Lumenis, CA)	242 µm	40 W (0.5 J, 80 Hz, short pulse)	100 s	High irrigation: pressure bag inflated to 150 mmHg and placed at 100 cm height, equivalent to 304 cm of gravity irrigation Medium irrigation consisted of a saline bag at 100 cm height No irrigation	t_{43} was exceeded for all trials with no irrigation. The mean time to reach the threshold of thermal injury: - 12.7 s (range 2–37 s) for no irrigation - 17.8 s (range 5–30 s) for medium irrigation
Belle JD, 2022	Ureter	3-dimensional printed kidney-ureter model	Dornier 30 W Ho:YAG	200 µm	3.6, 10, 20, and 30 W	60 s	35 cc/min	
			Olympus 100 W Ho: YAG					At 30 W, the TFL exceeded 43 °C
			Olympus 60 W TFL					The TFL generated higher average ureteral fluid temperatures than the Dornier and Empower HL at all power settings tested
Dau JJ, 2021	Kidney	In vitro caliceal mode	Ho: YAG (pulse 120; Lumenis, CA)	242 µm	0.5 J · 80 Hz (40 W)	60 s	0, 8, 12, 15, and 40 mL/minute	For trials using RT irrigation, average peak temperatures were: 58.6 °C ± 0.4 °C for 8 mL/min, 53.1 °C ± 0.4 °C for 12 mL/min, 48.5 °C ± 0.2 °C for 15 mL/min, 32.9 °C ± 0.2 °C for 40 mL/min

Table 1 (continued)

Author and year	Assessed area	Model for the experiments	Laser type	Fiber size	Laser settings	Duration of laser activation	Irrigation fluid flow rate	Maximum temperature
								For trials using CH irrigation were: 56.4 °C ± 0.4 °C for 8 mL/min, 48.0 °C ± 0.2 °C for 12 mL/min, 43.0 °C ± 0.5 °C for 15 mL/min, 20.7 °C ± 0.2 °C for 40 mL/min
Dau JJ, 2022	Kidney	Anesthetized pigs	Ho: YAG (pulse 120; Lumenis, CA)	230 µm (Moses 200 D/F/L; Lumenis)	30 W (0.5 J·60 Hz, short pulse)	60 s	8, 12 and 15 mL/minute	Mean calculated thermal dose was inversely related to irrigation rate and was generally highest with WM irrigation and lowest with CH irrigation The mean time to threshold of thermal injury was 9, 15, and 23 s for WM, RT, and CH irrigation, respectively, at 8 mL/min irrigation

Table 1 (continued)

Author and year	Assessed area	Model for the experiments	Laser type	Fiber size	Laser settings	Duration of laser activation	Irrigation fluid flow rate	Maximum temperature
Gallegos H, 2021	Kidney	ex vivo porcine model	Ho: YAG	275 µm	Frequencies: 5, 10, and 15 Hz X Energies: 0.5, 0.8, 1, and 1.5 J	60 s	8.5, 9.5, and 11.1 mL/min	Irrigation height was founded to be significant in the DT determination. 50 cm H_2O irrigation height decreased the DT by 4.8 °C compared to 30 cm H_2O independent of the use of access sheath and laser configuration The use of an access sheath provides lower intrarenal temperatures regardless of laser configuration and water height
Noureldin YA, 2020	Kidney	Live-anesthetized porcine model	Ho: YAG (pulse 120; Lumenis, CA)	200 µm	20 W, 40 W, and 60 W	60 s	1 m gravity irrigation or manual pump irrigation 1 pump every 3 s	When UAS 12/14 was used the maximum IRT was detected equal to 63.4 °C at 40 W and equal to 74.5 °C at 60 W with gravity irrigation With manual pump irrigation temperatures reaching the threshold of 54 °C were not noted regardless of the laser power setting with or without the presence of a UAS
Hardy LA, 2015	Ureter	In vitro ureter model	100 W TFL (IPG Photonics, Oxford, MA)	100–244 µm	Pulse energy of 35 mJ, pulse duration of 500 µs, and pulse rates of 150, 300, or 500 Hz	As much as required for complete stone ablation	22.7 ml/min	33 ± 3 °C, 33 ± 7 °C, and 39 ± 6 °C for TFL at pulse rates of 150, 300, and 500 Hz, respectively

Table 1 (continued)

Author and year	Assessed area	Model for the experiments	Laser type	Fiber size	Laser settings	Duration of laser activation	Irrigation fluid flow rate	Maximum temperature
			20 W Ho: YAG laser (Medilas H20, Dornier MedTech, Wessling, Germany)	270–464 µm	600 mJ, 350 µs, and 6 Hz	As much as required for complete stone ablation	13.5 ml/min	Mean peak saline temperature: 24 ± 1 °C
Hein S, 2018	Kidney	In vitro kidney model	100 W Ho: YAG	272 µm or 940 µm	-15 W (0.5 J/30 Hz/150 µs) and 45 W (1.5 J/30 Hz/150 µs) -18 W (1.0 J/18 Hz/400 µs vs. 4.5 J/4 Hz/400 µs) and 54 W (2.0 J/2 Hz/400 µs vs. 4.5 J/12 Hz/400 µs) -18 W (4.5 J/4 Hz/400 µs) and 100 W (4.5 J/22.3 Hz/400 µs)	120 s	0, 5, 10, 16.65, 30, 40, 50, 75, and 100 ml/min	Laser application without irrigation results in a quick increase in temperature of up to Δ28 K, rising to 68 °C at 100W High irrigation rates of 100 ml/min result in a temperature rise of 5 K at 100 W -During experiments with renal calculi, the temperature rise was quicker, more turbulent, and 12.9% higher than that reached in the blank test
Hein S, 2020	Kidney	Ex vivo porcine kidney model	100-W Ho: YAG laser (Sphinx, LISA laser products OHG, Katlenburg-Lindau, Germany)	272 µm, 550 µm, 940 µm	Varying between 5 and 100 W	Na	0–100 ml/min	ΔT for irrigation rates ≥ 30 ml/min: ΔT = 15 K × (power [W]/irrigation [ml/min])
Khajeh NR, 2022	Kidney	In vitro experimental model	Ho: YAG	230 µm	40 W (0.5 J · 80 Hz, SP)	60 s	0, 8, 15, and 40 mL/min	Peak temperature and rise time were inversely related to irrigation rate -Smaller volumes receive greater thermal dose and reach threshold of tissue injury more rapidly than larger volumes

Table 1 (continued)

Author and year	Assessed area	Model for the experiments	Laser type	Fiber size	Laser settings	Duration of laser activation	Irrigation fluid flow rate	Maximum temperature
Peteinaris A, 2022	Kidney	Live-anesthetized porcine model	Ho: YAG (pulse 120; Lumenis, CA)	200 µm	20W (1 J, 20 Hz), 40W (1 J, 40 Hz), 60 W (2 J, 30 Hz) MOSES™ pulse delivery vs conventional pulse delivery technology	30 s	1 m Gravity irrigation	For 60 W both the MOSES and the conventional laser exceeded the safety threshold of 54 °C in approximately 10 s reaching the hazardous temperature of 66.4 °C in 18 s
							Manual irrigation set at 1 pump every 3 s	For 60 W, the MOSES laser was close to a highest temperature of 42 °C and the standard laser close to 44 °C throughout the 30 s recording
Sierra A, 2023	Kidney and Ureter	In vivo porcine model	Ho: YAG (Cyber: Ho 150 WTM) TFL (Fiber dust)	200 µm	0.5 J/10 Hz, 0.5 J/20 Hz, 0.7 J/10 Hz, 0.7 J/20 Hz, 1 J/12 Hz, 1 J/20 Hz	3 min, 7 min, 10 min	Continuous irrigation at 40 cmH_2O	TFL is safe when working with 20 W in the kidney and 12 W in the ureter
Taratkin M, 2020	Not specified	In vitro experimental model	Ho:YAG (100 W, Lumenis, Yokneam, Israel	200 µm	0.2 J X 40 Hz (8 W)	60 s	Precise flow control 0, 10, 35 mL/min	With no flow temperature rise: 10.9 ± 0.5 At 35 mL/min $^{\Delta T}$local: 2.8 ± 0.5
			Super-pulse NTO IRE-Polus, Russia					With no flow temperature rise: 11 ± 0.5 At 35 mL/min $^{\Delta T}$local: 1.9 ± 0.5
Teng JF, 2021	Kidney	Human beings	Ho: YAG	200 µm	0.5 J/20 Hz and 1 J/20 Hz	60 s	0, 15 ml/min or 30 ml/ min	Temperature rise: 1 J/20 Hz, 15 ml/ min: 4.91 ± 0.58 0.5 J/20 Hz, 30 ml/ min:1.50 ± 0.44,

Table 1 (continued)

Author and year	Assessed area	Model for the experiments	Laser type	Fiber size	Laser settings	Duration of laser activation	Irrigation fluid flow rate	Maximum temperature
Winship B, 2019	Ureter	Benchtop ureteral model	Ho: YAG (Pulse 120H; Lumenis, Yokneam, Israel	365 µm	0.6 J/6 Hz, 0.8 J/8 Hz, 1 J/10 Hz, 1 J/20 Hz, 0.2 J/80 Hz	45 s	0-, 100-, and 200-mm Hg	Flexible scope: At 200 mm Hg, changes > 6 °C occurred at 1 J/10 Hz (15 s), 0.2 J/80 Hz (3 s), and 1 J/20 Hz (2 s) At 0 mm Hg, all settings produced changes > 6 °C within 3 s, except 0.6 J/6 Hz (35 s)
Wriedt R, 2023	Kidney	Ex vivo porcine kidney model	Ho: YAG (Sphinx Junior 30 W, LISA, Germany)	550 µm	14 W = 1.2 J, 12 Hz, 90 µs pulse duration 30 W = 3.3 J, 9 Hz, 230 µs pulse duration	5 or 10 s	10, 30, 50, 70 and 100	At high irrigation rates (I) of I ≥ 50 ml/min, CEM_{43} remained below the threshold of 120 min at any setting except for 10 s laser/10 s delay
Williams JG, 2021	Kidney	Experimental model	Ho: YAG					Mathematical model

WM irrigation: Warmed irrigation, RT irrigation: Room temperature irrigation, CH irrigation: Chilled İrrigation, DT: Delta temperature, $^{\Delta T:}$ Temperature change

It has been demonstrated that the use of room temperature irrigation fluid during endoscopic surgeries may result in a decrease in core body temperature, even leading to hypothermia. The absorption of irrigation fluid and the circulation of blood through the surgical site exposed to a large volume of room temperature irrigation fluid can cause a decrease in the patient's core body temperature. Hypothermia is a serious and sometimes troublesome reality, particularly for anesthesiologists. Therefore, according to the results of a meta-analysis, it was recommended to use warmed irrigation fluid to decrease heat loss and the risk of perioperative shivering and hypothermia [24]. However, when trying to prevent hypothermia, one must also be aware of excessive temperature rise during laser lithotripsy. This is because all newly generated heat by the laser would be added to the basal fluid temperature, which might facilitate exceeding 43 °C, the threshold for tissue damage.

Ultimately, the issue of uncontrolled temperature increase during laser lithotripsy is multifactorial and requires careful consideration of various parameters, including laser settings, irrigation fluid rate and temperature, and fluid volume at the lased area. To address this issue, future research is needed to develop laser systems with improved temperature control mechanisms and to explore novel methods for monitoring physical conditions during laser energy application. Additionally, the development of advanced monitoring systems is of utmost importance to allow physicians to monitor temperature changes and other physical conditions during endourology procedures. With these advancements, we can ensure safer and more effective procedures, minimizing the risk of tissue damage and other adverse events associated with uncontrolled temperature increase.

Limitations

Our study is not without limitations. First of all, this is a narrative review not a systematic review aiming to take a snapshot of current literature. Given the wide extension of the topic, it is hard to conduct a systematic review, since there are too many variables effecting temperature alterations during lithotripsy which must take into consideration. It was also not possible to pool the data and perform a meta-analysis, because there was no structured setup for the experiments and study design was different in almost all studies. The used equipment i.e., device for temperature measurement was different and some studies were in vitro studies using animal kidneys and some were experimental settings mimicking kidney anatomy.

Conclusion

With the advancement of endoscopic instruments and progress in laser technology, endoscopic surgery for stone removal has become the preferred treatment for urolithiasis. High-powered lasers enable the treatment of large stones through retrograde intrarenal surgery or percutaneous nephrolithotomy. Nevertheless, high power required for rapid disintegration also entail limitations such as increased intrarenal temperature, poor vision caused by the snowstorm effect during dusting and prolonged operation times, particularly for retrograde intrarenal surgery. To address excessive temperature rise, urologists must establish a balance between laser power, lasing time, and irrigation fluid rate and temperature.

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Declarations

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主题论文

高温已开启：温度过度升高对输尿管和肾结石激光治疗并发症的影响

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摘要

目的 尿科领域技术进步导致尿路结石治疗模式发生转变
当前临床正逐步转向微创性泌尿系统介入治疗，如输尿管镜检查和经皮肾镜碎石术。然而，激光碎石术中可能引发的热损伤问题引发关注——研究表明，即使采用常规低功率激光设置，也可能超过细胞热损伤阈值（43°C）。本综述旨在通过分析现有激光系统治疗过程中导致温度升高的因素，评估其对患者治疗效果的影响。

材料与方法 为筛选纳入研究，我们在PubMed等在线数据库中进行了检索。Google Scholar。关键词如“温度”或“热量”分别与“碎石术”、“肾镜碎石术”、“输尿管镜检查”或“逆行肾内手术”进行组合，既可单独使用，也可多种方式组合。

研究结果 为缓解温度上升问题，学界提出了多种策略，例如降低激光能量或频率、缩短延长激光激活时间、提高灌洗液流速，并采用室温或冰水进行冲洗。需要特别注意的是，由于可能引发肾内压升高及相关感染并发症，应谨慎采用较高流速的灌洗液。使用输尿管通路鞘（UAS）可有效促进灌洗液排出，从而降低盆腔内压和肾内液体温度。

结论 在激光功率、激光激活持续时间和冲洗液速率和温度之间取得平衡对泌尿科医生而言，控制体温过度升高至关重要。

关键词 尿路结石·尿道内手术·热损伤·激光碎石术

介绍

尿路结石是一种常见泌尿系统疾病，患病率估计在1%至15%之间。该病的发病率在全球范围内存在差异，且过去数十年间呈现持续上升趋势[1]。对于大多数尿路结石病例，药物治疗效果有限，而对有症状患者而言，手术干预仍是主要治疗手段。虽然传统开放性碎石术曾经是首选的外科手术方式，技术进步已将标准治疗转移到微创的尿路内介入治疗，如输尿管镜和经皮肾镜碎石术。冲击波碎石术也被认为是治疗上尿路结石的可行选择[2]。

激光技术在泌尿外科的应用最早可追溯至皮尔森团队的开创性实验，他们首次展示了激光对犬类膀胱的治疗效果。随后，马尔瓦尼团队利用红宝石晶体激光器开展了尿路结石碎石研究。然而，这种红宝石激光器因产生过热现象导致结石汽化，最终被证明在泌尿外科应用中效果欠佳。随着技术发展，Nd：YAG（弗雷迪）和钬铝石榴石（Ho：YAG）等脉冲波激光器相继问世，如今已成为泌尿外科领域不可或缺的重要诊疗工具[3]。

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细胞热损伤的临界温度为43℃，研究发现即使采用常规低功率激光设置，在肾盏和输尿管模型中仍可能超过该阈值。激光激活时长、灌注液体积、脉冲能量及频率等因素都会影响累积产热量，从而导致碎石术中组织损伤的风险[4]。

本综述旨在识别当前激光治疗中导致温度升高的因素，并评估其对患者预后的影响。通过研究，我们希望制定有效策略来缓解这些情况，从而降低激光治疗尿路结石并发症的风险。

材料和方法

在研究筛选过程中，我们通过PubMed和谷歌学术平台开展在线检索，不限时间限制，采用“温度”或“热”等关键词与“碎石术”、“肾镜碎石术”、“输尿管镜检查”或“逆行肾内手术”等术语单独或组合检索。同时查阅所有纳入研究的参考文献，以发现可能与本研究相关的其他信息来源。为确保结果一致性，我们将符合条件的研究语言限定为英文。纳入研究的包括：与碎石术中温度升高现象相关的现有研究（需结果具有一致性）以及预防温度升高的相关研究。排除了相关主题的综述性文献。记录了研究作者及发表年份、评估尿路温度升高的部位、实验模型、激光类型、光纤尺寸、激光参数设置、激光激活时长、冲洗液流速及温度状态等信息。

文献综述

激光器类型和温度

在另一项研究中，莫利纳等人[2] 本研究通过离体猪肾输尿管模型，系统分析了两种激光系统（120W Ho：YAG激光器，型号P120，以色列Lumenis公司；60W SPTF激光器，美国马萨诸塞州奥林巴斯公司）在输尿管碎石术中的温度分布特征。实验采用室温（27℃）生理盐水通过手动泵系统进行冲洗。研究发现，两种激光系统的温度曲线始终低于细胞损伤临界值（43℃）。特别值得注意的是，在粉尘模式（0.3焦耳，70赫兹，长脉冲）下，Ho：YAG激光器的温度中位数增幅高于SPTF激光器（40.6°C对比35.8 °C，各自地，p=0.064）。

Belle等人[6] 本研究对比了铥光纤激光器（TFL）与钬：钇铝石榴石（Ho：YAG）激光器在输尿管结石碎石术中的温度差异。结果显示，TFL在3.6W、10W和30W三种功率设置下产生的温度均最高，与德国多尼尔公司Medilas H SolvoHL（30W）和美国奥林巴斯公司Empower HL（100W）激光器相比。当功率为20W时，TFL（40.93°C）与EmpowerHL（41.17°C，p>0.05）的温度差异无统计学意义。但当功率提升至30W时，TFL的最高温度达到44.37°C，显著超出临床安全阈值。

Hardy等人[10] 比较了Ho：YAG和TFL在体外输尿管模型中对温度的影响。他们使用了Ho：YAG激光器，参数为600 mJ、350μs、6 Hz，以及TFL激光器，参数为35 mJ、500μs、150–500 Hz。生理盐水冲洗流速分别为TFL的22.7 ml/min和钬激光的13.7 ml/min。研究发现，钬激光的平均峰值冲洗液温度为24±1°C，而TFL在脉冲频率分别为150、300和500 Hz时的温度分别为33±3°C、33±7°C和39±6°C。研究人员得出结论，为了避免过度热升并提供足够的安全裕度，TFL碎石术应采用低于500 Hz的脉冲频率和/或增加冲洗流速。

在另一项实验研究中，Sierra等人[15] 比较Ho：YAG和TFL在猪体内模型和输尿管体外模型中的安全性。在最大20 W功率和逐渐降低的灌注（40cmH_2O连续）下，TFL达到的温度为40.2°C，Ho：YAG激光达到的温度为41°C。

同样，Taratkin等人[16] 研究人员在体外模型中研究了Ho：YAG激光与新型TFL在激光碎石术中的温度变化曲线。结果显示，两种激光产生的温度升高幅度相近，且所消耗能量与系统吸收热量相当。在20瓦功率下未使用冲洗时，Ho：YAG激光的温度升高为10.9±0.5°C，而超脉冲TFL则达到11.0±0.5°C。

激光设置、灌注流速和温度

Wollin等人在他们的研究中[1] 在体外环境中研究了激光设置和冲洗流速对输尿管碎石术期间输尿管温度的影响。具体而言，他们使用了200μm的激光器，脉冲能量和频率各不相同（0.2 J/50 Hz、0.6 J/6 Hz、0.8 J/8 Hz、1 J/10 Hz和1 J/20 Hz），在允许设定室温流速（100、50和0 mL/分钟）的管路系统中持续60秒。他们的研究结果表明，在100 mL/min的冲洗流速下，只有最高激光设置（1 J/20 Hz）产生了30.7°C的最大温度，这被认为在临床上不显著。然而，在没有冲洗液流的情况下，所有最大温度都超过了

细胞热损伤的阈值（43℃）。此外，在最高激光设置（1J/20Hz）且无冲洗的情况下，他们的研究中最高温度超过100°C[1]。

莫利纳等人[3] 研究人员对比了绵羊尿道在有无灌洗条件下的Ho：YAG激光碎石术温度变化。数据显示，未灌洗的完整尿道模型温度升高幅度显著大于灌洗组，分别为49.5±2.3°C和37.4±2.5°C。

阿尔杜基等人[5] 研究人员在体外猪模型中研究了高功率Ho：YAG激光碎石术过程中膀胱腔内液体的温度变化。实验采用Ho：YAG激光器，功率设置为0.5焦耳×80赫兹=40瓦，并分别设置高、中、低三种灌注模式。结果显示，无灌注、中等灌注和高灌注模式下的峰值温度分别为84.8°C、63.9°C和43.6°C。

海因等人[11] 利用体外模型模拟肾盂并评估Ho：YAG碎石术期间的温度变化。结果显示，未进行冲洗时，激光应用导致温度快速上升至Δ28 K，在100 W时升至68°C。然而，更高的冲洗速率会导致温度上升幅度降低。在最高冲洗速率100 ml/min和最高激光功率设置（100 W）下，温度仅上升5 K。

滕等人[17] 在真实场景中，研究人员开展了一项研究，以评估使用柔性URS进行Ho：YAG碎石术时肾盏内灌注液温度的变化。作者发现，在功率设置为1 J/20 Hz且灌注流速为15 ml/min的情况下，温度升幅显著高于其他组。此外，在相同激光设置下，灌注流速较低的组别温度升高幅度也显著更大。当未进行灌注时，以1 J/20 Hz达到43°C所需时间显著短于0.5 J/20 Hz的条件。

在另一项研究中，Winship等人[19] 本研究采用Ho：YAG激光器，通过柔性与半刚性输尿管镜对台式输尿管模型进行温度升高的研究。在不同激光能量设置下，当使用半刚性镜管配合100毫米汞柱的灌注系统时，仅1焦耳/20赫兹的激光参数能使温度升高超过6摄氏度。激光停止后，温度在2秒内即恢复至接近基线水平。

阿尔杜基等人[4] 研究人员采用Ho：YAG激光器（脉冲120；Lumenis）在体外实验性膀胱模型中，研究了踏板激活对液体温度及热分布的影响。实验表明，延长踏板激活时间会导致峰值温度升高并加剧热效应。当采用30秒开/15秒关的激光激活模式，以50%的激光器工作周期（ODC=激光时间/碎石时间）施加40瓦功率时，系统在9秒内即达到热损伤阈值（43°C）。

Wriedt等人[20] 在离体猪肾脏模型中，使用不同的碎石参数评估了磁共振成像对组织加热的影响。作者报告称，当使用30瓦激光应用10秒时，为避免超过120分钟的腔内碎石$_{43}$，冲洗速率至少需要达到70 ml/min。此外，在使用人结石进行的实验中，他们观察到肾盏壁局部温度升高，认为这是由于加热后的碎石碎片未从肾脏手术区域排出所致。

肾盂肾盏体积和温度

卡杰等人[13] 研究了Ho：YAG激光碎石术中肾盂肾盏体积与温度升高的关系。研究结果表明，温度升高和激光激活产生的热剂量与各模型中的液体体积及灌注速率呈负相关。在所有模型中，通过1分钟连续激光激活获得的灌注速率为40 mL/min时，测得的安全温度低于组织损伤阈值[13]。

脉冲调制类型和温度

皮蒂纳里斯等人的一项研究[14]本研究在活体麻醉猪模型中，将新引入的钬脉冲调制系统（Moses）与传统脉冲输送技术在输液温度（IFT）上的效果进行了对比。研究将危险IFT阈值设定为54°C。结果显示，无论是Moses系统还是传统60瓦激光激活技术，在重力输液条件下均会导致温度显著升高：约10秒内温度超过54°C安全阈值，18秒内达到危险温度66.4°C。然而，采用手动泵输液的任何设置条件下，IFT均未超过54°C。

温希普等人[18] 本研究通过实验性输尿管模型，系统探究了钬：钇铝石榴石（Ho：YAG）脉冲类型（短脉冲SP、长脉冲LP、莫塞斯接触Mc、莫塞斯距离MD）对灌注液温度的影响。实验数据显示：在1焦耳/20赫兹的参数设置下，长脉冲LP产生的温度基线变化最大；且所有脉冲类型在相同参数设置下，热剂量均在3秒激活时间内突破损伤阈值。

建议温度升高的公式

在另一项研究中，海因等人[12] 在离体猪肾脏模型中研究了Ho：YAG激光在逆行肾内手术和经皮肾镜碎石术中的热效应。研究人员根据其结果提出了一种计算温度变化的公式，适用于灌注速率高于30毫升/分钟的情况：ΔT=15 K×（功率[W]/灌注[ml/min]）。

最后，Williams等人[21] 研究人员开发了一个数学模型，用于预测碎石术中激光对肾脏温度的影响。该模型基于肾体积、冲洗流速、冲洗液温度和激光功率四个参数。研究团队建议临床医生使用室温冲洗液进行冲洗，并避免过度使用激光。他们还提出通过调节冲洗液的流入量（即加压冲洗液）或流出量（即使用UAS）来调整冲洗液流量。

温度升高的可能预防措施

在他们的研究中，Dau等人[7] 研究了冷却灌洗对体外模型中肾盏液温度及达到热损伤阈值所需时间的影响。实验使用120 W Ho：YAG激光器（pulse120；Lumenis，CA），以0.5 J·80 Hz（40 W）的设置在短脉冲模式下持续60秒。在室温（19°C）灌洗时28秒内达到热损伤阈值，而使用8 mL/min冷却灌洗（1°C）时则需33秒。当灌洗流速为12 mL/min时，室温灌洗46秒内即可达到阈值，但冷却灌洗则无法实现。另一项研究评估并比较了输尿管镜激光碎石术中冷却灌洗（4°C–1°C）、室温（RT）（20°C–1°C）和温水（WM）灌洗（37°C–1°C）的热效应，实验采用活体猪模型。研究人员得出结论：与室温或温水溶液灌洗相比，输尿管镜激光碎石术中使用冷却生理盐水灌洗可减缓温度上升、降低峰值温度，并延长达到热损伤的时间[7]。

加列戈斯等人在研究中发现[8] 研究表明，使用输尿管套管（UAS）可有效降低肾内温度，且该效果不受激光配置和灌洗液高度的影响。在灌洗液高度50厘米$_2$ H_2O、能量1焦耳、频率15赫兹的条件下，未使用UAS时每分钟温度升高值更高（5.8°C对比3.8°C）[8]。类似地，努雷丁等人[9]研究人员在活体麻醉猪模型中研究了灌注速率和UAS尺寸对输尿管软镜检查期间肾内温度的影响。研究发现，采用重力灌注方式（即手术台上方1米处放置液体袋）且未使用UAS时，即使激光功率低至20瓦、仅持续20秒激活，肾内温度仍可能危险升高至54°C。而采用泵式灌注方式时，若以最高功率60瓦持续60秒激活激光，即便不使用UAS，肾内温度仍能保持在安全范围内[9]（表1）。

讨论

针对激光碎石术中温度变化的研究已开展大量实验，研究者采用多种实验模型和激光设备进行探索。导致温度升高的因素包括激光类型、激光参数设置（高功率、高频）、冲洗液流速、激光激活时间、腔室内液体量以及碎石过程中产生的热能积聚。目前内窥镜碎石术主要使用的两种激光器是钬：钇铝石榴石（Ho：YAG）激光器和铥激光器，这些系统经过多年改良已实现显著功率提升。最新研发的碎石激光技术包括：采用莫尔斯技术的Ho：YAG脉冲调制技术、脉冲式铥钇铝石榴石激光器，以及铥光纤激光器。

功率增加会导致温度升高，临床医生必须平衡多个变量以避免不良影响。为了降低温度升高，可以考虑修改激光能量或频率、减少激光激活持续时间、增加冲洗液流速、使用室温或冷水冲洗等方法。

虽然提高灌洗液流速可能是降低温度升高的一个选择，但必须考虑到肾内压力升高及相关感染并发症的风险。当盆腔肾内压力超过30-35毫米汞柱时[22]，可能发生肾盂静脉反流，因此在增加流速或抬高灌洗液袋时需注意防范。使用输尿管套管（UAS）可促进灌洗液排出，不仅能降低盆腔压力，还能减少肾内液体温度[9]，但UAS的使用也可能引发输尿管损伤和狭窄等并发症。采用新型压力控制式UAS可能解决这一问题[23]，但其实际应用价值仍需进一步研究验证。

激光器的参数设置和脉冲持续时间是决定热能输出的关键因素，总能量的计算公式为“总能量=脉冲能量×频率”。因此，在低灌溉速率条件下，若需使用高脉冲能量或高频率，必须特别注意控制激光脉冲时间。

激光作用区域的液体量与温度升高相关。在相同能量条件下，液体量越少，升温速度越快。因此，在肾盏或输尿管等相对狭窄的空间使用激光时，必须注意避免温度过高。

除上述问题外，灌注液的初始温度是另一个可能导致激光碎石术过程中温度升高的因素。

表1激光对肾内温度影响的研究描述和显著结果

作者和年份	评估面积	实验模型	激光类型	纤维尺寸	激光设置	激光激活持续时间	灌注液流速	最高温度
Molina WR，2021	输尿管	猪离体输尿管-肾脏	Ho：YAG 激光（型号 P120，Lumenis Ltd.，以色列）	200 μm	粉尘：0.3 J，70 Hz，长脉冲。碎裂：0.8 J，8 Hz，短脉冲	5 s	手动泵送系统	碎裂时的温度中位数：Ho：YAG为30.0 °C，SPTFL为33.3 °C（p=0.004）；粉尘处理时的温度中位数：Ho：YAG为40.6 °C，SPTFL为35.8 °C（p=0.064）
			超脉冲铥光纤（SPTFL）（SOLTIVE™Olympus，MA）		粉尘：0.1 焦耳，200 赫兹；SP碎裂：0.8焦耳，8 赫兹；短脉冲（SP）和			
Molina WR，2015	输尿管	离体绵羊输尿管模型	Ho：YAG 激光（Dornier Medi 拉斯，肯尼索，乔治亚州）	365 μm	10W＝1 J×10 Hz	3 s	8 mL/s	测得温度：灌注时37.4 °C，非灌注时49.5 °C。输尿管外壁热扩散范围：灌注时0.9±0.1厘米，非灌注时1.1±0.1厘米。
Aldoukhi AH，2021	肾脏	人和体外肾盏模型	Ho：YAG（脉冲120；Lumenis，CA）	242 μm	采用五种不同模式进行1200焦耳(J)功率的60秒治疗：0.5 J · 80 Hz（40瓦）50%ODC（30秒/30秒），0.5 J · 80 Hz（40瓦）50%ODC（15秒/15秒 · 2次），0.5 J · 80 Hz（40瓦）50%ODC（10秒/10秒 · 3次），0.5 J · 80 Hz（40瓦）50%ODC（5秒/5秒 · 6次），0.5 J · 40 Hz（20瓦）100%ODC	ODC（操作员工作周期）＝激光时间/碎石时间	蠕动泵（Masterflex：Cole Parmer，IL）以8 mL/min的速度运行	当激光器以40W功率以30秒/15秒的开关模式启动时，9秒后即可达到t_{43}=120等效分钟数

表1（续）

作者和年份	评估面积	实验模型	激光类型	纤维尺寸	激光设置	激光激活持续时间	灌注液流速	最高温度
Aldoukhi AH, 2018	肾脏	猪体内	Ho：YAG（脉冲120；Lumenis，CA）	242 μm	40 W (0.5 J, 80 Hz，短脉冲）	100 s	高灌：将压力袋充气至150 ㎜Hg，置于100 ㎝高度，相当于304 ㎝重力灌溉。中灌由100 ㎝高度的生理盐水袋组成，不灌溉	所有未进行冲洗的试验中，t43值均被超过。达到热损伤阈值的平均时间：未冲洗组为12.7秒（范围2-37秒），中等冲洗组为17.8秒（范围5-30秒）。
Belle JD，2022	输尿管	三维打印肾输尿管模型	Dornier 30 W Ho：YAG	200 μm	3.6、10、20和30 W	60 s	35 cc/min	
			Olympus 100 W Ho：YAG					在30 W时，TFL超过43°C
			Olympus 60 W TFL					在所有测试功率设置下，TFL产生的输尿管液体平均温度均高于Dornier和Empower HL
Dau JJ, 2021	肾脏	体外杯状模式	Ho：YAG（脉冲120；Lumenis，CA）	242 μm	0.5 J · 80 Hz (40 W)	60 s	0、8、12、15和40 mL/minute	采用RT冲洗方式的试验中，平均峰值温度为：58.6 °C±0.4 °C for 8mL/min, 53.1 °C±0.4 °C for 12mL/min, 48.5 °C±0.2 °C for 15mL/min, 32.9 °C±0.2 °C for 40mL/min

表1（续）

作者和年份	评估面积	实验模型	激光类型	纤维尺寸	激光设置	激光激活持续时间	灌注液流速	最高温度
								对于使用CH冲洗的试验，如下所示： 56.4 °C±0.4 °C for 8 mL/min, 48.0 °C±0.2 °C for 12 mL/min, 43.0 °C±0.5 °C for 15 mL/min, 20.7 °C±0.2 °C for 40 mL/min
Dau JJ, 2022	肾脏	麻醉猪	Ho：YAG（脉冲120；Lumenis，CA）	230 μm（摩西200 D/F/L; Lumenis)	30 W（0.5 J·60 Hz，短脉冲）	60 s	8、12和15 mL/分钟	计算得出的平均热剂量与灌注速率呈负相关，且通常在WM灌注时最高，在CH灌注时最低。在8 mL/min的灌注条件下，热损伤阈值的平均时间分别为WM灌注9秒、RT灌注15秒和CH灌注23秒。

表1（续）

作者和年份	评估面积	实验模型	激光类型	纤维尺寸	激光设置	激光激活持续时间	灌注液流速	最高温度
Gallegos H，2021	肾脏	猪离体模型	Ho: YAG	275 μm	频率：5、10和15Hz X 能量：0.5、0.8、1和1.5 J	60 s	8.5、9.5和 11.1 mL/min	灌溉高度被确定为DT测定中的重要因素。与30厘米水灌溉高度相比，50厘米水灌溉高度使DT降低了4.8 °C，且与使用接入鞘和激光配置无关。 无论激光配置和水位如何，使用导管鞘都能降低肾内温度
Noureldin YA, 2020	肾脏	实时麻醉 猪模型	Ho：YAG（脉冲120；Lumenis，CA）	200 μm	20 W、40 W和60 W	60 s	1米重力灌溉或手动泵灌溉，每3秒使用1次泵送	使用UAS 12/14时，重力灌溉条件下测得的最大灌溉温度（IRT）为：40瓦时63.4 °C，60瓦时74.5 °C。 无论是否使用激光功率调节，手动泵灌溉时温度均未达到54 °C的临界值，无论是否使用UAS。
Hardy LA 2015	输尿管	体外输尿管模型	100 W TFL（IPG Photonics，马萨诸塞州牛津市）	100–244 μm	脉冲能量35mJ，脉冲持续时间 500 μs，以及150、300或500 Hz的脉冲频率	完全石刀消融所需的全部能量	22.7 ml/min	当脉冲频率分别为150、300和500赫兹时，TFL的温度分别为33 ± 3 °C、33 ± 7 °C和39 ± 6 °C。

表1（续）

作者和年份	评估面积	实验模型	激光类型	纤维尺寸	激光设置	激光激活持续时间	灌注液流速	最高温度
			20 W Ho: YAG 激光（美迪拉斯）H20，Dornier MedTech，Wessling，德国）	270–464 μm	600 mJ，350μs，和 6 Hz	完全石刀消融所需的剂量	13.5 ml/min	平均峰值盐水温度：24±1 °C
Hein S，2018	肾脏	体外肾模型	100 W Ho: YAG	272 μm或940μm	-15 W (0.5 J/30 Hz/150 μs) and 45 W (1.5 J/30 Hz/150 μs) -18 W (1.0 J/18 Hz/400 μs vs. 4.5 J/4 Hz/400 μs) and 54 W (2.0 J/2 Hz/400 μs vs. 4.5 J/12 Hz/400 μs) -18 W (4.5 J/4 Hz/400 μs) and 100 W (4.5 J/22.3 Hz/400 μs)	120 s	0, 5, 10, 16.65, 30, 40、50、75和100 ml/min	不进行冲洗的激光应用会导致温度快速上升，最高可达28K，温度升至68°C时达到100W 灌溉率高达100 ml/min时，温度会上升5 K，此时功率为100 W。 在肾结石实验中，温度上升速度更快、波动更剧烈，且比空白对照组高出12.9%。
Hein S，2020	肾脏	猪离体肾脏模型	100-W Ho: YAG 激光（Sphinx，Lisa 激光产品 OHG，德国卡特伦堡-林道）	272 μm, 550 μm, 940 μm	5至100 W之间	Na	0–100 ml/min	ΔT当灌溉速率≥30 ml/min时：ΔT＝15 K×(power [W]/irrigation [ml/min])
Khajeh NR，2022	肾脏	体外实验模型	Ho: YAG	230 μm	40 W (0.5 J · 80 Hz, SP)	60 s	0、8、15和40 mL/min	峰值温度和上升时间与灌溉速率呈负相关 -较小体积的受热剂量更高，且比较大体积更快达到组织损伤阈值

表1（续）

作者和年份	评估面积	实验模型	激光类型	纤维尺寸	激光设置	激光激活持续时间	灌注液流速	最高温度
Peteinaris A，2022	肾脏	实时麻醉猪模型	Ho：YAG（脉冲120；Lumenis，CA）	200 μm	20W (1 J, 20 Hz), 40W (1 J, 40 Hz), 60 W (2 J, 30 Hz) Moose™脉冲输送技术与传统脉冲输送技术的对比	30 s	1 m重力灌溉	当功率为60瓦时，无论是Moses激光器还是传统激光器，温度均超过54°C的安全阈值，这一情况在约10秒内达到66.4°C的危险温度18 s
							人工灌溉设置为每3秒1次泵送	在60瓦功率下，摩西激光器的温度接近42°C的峰值，而标准激光器则接近44°C，这一温度持续了30秒的记录。
Sierra A，2023	肾脏和输尿管	猪体内模型	Ho：YAG（网络：Ho 150 WTM) TFL（纤维粉尘）	200 μm	0.5 J/10 Hz, 0.5 J/20 Hz, 0.7 J/10 Hz, 0.7 J/20 Hz, 1 J/12 Hz, 1 J/20 Hz	3 min, 7 min, 10 min	持续灌注40 cmH $_2$O	当肾脏功率为20 W、输尿管功率为12 W时，TFL是安全的
Taratkin M, 2020	未指定	体外实验模型	Ho：YAG（100瓦，Lumenis，以色列Yokneam） 超脉冲NTO IRE-Polus，俄罗斯	200 μm	0.2 J X 40 Hz (8 W)	60 s	精确流量控制0、10、35 mL/min	无流量温度上升：10.9±0.5 在35 mL/min $^{\Delta T}$本地条件下：2.8±0.5 无流量温度上升：11±0.5 在35 mL/min $^{\Delta T}$本地条件下：1.9±0.5
Teng JF，2021	肾脏	人类	Ho: YAG	200 μm	0.5 J/20 Hz和1 J/20 Hz	60 s	0,15 ml/min或30 ml/ min	温度上升：1 J/20 Hz, 15 ml/ min: 4.91 ± 0.58 0.5 J/20 Hz, 30 ml/ min: 1.50±0.44,

表1（续）

作者和年份	评估面积	实验模型	激光类型	纤维尺寸	激光设置	激光激活持续时间	灌注液流速	最高温度
Winship B, 2019	输尿管	台式输尿管模型	Ho：YAG（脉冲120 H；Lumenis，以色列约克尼姆）	365 μm	0.6 J/6 Hz, 0.8 J/8 Hz, 1 J/10 Hz, 1 J/20 Hz, 0.2 J/80 Hz	45 s	0-、100-和200-毫米汞柱	在200毫米汞柱压力下，温度变化超过6 °C的情况发生于 1 10 Hz（15 s）、0.2 J/80 Hz（3 s）和1 J/20 Hz（2 s） 在0mmHg时，所有设置产生的变化＞6 °C 3 秒内，0.6 J/6 Hz（35秒）除外
Wriedt R，2023	肾脏	猪离体肾脏模型	Ho: YAG（Sphinx Junior 30 W，德国丽莎）	550 μm	14 W=1.2 J，12 Hz，90 μs脉冲持续时间 30 W=3.3 J，9 Hz，230 μs脉冲持续时间	5或10秒	10、30、50、70和100	高灌水 当 I≥50 ml/min 时，CEM_{43}的转换率(I)在除任何设置外均低于120分钟的阈值。 10 s激光/10 s延迟
Williams JG，2021	肾脏	实验模型	Ho: YAG					数学模型

WM**灌注**：温水灌注，RT灌注：室温灌注，CH灌注：冷水灌注，DT：温差，ΔT：温度变化

研究表明，在内窥镜手术中使用室温冲洗液可能导致患者核心体温下降，甚至引发低体温症。当大量室温冲洗液接触手术部位时，其吸收作用和血液循环过程会降低患者核心体温。低体温症对麻醉医师而言是严重且棘手的临床问题。因此，根据一项荟萃分析结果，建议使用温热冲洗液以减少热量流失，并降低围手术期颤抖和低体温症风险[24]。但需注意的是，在尝试预防低体温症时，还需警惕激光碎石术中温度过度升高的风险。这是因为激光产生的全部新热量会叠加到基础冲洗液温度上，可能导致温度超过43°C——这是组织损伤的临界值。

激光碎石术中温度失控的问题具有多重成因，需要综合考量激光参数、灌洗液流速与温度、术区液体量等关键因素。为解决这一难题，未来研究需重点开发具备智能温控系统的激光设备，并探索创新的实时监测技术。此外，建立先进的术中监测系统对医生掌握温度变化等生理指标至关重要。通过这些技术突破，我们不仅能确保手术安全高效，更能有效降低因温度失控引发的组织损伤等并发症风险。

限制

本研究存在若干局限性。首先，本研究属于叙述性综述而非系统性综述，旨在对现有文献进行快照式梳理。鉴于研究主题范围广泛，开展系统性综述存在困难，因为影响碎石术中温度变化的变量过多，需要综合考量。此外，由于实验设计缺乏统一框架且研究方案差异显著，我们无法整合数据进行荟萃分析。所使用的测量设备（如温度监测装置）各不相同，部分研究采用动物肾脏的体外实验，另一些则通过模拟肾脏解剖结构的实验设置展开。

结论

随着内窥镜器械的升级与激光技术的进步，内窥镜碎石术已成为治疗尿路结石的首选方案。高功率激光设备可通过逆行肾镜手术或经皮肾镜碎石术处理大结石。然而，高强度激光在快速碎石的同时也存在局限性：不仅会导致肾盂温度升高，除尘时的“雪暴效应”会引发视野模糊，且逆行肾镜手术的耗时较长。为解决温度过高问题，泌尿科医生需要在激光功率、照射时间和冲洗液流速及温度之间找到最佳平衡点。

作者贡献：ST：项目开发、数据收集、数据分析、论文撰写和编辑。MFB：数据收集、论文撰写。AO：数据收集、论文撰写。CG：项目开发、论文编辑。AM：项目开发、论文撰写和编辑。

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ORIGINAL ARTICLE

WATTS happening? Evaluation of thermal dose during holmium laser lithotripsy in a high-fidelity anatomic model

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Abstract

Purpose To evaluate the thermal profiles of the holmium laser at different laser parameters at different locations in an in vitro anatomic pelvicalyceal collecting system (PCS) model. Laser lithotripsy is the cornerstone of treatment for urolithiasis. With the prevalence of high-powered lasers, stone ablation efficiency has become more pronounced. Patient safety remains paramount during surgery. It is well recognized that the heat generated from laser lithotripsy has the potential to cause thermal tissue damage.

Methods Utilizing high-fidelity, 3D printed hydrogel models of a PCS with a synthetic BegoStone implanted in the renal pelvis, laser lithotripsy was performed with the Moses 2.0 holmium laser. At a standard power (40 W) and irrigation pressure (100 cm H_2O), we evaluated operator duty cycle (ODC) variations with different time-on intervals at four different laser settings. Temperature was measured at two separate locations—at the stone and away from the stone.

Results Temperatures were highest closest to the laser tip with a decrease away from the laser. Fluid temperatures increased with longer laser-on times and higher ODCs. Thermal doses were greater with increased ODCs and the threshold for thermal injury was reached for ODCs of 75% and 100%.

Conclusion Temperature generation and thermal dose delivered are greatest closer to the tip of the laser fiber and are not dependent on power alone. Significant temperature differences were noted between four laser settings at a standardized power (40 W). Temperatures can be influenced by a variety of factors, such as laser-on time, operator duty cycle, and location in the PCS.

Keywords Thermal dose · Temperature · Laser lithotripsy · Holmium · Anatomic model

Abbreviations

RIRS	Retrograde intrarenal surgery
Ho: YAG	Holmium: Yttrium–Aluminum–Garnet
TD_{43}	Thermal dose threshold of injury at 43 °C
CEM	Cumulative equivalent
URS	Ureteroscopy
PCS	Pelvicalyceal collecting system
CFD	Computational fluid dynamics
PVA	Polyvinyl alcohol
ODC	Operator duty cycle
DICOM	Digital imaging and communications in medicine
CAD	Computer-aided design
UPJ	Ureteropelvic junction

Introduction

Retrograde intrarenal surgery (RIRS) is a common treatment for urolithiasis. Advances in laser technology have been integral for success with Holmium: Yttrium–Aluminum–Garnet (Ho:YAG) as a standard lithotripsy laser for its ability to pulverize stones of many compositions [1]. Ho:YAG fragmentation occurs predominantly through photothermal effects with some photoacoustic contribution [2]. The stone absorbs laser energy leading to fragmentation and melting. Energy generation during lasing is the main mechanism of

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heat production, increasing fluid temperatures potentially causing thermal tissue injury [3–5].

High-powered lasers (≥ 100 W) can deliver energy at greater frequencies (> 120 Hz), improving treatment efficiency. As power increases, so does heat generated. It is crucial to determine the most efficient method of lithotripsy while preserving patient safety. The threshold of thermal injury (TD_{43}) is the thermal dose, in cumulative equivalent minutes (CEM), held at 43 °C. Tissue denaturation occurs when $TD_{43} \geq 120$ min ($TD_{43} = 120$ CEM); this was first evaluated by Sapareto and Dewey with further evaluation during ureteroscopy (URS) in contemporary studies [6–8]. Current in vitro models have produced valuable information but may be challenging to translate clinically. In vivo and ex vivo animal models more closely simulate human RIRS but are expensive, may not replicate human anatomy, and encompass ethical dilemmas.

The goal of this study was to build on prior studies, using a high-fidelity anatomic human kidney model of a pelvicalyceal collecting system (PCS) which has previously been validated with mechanical and computational fluid dynamics (CFD) testing [9]. Thermal properties of polyvinyl (PVA) hydrogel have been validated as an accurate analog of human tissue [10, 11]. The aims of this study are:

1. Evaluate the temperature profile of the Moses 2.0 Ho:YAG laser at and away from the stone for four different 40 W laser settings using four operator duty cycles (ODCs) with three time-on intervals.
2. Evaluate and compare time to TD_{43} for each laser setting.

Materials and methods

Simulation model fabrication

Digital Imaging and Communications in Medicine (DICOM) data from a patient's CT scan were segmented into a 3D computer-aided design (CAD) model using Mimics software (Materialize, Leuven, Belgium). The 3D CAD model (PCS; PCS volume = 25.1 ml) was 3D printed using hydrogel filament (Fusion3 Design, Greensboro, NC) with a synthetic BegoStone (10:1 powder-to-water ratio by weight) positioned in the renal pelvis and coated with a second PVA mixture (Figure S1A & B). This was then implanted into a hydrogel kidney block. The final product underwent extensive mechanical and CFD testing to replicate PCS properties, stone lithotripsy, and fluid flow (Figure S1C & D) [10].

Laser lithotripsy

Lithotripsy was performed at a standardized power (40 W, short pulse width, Moses technology activated) with continuous normal saline irrigation (100 cm $H_2O = 17.9$ ml/min) via retrograde access with a flexible ureteroscope (LithoVue, Boston Scientific) and a 200 µm Ho:YAG laser fiber (Moses 2.0, Boston Scientific; Figure S2). 40 W was selected for the standardized power given the ability to test four laser settings—two fragmentation (1 J × 40 Hz, 2 J × 20 Hz) and two dusting (0.5 J × 80 Hz, 0.4 J × 100 Hz). We evaluated 3 ODCs (50, 75, and 100%) with different laser-on (30, 60, and 120 s) times. Each experiment consisted of 10 ODCs (1 ODC = one laser-on/pedal activated and one laser-off/pedal off sequence. Also defined as laser time-on divided by total lithotripsy time); the 100% ODC consisted of pedal-on time of 12 min straight with no laser-off time. Ten permutations of each laser setting were tested. A total of 80 (40 tests × 2 runs) experiments were performed. Temperature was measured continuously.

Data collection and analysis

Fluid temperature was recorded with K-type needle thermocouple probes and data logger (Omega, Norwalk, CT) at two positions within the PCS—at the stone (renal pelvis) and away from the stone (upper pole calyx). Thermal dose was calculated with the Sapareto and Dewey formula. Thermal dose is an accepted measure of thermal load and has been extensively tested with the known TD_{43} of human tissue being sustained at 43 °C for 120 min when tissue denaturation occurs and is measured in CEM ($TD_{43} = 120$ CEM) [7, 8, 12–15]. Statistical analysis for thermal dose was analyzed via area under the curve (AUC) and Kruskal–Wallis comparison. Temperature data were analyzed via linear regression in a third-order polynomial (Prism 9). $p < 0.05$ was considered statistically significant.

Synthesized (37 °C starting temperature) data were calculated by taking the difference from 37 °C and the baseline experimental data, then adding this difference to experimental starting temperature (room temperature). Synthesized thermal dose data were calculated from the synthesized temperature data in the same manner as the experimental data.

Results

Fluid temperature increased during all tests. For 100% ODC, recorded temperatures continuously increased until a plateau. At 50% and 75% ODCs, a sinusoidal temperature curve resulted in correlation with laser-on period of the ODC. The

highest cumulative thermal doses and maximum temperatures were recorded mostly at the stone and during longer laser-on times. 100% ODCs delivered the greatest cumulative thermal dose (Fig. 1).

Table 1 shows the thermal dose, time to TD_{43}, and statistical comparisons at versus away from the stone. For 100% ODC, the cumulative thermal dose and time to TD_{43} at the stone was highest/fastest for 2 J × 20 Hz (23,812.3CEM/270 s) and lowest/longest for 0.4 J × 100 Hz (1193.9CEM/490 s); 1 J × 40 Hz was 3994.4CEM/360 s and 0.5 J × 80 Hz was 1289.02CEM/300 s. Away from the stone, the highest/fastest was 2 J × 20 Hz (48,273.2CEM/350 s) and lowest/longest was for 1 J × 40 Hz (81.02CEM/threshold not reached); 0.5 J × 80 Hz was 3757.4CEM/400 s and 0.4 J × 100 Hz was 1193.9/490 s. There was a statistically significant difference between the thermal doses at and away from the stone for 1 J × 40 Hz ($p < 0.0001$) and 0.5 J × 80 Hz ($p = 0.008$).

For 75% ODC, TD_{43} was exceeded during 30 s on/10 s off only for 2 J × 20 Hz away from the stone (156.5 CEM). For 60 s on/20 s off, TD_{43} was reached both at and away from the stone for 2 J × 20 Hz (804.2 and 627.9 CEM), it was reached at the stone only for 1 J × 40 Hz (374.2 CEM) and 0.5 J × 80 Hz (1270.6 CEM). TD_{43} was not reached for 0.4 J × 100 Hz. For 120 s on/40 s off, the threshold was reached for each laser setting at and away from the stone except for 0.4 J × 100 Hz where it was only reached at the stone. The TD_{43} was not reached for any laser settings tested at 50% ODC.

Generally, fragmentation settings delivered higher thermal doses at the stone (0.5 J × 80 Hz had the highest cumulative thermal dose for 75% ODC, 60 s on/20 s off and 50% ODC, and 120 s on/120 s off) and away from the stone (Table S1).

As laser-on time increased, so did the thermal dose. For both the 50% and 75% ODCs, a laser-on time of 120 s delivered the greatest cumulative thermal dose for each laser setting. Table S2 depicts the comparison of thermal dose for ODC- time-on of 50% and 75% ODC separately of each laser setting. When comparing data for 50% ODC, at the stone, all laser-on permutations were significantly different except for 30 s on versus 60 s on for 0.4 J × 100 Hz. For 50% ODC away from the stone, a significant difference was achieved for each comparison except for 30 s on versus 60 s on for 0.5 J × 80 Hz and during 60 s on versus 120 s on for 1 J × 40 Hz and 2 J × 20 Hz. Evaluating 75% ODC, there were statistically significant differences for each time-on cycle except for 0.5 J × 80 Hz for 60 s on/20 s off versus 120 s on/40 s off at the stone and 30 s on/10 s off versus 60 s on/20 s off for 2 J × 20 Hz away from the stone.

Considering laser-off times independent of laser-on times, comparing between 50% versus 75% ODC (30 s on/30 s off versus 30 s on/10 s off, 60 s on/60 s off vs 60 s on/20 s off, and 120 s on/120 s off versus 120 s on/40 s off), a significant difference ($p < 0.0001$) for each ODC permutation at all four laser settings was recorded both at and away from the stone.

When adapting our experimental data to synthesize simulated data at a starting temperature of 37 °C, maximal temperatures were higher and every trial exceeded TD_{43} at both locations except 2 J × 20 Hz, 30 s on/30 s off away from the stone. The time to TD_{43} was reached significantly faster when starting at body temperature. Similar statistical results were appreciated for this synthesized data as well.

Complete temperature data, 50% ODC graphs, and synthesized data for the body-temperature analyses are included in the supplemental material.

Discussion

This study demonstrated significant differences in temperature and thermal dose between four laser settings while varying frequency, energy, and ODC with a standardized power (40 W) and irrigation (17.9 ml/min). When evaluating these results and data, it is important to recognize that, while this high-fidelity model can simulate the PCS during URS, it is not able to fully replicate the surgical environment and every confounding variable that is present during RIRS and laser lithotripsy. Additionally, these studies were performed via in vitro anatomic model at room temperature. We do acknowledge that the raw data may not provide a completely accurate clinical correlation; however, correcting for the baseline starting temperature with the synthesized data, this may allow for a stronger consideration with regards to a more accurate clinical correlation.

While significant differences were recognized, there were no overall trends related to fluid temperatures with relation to the frequency or energy tested. Regardless of ODC and laser settings, the total energy delivered was consistent based on laser-on time (30 s-on = 12 ± 0.2 kJ, 60 s-on = 24 ± 0.1 kJ, 120 s-on = 48 ± 0.1 kJ, 100% = 28.3–30.1 kJ). If the dogma and laws of thermodynamics state that power determines temperature independent of frequency and energy held true [8, 16–18], closer results should have been expected between laser settings. A possible explanation, based on expert opinion, is that even though the laser system was set to 40 W, total power may not be delivered consistently during lasing. The FDA requires Ho:YAG lasers produce an output within 15% of the power setting displayed. Based on flashlamp laser technology, some energy pulses may be closer to the selected settings than others. Power output has been found to fluctuate with the temperatures inside of the laser system, which varies with duration of laser activation.

In a survey of 414 urologists, 67% of responses indicated that dusting (high frequency/low energy) was preferred [19]. Urologists must proceed judiciously as high-powered lasers

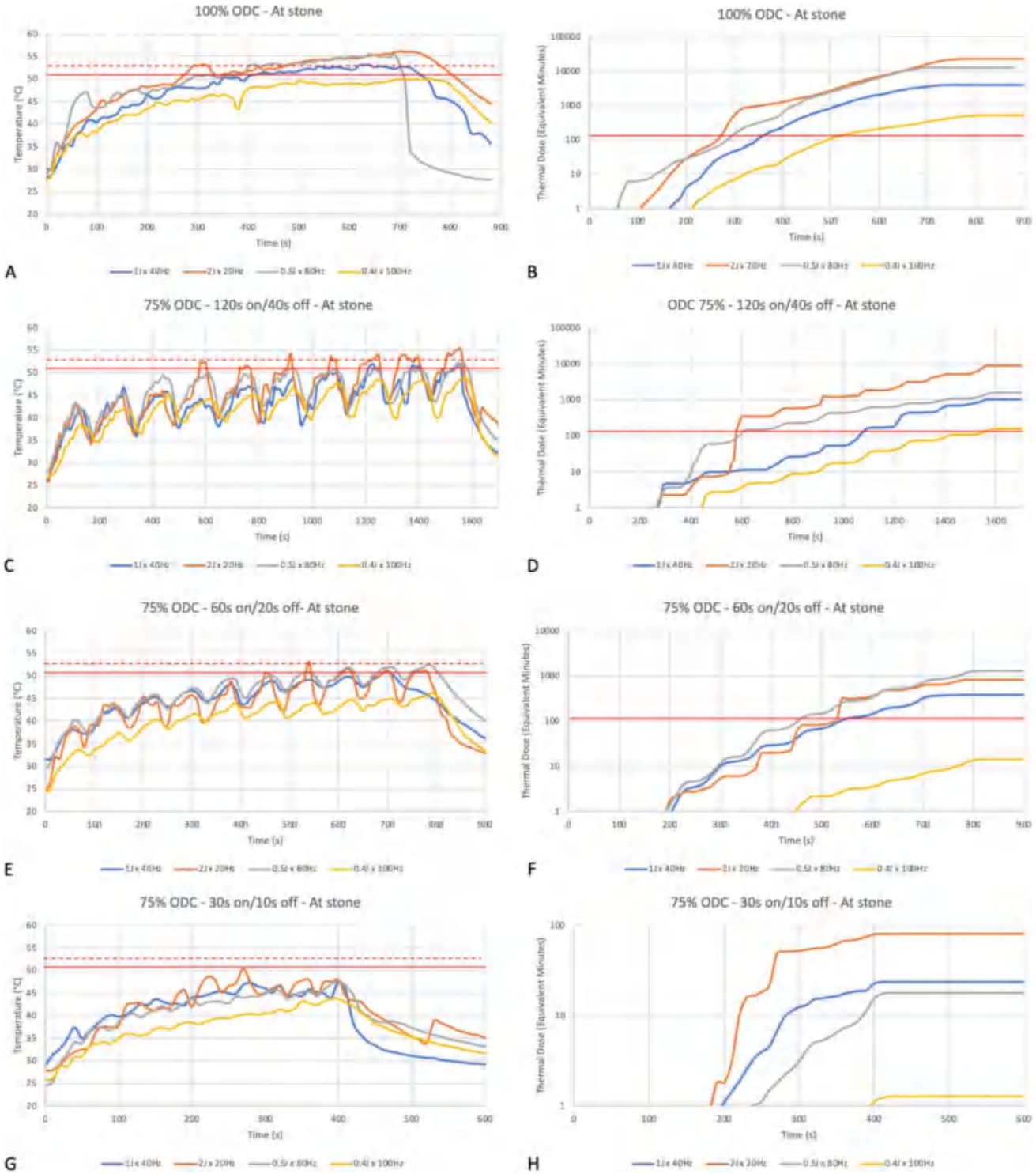


Fig. 1 Temperature and thermal dose graphs of each laser setting at the stone. Critical temperatures of 51 °C (solid red line) and 53 °C (dashed red line) are on temperature graphs. TD_{43} (solid red line) is on the thermal dose graphs. 100% ODC (**A**) temperature and (**B**) thermal dose. 75% ODC: 120 s on/40 s off (**C**) temperature and (**D**) thermal dose; 60 s on/20 s off (**E**) temperature and (**F**) thermal dose; 30 s on/10 s off (**G**) temperature and (**H**) thermal dose

Table 1 Room temperature (experimental) and 37 °C (synthesized) data for cumulative thermal dose (CEM), time to TD_{43}, and statistical comparison at the stone versus away from the stone

Laser setting	ODC	Time on (s)/time off (s)	Cumulative thermal dose (CEM)		Time to thermal injury threshold (s)		P at versus away from Stone
			At stone	Away from stone	At stone	Away from stone	
Experimental starting temperature at room temperature							
1 J × 40 Hz	100%		**3994.372408**	81.01790325	360	NR	< 0.0001
	75%	30/10	23.74853563	5.44836126	NR	NR	< 0.0001
		60/20	**374.2499514**	61.7420721	570	NR	< 0.0001
		120/40	**1008.87866**	**370.2939787**	1080	1060	0.0141
	50%	30/30	1.184148196	0.003849885	NR	NR	< 0.0001
		60/60	6.533942312	2.584527506	NR	NR	0.0101
		120/120	17.34302074	1.170469434	NR	NR	< 0.0001
2 J × 20 Hz	100%		**23,812.30995**	**48,273.20725**	270	350	0.4059
	75%	30/10	79.15143878	**156.5133206**	NR	390	0.1908
		60/20	**804.2165105**	**627.9591831**	540	560	0.4538
		120/40	**8944.85014**	**4270.637634**	580	690	0.0307
	50%	30/30	0.016903765	0.000624035	NR	NR	< 0.0001
		60/60	2.541680503	5.39947926	NR	NR	0.0321
		120/120	73.32476729	6.34378446	NR	NR	< 0.0001
0.5 J × 80 Hz	100%		**12,897.02513**	**3757.371719**	300	400	0.008
	75%	30/10	17.77461774	0.625119376	NR	NR	< 0.0001
		60/20	**1270.627218**	87.21824929	470	NR	< 0.0001
		120/40	**1568.099796**	**566.4515832**	610	940	< 0.0001
	50%	30/30	0.019893315	0.003267131	NR	NR	0.0023
		60/60	0.835863942	0.016868467	NR	NR	< 0.0001
		120/120	49.59701998	9.762252576	NR	NR	< 0.0001
0.4 J × 100 Hz	100%		**496.7329568**	**1193.887628**	520	490	0.0951
	75%	30/10	1.272085656	0.022888439	NR	NR	0.003
		60/20	14.40175912	9.806241275	NR	NR	0.4042
		120/40	**160.0905257**	28.62056023	1550	NR	< 0.0001
	50%	30/30	0.027268611	0.001571028	NR	NR	< 0.0001
		60/60	0.091726583	0.040731872	NR	NR	0.0533
		120/120	7.797394552	1.332162056	NR	NR	< 0.0001
Synthesized starting temperature of 37 °C							
1 J × 40 Hz	100%		**1,908,310.053**	**3222.019151**	125	395	< 0.0001
	75%	30/10	**7322.655539**	**913.1144351**	145	285	< 0.0001
		60/20	**16,378.61107**	**8254.505973**	225	295	0.0260
		120/40	**1,739,669.622**	**407,362.0577**	115	235	0.0034
	50%	30/30	**1443.021766**	**146.2747411**	280	580	< 0.0001
		60/60	**10,627.60964**	**3768.877438**	275	190	0.0251
		120/120	**81,137.7316**	**8242.847493**	115	320	< 0.0001
2 J × 20 Hz	100%		**2,843,906.409**	**15,214,508.32**	105	135	0.0932
	75%	30/10	**46,790.00092**	**160,584.8182**	115	110	0.0199
		60/20	**4,502,069.297**	**3,397,500.191**	85	120	0.3611
		120/40	**21,788,051.72**	**7,106,049.871**	95	115	0.0252
	50%	30/30	**141.4346719**	107.4275158	620	NR	> 0.9999
		60/60	**5230.702309**	**6402.409149**	385	300	> 0.9999
		120/120	**45,458.29682**	**3332.703988**	125	615	< 0.0001

Table 1 (continued)

Laser setting	ODC	Time on (s)/ time off (s)	Cumulative thermal dose (CEM)		Time to thermal injury threshold (s)		P at versus away from Stone
			At stone	Away from stone	At stone	Away from stone	
0.5 J × 80 Hz	100%		**4,064,796.22**	**634,663.1546**	55	155	0.0003
	75%	30/10	**109,286.5641**	**1746.843721**	115	240	< 0.0001
		60/20	**325,400.0589**	**25,879.8443**	140	270	< 0.0001
		120/40	**831,654.9703**	**172,884.6415**	105	275	< 0.0001
	50%	30/30	**511.5047966**	**155.9222927**	360	530	0.0200
		60/60	**4069.699667**	**202.5558009**	340	1130	< 0.0001
		120/120	**365,374.0152**	**91,416.32437**	55	85	< 0.0001
0.4 J × 100 Hz	100%		**413,479.7619**	**752,733.7017**	145	165	> 0.9999
	75%	30/10	**4010.392836**	**355.5392631**	225	310	0.0603
		60/20	**86,184.97564**	**65,075.70654**	195	215	0.7942
		120/40	**211,310.8757**	**24,788.63573**	255	295	< 0.0001
	50%	30/30	**895.0846398**	**129.6287396**	275	500	0.0045
		60/60	**2527.187859**	**551.2766972**	400	620	0.0003
		120/120	**70,227.88752**	**23,026.15331**	105	150	< 0.0001

Bold indicate test that exceeded threshold of thermal injury. NR indicates that the threshold of thermal injury was not reached. Statistics comparing thermal dose and calculated with Kruskal–Wallis

pose the risk of thermal injury. Human tissue can be rendered nonviable after sustaining a thermal dose equivalent of 43 °C for 120 min, 21.8 s at 51 °C, 15 s at 53 °C, and only 1 s at 56 °C; thus, temperature and thermal dose are not linearly related [6–8]; even TD_{43} of as little as 20 min may result in minor renal thermal injury [20]. We demonstrated that higher cumulative thermal doses were generated with longer laser-on times and higher ODCs for all laser settings.

The Laser Research Lab at the University of Michigan has extensively evaluated laser parameters and thermal dose via in vitro bench models and computational modeling. They have evaluated laser power (2.5–50 W), frequency (5–80 Hz), irrigation rate (0–40 ml/min) and temperature (~0 °C and 19 °C), and ODC (50–100%) [7, 8, 12–15]. They sought to adapt their findings into an in vivo porcine model. Continuous temperature monitoring was performed as irrigation rates were manipulated with a standardized power (40 W) and lasing time (100 s). They found that temperatures capable of tissue damage were easily achieved but can be negated by increasing irrigation flow [21].

Our study demonstrated that greater temperatures and thermal doses were delivered with higher ODCs and longer laser-on times. The TD_{43} was reached for ODCs of 100% and 75%. These findings support previously published studies that the threshold for thermal injury was only exceeded for ODCs ≥ 70% while this threshold was reached quicker at higher ODCs [13]. Aldoukhi, et al. performed a chart review of 63 URS cases and determined that mean ODCs are 32%, while the ODC was 63% during the 60 s of greatest power delivered [15]. These findings along with the results of our study indicate that the ODC, laser-on time, and off-times play a crucial role in regulating the fluid temperatures during laser lithotripsy. Advancements in laser technology provide more opportunity in managing large renal stones via RIRS with prolonged ODCs due to wider range of settings and availability of pulsed lasers that limit retropulsion.

Maxwell, et al. compared a simulation with their in vitro test tube model. They recognized that heat was delivered away from the laser tip toward the distal end of the test tube and bounced back to the opening of the tube, causing a more uniform temperature throughout their system [7]. In our study, maximal temperatures and thermal doses were most often recorded at the probe closest to the tip of the laser fiber. Temperatures and thermal dose variations between probe locations can be attributed to ureteroscope manipulation while lasing along with positioning of the stone and laser tip in the PCS. It is important to recognize that the location of the laser tip and stone are decisive in the thermal loads.

It is important to recognize that the power was standardized in this study due to the ability to manipulate the frequency and energy without changing power and 40 W is a high power which can result in dangerous fluid temperatures during RIRS. There have been recommendations to consider performing lithotripsy in the kidney at a power less than 30 W to minimize the risk of thermal injury [16]. Even when higher power settings are utilized, the risk of thermal injury

can be mitigated by taking breaks from lasing, increasing irrigation rates, or using cooled irrigation.

This study had several strengths. First, this study evaluated four factors: temperature, thermal dose, ODC, and laser-on time in an anatomically correct, high-fidelity model. Second, we were able to evaluate thermal load in multiple locations in the PCS. Finally, we were able to measure the temperatures during active lithotripsy. While prior studies have compared some of these factors affecting fluid temperature, the majority of these studies focus on fewer variables [7, 8, 12, 13, 15]. The majority of studies analyzing thermal dose were performed via in vivo or ex vivo animal models or in vitro glass test tube models.

There are several limitations in this study. We acknowledged that these tests were performed on a model starting at room temperature. Despite the lower starting temperature, we demonstrated that dangerous temperatures can be achieved with aggressive lasering. Our results even more strongly demonstrated that TD_{43} can be reached easily starting at corporal temperature based on our more detailed calculations to simulate starting at body temperature. We also recognize that this model only includes a partial ureter segment and this may lead to difficulty transferring results to clinical situations. While some of the data presented may be challenging to correlate to the surgical environment, it is paramount to recognize that dangerous thermal loads can easily be reached in a clinical setting if one is not diligent during laser lithotripsy. Further studies are indicated to pursue increasingly accurate simulations of RIRS for laser lithotripsy.

Conclusion

This study demonstrated that higher temperatures, greater cumulative thermal dose, and TD_{43} were reached faster closer to the tip of the Ho:YAG laser fiber, with longer laser-on times, coupled with shorter laser-off times, and higher ODCs. Both frequency and energy are crucial in temperature generation and thermal dose delivered, even at a standardized power. Fragmentation settings in general elicited greater thermal doses during Ho:YAG RIRS laser lithotripsy compared with dusting settings. Further studies and model development may allow for a more accurate clinical correlation during in vitro laser studies.

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Author contributions CW: project development, data collection, data analysis, and manuscript writing; AS: data collection and data analysis; DP: data analysis and manuscript writing; KD: data analysis and manuscript writing; LS: project development, data collection, and data analysis; NS: project development, data collection, and data analysis; TO: project development and manuscript writing; SQ: project development and data analysis; AG: project development, data collection, and data analysis. All of the listed authors have contributed substantially to the production of this research and manuscript.

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Declarations

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原文

发生了什么？高保真解剖模型中钬激光碎石术热剂量的评估

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摘要

目的：评估钬激光在不同激光参数下，于人体不同部位的热分布情况。

体外解剖盆腔肾盂集合系统（PCS）模型。激光碎石术是治疗尿路结石的基础疗法。随着高功率激光技术的应用，结石消融效率显著提升。手术中患者安全始终是首要考量。众所周知，激光碎石术产生的高温可能造成组织热损伤。

方法：采用高保真3D打印水凝胶模型的PCS，将合成BegoStone植入肾脏

在进行盆腔激光碎石术时，我们使用Moses 2.0钬激光器。在标准功率（40W）和灌注压力（100cm $_2$ H₂O）条件下，我们评估了在四种不同激光设置下，操作员工作循环（ODC）随不同工作时间间隔的变化情况。温度分别在结石位置和远离结石的位置进行测量。

结果激光头附近温度最高，远离激光头时温度逐渐降低。流体温度升高

随着激光作用时间延长和ODC值升高，热剂量也随之增加，当ODC值达到75%和100%时，热损伤阈值被触发。

结论激光光纤尖端附近温度生成和热剂量递送最大，且不

仅依赖功率。在40 W标准功率下，四种激光设置显示出显著的温度差异。温度受多种因素影响，包括激光开启时间、操作员工作周期以及在PCS中的位置。

关键词热剂量·温度·激光碎石术·钬·解剖模型

缩写

RIRS逆行肾内手术

Ho：钇铝石榴石（YAG）；Holmium：钇铝石榴石（Yttrium–Aluminum–Garnet）

TD_{43}	43°C时的热剂量损伤阈值
厘米	累计等效
单位	输尿管镜检查
pc	肾盂肾盏集合系统
CFD	计算流体动力学
PVA	聚乙烯醇
鸟氨酸脱羧酶	操作员值班周期
dicom数字图像与通信	医学
CAD	计算机辅助设计
UPJ	输尿管肾盂连接处

介绍

逆行肾内碎石术（RIRS）是治疗尿路结石的常用方法。激光技术的进步对治疗效果至关重要，钬铝石榴石（Ho：YAG）作为标准碎石激光器，因其能粉碎多种成分的结石而被广泛采用[1]。Ho：YAG碎石过程主要通过光热效应实现，同时伴有光声效应的辅助作用[2]。结石吸收激光能量后发生碎裂和熔融，而激光工作时产生的能量生成是其主要作用机制。

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热量产生，流体温度升高可能造成热组织损伤[3-5]。

大功率激光（≥100瓦）能在更高频率（>120赫兹）下输出能量，显著提升治疗效率。但功率越高，产生的热量也越大。在确保患者安全的前提下，选择最高效的碎石方法至关重要。热损伤阈值（TD_{43}）是指在43℃环境下能承受的热剂量，单位为累积当量分钟（CEM）。当TD_{43}≥120分钟（即$_{TD\ 43}$=120 CEM）时，组织会发生变性。这一标准最初由萨帕雷托和杜威提出，并在后续输尿管镜检查（URS）研究中得到验证[6–8]。虽然现有体外模型提供了宝贵数据，但其临床转化仍面临挑战。相比之下，活体和离体动物模型虽能更贴近人体RIRS（输尿管结石）的生理特征，但存在成本高昂、解剖结构难以复现以及伦理争议等局限性。

本研究旨在基于既往研究成果，采用经机械测试与计算流体动力学（CFD）验证的高精度解剖学人肾模型构建盆腔肾盂集合系统（PCS）[9]。聚乙烯醇（PVA）水凝胶的热学特性已被证实可精准模拟人体组织[10，11]。本研究的主要目标包括：

1. 本研究通过四种不同40瓦激光功率设置，采用四种操作员工作周期（ODCs）及三种开启时间间隔，系统评估了Moses 2.0 Ho：YAG激光器在石料表面及远离石料区域的温度分布特征。
2. 评估并比较每个激光设置的TD时间$_{43}$。

材料和方法

模拟器制造

使用比利时鲁汶Materialize公司开发的Mimics软件，将患者CT扫描的数字医学影像与通信（DICOM）数据分割为三维计算机辅助设计（CAD）模型。该三维CAD模型（PCS，体积25.1毫升）采用北卡罗来纳州格林斯伯勒Fusion3Design公司生产的水凝胶线材进行3D打印，其中合成BegoStone材料（粉末与水重量比10：1）被精准定位在肾盂区域，并覆盖第二层聚乙烯醇（PVA）混合涂层（图S1A和B）。随后将模型植入水凝胶肾脏模型中。最终产品经过全面的力学测试和流体动力学模拟测试，成功复现了PCS的物理特性、结石碎石效果及流体流动状态（图S1C和D）[10]。

激光碎石术

碎石术采用标准化功率（40 W，短脉冲宽度，激活Moses技术）进行，通过逆行通道使用柔性输尿管镜（LithoVue，Boston Scientific）和200μm Ho：YAG激光光纤（Moses 2.0，Boston Scientific；图S2）进行连续生理盐水冲洗（100 cm H_2O=17.9 ml/min）。选择40 W作为标准化功率，因为可以测试四种激光设置——两种碎石模式（1 J×40 Hz，2 J×20 Hz）和两种碎粉模式（0.5 J×80 Hz，0.4 J×100 Hz）。我们评估了三种ODC（50%、75%和100%）在不同激光开启时间（30、60和120秒）下的效果。每个实验包含10个ODC（1 ODC=一个激光开启/踏板激活和一个激光关闭/踏板关闭序列；激光开启时间除以总碎石时间）；100% ODC的踏板开启时间为12分钟，无激光关闭时间。每种激光设置测试了10种排列组合。总共进行了80次实验（40次测试×2次运行），温度持续监测。

数据收集和分析

使用K型针式热电偶探头和数据记录仪（Omega公司，康涅狄格州诺沃克市）在PCS系统内的两个位置——结石部位（肾盂肾盏）和远离结石部位（上极盏）记录液体温度。热剂量采用Sapareto和Dewey公式计算。热剂量是公认的热负荷测量指标，其已通过大量实验验证$_{：当人体组织发生变性时}$，以43°C为基准温度可维持$_{43}$分钟，此时热剂量$TD43_{43}$为120单位[7，8，12–15]。热剂量的统计分析采用曲线下面积（AUC）和Kruskal-Wallis检验。温度数据通过三次多项式线性回归分析（Prism9软件）处理，p<0.05视为具有统计学意义。

合成数据（起始温度37°C）的计算方法是：先将37°C与基线实验数据相减，再将所得差值加到实验起始温度（室温）上。合成热剂量数据的计算方式与实验数据相同，均基于合成温度数据进行。

结果

所有测试中液体温度均持续升高。当使用100%ODC时，记录的温度持续上升直至达到稳定状态。在50%和75%ODC条件下，温度曲线呈现正弦波形，与ODC的激光开启周期存在相关性。

累积热剂量和最高温度记录显示，主要在石质区域且激光照射时间较长时达到峰值。其中，100%ODCs组的累积热剂量最大（图1）。

表1展示了结石位置与远离结石位置时的热剂量、热剂量达到时间$_{43}$及统计学对比结果。对于100%ODC能量密度，结石位置的累积热剂量和达到热剂量时间$_{43}$分别以2 J×20 Hz（23,812.3CEM/270秒）最快/最高，0.4 J×100 Hz（1193.9 CEM/490秒）最慢/最长；1 J×40 Hz为中等（3994.4CEM/360秒），0.5 J×80 Hz为最低（1289.02CEM/300秒）。远离结石位置时，最快/最高值为2 J×20 Hz（48,273.2CEM/350秒），最低/最长值为1 J×40 Hz（未达到统计学显著性，即未达到显著性水平，记为“未达到”）；0.5 J×80 Hz为中等（3757.4 CEM/400秒），0.4 J×100 Hz为最低（记为“1193.9/490秒”）。1 J×40 Hz（p<0.0001）和0.5 J×80 Hz（p=0.008）在结石位置与远离结石位置时的热剂量存在统计学显著差异。

在75%ODC条件下，仅当使用2 J×20 Hz能量密度且远离结石时（156.5 CEM），TD$_{43}$在30秒开启/10秒关闭模式下被突破。对于60秒开启/20秒关闭模式，TD$_{43}$在2 J×20 Hz能量密度下，无论是否靠近结石均达到阈值（分别为804.2 CEM和627.9 CEM），而1 J×40 Hz仅在结石处达到（374.2 CEM），0.5 J×80 Hz则在结石处达到（1270.6 CEM）。0.4 J×100 Hz未达到TD$_{43}$阈值。120秒开启/40秒关闭模式下，除0.4 J×100 Hz仅在牙结石处达到阈值外，其他激光设置在结石处和远离结石处均达到阈值。50%ODC测试的所有激光设置均未达到TD阈值。

总体而言，碎裂设置在结石部位（0.5 J×80 Hz在75%ODC、60秒开/20秒关和50%ODC、120秒开/120秒关时累积热剂量最高）和结石部位外（表S1）均能提供更高热剂量。

随着激光开启时间的延长，热剂量也随之增加。对于50%和75%的ODC设置，120秒的激光开启时间在各激光设置中均产生了最大的累积热剂量。表S2展示了50%和75% ODC开启时间下，不同激光设置的热剂量对比数据。在结石位置进行50%ODC时，除0.4焦耳×100赫兹的30秒与60秒开启时间外，其他所有激光开启时间组合均存在显著差异。对于结石位置外的50%ODC，除0.5焦耳×80赫兹的30秒与60秒开启时间外，其他所有对比均呈现显著差异；而在1焦耳×40赫兹和2焦耳×20赫兹条件下，60秒与120秒开启时间的对比也显示出显著差异。评估75%ODC时，除结石位置外的0.5焦耳×80赫兹外，所有开启时间周期均存在统计学显著差异：结石位置的60秒/20秒与120秒/40秒开启时间，以及2焦耳×20赫兹的30秒/10秒与60秒/20秒开启时间均存在显著差异。

考虑到激光关闭时间与开启时间无关，比较50%与75%的ODC（30秒开/30秒关与30秒开/10秒关，60秒开/60秒关与60秒开/20秒关，在结石位置和远离结石位置时，两种激光设置（120秒开/120秒关与120秒开/40秒关）的ODC置换均显示出显著差异（p<0.0001）。

在将实验数据适配以在37°C初始温度下合成模拟数据时，最大温度值更高，且除2 J×20 Hz、30秒开/30秒关的石块远离位置外，所有试验均超过阈值温度$_{43}$。从体温开始时达到阈值温度$_{43}$的时间显著缩短。这种合成数据也显示出相似的统计学结果。

完整的温度数据、50%ODC曲线以及用于体温分析的综合数据均收录于补充材料中。

讨论

本研究在频率、能量和ODC参数变化时，展示了四种激光设置在温度和热剂量上的显著差异，同时保持了标准化功率（40 W）和灌注（17.9 ml/min）。在评估这些结果和数据时，重要的是要认识到，虽然这种高保真模型可以在URS期间模拟PCS，但它无法完全复制手术环境以及RIRS和激光碎石术期间存在的所有干扰变量。此外，这些研究是在室温下的体外解剖模型中进行的。我们承认原始数据可能无法提供完全准确的临床相关性；然而，通过使用合成数据校正基线起始温度，这可能有助于更准确地考虑临床相关性。

虽然研究发现存在显著差异，但就流体温度与测试频率或能量之间的整体趋势而言，并未发现明显关联。无论ODC参数和激光器设置如何调整，基于激光开启时间计算的总能量始终稳定（30秒开启=12±0.2千焦，60秒开启=24±0.1千焦，120秒开启=48±0.1千焦，100%功率=28.3–30.1千焦）。若热力学定律中“功率决定温度而频率和能量无关”的理论成立[8，16–18]，理论上不同激光设置间应呈现更接近的结果。专家推测，尽管激光系统设定为40瓦，但实际输出功率在激光工作时可能存在波动。根据美国食品药品监督管理局（FDA）规定，钬：钇铝石榴石（Ho：YAG）激光器的输出功率需在设定值的15%范围内。基于闪光灯激光技术原理，部分能量脉冲可能比其他脉冲更接近设定值。研究发现，激光系统内部温度随工作时长变化会产生波动，从而导致功率输出不稳定。

在一项针对414名泌尿科医生的调查中，67%的受访者表示更倾向于使用高频低能激光碎石[19]。泌尿科医生必须谨慎使用高功率激光

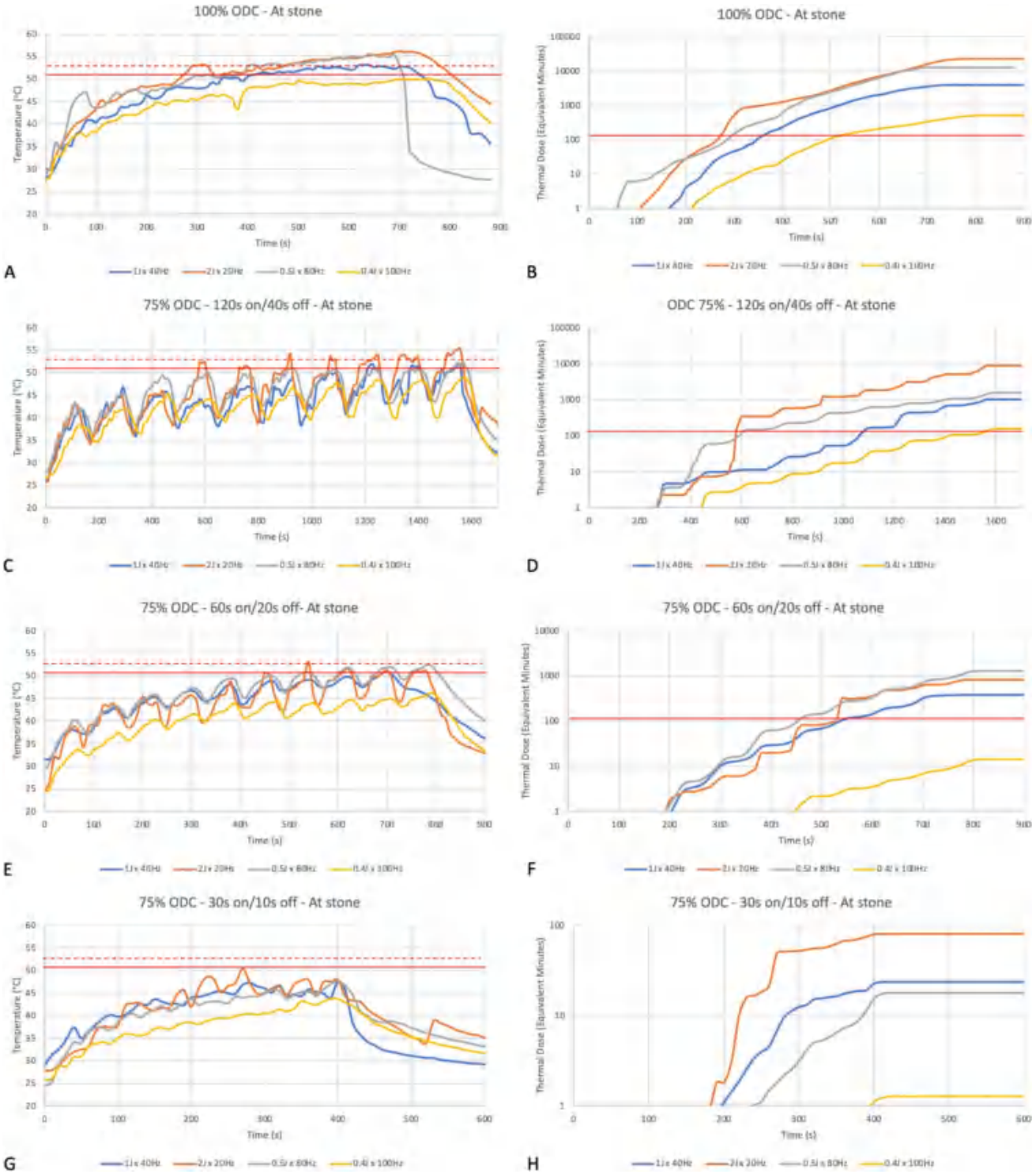


图1每个激光设置在结石处的温度和热剂量曲线。温度曲线上的临界温度为51°C（红色实线）和53°C（红色虚线）。热剂量曲线上的$_{TD43}$（红色实线）为。100%ODC（**A**）温度和（**B**）热剂量。75%ODC：120秒开/40秒关（**C**）温度和（**D**）热剂量；60秒开/20秒关（**E**）温度和（**F**）热剂量；
30秒开/10秒关（**G**）温度和（**H**）热剂量

表1展示了室温（实验）与37°C（合成）条件下累积热剂量（CEM）、至TD时间$_{43}$及石体与非石体对比的统计学比较数据

激光设置	ODC持续时间（秒）/休息时间(s)		累积热剂量（CEM）		达到热损伤阈值的时间(s)		P与对比
			在石头上	远离石头	在石头上	远离石头	远离石头
实验起始温度为室温			*擦除*				
1 J×40 Hz	100%		**3994.372408**	81.01790325	360	编号	<0.0001
	75%	30/10	23.74853563	5.44836126	编号	编号	<0.0001
		60/20	**374.2499514**	61.7420721	570	编号	<0.0001
		120/40	**1008.87866**	**370.2939787**	1080	1060	0.0141
	50%	30/30	1.184148196	0.003849885	编号	编号	<0.0001
		60/60	6.533942312	2.584527506	编号	编号	0.0101
		120/120	17.34302074	1.170469434	编号	编号	<0.0001
2 J×20 Hz	100%		**23,812.30995**	**48,273.20725**	270	350	0.4059
	75%	30/10	79.15143878	**156.5133206**	编号	390	0.1908
		60/20	**804.2165105**	**627.9591831**	540	560	0.4538
		120/40	**8944.85014**	**4270.637634**	580	690	0.0307
	50%	30/30	0.016903765	0.000624035	编号	编号	<0.0001
		60/60	2.541680503	5.39947926	编号	编号	0.0321
		120/120	73.32476729	6.34378446	编号	编号	<0.0001
0.5 J×80 Hz	100%		**12,897.02513**	**3757.371719**	300	400	0.008
	75%	30/10	17.77461774	0.625119376	编号	编号	<0.0001
		60/20	**1270.627218**	87.21824929	470	编号	<0.0001
		120/40	**1568.099796**	**566.4515832**	610	940	<0.0001
	50%	30/30	0.019893315	0.003267131	编号	编号	0.0023
		60/60	0.835863942	0.016868467	编号	编号	<0.0001
		120/120	49.59701998	9.762252576	编号	编号	<0.0001
0.4 J×100 Hz	100%		**496.7329568**	**1193.887628**	520	490	0.0951
	75%	30/10	1.272085656	0.022888439	编号	编号	0.003
		60/20	14.40175912	9.806241275	编号	编号	0.4042
		120/40	**160.0905257**	28.62056023	1550	编号	<0.0001
	50%	30/30	0.027268611	0.001571028	编号	编号	<0.0001
		60/60	0.091726583	0.040731872	编号	编号	0.0533
		120/120	7.797394552	1.332162056	编号	编号	<0.0001
合成起始温度为37°C							
1 J×40 Hz	100%		**1,908,310.053**	**3222.019151**	125	395	<0.0001
	75%	30/10	**7322.655539**	**913.1144351**	145	285	<0.0001
		60/20	**16,378.61107**	**8254.505973**	225	295	0.0260
		120/40	**1,739,669.622**	**407,362.0577**	115	235	0.0034
	50%	30/30	**1443.021766**	**146.2747411**	280	580	<0.0001
		60/60	**10,627.60964**	**3768.877438**	275	190	0.0251
		120/120	**81,137.7316**	**8242.847493**	115	320	<0.0001
2 J×20 Hz	100%		**2,843,906.409**	**15,214,508.32**	105	135	0.0932
	75%	30/10	**46,790.00092**	**160,584.8182**	115	110	0.0199
		60/20	**4,502,069.297**	**3,397,500.191**	85	120	0.3611
		120/40	**21,788,051.72**	**7,106,049.871**	95	115	0.0252
	50%	30/30	**141.4346719**	107.4275158	620	编号	>0.9999
		60/60	**5230.702309**	**6402.409149**	385	300	>0.9999
		120/120	**45,458.29682**	**3332.703988**	125	615	<0.0001

表1（续）

激光设置	马氢酸脱羧酶	开启时间（秒）/休息时间(s)	累积热剂量（CEM）		达到热损伤阈值的时间(s)		P与对比
			在石头上	远离石头	在石头上	远离石头	远离石头
0.5 J×80 Hz	100%		**4,064,796.22**	**634,663.1546**	55	155	0.0003
	75%	30/10	**109,286.5641**	**1746.843721**	115	240	<0.0001
		60/20	**325,400.0589**	**25,879.8443**	140	270	<0.0001
		120/40	**831,654.9703**	**172,884.6415**	105	275	<0.0001
	50%	30/30	**511.5047966**	**155.9222927**	360	530	0.0200
		60/60	**4069.699667**	**202.5558009**	340	1130	<0.0001
		120/120	**365,374.0152**	**91,416.32437**	55	85	<0.0001
0.4 J×100 Hz	100%		**413,479.7619**	**752,733.7017**	145	165	>0.9999
	75%	30/10	**4010.392836**	**355.5392631**	225	310	0.0603
		60/20	**86,184.97564**	**65,075.70654**	195	215	0.7942
		120/40	**211,310.8757**	**24,788.63573**	255	295	<0.0001
	50%	30/30	**895.0846398**	**129.6287396**	275	500	0.0045
		60/60	**2527.187859**	**551.2766972**	400	620	0.0003
		120/120	**70,227.88752**	**23,026.15331**	105	150	<0.0001

加粗表示温度超过热损伤阈值的测试结果，NR表示未达到热损伤阈值。统计学比较热剂量与Kruskal-Wallis检验计算结果。

存在热损伤风险。人体组织在承受43°C热剂量当量120分钟、51°C21.8秒、53°C15秒以及56°C仅1秒后，可能变得无法存活；因此，温度与热剂量并非线性相关[6–8]；即使热剂量当量$_{43}$仅20分钟也可能导致轻微肾热损伤[20]。我们证明，所有激光设置下，激光开启时间越长、光密度值（ODCs）越高，累积产生的热剂量就越大。

密歇根大学激光研究实验室通过体外实验模型和计算建模，对激光参数和热剂量进行了广泛评估。他们评估了激光功率（2.5–50 W）、频率（5–80 Hz）、冲洗速率（0–40 ml/min）和温度（约0°C和19°C），以及ODC值（50–100%）[7，8，12–15]。他们试图将这些发现应用于活体猪模型。在保持标准功率（40 W）和激光时间（100 s）的情况下，通过调节冲洗速率进行连续温度监测。研究发现，虽然很容易达到可造成组织损伤的温度，但通过增加冲洗流量即可消除这种损伤[21]。

我们的研究表明，随着ODC值升高和激光作用时间延长，治疗过程中产生的温度和热剂量也随之增加。当ODC值达到100%和75%时，治疗时长TD $_{43}$会达到阈值。这些发现支持了既往研究结论：热损伤阈值通常在ODC≥70%时才会被突破，且该阈值在ODC值较高时达到得更快[13]。阿尔杜基（Aldoukhi）团队通过对63例上尿路结石（URS）病例的病历分析发现，平均ODC值为32%，而热损伤阈值（ODC）则达到63%。在60秒最大功率输出期间[15]，这些发现结合本研究结果表明，激光头（ODC）、激光开启时间与关闭时间对调控激光碎石术中的液体温度具有关键作用。随着激光技术的进步，由于脉冲激光器能有效抑制后向冲击波，加之更广泛的参数设置范围，使得通过超声碎石术（RIRS）处理大型肾结石时延长碎石时间成为可能。

麦克斯韦团队将模拟实验与体外试管模型进行对比研究。他们发现热量从激光头端向外传导至试管远端后反弹回管口，这种能量传递方式使整个系统温度分布更加均匀[7]。在我们的研究中，最高温度和热剂量通常出现在最靠近激光光纤尖端的探头位置。不同探头位置的温度与热剂量差异，主要源于输尿管镜操作时的激光照射位置、结石定位方式以及激光头在碎石系统中的摆放位置。需要特别指出的是，激光头与结石的位置关系对热负荷产生决定性影响。

需要特别说明的是，本研究之所以采用标准化功率设置，是因为在保持功率不变的前提下可以灵活调节频率和能量输出。需要强调的是，40瓦属于高功率参数，可能导致体外冲击波碎石术（RIRS）过程中液体温度升高，存在安全隐患。目前医学界建议，肾脏碎石治疗应选择功率低于30瓦的参数设置，以最大限度降低热损伤风险[16]。即使采用更高功率参数，仍需警惕热损伤风险。

可通过暂停激光作业、提高灌溉频率或采用冷却灌溉来缓解。

本研究具有多项优势。首先，我们通过解剖学精确的高保真模型，系统评估了温度、热剂量、ODC值及激光照射时间四个关键参数。其次，能够在碎石系统（PCS）的多个部位同步监测热负荷。最后，成功实现了碎石术过程中温度的实时测量。尽管既有研究对比过影响液体温度的某些因素，但多数研究仅聚焦少数变量[7，8，12，13，15]。值得注意的是，热剂量相关研究多采用动物活体/离体模型或玻璃试管体外实验进行。

本研究存在若干局限性。我们承认这些实验是在室温条件下启动的模型进行的。尽管初始温度较低，但通过激进的激光治疗仍能达到危险温度。基于更详细的计算模拟（假设从体温开始），我们的结果更有力地证明了在体温条件下启动时，热损伤阈值（TD）$_{43}$可能轻易达到危险水平。同时需要指出，该模型仅包含部分输尿管段，这可能导致临床应用时结果转移存在困难。虽然部分数据可能难以与手术环境对应，但必须认识到：在临床环境中，若操作人员在激光碎石术中不够谨慎，极易产生危险热负荷。未来研究应致力于开发更精确的激光碎石术热损伤阈值（RIRS）模拟模型。

结论

本研究表明，随着激光运行时间延长、关闭时间缩短以及氧损伤系数（ODC）升高，钬：钇铝石榴石（Ho：YAG）激光光纤尖端附近温度更快上升，累积热剂量（TD）和热剂量$_{43}$值也更高。即使在标准化功率下，频率和能量对温度生成及热剂量传递仍起关键作用。相较于碎石模式，碎石碎石术（Ho：YAG RIRS laser lithotripsy）的碎石设置通常会引发更高热剂量。未来研究和模型开发有望在体外激光实验中建立更精准的临床相关性。

补充信息在线版本包含可在https://doi.org/10.1007/s00345-024-04821-9上获得的补充材料。

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作者贡献：CW：项目开发、数据收集、数据分析及论文撰写；AS：数据收集与数据分析；DP：数据分析及论文撰写；KD：数据分析及论文撰写；LS：项目开发、数据收集与数据分析；NS：项目开发、数据收集与数据分析；TO：项目开发及论文撰写；SQ：项目开发与数据分析；AG：项目开发、数据收集与数据分析。所有署名作者均对本研究及论文的完成作出了实质性贡献。

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声明

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知情同意本研究不需要知情同意。

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ORIGINAL ARTICLE

Assessing renal tissue temperature changes and perfusion effects during laser activation in an in vivo porcine model

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Abstract

Introduction High fluid temperatures have been seen in both in vitro and in vivo studies with laser lithotripsy, yet the thermal distribution within the renal parenchyma has not been well characterized. Additionally, the heat-sink effect of vascular perfusion remains uncertain. Our objectives were twofold: first, to measure renal tissue temperatures in response to laser activation in a calyx, and second, to assess the effect of vascular perfusion on renal tissue temperatures.

Methods Ureteroscopy was performed in three porcine subjects with a prototype ureteroscope containing a temperature sensor at its tip. A needle with four thermocouples was introduced percutaneously into a kidney with ultrasound guidance to allow temperature measurement in the renal medulla and cortex. Three trials of laser activation (40W) for 60 s were conducted with an irrigation rate of 8 ml/min at room temperature in each subject. After euthanasia, three trials were repeated without vascular perfusion in each subject.

Results Substantial temperature elevation was observed in the renal medulla with thermal dose in two of nine trials exceeding threshold for tissue injury. The temperature decay time ($t½$) of the non-perfused trials was longer than in the perfused trials. The ratio of $t½$ between them was greater in the cortex than the medulla.

Conclusion High-power laser settings (40W) can induce potentially injurious temperatures in the in vivo porcine kidney, particularly in the medullary region adjacent to the collecting system. Additionally, the influence of vascular perfusion in mitigating thermal risk in this susceptible area appears to be limited.

Keywords In vivo porcine model · Temperature · Thermal injury · Safety · Ureteroscopy

Introduction

Laser lithotripsy with higher-power laser settings not only can yield smaller stone fragments [1] and faster endoscopic treatments [2] but also imposes a thermal risk to the adjacent renal and ureteral tissues. Several computer simulations, in vitro experiments, and in vivo pre-clinical studies have demonstrated high fluid temperature up to 70 degrees Celsius when utilizing 40 Watt laser settings [3–9].

A clinical study evaluating fluid temperature during Ho:YAG laser lithotripsy of ureteral stones [10] also revealed that temperature of the ureteral fluid exceeded 56 degrees Celsius in most patients, including some treated with 10 Watt laser settings. Additionally, following the introduction of the Thulium Fiber Laser (TFL) several years ago, incidents of ureteral thermal injuries were reported, leading to an Urgent Medical Device Correction by the manufacturer not to exceed 20 W settings in the ureter [11].

Despite this collection of data on temperature elevation from laser activation and several reports of thermal tissue injury, exploration of the relationship between calyceal fluid temperatures and renal tissue temperatures has thus far been limited to a single in vivo porcine study by Okhunov et al. that examined temperature in the collecting system, papilla, medulla, and cortex during ureteroscopy [12]. Only minimal tissue temperature elevation was observed in the papilla in several trials; however, the cessation of laser activation when a ureteroscope thermocouple reached 44 °C (occurring in as quickly as 4 s in some cases) precluded a full sampling of the thermal conditions experienced during ureteroscopy

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[12]. For example, laser lithotripsy in a small calyx with a tight infundibulum (limiting irrigation) with longer periods of laser activation can produce higher and sustained temperatures—between 60 and 80 °C. [4] Thus, it is important to challenge the hypothesis that parenchymal tissue will not experience meaningful temperature elevation with laser activation in a calyx under this more expansive range of conditions as well.

Additionally, the distribution of blood vessels in different regions of the kidney must be considered to more fully understand heat transfer and heat-sink effects within different regions of the kidney. Hence, the objectives of this study were twofold: first, to measure renal tissue temperatures in response to laser activation in a calyx, and second, to assess the effect of vascular perfusion on renal tissue temperatures.

Methods

After obtaining approval from the Institutional Animal Care and Use Committee (IACUC), three female Yorkshire cross pigs (45–55 kg) were anesthetized with telazol and xylazine, intubated, and positioned supine. Animals were ventilated via positive pressure ventilation and maintained under anesthesia with isoflurane and oxygen. Intravenous fluid was provided (0.9% NaCl) and animals were continuously monitored via pulse oximetry and core body temperature.

At the beginning of each procedure, a flexible cystoscope (CYF-3; Olympus) was inserted into the bladder and used to identify the ureteral orifices and advance a 0.035-inch guidewire (Sensor; Boston Scientific) up the ureter. After visualization of the ureter and collecting system with a single-use ureteroscope (LithoVue; Boston Scientific), the initial guidewire was exchanged for a 0.035-inch Amplatz Superstiff guidewire (Boston Scientific).

An Outflow Resistance Altering Tool (ORAT) was passed over the wire into the proximal ureter or renal pelvis. The ORAT is essentially a modified Ureteral Access Sheath (UAS) that allows for adjustment of the outflow resistance to simulate various clinical scenarios, ranging from a narrow ureter to use of an access sheath [13]. In this particular study, the outflow resistance was adjusted to achieve a targeted IRP of 40 cmH_2O while maintaining an irrigation rate of 8 ml/min at room temperature. A prototype flexible ureteroscope with a temperature sensor located at its tip was inserted through the ORAT and fixed in a lower pole calyx for the duration of the trials using an endoscopic fixation device (CystoAssist; Mediflex). A 6 Fr ureteral access catheter (Axxcess; Boston Scientific) was placed into the bladder to maintain drainage.

A multipoint temperature sensing (MTS) needle (MultiPoint 1.5 Thermal Sensor, Boston Scientific) with thermal sensors located 5, 15, 25, and 35 mm from the needle tip was inserted percutaneously with ultrasound guidance through the kidney to the calyx in which the ureteroscope was located. This positioning was intended to locate the four MTS sensors in the collecting system, renal medulla (5 mm from the collecting system), outer region of the renal cortex, and outside the renal capsule, as depicted in Fig. 1. To facilitate data collection, the connectors of the MTS were modified for compatibility with a standard thermocouple data logger (TC-08, Pico Technology).

The ureteroscope position was checked to ensure the laser fiber was not trained directly on the MTS and was not too close to urothelial tissue. A peristaltic pump (Masterflex™ L/S™) delivered 0.9% NaCl irrigation at 8 ml/min at room temperature. A Ho:YAG laser at 40 Watt settings (0.5 J pulse energy, 80 Hz frequency) was activated for 60 s for each trial. Three trials were conducted consecutively in the same calyx in each subject. Adequate time was allotted between trials to ensure temperatures returned to baseline at all thermal sensors before initiating subsequent trials.

Upon completing the experiment, the kidney was carefully harvested with the needle position maintained, and the



Fig. 1 Placement of the MTS within the renal parenchyma. The green marks indicate the locations of the thermal sensors

kidney was sectioned to correlate the temperature sensors' locations with anatomic landmarks (Fig. 1).

A customized MATLAB code was utilized to align the laser and temperature data and perform further calculation. In each trial, thermal dose was computed for each temperature sensor by applying the Dewey and Sapareto methodology to the corresponding temperature curve [14]. Thermal dose is a way to quantify the biological risk of thermal injury, and it depends on the magnitude of temperature elevation and the period of time exposed to elevated temperatures. The threshold for thermal tissue injury and cell death has been established as 120 equivalent minutes [14, 15], which means maintaining a temperature of 43 °C for 120 min. This is equivalent to 44 °C for 60 min, 45 °C for 30 min, and so forth. Even short (1 s) exposures to a temperature of 56 °C will also reach the threshold of thermal injury.

To evaluate the impact of vascular perfusion, temperature decay was examined in the medullary and cortical portions of the kidney. Following euthanasia, additional non-perfusion trials were conducted in the same calyces in each pig. Since core temperature decayed rapidly after euthanasia, a direct comparison of temperatures and thermal dose between perfused and non-perfused trials was not meaningful. Instead, the half-life ($t½$) of temperature decay after laser deactivation was determined from each trial by measuring the time between temperature at the end of laser activation and the midpoint toward baseline temperature. To facilitate comparison, a ratio of $t½$ values for perfused and non-perfused trials was calculated.

Results

Time–temperature curves from each temperature sensor are displayed in Fig. 2. Each curve represents the range of temperatures from three trials. The red line at the bottom designates the 60-s period of laser activation at 40 W settings. Temperature of the collecting system fluid exceeded 60 °C in each trial. Thermal energy propagated into the medulla with peak temperatures ranging from 48 to 52 °C. Cortical temperatures also increased with peak values recorded between 38 and 48 °C. No significant elevation in temperature was observed outside the renal capsule. Following deactivation of the laser, temperature decayed to baseline.

The calculated thermal dose in the medulla of subject #3 ranged from 119 to 380 equivalent minutes. Two of the trials

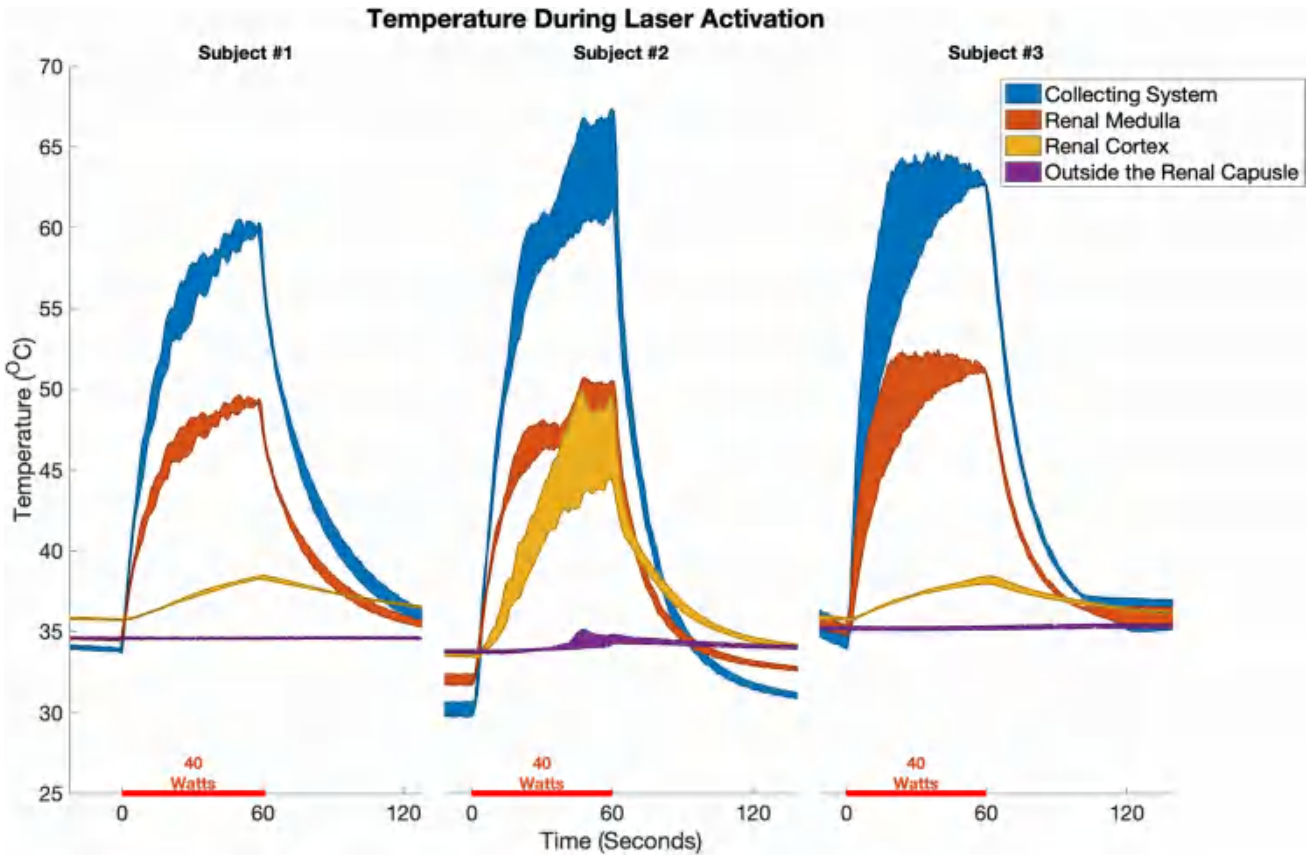


Fig. 2 Time–temperature curves for each subject. Each curve represents the range of temperatures from the three trials conducted. The red line at the bottom designates the 60-s period of laser activation at 40 W settings

exceeded the threshold for thermal injury (120 equivalent minutes), while the third trial was just short. Thermal dose in the medulla of the other subjects ranged from 20 to 55 but did not exceed the thermal threshold for tissue injury (Table 1).

When comparing temperature decay, the ratio of *t½* for non-perfused trials averaged 1.48 ± 0.14 (range 1.3–1.6) times longer in the medullary tissue and 2.6 ± 1.28 (range 1.7–4.1) times longer in the cortical tissue (Fig. 3).

Discussion

This in vivo study utilized MTS to assess the change in temperature within the collecting system, renal medulla, renal cortex, and outside the renal capsule during laser activation in a renal calyx. In the first part of this study, a consistent gradation in temperature was noted from the collecting system to outside of the renal capsule. Substantial temperature elevation was observed in the renal medulla with thermal dose in two of nine trials exceeding threshold for tissue injury.

Table 1 Mean and maximum calculated t43 values of the different thermal sensors across all subjects and trials

	Mean thermal dose	Max thermal dose
Collecting system	709,300	3,954,200
Renal medulla	90	380
Renal cortex	3	24
Outside renal capsule	0	0

These findings diverge from the study conducted by Okhunov et al. [12] primarily due to variations in the study design. Okhunov's study consisted of two main parts. In the first part, the temperature in the collecting system was limited to a maximum of 44 degrees Celsius. However, this temperature limit makes it highly improbable to surpass the threshold for thermal injury. Thus, it does not fully encompass the range of clinical scenarios, as observed in numerous in vitro, pre-clinical in vivo studies, and clinical studies [3–8].

In the second part of Okhunov's study, restrictions were placed on the highest power output, which was capped at 30 Watts. Additionally, an operator duty cycle known to mitigate temperature elevation was imposed on laser activation [16, 17]. Although Okhunov's study conditions, which incorporate robust temperature mitigation techniques, reflect good clinical practice and provide protection under ideal circumstances, not all ureteroscopic cases can be performed under such ideal circumstances. When assessing the risk of thermal injury, it is essential to explore the limits at which high temperatures may be encountered.

The kidneys receive substantial blood flow, approximately 20% of the overall circulation [18]. It seems reasonable to assume that vascular perfusion alone could mitigate temperature elevation from laser activation. A cooling effect has been observed in radiofrequency ablation, where perfusion-mediated tissue cooling has reduced the extent of coagulation necrosis during tumor ablation [19]. However, the dynamics in the kidney are more intricate than the simplified heat diffusion and conduction equation, primarily due to the non-uniform distribution of blood supply within the organ [20].

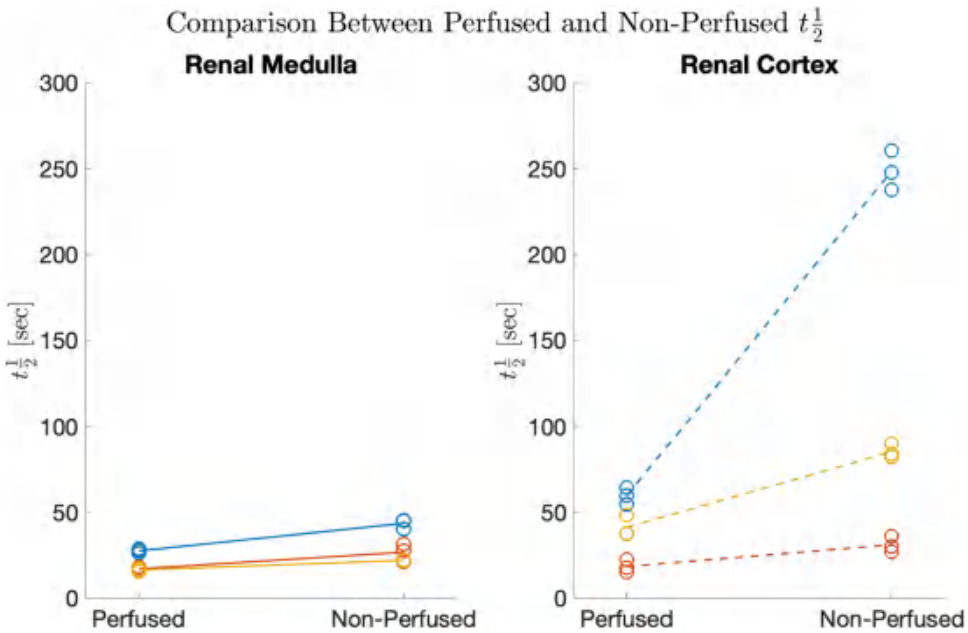


Fig. 3 Comparison of temperature decay (*t½*) between perfused and non-perfused trials, represented by different colors for each subject. The left panel displays the medulla, while the right panel displays the cortex

In the second part of this study, three additional trials were carried out in each porcine subject after euthanasia, without vascular perfusion. Unsurprisingly, the temperature decay time ($t½$) of the non-perfused trials was longer than in the perfused trials. However, the ratio of $t½$ between the non-perused and perfused trials was greater in the cortex than the medulla. This suggests that the vascular heat-sink effect in the cortex is more pronounced than in the medulla. On this basis, the medulla of the kidney appears to be more susceptible to thermal injury than the cortex.

This study has certain limitations. First, the use of the MTS needle with thermal sensors positioned 10 mm apart resulted in only two thermosensors being positioned within the renal parenchyma. Furthermore, our experiment utilized only one needle. Therefore, while this study demonstrates a genuine thermal risk to areas of the kidney adjacent to the calyx in which laser activation occurs, it does not provide a comprehensive thermal assessment of the entire renal parenchyma.

Second, the assessment of the role of perfusion in thermal mitigation, specifically the contribution of convection to thermal spread, was only conducted in a comparative manner and did not quantitatively evaluate perfusion. This is important to note since rapid changes in blood flow during the time of laser activation may be induced due to a combined effect of the intrarenal pressure and potentially temperature changes caused by the laser activation itself. However, our study provides evidence indicating the presence of a thermal injury risk in the renal medulla during ureteroscopy, which exhibits lower perfusion compared to the cortex.

Future studies will focus on thermal mapping of the kidney during laser activation with increased sampling and spatial resolution. This will enable the development of a mathematical model linking thermal dose in the collecting system fluid to thermal injury risk in various kidney regions.

Conclusion

High-power laser settings (40 W) with lower irrigation rates can induce potentially injurious temperatures in the in vivo porcine model, particularly in the medullary region adjacent to the collecting system. Additionally, the influence of vascular perfusion in mitigating the thermal risk in this susceptible area appears to be limited.

Authors contribution R Marom: Project development, Data Collection, Manuscript writing, Data analysis. WW Roberts: Manuscript writing/editing, Data analysis, Critical Revision, Study management. JJ Dau: Manuscript editing. KR Ghani: Manuscript editing. TL Hall: Manuscript editing.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest K.R.G. has consulting relationships with Boston Scientific, Ambu, Olympus, Coloplast, and Karl Storz. W.W.R. has a consulting relationship with Boston Scientific. R.M., J.J.D., and T.L.H. have no disclosures.

Ethical approval All procedures performed in the study involving animal subjects were in accordance with the ethical standards of the institutional research committee and were approved by the University of Michigan's Institutional Animal Care and Use Committee (IACUC).

Disclaimer The prototype ureteroscope used in this study was a concept device/technology, which was not available for sale at the time the study was conducted. Pre-clinical study results may not necessarily be indicative of clinical performance.

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原文

活体猪模型中激光激活过程中肾组织温度变化及灌注效应的评估

Ron Marom[1] · Julie J. Dau[1] · Khurshid R. Ghani[1] · Timothy L. Hall[2] · William W. Roberts[1,2]

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摘要

引言激光碎石术的体外和体内研究均显示液体温度升高，但肾实质内部的热分布尚未得到充分阐明。此外，血管灌注的散热效应仍存在争议。本研究旨在实现双重目标：首先测量肾盏区域激光激活时的肾组织温度变化，其次评估血管灌注对肾组织温度的影响。

方法使用配备温度监测功能的原型输尿管镜对三头猪实施了输尿管镜检查。传感器位于其尖端。在超声引导下，将带有四个热电偶的针头经皮插入肾脏，以测量肾髓质和皮质的温度。在室温下，以8 ml/min的灌注速率对每位受试者进行了三次激光激活（40W）60秒的试验。实施安乐死后，每位受试者在无血管灌注的情况下重复进行了三次试验。

结果在九项试验中，有两项发现肾髓质温度随热剂量增加而显著升高组织损伤的临界温度。非灌注试验的温度衰减时间（t ½）比灌注试验长。t ½的比值在皮质中比在髓中大。

结论高功率激光设置（40W）可在猪肾脏体内诱导具有潜在损伤性的温度，尤其是在邻近集合系统的髓质区域。此外，血管灌注对缓解该易感区域热风险的作用似乎有限。

关键词体内猪模型·温度·热损伤·安全性·输尿管镜检查

介绍

采用高功率激光设置进行碎石术不仅能产生更小的结石碎块[1]和更快的内镜治疗速度[2]，但同时也给邻近的肾组织和输尿管组织带来热损伤风险。多项计算机模拟、体外实验及临床前研究显示，使用40瓦激光设置时，液体温度可高达70摄氏度[3-9]。

一项评估输尿管结石Ho：YAG激光碎石术中液体温度的临床研究[10]研究显示，多数患者输尿管液温超过56摄氏度，其中部分患者使用10瓦激光治疗。此外，自数年前引入铥光纤激光（TFL）以来，输尿管热损伤事件频发，促使制造商紧急发布医疗器械修正案，规定输尿管激光功率不得超过20瓦[11]。

尽管已有大量关于激光激活引发的温度升高的数据记录，以及多篇关于热损伤组织的报道，但关于盏状窝液体温度与肾组织温度关系的研究，目前仅限于奥赫诺夫团队在猪体内进行的一项研究。该研究通过尿路镜检查，检测了收集系统、乳头、髓质和皮质的温度变化[12]。多项试验显示，乳头组织的温度升高幅度微乎其微；然而，当尿路镜热电偶温度达到44°C时（某些情况下仅需4秒即可触发激光关闭），导致无法完整采集尿路镜检查期间的热环境数据。

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[12]例如，对于小叶盏且漏斗部狭窄（限制冲洗）的情况，采用较长的激光激活时间进行碎石术，可使温度持续升高至60-80°C。[4] 因此，有必要对以下假设提出质疑：在更广泛的实验条件下，激光激活下叶状结构的实质组织不会出现显著的温度升高。

此外，要全面理解肾脏各区域的热传递与散热效应，必须考虑其血管分布特征。本研究旨在实现双重目标：首先测量肾盏区域激光激活后的组织温度变化，其次评估血管灌注对肾组织温度的影响。

方法

在获得机构动物护理与使用委员会（IACUC）的批准后，三头雌性约克夏杂交猪（45–55公斤）被用特拉唑和木糖素麻醉，插管后仰卧位。动物通过正压通气进行通气，并在异氟烷和氧气麻醉下维持。静脉输注液体（0.9%氯化钠），并通过脉搏血氧饱和度和核心体温持续监测动物状况。

在每次操作开始时，医生会先将柔性膀胱镜（型号CYF-3；奥林巴斯）插入膀胱，用于定位输尿管开口并推进0.035英寸导丝（Sensor；波士顿科学）。当使用一次性输尿管镜（LithoVue；波士顿科学）观察输尿管及收集系统后，将初始导丝更换为0.035英寸的Amplatz Superstiff导丝（波士顿科学）。

将一种流出阻力调节工具（ORAT）沿导丝送入近端输尿管或肾盂。ORAT本质上是一种改良的输尿管通路鞘（UAS），可调节流出阻力以模拟各种临床场景，范围从狭窄输尿管到使用通路鞘[13]。在本研究中，通过调节流出阻力，在室温下保持8 ml/min的灌洗速率的同时，实现了40 cmH $_2$O的目标尿流率（IRP）。将带有温度传感器的原型柔性输尿管镜通过ORAT插入，并使用内镜固定装置（CystoAssist；Mediflex）在试验期间固定于下极盏部。为维持引流，将6 Fr输尿管通路导管（Axxcess；Boston Scientific）置入膀胱。

多点温度传感（MTS）针（MultiPoint 1.5 Thermal Sensor，Boston Scientific），其热传感器分别位于距针尖5、15、25和35毫米处

空斯普林格

在超声引导下，经肾脏皮下穿刺至盏部（输尿管镜所在位置），将MTS传感器组置入该区域。该定位方案旨在将四个传感器分别部署于集合系统、肾髓质（距集合系统5毫米处）、肾皮质外缘及肾包膜外侧，具体位置如图1所示。为便于数据采集，我们对MTS传感器的连接器进行了改造，使其与标准热电偶数据记录仪（型号TC-08，Pico Technology）兼容。

检查输尿管镜位置以确保激光光纤未直接对准MTS且未过于接近尿路上皮组织。蠕动泵（Masterflex™L/S™）在室温下以8 ml/min的流速输送0.9%氯化钠冲洗液。每次试验中，使用40瓦霍氏钇铝石榴石激光器（脉冲能量0.5焦耳，频率80赫兹）持续激活60秒。每位受试者在同一盏盏叶内连续进行三次试验。试验间留有充足时间以确保所有热传感器温度恢复至基线值，随后再开始下一次试验。

实验完成后，肾脏被小心取出，同时保持针头位置不变，随后



图1 MTS在肾实质中的定位。绿色标记表示热传感器的位置

对肾脏进行切片处理，以将温度传感器的位置与解剖标志进行关联（图1）。

本研究采用定制的MATLAB代码对激光与温度数据进行对齐处理并开展后续计算。每次实验中，通过将杜威-萨帕雷托法应用于对应温度曲线[14]，为每个温度传感器计算热剂量。热剂量是量化热损伤生物学风险的指标，其数值取决于温度升幅的大小及暴露于高温环境的时间长短。目前热组织损伤与细胞死亡的临界值被确定为120等效分钟[14，15]，这意味着当温度维持在43°C时

120分钟。这相当于在44°C下持续60分钟，或在45°C下持续30分钟，依此类推。即使短至1秒的56°C高温暴露，也会达到热损伤的临界点。

为评估血管灌注的影响，研究人员对肾脏髓质和皮质区域的体温衰减情况进行了检测。实施安乐死后，研究者在每头猪的同侧肾盏中进行了额外的非灌注实验。由于核心体温在安乐死后迅速下降，因此无法直接比较灌注与非灌注实验中的体温变化及热剂量差异。有意义。相反，通过测量激光激活结束时的温度与基线温度中点之间的间隔时间，确定了激光失活后温度衰减的半衰期（t ½）。为了便于比较，计算了灌注和非灌注试验的t ½值的比值。

结果

各温度传感器的温度-时间曲线如图2所示。每条曲线代表三次实验的温度范围。底部红线标示了40瓦激光设置下60秒的激活周期。采集系统液体温度在每次实验中均超过60°C。热能向髓质区域传导，峰值温度介于48至52°C之间。皮质温度同样升高，峰值记录在38至48°C区间。在肾包膜外未观察到显著温度升高。激光停用后，温度逐渐回落至基线水平。

受试者3的髓质中计算出的热剂量范围为119至380等效分钟。其中两项试验

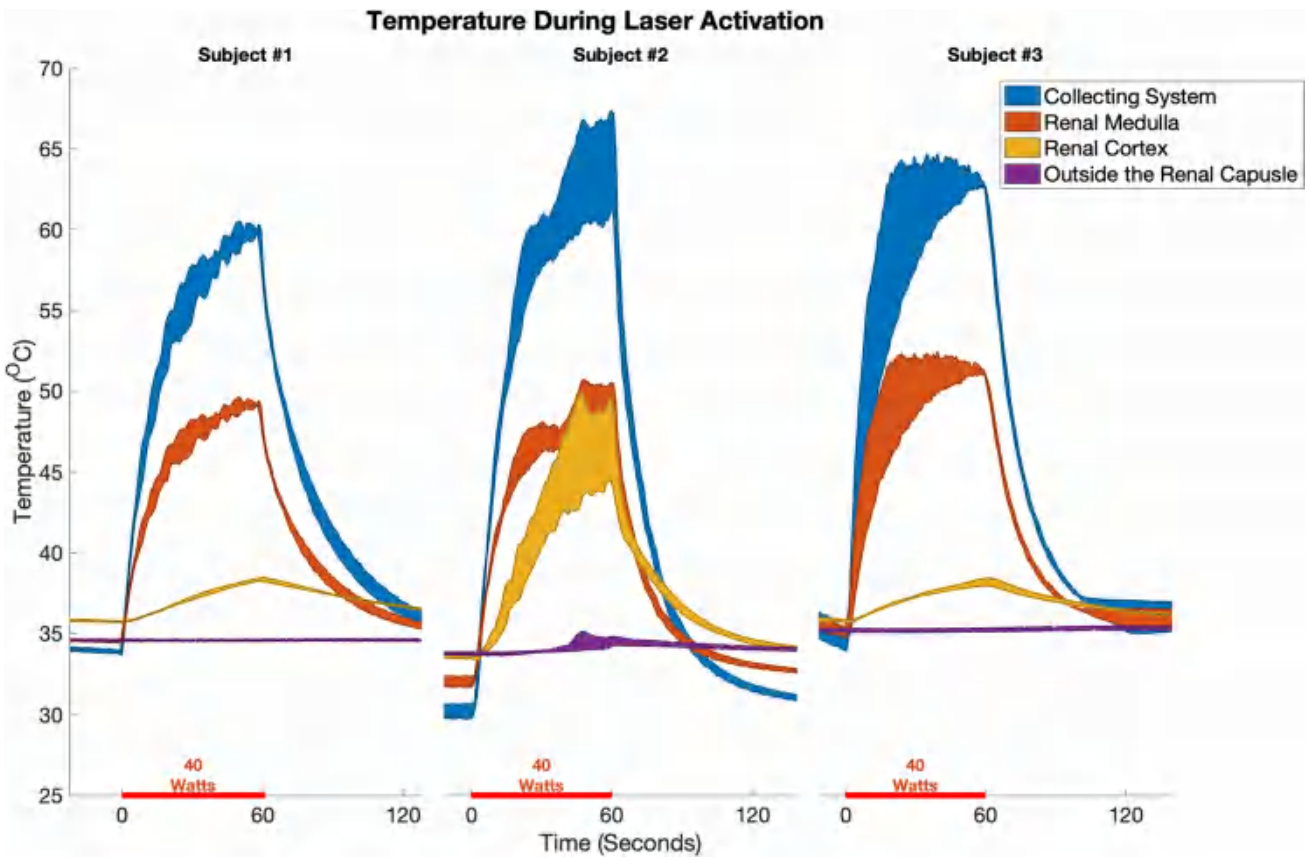


图2为各受试者的时间-温度曲线，每条曲线代表三次试验的温度范围，底部红线表示40W激光激活60秒的周期

超过了热损伤的阈值（120分钟等效时间），而第三次试验刚好未超过。其他受试者脊髓中的热剂量范围为20到55，但没有超过组织损伤的热阈值（表1）。

在比较温度衰减时，非灌注试验的t ½比值在髓质组织中平均长1.48±0.14倍（范围1.3-1.6倍），在皮质组织中平均长2.6±1.28倍（范围1.7-4.1倍）（图3）。

讨论

本项体内研究采用MTS技术，监测肾盏激光激活过程中收集系统、肾髓质、肾皮质及肾包膜外温度变化。研究初期发现，温度从收集系统向肾包膜外呈梯度递增。在九次实验中，有两次肾髓质温度显著升高，其热剂量已超过组织损伤阈值。

表1所有受试者和试验中不同热传感器的平均和最大计算t43值

	平均热剂量	最大热剂量
收集系统	709,300	3,954,200
肾髓质	90	380
肾皮质	3	24
肾外囊	0	0

这些发现与奥赫诺夫等人[的研究结果存在差异。12]这主要源于研究设计的差异。奥赫诺夫的研究包含两个主要部分。在第一部分中，采集系统的温度被限制在最高44摄氏度。然而，这种温度上限使得超过热损伤阈值的可能性极低。因此，该研究未能完全涵盖临床场景的多样性，正如我们在大量体外实验、临床前体内研究及临床试验中所观察到的[3–8]。

在奥赫诺夫研究的第二阶段，研究人员对最高功率输出进行了限制，将其上限设定为30瓦。此外，还对激光激活施加了已知能降低温度升高的操作员工作周期[16，17]。尽管奥赫诺夫的研究条件采用了完善的温度控制技术，符合良好的临床实践标准，并在理想条件下提供了保护措施，但并非所有输尿管镜手术都能在如此理想的条件下进行。在评估热损伤风险时，必须探索高温可能达到的极限值。

肾脏的血流量占全身循环总量的约20%[18]。可以合理推测，仅通过血管灌注作用就能缓解激光激活引发的温度升高。在射频消融术中已观察到冷却效应，其中灌注介导的组织冷却作用可减少肿瘤消融过程中的凝固性坏死[19]。然而，肾脏的动态变化比简化版的热扩散与传导方程更为复杂，这主要源于器官内部血液供应分布的不均匀性[20]。

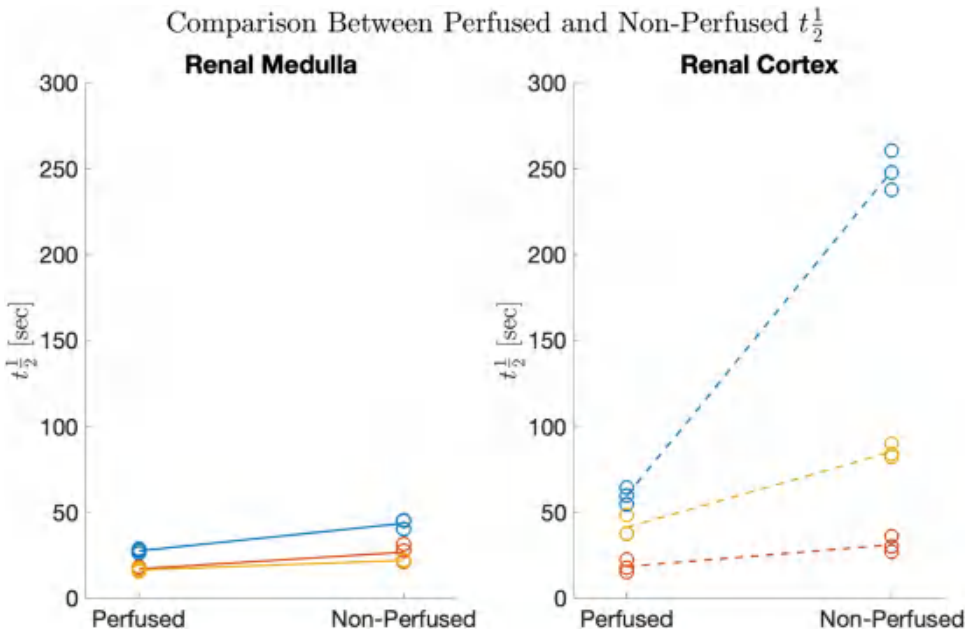


图3血液灌注与非灌注试验的温度衰减（t ½）对比，不同颜色代表不同受试者。左图显示延髓，右图显示大脑皮层

在本研究的第二阶段，我们对每只接受安乐死处理的猪只进行了三次额外实验，这些实验均未进行血管灌注。不出所料，未灌注组的体温衰减时间（t ½）明显长于灌注组。但值得注意的是，皮层区域未灌注与灌注组的t ½比值差异大于脊髓区域。这表明皮层的血管散热效应比脊髓更为显著。由此可以推断，肾脏的脊髓区域比皮层更容易受到热损伤。

本研究存在若干局限性。首先，采用间距10毫米的MTS针头搭配热传感器时，仅有两个传感器能定位在肾实质内。其次，实验仅使用单根针头。因此，尽管本研究证实了激光激活区域邻近肾盏的肾脏组织确实存在热损伤风险，但未能对整个肾实质进行全面的热学评估。

其次，关于灌注在热缓解中的作用评估——特别是对流对热扩散的贡献——仅以比较方式展开，未对灌注进行定量分析。这一点需要特别注意，因为在激光激活期间，肾内压力与激光激活本身可能引发的温度变化共同作用，可能导致血流快速变化。不过，我们的研究提供了证据表明：在输尿管镜检查过程中，肾髓质存在热损伤风险，其灌注水平较肾皮质更低。

未来研究将重点开展肾脏激光激活过程中的热成像分析，通过提升采样频率和空间分辨率，建立数学模型，将采集系统液体中的热剂量与肾脏不同区域的热损伤风险相关联。

结论

高功率激光（40瓦）配合较低的冲洗速率，可能在猪体内模型中引发损伤性温度，尤其在靠近收集系统的髓质区域。此外，血管灌注对缓解该敏感区域热风险的作用似乎有限。

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免责声明本研究中使用的输尿管镜原型是概念器械/技术，研究进行时未上市。临床前研究结果不一定能反映临床性能。

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UROLOGY - ORIGINAL PAPER

Comparison of temperature and renal tissue thermal damage by holmium laser with different energy parameters during lithotripsy: in vitro porcine kidney model

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Abstract

Objective Holmium laser percutaneous nephrolithotripsy was simulated by porcine kidney calculus model in vitro to investigate thermal damage of renal tissue by different energy parameters of the holmium laser.

Methods We placed human kidney calculus specimen in fresh vitro porcine kidney, then insert thermocouple temperature probes into the submucosa of the renal pelvis and reheated in a 37 °C water bath. A percutaneous nephrological sheath was used to penetrate the renal parenchyma with a moderate irrigation rate of 30 ml/min at 18 ℃. The Holmium laser was used to fragment the stones under a nephroscope, and the temperature was recorded.

Results The four independent models were lithotripsy with 30 W and 60 W laser for 5 and 10 min, respectively; the mean temperature of 30 W vs. 60 W within 5 min was 36.06 °C vs. 39.21 °C ($t=5.36$, $P<0.01$) and the highest temperature was 43.60 °C vs. 46.60 °C; the mean temperature of 30 W vs. 60 W within 10 min was 37.91 °C vs. 40.13 ℃ ($t=5.28$, $P<0.01$), maximum temperature 46.80 ℃ vs. 49.20 ℃. Pathologically, each kidney was observed to have different degrees of thermal damage lesions, and the higher power and longer time the more severe the injury, but the injury was mainly limited to the uroepithelial and subepithelial tissues, with rare damage to renal tubules.

Conclusion The higher laser excitation power and longer duration raised the intrarenal temperature significantly and caused a certain degree of thermal damage to the kidney tissue, but overall it was found to be safe and reliable. Urologists can avoid further side effects through surgical expertise.

Keywords Holmium laser · Lithotripsy · Thermal damage · Intrarenal temperature

Background

The incidence of urinary calculus is gradually increasing worldwide, and in some cases, complex calculus require surgical intervention. With the continuous development of minimally invasive surgery, the treatment of upper urinary tract stones has shifted from open surgery to endoluminal surgery. Percutaneous nephrolithotomy (PCNL) and flexible ureteroscopy (FURS) are widely performed in clinical practice due to their less invasive nature, precise efficacy, and maturity of application [1]. The advancement of lithotripsy energy output modalities has also contributed to the progress of minimally invasive surgery. Since the 1980s, lasers have been officially used in medicine, and the unique physical effect of the holmium laser on human calculus makes it highly efficient for lithotripsy. Although it has been shown that the thulium fiber laser is not inferior for this purpose, the holmium laser remains a state-of-the-art device for endoscopic lithotripsy [2]. The holmium laser is the most commonly used laser in urology surgery due to its outstanding advantages, with approximately 95% of its energy absorbed by the surrounding 5 mm water medium and good directivity [3].

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However, despite the increasing popularity of the holmium laser, we have observed that patients undergoing holmium laser lithotripsy exhibit a higher frequency of complications such as ureteral and pelvic stenosis adhesions or even impaired renal function [4]. Most previous thermal studies on the holmium laser did not consider the absorption of laser energy by calculus or discuss tissue pathological changes in depth. Therefore, our study aimed to simulate reality with a more detailed experiment.

Materials and methods

Experimental model

Kidney model

Fresh porcine kidney models were obtained directly from a meat plant and stored in frozen transit at − 4 to 0 °C. The kidneys were used for the study within one hour of isolation. Porcine kidney morphology and size were basically the same, no other lesions, perirenal fat, envelope were trimmed and cleaned before the experiment operating.

Calculus

The human urinary calculus used in this study underwent harmless treatment and compositional analysis. The primary components of these calculus are calcium oxalate dihydrate and calcium oxalate pentahydrate, which are the most prevalent types. The calculus were surgically extracted from the kidney or ureter, and patients provided informed consent for the use of their calculus specimens in this research. The calculus were then reduced and polished to a size of approximately 2–2.5 cm and inserted into the incision made in the porcine renal pelvis. Subsequently, the assembly system was sutured using silk thread (Fig. 1).

Equipment

The equipment included holmium laser lithotripsy system (HZ Series, Potent Optoelectronics, China), endoscopic monitoring system (Richard Wolf, Germany), nephroscope (F9.5, Richard Wolf, Germany), renal puncture sheath (F20, Veili Medical, China), thermostatic water bath system (HH420, YuNuo Instrument, China), thermocouple thermometer and probe (TA612 Series, Suzhou TASI Electronics, China), lavage pump (Fig. 2).

Procedure

1. A fresh vitro porcine kidney combined with a urinary calculus model was prepared. Two thermocouple temperature probes were inserted into the kidney tissue in the proposed lithotripsy area, with a probe phase distance of 1 cm. The probes were positioned as close as possible to the urothelial layer of the collecting system, approximately 5 mm away from the epithelial tissue, ensuring avoidance of penetration into the renal pelvis cavity.
2. The porcine kidneys were rewarmed in a 37 ℃ thermostatic saline bath. The experiment was started by monitoring the kidney temperature until it reached 37 ℃. The renal pelvis was punctured with an F20 nephroscopic sheath, and the nephroscope combined with a holmium laser was used to smash the stones in the kidney. Machine-controlled continuous saline irrigation was used at a uniform moderate rate of 30 ml/min and an irrigation fluid temperature of 18 °C (room temperature). Following urologists' surgical habits, the holmium laser was activated in a trial by the same surgeon for 20–25 s per continuous relay with a 5 s pause. The urologist who conducted the trial was surgically experienced, with more than 10 years of experience in the specialty, and performed approximately 200 laser lithotripsy procedures per year.
3. Experimental groups: The study was divided into four groups with different laser parameters: Group A setting 30 W (2 J, 15 Hz), for 5 min; Group B setting 60 W (3 J, 20 Hz), 5 min; Group C setting 30 W (1 J, 30 Hz), 10 min; Group D setting 60 W (2 J, 30 Hz), 10 min.
4. Once the allotted time for each group was reached, lithotripsy was discontinued, and the kidney was dissected to visually assess histopathological changes within the lithotripsy area. Tissue samples from potential thermal damage sites were collected and preserved in formalin. Microscopic examination of the prepared tissue sections was subsequently conducted to observe any pathological alterations.

Data statistics

Temperature recording software was provided by TASI, Inc. with a recording interval of 5 s. Two probe temperature data within the same kidney model were recorded by taking the average value after data export. All data were imported into Microsoft Excel and SPSS 22.0 to produce graphs. The mean temperature of each group was compared, and the difference was examined by t test, the calibration level $\alpha = 0.05$.

Results

In each group, two kidney models were employed for two independent trials. The maximum temperature for Group A in two trials was 43.60 ℃., the mean temperature was

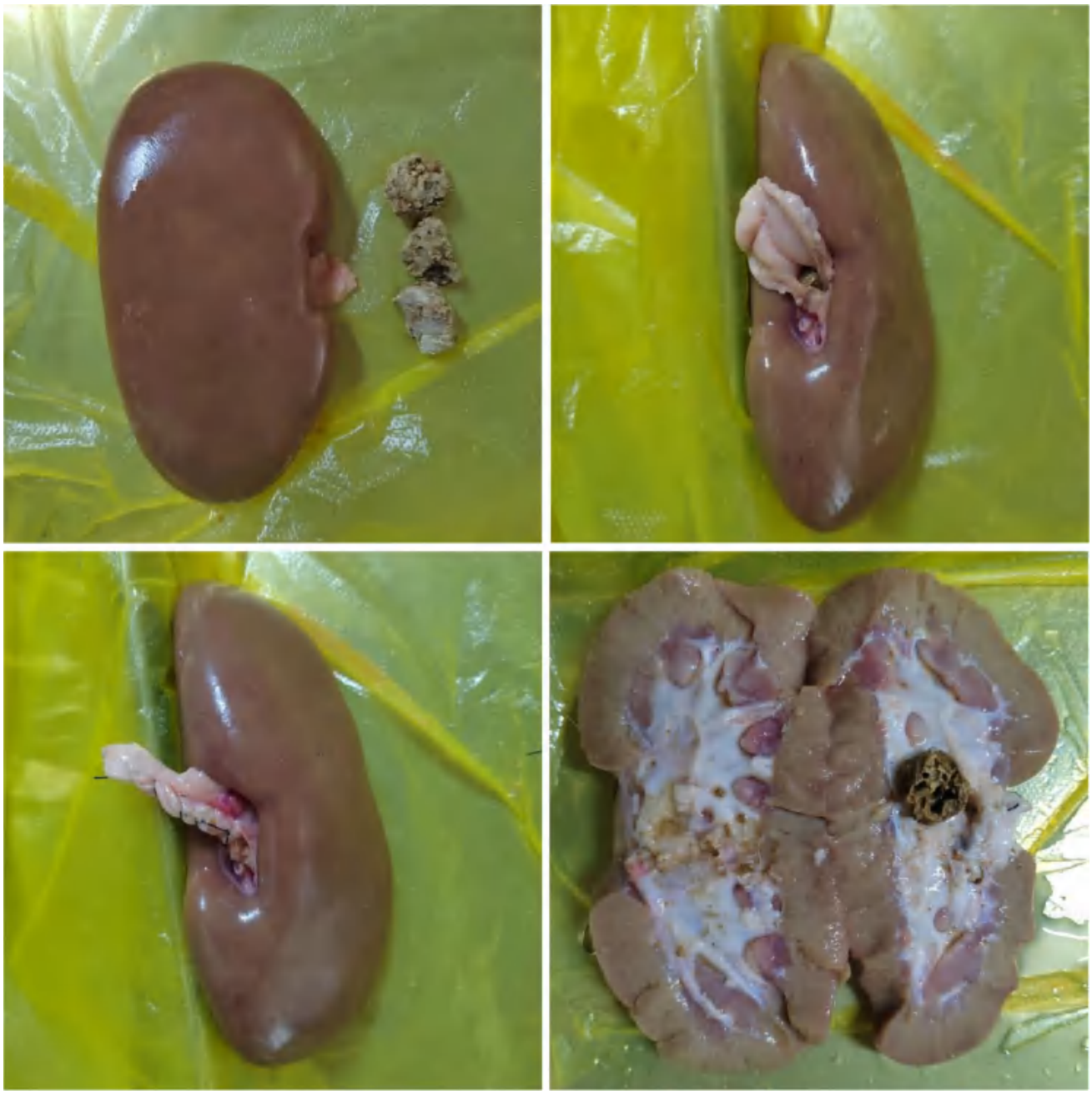


Fig. 1 Porcine kidney with calculus model

36.01 ℃ and 36.10 ℃. While the maximum temperature of Group B was 46.60 ℃, the mean temperature was 39.39 ℃ and 39.02 ℃. The temperature profiles of Group A and B are shown in Fig 3a, b. After data consolidation, the mean temperature in Group B was higher than in Group A(39.21 °C vs. 36.06 °C, $t = 5.36$, $P = 0.00$), and the heat generated by the 60 W laser during the 5 minute laser lithotripsy had a greater effect on the increased kidney temperature.

A comparison was made between Group C, where Holmium laser excitation was performed for 10 min, and Group D. The maximum temperature of Group C was 46.8 °C with mean temperatures of 37.56 °C and 38.25 °C in both trials. While the maximum temperature of Group D was 49.2 °C with mean temperatures of 40.08 °C and 40.18 °C, respectively (Fig. 3c, d). Group D, with 60 W laser for 10 min, when compared to Group C (30 W), had more significant elevation of renal parenchymal temperature and may have caused thermal damage to the tissue (40.13 °C vs. 37.91 °C, $t = 5.28$, $P = 0.00$).



Fig. 2 Equipment and procedure

We dissected each kidney after laser excitation. For each kidney we took 3–5 pieces of tissue for pathological observation, near the thermocouple probe. Mild to moderate thermal damage was more common in Group A and C. Microscopically, the mucosal epithelium of the renal pelvis was detached from the underlying tissue to varying degrees, with some of the superficial umbrella cells only missing and some of the whole layer missing, exposing the bare basement membrane and edema of the mucosal lamina propria (Fig. 4a, b). More severe thermal damage was seen in specimens from groups B and D. The mucosal epithelium was degenerated and detached, with edema of the lamina propria and varying degrees of degeneration and necrosis of the mucosal muscle, myocytes and collagen fibers of the outer membrane (Fig. 4c). We classified the damage in the 53 pathological sections produced, defining 19 sections with severe thermal damage, 2 in Group A, 4 in Group B, 5 in Group C, and 8 in Group D; 24 sections with moderate thermal damage, 8 in Group A, 6 in Group B, 6 in Group C and 4 in Droup D, respectively; and 10 sections with mild damage, 3 in Group A, 3 in Group B, 2 in Group C and 2 in Group D. Ranking the proportion of severe thermal injuries from highest to lowest, we had Group D at 57.1%, Group C at 38.5%, Group B at 30.8%, and Group A at 15.4%.

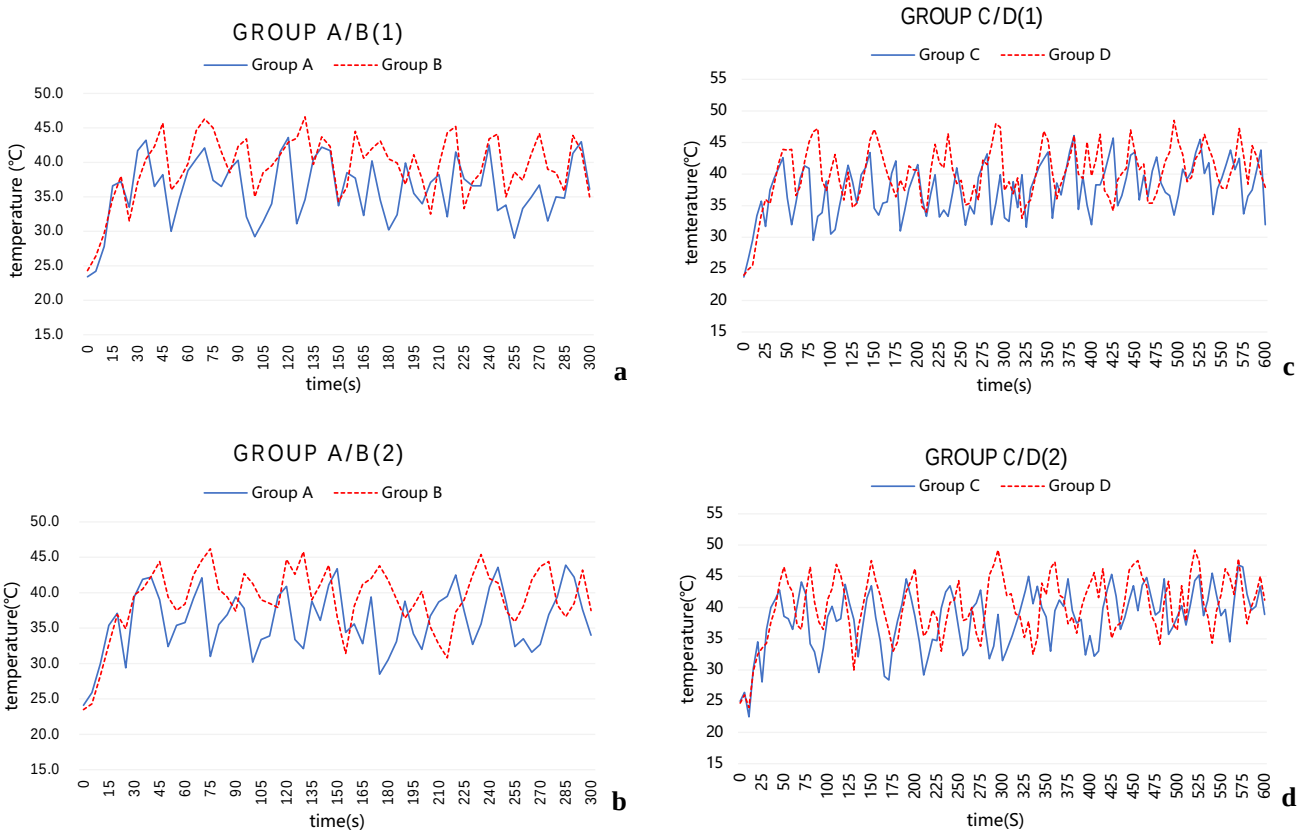


Fig. 3 Temperature profiles of different laser energy parameters. **a** Group A/B 1st trail. **b** Group A/B 2nd trail. **c** Group C/D 1st trail. **d** Group C/D 2nd trail

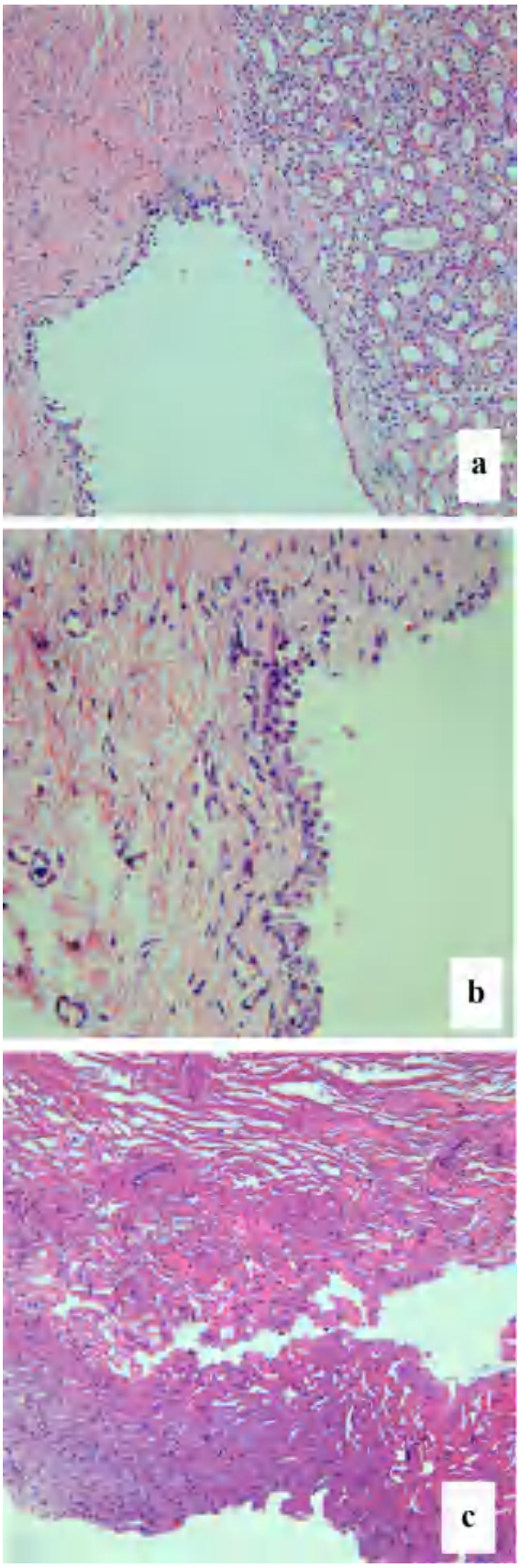


Fig. 4 Pathological pictures of thermal damage renal tissue. **a** Mild. **b** ▸ Moderate. **c** Severe

Discussion

Holmium laser lithotripsy has emerged as the preferred treatment modality for urolithiasis. However, most of the previous experiments on isolated animal organs or equipment were only for the purpose of observing temperature changes, and less attention was paid to actual histopathological damage [5]. In vivo animal experiments fully consider the influence of blood flow on temperature changes, and the monitored temperature is closer to reality [6]. However, creating a urinary calculus model in vivo animals is very difficult, and the accuracy of temperature monitoring is not as good as that in vitro. Moreover, model consistency and sample size are both major challenges to controlling bias. Our study innovatively integrates the advantages of in vitro and in vivo experiments, especially in the production of calculus models and pathological observation, which better simulates the actual situation compared with previous studies.

Holmium laser primarily relies on the photothermal mechanism of lithotripsy, where the aqueous medium at the tip of the transmitting fiber absorbs energy and undergoes rapid vaporization to form microbubbles [7]. However, not all of the energy is absorbed by the water and transmitted to the target stone. This laser-emitted energy that does not reach the stone can spill out, elevating intrarenal temperature, damaging the urinary epithelium, and possibly creating complications [8]. Direct impact of laser energy on the flushing fluid is less likely to occur in real procedures. Therefore, we included human calculus samples in our study.

The water flow rate is one of the most important factors affecting the temperature during lithotripsy [8]. A higher water flow rate can significantly lower intrarenal temperature; however, it also leads to increased intrarenal pressure, thereby augmenting the risk of infection. Several studies have pointed out that the water flow rate, the risk is higher, and the temperature after 10 and 60 s of laser activation did not exceed 38.5 °C at a rinse fluid flow rate of 40 mL/min, regardless of the laser configuration [9]. Actual operations encompass intricate factors, including bleeding and infection. To ensure operational safety, urologists often adjust the flow rate to its lowest value, ensuring a clear visual field through the nephroscope's water valve, thus rendering quantification of flow velocity challenging. Hence, we standardized the ideal perfusion flow rate at 30 mL/min. We employ constant pressure pump irrigation without considering factors like lithotripsy discharge and optimal field of view clarity, eliminating the need for manual adjustment of the nephroscope's water valve. Aligned with our surgical practice, the laser was activated for approximately 25 s,

paused for 5 s to enable efficient cooling of the kidney by the irrigation fluid, thus explaining the peaks and valleys observed in our temperature profile.

The proportion of laser energy reaching the stone can be used to estimate the efficiency of laser lithotripsy. An in vitro study reported that 52% of the emitted pulses reached the stone when using a frequency of 20 Hz; when using a frequency of 50 Hz, only 23% reached the target, and at 80 Hz only 4% [10]. It seems that the frequency of laser and lithotripsy efficiency is inversely proportional at a constant power level. Thus, we used different frequency settings in groups A and C with a laser power of 30 W, 15 Hz in Group A vs. 30 Hz in Group C. During the first 5min of intermittent excitation, no significant difference in mean temperature (36.06 ℃ vs. 36.36 ℃, $t=0.52$, $P>0.05$). Similarly, in groups B and D with laser power of 60W set at frequencies of 20 Hz and 30 Hz, the mean temperatures were almost the same (39.21 ℃ vs. 39.27 ℃, $t=0.09$, $P>0.05$). We believe that under sufficient lavage and good laser excitation habit, the residual energy has minimal impact on the renal temperature.

A comparative study of high-power vs. low-power laser lithotripsy showed significantly shorter procedure times but higher joules/mm^3 values for high-power lasers [11]. In another laboratory study simulating the renal calyx, the authors investigated the use of different energies and frequencies to measure the temperature of the medium at various irrigation flows. They found that the higher the delivered energy, the greater the increase in fluid temperature, reaching 50 °C and 70 °C in 10 s and 60 s, respectively, without irrigation [9]. However, most experiments still did not include the calculus factor.

We observed that as the power increased, the energy spillover grew greater, and the intrarenal temperature rose higher and faster, obviously. But the exponential increase in power does not result in a significant increase in temperature. Instead, the higher power may lead to increased lithotripsy efficiency and a decrease in operative time, ultimately translating to a lower risk of bleeding and infection. Although a recent meta-analysis showed no evidence of an advantage of higher power lasers over lower power lasers in terms of shorter operative times when dealing with same volume calculus [12], this is strongly correlated with the fact that calculus composition varies in different populations. Therefore, the surgeon must fully evaluate the mutual advantages and disadvantages of laser thermal damage and procedure time within the context of the actual situation, such as the patient's calculus location, load and infection status.

Thermal damage to tissues depends on the temperature reach and its ability to be sustained over time (thermal dose), which it was showed that tissue and cellular damage occurs at 43 °C and maintain 240 min [13]. A human body temperature exceeding 42 °C can causes substantial cellular damage, when the local temperature is > 45 °C, there will be damage to tissue, and when the local temperature is > 60 °C, the tissue proteins are thermally coagulated and denatured and irreversible damage occurs [14]. In a study, rabbit kidneys were placed in a closed container and subjected to holmium laser excitation, and there was an increase in water temperature and rabbit kidney tissue damage for a certain period of time, but it did not have the conditions of flowing water flushing and energy absorption by stones also [15]. Our results the submucosal mean temperature did not exceed 40 °C during the trail in all groups; the highest temperature was observed in Group D (60 W), at 49.2 °C. In each group, there were periods during which the temperature exceeded 42 °C, but thanks to the intermittent laser excitation and constant-rate irrigation as in human surgery, the high-temperature periods were relatively brief, lasting only about 20 s, and the temperature dropped back quickly after the pause in laser excitation.

After completely recording the temperature data for each individual model, the porcine kidney was promptly handed over to an assistant for dissection. Different degrees of thermal damage lesions were observed visually within each renal parenchyma, as the laser excitation time was longer and the number of lesions was higher in Groups C and D. We mainly excised the tissues near the temperature probe for pathological analysis. It was found in the specimen sections that Group D had the most serious lesions. The number of pathological section with serious urothelium thermal damage accounted for 57.1%, while Group A, the least, was only 15.4%. Thus, we can judge that the higher power and longer Holmium laser excitation caused more thermal damage to the kidney urothelium tissues. At the same time, we also observed very limited degenerative necrosis of the submucosal tissue glomeruli and tubules at the injury site (< 25%, mild) from all sections. Notably, despite Groups B and C having similar maximum temperatures, Group C had a lower mean temperature and a higher percentage of severe thermal injuries.We believe that tissue injury is not only caused by transient high temperatures but is also influenced by the duration of exposure to those temperatures. Evidently, renal tissue in Group C remained within the damaging temperature range for a longer duration.

However, the study has some limitations. Although only two kidney models were used per group, their temperature characteristics were largely consistent within each group. This suggests that the experiments are reproducible and the experimental data is scientifically reliable. Because of the isolated organ experiment, we could not simulate the effect of blood flow on the renal temperature. In vivo conditions, actual renal temperatures may be lower due to blood flow's regulatory effects. The thermal damage observed in our study represents a short-term complication; however, ex vivo organ experiments cannot provide insights into long-term

consequences, which must be observed in real-world clinical settings.

Conclusion

In conclusion, various energy parameter configurations of holmium laser during PCNL result in differing degrees of thermal damage to the kidney. Higher laser power and longer time for a certain irrigation speed lead to higher intrarenal temperature and more tissue damage, but the effect of rapid and high-power excitation on intrarenal temperature is not a concern. Moderate irrigation and intermittent laser excitation habits are very good at avoiding excessive elevation of intrarenal temperature. Little damage to the renal tubules from heat was observed in vitro experiment, with effects mostly limited to the renal mucosa and subepithelium. Overall, under various parameter settings, holmium laser applications for lithotripsy are generally safe and reliable. Urologists can confidently rely on their surgical expertise to minimize any additional side effects.

Author contributions WW: project development, data management, manuscript writing. ZX: project development, manuscript writing. MC: data management, manuscript editing. LX: data collection, pathological observation. YM: data collection. HZ: data collection.

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Data availability All relevant data are within the paper. The original data are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declared no potential conflict of interest with respect to the research, author-ship, and publication of this manuscript.

Ethical approval Medical Ethics Committee of Foshan Hospital of Traditional Chinese Medicine. IRB No. 2021138.

Informed consent The experimental calculus was surgically removed from human. Patients signed informed consent for the calculus to be used in this study.

Approval of the research protocol by an institutional reviewer board Foshan Health Commission Medical Research Project (China).

Registry and the registration no. of the study/trial N/A.

Animal studies N/A.

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泌尿外科-原始论文

温度与肾组织热损伤的比较在碎石术过程中采用不同能量参数的钬激光：猪肾体外模型

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摘要

目的本研究通过猪肾结石模型体外模拟钬激光经皮肾结石碎石术，以进行研究利用钬激光的不同能量参数，有效抑制肾脏组织的热损伤。

方法将人肾结石标本置于新鲜猪肾组织中，随后插入热电偶进行温度监测。将探针插入肾盂黏膜下层，并在37°C的水浴中重新加热。使用经皮肾鞘以中等灌注速率30 ml/min在18℃下渗透肾实质。采用钬激光在肾镜下碎石，并记录温度。

结果四个独立模型分别为：使用30瓦和60瓦激光分别进行5分钟和10分钟的碎石术；平均30W与60W组5分钟内的温度分别为36.06℃与39.21℃（t=5.36，P<0.01），最高温度分别为43.60℃与46.60℃；10分钟内的平均温度分别为37.91℃与40.13℃（t=5.28，P<0.01），最高温度分别为46.80℃与49.20℃。病理观察发现，每只肾脏均存在不同程度的热损伤病变，功率越高、时间越长损伤越严重，但损伤主要局限于尿路上皮和上皮下组织，肾小管损伤罕见。

结论激光能量功率越高、作用时间越长，肾内温度升高越显著，导致虽然对肾脏组织造成一定程度的热损伤，但总体上被证明是安全可靠的。泌尿科医生可通过手术技术避免进一步的副作用。

关键词钽激光·碎石术·热损伤·肾内温度

背景

全球尿路结石发病率持续攀升，部分复杂病例需通过手术治疗。随着微创手术技术的不断进步，上尿路结石的治疗方案碎石技术已从开放手术转向内镜手术。经皮肾镜碎石术（PCNL）和输尿管软镜术（FURS）因其微创特性、精准疗效及成熟应用，在临床实践中得到广泛应用[1]。碎石能量输出模式的进步也推动了微创手术的发展。自20世纪80年代起，激光技术正式应用于医学领域，钬激光对结石的独特物理作用使其在碎石术中表现出色。尽管铥光纤激光在该领域已证明不逊色，但钬激光仍是内镜碎石术的顶尖设备[2]。由于其显著优势——约95%的能量可被周围5毫米水介质吸收且具有良好定向性[3]，钬激光成为泌尿外科手术中最常用的激光设备。

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然而，尽管钬激光的普及率持续攀升，但我们观察到接受钬激光碎石术的患者并发症发生率更高，例如输尿管狭窄、盆腔粘连甚至肾功能受损[4]。以往大多数关于钬激光的热效应研究，既未考虑结石对激光能量的吸收效应，也未深入探讨组织病理学变化。因此，本研究旨在通过更精细的实验设计，还原临床真实场景。

材料和方法

实验模型

肾脏模型

新鲜猪肾样本直接从肉类加工厂获取，经冷冻运输后保存于-4至0℃的低温环境中。样本在分离后一小时内即用于实验。所有猪肾的形态与尺寸基本一致，实验前已去除肾周脂肪及包膜等组织，并进行彻底清洁。

微积分

本研究采用的人体尿路结石样本均经过无害化处理并完成成分分析。这些结石主要由草酸钙二水合物和草酸钙五水合物构成，属于最常见的类型。研究人员通过手术方式从患者肾脏或输尿管中取出结石样本，并获得患者对其样本用于本研究的知情同意。随后将结石研磨抛光至约2-2.5厘米大小，置入猪肾盂切口处。最后使用蚕丝线缝合组装系统（图1）。

设备

设备包括钬激光碎石系统（HZ系列，Potent Optoelectronics，中国）、内窥镜监护系统（Richard Wolf，德国）、肾镜（F9.5，Richard Wolf，德国）、肾穿刺鞘（F20，Veili Medical，中国）、恒温水浴系统（HH420，YuNuo Instrument，中国）、热电偶温度计和探头（TA612系列，Suzhou TASI Electronics，中国）、冲洗泵（图2）。

操作步骤

1. 研究人员制备了新鲜的体外培养猪肾，并结合尿路结石模型进行研究。两个热电偶tem-

将温度探头插入肾脏组织的碎石术预定区域，探头与组织表面保持1厘米间距。探头尽可能靠近集合系统的尿路上皮层，与上皮组织保持约5毫米距离，确保探头不会穿透至肾盂腔。

2. 将猪肾脏置于37℃恒温盐水浴中复温。实验开始时监测肾脏温度，直至达到
37 ℃。使用F20肾镜鞘管穿刺肾盂后，通过结合钬激光的肾镜对肾脏结石进行碎石。采用机器控制的连续盐水灌洗，以30毫升/分钟的均匀中等流速进行，灌洗液温度为18℃（室温）。根据泌尿外科医生的手术习惯，同一位外科医生在试验中以20-25秒的连续循环配合5秒暂停的方式激活钬激光。进行试验的泌尿外科医生具有丰富的手术经验，拥有超过10年的专业领域经验，每年完成约200例激光碎石手术。
3. 实验分组：本研究将受试者分为四组，各组采用不同激光参数设置，其中A组为初始参数组。
30 A组：2焦耳（15赫兹）功率，持续5分钟；B组：60焦耳（20赫兹）功率，持续5分钟；C组：30焦耳（30赫兹）功率，持续10分钟；D组：60焦耳（30赫兹）功率，持续10分钟。
4. 当各组完成规定时间后，立即停止碎石术，对肾脏进行解剖以直观观察碎石区域的组织病理学变化。随后采集可能受热损伤部位的组织样本，并用福尔马林保存。最后对制备好的组织切片进行显微镜检查，以观察是否存在病理改变。

数据统计

温度记录软件由TASI公司提供，记录间隔为5秒。通过数据导出后取平均值，记录了同一肾脏模型内的两个探头温度数据。所有数据均导入Microsoft Excel和SPSS 22.0以生成图表。比较了各组的平均温度，并通过*t检验*检验差异，校准水平 α=0.05。

结果

每组采用两种肾脏模型进行两次独立试验。A组在两次试验中的最高温度为43.60℃，平均温度为

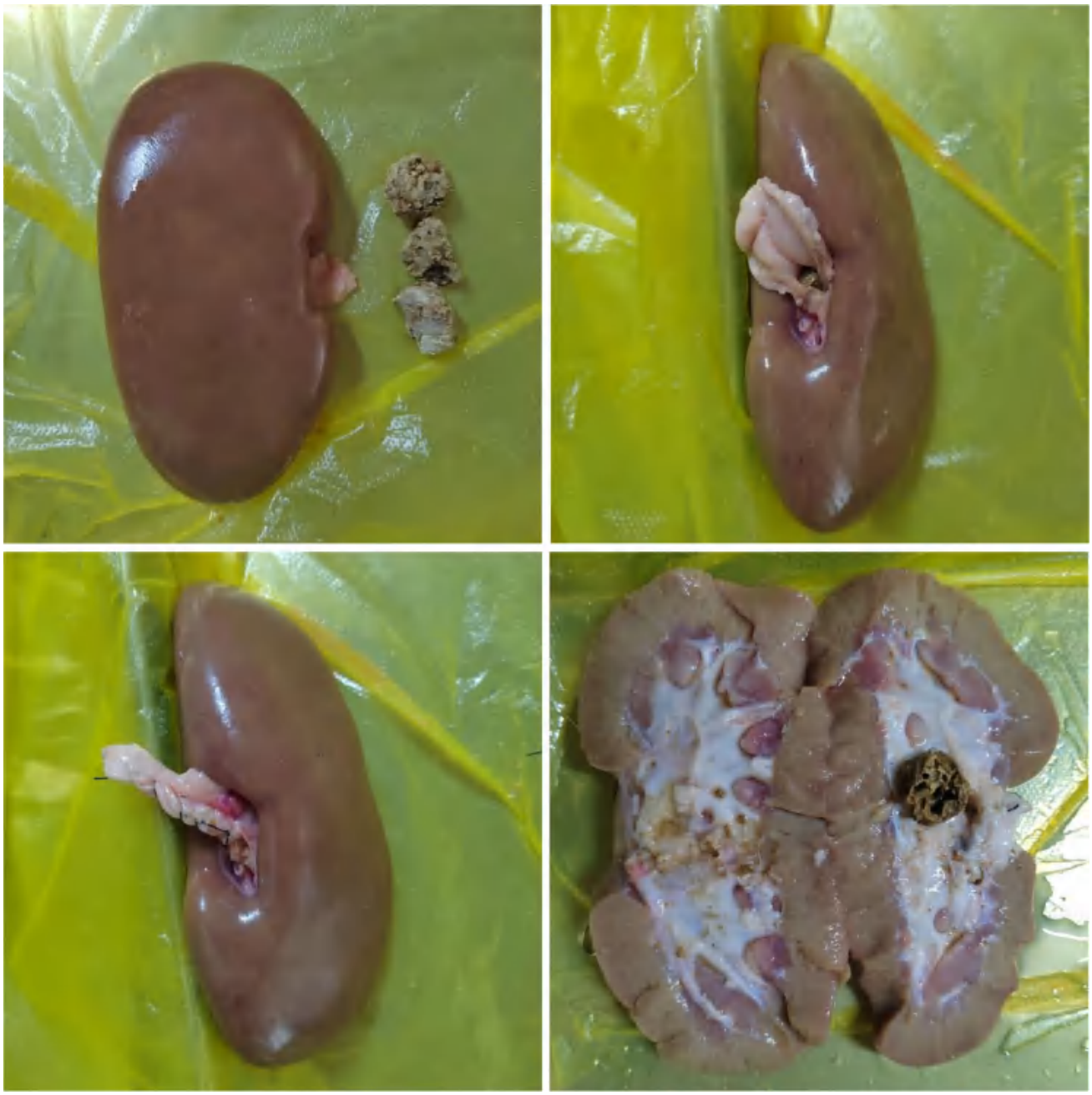


图1带结石的猪肾脏模型

36.01 ℃和36.10℃。B组最高温度为46.60℃，平均温度为39.39℃和39.02℃。A组和B组的温度曲线如图3 a、b所示。数据合并后，B组的平均温度高于A组（39.21℃ vs.36.06℃，t=5.36，P=0.00），并且60W激光在5分钟的激光碎石术期间产生的热量对肾脏温度的升高有更大的影响。

研究人员对C组（接受10分钟钬激光激发）与另一组进行了对比。

D组。C组的最高温度为
46.8 在两次试验中，温度均达到37.56°C和38.25°C。而该组的最大温度为
D值为49.2°C，平均温度为40.08°C。
40.18 °C，分别（图3 c、d）。与使用30W激光的C组相比，使用60W激光照射10分钟的D组，肾实质温度升高更显著，可能对组织造成热损伤（40.13°Cvs37.91°C，t=5.28，P=0.00）。



图2设备及流程

我们对每个肾脏进行激光激发后解剖。每个肾脏取3-5块组织用于病理学观察，取自热电偶探头附近区域。轻度至A组和C组的中度热损伤更为常见。显微镜下可见肾盂黏膜上皮与下方组织不同程度脱离，部分浅层伞状细胞仅缺失，部分则缺失整个细胞层，暴露出裸露的基底膜及黏膜固有层水肿（图4 a、b）。B组和D组标本显示更严重的热损伤：黏膜上皮发生变性脱落，固有层水肿伴黏膜肌层、肌细胞及外膜胶原纤维不同程度的变性坏死（图4 c）。通过对53例病理切片的损伤分级，共定义19例重度热损伤：A组2例，B组4例，C组5例，D组8例；24例中度热损伤：A组8例，B组6例，C组6例，D组4例；10例轻度损伤：A组3例，B组3例，C组2例，D组2例。按重度热损伤比例从高到低排序，D组占比最高达57.1%，C组为38%。5%，B组为30.8%，A组为15.4%。

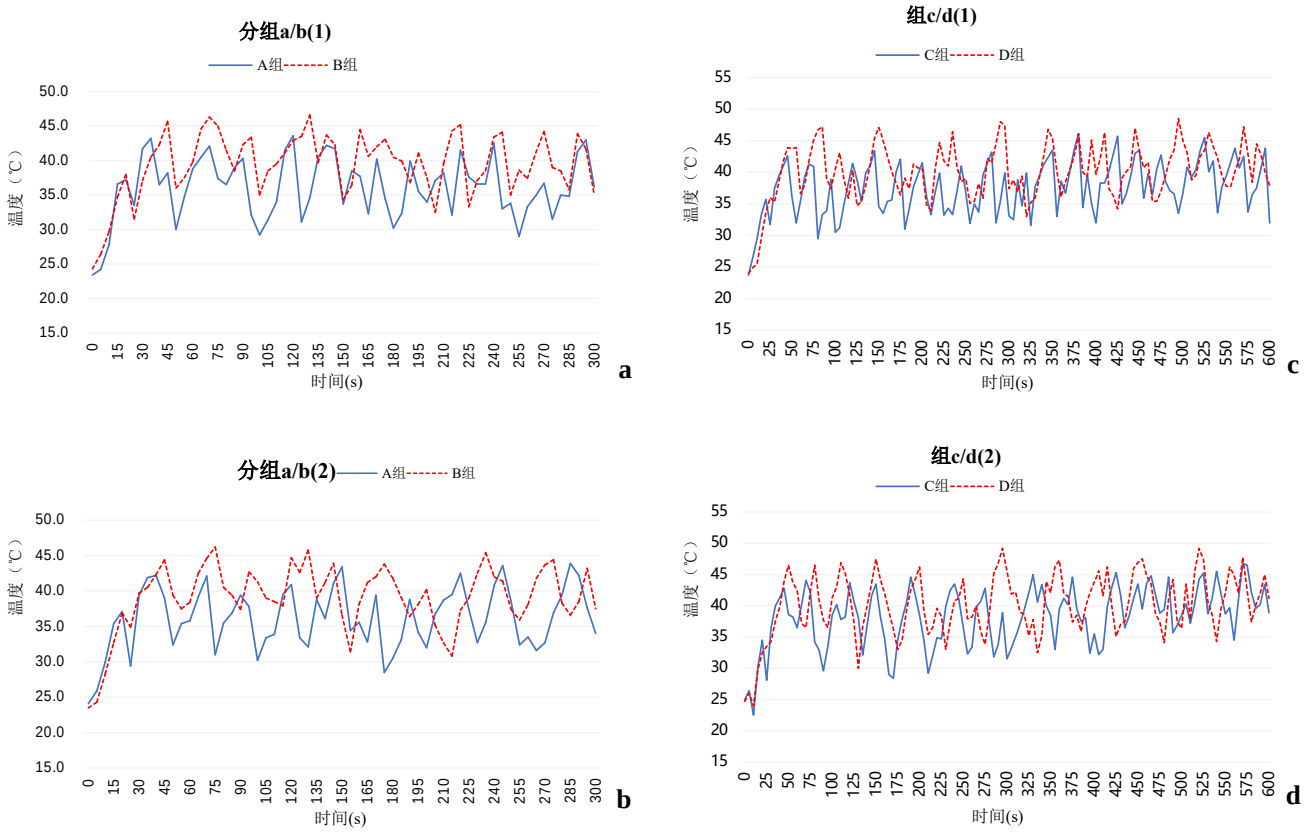


图3不同激光能量参数的温度分布曲线。**a**组A/B第一次试验。**b**组A/B第二次试验。**c**组C/D第一次试验。**d**组C/D第二次试验。

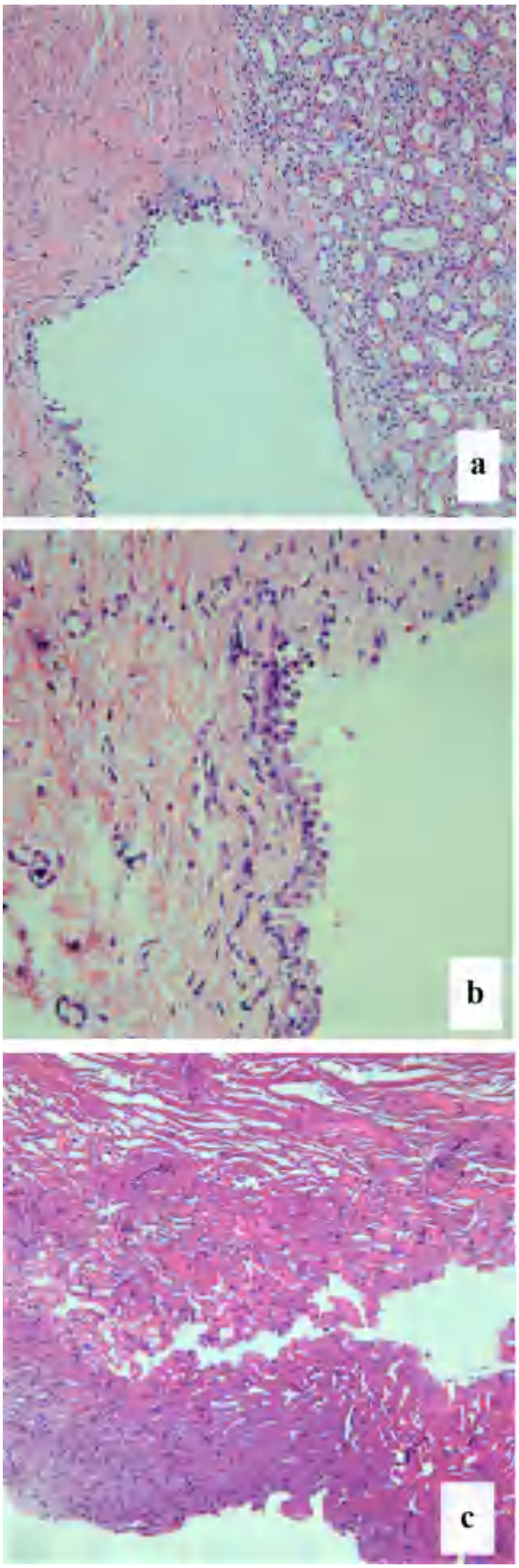


图4热损伤肾组织病理图片。**a**轻度。**b** Š中度。**c**重度

讨论

钬激光碎石术已成为治疗尿路结石的首选方案。然而，以往针对孤立动物器官或设备的实验大多仅用于观察温度变化，对实际组织病理损伤的关注较少[5]。活体动物实验充分考虑了血流对温度变化的影响，监测温度更贴近实际情况[6]。但活体动物建立尿结石模型难度较大，且温度监测精度不及体外实验。此外，模型一致性与样本量不足都是控制偏差的主要挑战。本研究创新性地整合了体外与活体实验的优势，特别是在结石模型制备和病理观察方面，相比以往研究更能模拟真实临床场景。

钬激光治疗主要通过碎石的光热机制发挥作用，其工作原理是：传输光纤尖端的水介质吸收能量后迅速汽化形成微气泡[7]。但并非所有能量都能被水介质吸收并传递至结石部位。未抵达结石的激光能量会外泄，导致肾内温度升高、损伤尿路上皮组织，甚至可能引发并发症[8]。在实际临床操作中，激光能量直接作用于冲洗液的情况较为少见。因此，我们在研究中采用了人类结石样本进行验证。

水流速率是影响碎石术期间温度的最重要因素之一[8]。较高的水流速率可显著降低肾内温度，但也会导致肾内压力升高，从而增加感染风险。多项研究表明，水流速率越高，感染风险越大。在冲洗液流速为40 mL/min时，无论激光配置如何，激光激活10秒和60秒后的温度均未超过38.5°C[9]。实际操作涉及出血和感染等复杂因素。为确保手术安全，泌尿科医生通常将流速调整至最低值，以确保通过肾镜水阀获得清晰视野，这使得流速量化变得困难。因此，我们将理想的灌注流速标准化为30 mL/min。我们采用恒压泵冲洗，无需考虑碎石术排出液和最佳视野清晰度等因素，从而消除了手动调节肾镜水阀的需要。根据手术规范，激光器持续工作约25秒。

暂停5秒以促进灌注液对肾脏的高效冷却，这解释了温度曲线中出现的波动现象。

激光能量到达结石的比例可用于评估激光碎石术的效率。一项体外研究表明，当使用20Hz频率时，52%的发射脉冲能到达结石；使用50Hz频率时仅有23%达到目标，而80Hz时仅剩4%[10]。在功率恒定条件下，激光频率与碎石效率呈反比关系。因此，我们在A组和C组分别采用30W功率的激光器，设置15Hz与30Hz两种频率。间歇性激发的前5分钟内，两组平均温度无显著差异（36.06 ńý 对比36.36 ńý，t=0.52，P>0.05）。类似地，在B组和D组中，60W功率的激光器以20Hz和30 Hz频率设置时，平均温度几乎相同（39.21 ńý 对比39.27 ńý，t=0.09，P>0.05）。我们认为在充分冲洗和良好激光激发习惯下，残留能量对肾脏温度的影响微乎其微。

一项高功率与低功率激光碎石术的对比研究表明，高功率激光的手术时间显著缩短，但焦耳/毫米^{3}值更高[11]。另一项针对肾盏结构的实验室模拟研究中，研究人员通过调节不同能量和频率参数，测量了不同冲洗流量下介质温度的变化。实验发现，能量输出越高，介质温度升幅越大——在无冲洗条件下，温度分别在10秒和60秒内达到50°C和70°C[9]。不过需要指出的是，多数实验仍未纳入结石因素的考量。

我们观察到，随着功率增加，能量溢出效应显著增强，肾内温度上升幅度和速度也明显加快。但功率的指数级增长并不会导致温度显著升高。相反，更高功率可能提升碎石效率并缩短手术时间，最终降低出血和感染风险。尽管近期荟萃分析显示，在处理相同体积结石时，高功率激光在缩短手术时间方面并未优于低功率激光[12]，但这与结石成分在不同人群中的差异密切相关。因此，外科医生必须根据患者结石位置、结石负荷及感染状况等实际情况，全面权衡激光热损伤与手术时间的利弊得失。

组织的热损伤取决于温度达到的程度及其持续时间（热剂量），研究表明，组织和细胞损伤发生在43°C并持续240分钟[13]。当人体温度超过42°C时，可造成严重损伤。当局部温度超过45°C时，细胞组织会受到损伤；当温度超过60°C时，组织蛋白会发生热凝固和变性，导致不可逆损伤[14]。有研究将兔肾置于密闭容器中进行钬激光照射，虽然在一定时间内水温升高且兔肾组织受损，但缺乏水流冲洗和结石能量吸收的条件[15]。我们的实验结果显示，所有组别在试验过程中黏膜下平均温度均未超过40°C，其中D组（60瓦）温度最高达到49.2°C。各组均出现温度超过42°C的时段，但由于采用了与人体手术相同的间歇性激光照射和恒定流速冲洗技术，高温持续时间较短，每次仅约20秒，且在激光照射暂停后温度会迅速回落。

在完成各模型温度数据记录后，研究人员立即把猪肾交给助手进行解剖。通过观察发现，随着激光激发时间延长和病灶数量增加，C组和D组肾实质内可见不同程度的热损伤病灶。我们主要切除温度探头附近的组织进行病理分析。切片结果显示，D组损伤最为严重，严重尿路上皮热损伤的病理切片占比达57.1%，而A组仅占15.4%。由此可见，高功率和长脉冲的钬激光对肾尿路上皮组织损伤更严重。同时，所有切片显示损伤部位的肾小球和肾小管间质组织退行性坏死程度极轻微（<25%，轻度）。值得注意的是，尽管B组和C组最高温度相近，但C组平均温度更低，且严重热损伤比例更高。我们认为，组织损伤不仅由短暂的高温引起，还受暴露于这些温度的持续时间影响。显然，C组的肾组织在更长时间内仍处于损伤温度范围内。

不过，本研究存在一些局限性。虽然每组仅使用了两种肾脏模型，但各组温度特征基本一致。这表明实验具有可重复性，实验数据在科学上具有可靠性。由于采用离体器官实验，我们无法模拟血流对肾脏温度的影响。在体内条件下，由于血流的调节作用，实际肾脏温度可能更低。本研究观察到的热损伤属于短期并发症；然而，离体器官实验无法提供关于长期影响的深入见解。

这些后果必须在真实临床环境中加以考量。

结论

综上所述，钬激光在体外冲击波碎石术（PCNL）中采用不同能量参数配置时，会对肾脏造成不同程度的热损伤。当激光功率较高且冲洗速度固定时，持续时间较长会导致肾内温度升高和组织损伤加剧，但快速高功率激发对肾内温度的影响无需过分担忧。采用适度冲洗与间歇性激光激发的常规操作，能有效避免肾内温度过度升高。体外实验显示，热损伤对肾小管的影响微乎其微，主要损伤部位集中在肾黏膜和上皮下层。总体而言，无论参数设置如何，钬激光在碎石术中的应用都具有安全可靠的特点。泌尿科医生完全可以通过娴熟的手术操作，将潜在副作用控制在最低限度。

作者贡献WW：项目开发、数据管理、论文撰写。ZX：项目开发、论文撰写。MC：数据管理、论文编辑。LX：数据收集、病理学观察。YM：数据收集。HZ：数据收集。

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声明

利益冲突作者声明在研究、作者和出版本手稿方面没有潜在的利益冲突。

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知情同意本研究通过手术从患者体内取出结石，所有患者均签署了知情同意书，同意将结石用于本研究。

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注册号和研究/试验注册号无。

动物研究N/A。

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Original Article
Clinical Investigation

Japanese survey of perioperative complications and ureteral stricture after ureteroscopy with laser lithotripsy for upper urinary tract stones in multicenter collaborative study

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Abbreviations & Acronyms
BMI = body mass index
CROES = Clinical Research Office of Endourological Society
ESUT = European Society of Uro-technology
EULIS = European Association of Urologists Sections of Urolithiasis
HU = Hounsfield unit
IQR = interquartile range
JSER = Japanese Society of Endourology and Robotics
PULS = proposed postoperative ureteroscopic lesion scale
SWL = shockwave lithotripsy
URS = ureteroscope
URS-L = ureteroscopy with laser lithotripsy

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Objectives: This study aimed to investigate perioperative complications and the details of postoperative ureteral stricture after ureteroscopy with laser lithotripsy (URS-L) for upper urinary tract stones in Japan.

Methods: Patient data on intra- and postoperative complications after ureteroscopy using URS-L were retrospectively collected from multiple centers in Japan between April 2017 and March 2020 with the cooperation of the Japanese Society of Endourology and Robotics. Data included the number of patients undergoing URS-L, number and type of intra- and postoperative complications, and detailed characteristics of postoperative ureteral stricture.

Results: In total, 14 125 patients underwent URS-L over 3 years at 82 institutions. Annual URS-L numbers gradually increased from 4419 in 2017, to 4760 in 2018, and 4946 in 2019. The total complication rate was 10.5%, which was divided into intra-operative complications in 1.40% and postoperative complications in 9.18%. The annual incidences of intra- and postoperative complications were not significantly different from year to year ($p = 0.314$ and $p = 0.112$). Ureteral perforation, ureteral avulsion, and the intra-operative conversion rate were 1.35%, 0.03%, and 0.02%, respectively. Fever >38°C, septic shock, blood transfusion, and postoperative mortality were 7.44%, 0.81%, 0.07%, and 0.04%, respectively. Ureteral stricture occurred in 0.8% of cases. The median length of stricture site was 10.0 mm and the success rate of stricture treatment was 54.6%.

Conclusion: Although URS-L utilization has increased in Japan, the annual complication rate has remained steady. Although URS-L is a useful and less invasive procedure, devastating complications can still occur.

Key words: postoperative complication, ureteral stricture, ureteroscopy with laser lithotripsy.

INTRODUCTION

The prevalence of urolithiasis in the upper urinary tract has been increasing globally due to metabolic syndrome, climate change, and increased utilization of diagnostic modalities such as CT and ultrasonography.[1] Current treatment regimens for upper urinary tract stones have also shifted: while the use of shockwave lithotripsy (SWL) has decreased, use of ureteroscopy (URS) has significantly increased with the development of laser technologies and the

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evolution of flexible URS.[2] Lithotripter devices to break apart the stones have gradually changed from pneumatic lithotripter systems to holmium YAG lasers and thulium fiber lasers in Japan as a result of development of finer laser fibers, along with increased flexibility, versatility, and usability of these lasers.[3] These laser lithotripsic devices are also quite effective for breaking ureteral stones than kidney stones. In addition, the introduction of flexible URS systems has also increased the range of treatment indications for ureteral stones and kidney stones.

Thus, we refer to this as the "ureteroscopy era with lasers" for stone management. However, as new technology results in novel discoveries and improved clinical efficacy, it is also accompanied by critical risks such as unknown complications and variable clinical outcomes. In this study, we aimed to survey recent intra- and postoperative complications after ureteroscopy with a holmium YAG laser for upper urinary tract stones in Japan. In addition, we also investigated the details of postoperative ureteral stricture.

METHODS

Study design and patients

We retrospectively collected patient data on intra- and postoperative complications after URS-L for upper urinary tract stones. Data were collected from multiple Japanese centers between April 2017 and March 2020 and were acquired with the cooperation of the Japanese Society of Endourology and Robotics (JSER). This study was approved by the institutional review board at Kobe University (No. B190331). We acquired patient consent by an opt-out approach at each institution. We retrospectively extracted only relevant data from each patient's medical record at each participating institution.

Data collection

The following postoperative early complication data were collected from each institution for incidents <1 month after ureteroscopy: annual cases of URS-L, number of ureteral perforations, number of ureteral avulsions, frequency of conversion to open or laparoscopy as an intra-operative complication, number of patients with fever >38°C, frequency of septic shock, blood transfusion, or subcapsular hematoma, and mortality. The number of ureteral strictures, which were diagnosed after 1 month postoperatively, were collected as postoperative late complications. Additionally, we collected the characteristics of patients with postoperative ureteral stricture including age, gender, body mass index (BMI), preoperative hydronephrosis status, preoperative stent placement, stone location, maximum stone size, and stone density by Hounsfield Unit (HU).

Furthermore, we collected data on the diagnostic method, surgical and clinical outcomes: diagnostic imaging studies, time to diagnosis of ureteral stricture after URS-L, length of ureteral stricture, location of ureteral stricture, treatment methods, and success rate of stricture treatment. Additionally, we defined the criteria for specific complications by the following: ureteral perforation was defined as injury involving the full thickness of the ureteral wall, including the adventitia with retroperitoneal fat; fever was indicated by a temperature greater than 38°C related to surgery occurring even once within 1 month after URS-L; septic shock was indicated by unstable mean blood pressure less than 65 mmHg despite fluid infusion and due to infectious status related to surgery; and ureteral stricture was defined as worse hydronephrosis or hydronephrosis equivalent to that before surgery as assessed by postoperative CT or ultrasound sonography. The success of stricture treatment was defined as the amelioration of postoperative hydronephrosis compared with preoperative status.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 26. Continuous variables and nominal variables from retrospectively collected clinical data were described as medians with interquartile ranges (IQR) and numbers with percentages, respectively. Moreover, Pearson's v^2-test was used for univariate analysis to compare data for complications between each year. Statistical significance was set at a two-sided p-value of <0.05.

RESULTS

URS-L for upper urinary tract stones was performed on 14 125 patients at 82 institutions between April 2017 and March 2020. Annual URS-L numbers gradually increased from 4419 in 2017 to 4760 in 2018 and 4946 in 2019 (Figure 1). The total complication rate was 10.5%, including intra-operative complications in 1.40% of cases and postoperative complications in 9.18% of cases. Of the intra-operative complications, ureteral perforation, ureteral avulsion, and conversion to open/laparoscopy rates were 1.35%, 0.03%, and 0.02%, respectively. Postoperative early complication rates for events occurring less than 1 month after ureteroscopy were fever >38°C (7.44%), septic shock (0.81%), blood transfusion (0.07%), subcapsular hematoma (0.05%), and mortality (0.04%). The incidence of ureteral stricture as a postoperative late complication was 0.8% (Table 1). Annual incidence rates of intra- and postoperative complications were not significantly different from year to year ($p = 0.314$ and $p = 0.112$; Figure 2). Annual incidence rates of ureteral perforation, fever, septic shock, and ureteral stricture were also not significantly different from year to year ($p = 0.163$, $p = 0.182$, $p = 0.906$, and $p = 0.635$; Figure 3).

From 108 ureteral strictures, which were diagnosed after 1 month postoperatively, 68.4% were diagnosed within 3 months after ureteroscopy by using CT in 42.5% of cases and by ultrasound in 17.5% of cases. The median length of ureteral stricture was 10.0 mm. The most frequently occurring stricture site was in the proximal ureter (38.8%), followed by the distal ureter (24.0%) and the middle ureter (22.2%). The most often selected treatment for ureteral stricture was transurethral balloon dilation. (54.6%) followed by observation (22.2%), ureteroureterostomy (10.1%), and ureteral stent/nephrostomy replacement (10.1%). The total success rate of stricture treatment was 54.6%. Transurethral balloon dilation was the most effective method of all the procedures (Table 2).

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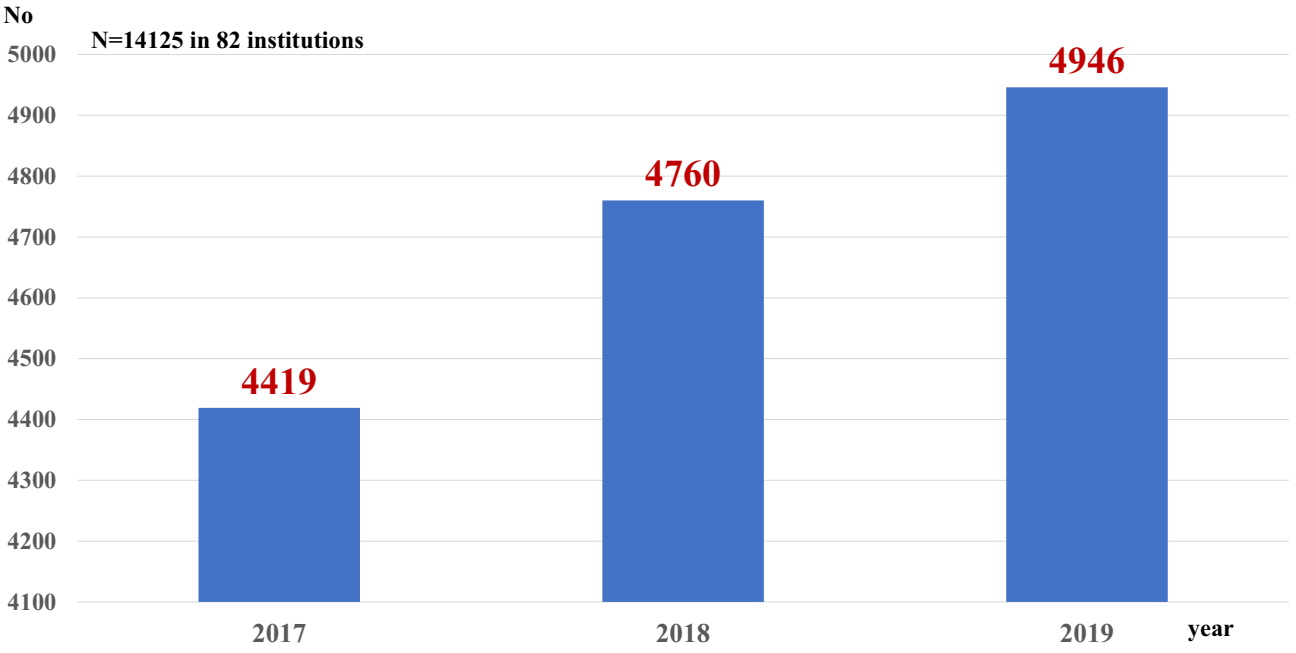


FIGURE 1 Rates of ureteroscopy for upper urinary tract stones by laser lithotripsy in Japan.

TABLE 1 Intra- and postoperative complications after ureteroscopy with laser lithotripsy.

Total complication rate (n, %)	1496 (10.5)
Intra-operative complication rate (n,%)	199 (1.40)
Ureteral perforation	191 (1.35)
Ureteral avulsion	5 (0.03)
Conversion to open/laparoscopy	3 (0.02)
Postoperative early complication rate (<1 month) (n, %)	1189 (8.41)
Fever-up (>38°C)	1051 (7.44)
Septic shock	115 (0.81)
Blood transfusion	10 (0.07)
Sup-capsular hematoma	7 (0.05)
Mortality	6 (0.04)
Postoperative late complication (n, %)	108 (0.80)
Ureteral stricture	108 (0.80)

Note: N = 14 125.

DISCUSSION

In this survey, we found that annual URS-L cases for upper urinary stones in Japan have gradually increased. Although the total complication rate was 10.5%, including intra-operative complications in 1.40% of cases and postoperative complications in 9.18% of cases, the annual incidence rates of intra- and postoperative complications were not significantly different year over year.

The trend of surgical procedures for stone management in the upper urinary tract has changed with the expanded use of laser technology and the innovation of the flexible ureteroscope. In 2014, Ordon et al. found that in an analysis of administrative databases, of 194 781 kidney stone treatments performed between 1991 and 2010, URS utilization significantly increased from 25% in 1991 to 59% in 2010. Conversely, SWL utilization decreased from 69% in 1991 to 34%

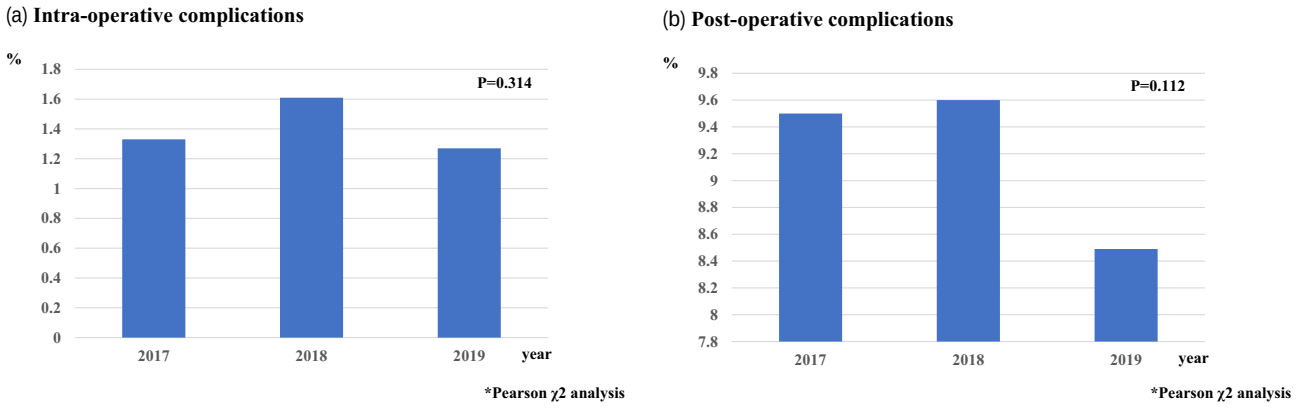


FIGURE 2 Perioperative complication rate for ureteroscopy with laser lithotripsy. (a) Intra-operative complications. (b) Postoperative complications.

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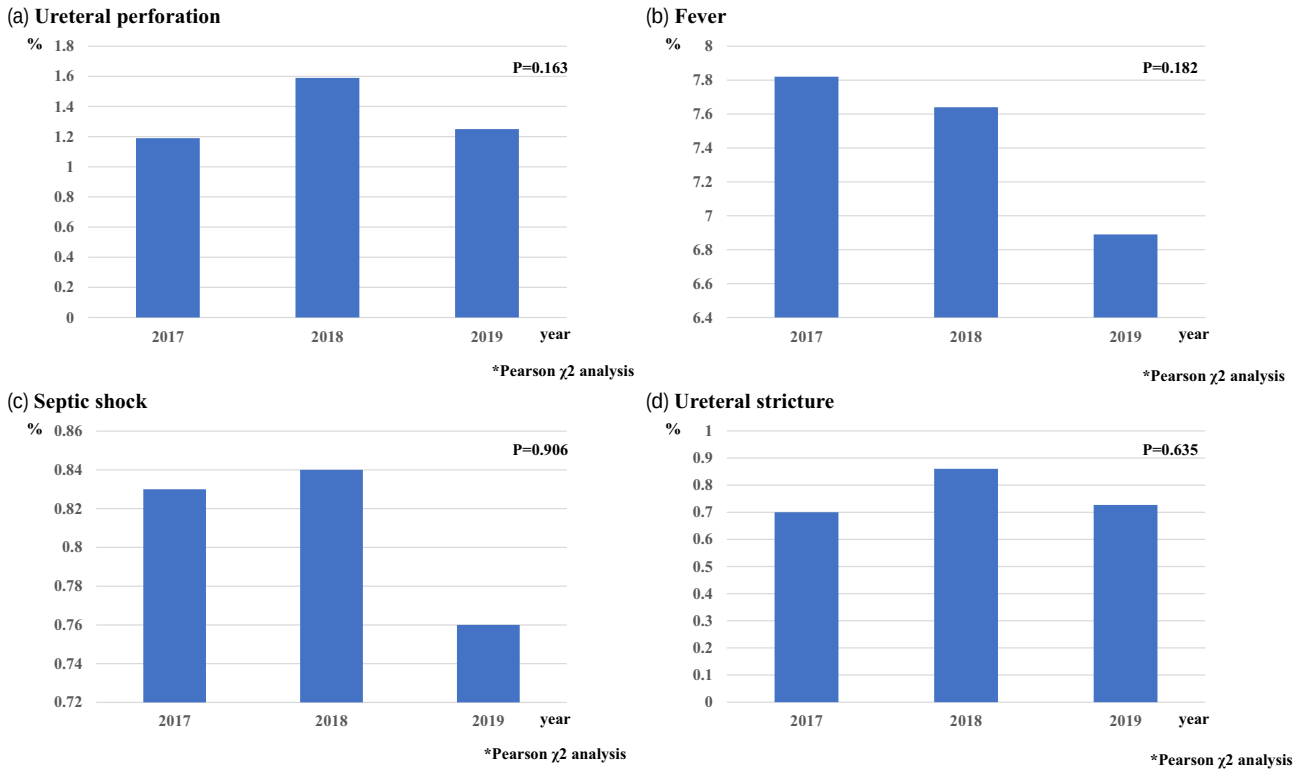


FIGURE 3 Major complication rates for ureteral perforation, fever, septic shock, and ureteral stricture during and after ureteroscopy with laser lithotripsy. (a) Ureteral perforation, (b) Fever, (c) Septic shock, (d) Ureteral Stricture.

in 2010 and was inferior to URS.[4] Additionally, Herout et al. showed that the number of URS significantly increased by 143% between 2006 and 2019.[5] Likewise, Isotani et al reported in 2019 that the annual trend of URS utilization in Japan has been increasing and surpassed the number of SWL performed per year in 2014.[2]

With the current rise in URS utilization, novel technologies might bring additional complications and increase the rate of perioperative complications. The EAU guidelines describe that the overall complication rate after URS is 9%–25%, however, most complications are minor and do not require surgical intervention.[6] According to a global study by the Clinical Research Office of the Endourological Society (CROES), there was a complication rate of 7.4% out of 11 885 patients, including 4.2% intra-operative, 2.6% postoperative, and 0.5% both intra- and postoperative complications, almost all of which were minor complications. However, it should be noted that critical complications still occurred.[7] In the present study, the total complication rate out of 14 125 patients undergoing URS with laser lithotripsy was 10.5%, including intra-operative complications in 1.40% and postoperative complications in 9.18%, which were equivalent to another report. However, severe complications still occurred in our study.

Ureteral perforation, which is a devastating intra-operative complication, occurs in 0.3%–7.4% of cases as a result of ureteroscopic surgery with a ureteral access sheath, laser emission, basketing, and from the ureteroscope itself.[8] Currently, ureteral wall injury as an intra-operative major complication is classified by endoscopic grade. Traxer et al. initially suggested the intra-operative endoscopic classification of ureteral wall injury when using a ureteral access sheath.[9] Subsequently, Schoentaler et al. proposed a postoperative ureteroscopic lesion scale (PULS).[10] In accordance with the Traxer grading system, 13.3% of cases using a 12/14F ureteral access sheath resulted in a damaged ureteral wall involving muscle layers.[9] The ureteral perforation rate in our study was relatively lower, at 1.35%. On the contrary, although ureteral avulsion is a relatively rare intra-operative complication with an incidence of 0.04%–0.9% during ureteroscopy, it is one of the most calamitous complications.[8] Our rate of ureteral avulsion in this study was 0.03%, which was not a lower rate because upper urinary stones are considered a benign disease. Therefore, it is necessary to avoid this serious complication. Once ureteral avulsion has occurred, immediate repair is required, or repair can be performed as a staged procedure. In our study, 0.02% of patients converted from URS to open or laparoscopic procedures due to ureteral avulsion.

Postoperative fever is a well-known early complication following URS, with a reported rate between 0.2% and 15%.[8] In our study, 7.44% of patients experienced fever >38°C postoperatively. Furthermore, urosepsis, which is defined as sepsis resulting in life-threatening organ dysfunction caused by urogenital tract infection is also a serious complication with an incidence between 0.1% and 4.3% post-ureteroscopy.[11] Urosepsis accompanied by septic shock occurs with a frequency of 0.3% to 4.6%, resulting in a mortality rate of 28.3–41.1%.[12,13] The rate of septic shock in our study was 0.81%.

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TABLE 2 Characteristics and outcomes of postoperative ureteral stricture after ureteroscopy with laser lithotripsy.

N = 108 Age (year, median, IQR)	63.0 (54.0–71.0)
Gender (No, %)	M: 72 (66.6), F 36 (33.3)
BMI (kg/m^2, median, IQR)	24.4 (22.1–27.2)
Pre-operative hydronephrosis (No, %)	85 (78.7)
Pre-ureteral stenting (No, %)	31 (28.7)
Stone location (No, %)	
Ureteral orifice	1 (0.9)
Distal ureter	17 (15.7)
Middle ureter	23 (21.2)
Proximal ureter	47 (43.5)
Ureter-pelvic junction	14 (12.9)
Kidney	6 (5.5)
Max stone size (mm, median, IQR)	10.2 (7.4–13.5)
CT-value (HU, median, IQR)	1070.5 (781.5–1320.5)
Diagnosed period of ureteral stricture after ureteroscopy	
POD 1 months	33 (30.5)
POD 1–3 months	41 (37.9)
POD 3–6 months	23 (21.2)
POD 6–12 months	8 (7.4)
POD > 12 months	3 (2.7)
Diagnostic imaging study (No, %)	
CT	46 (42.5)
Ultrasound	19 (17.5)
IVP	1 (0.9)
RP	20 (18.5)
Ureteroscopy	19 (17.5)
Others	3 (2.7)
Length of ureteral stricture (mm median, IQR)	10.0 (5.0–17.0)
Location of ureteral stricture (No, %)	
Ureteral orifice	2 (1.8)
Distal ureter	26 (24.0)
Middle ureter	24 (22.2)
Proximal ureter	42 (38.8)
Ureter-pelvic junction	14 (12.9)
Treatment of ureteral stricture (No, %)	
Transurethral balloon dilation	59 (54.6)
Ureteroureterostomy (Open or laparoscopic)	11 (10.1)
Nephrectomy	2 (1.8)
Ureteral stent or nephrostomy replacement	11 (10.1)
Observation	24 (22.2)
Success rate (No, %)	
Total	59 (54.6)
Transurethral balloon dilation	37 (62.7)
Ureteroureterostomy (Open or laparoscopic)	5 (45.4)
Ureteral stent or nephrostomy replacement	11 (100)
Observation	7 (29.1)

Abbreviations: BMI, body mass index; HU, Hounsfield Unit; IQR, interquartile range; IVP, intravenous pyelogram; POD, postoperative day; RP, retrograde pyelogram.

Blood transfusion following URS for stone treatment is also an early complication, with 1.3%–1.6% incidence.[14,15] Intra-operative bleeding during URS often occurs as a result of ureteral wall injury due to the use of a ureteral access sheath or laser shooting, renal injury due to laser shooting, or renal fornix rupture from high intrarenal pressure. High intrarenal pressure, as well as longer operation time and higher irrigation perfusion pressure intra-operatively are also causes of subcapsular perirenal hematoma, exhibiting 0.4% –2.2% incidence.[16] Patients continuing to take anticoagulation or antiplatelet agents prior to surgery often continue to bleed more intra- and postoperatively.[17,18] In our study, there were 0.07% patients who underwent blood transfusion and 0.05% who experienced subcapsular hematoma, both of which were observed at a relatively lower rate than that previously reported.

Although ureteroscopy for stone management is a safe and minimally invasive procedure, lethal morbidities have occurred. According to a current systematic review from the European Association of Urologists Sections of Urolithiasis (EULIS) and Uro-technology (ESUT), Bhanot et al. demonstrated that there were 72 patient deaths in 15 studies following URS. For the 42 patients in which the etiology could be determined, causes of death included sepsis in 57.1%, multiple organ dysfunction, cardiac-related incidences such as infarction of arrhythmia in 14.2%, hemorrhagic complications in 4.7%, and respiratory-related incidences such as lung thromboemolisms in 7.1%.[19] The mortality rate following URS in the present study was 0.04% which was not a lower incidence than that reported previously.

Ureteral stricture is a major late postoperative complication, with up to 3% incidence.

Ureteral stricture was defined as the focal narrowing of the ureter at the site of previous stone impaction with identifiable hydroureteronephrosis on IVP or retrograde pyelography for generations.[20] However, the usage of contrast agents currently should avoid to be less contrast allergy when anatomical condition before stone surgery is evaluated. In addition, there are not only site of previous stone impaction but also the other site of ureter due to excessive manipulation of ureteroscope and stone basket, miss laser shooting, thermal injury due to leaser setting as well as impacted stone.[21] Therefore, ureteral stricture was defined as worse hydronephrosis or hydronephrosis equivalent to that before surgery in our present study. Especially, the thermal injury might be one of the latest causes to postoperative ureteral stricture when shooting the laser into ureter. Intrarenal temperatures during ureteroscopic laser lithotripsy correlated directly with the laser power setting.[22] In our study, the rate of ureteral stricture was 0.8%. Sunaryo et al. reported that ureteral stricture developed in 2.9% of patients after URS.[23] Some causes of ureteral stricture formation following URS are classified as iatrogenic factors, including ureteral wall injury due to direct and indirect thermal injury, ischemia of the ureteral mucosa due to use of a ureteral access sheath, remaining stone fragments within the mucosa, and intrinsic stone factors such as impacted stone and stone size. Once a ureteral stricture has occurred postoperatively, a complete cure is difficult to achieve. From a population-based assessment, Sunaryo et al. reported that 35% of ureteral strictures required drainage including placement of a ureteral stent or percutaneous nephrostomy, 21% required endoscopic intervention, 4.8% required ureteral reconstruction, and 1.7% underwent simple nephrectomy.[23] In our study, intervention for postoperative ureteral strictures was performed as follows: 54.6% underwent transurethral balloon dilation, 10.1% underwent ureteroureterostomy, 1.8% underwent nephrectomy, 10.1% underwent ureteral stent or nephrostomy replacement, and 22.2% continued observation. The success

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rate is dependent on the kind of interventional procedure performed. Xiong et al. reported that the overall success rate was 60.9% with endourological intervention for post ureteroscopic ureteral stricture; however, 97.3% underwent reconstructive surgery.[24] In our study, the total success rate for resolution of ureteral stricture was 54.6%, and out of all the interventions, transurethral balloon dilation and ureteroureterostomy successfully managed strictures in 62.7% and in 45.4%. of cases, respectively.

This study has some limitations. First, as a main limitation, the data in this study were collected from experienced institutions actively performing stone surgeries. Therefore, institutions where limited numbers of annual stone surgeries were performed were not included. Second, we collected data on only major complications after URS-L. Therefore, data on minor complications, like breakage of URS, postoperative pain, and ureteral stent-related events, were not collected. Third, we could not analyze the difference between complications related to ureteral versus kidney stones or rigid versus flexible URS because that data was not available from the patient's chart. Fourth, ureteral strictures were diagnosed after 1 month postoperatively using a mix of US and CT. In some cases, postoperative hydronephrosis might mitigate at 2, or 3 months after operation. And then, to compare the degree of hydronephrosis between pre-operation and post-operation, we used the mix evaluation image of US and CT. Nevertheless, to the best of our knowledge, this is the first report to have reported the rates of intra- and postoperative complications after URS-L for upper urinary tract stones in Japan. Additionally, we evaluated the rates of postoperative ureteral stricture. In conclusion, although URS-L utilization has increased in Japan with increasing technological advancements, the annual complication rate has remained steady. Although URS-L is a useful and minimally invasive procedure, devastating complications have still occurred. Careful management for URS-L is needed to prevent additional invasive procedures.

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AUTHOR CONTRIBUTIONS

Takaaki Inoue: Conceptualization; Methodology; Software; Data curation; Formal analysis; Investigation; Project administration; Writing – original draft. Hirokazu Tanaka: Data curation. Tomoko Masuda: Data curation. Akinori Iba: Data curation. Mitsuhiro Tambo: Data curation. Shinsuke Okada: Data curation; Writing – review & editing. Terunobu Hou: Data curation. Ryoji Takazawa: Data curation. Hirofumi Izaki: Data curation. Shuzo Hamamoto: Data curation; Writing – review & editing. Masato Fujisawa: Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

None declared.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

Yes (No. B190331).

INFORMED CONSENT

Yes due to Opt-out in our hospital.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL

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ANIMAL STUDIES

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Editorial Comment

Editorial Comment on Japanese survey of perioperative complications and ureteral stricture after ureteroscopy with laser lithotripsy for upper urinary tract stones in multicenter collaborative study

In this study, Inoue et al. have comprehensively catalogued the key adverse effects associated with ureteroscopy (URS) and laser lithotripsy among a sample exceeding 14 000 patients in Japan.[1] Rates of intra and postoperative complications were reported at 1.4% and 9.2%, respectively. The latter included fever (7.4%) and septic shock (0.8%). The successful execution of orchestrating data collection from 82 contributing centers should be highly lauded. The fruits of this collaborative labor is the development of real-world reference data at a national level. While URS has become the stone intervention of choice among many urologists worldwide, the associated morbidity burden cannot be overlooked. The reported mortality of 0.07% in this study reminds us that deaths related to kidney stones and their surgical removal can and do occur.[2] Therefore, while URS is commonly purported as a procedure of "no limits," there do exist certain patient groups, for example, extreme elderly where highly selective patient selection is critical. In a recent study of URS in patients ≥85 years, the overall complication rate was 47% while the mortality was 23% at 1 year.[3]

In the operation theater, it is imperative that the surgeon takes ownership of how their incorrect technique and improper use of equipment can potentially lead to complications. This is highly relevant for ureteral strictures, which Inoue et al. reported to have occurred in 0.8% of the study sample. Newer generation laser systems offer the option of high-power settings. While it can be tempting to select these automatically in the pursuit of zero residual fragments, care and caution is required. A recent prospective trial of intrarenal temperature during URS in a clinical setting found that the threshold for cellular thermal injury (43°C) was reached in as quickly as 12 s when 30 W was applied.[4] The argument for employing only lower settings during stone lithotripsy is therefore mounting. Currently, however, practice patterns for laser settings do vary widely and the large variation in company pre-settings likely fuels this further. While there are some recommendations among experts now available, more research is needed in order to determine what is truly considered safe. This needs to be complemented by further research into laser activation times and patterns. Debate and controversy also persist surrounding the relationship between ureteral access sheath use and ureteral stricture formation. The introduction of vacuum-assisted access sheaths will likely see use of sheaths heightened further in clinical practice.[5] Like with high-power settings, while their potential to increase stone free rate attracts most attention when they are discussed, it is important to not overlook their potential link to later stricture formation.

The findings from Inoue et al. therefore prompt us to reflect on how complications like strictures can occur and what steps

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原文
临床研究

一项多中心合作研究对激光碎石术治疗上尿路结石术后围手术期并发症及输尿管狭窄的日本调查

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3 4 5 6 7 8 9 10 11 11 11

随着更精细激光光纤的开发，日本的[2]灵活输尿管碎石系统逐渐从气动碎石系统升级为钬YAG激光器和铥光纤激光器，这些设备在灵活性、多功能性和易用性方面都有显著提升。[3]这类激光碎石设备对输尿管结石的治疗效果甚至优于肾结石。此外，灵活输尿管碎石系统的引入，也使得输尿管结石和肾结石的治疗适应症范围得到拓展。

因此，我们将这一时期称为“激光输尿管镜时代”，用于结石治疗。然而，随着新技术带来新发现和临床疗效的提升，也伴随着未知并发症和疗效差异等关键风险。本研究旨在调查日本采用钬YAG激光输尿管镜治疗上尿路结石术后近期并发症情况，并详细探讨术后输尿管狭窄的具体表现。

方法

研究设计和患者

本研究通过回顾性分析收集了经尿道碎石术（URS-L）治疗上尿路结石术后患者术中及术后并发症的相关数据。数据采集时间为2017年4月至2020年3月期间，由日本内镜泌尿外科与机器人学会（JSER）协助完成。该研究经神户大学机构审查委员会批准（编号B190331），所有参与机构均采用自愿退出机制获取患者知情同意。我们仅从各参与机构患者病历中提取了相关数据。

数据收集

我们从各医疗机构收集了输尿管镜术后早期并发症数据，涵盖术后1个月内发生的事件：输尿管镜下输尿管结石（URS-L）年发病率、输尿管穿孔数量、输尿管夹层数量、术中转为开放手术或腹腔镜手术的频率、发热（体温＞38℃）患者数量、脓毒性休克发生率、输血次数及肾包膜下血肿情况，以及死亡率。术后1个月确诊的输尿管狭窄病例被列为术后晚期并发症。此外，我们还收集了术后输尿管狭窄患者的特征数据，包括年龄、性别、体重指数（BMI）、术前肾积水状态、术前支架置入情况、结石位置、最大结石尺寸以及按亨氏单位（HU）计算的结石密度。

此外，我们系统收集了诊断方法、手术及临床疗效的相关数据，具体涵盖：诊断影像学检查、经尿道输尿管镜检查（URS-L）后输尿管狭窄的诊断时间、狭窄长度、狭窄部位、治疗方式及狭窄治疗成功率。同时，我们根据以下标准明确了特定并发症的界定：输尿管穿孔定义为累及输尿管壁全层的损伤，包括外膜层。腹膜后脂肪堆积；发热指体温超过38℃且在URS-L术后一个月内至少发生过一次相关手术；脓毒性休克指尽管输液仍存在低于65mmHg的不稳定平均血压，且与手术相关的感染状态有关；输尿管狭窄定义为术后CT或超声检查显示的更严重肾积水或与术前相当的肾积水。狭窄治疗的成功定义为术后肾积水较术前状况有所改善。

统计分析

本研究采用IBM SPSS Statistics 26版软件进行数据分析。回顾性临床数据中的连续变量和名义变量分别以中位数（带四分位距IQR）和频数（百分比）呈现。通过皮尔逊x^2 [2]检验进行单因素分析，比较不同年份的并发症发生率。统计学显著性水平设定为双侧p值<0.05。

结果

2017年4月至2020年3月期间，82家医疗机构共对14 125 名患者实施了上尿路结石的逆行性尿路镜碎石术（URS-L）。每年URS-L手术数量逐年递增，从2017年的4419例增至2018年的4760例，2019年达到4946例（图1）。总体并发症发生率为10.5%，其中术中并发症占1.40%，术后并发症占9.18%。术中并发症中输尿管穿孔、输尿管剥离和转为开放/腹腔镜手术的发生率分别为1.35%、0.03%和0.02%。术后早期并发症（输尿管镜术后1个月内发生）包括发热>38°C（7.44%）、脓毒性休克（0.81%）、输血（0.07%）、肾盂下血肿（0.05%）及死亡（0.04%）。术后晚期并发症输尿管狭窄的发生率为0.8%（表1）。术中和术后并发症的年发生率无显著差异（p=0.314 和p=0.112；图2）。输尿管穿孔、发热、脓毒性休克和输尿管狭窄的年发病率也与年与年之间无显著差异（p=0.163、p=0.182、p=0.906和p=0.635；图3）。

在术后1个月确诊的108例输尿管狭窄病例中，68.4%的病例通过CT检查在输尿管镜检查后3个月内确诊（占42.5%），超声检查占17.5%。输尿管狭窄的中位长度为10.0毫米。最常见的狭窄部位是近端输尿管（38.8%），其次是远端输尿管（24.0%）和中段输尿管（22.2%）。治疗选择方面，经尿道球囊扩张术占比最高（54.6%），其次是观察治疗（22.2%）、输尿管吻合术（10.1%）和输尿管支架/肾造瘘术（10.1%）。输尿管狭窄治疗的总体成功率为54.6%。经尿道球囊扩张术是所有治疗手段中效果最佳的（见表2）。

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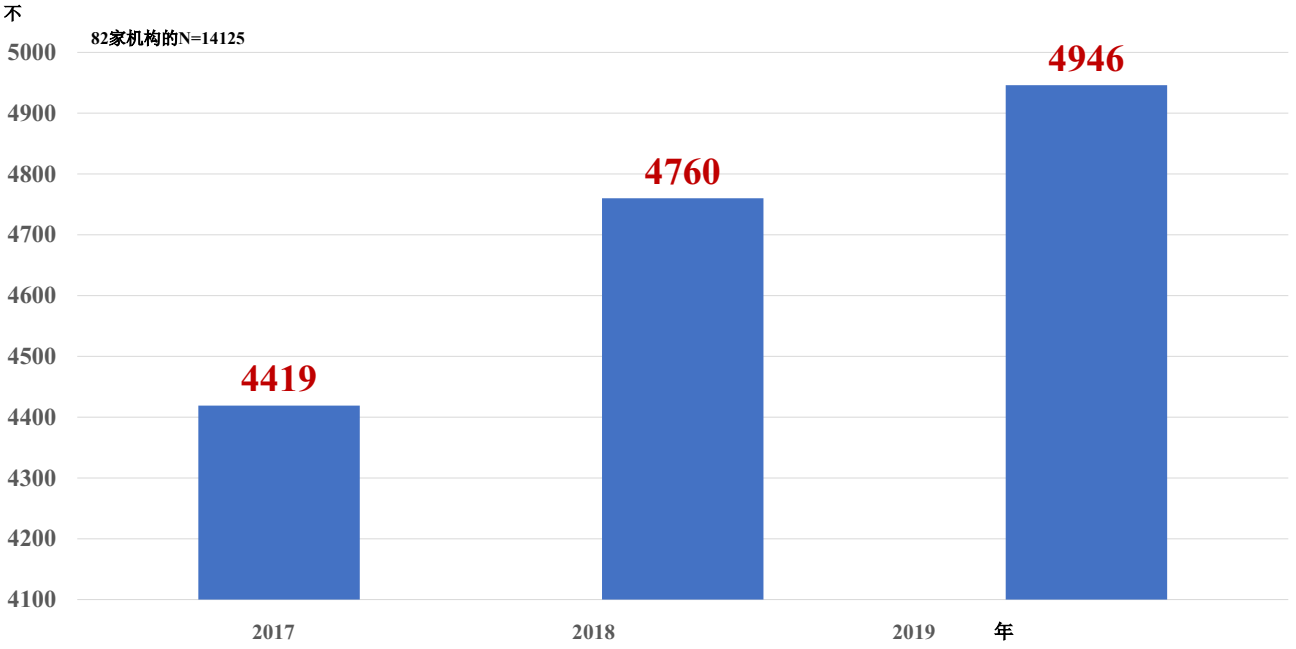


图1日本采用激光碎石术治疗上尿路结石的输尿管镜检查率

表1激光碎石输尿管镜术后并发症分析

总并发症率（n，%）	1496 (10.5)
术中并发症发生率（n，%）	199 (1.40)
输尿管穿孔	191 (1.35)
输尿管剥离	5 (0.03)
转为开腹/腹腔镜手术	3 (0.02)
术后早期并发症发生率（<1个月）（n，%）	1189 (8.41)
发热（>38°C）	1051 (7.44)
脓毒性休克	115 (0.81)
输血	10 (0.07)
囊膜上血肿	7 (0.05)
死亡率	6 (0.04)
术后晚期并发症（n，%）	108 (0.80)
输尿管狭窄	108 (0.80)

注：N=14 125。

讨论

本次调查发现，日本每年上尿路结石（URS-L）病例数呈持续上升趋势。尽管总并发症发生率达10.5%，其中术中并发症占1.40%，术后并发症占9.18%，但术中与术后并发症的年发生率均未达到显著水平。
与往年相比有显著差异。

随着激光技术的广泛应用和柔性输尿管镜的创新，上尿路结石的外科治疗方式发生了显著变化。2014年，Ordon团队通过分析1991至2010年间194,781例肾结石治疗的行政数据库发现，经尿道输尿管镜（URS）的使用率从1991年的25%显著提升至2010年的59%。而经皮肾镜取石术（SWL）的使用率则从1991年的69%下降至2010年的34%。

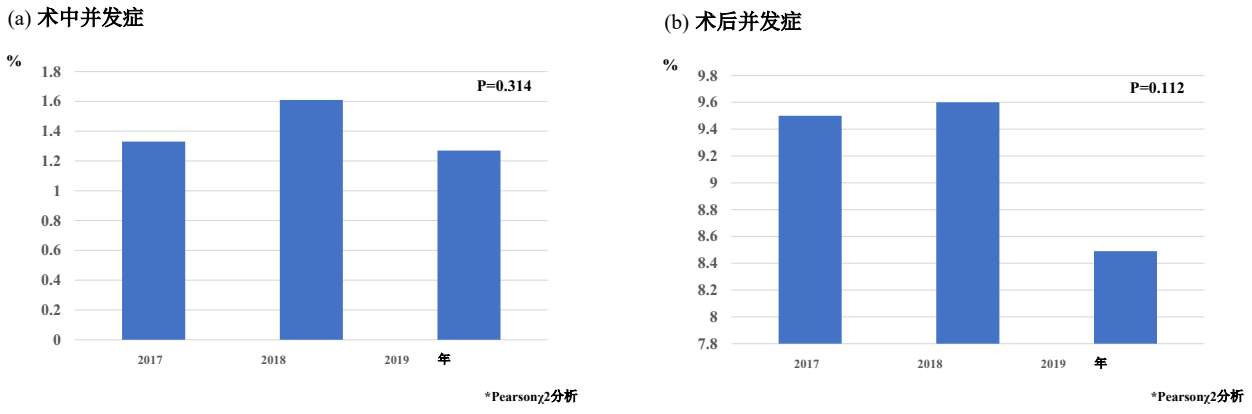


图2激光碎石联合输尿管镜检查的围手术期并发症发生率。(a)术中并发症。(b)术后并发症。

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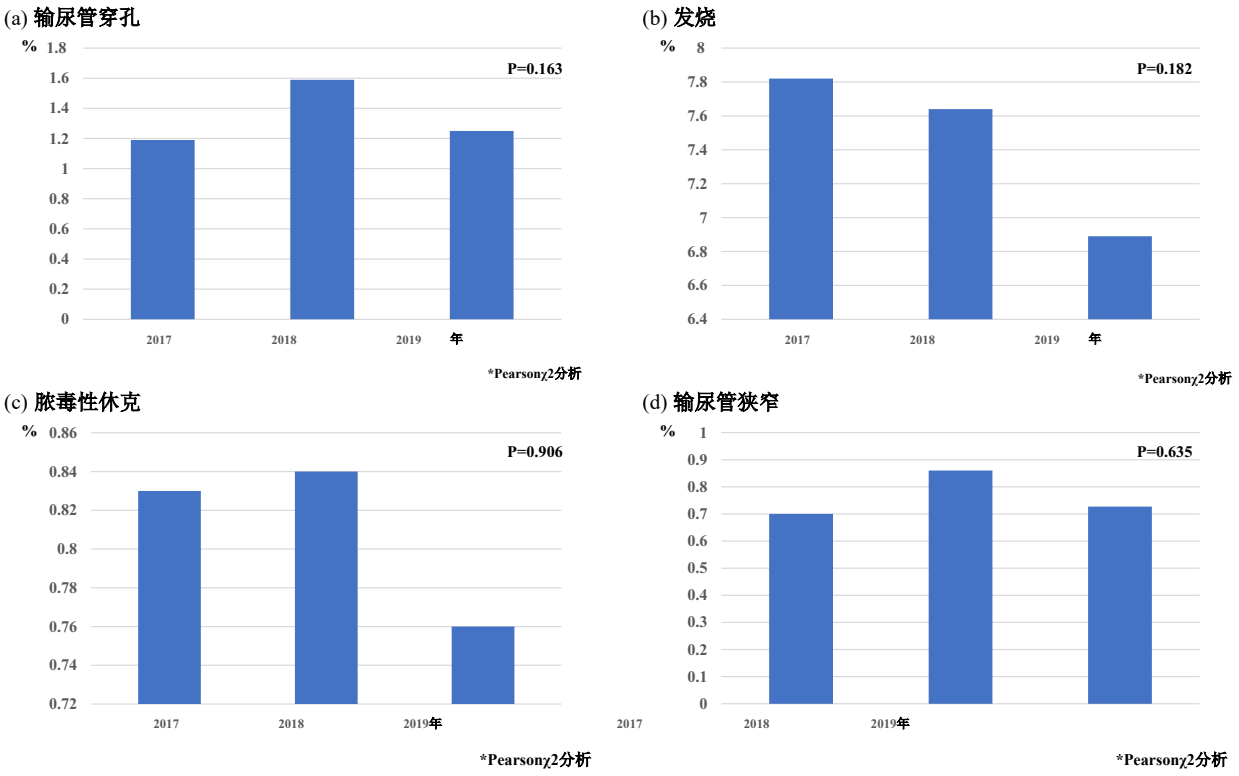


图3激光碎石输尿管镜检查术中及术后输尿管穿孔、发热、脓毒性休克和输尿管狭窄的主要并发症发生率。(a)输尿管穿孔，(b)发热，(c)脓毒性休克，(d)输尿管狭窄。

2010年，其数量低于URS。[4]此外，Herout等人显示，2006年至2019年间URS数量显著增加143%。[5]同样，Isotani等人在2019年报告称，日本URS使用量的年度趋势一直在增加，并且在2014年超过了每年进行的SWL数量。[2]

随着经尿道碎石术（URS）应用的日益普及，新型技术的引入可能引发更多并发症，从而增加围手术期并发症的发生率。欧洲泌尿外科学会（EAU）指南指出，URS术后总体并发症发生率为9%-25%，但多数并发症属于轻微范畴，无需手术干预。[6]根据内镜泌尿外科学会（CROES）临床研究办公室的全球研究数据显示，在11,885例患者中，并发症发生率为7.4%，其中术中并发症占4.2%，术后并发症占2.6%，术中术后并发症合计0.5%，且绝大多数为轻微并发症。但需注意的是，仍存在严重并发症的发生。[7]本研究对14,125例采用激光碎石术联合URS的患者进行分析，结果显示总并发症发生率为10.5%，其中术中并发症占1.40%，术后并发症占9.18%，该数据与另一项研究结果基本一致。但需要强调的是，本研究中仍存在严重并发症的发生。

输尿管穿孔作为极具破坏性的术中并发症，发生率在0.3%-7.4%之间，主要由输尿管镜手术中的尿道套管、激光发射、篮式电切操作及内窥镜本身引发。[8]当前该并发症的严重程度已通过内镜分级系统进行分类。Traxer等学者最初提出研究建议在使用输尿管套管时，术中应通过内镜对输尿管壁损伤进行分类。[9]此后，Schoentaler团队提出了术后输尿管镜损伤评分标准（Puls）。[10]根据Traxer分级系统，使用12/14F输尿管套管的病例中，13.3%出现累及肌层的输尿管壁损伤。[9]本研究中输尿管穿孔发生率相对较低，仅为1.35%。值得注意的是，尽管输尿管剥离术是输尿管镜检查中较为罕见的术中并发症（发生率0.04%-0.9%），但其危害性极高。[8]本研究中输尿管剥离术发生率为0.03%，这一比例并不低，因为上尿路结石本身属于良性病变。因此必须避免这种严重并发症。一旦发生输尿管剥离术，需立即进行修复，或分阶段实施修复。本研究中，仅有0.02%的患者因输尿管剥离术需要从经尿道输尿管镜手术转为开放手术或腹腔镜手术。

输尿管镜手术后发热是该手术常见的早期并发症，文献报道发生率介于0.2%至15%之间。[8]本研究数据显示，术后发热体温超过38℃的患者比例达7.44%。尿脓毒症作为严重并发症，其定义为泌尿生殖道感染引发危及生命的器官功能障碍，发生率在输尿管镜术后0.1%至4.3%之间。伴有脓毒性休克的[11]尿脓毒症发生率0.3%至4.6%，死亡率28.3-41.1%。[12,13]本研究中脓毒性休克的发生率为0.81%。

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表2激光碎石输尿管镜术后输尿管狭窄的临床特征与治疗效果

N=108（年龄，年，中位数，IQR）	63.0 (54.0–71.0)
性别（否，%）	M: 72 (66.6), F 36 (33.3)
BMI（kg/m^2，中位数，IQR）	24.4 (22.1–27.2)
术前肾积水（否，%）术前输尿管支架置入术（否，%）	85 (78.7) 31 (28.7)
结石位置（无，%）	
输尿管开口远端输尿管中段输尿管近端输尿管	1 (0.9)17 (15.7) 23 (21.2) 47 (43.5) 14 (12.9) 6 (5.5)
结石最大尺寸（毫米，中位数，IQR）；CT值（HU，中位数，IQR）	10.2 (7.4–13.5) 1070.5 (781.5–1320.5)
输尿管镜检查后诊断的输尿管狭窄期	
POD 1个月	33 (30.5)
POD 1-3个月	41 (37.9)
POD 3-6个月	23 (21.2)
6-12个月POD	8 (7.4)
POD>12个月	3 (2.7)
诊断性影像学检查（否，%）	
Ct	46 (42.5)
超声	19 (17.5)
IVP	1 (0.9)
Rp	20 (18.5)
输尿管镜检查	19 (17.5)
其他	3 (2.7)
输尿管狭窄长度（mm，中位数IQR）：10.0（5.0-17.0）；狭窄部位分布（例数，%）	
输尿管口	2 (1.8)
输尿管远端	26 (24.0)
中输尿管	24 (22.2)
近端输尿管	42 (38.8)
输尿管-盆腔连接处	14 (12.9)
输尿管狭窄治疗（否，%）	
经尿道球囊扩张术	59 (54.6)
输尿管尿路造口术（开放或腹腔镜）11例（10.1）肾切除术	2 (1.8)
输尿管支架或肾造瘘术置换11（10.1）	
观察结果	24 (22.2)
成功率（否，%）	
总计	59 (54.6)
经尿道球囊扩张术	37 (62.7)
输尿管尿路造口术（开放或腹腔镜）5例（45.4）	
输尿管支架或肾造瘘术置换11（100）	
观察结果	7 (29.1)

缩写：BMI，体重指数；HU，亨氏单位；IQR，四分位距；IVP，静脉肾盂造影；POD，术后日；RP，逆行肾盂造影。

经输尿管肾镜取石术后输血是该手术的早期并发症之一，发生率为1.3%-1.6%。[14,15]术中出血常由输尿管穿刺鞘或激光碎石导致的输尿管壁损伤、激光碎石引发的肾脏损伤，或因肾内高压导致的肾圆韧带破裂所致。此外，肾内高压、手术时间延长以及术中灌注压升高也是引发肾周囊下血肿的因素，其发生率为0.4%。
-2.2%的发病率。[16]患者继续服用抗凝剂或者在手术前使用的抗血小板药物通常在术中和术后继续出血。[17,18]在我们的研究中，有0.07%的患者接受了输血，0.05%的患者发生了包膜下血肿，这两者都比之前报道的相对较低。

尽管输尿管镜取石术是一种安全且微创的治疗手段，但仍有致死性并发症发生。根据欧洲泌尿外科学会泌尿系结石分会（EULIS）与泌尿技术分会（ESUT）最新发布的系统综述，Bhanot等学者的研究显示，在15项输尿管镜取石术（URS）相关研究中，共有72例患者死亡。在42例明确病因的病例中，死亡原因包括：脓毒症57.1%、多器官功能障碍14.2%、心脏相关并发症（如心肌梗死和心律失常）4.7%、出血性并发症4.7%，以及呼吸系统相关事件（如肺血栓栓塞）7.1%。[19]本研究显示URS术后死亡率为0.04%，这一数据与既往报道的发病率持平。

输尿管狭窄是术后晚期的主要并发症，发生率高达3%。

输尿管狭窄的定义是：在既往结石嵌顿部位出现输尿管局灶性狭窄，并通过IVP或历代逆行肾盂造影检查可明确显示输尿管肾积水。[20]然而，当前使用造影剂时应避免因术前解剖结构评估导致的造影剂过敏反应。此外，除结石手术前的结石嵌顿部位外，输尿管镜和碎石篮操作过度、激光照射遗漏、激光设置不当引发的热损伤以及结石残留等因素，都可能导致输尿管狭窄的发生。[21]因此，本研究将输尿管狭窄定义为术后出现比术前更严重的肾积水或等同程度的肾积水。特别值得注意的是，当将激光射入输尿管时，热损伤可能是术后输尿管狭窄的最新诱因之一。输尿管镜激光碎石术期间的肾内温度与激光功率设置直接相关。[22]本研究中输尿管狭窄发生率为0.8%。孙亚罗等学者曾报道，经尿道碎石术后2.9%的患者会出现输尿管狭窄。经尿道输尿管结石碎石术（URS）术后输尿管狭窄的成因可分为医源性因素和结石本身因素。医源性因素包括直接或间接热损伤导致的输尿管壁损伤、使用输尿管套管造成的黏膜缺血、黏膜内残留结石碎片，以及结石因素如结石嵌顿和结石大小。术后一旦形成输尿管狭窄，往往难以完全治愈。Sunaryo等学者基于人群研究数据显示：35%的狭窄病例需通过置入输尿管支架或经皮肾造瘘术进行引流，21%需内镜介入治疗，4.8%需输尿管重建，1.7%需单纯肾切除术。[23]本研究中术后狭窄干预方案如下：54.6%采用经尿道球囊扩张术，10.1%实施输尿管吻合术，1.8%进行肾切除术，10.1%更换输尿管支架或肾造瘘装置，22.2%采取观察治疗。手术成功率

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成功率取决于所采用的介入手术类型。Xiong等学者报告称，采用经尿道介入治疗输尿管镜术后输尿管狭窄的总体成功率为60.9%，但97.3%的患者需要接受重建手术。[24]在我们的研究中，输尿管狭窄完全缓解的总体成功率为54.6%，在所有介入治疗中，经尿道球囊扩张术和输尿管吻合术分别成功处理了62.7%和45.4%的病例。

本研究存在若干局限性。首先，作为主要局限，本研究数据采集自常年开展结石手术的成熟医疗机构，因此未纳入年手术量较少的机构。其次，我们仅收集了经尿道碎石术后（URS-L）的主要并发症数据，未纳入输尿管结石、术后疼痛及输尿管支架相关事件等次要并发症数据。第三，由于患者病历中未提供相关数据，我们无法分析输尿管结石与肾结石、刚性输尿管碎石术与柔性输尿管碎石术相关并发症的差异。第四，输尿管狭窄诊断采用超声与CT联合影像检查，术后1个月进行评估。部分病例术后2-3月可能出现肾积水缓解现象，为比较术前术后肾积水程度，我们采用超声与CT的联合影像评估。尽管如此，据我们所知，这是
首份报告中已报告术中及术后发生率
经尿道碎石术后出现上尿路结石并发症
在日本。此外，我们还评估了术后并发症的发生率。
我曾患有输尿管狭窄。总之，尽管随着技术进步，日本对URS-L的应用有所增加
尽管取得进展，但年并发症率仍居高不下
尽管URS-L是一种实用且微创的手术，但仍会出现严重并发症。因此，需谨慎管理URS-L，以避免进一步进行侵入性操作。

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数据管理。Mitsuhiro Tambo：数据管理。Shinsuke
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知情同意

是，因为在我院实行了选择退出机制。

注册表和注册号
研究/试验的

N/A.

动物研究

N/A.

资金信息

就目前情况而言，我们没有相关的资金
文章

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编辑评论

多中心协作研究中日本对输尿管镜联合激光碎石术治疗上尿路结石围手术期并发症及输尿管狭窄的调查编辑评论

在本研究中，井上团队对日本超过14,000名患者的输尿管镜检查（URS）和激光碎石术相关主要不良反应进行了全面统计。术中并发症发生率为1.4%，术后并发症发生率为9.2%，后者包括发热（7.4%）和脓毒性休克（0.8%）。82家合作中心协同完成数据收集的高效运作值得高度赞扬。这项协作成果构建了国家级真实世界参考数据。尽管输尿管镜检查已成为全球泌尿科医生首选的结石干预手段，但其伴随的并发症负担不容忽视。本研究报道的0.07%死亡率提醒我们，与肾结石及其手术切除相关的死亡确实可能发生。[2]因此，虽然输尿管镜检查常被誉为“无限制”的手术，但某些特定患者群体（如高龄患者）仍需严格筛选。近期一项针对85岁以上患者的研究显示，输尿管镜检查的总体并发症发生率达47%，1年死亡率达23%。[3]

在手术室中，外科医生必须对自己的错误操作负责。设备使用不当可能引发并发症，这一点在输尿管狭窄治疗中尤为关键。井上团队的研究数据显示，该病症在样本中发生率高达0.8%。新一代激光系统具备高功率调节功能，虽然追求零残留碎石时可能倾向于自动选择高功率，但必须保持谨慎。近期一项临床研究发现，当使用30瓦功率进行输尿管碎石术时，仅需12秒即可达到细胞热损伤阈值（43℃）。[4]因此，主张在碎石术中优先选择低功率的呼声日益高涨。然而当前激光功率的临床实践差异显著，不同厂商预设参数的差异可能加剧这种不一致性。尽管专家已提出部分建议，但要确定真正安全的功率阈值仍需更多研究。同时，关于激光激活时长和模式的研究也应同步推进。关于输尿管套管与输尿管狭窄形成的关系，学界至今仍存在争议。随着真空辅助输尿管套管的引入，这类器械在临床应用中的使用频率预计将进一步提升。[5]与高功率设备类似，虽然这类器械在提高无结石率方面的潜力最受关注，但其可能引发的术后狭窄风险同样不容忽视。

因此，井上等人研究结果促使我们思考狭窄等并发症的形成机制及应对措施。

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Review

Factors affecting the thermal effects of lasers in lithotripsy: A literature review

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Thermal effect;
Operator duty cycle

Abstract Objective: The use of lasers has been an important part of urology in the treatment of stone and prostate disease. The thermal effects of lasers in lithotripsy have been a subject of debate over the years. The objective of this review was to assess the current state of knowledge available on the thermal effects of lasers in lithotripsy, as well as explore any new areas where studies are needed.

Methods: In August 2022, a keyword search on Google Scholar, PubMed, and Scopus for all papers containing the phrases "thermal effects" AND "laser" AND "lithotripsy" AND "urology" was done followed by citation jumping to other studies pertaining to the topic and 35 relevant papers were included in our study. The data from relevant papers were segregated into five groups according to the factor studied and type of study, and tables were created for a comparison of data.

Results: Temperature above the threshold of 43 °C was reached only when the power was >40 W and when there was adequate irrigation (at least 15e30 mL/min). Shorter lasing time divided by lithotripsy time or operator duty cycles less than 70% also resulted in a smaller temperature rise.

Conclusion: At least eight factors modify the thermal effects of lasers, and most importantly, the use of chilled irrigation at higher perfusion rates, lower power settings of <40 W, and with a shorter operator duty cycle will help to prevent thermal injuries from occurring. Stones impacted in the ureter or pelvi-ureteric junction further increase the probability of thermal injuries during laser firing.

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1. Introduction

Laser is an acronym for "light amplification by stimulated emission of radiation". In 1968, Mulvaney and Beck [1] published a study on the fragmentation of calculi using a ruby crystal laser, which was one of the first studies in laser lithotripsy. The use of lasers has been an important part of urology in the treatment and management of stone diseases and benign prostatic hyperplasia especially after the 1980s. The urological community would benefit from a review article that provides an overview of the current state of knowledge on the thermal effects of lasers, as well as identifies potential new areas of research that require further investigation. Also, the safety of the long-term use of lasers on injury to the pelvicalyceal system and the ureters as well as the factors that may lead to causation of this photothermal injury is not well documented and requires further detailed studies.

During laser lithotripsy, the operator can modify three factors to achieve the necessary effect of stone fragmentation: pulse energy (J), pulse frequency (Hz), and pulse duration (ms). Any changes in energy and frequency can change the power (W), and higher power results in higher temperatures and therefore thermal damage [2]. This thermal damage occurs as a result of the photothermal effect of lasers leading to absorption of the heat energy by the surrounding tissue [3].

Temperature measured using thermocouples placed near the laser probe has been the surrogate used in various experimental studies to extrapolate on safety of in vivo laser use. Sapareto and Dewey [4] proposed a "time e temperature relationship" for tissue thermal damage stating that for every 1 °C exceeding the "threshold (43 °C)", the time required to cause damage to the same number of cells will decrease by half. For example, when the tissue is in a 45 °C environment for 15 s, the degree of thermal damage to cells is similar to that at 44 °C for 30 s or 43 °C for 1 min. Most of the articles in this review used this temperature threshold as the standard for assessing the thermal end point.

A long-term sequela of thermal injury of particular concern is that of ureteral strictures. It was found to be approximately three times more common in patients treated by laser lithotripsy over pneumatic lithotripsy in a meta-analysis study [5]. However, a prospective study published in 2019 found that the incidence rate was quite low (1.5%) and seen mostly in the presence of stone impaction [6]. Whether this result was due to an increase in the local temperature or direct injury to the surrounding tissue could not be determined. This is an area of interest which may need further investigation and can be considered for future studies.

The objectives of this review article were to study the following questions in relation to lasers in lithotripsy.

i. What were the factors affecting the thermal effects of lasers on non-target tissue during lithotripsy?
ii. Was the thermal injury to non-target tissue during laser lithotripsy significant?
iii. What were the areas that need further investigation to prevent laser-related injuries?

2. Materials and methods

In August 2022, a keyword search on Google Scholar, PubMed, and Scopus for all papers containing the keywords "thermal effects" AND "laser" AND "lithotripsy" AND "urology" was done in various combinations, followed by citation jumping to other studies pertaining to the topic. All accepted and published English language full articles were studied and filtered wherein articles not pertaining to the aims of our review were excluded by reading the title, abstract, and full article. Thirty-five relevant papers were included in our study and the findings are presented as a narrative literature review.

There were several factors that stood out while the review was conducted and they were segregated into five groups according to the factor studied and type of study, and tables were created for a comparison of data.

3. Results

3.1. Irrigation

The majority of the studies were done on irrigation (its presence or absence, with irrigation pump or only gravity, and chilled or warm). Out of 12 studies, two were in vivo in sheep or pig [7,8], two were ex vivo [9,10], while the remaining eight [2,11e17] were in vitro studies. They all used thermocouples for measuring the temperature but the placement of the probe was inconsistent among the studies. An average distance of 0.5 mm from the laser tip is ideal corresponding to the depth of penetration of holmium:yttrium-aluminium-garnet (Ho:YAG) laser in the water medium [18].

One of the first laser thermography study was conducted in 2015 by Molina et al. [9], where two ex vivo models (clinical model and open ureteral model) were studied for temperature rises during Ho:YAG laser with 365 mm firing at 10 W (1 J/10 Hz). They showed an increase in the temperature during laser activation and that ureteral thermal values decreased with saline irrigation. This was further cemented in 2016 by Butticè et al. [11], when they compared 200 mm with 272 mm fibers in a bench model inserted into a saline-filled heating tank at two temperatures (room 24.5 °C and body 36.5 °C). They found that when the irrigation was open, the maximum temperature limit was never reached. Dau et al. [8,16] conducted studies in vivo (in 2022) and in vitro (in 2021), respectively, most importantly studying the effect of chilled irrigation on caliceal fluid temperatures and the laser heating of fluid with and without stone ablation. They showed that the temperature rise and thermal dose during lithotripsy, especially at higher power were reduced by using chilled irrigation at 1 °C as compared to room temperature irrigation at 19 °C.

More studies since then have come to similar conclusions in various different settings as enumerated in Tables 1 and 2, and the general consensus was that irrigation is essential during laser activation preferably at higher flow rates and higher pressure. Most studies showed a temperature beyond the threshold of 43 °C, only at higher power settings (≥40 W), and the power of the laser must be regulated to stay below the threshold. One article also showed that high

Table 1 Studies pertaining to irrigation with the holmium:yttrium-aluminium-garnet laser.

Study	Study subject	Laser fiber used (mm)	Lasing time	Power setting (W or J/Hz)	Irrigation setting	Temperature recorded (°C)	Mode of temperature measurement
Molina et al., 2015 [9]	Ovis aries	365	NA	1/10	• With • Without	• 37.4±2.5[a] • 49.5±2.3[a]	• Temperature on external surface using Infrared Fluke Ti55 Thermal Imager
Butticè et al., 2016 [11]	Bench model with saline heating tank	200 or 272	Stopped when a limit reached	0.5/20, 1/10, 2/5, 3/5, or 4/5	• With or without	• Threshold surpassed when irrigation not used	• Endotracheal thermometer inside the model
Aldoukhi et al., 2017 [12]	Glass test tube	200	1 min	(0.5e1)/(10e80)	• 0, 7e8, 14e15, or 38e40 mL/min	• Max 70.3±2.7[a] at 40 W, no irrigation	• Thermocouple placed 5 mm from bottom of the test tube
Aldoukhi et al., 2018 [7]	Pig	242	1 min	0.5/80	• 0.1, 15, or 40 mL/min	• 0.1 mL/min: 84.8 • 15 mL/min: 63.9 • 40 mL/min: 43.6	• Thermocouples in calyx, by open exposure, puncture, and retrograde beside the scope
Wollin et al., 2018 [2]	PVC tubing	200	1 min	(0.2e1)/(6e50)	• 0, 50, or 100 mL/min	• 0 mL/min: >100 • 50 mL/min: >43.4 • 100 mL/min: 30.7	• Probe tip thermometer placed 1 mm from tip of fiber
Hein et al., 2018 [13]	20 mL test tube in water bath	272 or 940	2 min	0.5/33, 1/18, 1.5/30, 2/2, or 4.5/(4,12, or 22.3)	• 0e100 mL/min	• Max 68 at 100 W	• Thermocouple in the test tube and water bath
Winship et al., 2019 [17]	Saline bag with reservoir	365	45 s	(0.2e1)/(6e80)	• 0, 100, or 200 mmHg	• Threshold >6 rose at 100 mmHg and below	• Thermocouple placed adjacent to the fiber
Hein et al., 2020 [10]	Porcine kidney in water bath	272, 550, or 940	1min	5e100 W	• 0e100 mL/min	• Critical temperature rose above 30 W	• Three thermocouples in kidney with one flexible thermocouple placed 4 mm proximal to fiber
Ghanim et al., 2020 [14]	Water tank with PVC pipe	365	70 s	(0.375, 0.675, or 1)/20	• 0, 1, 10, or 30 mL/min	• Max 70 at high power and closest to thermometer	• Thermometer in one end of the PVC tube
Liang et al., 2020 [15]	Ligated F20 rubber tube	200	3, 5, or 10 s	(0.5, 1, 1.5, 2, or 3)/(10 or 20)	• 10, 15, 20, or 30 mL/min	• Max 78 at 30 W power at 10 mL/min	• Thermocouple 5 mm from bottom of the tube

(continued on next page)

Table 1 (continued)

Study	Study subject	Laser fiber used (mm)	Lasing time	Power setting (W or J/Hz)	Irrigation setting	Temperature recorded (°C)	Mode of temperature measurement
Dau et al., 2021 [16]	Glass test tube in water bath	242	1 min	0.5/80	• Chilled irrigation at 1 °C and room temperature at 19 °C at 0, 8, 12, 15, or 40 mL/min	• Threshold temperature delayed in chilled	• Wire thermocouple 3 mm proximal to the ureteroscope tip
Dau et al., 2022 [8]	Female Yorkshire pig	242	1 min	NA	• Chilled irrigation at 1 °C to 4 °C and room temperature at 19 °C at 0e40 mL/min	• Threshold temperature delayed in chilled	• Thermocouple fixed 5 mm from the ureteroscope tip

Max, maximum; NA, not available; PVC, polyvinyl chloride.
[a] Mean±standard deviation

energy (3.0 J) and low frequency (10 Hz) mode has slightly less thermal damage than its counterpart settings at the same power [15] and needs further evaluation.

The use of ureteric access sheath (UAS) and its effect on the intrarenal temperature were also studied by one group [19]. They found that the UAS decreases intrarenal temperatures at a power setting of 20 W, when compared with not using one. At a power setting greater than 40 W, however, the protective effect was lost and only remedied by increasing irrigation rates [19]. This study also compared the use of the manual pump with the gravity pump for irrigation, and observed that the dangerous threshold temperature was never reached with the manual pump (0.33 pumps/s), but the temperature rise was detrimental at the higher power of >40 W with the gravity pump. Therefore, this indicates that the manual pump could be preferred over the simple gravity irrigation.

3.2. Type of laser

Apart from the Ho:YAG laser, another laser being used frequently recently in lithotripsy is the thulium:YAG (Th:YAG) laser. Since the Th:YAG (2000 nm) laser has a slightly lesser wavelength compared with the Ho:YAG (2140 nm), the depth of penetration is also less. The power efficiency of Th:YAG laser is also said to be five times more than the Ho:YAG laser [18]. But the main advantage during lithotripsy for the Th:YAG is that it is a continuous wave laser, which is better suited for tissue ablation; to overcome this, a thulium fiber laser (TFL; 1940 nm wavelength) was introduced, which was a thulium ion laser with semiconductor diodes instead of a flash pump [20]. This TFL had both the continuous and pulsed wave modes.

The major aspects of studies comparing the Ho:YAG with thulium laser have been summarized in Table 3. In 2016, Kallidonis et al. [21,22] performed two separate studies to evaluate the effect of the Th:YAG laser when compared with Ho:YAG laser. One was ex vivo in the porcine upper urinary tract, while the other was an in vitro model. They showed comparable results in both studies while studying the temperature rises using both lasers, and concluded that up to 20 W Th:YAG laser was a safe alternative to the Ho:YAG laser, with adequate irrigation. Similar results were obtained by Taratkin et al. [23] and Peng et al. [24] when comparing the Ho:YAG laser with the TFL, finding that irrigation reduced the respective temperatures in the same manner for both lasers.

More recently, Molina et al. [25] compared the temperature rise seen during the super pulse TFL versus the high power Ho:YAG laser during dusting and fragmenting separately in ex vivo porcine kidneys. The intra-luminal temperature rise during laser activation was equivalent during dusting and higher in the super pulse TFL during fragmentation, but neither reached the threshold for thermal injury based on the duration of exposure. Therefore, there seems to be a risk of an increased temperature rise with a TFL during fragmentation, but it warrants further investigation.

3.3. Operator duty cycle (ODC) and pedal time

The ODC indicates the ratio of "on/off" of the laser power. The higher the "duty", the higher the ratio of "on"

Table 2 Inferences from the irrigation studies.

Study	Inference
Molina et al., 2015 [9]	• The study was one of the first studies that showed an increase in the temperature during laser activation and that ureteral thermal values decreased with saline irrigation
Butticè et al., 2016 [11]	• Rapid increases of temperature must be avoided when irrigation is closed and water at lower temperatures during irrigation helped delay the rise of temperature
Aldoukhi et al., 2017 [12]	• The highest temperature seen with 1 J/40 Hz power and no irrigation, counter measures for same can be exploited by urologists
Aldoukhi et al., 2018 [7]	• Thermal damage threshold reached in no and medium irrigation but not in high irrigation, so high-power lasers pose a threat for thermal damage at lower irrigation rates
Wollin et al., 2018 [2]	• Despite increasing laser settings, adequate irrigation can maintain relatively stable temperatures within an in vitro ureteral system
Hein et al., 2018 [13]	• Laser devices should, therefore, always be applied in conjunction with continuous, closely monitored irrigation whenever performing holmium:yttrium-aluminium-garnet laser lithotripsy
Winship et al., 2019 [17]	• High temperatures were achieved in as little as 1 s at common irrigation pressure and laser settings, particularly with a flexible ureteroscope and power $\geq$10 W; however, with laser cessation, temperatures quickly returned to a safe level at each irrigation pressure
Hein et al., 2020 [10]	• A formula to calculate the approximate DT for irrigation rates $\geq$30 mL/min was developed: DT Z 15 K$\times$(power [W]/irrigation [mL/min])
Ghanim et al., 2020 [14]	• All three parameters (pulse energy, irrigation rate, and distance) showed highly significant effect on measured temperatures; the holmium:yttrium-aluminium-garnet laser might be safely provided when there was sufficient irrigation with optimal selected laser power
Liang et al., 2020 [15]	• Safe temperature of laser firing can be ensured at laser power less than 10 W, irrigation greater than 30 mL/min, and high-energy low-frequency firing
Dau et al., 2021 [16] and Dau et al., 2022 [8]	• Chilled irrigation slows temperature rise, decreases plateau temperature, and lowers thermal dose during high-power laser lithotripsy

compared with "off", and therefore, it gives more output energy. The 100% ODC means continuous on, which is the continuous wave cutting [26]. In the setting of lithotripsy, it may be calculated as lasing time divided by lithotripsy time.

In 2021, Aldoukhi et al. [27] performed in vitro tests, wherein 1200 J of laser energy was applied in five different patterns at 20 W average power for 60 s. The mean ODC was 32% overall among the five patterns and the mean time of pedal activation was 3.6 s. In vitro studies revealed a longer pedal activation time produced a higher peak temperature and thermal dose. Louters et al. [28] in 2022, conducted a similar study to determine the effect of the ODC on the thermal dose delivered. A higher ODC resulted in a greater maximum temperature and thermal dose, with an ODC $\geq$70% exceeding the threshold of 43 °C. Use of a 50% ODC compared with 60% of the ODC resulted in a ten-fold increase in time required to reach the threshold of thermal injury and an eight-fold increase in maximal allowable energy. These studies fortify the statement that judicious laser ODC control can help to prevent thermal damage from lasers.

3.4. In vivo studies

One of the only in vivo studies was conducted in patients undergoing ureteroscopy laser lithotripsy for stone disease in China in 2019 by Wang et al. [29]. A total of 30 patients (16 males and 14 females) with a mean age of 47.4 (standard deviation 13.7) years, and a mean calculi diameter of 14.2 (standard deviation 8.1) mm, undergoing ureterorenoscopic lithotripsy were studied. A temperature measurement guidewire was inserted and extended slightly beyond the ureteroscope, while the other end was connected to a thermometer that fed real-time temperature change data to a computer.

The highest temperatures in the 30 sets of data were all higher than 43 °C (100%), with 19 sets (63.3%) having peak temperatures higher than 56 °C. This study showed that with the increase in the power of the holmium laser, or with impacted calculi, the increase in the temperature of the lavage solution around the calculi was even greater, often exceeding the temperature that could be safely tolerated by the tissue; therefore, temperature might be one of the factors that caused ureteral thermal injury and resulted in postoperative strictures [24]. However, the study by Wang et al. [29] was not without limitations as it only studied the thermal effect with respect to the laser power, and also the surgeon was different for each case, which meant the laser settings, time of lasing, and intraoperative conditions were different for each case.

3.5. Other factors like volume and pulse duration

In 2022, Dau et al. [30] performed an in vitro study keeping the laser fiber above the stone at 3.5 mm (no ablation) and 0.5 mm (ablation), and the temperature of the fluid was recorded using two thermocouples once per second, to determine the percentage of applied laser energy that is converted to heat and the percentage used for stone ablation. They found that even under conditions of energy-efficient stone ablation, the majority of applied laser energy (91%e96%) was converted to heat [30]. The pelvicalyceal volume in which laser activation occurs was also later found to be an important factor in the thermal effects caused

Table 3 Studies pertaining to the type of lasers.

Study	Study subject	Laser studied	Laser fiber diameter or type	Lasing time	Power settings (W), energy (J)/frequency (Hz)	Irrigation setting	Temperature recorded (°C)
Kallidonis et al., 2016 [21]	Pig	Ho:YAG vs. Th:YAG	Continuous wave	NA	• 10 W, 20 W, 30 W, or 40 W	• With	• 33.5
Kallidonis et al., 2016 [22]	Burette with a stopcock and a 40 mL vessel	Ho:YAG vs. Th:YAG	Both pulsed and continuous waves	10 min	• 5 W, 10 W, 20 W, 50 W, or 100 W	• Without	• 45.6e68.7
Taratkin et al., 2020 [23]	In vitro model	Ho:YAG vs. SP TFL	200 μm	1 min	• 40 W, 0.2 J	• 0 or 35 mL/min	• Temperature reduction after irrigation - Ho:YAG: 2.6 - TFL: 1.9
Peng et al., 2020 [24]	Test tube in water tank	TFL	Continuous wave	1 min	• Different settings up to 30 W	• 0, 15, 25, or 50 mL/min	• 0 and 15 mL/min: more than 6.5 °C rise above threshold seen; 25 and 50 mL/min: no rise of temperature over threshold
Molina et al., 2021 [25]	Porcine kidney	Ho:YAG vs. SP TFL	200 μm	5 s each for 15 times	• Ho:YAG dusting: 0.3 J/70 Hz; SP TFL dusting: 0.1 J/200 Hz; fragmenting: 0.8 J/8 Hz	• With	• During fragmenting setting - Ho:YAG: 30 - SP TFL: 33.3 • During dusting setting - Ho:YAG: 35.8 - SP TFL: 40.6

Ho:YAG, holmium:yttrium-aluminium-garnet; Th:YAG, thulium:yttrium-aluminium-garnet; TFL, thulium fiber laser; SP, super pulse; NA, not available.

by lasers [31]. The authors found that the volume of fluid in each model was inversely related to the extent of temperature elevation. Therefore, the thermal dose in laser firing reached the threshold for injury faster in smaller volumes. Louters et al. [32] performed a study to determine the volume of fluid mixing during laser activation in a plastic tube with dyed irrigation by evaluating the distance travelled by the dyed fluid during laser activation. The volume of total fluid mixing within the ureter model was found to be small, thus conferring a greater risk of ureteral thermal injury.

The pulse duration of laser activation has also been found to play a role in the thermal effects in a study by Sugiwaka et al. [33] in 2022, where the bubble behavior and temperature distribution around bubbles were studied in an in vitro experiment. They found long pulse bubbles had a higher temperature around the bubble and may lead to increased thermal damage to surrounding tissue. The factors mentioned above have not been studied in detail enough to know whether they influence the thermal damage to much extent. However, they should be considered in subsequent analyses, as preliminary studies show that they do play a role.

The main study parameters and settings with respect to these factors are listed in Table 4.

4. Discussion

The use of lasers for lithotripsy is widespread with newer technology and different lasers being developed for this specific purpose. The photothermal effect as mentioned earlier is the main mechanism for the fragmentation of stones, but there are some factors of the laser and fiber used that can modify these effects to a certain extent. At higher power, irrigation is required at higher flow rates to keep temperatures low. However, one must be judicious as overzealous pumping of irrigation can lead to pyelovenous backflow and extravasation due to an increased intrarenal pressure [34].

High-power laser energy can cause a significant increase in fluid temperature in the collecting system and ureter, leading to histologic injury in the surrounding tissue [2,7,12,17]. It is crucial to develop methods to predict and control the thermal dose to ensure patient safety during high-power laser lithotripsy. As mentioned earlier, the time duration of temperature also plays an important role as elucidated in the "time–temperature relationship" by Sapareto and Dewey [4]. This is further encountered as the ODC, or the time duration of "on/off". One study has shown that while the temperature may reach below the threshold between laser firing attempts, the thermal dose is cumulative and can reach very large proportions [27]. Therefore, it is essential that these factors which may lead to an increased thermal dosage are studied in order to prevent thermal damage, especially in the in vivo settings. This study attempted to consolidate the various factors that modify the thermal effects of lasers, so that future studies may concentrate their efforts in studying these factors in detail.

From our review, it can be inferred that there are at least eight factors that modify the thermal effects of lasers:

i. Irrigation: the irrigation at higher perfusion flow rates with open systems, at higher pressure, and chilled irrigation over warm irrigation provided better control of the temperature rise during laser lithotripsy. A UAS when feasible may be recommended to reduce temperatures.
ii. The type of laser: the TFL may have slightly higher potential for damage, but further studies are required.
iii. Power settings: in general, higher power means increased risk for damage. Staying below a maximum of 40 W is advisable.
iv. The ODC and pedal time: the higher ODC (on time > off time) and longer pedal times increase risk for injury. Intermittent lasing should be advocated as opposed to continuous.
v. Pulse duration: longer pulse duration increase temperature around bubble and thereby can cause damage.
vi. Volume of fluid: this includes the total pelvicalyceal volume in which laser activation occurs as well as the volume of fluid mixing, with lower fluid volumes resulting in increased thermal doses.
vii. The distance from stone: preliminary studies show that the energy transfer may be equivalent at further distances as well; however, more studies are needed to come to an apt conclusion.
viii. Stone impaction: with impacted stones, the temperature of the lavage solution was significantly higher, often exceeding the temperature that could be safely tolerated by the tissue.

There are plenty of studies to show the importance of the first three factors, and further studies should focus on the remaining lesser researched factors to ensure that thermal injury can be completely avoided during laser activation.

The major deficiency in the studies was that none of them assessed how the temperature changes actually affect the physiology of the pelvi-ureteric system and kidney function due to their in vitro nature. There are obvious ethical issues that come up as well that prevent one from experimenting at higher temperature at the cost of safety. However, one is encouraged to pursue more randomized control human studies comparing temperature changes at laser settings below 40 W, at different irrigation rates (preferably chilled), and at lower ODCs (i.e., intermittent activation) in order to find the ideal settings for safety. The use of a UAS and manual pump during irrigation can also be seen to help mitigate the temperature rise seen during laser activation, and more studies are advised comparing the manual pump with gravity irrigation both with and without access sheaths.

Our study had some limitations notably that the reviewed data were mostly from experimental studies conducted on various in vitro, in vivo, and ex vivo subjects, and not clinical data from patients. Also notably, it was a narrative study that reflects the heterogeneity of data, such as the various laser settings, lasers used, and flow rates. As the adage goes, "prevention is better than cure", and additional research is required to prevent laser thermal damage.

Table 4 Other factors affecting thermal damage by lasers.

Study	Factor studied	Study subject	Laser studied	Laser fiber diameter and laser setting	Lasing time	Power settings (J/Hz)	Irrigation setting	Temperature recorded
Dau et al., 2022 [30]	Percentage of laser energy converted to heat	Double walled glass Dewar	Moses 200 D/F/L	200 μm, short pulse and Moses distance modes	30 s	0.5/5	NA	• Rise in control: 1.03±0.01 °C[a] • Rise in experiment: 0.99±0.06 °C[a]
Rezakahn Khajeh et al., 2022 [31]	Pelvicalyceal system volume	Glass tubes of different volumes in the water tank	Ho:YAG laser	230 μm	1 min	0.5/80	0, 8, 15, or 40 mL/min	• Threshold reached faster in smaller volume
Tsaturyan et al., 2022 [36]	Continuous prolonged activation	20 mL syringe with the access sheath	Ho:YAG laser	Continuous wave	10 min	(0.3, 1, or 1.5)/40	10, 20, or 30 mL/min	• Max 83 °C at 10 mL/min
Sugiwaka et al., 2022 [33]	Pulse duration	In vitro model	NA	Pulsed wave	NA	NA	NA	• NA
Louters et al., 2022 [32]	Volume of fluid mixing	Plastic tube	Ho:YAG laser	NA	NA	0.5/40	8e40 mL/min	• Threshold crossed at lower irrigation rates with the mixing volume only 1.26±0.10 cm^3[a]

Ho:YAG, holmium:yttrium-aluminium-garnet; Max, maximum; NA, not available.
[a] Mean±standard deviation.

5. Future perspective

It is well known that the theoretical depth of penetration of the Ho:YAG laser into tissue is only 0.4 mm, but there has been speculation that the actual depth of penetration exceeds it [35]. This may account for the thermal damage seen during the use of lasers. However, whether the injury was related to contact damage or due to the thermal effects of the heat generated by laser firing has not been studied in depth. Whether it is due to either cause, the risks that stem from thermal damage cannot be easily ignored and thus the factors which may influence this damage have to be studied thoroughly.

Many studies in the past decade have been dedicated to studying the effects of irrigation on the thermal damage caused; however, the recent studies focused more on other factors such as pulse duration, ODC, type of laser, and in vivo studies. These need to be studied further in detail to fill the voids in our knowledge regarding the impact these factors have on laser related injury. In addition, there is a lack of studies which consider patient factors like age, degree of hydronephrosis, and coexisting infections; this may confound the temperature rise seen. However, this is probably due to the fact that the majority of studies are in vitro ones, and when in vivo studies are done in the future, these factors should be studied prudently.

6. Summary

This review explores the thermal effects of lasers in urology, particularly in lithotripsy for stone and prostate disease. The study was conducted by searching for relevant papers on thermal effects, lasers, lithotripsy, and urology. A total of 35 papers were included in the study, and the results were categorized into five groups for analysis. The findings reveal that temperatures above 43 °C are typically reached with laser power exceeding 40 W and sufficient irrigation (at least 15e30 mL/min). Shorter lasing times and an ODC of less than 70% also lead to smaller temperature increases. The study concludes that several factors influence the thermal effects of lasers including the irrigation, type of laser, power, ODC, pulse duration, volume of fluid, and stone impaction. The key recommendations from the study include the use of chilled irrigation at higher perfusion rates, lower power settings (<40 W), and a shorter ODC to prevent thermal injury, especially in cases involving impacted stones.

7. Conclusion

The thermal effect of lasers with respect to urology is one of the up-and-coming areas of research, even though studies date almost back to 2015. A better understanding of the thermal injury that may result from lasers is essential to prevent the improper technique and consequent sequelae. The use of chilled irrigation at higher perfusion rates, lower power settings of <40 W, and with a shorter ODC will help to prevent thermal injuries from occurring, especially during stone impaction. This review article hopes to highlight the important lessons to be learnt from previous studies and encourage the reader to endeavor into the various gaps in knowledge which are present to further ensure safe and efficient laser usage.

Author contributions

Study concept and design: Kiron Krishnaprasad.
Data acquisition: Kiron Krishnaprasad, Ravi Teja Pathi.
Data analysis: Kiron Krishnaprasad.
Drafting of manuscript: Kiron Krishnaprasad, Ravi Teja Pathi.
Critical revision of the manuscript: Kiron Krishnaprasad, Mustafa Nazar.

Conflicts of interest

The authors declare no conflict of interest.

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评审

影响激光碎石热效应的因素：文献综述

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关键词肾结石；
激光碎石术；冲洗；热效应；
操作员值班周期

摘要目的：激光技术在泌尿外科治疗结石及前列腺疾病中具有重要地位。然而，激光碎石术中的热效应问题多年来始终存在争议。本综述旨在系统梳理当前关于激光碎石术热效应的研究现状，并探索亟待深入研究的新领域。

研究方法：2022年8月，我们通过谷歌学术、PubMed和Scopus数据库进行关键词检索，筛选出包含“热效应”、“激光”、“碎石术”和“泌尿外科”等关键词的论文。通过文献跳跃法获取相关研究后，最终纳入35篇相关论文。根据研究因素和研究类型对数据进行五类分组，并制作表格进行数据对比分析。

结果：只有当功率>40 W且存在充足灌注（至少15-30 mL/min）时，温度才会超过43 ℃的阈值。激光作用时间较短或碎石时间，以及操作员工作周期低于70%，也会导致温度升高幅度减小。

结论：至少有八个因素会影响激光的热效应，其中最关键的是采用低温冲洗配合高灌注速率、功率设置低于40瓦以及缩短操作者工作周期，这些措施能有效预防热损伤的发生。当结石阻塞输尿管或肾盂输尿管连接部时，激光治疗过程中热损伤的风险会显著增加。ª2025《亚洲泌尿外科杂志》编辑部。本文由爱思唯尔出版集团负责制作与托管。本刊为CC BY-NC-ND许可协议（知识共享署名-非商业性使用-禁止演绎http://creativecommons.org/licenses/by-nc-nd/4.0/）下的开放获取期刊。

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1. 介绍

激光是“通过受激发射放大光”的缩写。1968年，穆尔瓦尼和贝克[1]发表了关于使用红宝石晶体激光器粉碎结石的研究，这是激光碎石术的早期研究之一。自20世纪80年代以来，激光技术在泌尿科领域发挥着重要作用，尤其在治疗结石疾病和良性前列腺增生方面成效显著。泌尿学界亟需一篇综述文章，既能全面梳理当前激光热效应的研究进展，又能明确需要深入探索的潜在研究方向。此外，激光长期使用对盆腔肾盂系统和输尿管造成的损伤风险，以及引发这种光热损伤的具体因素，目前尚未得到充分论证，亟需开展更深入的专项研究。

在进行激光碎石术时，操作者可通过调节三个关键参数来实现结石粉碎效果：脉冲能量(J)、脉冲频率（Hz）和脉冲持续时间（μs）。能量和频率的任何调整都会改变功率(W)，功率越高温度随之升高，从而引发热损伤[2]。这种热损伤源于激光的光热效应，即周围组织吸收热能所导致的[3]。

在多种实验研究中，研究人员常采用激光探头附近的热电偶测温数据作为替代指标，用于评估体内激光治疗的安全性。萨帕雷托和杜威[4]提出了一种组织热损伤的“时间-温度关系”理论，指出当温度超过“阈值（43·℃）”1 ℃时，造成相同数量细胞损伤所需时间将缩短一半。例如，当组织在45·℃环境中持续15秒时，其热损伤程度相当于44·℃环境30秒或43·℃环境1分钟的损伤效果。本综述中大多数文献都将这一温度阈值作为评估热损伤终点的标准。

热损伤的长期后遗症中，输尿管狭窄尤为值得关注。一项荟萃分析研究[5]显示，接受激光碎石术治疗的患者发生该并发症的概率是气压碎石术患者的三倍左右。然而2019年发表的前瞻性研究发现，其发生率其实相当低（1.5%），且主要出现在结石嵌顿的情况下[6]。目前尚无法确定这一结果是由于局部温度升高所致，还是周围组织受到直接损伤。这一研究方向值得深入探讨，未来可作为重点研究课题。

本综述旨在探讨激光碎石术的相关问题。

i. 在碎石术过程中，哪些因素会影响激光对非靶组织的热效应？

ii.激光碎石术中非目标组织的热损伤是否显著？

iii.需要进一步调查哪些领域以预防激光相关伤害？

2. 材料和方法

2022年8月，我们在谷歌学术、PubMed和Scopus数据库中对包含“热效应”、“激光”、“碎石术”和“泌尿外科”关键词的论文进行了多组组合检索，并通过引文跳转至相关研究文献。我们系统筛选了所有被接受并发表的英文全文论文，通过阅读标题、摘要和全文内容，排除了与本综述研究目的无关的文献。最终纳入35篇相关论文，以叙述性文献综述的形式呈现研究结果。

在进行审查时，有几个突出的因素，根据研究因素和研究类型，将它们分成了五组，并创建了表格来比较数据。

3. 结果

3.1. 灌溉

大多数研究集中在灌溉系统（包括是否存在灌溉系统、是否配备灌溉泵、是否采用重力灌溉，以及是否使用冷水或温水）方面。在12项研究中，有两项采用活体实验（绵羊或猪）[7，8]，两项为离体实验[9，10]，其余八项[2，11-17]为体外实验。所有研究均采用热电偶进行温度测量，但不同研究中探头的放置位置存在差异。激光头与目标组织的平均距离为0.5毫米，这一距离与钬铝石榴石（Ho：YAG）激光在水介质中的穿透深度最为匹配[18]。

莫利纳等人于2015年率先开展了激光热成像研究。9]本研究采用两种离体模型（临床模型与开放输尿管模型），测试了10瓦功率（1焦耳/10赫兹）365μm脉冲Ho：YAG激光治疗时的温度升高情况。实验数据显示，激光激活期间温度显著上升，而输尿管热值在生理盐水冲洗后有所下降。该结论于2016年被Buttice等人进一步证实。11]在实验台上，研究人员将200μm与272μm纤维置于装有生理盐水的加热槽中，分别在室温（24.5·℃）和体温（36.5·℃）下进行对比。当冲洗系统处于开启状态时，温度始终未达到极限值。Dau等人[8,16]研究人员分别于2022年开展体内研究，2021年进行体外研究，重点考察了冰水冲洗对结石周围液体温度的影响，以及激光加热液体时是否进行碎石手术的对比效果。研究发现，在碎石过程中（尤其是高功率操作时），采用-1℃冰水冲洗可显著降低温度升高幅度和热剂量，相较于19℃室温冲洗效果更佳。

此后多项研究在不同实验条件下得出了相似结论（详见表1和2），学界普遍认为：激光激活过程中必须进行灌溉，且建议采用更高流速和压力。多数研究显示，只有当功率设置达到40瓦及以上时，温度才会突破43·摄氏度的临界值，因此需通过调节激光功率确保温度始终低于该阈值。另有研究指出，高

表1 关于钬钇铝石榴石激光灌溉的研究。

研究	研究对象	激光光纤已使用（μm）	激光时间	功率设置（W或J/Hz）	灌注设置	记录温度（℃）	温度测量方式
Molina等人，2015[9]	绵羊	365	否	1/10	• 和 • 无	• 37.4±2.5[a] • 49.5±2.3[a]	• 使用红外线Fluke Ti55热成像仪测量外部表面温度
Buttice等人，2016[11]	带盐水加热槽的试验台模型	200或272	达到上限后停止	0.5/20、1/10、2/5、3/5或4/5	• 有或无	• 未使用灌注时超过阈值	• 模型内的气管内温度计
阿尔杜基等人，2017 [12]	玻璃试管	200	1 min	(0.5e1)/(10e80)	• 0、7-8、14-15 或38-40 mL/min	• 最大70.3±2.7 [a]，40 W，无灌注	• 热电偶5号mm，自试管底部起
阿尔杜基等人，2018 [7]	猪	242	1 min	0.5/80	• 0.1、15或40 mL/min	• 0.1 mL/min：84.8 • 15 mL/min：63.9 • 40 mL/min：43.6	• 通过开放暴露、穿刺及逆行方式在镜下观察杯状结构中的热电偶
Wollin等人，2018[2]	聚氯乙烯管	200	1 min	(0.2e1)/(6e50)	• 0、50或100 mL/min	• 0 mL/min：>100 • 50 mL/min：>43.4 • 100 mL/min：30.7	• 探针温度计放置在距离光纤尖端1 mm处
Hein等人，2018[13]	20 mL试管，置于水浴中	272或940 2分钟 0.5/33、1/18、1.5/30、2/2或		4.5/（4、12 或22.3）	• 0e100 mL/min •100 W时最大68 •测试管和水浴中的热电偶		
Winship等人，2019[17]	盐水袋和储液器	365	45 s	(0.2e1)/(6e80)	• 0、100或200 mmHg	• 阈值＞6在100 mmHg和以下上升	• 热电偶紧贴光纤放置●肾脏内设有三个热电偶，其中一个柔性热电偶位于光纤近端4毫米处
Hein等人，2020[10]	水浴中的猪肾脏	272、550或940	1min	5e100 W	• 0e100 mL/min	• 临界温度上升至30 W以上	
Ghanim等人，2020[14]	带聚氯乙烯管的水箱	365	70 s	（0.375,0.675，或1）/20	• 0、1、10或30 mL/min	• 高功率时最大值为70，且最接近温度计读数	• 聚氯乙烯管一端的温度计
梁等，2020 [15]	连接的F20橡胶管	200	3、5或10秒	（0.5、1、1.5、2或3）/（10或20）	• 10、15、20或30 mL/min	• 最大78，功率30瓦，流速10毫升/分钟	• 热电偶，距离管底5 mm

（续下页）

表1（续）

研究	研究对象	激光光纤所用（μm）	激光时间	功率设置（W或J/Hz）		灌注设置		（。C）	温度记录模式量度
				头部和肩部，在水浴中	玻璃试管	242	1 min	0.5/80	●供水点●阈值温度●3毫米金属丝热电偶
				2021年[16]				1。C和室温-	LED灯的布局 邻近输尿管-
									范围提示
								0时的19℃温度，	
								8、12、15或40 mL/min	
头部和肩部，2022 [8]	女性的约克夏猪	242	1 min	否				● 在●阈值温度下进行LED灌溉，热电偶固定于5毫米处	
								1。C至4。C，室温延迟至室内	从输尿管镜尖端
								温度为19℃	
								在0-40 mL/min时	

Max，最大值； NA，不是avai lab le；聚氯乙烯，polyviny l ch loride。
[a] Mean±标准差

能量（3.0J）和低频（10Hz）模式在相同功率下的热损伤略小于其对应设置[15]，需要进一步评估。

有研究团队[19]还探讨了输尿管套管（UAS）的使用及其对肾内温度的影响。研究发现，当功率设置为20瓦时，使用UAS可有效降低肾内温度，而未使用时则无此效果。但当功率超过40瓦时，这种保护作用会消失，此时只能通过提高冲洗速率来缓解[19]。该研究还对比了手动泵与重力泵的冲洗效果，发现手动泵（0.33次/秒）从未达到危险温度阈值，但在功率超过40瓦时，重力泵会导致温度升高。因此，这表明在冲洗过程中，手动泵可能比简单的重力冲洗方式更值得推荐。

3.2. 激光类型

除了钬：钇铝石榴石（Ho：YAG）激光器外，铥：钇铝石榴石（Th：YAG）激光器近年来在碎石术中也得到广泛应用。由于Th：YAG（2000纳米）激光波长比Ho：YAG（2140纳米）略短，其穿透深度也相应减少。据称Th：YAG激光器的功率效率是Ho：YAG的五倍[18]。但Th：YAG在碎石术中的主要优势在于其连续波特性，更适合组织消融；为此，研究人员推出了铥光纤激光器（TFL，波长1940纳米），这是一种采用半导体二极管替代闪光泵浦的铥离子激光器[20]。该TFL设备同时具备连续波和脉冲波两种工作模式。

表3概述了Ho：YAG与铥激光治疗的对比研究主要方面。2016年，Kallidonis等学者[21,22] 为评估Th：YAG激光与Ho：YAG激光的疗效差异，研究人员开展了两项独立研究。其中一项采用猪上尿路离体模型，另一项则使用体外实验模型。研究发现，两种激光在测量温度升高时效果相当，且在确保充分冲洗的前提下，20瓦Th：YAG激光可作为Ho：YAG激光的安全替代方案。塔拉特金团队[...]的研究也得出了类似结论。23] 以及彭等人[24] 在对比Ho：YAG激光与TFL时，发现两种激光的温度下降幅度完全一致，这表明两种激光的冲洗效果相当。

最近，Molina等人[25] 本研究通过体外猪肾脏实验，分别对比了超脉冲TFL与高功率Ho：YAG激光在碎石和碎石碎石过程中的温度升高情况。结果显示：激光激活时的腔内温度升高幅度在碎石过程中相当，而超脉冲TFL在碎石过程中温度升高更为显著，但两者均未达到基于暴露时间判定的热损伤阈值。因此，超脉冲TFL在碎石过程中可能存在温度升高的风险，但需进一步研究验证。

3.3. 操作员当班周期（ODC）和踩踏时间

ODC表示激光功率的“开/关”比。占空比越高，激光器“开”的时间就越长。

表2灌水研究的推论。

研究	推理
Molina等人，2015[9]	• 该研究是最早发现激光激活时温度升高的研究之一，同时发现输尿管热值随生理盐水冲洗而降低。
Buttice等人，2016[11]	• 在关闭灌溉系统时，必须避免温度快速上升；而灌溉过程中采用低温水则有助于延缓温度上升。
Aldoukhi等人，2017[12]	• 在1 J/40 Hz功率且无灌注的情况下测得的最高温度，泌尿科医生可利用针对该情况的对策
Aldoukhi等人，2018[7]	• 在无灌溉和中等灌溉条件下，热损伤阈值被达到，但在高灌溉条件下未达到，因此高功率激光在低灌溉率下对热损伤构成威胁
Wollin等人，2018[2]	• 尽管激光功率调高，但通过充分冲洗仍能维持体外输尿管系统内的相对稳定温度。
Hein等人，2018[13]	• 因此，进行钬：钇铝石榴石激光碎石术时，应始终将激光设备与持续、密切监测的灌注结合使用。
Winship等人，2019[17]	• 在常规灌注压力和激光参数下，使用柔性输尿管镜且功率≥10瓦时，仅需1秒即可达到高温；然而，当采用激光切割技术时—— 在不同灌溉压力下，温度迅速恢复至安全水平
Hein等人，2020[10]	• 开发了一个计算灌溉速率≥30 mL/min时近似ΔT的公式：ΔT=15 K×（功率[W]/灌溉[ML/min]）
Ghanim等人，2020[14]	• 所有三个参数（脉冲能量、灌注速率和距离）均对测量温度产生高度显著的影响；钬：钇铝石榴石激光器可能安全 当采用最佳激光功率进行充分灌注时可实现
梁等，2020[15]	• 在激光功率小于10 W、灌注量大于30 mL/min以及高能低频点火的情况下，可确保激光点火的安全温度。
Dau等人（2021）[16]和Dau等人，2022[8]	• 冷冻灌洗可减缓温度上升，降低平台温度，并降低高功率激光碎石术中的热剂量

与“关闭”状态相比，因此输出能量更大。100%ODC表示持续开启，即连续波切割[26]。在碎石术中，可计算为激光时间除以碎石时间。

2021年，阿尔杜基等人[27] 在体外实验中，研究人员采用20瓦平均功率的激光，以五种不同模式施加1200焦耳能量，持续60秒。结果显示，五种模式的平均ODC值均为32%，踏板激活平均时长为3.6秒。实验数据表明，延长踏板激活时间会显著提升峰值温度和热剂量。Louters等人[28] 2022年，研究人员开展了一项类似研究以评估脉冲能量密度（ODC）对热剂量的影响。研究发现，ODC值越高，最大温度和热剂量也越大，当光密度转换效率（ODC）≥70%时，温度会超过43 ℃的损伤阈值。与使用60%ODC值相比，采用50%ODC值时达到热损伤阈值所需时间增加十倍，最大允许能量则增加八倍。这些研究有力证明，通过合理调控激光ODC值，可有效预防激光引发的热损伤。

3.4. 体内研究

2019年，王等学者在中国开展了一项罕见的体内研究，对象是接受输尿管镜激光碎石术治疗结石的患者。29]本研究共纳入30例患者（男性16例，女性14例），平均年龄47.4岁（标准差13.7岁），结石平均直径14.2毫米（标准差8.1毫米），均接受输尿管肾镜碎石术。术中置入温度监测导丝并稍作延伸。输尿管镜的另一端连接着温度计，实时监测温度变化数据并传输至计算机。

在30组数据中，所有样本的最高温度均超过43 摄氏度（100%），其中19组（63.3%）的峰值温度甚至突破56 摄氏度。研究表明，随着钬激光功率的提升或结石受压程度加重，结石周围冲洗液的温度升高更为显著，常常超过组织安全耐受温度阈值。因此，温度可能是导致输尿管热损伤并引发术后狭窄的重要因素[24]。不过，王等学者的研究[29] 该研究存在局限性，仅考察了激光功率对热效应的影响，且不同病例的主刀医生存在差异，导致各病例的激光参数设置、激光持续时间及术中条件均不一致。

3.5. 其他因素，如音量和脉冲持续时间

2022年，Dau等人[30] 研究人员通过体外实验对比了两种激光光纤与结石的距离：3.5毫米（非消融模式）和0.5毫米（消融模式）。实验采用双热电偶实时监测液体温度，每秒记录一次数据，以确定激光能量转化为热能的比例及结石消融所占比例。研究发现，即便在能量高效消融条件下，仍有91%-96%的激光能量转化为热能[30]。后续研究还发现，激光激活发生的Pelvic Lyceal Volume（盆腔腔隙）是影响热效应的重要因素。

表3　与激光类型有关的研究。

研究	研究对象	激光研究	激光光纤直径或类型	激光时间功率设置(W)、能量(J)/频率	灌注设置	记录温度（℃）
卡利多尼斯等，2016 [21]	猪	Ho：YAG与Th：YAG连续波	数值孔径	• 10 W, 20 W, 30 W, or 40 W	• 和	• 33.5
卡利多尼斯等，2016年[22]	带旋塞的布雷特瓶（Ho：YAG与Th：YAG）和一个40 mL容器	脉冲模式及10分钟持续模式，连续不断的波	薄雾	功率分别为5 W、10 W、20 W、50 W或100 W	• 无	• 45.6e68.7
Taratkin等人，2020 [23]	体外模型	Ho：YAG vs.SP TFL 200 μm	1 min	• 40 W, 0.2 J	• 0 或 35 mL/min	• 冲洗后温度降低 - Ho:YAG: 2.6 - TFL: 1.9
Peng等人，2020年[24]	水箱中的试管TFL	连续波1分钟	●最多可设置为	30 W	• 0、15、25 或50 mL/min	• 0和15 mL/min：超过6.5 。C的温度上升超过阈值；25和50 mL/min：温度没有超过阈值
Molina等人，2021年[25]	猪肾脏	Ho：YAG vs.SP TFL 200 μm	每项耗时5秒：	●Ho：YAG抛光：0.3焦耳/15×70 Hz；SP TFL防尘：0.1 J/200 Hz；碎裂：0.8 J/8 Hz	• 和	• 正在设置片段 - Ho:YAG: 30 - SP TFL: 33.3 • 除尘设置期间 - Ho:YAG: 35.8 - SP TFL: 40.6

Ho：钇铝石榴石，钬：钇-铝石榴石；Th：钇铝石榴石（YAG）；TFL：铥　光纤激光器；SP：超脉冲；NA：不可用。

通过激光照射[31]。研究发现，各模型中的液体体积与温度升幅呈反比关系。因此，当液体体积较小时，激光照射产生的热剂量会更快达到损伤阈值。Louters等人[32] 研究人员通过测量激光激活过程中染色液体的移动距离，对塑料管内激光激活时的液体混合体积进行了研究。结果显示，输尿管模型内的液体混合总量较少，这会显著增加输尿管热损伤的风险。

Sugiwaka等人研究发现，激光激活的脉冲持续时间对热效应具有显著影响。33] 2022年的一项体外实验研究了气泡行为及其周围温度分布。研究发现，长脉冲气泡周围温度更高，可能导致周围组织热损伤加剧。目前上述因素尚未得到充分研究，尚无法确定其对热损伤的影响程度。不过，后续分析中应考虑这些因素，因为初步研究表明它们确实会产生影响。

这些因素的主要研究参数和设置列于表4。

4. 讨论

激光碎石技术已得到广泛应用，随着技术进步，针对该用途的新型激光设备和不同波长的激光器正不断研发。如前所述，光热效应是碎石的主要作用机制，但所用激光器和光纤的特性会在一定程度上影响这一效果。当功率较高时，需要加大冲洗流量以维持低温环境。但需谨慎操作，因为过度冲洗可能导致肾盂静脉逆流和肾盂渗漏，这是由于肾内压升高所致[34]。

高功率激光能量会导致收集系统和输尿管内的流体温度显著升高，进而引发周围组织的组织学损伤[2，7，12，17]。在进行高功率激光碎石术时，开发预测和控制热剂量的方法对保障患者安全至关重要。如前所述，温度持续时间同样扮演着关键角色，正如萨帕雷托和杜威提出的“时间-温度关系”理论所阐明的[4]。这种现象在“ODC”（即“开启/关闭”时间周期）中尤为明显。有研究表明，虽然温度可能在两次激光发射尝试之间降至阈值以下，但热剂量会持续累积，最终可能达到极高水平[27]。因此，必须深入研究可能导致热剂量增加的因素，以预防热损伤，特别是在体内实验环境中。本研究试图整合各种影响激光热效应的因素，以便未来的研究可以集中精力详细研究这些因素。

通过我们的综述可以推断，至少有八个因素会影响激光的热效应：

i. 灌注：在开放系统中采用高流量灌注、高压灌注及冷灌注，相较于温灌注更能有效控制激光碎石术中的温度升高。若条件允许，建议使用UAS设备以降低体温。

ii.激光类型：TFL可能具有稍高的损伤风险，但需进一步研究。

iii.功率设置：一般来说，功率越高，损坏风险越大。建议将功率控制在40瓦以内。

四、ODC与踏板时间：ODC值越高（开启时间长于关闭时间）且踏板时间越长，受伤风险越大。应提倡间歇性激光治疗，而非持续性治疗。

v. 脉冲持续时间：脉冲持续时间过长会升高气泡周围的温度，从而可能造成损伤。

六.液体体积：该指标包含激光激活发生的总骨盆肾盂体积及液体混合体积，液体体积越小，热剂量越高。

七.石头的距离：初步研究表明，能量传递在更远的距离上可能同样有效；然而，仍需更多研究才能得出确切结论。

viii.石头撞击：当存在结石阻塞时，冲洗液的温度会显著升高，通常会超过组织安全耐受的温度。

已有大量研究证实前三个因素的重要性，后续研究应重点探索其他较少被关注的因素，从而确保在激光激活过程中完全避免热损伤。

现有研究的主要缺陷在于，由于实验均采用体外环境，未能评估温度变化对盆腔输尿系统及肾脏功能的实际生理影响。此外，实验中涉及的安全风险也引发了伦理争议，限制了在更高温度下开展实验的可能性。但建议开展更多随机对照人体试验，通过对比40瓦以下激光功率、不同冲洗速率（优选冷却状态）以及间歇性激活（ODC）等参数，寻找安全阈值。值得注意的是，使用UAS和手动泵进行冲洗可有效缓解激光激活时的温度升高现象。建议进一步开展对比研究，验证手动泵与重力冲洗在使用导管鞘与不使用导管鞘两种情况下的效果差异。

本研究存在若干局限性：首先，所分析数据主要来自体外、体内及离体实验，而非临床患者数据；其次，研究采用叙述性研究设计，数据呈现异质性特征，包括不同激光参数设置、所用激光器及流速差异。俗话说“预防胜于治疗”，因此需要开展更多研究来预防激光热损伤。

表4 其他影响激光热损伤的因素。

研究	因素研究	研究对象	激光研究	激光光纤直径和激光设置	激光时间	电源设置（J/Hz）	灌注设置	记录的温度
Dau 等人，2022[30]	激光能量转化为热能的百分比	双层玻璃德瓦瓶	摩西200 D/F/L	200 μm、短脉冲和Moses距离模式	30 s	0.5/5	否	• 对照组血清中Rise的增加：1.03±0.01 °C[a] • 实验温度升高：0.99±0.06 °C[a]
Rezakahn Khajeh 等人，2022[31]	肾盂系统容积	水箱中不同体积的玻璃管	Ho：YAG激光	230 mm	1 min	0.5/80	0, 8, 15, 或40 mL/min	• 小号音量更快达到阈值
Tsaturyan 等人，2022[36]；Sugiwaka等人，2022[33]；Louters 等人，2022[32]	持续长时间激活 脉冲持续时间 液体混合体积	20 mL注射器，带穿刺鞘体外模型 否 塑料管	Ho：YAG激光 否 Ho：YAG激光	连续波 脉冲波 否	10 min 否 否	（0.3、1或1.5）/ 40 否 0.5/40	10, 20, 或30 mL/min NA 8e40 mL/min	• 最高83°C • 否 • 当灌溉率较低时，仅混合体积达到阈值1.26±0 10厘米^3[a]

Ho：钇铝石榴石；YAG：钇铝石榴石；Max：最大值；NA：不可用。[a]Mean±标准差

5. 未来展望

众所周知，钬掺杂钇铝石榴石（Ho：YAG）激光器的理论穿透深度仅为0.4毫米，但有推测认为实际穿透深度可能超过该数值[35]。这或许可以解释激光使用过程中观察到的热损伤现象。然而，这种损伤究竟是由接触损伤引起，还是源于激光发射产生的热效应，目前尚未得到深入研究。无论具体原因如何，由此引发的热损伤风险不容忽视，因此必须对可能影响该损伤的因素进行系统性研究。

过去十年间，大量研究致力于探究灌溉对热损伤的影响，但近期研究更多聚焦于脉冲持续时间、ODC值、激光类型及体内实验等其他因素。这些因素对激光相关损伤的影响仍需深入研究，以填补现有知识空白。此外，缺乏考虑患者年龄、肾积水程度及合并感染等个体差异的研究，可能导致观察到的温度升高现象被混淆。不过这可能是因为多数研究采用体外实验，未来开展体内实验时，这些因素需要谨慎考量。

6. 摘要

本综述探讨了激光在泌尿外科中的热效应，特别是在碎石术治疗结石和前列腺疾病中的应用。研究通过检索相关论文，涵盖热效应、激光、碎石术及泌尿外科领域，共纳入35篇论文，并将结果分为五类进行分析。研究发现，当激光功率超过40瓦且灌注充足（至少15-30 mL/min）时，温度通常会达到43 ℃以上。较短的激光作用时间和低于70%的ODC也会导致温度升高幅度减小。研究结论表明，影响激光热效应的因素包括灌注方式、激光类型、功率、ODC、脉冲持续时间、液体体积及结石嵌顿情况。研究的关键建议包括：在高灌注速率下使用冷却灌注、降低功率设置（<40瓦）以及缩短ODC以防止热损伤，尤其适用于结石嵌顿病例。

7. 结论

尽管相关研究可追溯至2015年，但激光在泌尿外科领域的热效应研究仍是新兴热点。深入理解激光可能引发的热损伤机制，对于避免操作不当导致的并发症至关重要。采用低温冲洗配合高灌注速率、功率设置低于40瓦且缩短ODC（激光脉冲持续时间）等措施，能有效预防热损伤，尤其在结石阻塞时更为关键。本文旨在梳理前人研究的重要经验，为临床医生提供参考，并鼓励学界深入探索该领域。

various gaps in knowledge which are present to further ensure safe and efficient laser usage.

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RESEARCH

Monitoring Intrarenal temperature changes during Ho: YAG laser lithotripsy in patients undergoing retrograde intrarenal surgery: a novel pilot study

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Abstract

Ho: YAG laser lithotripsy is widely used for urinary stone treatment, but concerns persist regarding its thermal effects on renal tissues. This study aimed to monitor intrarenal temperature changes during kidney stone treatment using retrograde intrarenal surgery with Ho: YAG laser. Fifteen patients were enrolled. Various laser power settings (0.8 J/10 Hz, 1.2 J/12 Hz) and irrigation modes (10 cc/min, 15 cc/min, 20 cc/min, gravity irrigation, and manual pump irrigation) were used. A sterile thermal probe was attached to a flexible ureterorenoscope and delivered into the calyceal system via the ureteral access sheath. Temperature changes were recorded with a T-type thermal probe with ±0.1 °C accuracy. Laser power significantly influenced mean temperature, with a 4.981 °C difference between 14 W and 8 W laser power ($p < 0.001$). The mean temperature was 2.075 °C higher with gravity irrigation and 2.828 °C lower with manual pump irrigation ($p = 0.038$ and $p = 0.005$, respectively). Body mass index, laser power, irrigation model, and operator duty cycle explained 49.5% of mean temperature variability (Adj. $R^2 = 0.495$). Laser power and operator duty cycle positively impacted mean temperature, while body mass index and specific irrigation models affected it negatively. Laser power and irrigation rate are critical for intrarenal temperature during Ho: YAG laser lithotripsy. Optimal settings and irrigation strategies are vital for minimizing thermal injury risk. This study underscores the need for ongoing research to understand and mitigate thermal effects during laser lithotripsy.

Keywords Retrograde intrarenal surgery · Ho:YAG laser · Intrarenal temperature · Laser lithotripsy

Introduction

Retrograde intrarenal surgery (RIRS) is a minimally invasive procedure used to treat urinary stones located within the kidney and upper urinary tract and has become increasingly popular as a first-line treatment for many patients [1]. Its success in achieving high stone clearance rates with minimal morbidity has contributed to its growing popularity and widespread adoption in clinical practice. Since its introduction in the 1990s, the Holmium: Yttrium-Aluminum-Garnet (Ho: YAG) laser has emerged as a standard tool in urological practice for intracorporeal treatment of urinary stone disease, displaying efficacy in fragmenting stones of various compositions [2].

With technological advancements, high-power laser systems have emerged as alternatives to traditional low-power laser systems in endourology. High-power Ho: YAG laser and Thulium Fiber Laser (TFL) systems are particularly noteworthy due to their high-frequency settings, which enable effective stone dusting and result in less retropulsion, making them ideal alternatives [3, 4]. The main concern regarding using these high-power laser systems is the increased risk of thermal tissue damage due to their ability to deliver higher energy transfer than traditional low-power

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laser settings [5]. TFLs offer advantages over other types of lasers due to their wavelength and mode of operation. However, it's important to note that thermal tissue damage can still occur with TFL procedures if the laser parameters are not properly controlled or if excessive energy is delivered to the tissue. Careful attention to settings and technique is necessary to ensure optimal outcomes and minimize adverse effects.

When laser energy is applied to the stone, it causes rapid vaporization of water molecules within the stone, leading to the generation of a shock wave that fragments the stone into smaller pieces. Additionally, laser energy absorbed by the calyceal fluid increases temperature locally.The main concern regarding the use of the Ho: YAG laser is its potential thermal effects on the surrounding urothelium and kidney tissue [6]. The extent of temperature increase depends on factors like laser power settings, laser application duration, irrigation rate, stone characteristics, and composition and volume of the calyceal fluid.

An increase in the intrarenal temperature (IRT) during laser lithotripsy of urinary system stones has been demonstrated in animal models and 3D modelling studies, with discussions on the effective parameters and outcomes of temperature increase [7–19]. However, the clinical significance of this temperature increase is still a topic of debate. While moderate temperature increases are generally well tolerated by the surrounding tissues, excessive heat could cause thermal injury to the renal parenchyma or surrounding structures. Studies have been designed with 43 °C as the threshold temperature value, based on research showing protein denaturation at 43 °C in the porcine urinary system [20]. Currently, few clinical studies have addressed the monitoring of IRT during laser lithotripsy for kidney stones [21–23].

The primary aim of this study was to monitor IRT changes during Ho: YAG laser treatment of kidney stones, while the secondary aim was to investigate the effects of different variables on the mean temperature.

Patients and methods

Patients undergoing flexible ureteroscopic Ho: YAG laser lithotripsy at our center from March to August 2023 were enrolled after ethics approval (Approval no. 2023/13). The inclusion criteria were as follows: (1) 18 years or older, (2) diagnosed with kidney stones, and (3) whose longest diameter of the stone was less than 2 cm. The exclusion criteria were (1) pediatric patients, (2) patients with congenital kidney/ureter anomalies, (3) patients with ureteral stricture or concurrent ureteral stone, and (4) patients who were pregnant or lactating. Informed consent was obtained from eligible patients before inclusion in the study.

Surgery was performed 7–10 days after inserting a 6/26 DJ stent (Boston Scientific, USA) to improve ureteral access sheath insertion success and reduce ureteral damage risk. All patients had a sterile urine culture five days before surgery. A single experienced surgeon (Y.B.) performed all operations.

We used a thermometer (model 88,598 4ch K SD Logger) capable of recording data at 1-second intervals for the temperature measurement system. The measurement range of the thermometer was − 200 °C to + 350 °C, with a measurement accuracy of ± 0.1 °C. It employs a T-type thermal probe with a diameter of 0.3 mm. To measure the IRT during the operation, the thermal probe was attached to a disposable flexible ureterorenoscope (WiScope®, Germany) with its tip 10 mm from the distal end (Fig. 1) and inserted

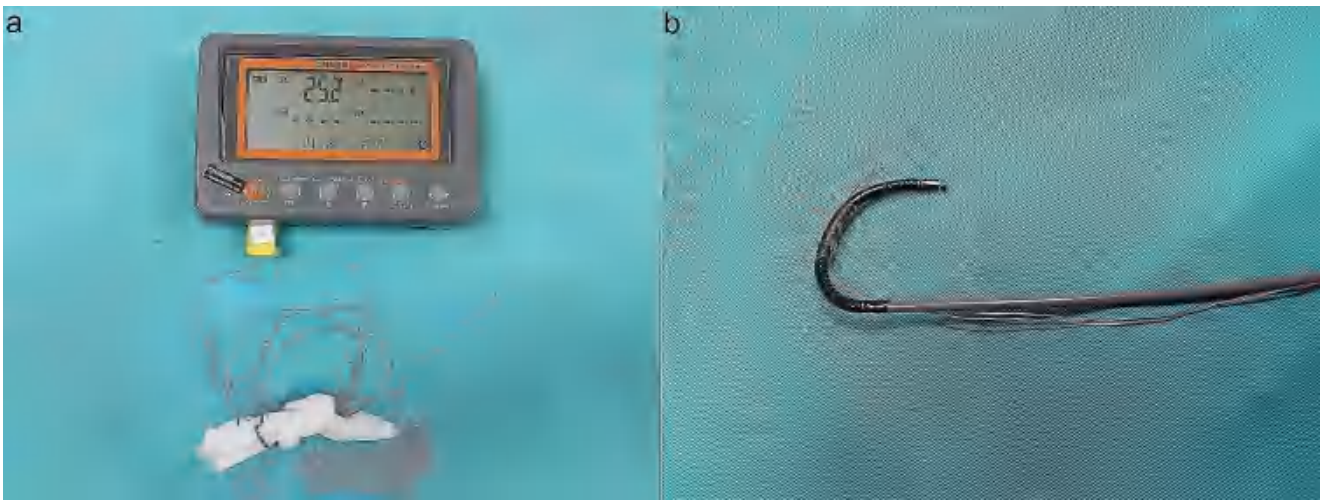


Fig. 1 Temperature measurement system **a** T-type wire temperature sensor and thermometer. **b** The temperature sensor secured to flexible ureterorenoscope

into the collecting system with a flexible ureterorenoscope through a 13/15 single lumen ureteral access sheath (Navigator™ HD, Boston Scientific, USA).

We utilized a holmium laser system (Sphinx Jr., Promed, Germany) equipped with a 272 µm laser fibre (FlexiFib, LISA Laser Products, Germany) to carry out lithotripsy. Each patient underwent lithotripsy using saline solution at room temperature (25.41 ± 2.82 °C). The experimental protocol included mechanical pump irrigation, specifically using a serum infusion pump, at flow rates of 10 ml/min, 15 ml/min, and 20 ml/min. The laser employed for this purpose was 8 W (0.8 J/10 Hz). In addition to the mechanical pump irrigation models, gravity (60 cm above the operating table) and manual pump (pumping as needed to enhance visualization quality) irrigation models were employed for the 14 W (1.2 J/12 Hz) laser setting.

When the flexible ureterorenoscope reached the calyceal system, temperature measurements began. The measurements ended when no clinically significant residual fragments (< 3 mm) were confirmed by endoscopic or fluoroscopic examination. For each study model, many characteristics were recorded, including lasing time (the duration of the active laser pedal on time), lithotripsy time (the time interval from the beginning of laser activation to the conclusion of the final laser activation, considering the durations of pedal on and off), operator duty cycle (ODC) (lasing time/lithotripsy time), total energy, and IRT.

Table 1 Perioperative and clinical characteristics of the patients

Characteristics	Overall ($n = 15$)
Gender, n (%)	
Male	8 (53)
Female	7 (47)
Age (years)	51,27 ± 15,50
Body mass index (kg/m^2)	26,43 ± 4,47
Stone side, n (%)	
Right	7 (47)
Left	8 (53)
Stone number, n (%)	
Single	13 (86)
Multiple	2 (14)
Stone location, n (%)	
Renal pelvis	9 (60)
Upper calyx	2 (13)
Middle calyx	2 (13)
Multiple calyx	2 (13)
Stone size (mm^2)	139,49 ± 15,07
Stone CT value (HU)	1240 (520–1520)
Opacity, n (%)	
Opaque	12 (80)
Non-opaque	3 (20)
Preoperative creatinine (mg/dL)	0,82 ± 0,13
Fluoroscopy time (sec)	18 (12–48)
Lasing time (min)	15,26 ± 7,04
Lithotripsy time (min)	20,44 ± 8,91
Total energy (J)	17188 ± 11430
Postoperative creatinine (mg/dL)	0,80 ± 0,12
Complication rate (%)	None
Postoperative stay (days)	1

CT computed tomography, *HU* hounsfield unit

Statistical analysis

The data were analysed using the Statistics Package for Social Sciences version 25 (IBM SPSS®, Armonk, NY). The Shapiro–Wilk test was used to verify normal distribution compliance. Normally distributed data are presented as the mean ± standard deviation, while nonnormally distributed data are presented as the median (minimum-maximum). For normally distributed data, repeated measures analysis of variance was used to compare the effects of different irrigation modes across different laser working modes, with multiple comparisons performed using the Bonferroni correction. For nonnormally distributed data, the Friedman test was used to compare the effects of different irrigation modes across different laser working modes, with multiple comparisons conducted using the Dunn test. Generalized linear mixed models were used to assess the effects of the independent variables on the mean temperature, with multiple comparisons performed using the Bonferroni correction. Linear regression analysis was used to identify predictors of mean temperature. $p < 0.05$ was considered to indicate statistical significance.

Results

Overall, 15 patients were included in our study. Table 1 shows the clinical and perioperative characteristics of the patients. The mean age was 51,27 ± 15,50 years, and the mean body mass index (BMI) was 26,43 ± 4,47 kg/m^2. The mean stone size was 139.49 ± 15.07 mm^2, and the stone location was the renal pelvis in 60% of patients.

For demonstration, the intrarenal temperature–time graph of "patient 2" is shown in Fig. 2. The IRT sharply decreased with irrigation before laser lithotripsy began, increased with decreasing irrigation rate at 8 W, and decreased with increasing irrigation rate at 14 W. There was a sharp decrease in IRT when transitioning from the gravity irrigation model to the manual pump irrigation model.

We analyzed temperature records from cases with around forty seconds of continuous laser activation, investigating different laser powers and irrigation settings. As the laser power increased and the irrigation rate decreased, the calyceal fluid heated more rapidly and eventually reached a plateau temperature. It was also noted that the time to reach the

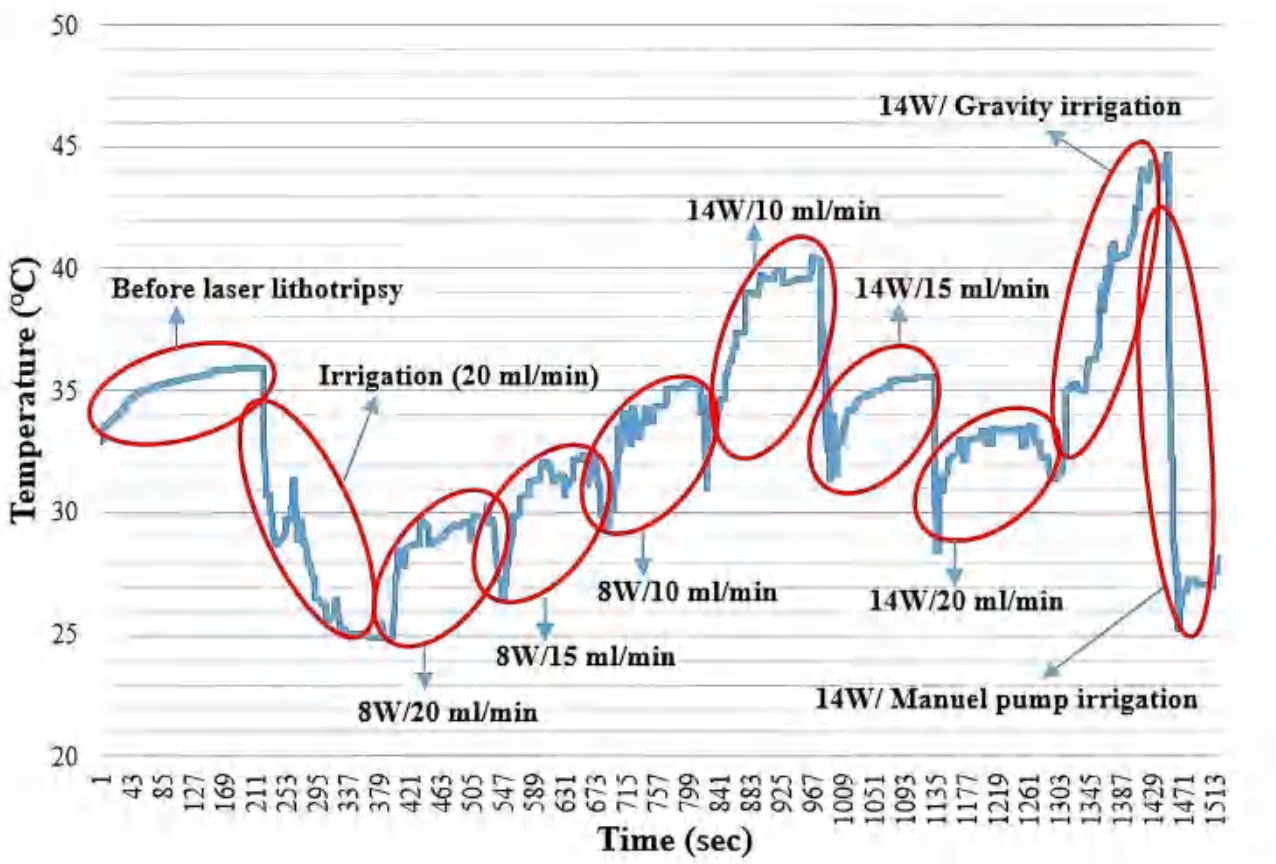


Fig. 2 The temperature-time graph of "patient 2"

plateau temperature was prolonged with a similar relationship between the laser power and irrigation model (Fig. 3).

The overall surgical parameters are summarized in Table 2. In the 8 W working model, the lowest minimum, mean, and maximum IRT were obtained in the 20 ml/min irrigation model (27.5 ± 2.8 °C, 30.2 ± 2.2 °C, and 31.7 ± 2.1 °C; $p = 0.017$, $p = 0.002$, and $p = 0.001$, respectively). In the 14 W working model, while the minimum and mean IRT values were lowest in the manual pump irrigation model (median 26.76 °C and 31.80 °C, respectively; $p < 0.001$), the lowest maximum IRT was obtained in the 20 ml/min irrigation model (35.21 ± 2.30 °C; $p = 0.005$). The total energy values in the 8 W and 14 W working models were comparable.

The effects of demographic and operative variables on the mean IRT are shown in Table 3. In the univariate analysis examining the purification effects, age, sex, stone size, stone computed tomography (CT) value, laser power, irrigation model, and ODC were the parameters that significantly affected the mean IRT. In the multiple analysis evaluating the interactions of parameters, unlike the results of the univariate analysis, sex was not found to have a significant effect on the mean temperature ($p = 0.616$). In contrast, total energy had a significant effect ($p = 0.012$). According to the standardized β coefficients, the laser power had the most significant effect on the mean IRT, with the mean IRT being 4.981 °C greater for the 14 W laser power than for the 8 W laser power ($p < 0.001$). Compared to the 20 ml/min irrigation model, the mean IRT value was 2.075 °C higher in the gravity irrigation model and 2.828 °C lower in the manual pump irrigation model ($p = 0.038$ and $p = 0.005$, respectively).

A multiple linear regression model was constructed to predict the mean IRT based on BMI, laser power, the irrigation model, and ODC (Table 4). The calculated regression model was statistically significant ($p < 0.001$). While laser power and ODC had positive effects on the mean IRT, increases in BMI and irrigation were expected to decrease the mean IRT. The current variables could explain approximately 49.5% of the mean IRT (Adj. $R^2 = 0.495$).

In the 8 W laser power treatment group, none of the irrigation treatments reached the threshold of 43 °C. Additionally, in the 14 W laser power group, one patient reached an

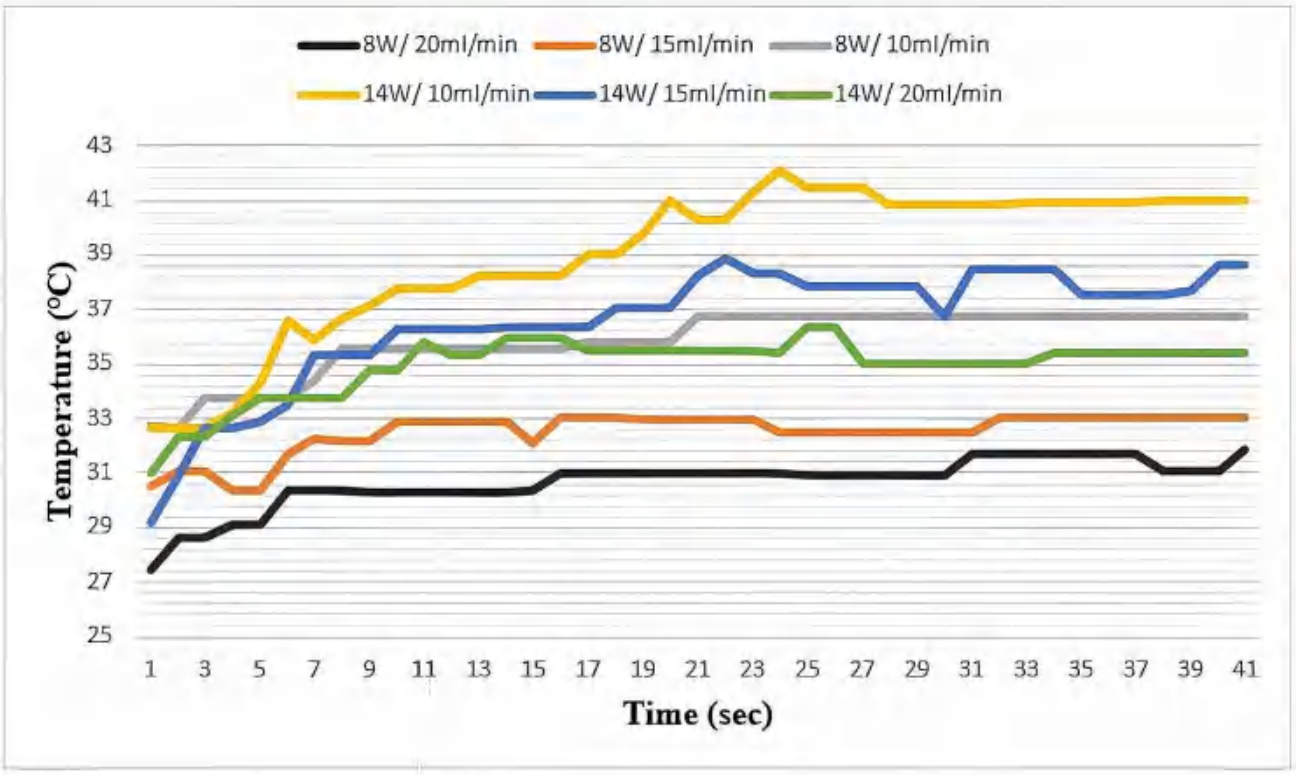


Fig. 3 Temperature-time curve at various power and irrigation settings

Table 2 Baseline characteristics and comparison of surgical parameters

	8 W						
	10 ml/min	15 ml/min	20 ml/min	Manuel pump	Gravity	Test statistic	*p*
Total Energy (J)	1069,7 ± 628,2	999,4 ± 377,1	883,8 ± 325,4	NA	NA	0,833	0,659**
Operator Duty Cycle	0,90(0,61 – 0,94)^{ab}	0,86(0,47 – 0,93)^{a}	0,91(0,52 – 1)^{b}	NA	NA	9,176	**0,01***
Temperature (°C)				NA	NA		
Minimum	30,7 ± 2^{a}	29 ± 2,7^{ab}	27,5 ± 2,8^{b}	NA	NA	8,174	**0,017****
Mean	33,7 ± 2,3^{a}	31,4 ± 2,3^{b}	30,2 ± 2,2^{b}	NA	NA	12,516	**0,002****
Maximum	35,1 ± 2,6^{a}	32,8 ± 1,7^{b}	31,7 ± 2,1^{b}	NA	NA	13,367	**0,001****
	14 W						
	10 ml/min	**15 ml/min**	**20 ml/min**	**Manuel pump**	**Gravity**	**Test statistic**	**p**
Total Energy (J)	2730,67 ± 2590,70	2076,22 ± 1702,33	1737,44 ± 1205,76	3470,33 ± 6801,19	2704,33 ± 4703,37	5,689	0,224**
Operator Duty Cycle	0,80 ± 0,14^{a}	0,72 ± 0,21^{ab}	0,69 ± 0,23^{ab}	0,60 ± 0,11^{b}	0,58 ± 0,25^{ab}	10,96	**0,027****
Temperature (°C)							
Minimum	32,65 (30,98 – 35,73)^{c}	31,38 (29,21–36,31)^{bc}	29,92 (27,04–33,93)^{b}	26,76 (25,28–29,21)^{a}	31,38 (28,46 – 33,34)^{bc}	22,922	**< 0,001***
Mean	37,67 (32,22–39,90)^{c}	36,27 (30,80 – 40,42)^{c}	34,06 (28,66 – 36,57)^{b}	31,80 (28,25–33,24)^{a}	36,51 (31,67 – 38,93)^{bc}	24,884	**< 0,001***
Maximum	39,53 ± 3,68^{b}	36,89 ± 3,02^{ab}	35,21 ± 2,30^{a}	38,62 ± 3,92^{ab}	40,01 ± 5,83^{ab}	15,039	**0,005****

*Friedman test, **Repeated measures analysis, $^{a-c}$There is no significant difference between irrigation models with the same letter

Table 3 Effects of independent variables on mean temperature

	Univariate					Multivariate				
	β1 (%95 CI)	S.E.M	β2	t	*p**	β1 (%95 CI)	S.E.M	β2	t	*p**
(Constant)						24,644 (20,843 – 28,444)	1,899	0,000	12,975	**< 0,001**
Age	-0,074 (-0,127 - -0,022)	0,026	-0,275	-2,819	**0,006**	-0,105 (-0,137 - -0,072)	0,016	-0,390	-6,475	**< 0,001**
Gender (Ref: male)	-2,087 (-3,345 - -0,829)	0,631	-0,318	-3,308	**0,001**	0,201 (-0,597–1)	0,399	0,031	0,504	0,616
BMI	-0,113 (-0,255–0,029)	0,071	-0,163	-1,593	0,116	0,064 (-0,018 – 0,145)	0,041	0,093	1,569	0,122
Stone size	0,024 (0,008 – 0,04)	0,008	0,292	2,997	**0,004**	0,019 (0,009 – 0,029)	0,005	0,231	3,769	**< 0,001**
Stone CT value	0,003 (0,001 – 0,005)	0,001	0,272	3,095	**0,003**	0,003 (0,001 – 0,005)	0,001	0,272	3,363	**0,001**
Laser power (Ref: 8 W)	3,515 (2,208–4,822)	0,655	0,522	5,364	**< 0,001**	4,981 (4,072 – 5,89)	0,454	0,740	10,965	**< 0,001**
Irrigation model (Ref: 20 ml/min)										
15 ml/min	1,763 (-0,273–3,798)	1,020	0,234	1,728	0,089	1,169 (0,257–2,082)	0,456	0,155	2,565	**0,013**
10 ml/min	2,719 (0,952–4,486)	0,885	0,361	3,071	**0,003**	-1,128 (-2,326–0,07)	0,599	-0,150	-1,885	0,064
Gravity	5,181 (2,894–7,468)	1,146	0,526	4,522	**< 0,001**	2,075 (-0,027 – 4,176)	1,050	0,211	1,976	**0,038**
Manuel pump	0,177 (-1,64 – 1,993)	0,910	0,018	0,194	0,847	-2,828 (-4,745 - -0,911)	0,958	-0,287	-2,952	**0,005**
Total energy	0 (-0,0002 – 0,0003)	0,000	0,030	0,280	0,780	-0,0002 (-0,0004 - -0,0001)	0,000	-0,232	-2,577	**0,012**
Operator Duty Cycle	6,568 (3,045 – 10,092)	1,767	0,390	3,718	**< 0,001**	3,997 (0,545–7,449)	1,725	0,238	2,317	**0,024**

BMI body mass index, *CT* computed tomography, *S.E.M* standart error of mean, *Generalized linear mixed models

Table 4 Analysis results on predictors of mean temperature

	β^1 (%95 CI)	β^2	t	*p**
(Constant)	29,227 (23,977–34,478)		11,111	**< 0,001**
BMI	-0,126 (-0,245 - -0,007)	-0,182	-2,118	**0,038**
Laser power	4,740 (3,462–6,018)	0,704	7,402	**< 0,001**
Irrigation model	-1,173 (-1,627 - -0,719)	-0,474	-5,160	**< 0,001**
Operator duty cycle	4,231 (1,091 – 7,371)	0,251	2,690	**0,009**

BMI *body mass index,* *Linear regression model (Stepwise method)

$p < 0{,}001$; $R^2 = 0{,}523$; Adj.$R^2 = 0{,}495$; Durbin-Watson = 1,611

IRT of 43 °C in the 10 ml/min irrigation model, and one patient reached this IRT in the gravity irrigation model.

Discussion

Our study revealed that in patients who underwent RIRS with a Ho: YAG laser, the laser power, irrigation model and ODC affect and predict the IRT. To our knowledge, this is the first clinical study to investigate the effects of variables other than laser power and irrigation models in RIRS patients treated with the Ho: YAG laser.

According to the essential laws of thermodynamics, in a constant environment, the amount of heat energy per unit time should remain constant, thus resulting in a constant temperature change ($Q = mc\Delta T$). Our study revealed that a continuous active laser could be used for forty seconds without interruption, i.e., when a constant amount of heat energy could be produced in a unit, the IRT increased for a period and then reached a plateau (Fig. 3). In this model, where the environment is not constant, the attainment of a plateau can be explained by the inflow of unheated irrigation fluid into the caliceal system and the outflow of heated irrigation fluid from the caliceal system. This phenomenon is consistent with previous studies reported in the literature [8, 19, 23, 24]. The fact that the IRT reaches a plateau at constant irrigation rates suggests that the mean IRT is a more important parameter than the peak IRT in clinical studies.

The laser settings are personalized. The pulse energy can then be gradually increased until an effective dusting or fragmentation effect is achieved. In our study, the laser power was the most effective parameter for determining the mean IRT. In the regression analysis evaluating predictors, it is predicted that there will be a 4.74 °C increase in the mean IRT with a one-unit increase in laser power (Table 4). In an experimental study by Aldoukhi et al., the highest

temperature (70.3 °C) was reached with 40 W laser power and no irrigation mode among laser powers ranging from 5 W to 40 W [8]. In the pig model study of Peteinaris et al., which considered 54 °C as the thermal threshold, the threshold value was reached with laser powers above 40 W in the gravity irrigation model. In contrast, a safe thermal range was maintained with 20 W and 40 W laser powers [25]. In the pig model study conducted by Noureldin et al., the IRT remained within safe ranges at 20 W laser power when an access sheath was used, and in the gravity irrigation model, threshold temperature values that could cause thermal damage in the urinary system were reached with higher laser powers [17].

The irrigation model has emerged as an influential parameter of IRT. According to a survey study conducted among urologists interested in endourology in 2019, 46% preferred manual pump irrigation, and 27% preferred gravity irrigation as an irrigation method [26]. In this study, the highest mean IRT values were obtained in the gravity irrigation model compared to those in the other irrigation models, while the lowest mean IRT was obtained in the manual irrigation model (Table 3). In the study by Peteinaris et al., the thermal threshold was reached in the gravity irrigation model at 40 W and 60 W laser powers with 30 s of laser activation, while the safe thermal range was maintained in the manual pump irrigation model under similar laser settings [27]. In another in vivo porcine model study, hazardous IRT values were reached in the gravity irrigation model at laser powers exceeding 40 W, regardless of the use of a ureteral access sheath. However, the manual pump irrigation model only reached the thermal threshold with 100 W laser power and without using a ureteral access sheath [25].

In daily practice, suspending irrigation flow can prevent stone retropulsion during lithotripsy. However, careful attention must be paid during this manoeuvre. In one patient in our study, the IRT increased by 9 °C in a very short period of 5 s during lithotripsy when irrigation was inadvertently closed, which is not known. An in vitro study by Buttice et al. demonstrated that irrigation limits temperature increase when any laser setting is used, and rapid increases occur when irrigation is closed [10]. Another experimental ureteroscopy model by Wolin et al. reached the threshold thermal value in all laser power models ranging from 3.6 W to 20 W without continuous irrigation [28]. Hein et al. reported that laser application without irrigation led to a rapid temperature increase of up to Δ28 K, reaching 68 °C at 100 W [24]. Considering all these findings, continuous irrigation flow is essential for maintaining a safe thermal range.

Louters et al.'s in vitro study investigating the effect of ODC on temperature showed that as ODC increased, higher temperatures were reached in shorter periods [29]. In an in vitro study by Aldoukhi et al., the thermal injury threshold was reached in as little as 9 s with 50% ODC at 40 W laser power [7]. An in vitro experiment suggested utilizing ODC as a method to restrict the increase in temperature in small cavities, such as the ureter or minor calyxes [30]. Pauchard et al.'s review on intrarenal temperature and pressure during RIRS suggested halting laser activation to mitigate the risk of high temperatures [31]. In our study, consistent with the literature, when laser activation was stopped during transitions between each working model, we observed a dramatic decrease in the IRT (Fig. 2). Additionally, according to both univariate and multivariate analyses, ODC had a positive effect on the mean IRT (Table 3).

In our study, the thermal threshold was not reached in any irrigation model at 8 W laser power. In contrast, at 14 W laser power, an IRT of 43 °C was reached in the 10 ml/min and gravity irrigation models. An in vitro study by Maxwell et al. modelled the human urinary system using laser powers ranging from 5 to 40 W and irrigation modes, including no irrigation, 15 ml/min, and 40 ml/min. Laser activation was performed for 60 s. Consistent with our study, they found that the thermal threshold was not reached with a laser power of 20 W or less and irrigation rates of 15 ml/min above [14]. Similarly, Teng et al. reported that in their clinical study, the IRT remained within a safe thermal range with low laser power (< 20 W) and an irrigation rate of at least 15 ml/min [23]. In a clinical study by Æsøy et al. utilizing a Thulium fibre laser, similar findings were reported where temperatures of 43 °C were not reached with laser powers of 5 W and 10 W and an irrigation rate of 15 ml/min [22]. Currently, there is no defined optimal laser setting or irrigation model for RIRS. However, low laser power (< 20 W) and moderate irrigation flow (15–30 ml/min) appear to be feasible options for managing the IRT [31].

We are aware that laser frequency is an important parameter affecting IRT. In an in-vitro study by Aldoukhi et al., it was found that at 20 Hz, only 52% of emitted pulses reached the stone, while at 50 Hz and 80 Hz, only 23% and 4% reached the stone, respectively [32]. Thus, with increased frequency, more energy will be absorbed in the liquid medium, leading to higher IRT. In their experimental ureteroscopic lithotripsy model, Liang et al. reported that higher frequencies at the same laser powers resulted in more heat production [33]. In an in-vitro study comparing low-frequency high single-pulse energy with high-frequency, low single-pulse energy models, Hein et al. associated higher frequency settings with 3.5% and 8.8% higher temperatures at low and high laser powers, respectively [24]. In a porcine model study by Gallegos et al., the IRT value was measured at the beginning of the study and one minute after laser use, and the difference between these two measurements was defined as delta temperature (DT). Energy, frequency, use of ureteral access sheath, and liquid height were

found to be parameters significantly affecting DT, with a predicted increase of 2.1 °C in DT at 15 Hz frequency compared to 5 Hz [34]. Maxwell et al. conducted a study with laser powers ranging from 5 to 40 W and different irrigation models, finding that peak temperature values were nearly the same at the same laser powers regardless of frequency and pulse setting [14].

Does IRT truly matter in clinical practice? Aldoukhi et al. performed intrarenal laser activation with a Ho: YAG laser at 40 W power for 60 s, without irrigation, and with low- and high-flow-rate irrigation in four in vivo pig models and achieved maximum IRTs of 84.8 °C, 63.9 °C and 43.6 °C, respectively. On histopathological examination, gross macroscopic changes were observed in the no-irrigation model. At the same time, it was reported that there were minimal changes in low-flow irrigation and no signs of thermal damage in high-flow irrigation [9]. Molina et al. created a ureteral stone model in ex vivo porcine models using manual irrigation, a Ho: YAG laser (6.4 W and 21 W), and a spTFL (6.4 W and 20 W). Both systems remained below the threshold temperature (43 °C). According to histopathological examination, there was no thermal damage to the ureters after lithotripsy [15]. Peteinaris et al. created a kidney stone model in two in vivo porcine models and performed laser lithotripsy using an 8 W Thulium fibre laser for 60 min. The IRT was between 44 °C and 46 °C in both models. The kidneys were histopathologically examined on the 7th and 14th days. On the 7th day, severe histopathological findings such as hemorrhagic areas, separated urothelium, fibrin accumulation, and inflammation in the lamina propria were observed, while on the 14th day, histopathology was reported as "minimal changes" [35]. Therefore, it is not easy to provide a definitive answer when evaluating these findings in light of the study findings. However, given the lack of sufficient evidence regarding the long-term effects of high temperatures, a lower IRT appears safer.

The thermal cytotoxic effect occurring in living tissues can be explained by the temperature and duration of exposure. Sapareto and Dewey developed an equation known as the cumulative equivalent minutes at 43 °C (CEM43) to assess the thermal dose, which is calculated based on an exposure time at a reference temperature of 43 °C [36]. Animal studies have shown that protein denaturation occurs in the urinary system at 43 °C [20], and a CEM43 duration exceeding 70 min leads to significant kidney damage [37]. Since there is no defined safe thermal dose for the human urinary system, we adopted 43 °C as the thermal threshold for our study based on the current literature.

During RIRS, delivering the probe to the calyceal system either retrogradely or percutaneously is necessary to enable IRT monitoring. Despite its fine calibration, which may influence irrigation flow and misrepresent actual IRT readings, the retrograde approach appears less morbid than percutaneous access. The retrograde method, contingent upon using a ureteral access sheath, is reliable. However, there is a need for more clinical studies regarding routine IRT monitoring during RIRS. Currently, flexible ureterorenoscopes capable of intrarenal pressure monitoring are used in clinical practice during RIRS [38], yet an instrument that facilitates IRT monitoring has yet to be developed. Future research in this area will inevitably involve the use of thermal probes.

The present study has several limitations. First, our study has a small sample size, which may introduce bias when estimating population means. Second, since each patient's calyceal anatomy and volume may vary, different IRT results may have been obtained with similar variables. Third, since it is not always possible to keep the laser fibre at the same distance from the stone and from the thermal probe, different IRT results may have been obtained with similar variables. Fourth, a multipoint thermal probe could not be utilized, and the temperature of each major calyx could not be measured; thus, the recorded temperature might not have accurately reflected the mean IRT. Fifth, as the recording device monitor could not provide real-time temperature information, laser activation was continued in cases where critical temperatures were reached. Sixth, due to the lack of chemical stone analysis, the possible effect on the temperature profile could not be investigated.

Conclusion

This preliminary study investigated the impact of Ho: YAG laser lithotripsy on intrarenal calyceal fluid temperature, focusing on the influence of laser power and irrigation rate. The results revealed that the Ho: YAG laser power and irrigation rate had opposite effects on the average temperature, with the laser power being the most influential parameter for temperature elevation. Continuous irrigation at a minimum rate of 15 ml/min helps maintain temperatures within the safe range, particularly at moderate laser powers. Furthermore, this study revealed ODC as a significant parameter affecting IRT, suggesting the importance of the periodic cessation of laser activation. These findings underscore the necessity for further clinical studies with larger populations to elucidate additional factors impacting IRT dynamics during laser lithotripsy.

Author contributions E.K.: Conceptualization, data curation, investigation, methodology, writing-orginal draft. Y.B.: Conceptualization, data curation, methodology, writing-review and editing. M.G.: Data curation, formal analysis. F.S.: Resources, data curation, formal analysis. O.K. and E.O.: Data curation, writing-review and editing. Y.K.Y.: Supervision, writing-review and editing. S.S.: Supervision, writing-review and editing. All the authors have read and approved the final

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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研究

逆行肾内手术患者Ho：YAG激光碎石术中肾内温度变化的监测：一项新的试点研究

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摘要

Ho：YAG激光碎石术在治疗尿路结石中应用广泛，但其对肾组织的热效应仍存在争议。本研究旨在通过逆行肾内手术结合Ho：YAG激光技术，监测肾结石治疗过程中肾内温度变化。共纳入15例患者，采用不同激光功率（0.8J/10Hz、1.2J/12Hz）和冲洗模式（10cc/min、15cc/min、20cc/min、重力冲洗及手动泵冲洗）。将无菌热探头连接于柔性输尿管肾镜，经输尿管套管引入盏状系统。使用T型热探头记录温度变化，精度达±0.1°C。激光功率对平均温度有显著影响，14W与8W功率组间温差达4.981°C（p<0.001）。重力冲洗组平均温度升高2.075°C，手动泵冲洗组则降低2.828°C（p=0.038和p=0.005）。体重指数、激光功率、冲洗模式及操作者工作周期共同解释了平均温度变异性的49.5%（调整后R^2=0.495）。激光功率和操作人员工作周期对平均体温有积极影响，而体重指数和特定灌注模式则会产生负面影响。在Ho：YAG激光碎石术中，激光功率和灌注速率对肾内温度起着关键作用。采用最佳参数设置和灌注策略，是降低热损伤风险的关键。本研究强调，需要持续开展研究以深入理解并减轻激光碎石术中的热效应。

关键词肾内逆行手术·Ho：YAG激光·肾内温度·激光碎石术

介绍

逆行肾内手术（RIRS）是一种微创治疗手段，专门用于处理肾脏及上尿路结石，现已成为众多患者的首选治疗方案[1]。该手术凭借其高结石清除率等显著优势，正逐渐成为临床治疗的热门选择。极低的发病率使其在临床应用中越来越受欢迎并得到广泛采用。自上世纪90年代问世以来，钬：钇铝石榴石（Ho：YAG）激光器已成为泌尿外科治疗尿路结石的标准工具，对各种成分的结石都具有碎石效果[2]。

随着技术进步，高功率激光系统已逐渐取代传统低功率激光系统，成为内镜泌尿外科领域的新型选择。其中，高功率钬掺杂钇铝石榴石（Ho：YAG）激光和铥光纤激光（TFL）系统尤为突出，其高频设置不仅能有效碎石，还能减少反冲现象，堪称理想替代方案[3，4]。但使用这类高功率激光系统时需注意，由于其能量传输能力远超传统低功率系统，可能导致组织热损伤风险显著增加。

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激光参数设置[5]。相比其他类型的激光器，TFLs（准分子激光）凭借其独特的波长和工作模式具有显著优势。但需特别注意的是，若TFL（准分子激光）治疗过程中激光参数控制不当，或向组织输送的能量过量，仍可能引发热损伤。因此必须严格把控参数设置与操作技巧，才能确保治疗效果最大化并最大限度降低副作用风险。

当激光能量作用于结石时，会引发结石内部水分子的快速汽化，从而产生冲击波将结石击碎成更小碎片。此外，被肾盏液吸收的激光能量还会导致局部温度升高。关于钬：钇铝石榴石（Ho：YAG）激光的主要争议在于其可能对周围尿路上皮和肾脏组织产生的热效应[6]。温度升高的程度取决于多种因素，包括激光功率设置、照射时长、冲洗速率、结石特性，以及肾盏液的成分和体积。

动物模型和三维建模研究表明，在进行尿路结石激光碎石术时，肾内温度（IRT）会升高，相关研究已探讨了温度升高的有效参数和治疗效果[7–19]。然而，这种温度升高的临床意义仍存在争议。虽然适度的温度升高通常能被周围组织良好耐受，但过量热量可能导致肾实质或周围结构的热损伤。基于猪尿路系统在43℃发生蛋白质变性的研究[20]，现有研究将43℃设为温度阈值。目前针对肾结石激光碎石术中肾内温度监测的临床研究仍较为有限[21–23]。

本研究的主要目的是监测Ho：YAG激光治疗肾结石过程中红外热疗（IRT）的变化，次要目的是探究不同变量对平均温度的影响。

患者和方法

2023年3月至8月期间，本中心在伦理委员会批准（批准号：2023/13）后，对接受经尿道输尿管镜钬：钇铝石榴石激光碎石术的患者进行入组研究。纳入标准为：(1)年满18周岁，(2)确诊为肾结石，(3)结石最长直径小于2厘米。排除标准包括：(1)儿童患者，(2)先天性肾/输尿管畸形患者，(3)存在输尿管狭窄或合并输尿管结石患者，(4)妊娠期或哺乳期患者。所有符合条件的患者在入组前均签署了知情同意书。

为提高输尿管套管置入成功率并降低输尿管损伤风险，医生在置入6/26 DJ支架（美国波士顿科学公司）后7-10天实施手术。所有患者术前5天均接受无菌尿培养。所有手术均由经验丰富的外科医生Y.B.单独完成。

我们采用了一款88,598型4通道KSD记录仪作为测温系统，该设备可实现1秒间隔的数据采集。其测量范围覆盖-200°C至+350°C，测量精度达±0.1°C，配备直径0.3毫米的T型热电偶探头。在手术过程中进行内镜热成像（IRT）检测时，将热电偶探头固定于一次性柔性输尿管肾镜（德国WiScope®品牌）上，探头尖端距离远端10毫米处（见图1）。

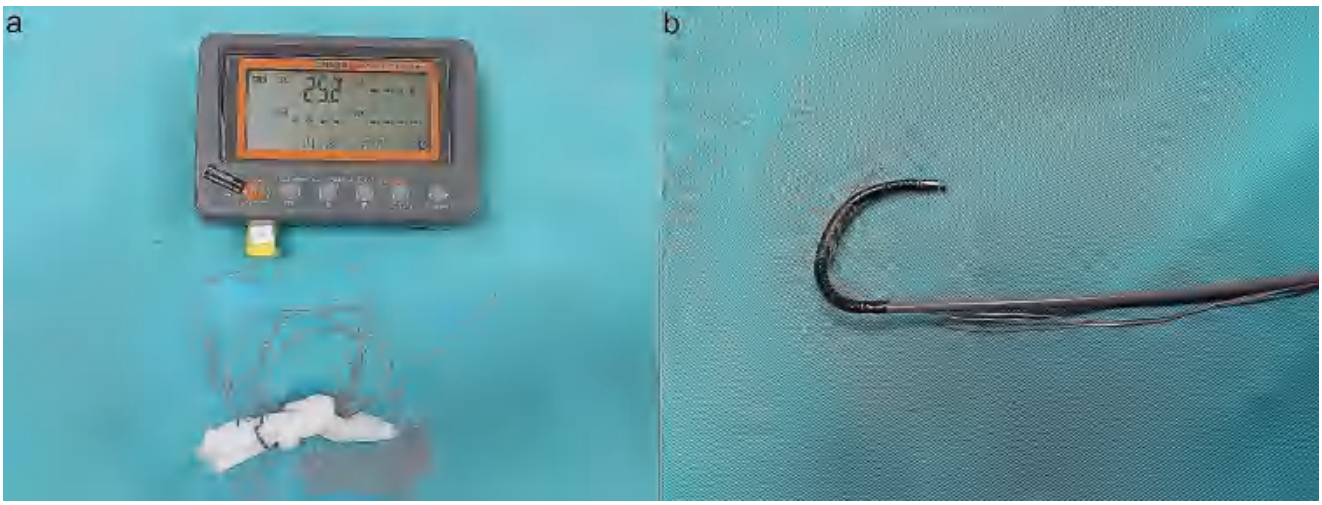


图1温度测量系统**a** T型导线温度传感器和温度计。**b**安装在输尿管肾镜上的温度传感器

通过13/15单腔输尿管导管鞘（Navigator™HD，美国波士顿科学公司），将输尿管肾镜插入收集系统。

我们使用了一套配备272μm激光光纤（FlexiFib，Lisa Laser Products，德国）的钬激光系统（Sphinx Jr.，Promed，德国）进行碎石术。每位患者均在室温（25.41±2.82°C）下使用生理盐水溶液进行碎石术。实验方案包括机械泵冲洗，具体采用血清输注泵，流速分别为10 ml/min、15 ml/min和20 ml/min。为此使用的激光功率为8 W（0.8 J/10 Hz）。除机械泵冲洗模式外，还采用了重力冲洗模式（手术台上方60厘米处）和手动泵冲洗模式（根据需要泵送以提高可视化质量），用于14 W（1.2 J/12 Hz）激光设置。

当软性输尿管肾镜抵达肾盏系统后，随即开始测量温度。若经内窥镜或X光检查确认无临床显著残留碎片（<3毫米），则停止测量。每个研究模型中，许多

表1患者围手术期及临床特征

特性	总体（*n*=15）
性别，n（%）	
男性	8 (53)
女性的	7 (47)
年龄（岁）	51,27±15,50
体重指数（kg/m²）	26,43±4,47
石方，n（%）	
右边的	7 (47)
左	8 (53)
石料数量，n（%）	
单曲	13 (86)
多选	2 (14)
石材位置，n（%）	
肾盂	9 (60)
上萼片	2 (13)
中萼片	2 (13)
多叶	2 (13)
石料尺寸（mm²）	139,49±15,07
CT值（HU）	1240 (520–1520)
不透明度，n（%）	
不透明	12 (80)
不透明	3 (20)
术前肌酐（mg/dL）	0,82±0,13
透视时间（秒）	18 (12–48)
激光时间（min）	15,26±7,04
碎石时间（min）	20,44±8,91
总能量(J)	17188±11430
术后肌酐（mg/dL）	0,80±0,12
并发症发生率（%）	没有一个
术后住院天数	1

*CT*计算机断层扫描，*HU*（亨氏单位）

记录了以下参数：激光持续时间（激光踏板有效工作时长）、碎石时间（从激光启动到最终停机的总时长，包含踏板开启与关闭的间隔）、操作员工作周期（ODC，即激光持续时间与碎石时间之比）、总能量以及IRT。

统计分析

本研究采用社会科学统计软件包25版（IBM SPSS®，纽约州阿蒙克）进行数据分析。通过夏皮罗-威尔克检验验证数据正态分布情况，正态分布数据以均值±标准差表示，非正态分布数据则采用中位数（最小值-最大值）呈现。对于正态分布数据，采用重复测量方差分析比较不同激光工作模式下各灌溉模式的效果，并通过Bonferroni校正进行多重比较。针对非正态分布数据，使用Friedman检验比较不同激光工作模式下的灌溉效果，多重比较采用Dunn检验。通过广义线性混合模型评估自变量对平均温度的影响，多重比较同样采用Bonferroni校正。线性回归分析用于确定平均温度的预测因子，$p<0.05$被视为具有统计学显著性。

结果

总体而言，本研究共纳入15名患者。表1显示了患者的临床和围手术期特征。平均年龄为51.27±15.50岁，平均体重指数（BMI）为26.43±4.47 kg/m²。结石平均大小为139.49±15.07毫米²，60%的患者结石位于肾盂。

为便于理解，图2中显示了“患者2”的肾内温度-时间曲线。在开始激光碎石术前，随着冲洗开始，IRT急剧下降，当8W时，随着冲洗速率的降低，IRT增加，当14W时，随着冲洗速率的增加，IRT下降。当从重力冲洗模式转换为手动泵冲洗模式时，IRT急剧下降。

我们分析了持续约四十秒激光激活病例的温度记录，研究了不同激光功率和灌注参数的影响。随着激光功率增加和灌注速率降低，盏状体液升温速度加快，最终达到恒温状态。同时发现，达到该温度所需时间会相应缩短。

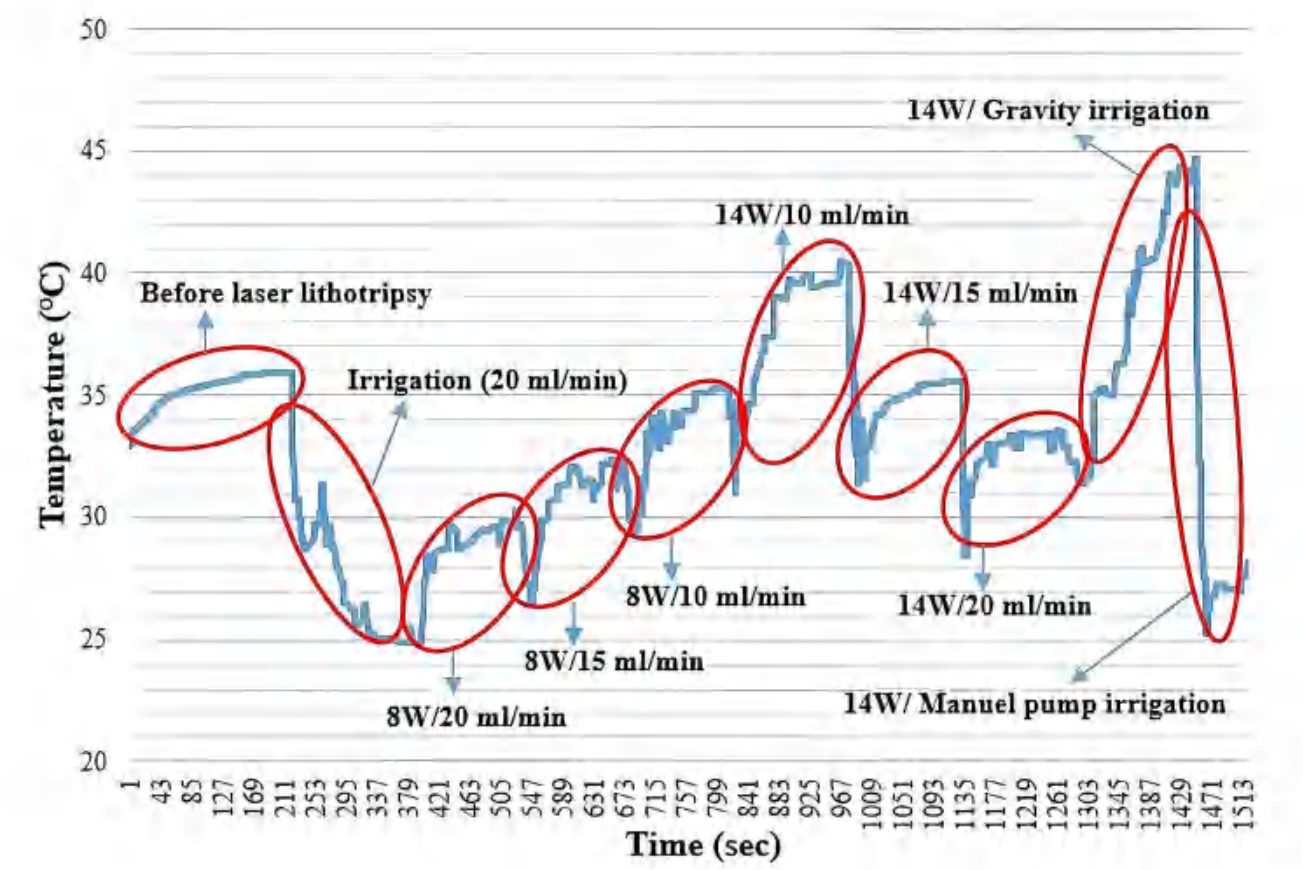


图2“患者2”的温度-时间曲线

平台温度持续升高，激光功率与灌注模式呈现相似的关联性（图3）。

整体手术参数总结于表2中。在8 W工作模型中，最低、平均和最高IRT值分别在20 ml/min灌洗模型中获得（27.5±2.8°C、30.2±2.2°C 和 31.7±2.1°C；p=0.017、p=0.002和p=0.001）。在14 W工作模型中，虽然手动泵灌洗模型的IRT最低值和平均值最低（中位数分别为26.76 °C和31.80°C；p<0.001），但20 ml/min灌洗模型的IRT最高值最低（35.21±2.30°C；p=0.005）。8 W和14 W工作模型的总能量值相当。

表3展示了人口统计学变量和手术参数对平均内镜取石术（IRT）时间的影响。在单因素分析中，年龄、性别、结石大小、结石CT值、激光功率、冲洗模式和ODC值是显著影响平均IRT时间的参数。而在评估参数交互作用的多因素分析中，与单因素分析结果不同，性别参数未显示出显著影响。对平均温度的影响（p=0.616）。相比之下，总能量具有显著影响（p=0.012）。根据标准化β系数，激光功率对平均IRT的影响最为显著，14 W激光功率的平均IRT比8 W激光功率高4.981°C（p<0.001）。与20 ml/min灌溉模型相比，重力灌溉模型的平均IRT值高2.075°C，而手动泵灌溉模型则低2.828°C（分别为p=0.038和p=0.005）。

我们构建了一个多元线性回归模型，用于预测基于BMI、激光功率、灌洗模式和ODC的平均IRT（见表4）。计算得出的回归模型具有统计学显著性（p<0.001）。虽然激光功率和ODC对平均IRT有正向影响，但BMI和灌洗模式的增加预计会降低平均IRT。这些变量可解释约49.5%的平均IRT（调整后R^2=0.495）。

在8瓦激光功率治疗组中，所有灌洗治疗均未达到43°C的阈值。此外，在14瓦激光功率组中，有1名患者达到了

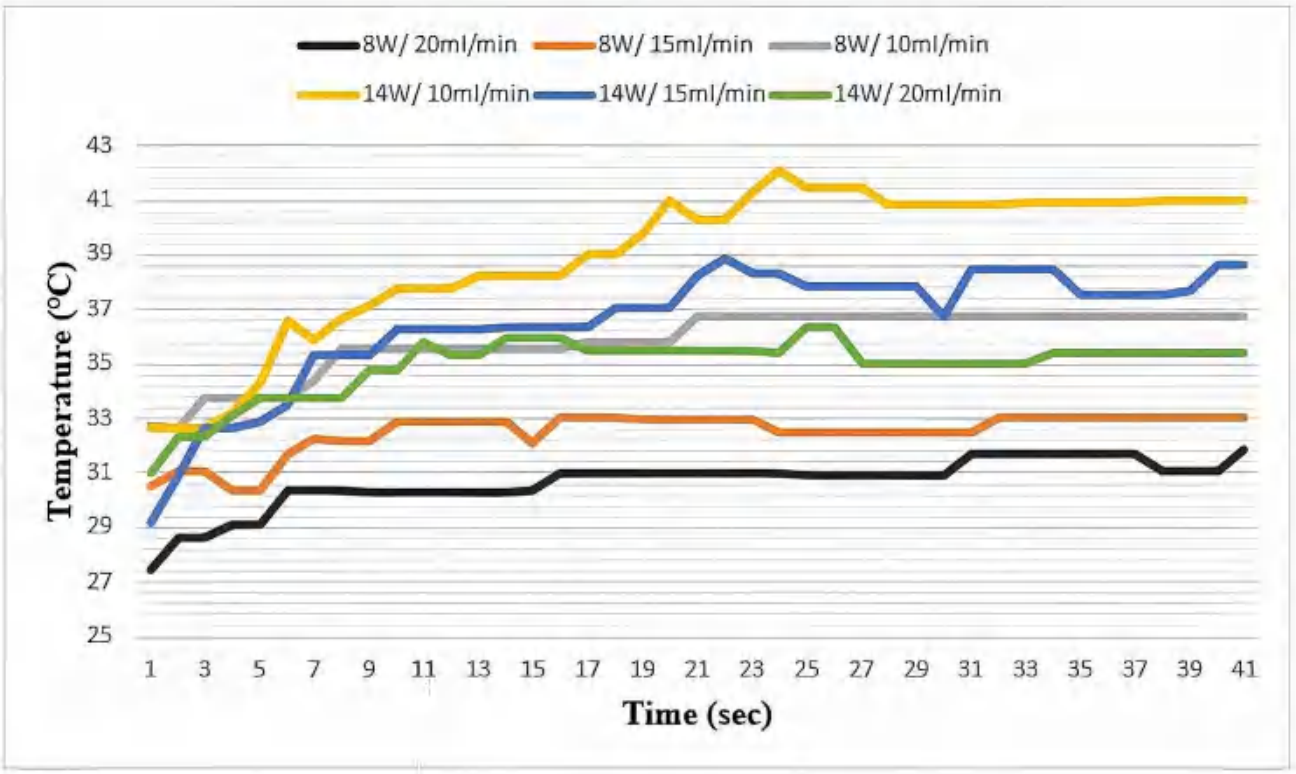


图3不同功率和灌溉设置下的温度-时间曲线

表2手术参数的基线特征和比较

	8 W						
	10 ml/min	15 ml/min	20 ml/min	手动泵	重力	检验统计量	*p*
总能量(J)	1069,7±628,2	999,4±377,1	883,8±325,4	否	否	0,833	0,659**
操作员值班周期	0,90（0,61-0,94）^{ab}	0,86（0,47-0,93）^{a}	0,91（0,52-1）^{b}	否	否	9,176	**0,01***
温度(°C)				否	否		
最小平均	30.7±2 ^{a}	29 ±2.7 ^{ab}	27.5±2.8 ^{b}	否	否	8,174	**0,017****
最大值	33,7±2,3^{a}	31.4±2.3 ^{b}	30.2±2.2 ^{b}	否	否	12,516	**0,002****
	35.1±2.6 ^{a}	32.8±1.7 ^{b}	31.7±2.1 ^{b}	否	否	13,367	**0,001****
	14 W						
	10 ml/min	**15 ml/min**	**20 ml/min**	**手动泵**	**重力**	**检验统计量**	**p**
总能量(J)	2730,67±2590,70	2076,22±1702,33	1737,44±1205,76	3470,33±6801,19	2704,33±4703,37	5,689	0,224**
操作员值班周期	0,80±0,14^{a}	0,72±0,21^{ab}	0,69±0,23^{ab}	0,60±0,11^{b}	0,58±0,25^{ab}	10,96	**0,027****
温度（℃）最小值、平均值、最大值	32,65（30.98-35.73）^{c}	31,38（29,21-36,31）^{bc} 36,27（30.80-40.42）^{c}	29.92（27.04–33.93）^{b} 34.06（28.66-36.57）^{b}	26,76（25,28–29,21）^{a} 31,80（28,25–33,24）^{a}	31,38（28.46-33.34）^{bc} 36.51（31.67-38.93）^{bc}	22,922	**＜0,001***
	37.67（32.22–39.90）^{c} 39.53±3.68 ^{b}	36.89±3.02 ^{ab}	35.21±2.30 ^{a}	38.62±3.92 ^{ab}	40.01±5.83 ^{ab}	24,884	**＜0,001***
						15,039	**0,005****

*Friedman检验，**重复测量分析，$^{a-c}$同一字母的灌注模型间无显著差异

表3自变量对平均温度的影响

	单变量					多变量				
	β1 (%95 CI)	S.E.M	β2	t	小于*	β1 (%95 CI)	S.E.M	β2	t	小于*
持续不断的						24,644 (20,843 – 28,444)	1,899	0,000	12,975	**< 0,001**
年龄	-0,074 (-0,127 - -0,022)	0,026	-0,275	-2,819	**0,006**	-0,105 (-0,137 - -0,072)	0,016	-0,390	-6,475	**< 0,001**
性别（参考：男性）	-2,087 (-3,345 - -0,829)	0,631	-0,318	-3,308	**0,001**	0,201 (-0,597–1)	0,399	0,031	0,504	0,616
[redacted]	-0,113 (-0,255–0,029)	0,071	-0,163	-1,593	0,116	0,064 (-0,018 – 0,145)	0,041	0,093	1,569	0,122
石料尺寸	0,024 (0,008 – 0,04)	0,008	0,292	2,997	**0,004**	0,019 (0,009 – 0,029)	0,005	0,231	3,769	**< 0,001**
CT石块值	0,003 (0,001 – 0,005)	0,001	0,272	3,095	**0,003**	0,003 (0,001 – 0,005)	0,001	0,272	3,363	**0,001**
激光功率（参考：8 W）	3,515 (2,208–4,822)	0,655	0,522	5,364	**< 0,001**	4,981 (4,072 – 5,89)	0,454	0,740	10,965	**< 0,001**
灌溉模型（参考：20 ml/min)										
15 ml/min	1,763 (-0,273–3,798)	1,020	0,234	1,728	0,089	1,169 (0,257–2,082)	0,456	0,155	2,565	**0,013**
10 ml/min	2,719 (0,952–4,486)	0,885	0,361	3,071	**0,003**	-1,128 (-2,326–0,07)	0,599	-0,150	-1,885	0,064
重力	5,181 (2,894–7,468)	1,146	0,526	4,522	**< 0,001**	2,075 (-0,027 – 4,176)	1,050	0,211	1,976	**0,038**
手动泵	0,177 (-1,64 – 1,993)	0,910	0,018	0,194	0,847	-2,828 (-4,745 - -0,911)	0,958	-0,287	-2,952	**0,005**
总能量	0 (-0,0002 – 0,0003)	0,000	0,030	0,280	0,780	-0,0002 (-0,0004 - -0,0001)	0,000	-0,232	-2,577	**0,012**
操作员值班周期	6,568 (3,045 – 10,092)	1,767	0,390	3,718	**< 0,001**	3,997 (0,545–7,449)	1,725	0,238	2,317	**0,024**

*BMI*体重指数，*CT*计算机断层扫描，*S.E.M*标准误差，*广义线性混合模型

表4平均气温预测因子分析结果

	β [1]（%95 CI）	β[2]	t	小于*
持续不断的	29,227 (23,977–34,478)		11,111	**< 0,001**
[redacted]	-0,126 (-0,245 - -0,007)	-0,182	-2,118	**0,038**
激光功率	4,740 (3,462–6,018)	0,704	7,402	**< 0,001**
灌注模型	-1,173 (-1,627 - -0,719)	-0,474	-5,160	**< 0,001**
操作员值班周期	4,231 (1,091 – 7,371)	0,251	2,690	**0,009**

BMI *体重指数*，*线性回归模型（逐步法）p<0,001；R^2=0.523；Adj.R^2= 0.495；Durbin-Watson=1.611

在10 ml/min的灌溉模型中，IRT为43°C，而在重力灌溉模型中，有一名患者达到了这一IRT。

讨论

本研究发现，对于接受Ho：YAG激光进行RIRS治疗的患者，激光功率、冲洗模式以及ODC的影响和预测作用均与术中恢复时间（IRT）相关。据我们所知，这是首个针对Ho：YAG激光治疗RIRS患者时，除激光功率和冲洗模式外其他变量影响的临床研究。

根据热力学基本定律，在恒定环境中，单位时间内的热能应保持恒定，从而导致温度变化恒定（Q=mcΔT）。我们的研究表明，连续工作40秒的主动激光器可保持恒定热能输出。

当灌溉速率在某一单位范围内变化时，灌溉温度（IRT）会先上升后趋于稳定（图3）。在该动态模型中，环境条件并非恒定，这种稳定状态的形成可归因于未加热灌溉液流入杯状系统，同时加热后的灌溉液从杯状系统流出。这一现象与文献中已有研究结果[8，19，23，24]的结论一致。值得注意的是，当灌溉速率保持恒定时，IRT仍能维持稳定水平，这表明在临床研究中，平均灌溉温度比峰值温度更具参考价值。

激光参数经过个性化设置。随后可逐步提升脉冲能量，直至达到理想的粉尘化或碎裂效果。本研究发现，激光功率是决定平均红外温度（IRT）的最关键参数。通过回归分析预测模型显示，激光功率每增加1个单位，平均IRT将提升4.74°C（表4）。Aldoukhi等人的实验研究中，最高

在5W至40W激光功率范围内，当功率为40W且不采用灌注模式时，温度可达到70.3°C[8]。Peteinaris等人在猪模型研究中将54°C作为热损伤阈值，发现重力灌注模型中需使用超过40W的激光功率才能达到该阈值。相比之下，采用20W和40W激光功率时则能维持安全热范围[25]。Noureldin团队的猪模型研究显示，使用套管导管时，20W激光功率可确保间质性肾炎（IRT）处于安全范围；而在重力灌注模型中，当激光功率更高时，才可能引发泌尿系统热损伤的临界温度值会被达到[17]。

灌注模式已成为影响红外热成像（IRT）效果的关键参数。2019年针对泌尿科医生开展的调查显示，46%的医生更倾向于手动泵灌注法，27%的医生偏好重力灌注法[26]。研究数据显示，重力灌注法的平均IRT值显著高于其他灌注模式，而手动灌注法的平均IRT值最低（见表3）。Peteinaris团队的研究表明，在重力灌注模式下，当激光功率达到40瓦和60瓦、激活时间30秒时，即可达到热阈值；而采用类似激光参数的手动泵灌注模式仍能保持安全热范围[27]。另一项活体猪模型研究发现，无论是否使用输尿管套管，重力灌注模式在激光功率超过40瓦时都会产生危险的IRT值。相比之下，手动泵灌注模式仅在使用100瓦激光功率且未使用输尿管套管时才会达到热阈值[25]。

在临床操作中，暂停冲洗液流动可有效避免碎石术中结石的逆向运动。但需特别注意操作时的谨慎性。本研究中有一例患者在碎石术过程中因意外关闭冲洗系统，导致术中温度在短短5秒内骤升9°C，具体机制尚不明确。布蒂斯团队的体外研究表明，无论采用何种激光参数，持续冲洗都能有效抑制温度升高，而关闭冲洗则会引发快速升温[10]。沃林团队的实验性输尿管镜模型显示，所有激光功率（3.6-20W）在不持续冲洗时均达到热阈值[28]。海因团队报告称，无冲洗状态下激光应用会导致温度快速攀升，最大增幅达28K，100W功率时温度可飙升至68°C[24]。综合上述研究结果可知，持续冲洗对于维持安全热范围至关重要。

Louters等人的体外研究显示，ODC对温度的影响表明，随着ODC的增加，温度在更短时间内达到更高水平[29]。Aldoukhi等人的体外研究显示，热损伤阈值在40瓦激光功率下，仅需9秒即可实现50%的ODC[7]。体外实验表明，可将ODC作为限制输尿管或小盏等小腔体温度升高的方法[30]。Pauchard等人在关于肾内温度与压力的RIRS研究综述中指出，应暂停激光激活以降低高温风险[31]。本研究与文献一致地发现：当在各工作模型间切换时暂停激光激活，可显著降低IRT（图2）。此外，单因素和多因素分析均表明，ODC对平均IRT具有积极影响（表3）。

在我们的研究中，任何灌注模型在8 W激光功率下均未达到热阈值。相比之下，在14 W激光功率下，10 ml/min和重力灌注模型达到了43°C的IRT。Maxwell等人的一项体外研究使用5至40 W的激光功率和灌注模式（包括无灌注、15 ml/min和40 ml/min）对人类泌尿系统进行了建模。激光激活持续60秒。与我们的研究一致，他们发现当激光功率不超过20 W且灌注速率高于15 ml/min时，热阈值仍未达到[14]。类似地，Teng等人报告称，在其临床研究中，当激光功率低于20 W且灌注速率至少为15 ml/min时，IRT仍保持在安全热范围内[23]。Æsøy等人使用铥光纤激光器进行的临床研究也报告了类似结果，即在5 W和10 W激光功率及15 ml/min灌注速率下，温度未达到43°C[22]。目前，尚无针对RIRS的明确最佳激光设置或灌注模型。然而，低激光功率（<20 W）和中等灌注流量（15–30 ml/min）似乎是管理IRT的可行选择[31]。

我们深知激光频率是影响体外碎石术（IRT）的关键参数。Aldoukhi团队的体外研究显示，当频率为20赫兹时，仅有52%的发射脉冲能抵达结石；而频率提升至50赫兹和80赫兹时，这一比例分别降至23%和4%[32]。由此可见，随着频率升高，液体介质吸收的能量增加，导致体外碎石术温度升高。Liang等学者在输尿管镜碎石模型实验中发现，相同激光功率下高频模式产生的热量更多[33]。Hein团队通过对比低频高单脉冲能量与高频低单脉冲能量模型的体外研究发现，高频设置在低功率和高功率条件下分别使温度升高3.5%和8.8%[24]。Gallegos团队在猪模型研究中，分别于实验开始时和激光使用后1分钟测量IRT值，并将两次测量的温差定义为温度差（DT）。能量、频率、输尿管套管使用情况及液体高度等参数均需纳入考量。

研究发现，某些参数对DT有显著影响，与5Hz相比，15Hz频率下DT预测增加2.1°C[34]。Maxwell等人使用5-40W不同激光功率和不同冲洗模式进行研究，发现无论频率和脉冲设置如何，相同激光功率下的峰值温度值几乎相同[14]。

红外热（IRT）在临床实践中究竟有多重要？阿尔杜基团队在四只活体猪模型中采用Ho：YAG激光器进行肾内激光激活，功率40瓦持续60秒，未使用冲洗液，分别采用低流量和高流量冲洗，测得最高IRT值分别为84.8°C、63.9°C和43.6°C。组织病理学检查显示，未冲洗组出现肉眼可见的宏观改变，而低流量冲洗组仅有轻微变化，高流量冲洗组则未见热损伤迹象[9]。莫利纳团队在离体猪模型中通过手动冲洗、Ho：YAG激光器（6.4W和21W）及spTFL（6.4W和20W）构建输尿管结石模型，两种系统温度均低于临界值（43°C）。组织病理学检查证实碎石术后输尿管未出现热损伤[15]。皮泰纳里斯团队在两只活体猪模型中建立肾结石模型，使用8W铥光纤激光器进行60分钟激光碎石，两个模型的IRT值均在44°C至46°C之间。研究人员分别在第7天和第14天对肾脏进行了组织病理学检查。第7天的检查结果显示存在出血区域、尿路上皮分离、纤维蛋白沉积及固有层炎症等严重病理改变，而第14天的病理报告仅显示“轻微变化”35。因此，根据现有研究数据对这些病理变化进行定性评估存在较大难度。不过考虑到高温疗法长期影响的相关证据尚不充分，采用较低强度的红外线治疗似乎更为安全。

活体组织中产生的热细胞毒性效应，主要由温度和暴露时长决定。萨帕雷托与杜威提出的“43℃累积当量分钟（CEM43）”计算公式，专门用于评估热剂量——该数值基于43℃参考温度下的暴露时间计算得出[36]。动物实验表明，当尿路温度达到43℃时会发生蛋白质变性[20]，若CEM43持续时间超过70分钟，就会造成肾脏严重损伤[37]。鉴于目前文献尚未明确人体尿路系统的安全热剂量，本研究根据现有资料将43℃定为热损伤临界温度。

在RIRS手术中，为实现灌注热成像（IRT）监测，必须通过逆行或经皮途径将探头送入肾盏系统。尽管该系统具有精密的校准功能，但其校准可能影响灌注流量，导致IRT实际成像结果失真。

在临床操作中，逆行入路相比经皮入路显得更为安全。该方法需配合输尿管套管使用，具有较高的可靠性。不过，目前仍需更多关于输尿管热成像监测（IRT）在输尿管镜肾镜联合手术（RIRS）中常规应用的临床研究。当前临床实践中，虽然已采用可监测肾内压力的柔性输尿管肾镜进行RIRS操作[38]，但专门用于IRT监测的仪器尚未问世。未来该领域的研究必然需要热探针技术的介入。

本研究存在若干局限性。首先，样本量较小可能导致人口均值估算存在偏差。其次，由于患者肾盏解剖结构和体积存在个体差异，即使变量相似也可能获得不同的红外热成像（IRT）结果。第三，由于无法始终保持激光光纤与结石及热探头的距离恒定，变量相似时可能产生不同IRT结果。第四，由于未使用多点热探头且无法测量各主要肾盏温度，记录温度可能无法准确反映平均IRT值。第五，监测设备无法实时显示温度信息，导致在达到临界温度时仍继续激光激活。第六，由于缺乏结石化学成分分析，无法探究温度曲线可能受到的影响。

结论

这项初步研究调查了Ho：YAG激光碎石术对肾盏内液体温度的影响，重点关注激光功率和冲洗速率的作用。结果显示，Ho：YAG激光功率和冲洗速率对平均温度具有相反的影响，其中激光功率是温度升高的最重要参数。以最低15 ml/min的速率持续冲洗有助于将温度维持在安全范围内，尤其是在中等激光功率下。此外，本研究揭示ODC是影响IRT的重要参数，表明定期停止激光激活的重要性。这些发现强调了需要进行更大规模人群的临床研究，以阐明激光碎石术过程中影响IRT动态的其他因素。

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输尿管结石患者行输尿管镜下钬激光碎石术治疗后输尿管狭窄发生情况及影响因素分析

张恒志①

【摘要】 **目的：**分析输尿管结石患者行输尿管镜下钬激光碎石术治疗后输尿管狭窄发生情况及影响因素。**方法：**选择 2022 年 2 月—2023 年 2 月贵阳贵航医院收治的 329 例行输尿管镜下钬激光碎石术治疗的输尿管结石患者作为研究对象。观察治疗后输尿管狭窄发生情况，分为狭窄组（n=21）、非狭窄组（n=308），比较两组一般资料，分析输尿管结石患者行输尿管镜下钬激光碎石术治疗后输尿管狭窄发生的影响因素。**结果：**329 例行输尿管镜下钬激光碎石术治疗的输尿管结石患者中，21 例治疗后发生输尿管狭窄，输尿管狭窄发生率为 6.38%。两组性别、年龄、体重指数、结石部位、患侧、合并尿路感染、结石残余、双 J 管留置时间比较，差异无统计学意义（P>0.05）；两组病程、结石直径、肾积水严重、结石嵌顿、炎性黏膜包裹比较，差异有统计学意义（P<0.05）。logistic 回归分析结果显示，病程长、结石直径大、肾积水严重、结石嵌顿、炎性黏膜包裹为输尿管镜下钬激光碎石术治疗后输尿管狭窄发生的影响因素（P<0.05）。**结论：**输尿管镜下钬激光碎石术治疗后仍存在一定的输尿管狭窄发生风险，病程长、结石直径大、肾积水严重、结石嵌顿、炎性黏膜包裹为其影响因素。

【关键词】 输尿管结石　钬激光碎石术　输尿管镜　输尿管狭窄

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Analysis of the Occurrence and Influencing Factors of Ureteral Stricture in Ureteral Calculi Patients after Ureteroscopic Holmium Laser Lithotripsy/ZHANG Hengzhi. //Chinese and Foreign Medical Research, 2024, 22(17): 166-169

[Abstract] **Objective:** To analyze the occurrence and influencing factors of ureteral stricture in ureteral calculi patients treated by ureteroscopic holmium laser lithotripsy. **Method:** A total of 329 patients with ureteral calculi who underwent ureteroscopic holmium laser lithotripsy treatment in Guiyang Guihang Hospital from February 2022 to February 2023 were selected as the study objects. The incidence of ureteral stricture after treatment was observed and divided into the stenosis group (n=21) and the non-stenosis group (n=308). The general data of the two groups were compared to analyze the influencing factors the occurrence of ureteral stricture in patients with ureteral calculi treated by ureteroscopic holmium laser lithotripsis. **Result:** Among 329 patients with ureteral calculi treated by ureteroscopic holmium laser lithotripsy, a total of 21 cases developed ureteral stricture after treatment, and the incidence of ureteral stricture was 6.38%. There were no significant differences in gender, age, body mass index, stone site, affected side, combined urinary tract infection, stone residue, and indindment time of double J-tube between the two groups (P>0.05). There were statistically significant differences in the course of disease, stone diameter, severe hydronephrosis, stone incarceration and inflammatory mucosal encapsulation between the two groups (P<0.05). logistic regression analysis showed that long course of disease, large stone diameter, severe hydronephrosis,

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stone incarceration, and inflammatory mucosal encapsulation were the influencing factors of ureteral stricture after ureteroscopic holmium laser lithotripsy (P<0.05). **Conclusion:** Ureteroscopic holmium laser lithotripsy has a certain risk of ureteral stricture, and the influencing factors are long course of disease, large stone diameter, severe hydronephrosis, stone incarceration, and inflammatory mucosal encapsulation.

[Key words] Ureteral calculi Holmium laser lithotripsy Ureteroscopic Ureteral stricture

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输尿管结石是一个形成在输尿管中的固体结构，由于尿液中的某些物质沉积或结晶而形成，可以阻塞尿液的正常流动，并引起一系列的症状和并发症，导致尿液潴留，引起剧烈的腰背部疼痛、腹痛及尿频、尿急等不适症状[1]。输尿管镜下钬激光碎石术是一种治疗输尿管结石的微创手术，通过导入输尿管镜和钬激光设备可以精确地将激光能量聚焦在结石上，将结石分解成更小的颗粒，以便更容易排出体外[2]。然而，输尿管镜下钬激光碎石术治疗后仍然可能会出现术后输尿管狭窄，即输尿管内径变窄，会限制尿液的正常流动，引起尿液梗阻、尿痛、尿频等尿路症状，容易滞留尿液，增加尿路感染的风险，严重的输尿管狭窄还可能会导致肾脏受损，影响肾功能[3]。因此，需要采取预防措施来减少输尿管结石和术后输尿管狭窄的风险，现报告如下。

1 资料与方法

1.1 一般资料

选择 2022 年 2 月—2023 年 2 月贵阳贵航医院收治的 329 例行输尿管镜下钬激光碎石术治疗的输尿管结石患者作为研究对象。纳入标准：（1）符合《中国泌尿外科和男科疾病诊断治疗指南（2019 版）》[4]标准；（2）初次进行结石手术；（3）输尿管镜下钬激光碎石术适应证；（4）影像学确诊；（5）资料完整；（6）沟通、认知均正常；（7）单侧输尿管结石。排除标准：（1）精神障碍；（2）合并肾结石；（3）组织增生导致的输尿管狭窄；（4）输尿管狭窄病史；（5）多发输尿管结石；（6）既往有输尿管手术史；（7）严重躯体疾病。本研究经贵阳贵航医院医学伦理委员会批准，患者及家属知情同意。

1.2 方法

1.2.1 基线资料 设计一般资料调查表，仔细询问、调查并记录患者的相关资料，内容包括：（1）性别；（2）年龄；（3）体重指数；（4）病程；（5）结石直径；（6）结石部位（上段、中段、下段）；（7）患侧（左侧、右侧）；（8）肾积水程度（重度、轻中度）；（9）结石嵌顿（是、否）；（10）炎性黏膜包裹（是、否）；（11）合并尿路感染（是、否）；（12）结石残余（是、否）；（13）双 J 管留置时间（>4 周、≤4 周）。

1.2.2 输尿管狭窄评估及分组 输尿管狭窄判断：于输尿管镜下钬激光碎石术治疗后 3~6 周拔除双 J 管，并于拔除后的 1 周、2 周、1 个月、3 个月、6 个月进行复查，使用泌尿系彩超，如出现肾积水加重情况，需进一步进行 CT、造影等检查，若为输尿管狭窄造成肾积水加重，则判断为发生输尿管狭窄。观察治疗后输尿管狭窄发生情况，分为狭窄组（发生输尿管狭窄）、非狭窄组（未发生输尿管狭窄）。

1.3 统计学处理

本研究数据采用 SPSS 22.0 统计学软件进行分析和处理，计量资料以（$\bar{x} \pm s$）表示，采用 t 检验，计数资料以率（%）表示，采用 χ^2 检验，以 P<0.05 为差异有统计学意义。

2 结果

2.1 输尿管镜下钬激光碎石术治疗后输尿管狭窄的发生情况

329 例行输尿管镜下钬激光碎石术治疗的输尿管结石患者中，有 21 例治疗后发生输尿管狭窄，输尿管狭窄发生率为 6.38%。

2.2 狭窄组和非狭窄组一般资料比较

两组病程、结石直径、肾积水严重、结石嵌顿、炎性黏膜包裹比较，差异有统计学意义（P<0.05）；两组性别、年龄、体重指数、结石部位、患侧、合并尿路感染、结石残余、双 J 管留置时间比较，差异无统计学意义（P>0.05），见表 1。

2.3 输尿管镜下钬激光碎石术治疗后输尿管狭窄发生的影响因素分析

将输尿管狭窄发生情况作为应变量（发生输尿管狭窄 =1，未发生输尿管狭窄 =0），将病程（连续变量）、结石直径（连续变量）、肾积水程度（重度 =1，轻中度 =0）、结石嵌顿（是 =1，否 =0）、炎性黏膜包裹（是 =1，否 =0）作为自变量，经 logistic

回归分析结果显示，病程长、结石直径大、肾积水严重、结石嵌顿、炎性黏膜包裹为输尿管镜下钬激光碎石术治疗后输尿管狭窄发生的影响因素（P<0.05），见表 2。

表1 狭窄组和非狭窄组一般资料比较

组别	性别 [例（%）]		年龄	体重指数	病程
	男	女	[岁，（$\bar{x}\pm s$）]	[kg/m^2，（$\bar{x}\pm s$）]	[个月，（$\bar{x}\pm s$）]
狭窄组（n=21）	11（52.38）	10（47.62）	50.13 ± 5.52	22.12 ± 0.86	5.05 ± 0.50
非狭窄组（n=308）	175（56.82）	133（43.18）	50.87 ± 5.74	22.06 ± 0.79	4.13 ± 0.52
χ^2/t 值	0.158		0.573	0.335	8.204
P 值	0.691		0.567	0.738	<0.001

组别	结石直径	结石部位 [例（%）]			患侧 [例（%）]	
	[cm，（$\bar{x}\pm s$）]	上段	中段	下段	左侧	右侧
狭窄组（n=21）	1.93 ± 0.31	3（14.29）	10（47.62）	8（38.10）	11（52.38）	10（47.62）
非狭窄组（n=308）	1.38 ± 0.25	37（12.01）	141（45.78）	130（42.21）	168（54.55）	140（45.45）
χ^2/t 值	9.598		0.177		0.037	
P 值	<0.001		0.915		0.847	

组别	肾积水 [例（%）]		结石嵌顿 [例（%）]		炎性黏膜包裹 [例（%）]	
	重度	轻中度	是	否	是	否
狭窄组（n=21）	13（61.90）	8（38.10）	14（66.67）	7（33.33）	12（57.14）	9（42.86）
非狭窄组（n=308）	76（24.68）	232（75.32）	98（31.82）	210（68.18）	84（27.27）	224（72.73）
χ^2/t 值	13.808		10.633		8.488	
P 值	<0.001		0.001		0.003	

组别	合并尿路感染 [例（%）]		结石残余 [例（%）]		双 J 管留置时间 [例（%）]	
	是	否	是	否	>4 周	≤4 周
狭窄组（n=21）	12（57.14）	9（42.86）	2（9.52）	19（90.48）	11（52.38）	10（47.62）
非狭窄组（n=308）	122（39.61）	186（60.39）	18（5.84）	290（94.16）	125（40.58）	183（59.42）
χ^2/t 值	2.503		0.045		1.128	
P 值	0.114		0.832		0.288	

表2 输尿管镜下钬激光碎石术治疗后输尿管狭窄发生的影响因素分析

因素	B	SE	Wald χ^2 值	P 值	OR 值	95%CI
病程	3.134	0.611	26.288	<0.001	22.963	6.930，76.084
结石直径	6.250	0.996	39.387	<0.001	518.191	73.579，3 649.443
肾积水程度	1.602	0.468	11.691	0.001	4.961	1.981，12.423
结石嵌顿	1.455	0.479	9.238	0.002	4.286	1.677，10.954
炎性黏膜包裹	1.269	0.459	7.633	0.006	3.556	1.446，8.744

3 讨论

输尿管结石阻塞尿液流动，造成尿液在尿路内滞留，易导致细菌感染，引发尿路感染的症状，如尿道灼热、尿频、尿急、尿痛等[5]。而且，结石经过输尿管时，可能会刮伤或刺激输尿管壁，引发输尿管炎症，甚至导致输尿管损伤，增加出血的风险。相比传统的手术方法，钬激光碎石术对周围组织损伤较小，可以最大限度地保护输尿管壁和其他组织，采用经尿道方式进行，无须开放手术，减少了术后的恢复时间和并发症的风险[6]。

本研究结果显示，329 例行输尿管镜下钬激光碎石术治疗的输尿管结石患者中，21 例治疗后发生输尿管狭窄，输尿管狭窄发生率为 6.38%。说明输尿管镜下钬激光碎石术治疗后仍存在一定的输尿管狭窄发生风险。经 logistic 回归分析结果显示，病程长、结石直径大、肾积水严重、结石嵌顿、炎性黏膜包裹为输尿管镜下钬激光碎石术治疗后输尿管狭窄发生的影响因素。分析原因为：（1）病程长说明结石已经存在较长时间并积聚成较大的固体物质，会导致输尿管黏膜的慢性刺激和炎症反应，进一步损伤输尿管组织，可能导致输尿管内组织的瘢痕形成和纤维化，增加输尿管狭窄的风险[7]。长期存在

的结石可能会引起其他并发症，例如肾功能异常或尿路感染，这些并发症本身就可能对输尿管组织造成进一步的损伤，增加术后发生输尿管狭窄的风险[8]。（2）钬激光碎石术是一种常用于治疗输尿管结石的手术方法，使用钬激光器产生的高能量光束将结石碎成小颗粒，以便更容易通过尿道排出体外。然而，当直径较大的结石被钬激光碎石术分解时，其中的碎片可能会比较粗糙，并可引发输尿管黏膜的炎症和损伤[9]。这些炎症反应可能导致组织增生和瘢痕形成，最终导致输尿管狭窄。此外，输尿管直径大的结石由于占据了更多的空间，可能会对周围组织施加更大的压力，增加了狭窄发生的风险[10]。（3）肾积水是指尿液在肾脏内无法正常排出，导致肾盂和输尿管扩张，重度肾积水意味着结石阻塞了输尿管的通路，导致尿液无法顺利流动，这种持续的阻塞会对输尿管壁施加压力，并引起炎症反应和组织损伤，当结石被钬激光碎石术分解时，由于长期的阻塞已经引起了严重的组织改变，再加上手术过程中的刺激，可能会增加输尿管狭窄的风险[11]。（4）结石嵌顿意味着结石阻塞了尿液的流动，会对输尿管壁施加压力，并引起炎症反应和组织损伤，当结石被钬激光碎石术分解时，由于结石嵌顿导致的组织损伤已经存在，再加上手术过程中的刺激，可能会增加输尿管狭窄的风险[12]。在进行钬激光碎石术时，为了辅助操作，可能会插入导丝或支架来保持输尿管通畅，然而，当结石嵌顿存在时，导丝或支架可能会更难插入，或者可能会引起更多的刺激和损伤，进一步增加了输尿管狭窄的风险[13]。（5）炎性黏膜包裹的输尿管结石通常会引起强烈的炎症反应，这是由于结石与输尿管黏膜之间的持续摩擦和刺激，当进行钬激光碎石术分解结石时，释放的结石碎片可能会进一步加剧炎症反应，持续的炎症反应会导致组织增生和纤维化，增加了输尿管狭窄的风险[14-15]。

综上所述，输尿管镜下钬激光碎石术治疗后仍存在一定的输尿管狭窄发生风险，病程长、结石直径大、肾积水严重、结石嵌顿、炎性黏膜包裹为其影响因素。

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· 激光在泌尿外科领域的应用 ·

低功率钬激光瞬时切割对输尿管狭窄及组织纤维化的影响

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【摘要】　目的　探索钬激光瞬时切割损伤对猪输尿管狭窄及组织纤维化的影响。**方法**　选取 10 头白雌猪，在双侧输尿管距肾盂输尿管连接部 5、10、15、20 cm 处分别标记为 A、B、C、D 组，各组激光参数设置如下：A 组 0.5 J×20 Hz（短脉冲），B 组 1.0 J×10 Hz（短脉冲），C 组 0.5 J×20 Hz（长脉冲）和 D 组 1.0 J×10 Hz（长脉冲）。每组应用钬激光进行烧灼，能量设置统一为低功率（10 W），烧灼点取手术视野 6 点钟位置，烧灼时长约 1 s。术后留置双 J 管 1 个月。术后 4 个月处死实验猪并剖取双肾、输尿管以及膀胱标本，沿长轴剖开输尿管。按术中标记距离及肉眼所见记录各组烧灼点狭窄情况，截取各组烧灼点输尿管组织，行组织病理学 HE 染色及 Masson 染色，分析组织损伤及纤维化情况。**结果**　本研究 1 头实验猪术中未能找到左侧输尿管开口，3 头实验猪术后当天死亡。最终纳入 6 头猪，共 12 侧尿路标本进行分析，包含 48 个烧灼点。各烧灼点输尿管局部狭窄的发生率为 64.6%（31/48），其中重度狭窄发生率为 8.3%（4/48）。A、B、C、D 组狭窄发生率分别为 66.7%（8/12）、66.7%（8/12）、66.7%（8/12）、52.5%（8/12），各组在狭窄发生率（P = 1.000）及狭窄程度（P = 0.075）方面的差异均无统计学意义。组织病理学分析结果显示，A、B、C、D 组的组织损伤深度［（1 645.46 ± 277.01）、（1 976.59 ± 222.62）、（1 841.37 ± 189.59）、（2 055.66 ± 206.40）μm，P = 0.560］及胶原纤维面积百分比［（70.22 ± 1.75）%、（69.48 ± 1.34）%、（68.00 ± 2.03）%、（74.39 ± 1.20）%，P = 0.560］差异均无统计学意义。**结论**　即使在低功率设置下，钬激光对输尿管组织的瞬时切割仍会导致较高的输尿管狭窄发生率。钬激光频率及脉冲长度选择对输尿管狭窄的发生率、组织病理损伤及纤维化程度无显著影响。

【关键词】　输尿管；　狭窄；　热损伤；　激光碎石术；　动物实验
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Effect of low-power Holmium laser instant cutting on ureteral stricture and tissue fibrosis

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【Abstract】　Objective　To investigate the effects of Holmium laser instant cutting damage on ureteral stricture and tissue fibrosis in pigs. **Methods**　Ten female white pigs were selected, and the bilateral ureters were marked at 5 cm, 10 cm, 15 cm, and 20 cm from the ureteropelvic junction (UPJ), designated as groups A, B, C, and D, respectively. The laser parameters were set as follows: Group A 0.5 J×20 Hz (short pulse), Group B 1.0 J×10 Hz (short pulse), Group C 0.5 J×20 Hz (long pulse), and Group D 1.0 J×10 Hz (long pulse). Holmium laser ablation was performed at each group with a uniform low power setting (10 W) for approximately 1 second at the 6 o'clock position of the surgical field. A double J stent was placed for one month post-operation. The experimental pigs were euthanized three months after stent removal, and specimens of the kidneys, ureters, and bladder were collected. The ureters were longitudinally opened, and the stenosis at each marked ablation site was recorded and subjected to histopathological analysis. **Results**　In this study, 1 pig failed to find the left ureteral opening during the operation, and 3 pigs died after operation. Six pigs with a total of 12 ureteral specimens were finally included. The incidence of local ureteral stricture at the ablation sites was 64.6% (31/48), with severe stricture occurring at 8.3% (4/48). The incidence of stricture in group A, B, C, and D were 66.7% (8/12), 66.7% (8/12), 66.7% (8/12), and 52.5% (8/12), respectively. There was no significant difference in the incidence

($P=1.000$) and degree ($P=0.075$) of stricture among the groups. Histopathological analysis showed no significant differences in tissue damage depth[(1 645.46 ± 277.01) μm vs. (1 976.59 ± 222.62) μm vs. (1 841.37 ± 189.59) μm vs. (2 055.66 ± 206.40) μm, $P=0.560$] and collagen fiber area percentage [(70.22 ± 1.75)% vs. (69.48 ± 1.34)% vs. (68.00 ± 2.03)% vs. (74.39 ± 1.20)%, $P=0.560$] among the groups. **Conclusions** Even under low power settings, instant cutting of ureteral tissue by Holmium laser results in a high incidence of ureteral stricture. The frequency and pulse length of the Holmium laser have no significant effect on the incidence of ureteral stricture, histopathological damage, or the degree of fibrosis.

【Key words】 Ureter; Stricture; Thermal injury; Laser lithotripsy; Animal experiment
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目前,输尿管镜钬激光碎石术因其微创、精准的特点,已逐步成为治疗泌尿系结石的首选手术方法之一[1-2]。输尿管狭窄是输尿管镜钬激光碎石术后严重的长期并发症,发生率为 0.3% ~4.9%,且在过去几年呈上升趋势[3-5];若输尿管狭窄得不到及时有效的治疗,将可能对患者肾功能造成不可逆的损害,最终导致肾衰竭等严重后果[6],部分复杂性输尿管狭窄病例在后期修复性治疗方面往往面临巨大的挑战及风险[7-8],输尿管镜钬激光碎石术后输尿管狭窄的形成原因涉及多种因素,其中钬激光对输尿管直接或间接的损伤是其重要原因;既往研究结果显示,与气压弹道相比,钬激光碎石明显增加了输尿管狭窄的发生风险[9-10]。钬激光对输尿管组织的损伤主要来自于其直接切割效应及局部高温对周围组织的影响。近年来,关于钬激光引发的输尿管组织局部高温效应的研究逐渐增多;然而,关于钬激光瞬时切割作用对输尿管狭窄影响的研究尚未见报道。本研究于 2019 年 11 月至 2020 年 3 月通过建立钬激光瞬时切割输尿管损伤的动物模型,探讨钬激光瞬时切割性损伤对输尿管狭窄及组织纤维化的影响,并进一步探究不同能量参数设置在其中的作用。

材料与方法

一、研究对象及实验器材

以上海雌性白猪为实验对象,共 10 头,均为 6 个月龄,平均体重 60 kg, 饮食及排尿正常,由吴江市田宇生物科技有限公司提供;实验白猪自由饮食,适应性喂养 2 周后进行实验。实验采用 F8.55 一次性电子输尿管软镜(型号 US31B-12,上海英诺伟医疗器械股份有限公司)及大功率钬激光治疗机(型号 SRM-H3B,上海瑞柯恩激光技术有限公司)。

二、输尿管钬激光瞬时切割热损伤模型的建立

实验猪麻醉后使用输尿管软镜裸镜进入输尿管,行至肾盂输尿管连接部(ureteropelvic junction, UPJ)缓慢退镜,于双侧输尿管距离 UPJ 为 5、10、15、20 cm 处分别标记为 A、B、C、D 组。各组激光参数设置如下:A 组 0.5 J×20 Hz(短脉冲),B 组 1.0 J×10 Hz(短脉冲),C 组 0.5 J×20 Hz(长脉冲),D 组 1.0 J×10 Hz(长脉冲)。每组应用钬激光进行烧灼,能量设置统一为低功率(10 W), 烧灼点取手术视野 6 点钟位置,烧灼时长约 1 s。术后留置双 J 管 1 个月。术后 4 个月行输尿管镜检查,观察输尿管狭窄情况。处死实验猪后进行解剖,取双肾、输尿管以及膀胱标本。沿长轴剖开输尿管,按术中标记距离肉眼探查各组烧灼点狭窄情况,并截取各组烧灼点输尿管组织,分别进行组织病理学分析。

本研究中输尿管狭窄的判定标准:轻度狭窄为 F6 导管可通过,肉眼及镜下可见瘢痕形成及管腔变窄;重度狭窄为 F6 导管不能通过。

三、制片及病理学分析

送检标本经 4% 多聚甲醛固定,固定状态良好后,严格按照本单位病理实验检测 SOP 程序进行修剪、脱水、包埋、切片、染色、封片,最后镜检合格的样片。

病理学分析采用以下 3 种方法。①损伤深度分析:应用 Image-Pro Plus 6.0 软件,每张烧灼点病理切片选取 8 处,测量出组织的损伤深度并取平均值。②纤维化分析:病理切片行 Masson 染色,每组内每张切片随机挑选至少 3 个 200 倍视野进行拍照,应用 Image-Pro Plus 6.0 软件分别测量 Masson 染色阳性像素面积,结合视野像素面积,得出胶原纤维的面积百分比 = 胶原纤维像素面积/视野像素面积 × 100%。③组织学分析:病理切片 HE 染色,统计组织病变情况。

四、统计学方法

采用 SPSS 26.0 统计软件进行数据分析。计量资料均符合正态分布,以 $\bar{x} \pm s$ 表示,组间比较采用 ANOVA 方差分析;分类变量以频率和百分比表示,

组间比较采用χ^2检验或 Fisher 精确检验；多组独立样本的等级资料，组间比较采用 Kruskal-Wallis 检验。以 $P<0.05$ 为差异有统计学意义。

结　果

一、输尿管镜检查及狭窄率分析

本研究 1 头实验猪术中未能找到左侧输尿管开口，3 头实验猪术后当天死亡；最终纳入 6 头猪，共 12 侧尿路标本进行分析，包含 48 个烧灼点。输尿管软镜下可见烧灼点狭窄以轻度为主，狭窄段输尿管可见黏膜缺血、苍白、瘢痕形成等改变，重度狭窄可观察到输尿管管腔闭锁（图 1）。狭窄总发生率为 64.6%（31/48），轻度狭窄发生率为 56.3%（27/48），重度狭窄为 8.3%（4/48）。其中，A 组未狭窄占比为 33.3%（4/12），轻度狭窄为 41.7%（5/12），重度狭窄为 25.0%（3/12）；B 组未狭窄占比为 33.3%（4/12），狭窄为 66.7%（5/12）且均为轻度狭窄；C 组未狭窄占比为 33.3%（4/12），轻度狭窄为 58.3%（7/12），重度狭窄为 25.0%（3/12）；D 组未狭窄占比为 47.5%（5/12），轻度狭窄为 58.3%（7/12），无重度狭窄发生。4 组标本在狭窄发生率（$\chi^2=0.42$，$P=1.000$）及狭窄程度（$K=1.360$，$P=0.075$）方面，差异均无统计学意义。

二、病理分析结果

获得烧灼病理切片 48 份，输尿管狭窄程度较轻时，输尿管组织病变主要以黏膜上皮肿胀、缺失为主，固有层及肌层水肿，肌纤维间隙增宽并有炎症细胞浸润；随着狭窄程度加重，输尿管局部肌层肌纤维消失，被大量增生的结缔组织取代（图 2）。A、B、C、D 组的组织损伤深度分别为（1 645.46 ± 277.01）、（1 976.59 ± 222.62）、（1 841.37 ± 189.59）、（2 055.66 ± 206.40）μm，各组间差异无统计学意义（$F=0.056$，$P=0.560$）；4 组病理标本胶原纤维面积的百分比分别为（70.22 ± 1.75）%、（69.48 ± 1.34）%、（68.00 ± 2.03）%、（74.39 ± 1.20）%，各组差异无统计学意义（$F=2.331$，$P=0.560$）。

讨　论

在钬激光碎石过程中，随着患者的呼吸活动，钬激光对输尿管黏膜的误击时有发生；在输尿管肿瘤的输尿管镜治疗中，更是需要使用激光直接烧灼肿瘤周围的黏膜组织，以实现肿瘤的完全剥离。尽管目前关于钬激光碎石过程中误击输尿管导致术后输尿管狭窄的数据仍然缺乏，但既往文献结果显示上尿路上皮肿瘤在接受激光治疗后，输尿管狭窄的并发症发生率最高可达 28.8%[11]，从而提示钬激光对输尿管黏膜直接烧灼可能会增加输尿管狭窄风险。本研究主要是建立钬激光对组织直接切割损伤的模型，为高度模拟临床钬激光碎石过程中误击输尿管的情况，本研究设置瞬时烧灼时间为 1 s，结果显示在钬激光烧灼处理部位输尿管狭窄的发生率高达 64.6%，重度狭窄发生率高达 8.3%。这一结果显示了钬激光对组织的直接损伤作用，而这方面在既往文献中较少被深入探讨。

钬激光的功率和能量设置是输尿管镜腔内碎石手术中的关键参数，术者根据结石的具体情况选择不同的参数以达到最佳的碎石效果。然而，钬激光不同能量参数对输尿管接触性损伤的影响尚未见相关文献报道。本研究结果表明，在相同钬激光功率设置下，钬激光的频率及脉冲长度对输尿管狭窄的

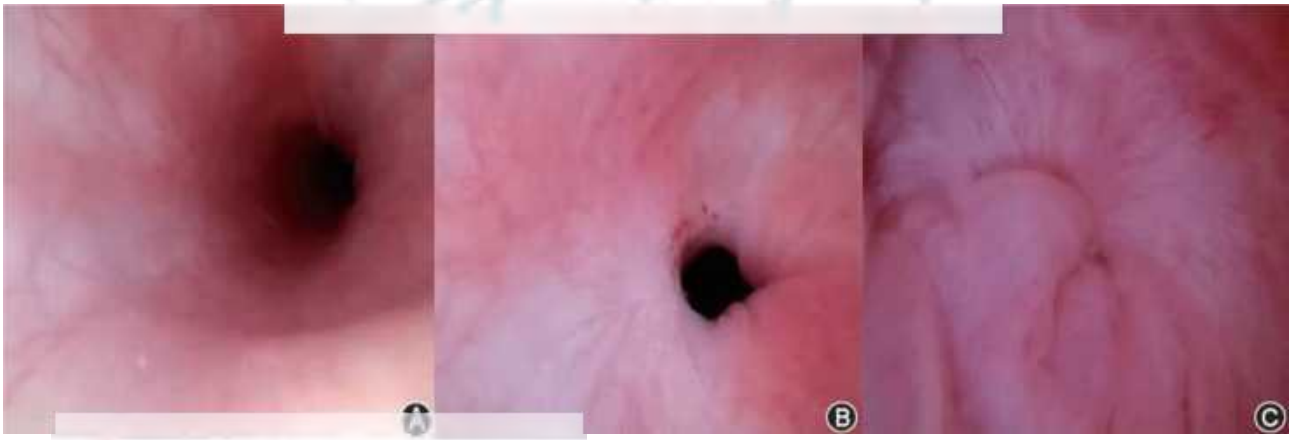


图 1　实验猪予钬激光瞬时切割输尿管损伤术后 4 个月输尿管软镜检查图像　A. 输尿管无狭窄，管腔通畅；B. 输尿管管腔轻度狭窄；C. 输尿管管腔完全闭锁

发生率、组织病理损伤及纤维化程度无显著影响。这一发现提示，在钬激光碎石术中，单纯通过调整频率和脉冲长度可能无法减少钬激光对输尿管组织的损伤。因此，术中采取各种策略避免钬激光误伤输尿管可能是降低输尿管狭窄的重要手段。目前关于钬激光功率及能量设置对输尿管损伤的研究主要集中在能量释放后局部温度升高的相关研究。已有研究结果表明，钬激光功率过高会增加肾脏热损伤的风险；当温度超过43℃时，高温导致的细胞毒性效应呈指数增加[12]。已有文献证实，高功率钬激光会导致局部温度迅速上升；但在低功率状态下，累积能量的发射也可能导致局部温度超过安全范围[13-14]。此外，脉冲模式对能量释放也有影响，长脉冲较短脉冲可能导致局部温度更高[15]。在本研究中，钬激光对输尿管进行瞬时切割，且在切割过程中保持输尿管软镜的正常灌注，因此，温度升高导致输尿管损伤的概率较小。

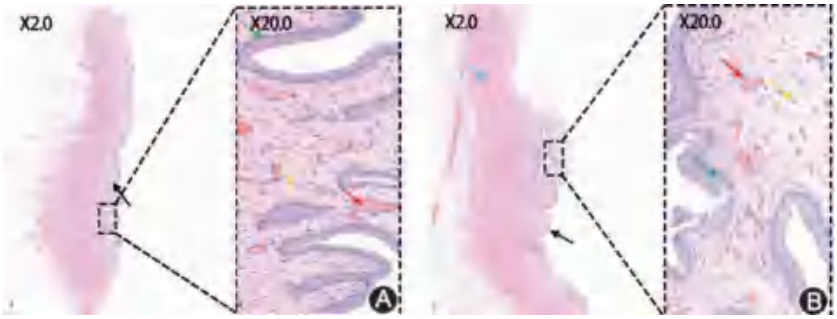


图 2　实验猪予钬激光瞬时切割输尿管后不同程度输尿管狭窄的组织学特征（HE 染色）A. 轻度狭窄段组织 HE 染色示，组织局部可见黏膜上皮细胞缺失（黑色箭头所示），较多上皮细胞肿胀，胞质疏松或呈空泡状（绿色箭头所示），固有层及肌层水肿，结缔组织排列疏松，肌纤维间隙增宽，较多血管淤血（红色箭头所示），并可见较多炎症细胞浸润（黄色箭头所示）；B. 重度狭窄段组织 HE 染色示，黏膜上皮细胞缺失（黑色箭头所示），较多上皮细胞肿胀，胞质疏松或呈空泡状（绿色箭头所示），固有层及肌层水肿，结缔组织排列疏松，肌纤维间隙增宽，较多血管淤血（红色箭头所示），并可见少量炎症细胞浸润（黄色箭头所示），肌层肌纤维消失，被大量增生的结缔组织取代（蓝色箭头所示）

钬激光的热效应对组织的损伤不仅包括温度升高的直接影响，还包括对光纤周围输尿管组织的广泛伤害。Ho 等[16]的研究结果显示，在热损伤的输尿管中，平滑肌消失，尿路上皮增生，周围软组织厚度增加，导致输尿管蠕动功能减弱，加重输尿管梗阻症状，进一步损害患肾功能。本研究得出类似的病理结果：当输尿管狭窄程度较轻时，主要表现为黏膜上皮坏死、脱落和缺失，受累输尿管的固有层常伴有炎症细胞浸润。随着狭窄的进展，固有层出现水肿，胶原纤维溶解，肌层平滑肌细胞开始出现坏死和溶解等病理改变。

尽管本研究提供了钬激光能量参数对输尿管损伤及纤维化影响的有价值数据，但仍存在局限性。首先，样本量较小，仅包括 10 头白雌猪，最终纳入分析的仅有 6 头，可能限制了结果的普遍性和统计学显著性。其次，本研究仅探讨了 10 W 功率下的不同频率和脉冲长度设置，未涉及其他能量水平。不同能量水平的钬激光可能对组织损伤和纤维化有不同影响，因此，未来研究应考虑更广泛的能量参数范围，以全面评估钬激光的效应。

综上所述，本研究建立了钬激光对输尿管瞬时切割的动物模型，结果显示即使在低功率设置下，钬激光的瞬时切割仍会导致较高的输尿管狭窄发生率，且部分病例出现重度狭窄。调整钬激光的频率及脉冲长度并未改善输尿管狭窄的发生率及组织纤维化的程度。因此，在进行输尿管镜钬激光碎石手术时，避免激光对输尿管组织的直接击打对于预防输尿管狭窄具有重要意义。

利益冲突　所有作者声明无利益冲突

作者贡献说明　彭泳涵：课题设计、论文撰写；李超、董浩：数据采集处理、图像采集；高小峰：研究指导、论文修改

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（以上名单全部按姓氏汉语拼音排序）

Turning up the HEAT

Surgical simulation of the Moses 2.0 laser in an anatomic model

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ABSTRACT

INTRODUCTION: With advancements in laser technology, urologists have been able to treat urinary calculi more efficiently by increasing the energy delivered to the stone. With increases in power used, there is an increase in temperatures generated during laser lithotripsy. The aim of this study was to evaluate the thermal dose and temperatures generated with four laser settings at a standardized power in a high-fidelity, anatomic model.

METHODS: Using high-fidelity, 3D-printed hydrogel models of a pelvicalyceal collecting system with a synthetic BegoStone implanted in the renal pelvis, surgical simulation of ureteroscopic laser lithotripsy was performed with the Moses 2.0 holmium laser. At a standard power (40 W) and irrigation pressure (100 cm H_2O), we evaluated operator duty cycle (ODC) variations with different time-on intervals at four different laser settings. Temperature was measured at two separate locations: at the stone and ureteropelvic junction.

RESULTS: Greater cumulative thermal doses and maximal temperatures were achieved with greater ODCs and longer laser activation periods. There were statistically significant differences between the thermal doses and temperature profiles of the laser settings evaluated. Temperatures were greater closer to the tip of the laser fiber.

CONCLUSIONS: Laser energy and frequency play an important role in the thermal loads delivered during laser lithotripsy. Urologists must perform laser lithotripsy cautiously when aggressively treating large renal pelvis stones, as dangerous temperatures can be reached. To reduce the risk of causing thermal tissue injury, urologists should consider reducing their ODC and laser-on time.

INTRODUCTION

Advancements in laser technology have allowed urologists to safely treat urolithiasis endoscopically for years. The holmium:yttrium-aluminum-garnet (Ho:YAG) laser has been accepted as a standard lithotripsy laser due to its ability to pulverize stones of many compositions.[1] With the increasing prevalence of high-powered lasers (≥100 W), more urologists have been utilizing this technology as they can deliver energy at higher frequencies (>120 Hz), leading to improved stone ablation efficiency and decreased operative time;[2] however, with increased power, there is increased heat generated. With this in mind, it is important to preserve patient safety while determining the most efficient method of stone ablation.

Lasers can be used for calculus ablation because the stone is able to absorb the emitted laser energy leading to stone fragmentation and melting; thus, temperature and thermal dose have been studied extensively. Thermal dose was first described by Sapareto and Dewey; it is the cumulative equivalent minutes, held at 43°C (TD_{43}), and is a standard measure for tissue denaturation occurring when TD_{43} ≥120 equivalent minutes.[3-5] Previously this lab, along with others, have attempted to study thermal loads during ureteroscopic (URS) laser lithotripsy.

The majority of these studies have been performed in low-fidelity in-vitro models consisting of test tubes or syringes or with ex-vivo porcine kidney models. The weakness of the

KEY MESSAGES

- The time to TD_{43} was generally faster at the stone.
- Temperatures and cumulative thermal doses were greater closer to the laser fiber tip.
- Longer laser-on times yielded greater cumulative thermal doses, while shorter laser-off intervals reached the TD_{43} faster.
- ODCs of ≥75% reached the threshold of thermal injury.

in-vitro models is that they may not accurately simulate surgical conditions. Conversely, while ex-vivo models may be the closest simulation to surgery, animal models encompass financial and ethical dilemmas.

The goal of our study was to improve upon and confirm our prior studies, using a validated high-fidelity anatomic human kidney model.[6] Using image segmentation, 3D printing, and hydrogel casting, a model inclusive of a complete pelvicalyceal collecting system (PCS) with a ureteral access sheath (UAS) simulating the full-length ureter and incorporating a 2 cm BegoStone was fabricated. This model was then submerged in a water bath maintained at 37°C.

The aims of this study were to:

1. Evaluate the temperature profile of the Moses 2.0 Ho:YAG laser at the stone and ureteropelvic junction (UPJ) for four different 40 W laser settings (two fragmentation and two dusting) using three operator duty cycles (ODCs).
2. Evaluate and compare time to TD_{43} for each laser setting.

METHODS

Simulation model fabrication

Digital Imaging and Communications in Medicine (DICOM) data from a patient's CT scan was segmented into a 3D computer-aided design (CAD) model using Mimics software (Materialize, Leuven, Belgium). The 3D CAD model (including the PCS/ureter) was 3D-printed using hydrogel filament (Fusion3 Design, Greensboro, NC) with a synthetic BegoStone (prepared with 10:1 powder to water ratio by weight) positioned in the renal pelvis and coated with a second polyvinyl alcohol (PVA) mixture (Figures 1A & B). This was then implanted into a hydrogel kidney block. The model was submerged in a warm water bath at anatomic temperature (starting temperature 37.0°C +/- 2.0°C); the water was circulated using a sous vide precision cooker (Anova Applied Electronics, San Fransisco, CA). The final product underwent extensive mechanical and computational fluid dynamic (CFD) testing to replicate PCS properties, stone lithotripsy, and fluid flow (Figures 1C & D).

Laser lithotripsy

URS laser lithotripsy was performed at a standardized power (40 W, short pulse width, Moses Technology activated) with continuous normal saline irrigation (17.5 ml/min) via retrograde access with a flexible ureteroscope (LithoVue, Boston Scientific, Marlborough, MA, U.S.) and a 200 µm Ho:YAG laser fiber (Moses 2.0, Boston Scientific, Marlborough, MA, U.S.) (Figure 2).

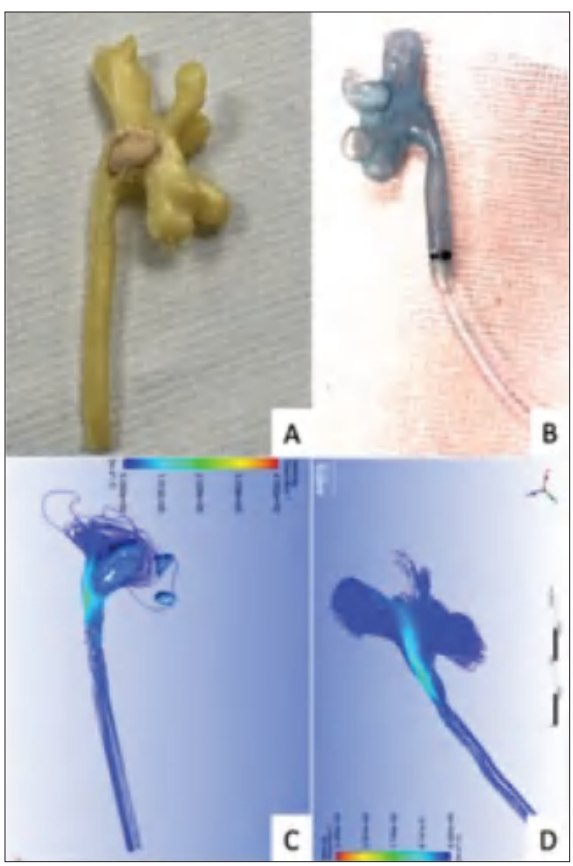


Figure 1. (A) 3D printed PVA PCS model with embedded BegoStone before coating with hydrogel. (B) Final hydrogel PCS model with drainage tubing secured acting as UPJ (stone inside model, unable to be visualized). (C&D) CFD testing of the model at 100 cm H_2O. CFD: computational fluid dynamic; PCS: pelvicalyceal collecting system; PVA: polyvinyl alcohol; UPJ: ureteropelvic junction.

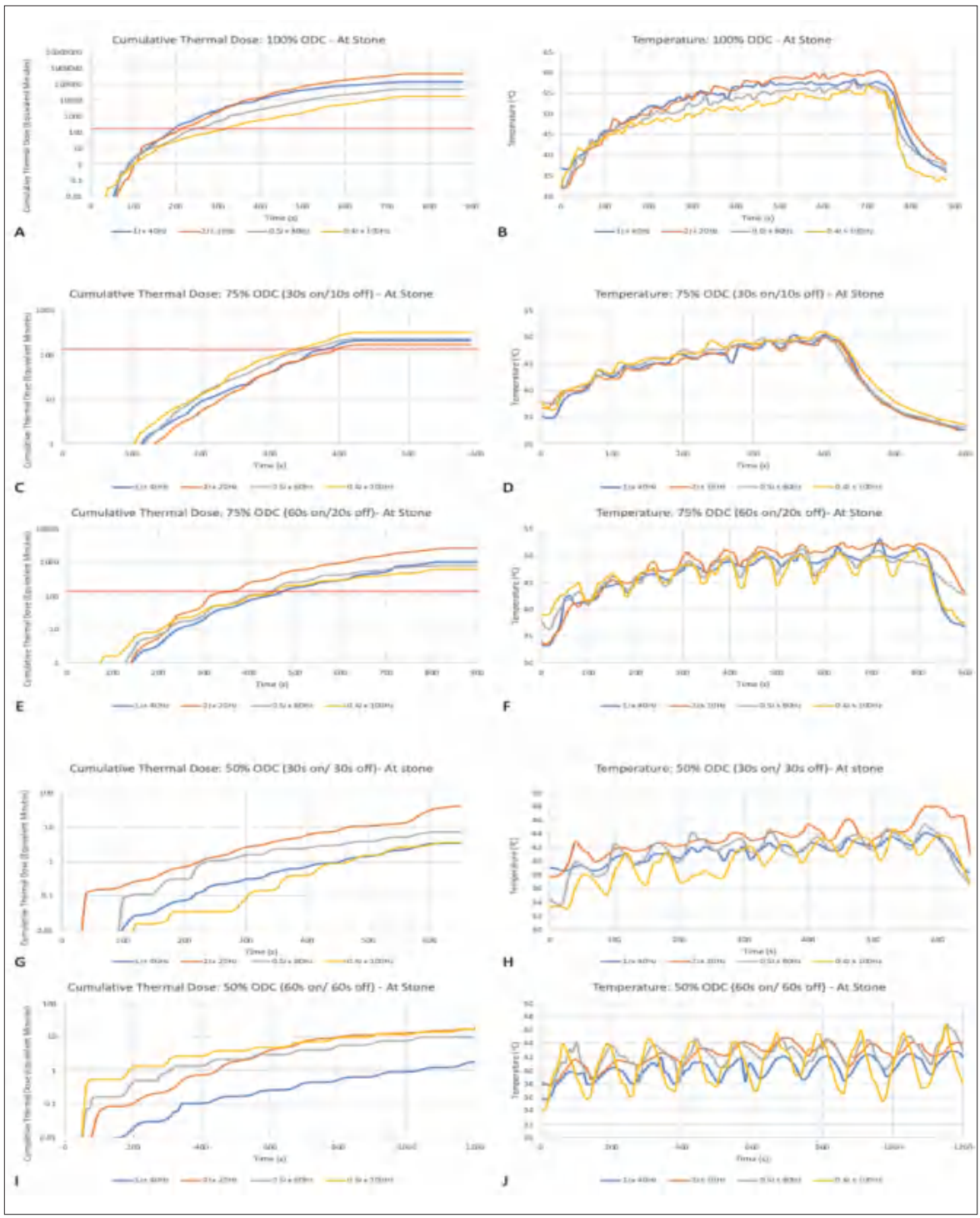


Figure 2. Temperature and thermal dose graphs of each laser setting at the stone. TD43 (solid red line) is on the thermal dose graphs. 100% operator duty cycle (ODC). (A) thermal dose; (B) temperature. 75% ODC: 30 seconds on/10 seconds off; (C) thermal dose and (D) temperature 60 seconds on/20 seconds off; (E) thermal dose and (F) temperature 50% ODC: 30 seconds on/30 seconds off; (G) thermal dose and (H) temperature 60 seconds on/60 seconds off; (I) thermal dose; and (J) temperature.

Table 1. Comparison of cumulative thermal dose, time to TD43, and statistical comparison at the stone vs. UPJ

Laser setting	ODC	Time on (s)/ time off (s)	Cumulative thermal dose (CEM)		Time to thermal injury threshold (s)		p at vs. away from stone
			At stone	Away from stone	At stone	Away from stone	
1 J x 40 Hz	100%		**93909.8907**	**134501.2717**	**200**	**195**	<0.0001
	75%	30/10	**221.6387713**	**206.1101383**	**380**	**370**	<0.0001
		60/20	**1125.62778**	**1025.910058**	**440**	**465**	<0.0001
	50%	30/30	3.569467179	3.071237613	NR	NR	<0.0001
		60/60	3.233970832	1.882688132	NR	NR	<0.0001
2 J x 20 Hz	100%		**318276.667**	**449089.338**	**195**	**205**	<0.0001
	75%	30/10	**187.32621**	**169.9063665**	**395**	**395**	0.0004
		60/20	**3398.569694**	**2690.290273**	**325**	**330**	<0.0001
	50%	30/30	51.75861439	39.50125173	NR	NR	<0.0001
		60/60	24.86021107	18.09596256	NR	NR	<0.0001
0.5 J x 80 Hz	100%		**62134.7335**	**51936.32456**	**230**	**230**	<0.0001
	75%	30/10	**344.6057609**	**228.1060048**	**320**	**350**	<0.0001
		60/20	**1253.588927**	**788.0238063**	**395**	**435**	<0.0001
	50%	30/30	11.20336357	7.050187058	NR	NR	<0.0001
		60/60	23.62071365	9.677738417	NR	NR	<0.0001
0.4 J x 100 Hz	100%		**18045.01532**	**8502.241086**	**295**	**315**	<0.0001
	75%	30/10	**316.2694821**	**242.2321829**	**330**	**380**	<0.0001
		60/20	**739.8320632**	**627.1075826**	**410**	**450**	<0.0001
	50%	30/30	3.071237613	3.569467179	NR	NR	<0.0001
		60/60	18.93383935	17.0028632	NR	NR	<0.0001

Bolded cells indicate tests that exceeded threshold of thermal injury. NR indicates that the threshold of thermal injury was not reached. Statistics comparing cumulative thermal dose and calculated with Kruskal-Wallis. UPJ: ureteropelvic junction.

A 12/14 Fr, 40 cm UAS was inserted just distal to the UPJ to simulate a complete ureteral length. Four laser settings – two fragmentation (1 J x 40 Hz and 2 J x 20 Hz) and two dusting (0.5 J x 80 Hz, 0.4 J x 100 Hz) were tested. We evaluated 3 ODCs (50, 75, and 100%) with different laser-on (30, 60, and 120 s) times. Each experiment consisted of 10 cycles (1 cycle = 1 laser-on/laser-off sequence = 1 ODC); the 100% ODC consisted of pedal-on time of 12 minutes straight with no laser-off time. Five permutations of each laser setting were tested. A total of 20 experiments were performed. Temperature was measured continuously with data analysis performed in 10-second intervals.

Data collection and analysis

Temperature was recorded with K-type needle thermocouple probes and data logger (Omega, Norwalk, CT) at two standard positions (registered in the model) in the PCS – at the stone (renal pelvis) and UPJ. Additionally, a third temperature probe was inserted into the hydrogel block. Thermal dose was calculated with the Sapareto and Dewey formula. Statistical analysis for thermal dose was analyzed via area under the curve (AUC) and Kruskal-Wallis comparison and temperature data was analyzed via non-linear regression in a third-order polynomial (Prism 9). $P<0.05$ was considered statistically significant.

RESULTS

When evaluating the cumulative thermal dose, it was found to be higher *at the stone* than at the UPJ for each laser setting tested. There was a statistically significant difference between cumulative thermal dose at the stone and UPJ for each laser setting tested (Table 1).

Table 2. Comparison of maximal temperature, and statistical comparison at the stone vs. UPJ

Laser setting	ODC	Time on (s)/ time off (s)	Maximum temperature (ºC)		p at vs. away from stone
			At stone	Away from stone	
1 J x 40 Hz	100%		**58.5**	**58.2**	<0.0001
	75%	30/10	**50.4**	**50.2**	<0.0001
		60/20	**52.9**	**51.6**	0.1618
	50%	30/30	44.1	43.1	0.0018
		60/60	42.8	43.3	0.1187
2 J x 20 Hz	100%		**60.5**	**59.9**	<0.0001
	75%	30/10	**50.1**	**50.1**	<0.0001
		60/20	**52.4**	**52.7**	0.0224
	50%	30/30	47.9	48.8	0.1638
		60/60	44.8	45.3	0.0301
0.5 J x 80 Hz	100%		**57.8**	**57.6**	<0.0001
	75%	30/10	**49.9**	**50.8**	<0.0001
		60/20	**51.2**	**52.1**	0.0014
	50%	30/30	45.2	44.4	<0.0001
		60/60	46.9	45.1	<0.0001
0.4 J x 100 Hz	100%		**56.7**	**55.3**	<0.0001
	75%	30/10	**50.8**	**49.9**	<0.0001
		60/20	**51.4**	**51.0**	<0.0001
	50%	30/30	44.4	43.8	<0.0001
		60/60	46.7	45.2	<0.0001

Bolded cells indicate tests that exceeded threshold of thermal injury. Statistics comparing temperature curves and calculated with non-linear regression in a third-order polynomial. UPJ: ureteropelvic junction.

The threshold of thermal injury was reached for the 100 and 75% ODCs both at the stone and UPJ but was not reached in any 50% ODC. The threshold of thermal injury was reached faster for 100% ODC than either of the 75% ODC time intervals. For the 75% ODCs, the 30 seconds on/10 seconds off time interval reached the threshold faster for all laser settings tested, except for 2 J x 20 Hz, where the 60 seconds on/20 seconds off interval was faster. The time to reach the threshold of thermal injury was typically faster at the stone compared to the UPJ except for 1 J x 40 Hz (100% ODC, 30 seconds on/10 seconds off), where the UPJ reached the threshold faster; while for 2 J x 20 Hz (30 seconds on/10 seconds off) and 0.5 J x 80 Hz (100% ODC) the threshold was reached at approximately the same time (Table 1).

The cumulative thermal dose was greater for each laser setting with greater ODCs both at the stone and UPJ. 2 J x 20 Hz delivered the greatest cumulative thermal dose for each time interval tested except for 30 seconds on/10 seconds off, where it delivered the lowest cumulative thermal dose. There was no other generalizable pattern appreciated between the laser settings otherwise when compared against one another (Tables 1 and 2).

Considering maximal temperatures at the stone vs. UPJ, the temperatures were higher at the stone in 13/20 tests, higher at the UPJ in 6/20 tests, and in one test, the maximal temperature was the same (2 J x 20 Hz, 30 seconds on/10 seconds off). There was a statistically significant difference in the temperature curves for all but three tests (1 J x 40 Hz – 60 seconds on/20 seconds off and 60 seconds on/60 seconds off, 2 J x 20 Hz – 30 seconds on/30 seconds off). Temperatures were hotter with greater ODCs for each laser setting both at the stone and at the UPJ. Considering the 75% ODCs, hotter maximal temperatures were recorded with a longer laser-on time (60 seconds on/20 seconds off) for each laser setting both at the stone and at the UPJ. Considering the 50% ODCs, there were mixed results as to which laser time-on cycle generated hotter maximal temperatures; for the fragmentation settings, the 30 seconds on/30 seconds off cycle yielded hotter temperatures, while for the dusting settings, the 60 seconds on/60 seconds off cycle was hotter. This held true both at the stone and at the UPJ (Table 2).

While there was not an apparent trend as to which laser setting produced the hottest temperatures, we did appreciate statistically significant differences between laser settings which demonstrates that frequency and energy can strongly influence temperature and thermal dose, even at a standardized power. For 100% ODC, 2 J x 20 Hz was hottest at the stone and UPJ, while 0.4 J x 100 Hz was the lowest for both. For the other 4 ODC/time-on intervals evaluated, there was no overall trend (Tables 1 and 2).

Temperatures of the hydrogel block started at 37.0°C +/- 2.1°C and increased 1.0°C +/- 2.0°C. There were no statistically significant changes in temperature measured at this location. It was observed that the temperatures increased slightly more when the starting temperature was lower (<37°C) opposed to a minimal temperature fluctuation at higher starting temperatures (≥37°C).

DISCUSSION

In this study, we were able to establish that temperatures and cumulative thermal doses were greater closer to the tip of the last fiber, which has also been recognized in previous studies.[7] Additionally, we demonstrated that energy and frequency play a significant role in the thermal load delivered, and the previously accepted concept that power is the sole determinant of temperature may not be entirely accurate.[5, 8-10] In general, greater thermal doses and maximal temperatures were achieved with greater ODCs and longer laser-on times for 100% and 75% ODCs, which is in agreement with previously published literature.[11,12] When comparing laser-on times for 75% ODC, 60 seconds on/20 seconds off delivered greater cumulative thermal doses and maximal temperatures for each laser setting both at the stone and UPJ.

Interestingly, when evaluating 50% ODCs, the fragmentation settings delivered greater cumulative thermal doses for shorter laser-on time (30 seconds on/30 seconds off) while the dusting settings delivered greater cumulative thermal doses for the longer laser-on time (60 seconds on/60 seconds off). When considering maximal temperatures, the same results held true, except for 1 J x 40 Hz at the UPJ (43.1°C for 30 seconds on/30 seconds off vs. 43.3°C for 60 seconds on/60 seconds off). This shows that the laser-off time may play a crucial role in fluid cool-down, as the longer the laser is off, the greater the opportunity that the fresh irrigation inflow can cool more of the PCS.

There have been numerous studies manipulating variables involved during URS laser lithotripsy. Dr. William Robert's laboratory at the University of Michigan has led many studies via in-vitro bench models and computational modelling. They have evaluated the Ho:YAG laser power (2.5–50 W), frequency (5–80 Hz), irrigation rate (0–40 ml/min), irrigation temperature (~0°C and 19°C), and ODC (≥50%).[4,5,11-14] Their work sought to adapt their previous findings to an in-vivo porcine model and found that temperatures capable of tissue damage were easily achieved but can be negated by increasing irrigation flow rate.[15] Other labs have also evaluated irrigation rates and have determined that increased irrigation rates can mitigate temperature increases during active lasing, as too can the use of a UAS.[16-18]

A recent study evaluated intraoperative irrigation fluid temperatures during URS treatment of urolithiasis. They compared laser settings of 1 J x 20 Hz and 0.5 J x 20 Hz with irrigation rates of 0 ml/min, 15 ml/min, and 30 ml/min. They found that with irrigation rates of 15 ml/min and 30 ml/min, a temperature of 43°C was not reached after 60 seconds straight of laser activation.[19] Our study used a UAS with a constant irrigation flow (100 cm H_2O=17.5 ml/min). We found that at a constant power, the threshold of thermal injury could be reached in as little as 195 seconds (2 J x 20 Hz at the stone and 1 J x 40 Hz at the UPJ). While there was a significant difference in power tested between Teng, et. al's study and ours, it is obvious that when treating larger stone burdens, urologists must be diligent when continuously lasing as temperatures can reach dangerous levels, even with UAS use.

It is important to consider that in this study, we were lasing a large calculus in the renal pelvis where there is more volume/area for fluid and irrigation flow. Previous studies have demonstrated that when lasing in smaller spaces, temperatures increased faster, and the threshold of thermal injury could be reached faster when compared to larger spaces.[20,21] In agreement with our prior evaluations and previous studies, the threshold of thermal injury was reached during ODCs greater than 70%.[11] This held true regardless of the laser settings tested and for laser-on time. Aldoukhi, et. al. performed a chart review of 63 URS cases and determined that during the 60 seconds of greatest power delivered, the ODC was 63%.[12]

Although studies have demonstrated that ODCs <70% are less likely to cross the threshold of thermal injury, it is important to consider that more powerful laser settings can deliver greater thermal loads in shorter amounts of time and with shorter ODCs. Additionally, when lasing in tighter spaces, such as a calyx opposed to the renal pelvis, it is reasonable to believe that the threshold of thermal injury could be reached even with lower ODCs or less powerful laser settings, particularly after a stone is broken; as the laser tip may be closer to the urothelium with no interruption from a stone, and it is not absorbing energy once pulverized. In an in-vitro model, it was found that the presence of a phantom BegoStone was related to lower rises in fluid temperatures when compared with no stone present at an array of powers tested (10, 20, 40, 60 W).[20]

It is recognized that BegoStones may possess distinctive photothermal properties compared with real urolithiasis during laser lithotripsy;[22] however, BegoStones are often accepted as a synthetic analogue for real urolithiasis during in-vitro urologic laser studies since they are able to be composed without significant difficulty in an efficacious manner and are able to be fabricated and reproduced with the same composition.

To date, this appears to be the first study evaluating thermal loads performed in a high-fidelity anatomic in-vitro model at anatomic temperature with a UAS used while actively lasing a phantom stone. Other studies have been performed using ex-vivo and in-vivo models with or without UAS that can simulate the complete ureteral length. It is well recognized that using a UAS can facilitate higher irrigation flow rates and modulate temperature increases more easily, in addition to reducing intrarenal pressures during irrigation.[17,23]

With regards to the power setting evaluated utilizing the Moses 2.0 Ho:YAG laser in this study, 40 W was chosen as the standard because this power allowed for the variation of both frequency and energy settings for four different laser settings — two dusting and two fragmentation — while maintaining constant power. It is recognized that urologists may commonly utilize lower power settings in clinical practice, however, the goal of this study was to evaluate variables besides power, since many previous studies have already compared different power settings.[4,5,13]

This study addressed some of the limitations of our previous studies which had been performed at room temperature. With this experimental model, we evaluated thermal dose and temperatures in the high-fidelity anatomic model performed at anatomic temperature with a UAS. This experimental design appears to be a quality, realistic in-vitro model for URS laser lithotripsy. The majority of previous studies have been performed with in-vitro test tube models or with ex-vivo porcine kidney models.

While we have addressed some limitations of our prior studies, we recognize that some limitations are present in this study. First, although this project was performed in a high-fidelity anatomic PCS model, some caution should be maintained when attempting to correlate this data to a surgical scenario. Second, only one PCS model was used in our evaluations in efforts to further reduce confounding variables influencing our results. Finally, although BegoStone models may simulate actual kidney stones, they may not act as an exact analogue. Our laboratory hopes to continue pursuing urologic laser research in the future, building on this study, and addressing some of these limitations.

This study had several strengths. First, this study evaluated four variables: laser frequency, laser energy, ODC, and laser time-on, in an anatomically correct, high-fidelity model that has been validated with mechanical and CFD testing; but this time, at anatomic temperature with the use of a UAS. Second, we were able to evaluate thermal load in two locations in the PCS. Finally, we were able to measure the temperatures while actively lasing a synthetic 2 cm calculus. The combination of these components into one model while analyzing four separate variables strengthens the results of this study. While prior studies have compared some of these factors affecting irrigation fluid temperature, the majority of these studies focus on fewer variables.

CONCLUSIONS

We were able to validate our previous studies and address several limitations with this experimental model. We confirmed that dangerous thermal loads can be delivered with greater ODCs and longer laser-on times. We demonstrated again that at a standardized power, energy and frequency manipulations can strongly influence thermal dose and temperatures. Based on the results of this study, it is important that urologists perform URS laser lithotripsy diligently, as irrigation fluid temperatures and cumulative thermal doses in the PCS can reach critical levels and potentially cause urothelial injury, regardless of laser setting.

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加大加热

解剖模型中Moses2.0激光器的手术模拟

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摘要

引言：随着激光技术的进步，泌尿科医生通过提高激光能量输送至结石的效率，能够更有效地治疗尿路结石。当激光功率增加时，激光碎石术过程中产生的温度也会随之升高。本研究旨在通过高保真解剖模型，评估在标准化功率条件下，四种不同激光设置所产生的热剂量和温度变化。

实验方法：采用高精度3D打印的肾盂输尿管集合系统水凝胶模型（模型中植入了合成贝戈斯通材料），使用摩西斯2.0钬激光系统进行输尿管镜激光碎石术的手术模拟。在标准功率（40瓦）和灌注压力（100厘米水柱）条件下，我们通过改变四个不同激光参数的开启时间间隔，评估了操作者工作循环（odC）的变化情况。温度测量在结石部位和输尿管肾盂连接处两个不同位置进行。

结果表明：随着臭氧浓度（odCs）的增加和激光激活时间的延长，累积热剂量和最高温度均显著升高。不同激光参数设置的热剂量和温度分布存在统计学显著差异，且激光光纤尖端附近的温度值更高。

结论：激光能量与频率在激光碎石术中对热负荷影响显著。泌尿科医生在对大型肾盂结石进行激进治疗时需格外谨慎，因可能产生危险温度。为降低热损伤风险，建议缩短激光脉冲宽度（odC）和激光持续时间。

介绍

激光技术的进步使泌尿科医生能够安全地通过内窥镜治疗尿路结石已有多年。钬钇铝石榴石（Ho：YAG）激光因其能粉碎多种成分的结石而被公认为标准碎石激光器。[1]随着高功率激光（>100W）的普及，越来越多的泌尿科医生开始采用这项技术，因为它们能以更高频率（>120 Hz）输送能量，从而提高结石消融效率并缩短手术时间；[2]但功率提升也带来了热量增加的问题。因此，在确定最有效的结石消融方法时，确保患者安全至关重要。

激光可应用于结石消融治疗，因其能有效吸收激光能量，促使结石碎裂并最终熔化。因此，温度与热剂量的研究已相当深入。热剂量最早由萨帕雷托和杜威提出，其定义为在43 ℃环境下保持的累积等效分钟数（td_{43}），该指标是衡量组织变性的标准参数，当td_{43}超过120等效分钟时即达到变性阈值。[3-5]此前本实验室联合多家机构，已着手研究输尿管镜（Urs）激光碎石术中的热负荷问题。

这些研究大多采用低保真度的体外模型，包括试管、注射器或离体猪肾模型。该模型的缺陷在于

重要消息

石头上的td时间$_{43}$通常更快。

■温度和累积热剂量在靠近激光光纤尖端处更大。

更长的激光开启时间产生更大的累积热剂量，而较短的激光关闭时间达到td $_{43}$更快。

■odCs ≥ 75%达到热损伤阈值。

体外模型的局限在于其无法准确模拟手术环境。而体外模型虽最接近真实手术，但动物模型却存在伦理与经济层面的双重困境。

本研究旨在通过采用经过验证的人体解剖肾脏高保真模型，改进并验证我们先前的研究成果。[6]我们运用图像分割、3D打印和水凝胶铸造技术，成功构建了一个包含完整肾盂肾盏集合系统（PCs）的模型，该模型配备模拟全长输尿管的输尿管套管（UAs），并内置2厘米长的贝戈斯通假体。随后将该模型浸入37 ℃恒温水浴中进行实验。

本研究旨在：

1.评估摩西的温度分布

2.0号手术刀：采用银离子激光对结石及输尿管肾盂连接处（UPJ）进行治疗，设置四种40瓦激光功率（含两种碎石模式和两种碎粉模式），并配合三种不同工作模式（odCs）。

2.评估和比较$_{43}$每个激光设置的td时间。

方法

模拟器制造

通过mimics软件（比利时鲁汶Materialize公司）将患者CT扫描的数字医学影像与通信（dICom）数据分割为三维计算机辅助设计（CAD）模型。该三维CAD模型（包含肾盂/输尿管）采用水凝胶线材（Fusion3设计，美国北卡罗来纳州格林斯博罗）进行3D打印，其中合成Begostone材料（按10：1重量比配制的粉末与水混合物）被定位在肾盂区域，并在其表面涂覆第二层聚乙烯醇涂层。

将全氟乙烯（PVA）混合物（图1A和B）植入水凝胶肾脏模型中。随后将模型置于解剖温度（初始温度37.0 ℃± 2.0℃）的温水浴中，使用安诺瓦应用电子公司（美国旧金山）的精密真空低温锅进行水循环。最终产品经过广泛的机械性能和计算流体动力学（CFD）测试，以模拟肾小管特性、结石碎石效果及流体流动状态（图1C和d）。

激光碎石术

采用标准化功率（40 W，短脉冲宽度，激活moses技术）进行Urs激光碎石术，通过逆行通道使用柔性输尿管镜（lithoVue，Boston Scientific，马尔伯勒，马萨诸塞州，美国）和200µm ho：yAg激光光纤（moses 2.0，Boston Scientific，马尔伯勒，马萨诸塞州，美国）进行连续生理盐水冲洗（17.5 ml/min）（图2）。

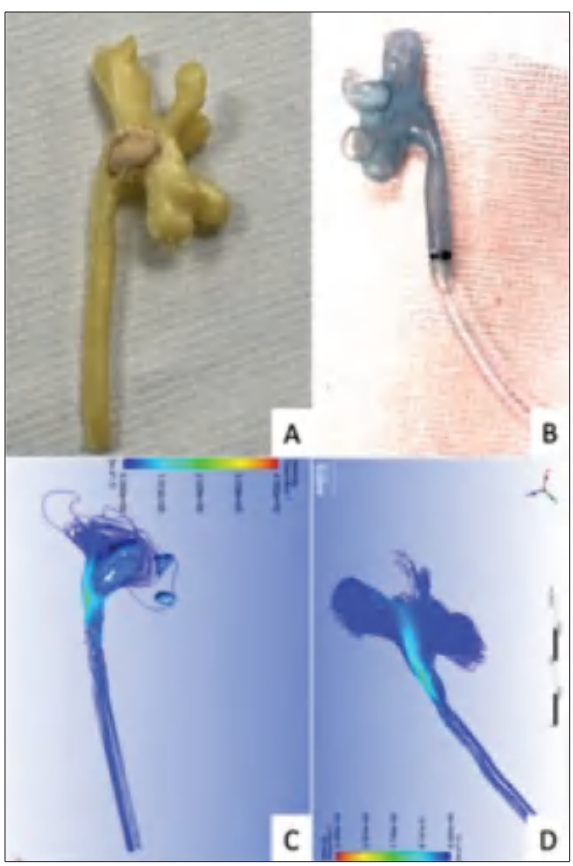


图1.(A)采用3D打印技术制作的PVA肾盂输尿管连接系统模型，内置BegoStone支架，表面未进行水凝胶包覆。(B)最终水凝胶成型的PCS模型，其内置引流管固定连接，可作为输尿管肾盂连接处（UPJ）使用（模型内部结石结构无法显示）。（C&D）该模型在100厘米水柱$_2$氧气环境下的计算流体动力学（CFD）测试。CFD：计算流体动力学；PCS：肾盂输尿管连接系统；PVA：聚乙烯醇；UPJ：输尿管肾盂连接处。

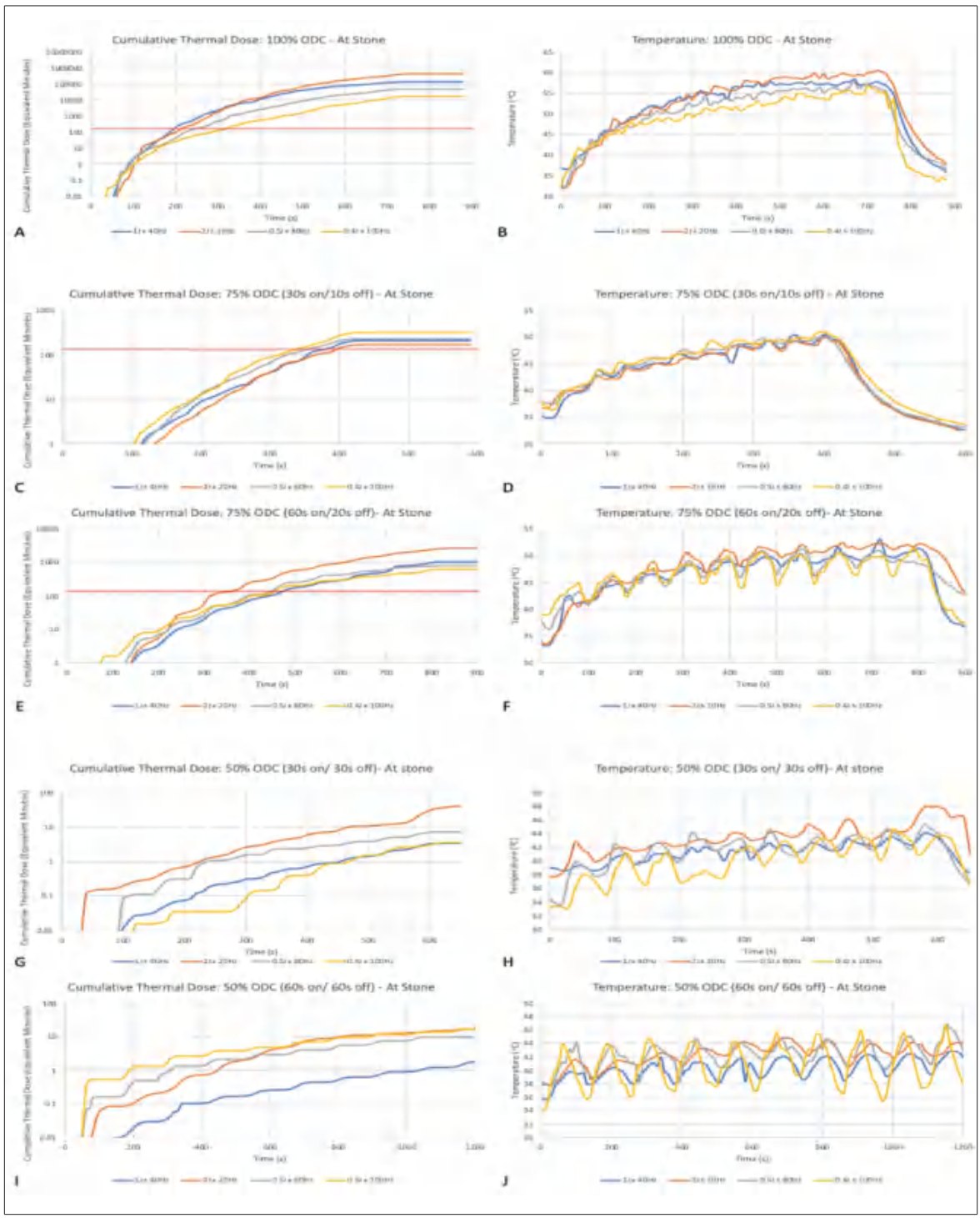


图2.各激光设置在结石处的温度与热剂量曲线。TD43（红色实线）对应热剂量曲线，显示100%操作员工作周期（ODC）。(A)热剂量；(B) 温度。75%ODC：30秒开/10秒关；(C)热剂量与(D)温度；60秒开/20秒关；(E)热剂量与(F)温度；50%ODC：30秒开/30秒关；(G)热剂量与(H)温度；60秒开/60秒关；(I)热剂量；(J)温度。

表1.石块与UPJ在累积热剂量、TD43时间及统计学比较上的对比

激光设置	当氢氟酸残酶	开启时间（秒）/休息时间(s)	累积热剂量（CEM）		热损伤阈值时间(s)		主场与客场石制
			在石头上	远离石头	在石头上	远离石头	
1 J x 40 Hz	100%		**93909.8907**	**134501.2717**	**200**	**195**	<0.0001
	75%	30/10	**221.6387713**	**206.1101383**	**380**	**370**	<0.0001
		60/20	**1125.62778**	**1025.910058**	**440**	**465**	<0.0001
	50%	30/30	3.569467179	3.071237613	编号	编号	<0.0001
		60/60	3.233970832	1.882688132	编号	编号	<0.0001
2 J x 20 Hz	100%		**318276.667**	**449089.338**	**195**	**205**	<0.0001
	75%	30/10	**187.32621**	**169.9063665**	**395**	**395**	0.0004
		60/20	**3398.569694**	**2690.290273**	**325**	**330**	<0.0001
	50%	30/30	51.75861439	39.50125173	编号	编号	<0.0001
		60/60	24.86021107	18.09596256	编号	编号	<0.0001
0.5 J x 80 Hz	100%		**62134.7335**	**51936.32456**	**230**	**230**	<0.0001
	75%	30/10	**344.6057609**	**228.1060048**	**320**	**350**	<0.0001
		60/20	**1253.588927**	**788.0238063**	**395**	**435**	<0.0001
	50%	30/30	11.20336357	7.050187058	编号	编号	<0.0001
		60/60	23.62071365	9.677738417	编号	编号	<0.0001
0.4 J x 100 Hz	100%		**18045.01532**	**8502.241086**	**295**	**315**	<0.0001
	75%	30/10	**316.2694821**	**242.2321829**	**330**	**380**	<0.0001
		60/20	**739.8320632**	**627.1075826**	**410**	**450**	<0.0001
	50%	30/30	3.071237613	3.569467179	编号	编号	<0.0001
		60/60	18.93383935	17.0028632	编号	编号	<0.0001

加粗单元格表示测试结果超过热损伤阈值，NR表示未达到该阈值。统计分析采用Kruskal-Wallis检验，比较累积热剂量。UPJ：输尿管肾盂连接处。

在膀胱颈（UPJ）远端插入12/14 Fr、40厘米的尿道扩张器（UAs）以模拟完整输尿管长度。测试了四种激光设置：两种碎石模式（1焦耳×40赫兹和2焦耳×20赫兹）以及两种碎石粉模式（0.5焦耳×80赫兹、0.4焦耳×100赫兹）。我们评估了三种碎石次数（50、75和100%），分别对应30秒、60秒和120秒的激光开启时间。每个实验包含10个周期（1个周期=1次激光开启/关闭序列=1次碎石次数）；100%碎石次数的实验采用连续12分钟的持续踩踏模式，不包含激光关闭时间。每种激光设置测试了五种组合方式，共进行20次实验。温度数据采用10秒间隔连续监测，并进行数据分析。

数据收集和分析

温度由K型针式热电偶探头与数据记录仪（Omega公司，诺沃克）进行记录。

Ct)在模型中注册的两个标准位置（位于肾盂和UPJ）的PCs区域进行测量。此外，第三个温度探头被插入水凝胶块中。热剂量通过萨帕雷托和杜威公式计算。热剂量的统计分析采用曲线下面积（AUC）和克鲁斯卡尔-沃利斯检验，温度数据则通过Prism 9软件中的三次多项式非线性回归进行分析。P<0.05被视为具有统计学意义。

结果

在评估累积热剂量时，发现*在每个测试激光设置下结石处*的累积热剂量高于UPJ处。在每个测试激光设置下，结石处与UPJ处的累积热剂量之间存在统计学显著性差异（表1）。

表2.石块与UPJ的最高温度及统计学对比

激光设置	当氧酸氢残酶	开启时间（秒）/休息时间(s)	最高温度（ºC）		主场与客场石制
			在石头上	远离石头	
1 J x 40 Hz	100%		**58.5**	**58.2**	<0.0001
	75%	30/10	**50.4**	**50.2**	<0.0001
		60/20	**52.9**	**51.6**	0.1618
	50%	30/30	44.1	43.1	0.0018
		60/60	42.8	43.3	0.1187
2 J x 20 Hz	100%		**60.5**	**59.9**	<0.0001
	75%	30/10	**50.1**	**50.1**	<0.0001
		60/20	**52.4**	**52.7**	0.0224
	50%	30/30	47.9	48.8	0.1638
		60/60	44.8	45.3	0.0301
0.5 J x 80 Hz	100%		**57.8**	**57.6**	<0.0001
	75%	30/10	**49.9**	**50.8**	<0.0001
		60/20	**51.2**	**52.1**	0.0014
	50%	30/30	45.2	44.4	<0.0001
		60/60	46.9	45.1	<0.0001
0.4 J x 100 Hz	100%		**56.7**	**55.3**	<0.0001
	75%	30/10	**50.8**	**49.9**	<0.0001
		60/20	**51.4**	**51.0**	<0.0001
	50%	30/30	44.4	43.8	<0.0001
		60/60	46.7	45.2	<0.0001

加粗单元格表示温度超过热损伤阈值的测试结果。温度曲线的统计分析采用非线性回归方法，通过三次多项式进行计算。UPJ：肾盂输尿管移行部

在结石和UPJ条件下，100%和75%的odC均达到了热损伤阈值，而50%的odC则未达到该阈值。相较于75%的odC时间间隔，100%的odC达到热损伤阈值的速度更快。对于75%的odC，除2焦耳×20赫兹设置外，所有测试激光参数中30秒开/10秒关的时间间隔都更快达到阈值，但2焦耳×20赫兹设置中60秒开/20秒关的时间间隔更快。除1焦耳×40赫兹（100%odC，30秒开/10秒关）外，结石部位达到热损伤阈值的时间通常比UPJ更快；而2焦耳×20赫兹（30秒开/10秒关）和0.5焦耳×80赫兹（100%odC）的阈值达到时间基本相同（见表1）。

随着激光设置的增强，结石部位和UPJ区域的累积热剂量均呈现上升趋势。在所有测试时间间隔中，2 J x 20 Hz的激光设置累积热剂量最高，但30秒开/10秒关的设置却最低。除上述差异外，其他激光设置间未发现其他具有普遍性的规律（参见表1和表2）。

在石料与UPJ设备的最高温度对比中，13/20次测试显示石料温度更高，6/20次测试显示UPJ温度更高，仅有一项测试（2焦耳×20赫兹，30秒开/10秒关）的最高温度相同。除三项测试外（1焦耳×40赫兹——60秒开/20秒关和60秒开/60秒关，2焦耳×20赫兹——30秒开/30秒关），其余测试的温度曲线均存在统计学显著差异。在石料和UPJ设备中，各激光设置的光密度值（odCs）越大，温度越高。以75%光密度值为基准，各激光设置的激光开启时间越长（60秒开/20秒关），石料和UPJ设备的最高温度均更高。以50%光密度值为基准，不同激光开启周期对最高温度的影响结果存在差异：碎石模式下30秒开/30秒关周期温度更高，而除尘模式下60秒开/60秒关周期温度更高。这一规律在石料和UPJ设备中均成立（表2）。

虽然不同激光设置产生的最高温度没有明显趋势，但我们确实观察到统计学意义上的显著差异，这表明即使在标准化功率下，频率和能量仍能显著影响温度和热剂量。对于100%臭氧浓度（odC），2焦耳×20赫兹的设置在结石和UPJ部位温度最高，而0.4焦耳×100赫兹的设置在这两个部位温度最低。对于其他4种臭氧浓度/持续时间组合，整体上未发现明显趋势（见表1和表2）。

水凝胶块的温度起始值为$^{37.0°C \pm 2.1°C}$，并以$^{1.0°C \pm 2.0°C}$的速率持续升高。该位置测得的温度未出现统计学显著变化。观察发现，当起始温度较低（$^{<37°C}$）时温度升高幅度略大，而当起始温度较高（>37 ℃）时温度波动幅度最小。

讨论

本研究证实，温度和累积热剂量在靠近最后一根光纤尖端的位置更高，这一发现与既往研究结果一致。[7]此外，我们证明能量和频率对热负荷具有显著影响，而传统观点认为功率是决定温度的唯一因素可能并不完全准确。[5,8-10]总体而言，当使用100%和75%的光密度时，光密度越高、激光开启时间越长，累积热剂量和最高温度就越高，这与已发表文献的结论一致。[11,12]在比较75%光密度的激光开启时间时，60秒开启/20秒关闭的模式在结石和UPJ部位的每个激光设置中，都能产生更高的累积热剂量和最高温度。

有趣的是，在评估50%臭氧浓度时，碎裂模式设置在较短激光开启时间（30秒开/30秒关）下能产生更高累积热剂量，而粉尘模式设置在较长激光开启时间（60秒开/60秒关）下则表现出更高累积热剂量。在考虑最高温度时，除UPJ模式下1焦耳×40赫兹的测试结果外（30秒开/30秒关$^{43.1°C}$对比60秒开/60秒关$^{43.3°C}$），其他条件均呈现相同规律。这表明激光关闭时间可能在流体冷却过程中起关键作用——激光关闭时间越长，新鲜灌注液流入冷却更多肺泡细胞的机会就越大。

在Urs激光碎石术中，已有大量研究对相关变量进行了操控。密歇根大学William Robert博士的实验室通过体外实验模型和计算建模开展了多项研究。他们评估了Ho：YAG激光功率（2.5-50 W）、频率（5-80 Hz）、冲洗速率（0-40 ml/min）、冲洗温度（约0 ℃和19 ℃）以及氧浓度（>50%）。[4,5,11-14]他们的研究试图将先前的发现应用于活体猪模型，发现能够造成组织损伤的温度很容易达到，但通过增加冲洗流速可以消除这种温度。[15]其他实验室也评估了冲洗速率，并确定增加冲洗速率可以减轻主动激光期间的温度升高，使用UAs同样可以达到这一效果。[16-18]

最近一项研究评估了在Urs治疗尿路结石期间术中冲洗液温度。他们比较了1 J x 20 Hz和0.5 J x 20 Hz的激光设置与0 ml/min、15 ml/min和30 ml/min的冲洗速率。他们发现，当冲洗速率为在15 ml/min和30 ml/min的条件下，连续60秒激光激活后仍未达到43 ℃的温度。[19]我们的研究使用了恒定灌注流量（100 cm^{-2} h=17.5 ml/min）的尿道成形器。我们发现，在恒定功率下，热损伤阈值最快可在195秒内达到（结石部位2焦耳×20赫兹，UPJ部位1焦耳×40赫兹）。尽管滕等人研究与我们的测试功率存在显著差异，但显然在治疗较大结石负荷时，泌尿科医生在连续激光治疗过程中必须格外谨慎，因为即使使用尿道成形器，温度也可能达到危险水平。

需要特别说明的是，本研究针对的是肾盂内较大的结石，该区域具有更大的容积和面积，有利于液体灌注与冲洗液流动。既往研究表明，相较于较小空间，激光治疗时温度上升更快，热损伤阈值可能更早达到。[20,21]与我们前期评估及既往研究结果一致，当结石占位率超过70%时即达到热损伤阈值。[11]这一结论不受测试的激光参数设置及激光作用时间的影响。Aldoukhi等学者通过对63例尿路结石病例的病历分析发现，在输送最大功率的60秒内，结石占位率可达63%。[12]

尽管研究表明光锥能量（odCs）低于70%时较难突破热损伤阈值，但需注意：高功率激光设备能在更短时间内产生更大热负荷，且光锥能量更低。此外，在膀胱颈与肾盂等狭窄空间进行激光治疗时，即使光锥能量较低或使用功率较小的激光设备，热损伤阈值仍可能被突破——特别是结石破碎后，此时激光尖端可能更接近尿路上皮，且碎石后不再吸收能量。体外实验显示，使用模拟贝戈斯结石时，与未放置结石的对照组相比，不同功率（10、20、40、60瓦）下液体温度升幅均有所降低。[20]

众所周知，与激光碎石术期间真正的尿路结石相比，Begostones可能具有独特的光热特性；[22]但是，在体外泌尿激光研究期间，Begostones通常被接受为真正的尿路结石的合成类似物，因为它们能够以有效的方式不费力地组成，并且能够以相同的组成进行制造和复制。

迄今为止，这似乎是首项在解剖温度条件下，于高保真解剖体外模型中进行热负荷评估的研究，该模型在使用超声导管（UAs）时同步对模拟结石进行激光治疗。其他研究已采用离体和体内模型进行实验，这些模型可模拟完整的输尿管长度，且部分研究使用了超声导管。学界普遍认为，使用超声导管不仅能提高冲洗流速、更精准地调控温度升高，还能有效降低冲洗过程中的肾内压。[17,23]

本研究采用moses2.0ho：yAg激光器评估功率参数时，将40瓦设定为标准功率。该功率值可在保持恒定功率的同时，实现频率与能量参数的四组不同激光模式调整——包含两种碎石模式和两种碎石粉碎模式。尽管泌尿科医生在临床实践中常采用较低功率，但本研究旨在突破单纯功率参数的局限，因为已有大量前期研究对比过不同功率设置的效果。[4,5,13]

本研究针对先前在室温环境下开展的研究存在局限性进行了改进。通过该实验模型，我们评估了在解剖温度条件下使用超声碎石仪（UAs）进行高精度解剖模型时的热剂量与温度参数。该实验设计为熊激光碎石术提供了一个高质量、高真实度的体外模型。值得注意的是，多数先前研究主要采用试管体外模型或离体猪肾模型进行实验。

尽管我们已对前期研究的局限性进行了改进，但本研究仍存在若干不足。首先，虽然本项目采用高精度解剖模型构建肾结石模型，但在将数据与实际手术场景对应时仍需保持审慎态度。其次，为最大限度减少干扰变量对结果的影响，本研究仅采用单一模型进行评估。最后，虽然Begostone模型能模拟真实肾结石，但其模拟效果可能无法完全复现真实病变。本实验室计划在后续研究中继续推进泌尿激光技术领域探索，基于本研究积累的经验，逐步解决上述局限性。

本研究具有多项优势。首先，我们通过解剖学精确的高保真模型（该模型已通过机械测试和CFd测试验证），评估了激光频率、激光能量、odC值及激光持续时间四个参数，且实验环境采用超声波阵列模拟解剖温度。其次，我们成功在人体解剖结构的两个特定部位评估了热负荷。

最终，我们成功实现了对合成2厘米结石进行激光治疗时的温度测量。通过整合这些组件构建单一模型并分析四个独立变量，本研究结果得到显著强化。尽管先前研究已探讨过影响灌注液温度的若干因素，但多数研究仅聚焦于较少变量。

结论

通过该实验模型，我们成功验证了前期研究结果并解决了若干局限性。我们证实，通过增加臭氧浓度和延长激光脉冲时间，可实现更高剂量的热负荷。研究再次表明，在功率、能量和频率标准化条件下，参数调整会显著影响热剂量和温度。本研究结果表明，泌尿科医生必须严格规范进行Urs激光碎石术操作——无论激光参数如何设置，输尿液温度和输尿管膀胱段的累积热剂量都可能达到临界值，进而引发尿路上皮损伤。

利益冲突声明：作者声明与本研究无任何个人或财务利益冲突。

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这篇论文已经过同行评审。

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RESEARCH

Temperature profile during endourological laser activation: introducing the thermal safety distance concept

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Abstract

Purpose To examine temporal-spatial distribution of heat generated upon laser activation in a bench model of renal calyx. To establish reference values for a safety distance between the laser fiber and healthy tissue during laser lithotripsy.

Methods We developed an in-vitro experimental setup employing a glass pipette and laser activation under various intra-operative parameters, such as power and presence of irrigation. A thermal camera was used to monitor both temporal and spatial temperature changes during uninterrupted 60-second laser activation. We computed the thermal dose according to Sapareto and Dewey's formula at different distances from the laser fiber tip, in order to determine a safety distance.

Results A positive correlation was observed between average power and the highest recorded temperature (Spearman's coefficient 0.94, $p < 0.001$). Irrigation was found to reduce the highest recorded temperature, with a maximum average reduction of 9.4 °C at 40 W ($p = 0.002$). A positive correlation existed between average power and safety distance values (Spearman's coefficient 0.86, $p = 0.001$). A thermal dose indicative of tissue damage was observed at 20 W without irrigation (safety distance 0.93±0.11 mm). While at 40 W, irrigation led to slight reduction in mean safety distance (4.47±0.85 vs. 5.22±0.09 mm, $p = 0.08$).

Conclusions Laser settings with an average power greater than 10 W deliver a thermal dose indicative of tissue damage, which increases with higher average power values. According to safety distance values from this study, a maximum of 10 W should be used in the ureter, and a maximum of 20 W should be used in kidney in presence of irrigation.

Keywords Stone · Laser temperature · Thermal dose · Thermal safety · *In-vitro* model

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Introduction

The physical principles of laser energy have revolutionized the endoluminal treatment of stone disease [1]. During laser lithotripsy, three major settings can be adjusted to adapt to different surgical conditions: pulse energy (J), pulse frequency (Hz), and pulse duration (µs). To regulate the total average power (W) given to the stone for ablation, the pulse energy and frequency are commonly titrated. High-power settings facilitate stone fragmentation or dusting regardless of stone size and composition [2]. Nevertheless, the potential benefit should be balanced with the increasing danger of thermal damage [3], a phenomenon that is temperature dependent.

The photothermal effect is the primary physical principle for the temperature to rise. The effects of this action on the surrounding tissues include coagulation, carbonization, and denaturation, ultimately leading to tissue scarring and fibrosis [4–6].

The extent of thermal damage is influenced by both the temperature of the tissue and the duration of heating. Traditionally, the formula developed by Sapareto and Dewey [7, 8] has been utilized to estimate tissue damage resulting from thermal exposure. This formula calculates the cumulative thermal dose necessary to achieve a specific biological effect, such as thermal necrosis or tissue ablation, typically observed at a temperature of 43 degrees Celsius lasting for at least 120 min. The cumulative equivalent minutes at 43 °C (CEM43) serve as a standardized measure of tissue heating, integrating both temperature and time factors of thermal energy delivery. In the context of lithotripsy, CEM43 is suggested as a relevant parameter for predicting tissue damage extent and optimizing safe laser parameters.

The aim of this study was to analyze the temporal-spatial distribution of generated heat following laser activation in a bench model of a renal calyx, in order to provide reference values for a safety distance between the laser fiber and healthy tissue during laser lithotripsy, based on CEM43 values.

Materials and methods

Experimental set-up

We developed an in-vitro experimental setup to study the variations in water temperature due to laser activation according to different intra-operative scenarios (Fig. 1). To simulate intra-operative conditions, we exploited a custom-built glass pipette with an open roof bulb simulating a renal calyx. The bulb diameter is 12 mm, while the opening is 10 mm. The stem of the bulb has a diameter of 5 mm, and it is 115 mm long. The glass pipette was filled with saline (NaCl 0.9%) and submerged in a container at 37 °C, replicating the temperature of the human body.

We tested our hypothesis in two different scenarios:

1. Laser activation without irrigation, with the laser fiber tip conducted at the center of the calix through a 4.8 Fr ureteral catheter (Coloplast, Humlebæk, Denmark, Fig. 1a).
2. Laser activation with irrigation, where a flexible ureteroscope (Lithovue, Boston Scientific, Marlborough, USA) was passed through a 12–14 Fr UAS (ReTrace, Coloplast, Humlebæk, Denmark) and conducted in the caliceal model. The laser fiber was then passed through the working channel of the scope and conducted at the

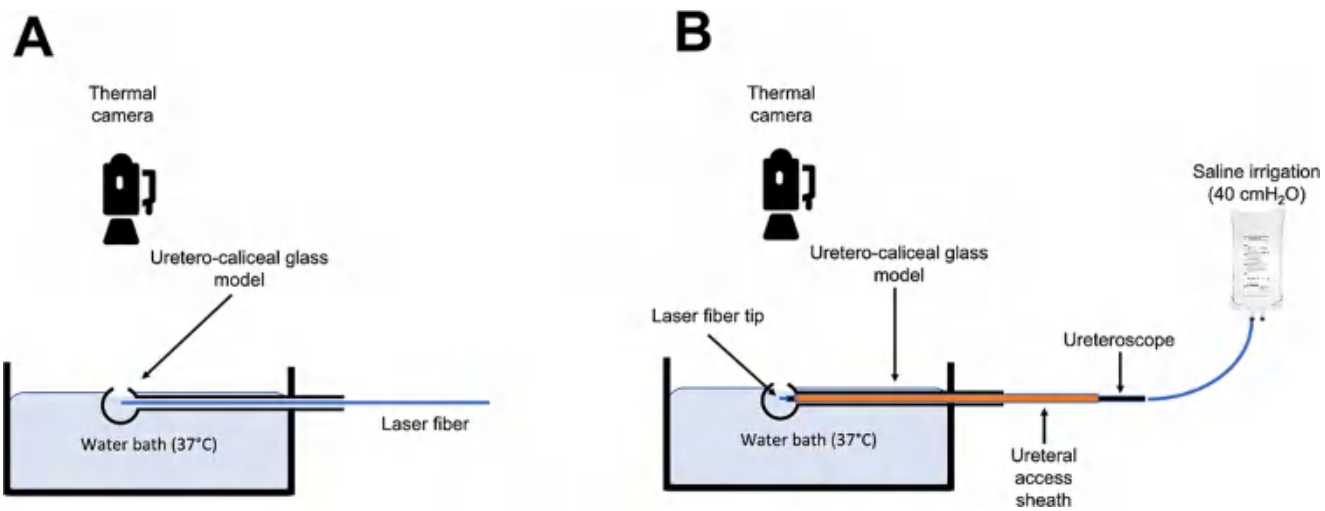


Fig. 1 Experimental setup for temperature recording during laser activation. **A**). Experimental setup in absence of irrigation **B**). Experimental setup in presence of irrigation

center of the laser. Saline at room temperature (21 °C) with a constant irrigating pressure of 40 cm H2O was used for irrigation (Fig. 1b). The irrigating pressure resulted in an average flow rate of 10 ml/min. The use of 12–14 Fr UAS enabled equilibrium between the inflow and outflow of fluid within the glass pipette, ensuring that the fluid level remained stable and prevented any overflow.

In both cases, a 200 µm laser fiber (Quanta System, Samarate, Italy) was used, with the laser fiber tip placed in a fixed position, 1 mm below the water surface. Laser fiber tip was cut before every test.

For live temperature monitoring during laser activation, a thermal camera set at 15 fps (FLIR E8 Pro, Teledyne FLIR LLC, Italy) was placed perpendicular to the open roof of the pipette. A thermal camera allows to keep track of both temporal and spatial changes in temperature.

All tests were performed using a high power Ho: YAG laser generator set with the lowest available peak power (Cyber Ho 150 W, Quanta System, Samarate, Italy). The spatial and temporal temperature fluctuations were documented and recorded during 60 s of uninterrupted laser activation, at different power and frequency settings with or without irrigation. Tested powers were 5 W, 10 W, 20 W, and 40 W. Each experimental configuration was repeated at least three times to ensure reliable results.

Image analysis

Image analysis was performed using FLIR Tools software version 6.x. The images were preprocessed to enhance image quality, remove noise, and normalize the temperature scale. Calibration was performed using reference objects with known temperatures to ensure accurate temperature measurements. To analyze the thermal images, a region of interest (ROI) was selected around the laser-irradiated area. The ROI consisted of a line perpendicular to the direction of the fiber laser, passing through the tip to capture the heat distribution accurately, over time. We exploited the customized image analysis algorithm to extract temperature information from the ROI.

Heat damage assessment

The effect of thermal damage on tissue depends on temperature and heating time. Dewey and Sapareto [7, 8] developed a metric known as thermal dose, which is calculated using the following experimental formula: $t_{43} = \sum_{t=0}^{t=end} R^{43-T} \Delta t$

where t represents the time in minutes, T denotes the temperature in degrees Celsius, and R is a constant that varies depending on T ($R = 0.5$ when $T > 43$, and $R = 0.25$ when $T < 43$). This formula enabled the computation of cumulative equivalent minutes at 43 °C (CEM43), which standardized cumulative temperature exposure across varying temperature profiles. Subsequently, a threshold of thermal injury of 120 equivalent minutes was established, consistent with existing literature [7, 8]. Accordingly, thermal damage is expected to occur when tissue is exposed to 43 °C for 120 min. Similarly, exposure to higher temperatures shortens the duration needed to obtain tissue damage.

Definition of safety distance

We utilized the collected data on temporal and spatial temperature variations during laser activation, captured by the thermal camera. Subsequently, we calculated CEM43 for every distance from the fiber tip to establish a safety margin for each power configuration, taking into account several surgical scenarios, i.e. presence or absence of irrigation.

Mean and standard deviation (SD) were calculated for each experimental replicate to analyze continuous variables. The comparison between different power settings was conducted using Student's t-test. The Spearman correlation was employed to examine the relationship between the average power and the highest recorded temperature, as well as between the average power and the safety distance values. The statistical analyses were performed using R software version 4.2.1 (www.r-project.org). All tests were two-sided, and a significance level of 0.05 was used.

Results

Recorded temperatures

Figure 2 shows an example of the spatial and temporal distribution of temperature obtained in a single replicate of our experimental setting. Highest temperature was recorded in proximity of the laser fiber, sharply declining when departing from it. Table 1 shows highest recorded temperatures 60 s after laser activations for all the analyzed scenarios. There was a statistically significant positive correlation between average power and highest recorded temperature (Spearman's correlation coefficient 0.94, $p < 0.001$). Highest temperature exceeded 43 °C with an average power ≥ 10 W in absence of irrigation. In presence of irrigation, highest temperature exceeded 43 °C with an average power ≥ 20 W. The use of irrigation was able to significantly lower highest recorded temperature with an average power ≥ 20 W, with a maximum average reduction of 9.4 °C at 40 W ($p = 0.002$).

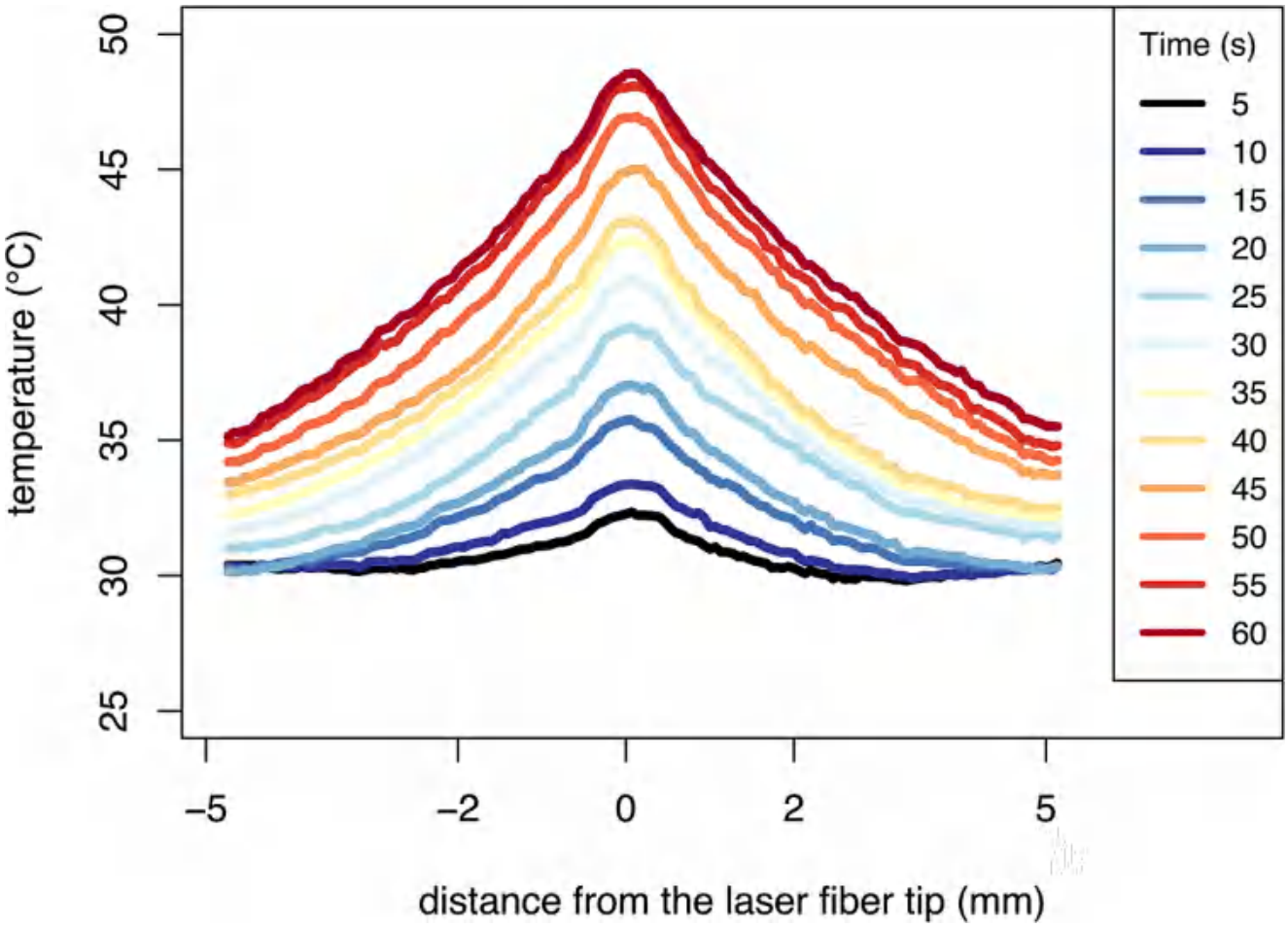


Fig. 2 Temporal and spatial distribution of recorded temperature during laser activation. The figure shows recorded temperatures for Ho: YAG laser according to the distance from the fiber tip and time of laser activation, when using 10 W of average power (5 J, 20 Hz, long pulse)

Table 1 Highest recorded temperature according to average power and use of irrigation

Average power	No irrigation, mean (SD)	Irrigation, mean (SD)	Temperature reduction	*p* value
5 W	40.1 (0.4) °C	39.1 (1.21) °C	1.0 °C	0.28
10 W	47.8 (0.3) °C	42.2 (2.2) °C	5.6 °C	0.04
20 W	56.4 (0.4) °C	50.7 (1.4) °C	5.7 °C	0.02
40 W	72.9 (0.9) °C	63.5 (0.9) °C	9.4 °C	0.002

Thermal dose and safety distance

A thermal dose indicative of tissue damage according to the CEM43 formula was observed with an average power of 20 W without irrigation, mean (SD) safety distance 0.93 (0.11) mm, and at 40 W irrespectively of the presence of irrigation (Fig. 3). For setting where CEM43 > 120 min, we estimated the thermal safety distance, defined as the distance from the laser fiber tip where thermal dose did not exceed the tissue damage threshold. There was a statistically significant positive correlation between average power and safety distance values (Spearman's correlation coefficient 0.86, $p = 0.001$). At maximum analyzed power, i.e. 40 W, irrigation provided a slight reduction in the mean (SD) safety distance, 4.47 (0.85) vs. 5.22 (0.09), although this difference was not statistically significant ($p = 0.08$).

Discussion

In this study, we report for the first time the temporal-spatial distribution of generated heat during laser lithotripsy. Using an in-vitro model, we described the rise in temperature as well as the thermal dose at different distances from the laser fiber tip. A rise in laser temperature > 43 °C was observed at 10 W without the use of irrigation and at 20 W in presence of irrigation. In order to better investigate the impact of generated heat, we estimated the thermal dose in terms

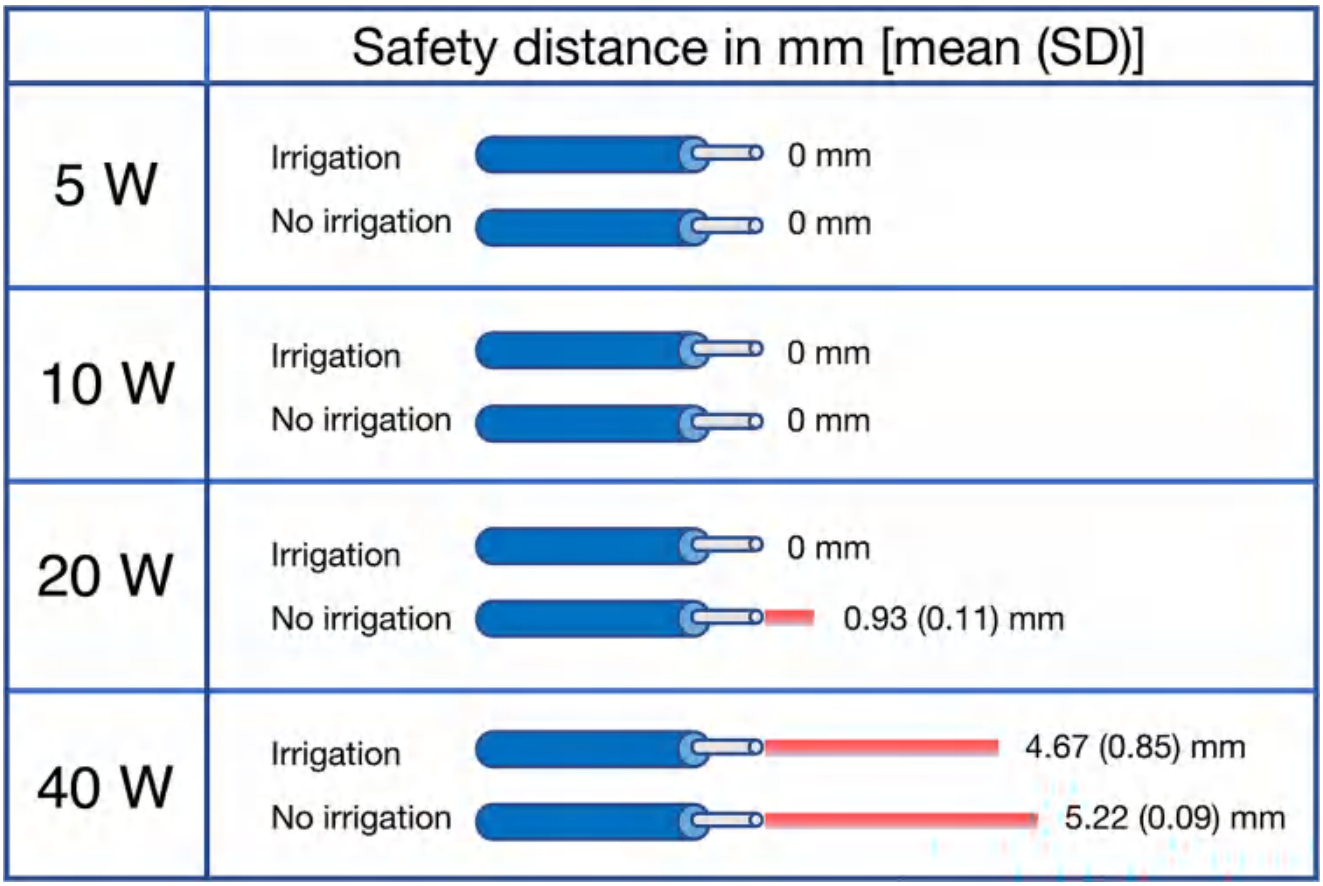


Fig. 3 Safety distance values according to the CEM43 formula for analyzed settings in presence and absence of irrigation (CEM43: cumulative equivalent minutes at 43 °C)

of CEM43 and defined the so-called thermal safety distance, i.e. the distance from the laser fiber tip where CEM43 remained below 120 min. We found that in the absence of irrigation, a thermal dose indicative of tissue damage was evident at 20 W, whereas in the presence of irrigation, it was instead evident at 40 W.

Several factors influence the thermal dose delivered during laser lithotripsy [9]. With regards to this, the choice of laser parameters is paramount: increasing average power of laser parameters [9, 10] invariably results in higher fluid temperature and thermal dose. It has been recommended that an average power > 25 W and > 15 W should not be used in the kidney and in the ureter, respectively [11]. Besides laser parameters, irrigation fluid is another important variable determining thermal dose values, influencing heat dissipation and cooling effects [12, 13]. Adequate irrigation helps mitigate thermal damage to surrounding tissues by dissipating heat and maintaining optimal operating conditions; however, increase in irrigation flow is likely paralleled by increase in intra-renal pressure, with possible drawbacks in terms of infectious complication risk. A recent bench [12] study showed that in order to mitigate the thermal effects of a 20 W laser regimen the irrigant flow should be set at 15 ml/s, i.e. elevating the water bag at 100 cm, far above the recommended 40 cmH20 threshold for irrigant pressure [14]. According to the same study, increasing power at 40 W required a 200 cmH_20 irrigant pressure in order to mitigate the thermal effect of such parameters [12].

It is therefore key not to focus only on temperature, but to stress the importance of the concept of thermal dose. Thermal tissue damage relies on both the degree of temperature increase and the duration it is sustained. Reporting outcomes solely based on peak temperature or time to reach a certain temperature may be misleading and provide an incomplete assessment of the risk of thermal injury. Sapareto and Dewey [7, 8] introduced the concept of thermal dose to standardize the relationship between temperature and time for tissues exposed to different temperatures. For instance, tissue maintained at 43 °C for 120 min accumulates the same thermal dose as tissue kept at 50 °C for 56 s or at 56 °C for 1 s [12]. Knowing the change in temperature and its temporal behavior, it is possible to estimate the cumulative equivalent minutes at 43 °C, and therefore to assess for any specific temperature record. This concept has

been confirmed in various tissue types, including the kidney [6]. Most soft tissues become nonviable with a CEM43 ranging surpassing 120 min [8, 15]. Our study stresses even more the importance of thermal dose over recorded temperature. An average power of 10 W without irrigation was shown to reach temperatures over 43 °C; however, thermal dose during the first 60 s of activation remained below the threshold of tissue damage. This happened also in the case of 20 W in presence of irrigation.

To date, proposed methodologies for investigating both temperature rise and thermal dose suffer from important limitations. The most evident is the lack of spatial definition, with point measurements which are unlikely to report a comprehensive scenario of heat diffusion and dissipation. Point estimates of temperature may be misleading, and considerably dependent on the distance from the selected point from the laser fiber tip. An important advantage of infrared thermometry is the temporal and spatial coverage of the changes in temperature [16], allowing us for the first time to define the concept of thermal safety distance.

There are clinically relevant implications in the results of our study. The safety distance values discourage the use of laser settings with an average power > 20 in the kidney, since thermal damage may arise even at 5 mm distance from the laser fiber tip. In the ureter, according to the safety distance values emerging from the current report, average power of laser settings should not overcome 10 W, since at 20 W tissue damage may arise up to 1 mm distance from the laser fiber tip. Preliminary clinical data seem to confirm this concept [17].

Our study is not devoid of limitation. First, being an in vitro study, our results will need to be substantiated in vivo. Second, the application of the thermal camera in an in vivo setting is not feasible at present, meaning that an alternative measurement modality will need to be implemented. Third, the implementation of stone into this model is experimentally not feasible, as the laser stone interaction would result in vertical movements, making signal to noise ratio of the thermal camera measurements too to be accurate. Fourth, the heat sink effect due to blood flaw was not recapitulated in our model, as the glassy pipet was bathing in a still medium. Firth, the small gap between the water surface and the laser tip could potentially affect the measured temperature due to heat dispersion as it passes through the medium. However, since the fiber laser is maintained in a fixed position, this error would be constant across all measurements, still allowing for comparisons among different conditions.

Conclusions

Our experimental configuration highlights several crucial clinical implications: (1) the experimental data about safety distance advise against employing laser settings with an average power exceeding 20 W within the kidney or 10 W within the ureter; (2) Irrigation has the potential to lower the highest recorded temperature; however, we observed a marginal reduction of the safety distance values at high power-settings (3) High power settings do not appear to be safe even in presence of irrigation.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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研究

内窥镜激光激活过程中的温度分布：引入热安全距离概念

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介绍

激光能量的物理原理彻底革新了腔内治疗结石疾病的方法[1]。在进行激光碎石术时，可通过调节脉冲能量(J)、脉冲频率（Hz）和脉冲持续时间（μs）这三个主要参数来适应不同手术需求。为了精确控制作用于结石的总平均功率(W)，通常需要对脉冲能量和频率进行微调。高功率设置能有效粉碎结石或使其碎裂成粉尘，无论结石大小和成分如何[2]。但需注意的是，这种潜在优势必须与热损伤风险的增加保持平衡[3]，而热损伤的发生具有温度依赖性特征。

光热效应是温度升高的主要物理原理，这种作用对周围组织的影响包括凝固、碳化和变性，最终导致组织瘢痕形成和纤维化[4—6]。

热损伤的程度受组织温度和加热时长的双重影响。传统上，萨帕雷托和杜威[7，8]提出的公式被用于评估热暴露导致的组织损伤。该公式通过计算达到特定生物效应（如热坏死或组织消融）所需的累积热剂量来实现，这种效应通常在43摄氏度持续至少120分钟的温度条件下出现。43℃累积等效分钟数（CEM43）作为组织加热的标准化指标，综合考量了热能传递的温度和时间因素。在碎石术中，CEM43被推荐为预测组织损伤程度和优化安全激光参数的重要参数。

本研究旨在通过激光碎石术实验模型，分析肾盏激光激活后产生的热量时空分布特征，基于CEM43值建立激光光纤与健康组织的安全距离参考标准。

材料和方法

实验设置

我们开发了一套体外实验装置，用于研究不同术中场景下激光激活引起的水温变化（图1）。为模拟术中条件，我们使用了一支定制的玻璃吸管，其顶部开有模拟肾盏的球形开口。该球形开口直径为12毫米，开口处直径为10毫米。球形开口的茎部直径为5毫米，长度为115毫米。玻璃吸管内填充了生理盐水（氯化钠0.9%），并浸入37°C的容器中，以模拟人体温度。

我们在两种不同场景下验证了假设：

1. 无需冲洗即可进行激光激活，具体操作是将激光光纤尖端经由4.8 Fr输尿管导管（丹麦Humlebæk公司Coloplast产品，见图1 a）导入杯状结构中心。
2. 采用激光联合灌洗技术进行激活，具体操作是将柔性输尿管镜（Lithovue，美国波士顿科学公司，马尔伯勒）经12-14 Fr UAS导管（ReTrace，丹麦科洛普拉斯公司，Humlebæk）插入膀胱杯模型。随后将激光光纤通过内镜工作通道引导至膀胱杯部位。

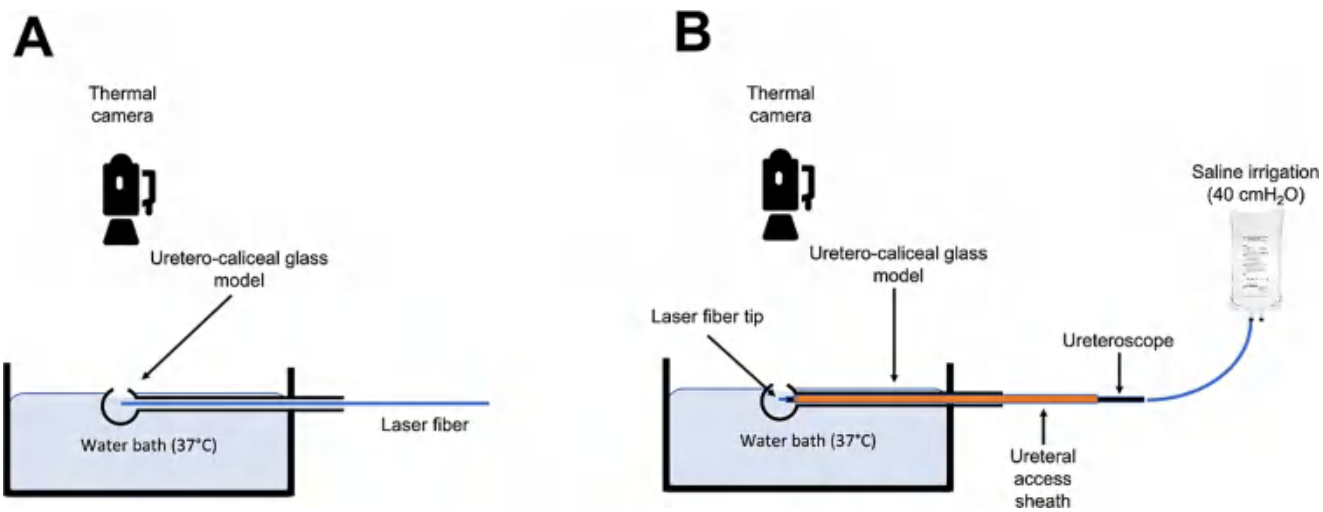


图1激光激活过程中温度记录的实验装置。**A)**无灌注的实验装置**B)**有灌注的实验装置

激光中心。使用室温（21°C）的生理盐水，以40厘米水柱的恒定灌注压力进行灌注（图1 b）。该灌注压力导致平均流速为10 ml/min。采用12−14 Fr UAS可使玻璃移液管内的液体流入与流出达到平衡，确保液位稳定并防止溢出。

两种情况下均采用200μm激光光纤（Quanta System，意大利萨马拉特），将光纤尖端固定于水下1毫米处。每次测试前均需对光纤尖端进行切割处理。

为实时监测激光激活过程中的温度，将热成像相机（FLIR E8 Pro，意大利Teledyne FLIR LLC公司）以15帧/秒的速率垂直安装在移液管的开口顶部。该设备可同步记录温度在时间和空间上的变化。

所有实验均采用高功率Ho：YAG激光发生器（Cyber Ho 150 W，Quanta System公司，意大利萨马拉特）进行，该设备具有最低可用峰值功率。在60秒连续激光激活期间，通过不同功率和频率设置（含/不含灌注）记录空间与时间温度波动。测试功率分别为5W、10W、20W和40W。每个实验配置至少重复三次以确保结果可靠性。

图像分析

图像分析采用FLIR Tools软件6.x版本完成。图像经过预处理以提升质量、消除噪声并标准化温度标度。通过已知温度的参考物体进行校准，确保温度测量的准确性。在热成像分析中，我们选取了激光照射区域周围的感兴趣区域（ROI）。该ROI由一条垂直于光纤激光器方向的线构成，该线穿过激光尖端以准确捕捉随时间变化的热分布。我们运用定制的图像分析算法，从ROI中提取温度信息。

热损伤评估

热损伤对组织的影响取决于温度
处理时间和加热时间。Dewey和Sapareto[7，8]开发了一个称为热剂量的指标，其计算使用以下实验公式：$t_{43}=\varepsilon^{t_{t=e}0^{和}R^{43-T}\triangle t}$，其中t表示时间（分钟），T表示温度（摄氏度），R是一个随T变化的常数（当T>43时R=0.5，当T>43时R=0.25）

T<43)。该公式实现了43℃条件下累积等效分钟数（CEM43）的计算，将不同温度曲线下的累积热暴露时间标准化。随后，我们根据现有文献[7，8]确立了120分钟热损伤阈值。这意味着当组织在43℃环境下暴露120分钟时，就会发生热损伤。类似地，暴露在更高温度下时，组织损伤所需的暴露时间会相应缩短。

安全距离的定义

我们利用热成像仪采集的激光激活期间温度时空变化数据，计算出光纤尖端各距离处的CEM43值，从而为不同功率配置建立安全裕度，同时考虑了手术场景中的多种情况，包括是否进行灌洗。

为分析连续变量，我们计算了每个实验重复的平均值和标准差（SD）。采用学生t检验对不同功率设置进行比较。通过斯皮尔曼相关系数分析平均功率与最高记录温度之间的关系，以及平均功率与安全距离值之间的关联。统计分析使用R软件4.2.1版（www.r-project.org）完成。所有检验均为双侧检验，显著性水平设定为0.05。

结果

记录的温度

图2展示了本实验单次重复中测得的温度时空分布示例。激光光纤附近测得最高温度，远离该区域时温度急剧下降。表1列出了所有实验场景中激光激活60秒后的最高温度记录。平均功率与最高温度呈现统计学显著正相关（斯皮尔曼相关系数0.94，p<0.001）。在未使用灌溉的情况下，当平均功率≥10W时，最高温度超过43°C；使用灌溉时，当平均功率≥20W时，最高温度同样超过43°C。研究表明，使用灌溉可显著降低平均功率≥20W时的最高温度记录，其中在40W功率下平均温度降幅最大，达到9.4°C（p=0.002）。

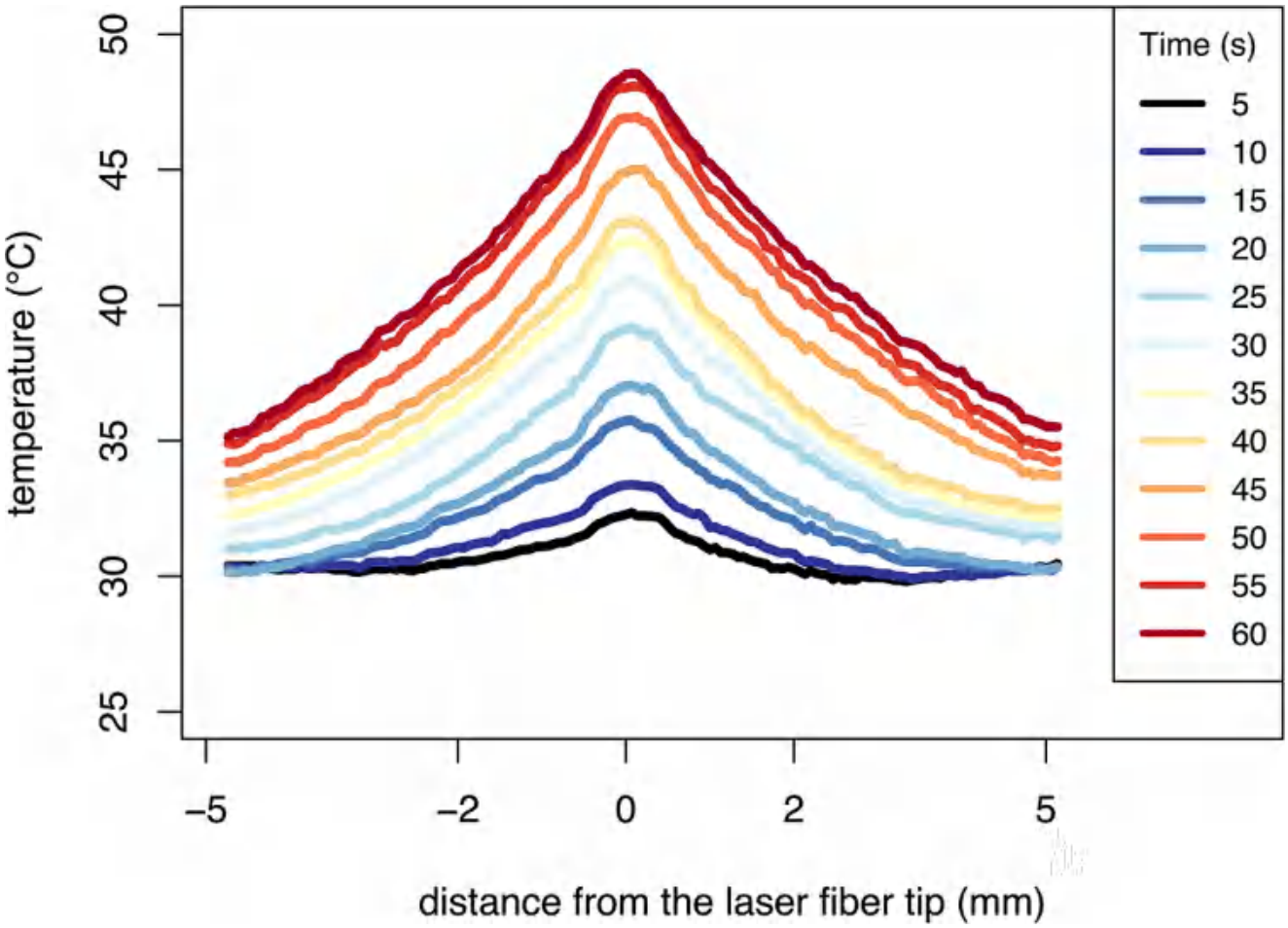


图2激光激活期间记录温度的时间和空间分布。该图显示了使用10W平均功率（5J，20Hz，长脉冲）时，Ho：YAG激光器根据光纤尖端距离和激光激活时间记录的温度。

表1根据平均功率和灌溉使用情况记录的最高温度

平均功率	无灌注，平均值（SD）	灌注，平均值（SD）	温度降低	p值
5 W	40.1 (0.4) °C	39.1 (1.21) °C	1.0 °C	0.28
10 W	47.8 (0.3) °C	42.2 (2.2) °C	5.6 °C	0.04
20 W	56.4 (0.4) °C	50.7 (1.4) °C	5.7 °C	0.02
40 W	72.9 (0.9) °C	63.5 (0.9) °C	9.4 °C	0.002

热剂量和安全距离

根据CEM43公式计算得出的热剂量指标显示，在未使用冲洗功能时，平均功率为20瓦时可观察到组织损伤迹象（平均安全距离0.93±0.11毫米，40瓦功率下该数值保持稳定）。对于CEM43值超过120分钟的治疗参数，我们通过热安全距离评估——即激光光纤尖端到热剂量未超过组织损伤阈值的最远距离。研究发现，平均功率与安全距离值之间存在统计学显著的正相关性（斯皮尔曼相关系数0.86，p=0.001）。在最大功率40瓦的测试条件下，使用冲洗功能可使平均热剂量值出现轻微下降。

（SD）安全距离，4.47（0.85）vs.5.22（0.09），尽管该差异无统计学意义（p=0.08）。

讨论

本研究首次揭示了激光碎石术过程中产生的热量在时空上的分布规律。通过体外模型，我们系统描述了激光光纤尖端不同距离处的温度升高情况及热剂量变化。实验数据显示：在10瓦功率下未使用冲洗时，激光温度升高超过43°C；而使用20瓦功率并配合冲洗时，温度增幅更为显著。为深入探究热量产生的影响，我们通过热剂量评估方法对相关参数进行了量化分析。

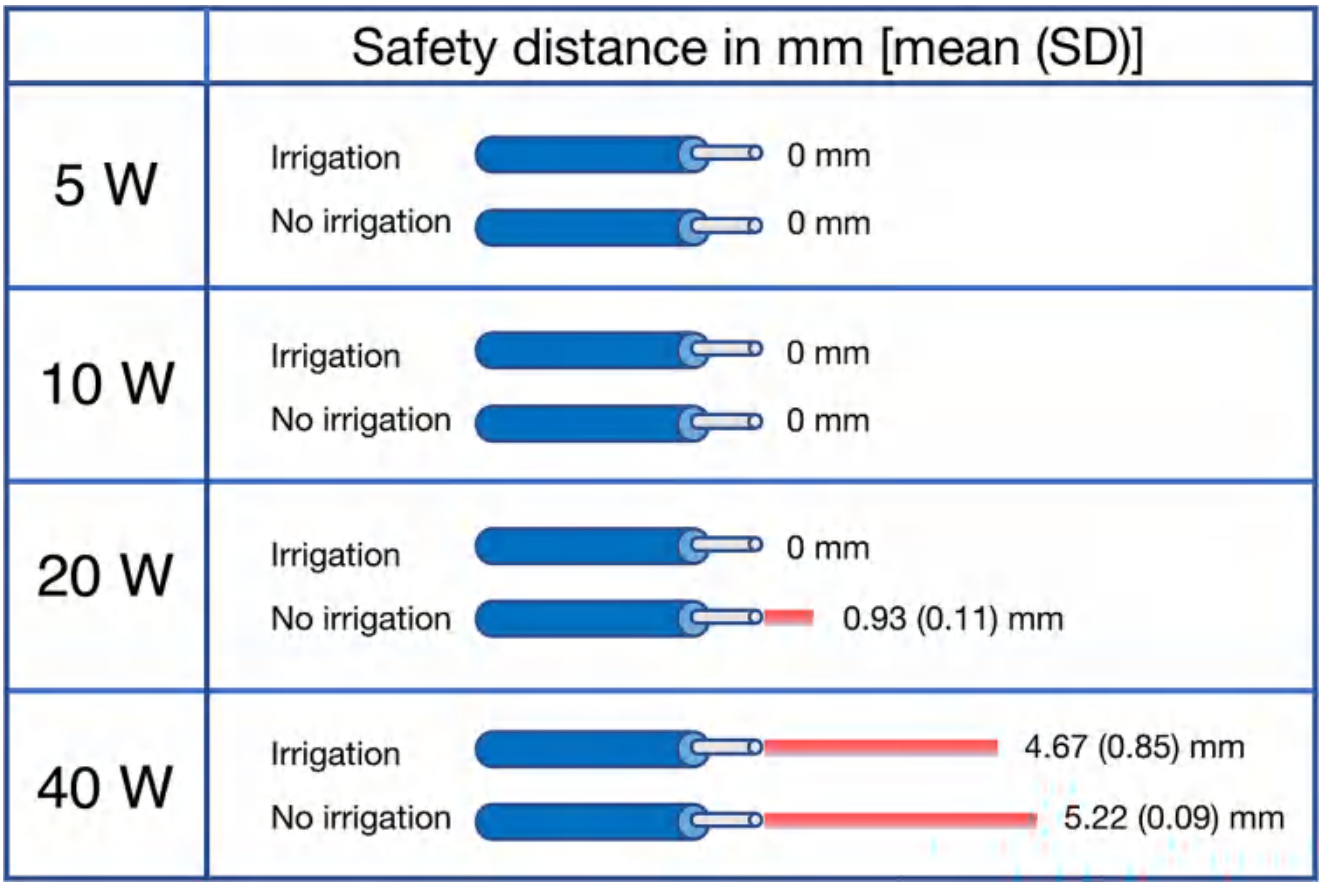


图3根据CEM43公式分析的设置在有无灌注情况下的安全距离值（CEM43：43°C下的累积等效分钟）

我们测定了CEM43的热效应，并定义了所谓的热安全距离——即激光光纤尖端持续保持CEM43值低于120分钟的区域。研究发现：在无灌注条件下，20瓦时即可检测到提示组织损伤的热剂量；而有灌注条件下，该阈值则需提升至40瓦才可检测到。

激光碎石术[9]过程中传递的热剂量受多重因素影响。其中激光参数的选择至关重要：平均功率越高[9，10]，液体温度和热剂量就越高。临床建议肾区平均功率不应超过25瓦，输尿管区域则不应超过15瓦[11]。除激光参数外，冲洗液也是决定热剂量的重要变量，它会影响热量散发和冷却效果[12，13]。适量冲洗液能通过散热维持最佳操作状态，有效减轻周围组织的热损伤；但冲洗流量增加可能伴随肾内压升高，从而增加感染并发症风险。最新实验室[12]研究表明，为减轻热效应

在20瓦激光治疗方案中，冲洗液流量应设置为15 ml/s，即将水袋抬高至100厘米，远高于推荐的40厘米水柱冲洗液压力阈值[14]。根据同一研究，当功率增加至40瓦时，需要200厘米水柱$_2$的冲洗液压力才能减轻此类参数的热效应[12]。

因此，我们不能只盯着温度数据，更要重视热剂量这个关键概念。组织热损伤的严重程度取决于温度上升幅度和持续时间。如果仅用峰值温度或达到特定温度所需时间来评估，可能会产生误导，无法全面评估热损伤风险。萨帕雷托和杜威[7，8]提出的热剂量概念，为不同温度环境下组织的温度-时间关系提供了标准化参照。例如，43℃持续120分钟的组织，其累积热剂量与50℃持续56秒或56℃持续1秒的组织相当[12]。通过掌握温度变化规律及其动态特征，我们就能估算出43℃条件下的累积等效时间，从而对任何特定温度记录进行风险评估。这一概念的提出，为热损伤评估提供了更科学的量化依据。

该现象已在多种组织类型中得到证实，包括肾脏[6]。当CEM43持续时间超过120分钟时，大多数软组织会失去活性[8，15]。我们的研究进一步强调了热剂量的重要性远超记录温度。数据显示，平均功率为10瓦且未进行冲洗时，温度可超过43°C；但激活启动后前60秒内的热剂量仍低于组织损伤阈值。即使在存在冲洗的情况下使用20瓦功率时，这一现象依然存在。

目前，针对温度升高和热剂量的研究方法仍存在明显局限。最突出的问题在于缺乏空间定义，仅凭点测量数据难以全面反映热量扩散与消散的完整过程。温度的点估计值可能具有误导性，且与激光光纤尖端到测量点的距离密切相关。红外测温技术的重要优势在于其能同时覆盖温度变化的时间维度和空间维度[16]，这使得我们首次能够明确界定热安全距离的概念。

本研究结果具有重要的临床意义。根据安全距离标准，肾脏部位的激光治疗应避免使用平均功率超过20瓦的激光设置，因为即使距离光纤尖端仅5毫米，也可能引发热损伤。对于输尿管部位，当前报告的安全距离数据表明，激光设置的平均功率不应超过10瓦——当功率达到20瓦时，距离光纤尖端仅1毫米处就可能造成组织损伤。初步临床数据似乎证实了这一观点[17]。

本研究存在若干局限性。首先，作为体外实验，我们的结果需要通过体内实验验证。其次，目前热成像相机在体内环境中的应用尚不可行，这意味着需要采用其他测量方式。第三，将结石植入该模型在实验层面不可行，因为激光与结石的相互作用会导致垂直位移，从而使热成像相机的信噪比无法准确测量。第四，由于玻璃移液管浸泡在静止介质中，我们的模型未能重现血液缺陷引发的散热效应。第五，水表面与激光尖端之间的微小间隙可能因介质中的热传导影响测量温度。不过，由于光纤激光器保持固定位置，这种误差在所有测量中保持恒定，仍可实现不同条件下的数据对比。

结论

我们的实验设计揭示了几个关键的临床意义：(1)安全距离的实验数据表明，肾脏内平均功率超过20瓦、输尿管内超过10瓦的激光设置不建议使用；(2)虽然冲洗可能降低最高记录温度，但我们发现高功率设置下的安全距离值仅有微小变化；(3)即使使用冲洗，高功率设置仍存在安全隐患。

无**致谢。**

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RESEARCH

An in vitro study of irrigation rate, operator duty cycle and intrarenal temperature in superpulse fiber thulium laser lithotripsy

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Abstract

Objective The present study aimed to examine the relationship between irrigation velocity, operator duty cycle (ODC), and intrarenal temperature during retrograde intrarenal surgery with a superpulse fiber thulium laser.

Methods Place the stones into the fresh isolated porcine kidneys, use puncture needle to place the temperature probe 2 mm around the stones, and place the pressure probes in the upper calyx, lower calyx, and renal pelvis. Place the entire setup in a 37 °C constant temperature water bath to simulate the human body environment. The laser power varies between 10 and 30 W, and the irrigation speed is 10-30 ml/min. Additionally, at a laser power of 20 W and an irrigation speed of 10 ml/min, different On-Duty Cycles (ODC) are set. Monitor the changes in temperature and pressure.

Results A direct proportionality of temperature in the kidney to the rate of irrigation has been reported between 10 W and 30 W laser powers. The percentage ratio of the rate of irrigation and power in the laser is 1:1, which can keep the temperature in the kidney at a safe level. At a laser power of 20 W and irrigation of 10 ml/min, the temperature inside the kidney increases sharply with the increase in ODC. By decreasing the ratio of ODC, the increase of temperature inside the kidney can be brought to a great reduction.

Conclusion Maintaining a 1:1 ratio between laser power and irrigation speed can effectively prevent thermal damage or injury to kidney tissue.Additionally, by adjusting the On-Duty Cycle (ODC) ratio, the intrarenal temperature can also be reduced.

Keywords Superpulse fiber thulium laser · Operator duty cycle (ODC) · Irrigation rate · Intrarenal temperature

Introduction

The continuous development of medical technology has resulted in the continued improvement of laser lithotripsy, which is now a mature treatment technique. Superpulsed fiber thulium laser with a 1940-nm wavelength has come to be one of the important candidates for lithotripsy. Due to the proximity of this wavelength to the absorption peak of water, the absorption coefficient of that wavelength in aqueous solutions is markedly higher than the conventional holmium laser at 2100 nm. This gives this wavelength a substantial edge over others in lithotripsy efficiency [1, 2]. Today, holmium laser lithotripsy is the preferred method for (flexible) URS, because of the wide range of applications and good outcomes in the procedure of lithotripsy [3]. What is more important is that besides showing stone-crushing efficiency superior to that with the holmium laser, the superpulsed fiber thulium laser also represents a new breakthrough in the treatment of the urinary tract stone, which features lower stone recoil force and thinner fiber diameter [4]. These features would thus indicate that the super-pulsed fiber thulium laser could be well applied and developed in the field of urinary stone treatment. The development of lithotripsy technology always attaches importance to the safety issue of laser lithotripsy as much as the stone comminution effect does. This work is aimed to optimize the temperature control and the irrigation flow rate during the process of laser lithotripsy to accomplish safe and effective therapy.

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Materials and methods

In vitro modeling

This study utilized fresh ex vivo porcine kidneys, sourced under conditions that strictly adhered to ethical protocols, with all pigs being humanely euthanized. The research was conducted with the approval of the Ethics Review Committee and was granted the corresponding ethical approval number [IACUC-202306-P-001].The calculi specimens were obtained from our calculi specimen library, all of which underwent compositional analysis and were confirmed to be calcium oxalate monohydrate stones (CT value: 890 ± 123 HU). The study employed a range of equipment, including a single-use electronic ureteroscope with an outer diameter of F8.6 (ZebraScope Anhui Happiness Factory Medical Equipment Co., Ltd), a ureteral access sheath (F11/13 Laikai Medical Devices (Beijing) Co., Ltd), a super-pulsed thulium fiber laser with a 200 μm laser fiber (A-ONE Laikai Medical Devices (Beijing) Co., Ltd) , a multi-channel real-time thermometer (NF4000P-8 Guangzhou Ruimanting Instrument Factory) , a precision constant-flow experimental pump (BT-100 Hebei Rongbai Electric Appliance Factory) , High-precision digital pressure gauge (DT-1 Shanghai Ruxiang Instrument Factory) , a temperature-controlled water bath, physiological saline, and other essential surgical instruments.

The procedure involved the careful placement of the calculi into the renal pelvis, with temperature probes inserted using a puncture needle, positioned approximately 2 mm from the calculi within the renal pelvis. Ureteral access sheath was carefully inserted and secured to the ureter with ligatures. The pressure transducer is placed in the upper calyx, lower calyx, and renal pelvis using the same puncture needle. The entire setup was immersed in a temperature-controlled water bath, with the temperature maintained at 37 °C to simulate the human body's environmental temperature.

Experimental procedures

The laboratory temperature is set at 25 °C. The laser lithotripsy power is set at 10 W (1.0 J × 10 Hz, 0.1 J × 100 Hz), 15 W (1.5 J × 10 Hz, 0.15 J × 100 Hz), 20 W (2.0 J × 10 Hz, 0.1 J × 200 Hz), 25 W (2.5 J × 10 Hz, 0.1 J × 250 Hz), and 30 W (1.0 J × 10 Hz, 0.1 J × 300 Hz). The irrigation speed is set at 10, 15, 20, 25, and 30 ml/min (the irrigation fluid is physiological saline, and the temperature is 25 °C). The continuous laser excitation time is 120 s.

For the laser lithotripsy power of 20 W (2.0 J × 10 Hz) and the irrigation speed of 10 ml/min (the irrigation fluid is physiological saline, and the temperature is 25 °C), each 20 s constitute an operational cycle. The laser operates in the ODC mode, with 10 different ODC modes set to simulate various surgical strategies: ODC10%: The laser is activated for 2 s and then turned off for 18 s. ODC20%: Activated for 4 s, then off for 16 s. ODC30%: Activated for 6 s, then off for 14 s. ODC40%: Activated for 8 s, then off for 12 s. ODC50%: Activated for 10 s, then off for 10 s. ODC60%: Activated for 12 s, then off for 8 s. ODC70%: Activated for 14 s, then off for 6 s. ODC80%: Activated for 16 s, then off for 4 s. ODC90%: Activated for 18 s, then off for 2 s. ODC100%: The laser is continuously activated for 20 s without an off cycle. Each cycle is repeated 6 times to form a large group experiment.

Both of the temperature and pressure probes monitor the parameter in real-time at a frequency of once per second and records changes. The above experiments are repeated 5 times for each set of parameters, and a new kidney is used for each repetition.

Data collection and analysis

The experiments have been conducted at least in quintuplicate, and the data are given as averages. Data were graphed using ggplot2 in R version 4.3.3. Values are presented as mean ± standard deviation. Statistical analysis was conducted by paired t-test between two groups and nonparametric rank sum tests using multiple samples for multiple groups. The significant difference was set at $p < 0.05$.

Results

Changes in intrarenal temperature during continuous laser lithotripsy

At a lithotripsy power of 10 W, with irrigation speeds of 10 ml/min, 15 ml/min, 20 ml/min, 25 ml/min, and 30 ml/min, the intrarenal temperature reached a steady state with steady-state temperatures of 38.6 °C, 35 °C, 33.1 °C, 31.7 °C, and 30.7 °C, respectively, none of which exceeded the safety threshold (Fig. 1). At a lithotripsy power of 15 W, the intrarenal temperature continued to rise with an irrigation speed of 10 ml/min. However, at irrigation speeds of 15 ml/min, 20 ml/min, 25 ml/min, and 30 ml/min, the intrarenal temperature reached a steady state with steady-state temperatures of 38.4 °C, 35.9 °C, 34.7 °C, and 34.4 °C, respectively, none of which exceeded the safety threshold (Fig. 2). At a lithotripsy power of 20 W, the intrarenal temperature continued to rise with irrigation speeds of 10 ml/min and 15 ml/min. However, at irrigation speeds of 20 ml/min, 25 ml/min, and 30 ml/min, the intrarenal temperature

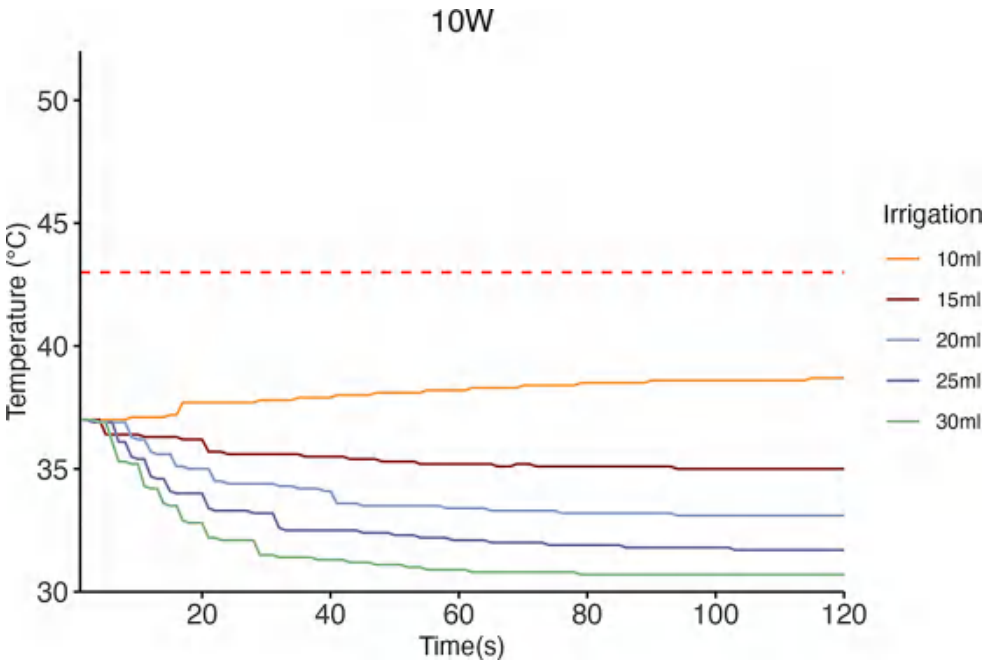


Fig. 1 Renal temperature at each irrigation speed at 10 W of gravel power

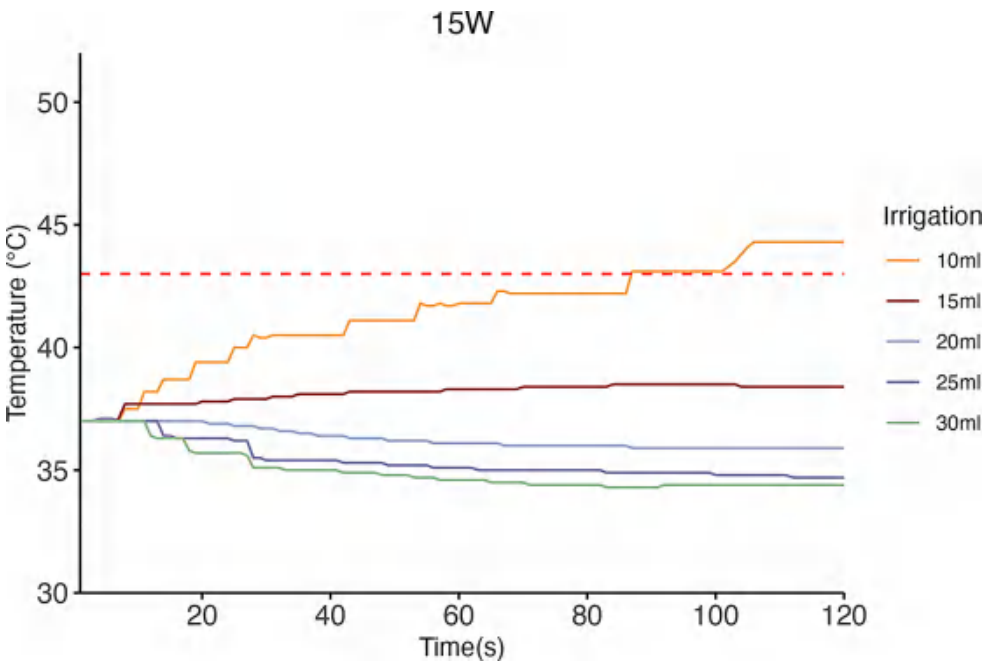


Fig. 2 Renal temperature at each irrigation speed at 15 W of gravel power

reached a steady state with steady-state temperatures of 38.7 °C, 36.3 °C, and 34.2 °C, respectively, none of which exceeded the safety threshold (Fig. 3). At a lithotripsy power of 25 W, the intrarenal temperature continued to rise with irrigation speeds of 10 ml/min, 15 ml/min, and 20 ml/min. However, at irrigation speeds of 25 ml/min and 30 ml/min, the intrarenal temperature reached a steady state with steady-state temperatures of 38.3 °C and 35.7 °C, respectively, neither of which exceeded the safety threshold (Fig. 4). At a lithotripsy power of 30 W, the intrarenal temperature continued to rise with irrigation speeds of 10 ml/min, 15 ml/min, 20 ml/min, and 25 ml/min. However, at an irrigation speed of 30 ml/min, the intrarenal temperature reached a steady state with a steady-state temperature of 37.5 °C, which did not exceed the safety threshold (Fig. 5). At different irrigation speeds, the intrarenal pelvic/calyceal pressure did not exceed 30mmH_2O (Table 1).

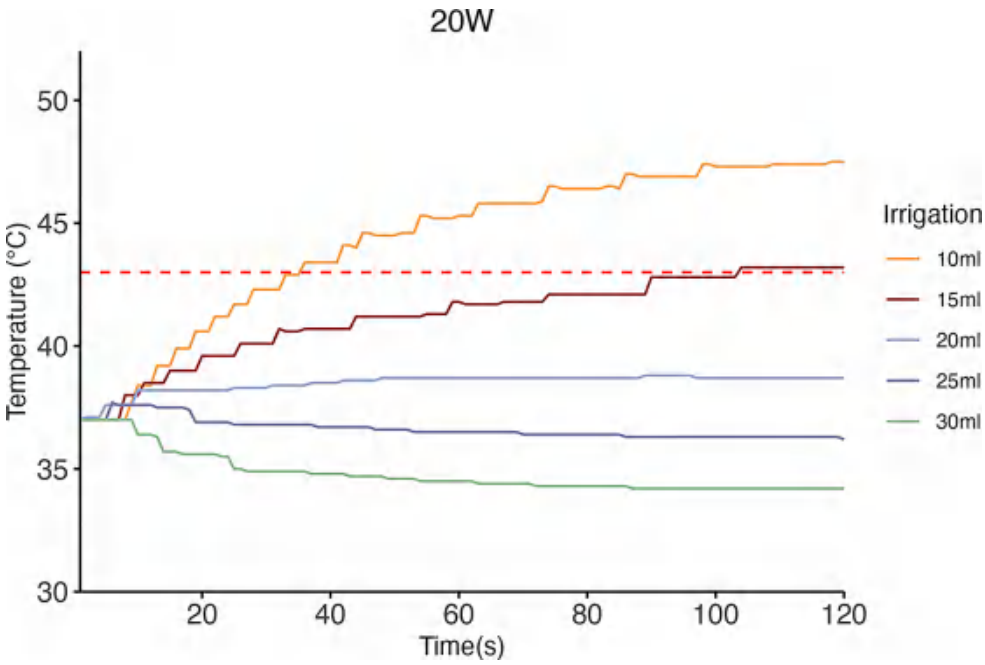


Fig. 3 Renal temperature at each irrigation speed at 20 W of gravel power

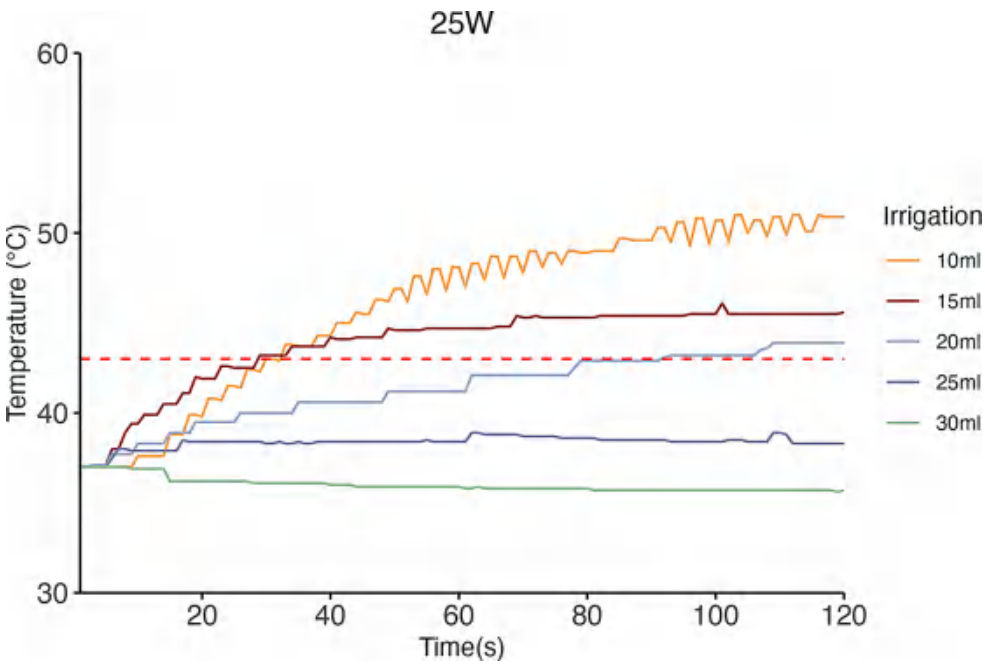


Fig. 4 Renal temperature at each irrigation speed at 25 W of gravel power

Changes in intrarenal temperature under different ODC ratios

When the On-Duty Cycle (ODC) is maintained below 60%, the steady-state intrarenal temperature tends to stabilize after reaching a certain value and does not further increase with the extension of time. In contrast, when the ODC exceeds 70%, the intrarenal temperature during the subsequent steady-state continues to rise over time (Fig. 6). With the increase of ODC, the highest intrarenal temperature shows a significant upward trend: ODC50%: 40.0 ± 0.52 °C; ODC 60%: 41.6 ± 0.38 °C; ODC 70%: 43.4 ± 0.48 °C; ODC 80%: 44.8 ± 0.73 °C; ODC 90%: 46.7 ± 0.54 °C (Table 2). When the ODC ratios are 70%, 80%, 90%, and 100%, respectively, the time for intrarenal temperature to reach the safety threshold temperature is 56.0 ± 1.0s, 51.8 ± 1.48s, 32.0 ± 1.58s, and 20.6 ± 1.14s, respectively (Table 3).

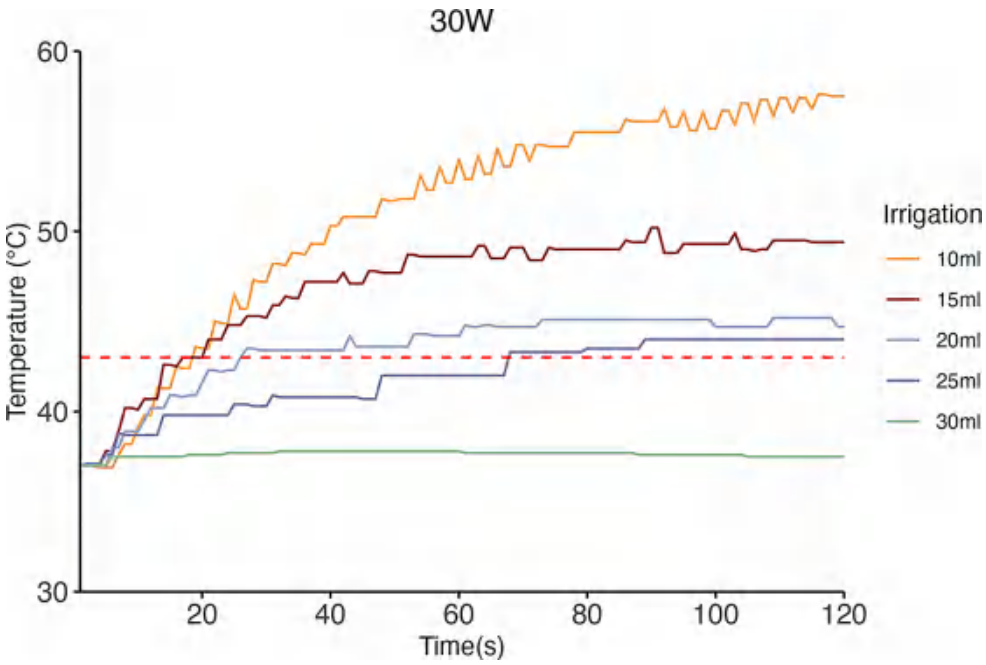


Fig. 5 Renal temperature at each irrigation speed at 30 W of gravel power

Table 1 The intrarenal pressure conditions under various irrigation speeds.（mmH_2O）

Irrigation speed	upper calyx	lower calyx	renal pelvis	F	*p*
10 ml/min	4.2 ± 0.07	3.85 ± 0.23	4.83 ± 0.09	33.46	<0.01
15 ml/min	4.6 ± 0.19	4.88 ± 0.08	5.48 ± 0.15	28.27	<0.01
20 ml/min	5.96 ± 0.04	6.08 ± 0.15	6.35 ± 0.12	10.05	<0.05
25 ml/min	6.18 ± 0.04	6.50 ± 0.28	9.08 ± 0.15	215.68	<0.01
30 mlmin	7.95 ± 0.54	8.65 ± 0.53	11.55 ± 0.15	54.82	<0.01

Table 3 The time required for different proportions of ODC to reach the safety threshold(s)

ODC Time	70%	80%	90%	100%
Time to reach the safety threshold	56.0 ± 1.0	51.8 ± 1.48	32.0 ± 1.58	20.6 ± 1.14

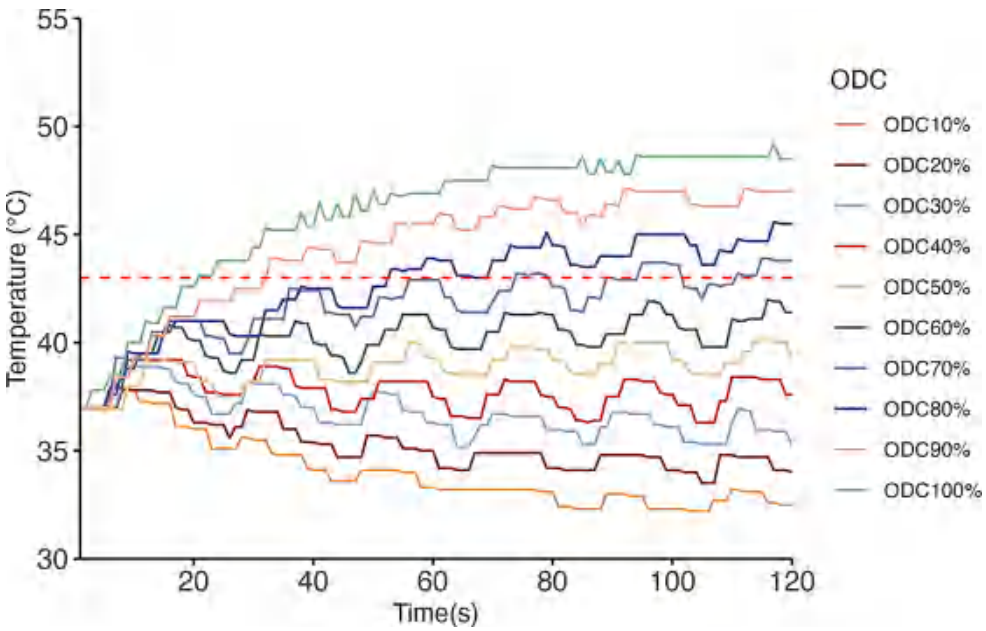


Fig. 6 Curve of renal temperature during the working cycle (ODC) of different proportions (laser power set to 20 W, irrigation speed is 10 ml/min)

Table 2 Different On-Duty Cycles (ODC) result in different intrarenal temperatures. (°C)

ODC	50%	60%	70%	80%	90%
Temperatures	40.0 ± 0.52	41.6 ± 0.38	43.4 ± 0.48	44.8 ± 0.73	46.7 ± 0.54

Discussion

Studies conducted earlier have shown that there is a considerable amount of cell necrosis in the human tissue above 43 °C temvperature and cell death further increases to 45 °C [5]. At a temperature of 60 °C, the proteins present in the tissue are irreversibly denatured; therefore, the structure of the tissue is permanently destroyed and its function is lost. This is why, to some extent, this is also considered as the temperature threshold for human tissue at 43 °C. During retrograde intrarenal surgery, the irrigation rate plays a very important factor in determining the temperature of the tissue [6]. The use of high irrigation rates will help avoid increased temperatures inside the kidney. A irrigation rate of 100 ml/min will maintain the temperature so that, even if the laser works continuously for one minute, the temperature does not exceed 38.5 °C [7]. But if the irrigation rate is too high, the intra-renal pressure will be increased, leading to postoperative pain and the patient being more prone to infection [8–10]. On the contrary, an inadequate irrigation rate might end up causing a high intraoperative temperature, leading to thermal injury in the tissues and affecting the visual field with an inability to wash away the stone powder in time, thus causing further damage to the tissues. And therefore, it is very important to measure the irrigation rate reasonably so that a surgical intervention in the patient can be safely made. In this experiment, we made a detailed observation and analysis of the temperature control used in laser lithotripsy. 10 W lithotripsy power and 10 ml/min irrigation rate kept the temperature of the kidney steady at a plateau in the early stage of the experiment, wherein this constant temperature was always below the safety threshold. The power of the laser had been increased to 15 W while proceeding with the experiment, although the irrigation rate remained the same. The temperature plateau reached 44 °C in the kidney, which was beyond the limit for safe human tissue. This damage was then effectively contained by increasing irrigation to a flow of 15 ml/min, such that the temperature was maintained at safe levels to prevent thermal injury. The results of the experiment show that with an increase in power, the temperature in the kidney grows appropriately to this change; conversely, an increase in the irrigation rate results in a decrease of the temperature in the kidney. Our observations correspond to the findings of Winship et al. [11], who conducted their experiments using 3.6 W, 6.4 W, 10 W, 16 W, and 20 W laser power with irrigation pressures of 0, 100, and 200 mmHg. These authors concluded that both the temperature in the kidney and the speed of irrigation determine the conducted temperature: the higher the laser power, the higher the temperature in the kidney; the faster the irrigation rate, the lower the temperature in the kidney [11]. The most striking result from this experiment is that when lithotripsy power and irrigation speed are varied together at a 1:1 ratio, the plateau temperature in the kidney stays below the safety threshold for all conditions. This approach is not only superior to the safety of the procedure but also provides physicians with a new way to adjust operational parameters in maximizing the benefit of lithotripsy while minimizing the possibility of thermal injury to the patient's kidney.

In our work, the 20 W lithotripter power and an irrigation flow rate of 10 mL/min were considered, paying particular attention to ODC values in a large range from 50 to 100%. This phenomenon is just the same as the classical sawtooth fluctuation wave which is corresponding to the laser periodical activation: the temperature in liquid increases rapidly when the laser is activated and decreases slowly to form a plateau when it is deactivated. The ODC ratio of the kidney showed a significantly raised level at the steady-state. This is similar to what was also observed in Louters et al. [12], so that a higher ODC increases temperature and energy release markedly. The steady-state renal temperature shows a trend of leveling off after attaining some value and does not increase further in case the ODC was kept below 60%. On the other hand, steady-state renal temperature increased to an increasing value after an ODC higher than 70%, and this may reflect increasing heat accumulation effect. It was also observed that a marked reduction in ODC, above an ODC of about 70%, considerably prolonged the time for which renal temperature to reach the safety threshold. This is likely due to the concordance with the results of Wanderling et al. [13]. The current theory is supported by the experimental results, which demonstrate that, over the very fine-tuning of the ODC required to minimize continuous activation time of the laser, the laser may be used for a greater length of time without crossing the safety temperature limit. One interesting point must be considered in this trial.

The experiment used a fixed superpulsed thulium fiber laser, one diameter of the fiber, and a ureteral guide sheath with a flexible ureteroscope. The effect of fiber diameter on temperature and size of the soft sheath is an area for future research. In addition, the fact that this was an in vitro experiment does not bring into play the physiological factors in the changes in temperature, like renal irrigation and urine production. More studies are essential to clarify whether experiments on animals present a solution to this problem. In a nut shell, the outcome of the study has indicated that the decrease in ODC ratio from applying retrograde intrarenal surgery can have the effect of substantially reducing the rise in renal temperature. This may provide a new safe and effective method for clinical application in surgery.

Conclusion

Therefore, reducing the ratio of ODC allows substantial relief in renal temperature elevation during super-pulse optical fiber thulium laser lithotripsy. When gravel power and irrigation speed have a 1:1 adjustment ratio, it can effectively keep renal temperature within safe limits, guarding against thermal injury of kidney tissue.

Author contributions Ding tianfu.Xu zheng.and Li jianxing. wrote the main manuscript text. Huang zhongyue. Xiao bo. and Huweiguo prepared all figures and table. All authors reviewed the manuscript.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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研究

超脉冲光纤铥激光碎石术中灌注率、操作者工作周期和肾内温度的体外研究

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摘要

目的本研究旨在探讨使用超脉冲光纤铥激光进行逆行肾内手术时，灌注速度、操作者工作周期（ODC）与肾内温度之间的关系。

方法将结石置于新鲜分离的猪肾中，用穿刺针将温度探头置于结石周围2毫米处，并将压力探头放置于上盏、下盏及肾盂。将整个装置置于37°C恒温水浴中以模拟人体环境。激光功率在10至30瓦之间变化，灌注速度为10-30 ml/min。此外，在激光功率为20瓦且灌注速度为10 ml/min时，设置不同的工作周期（ODC）。监测温度和压力的变化。

结果在10 W至30 W激光功率范围内，肾脏温度与灌注速率呈正比关系。激光功率与灌注速率的百分比比率为1：1，可将肾脏温度维持在安全水平。当激光功率为20 W且灌注速率为10 ml/min时，肾脏内部温度会随着ODC值的增加而急剧上升。通过降低ODC值的比率，可显著减少肾脏内部温度的升高。

结论保持激光功率与冲洗速度1：1的比率可有效防止肾脏组织的热损伤或损伤。此外，通过调整工作循环（ODC）比率，也可降低肾内温度。

关键词超脉冲光纤铥激光器·操作员工作周期（ODC）·灌注率·肾内温度

介绍

医疗技术的持续发展推动了激光碎石术的不断进步，这项技术现已发展成熟。采用1940纳米波长的超脉冲光纤铥激光器，已成为碎石治疗的重要候选方案。由于该波长与水分子吸收峰高度重合，其在水溶液中的吸收系数显著高于传统2100纳米钬激光。这种特性使得该波长在临床应用中展现出独特优势。

钬激光碎石技术在碎石效率方面具有显著优势[1，2]。目前，由于其广泛的应用场景和良好的治疗效果，钬激光碎石已成为（柔性）上尿路系统结石的首选方案[3]。更重要的是，超脉冲光纤铥激光器不仅展现出优于钬激光的碎石效率，更在尿路结石治疗领域实现了重大突破——该技术具有更低的结石反弹力和更细的光纤直径[4]。这些特性表明，超脉冲光纤铥激光器在尿路结石治疗领域具有广阔的应用前景。在碎石技术的发展过程中，激光碎石的安全性始终与结石粉碎效果同等重要。本研究旨在优化激光碎石过程中的温度控制和冲洗液流速，以实现安全有效的治疗效果。

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材料和方法

体外建模

本研究采用新鲜离体猪肾样本，所有实验均在严格遵循伦理规范的条件下获取，所有实验猪均经过人道安乐死处理。研究获得伦理审查委员会批准，并取得伦理批件号[IACUC-202306-P-001]。结石样本取自本机构结石标本库，经成分分析确认为草酸钙单水合物结石（CT值：890±123 HU）。实验设备包括：外径F8.6的一次性电子输尿管镜（安徽幸福工厂医疗器械有限公司）、输尿管套管（F11/13莱凯医疗器械（北京）有限公司）、配备200μm光纤的铥光纤超脉冲激光器（A-ONE莱凯医疗器械（北京）有限公司）。（有限公司）配备多通道实时温度计（NF4000P-8广州瑞曼婷仪器厂）、精密恒流实验泵（BT-1河北荣柏电器厂）、高精度数字压力表（DT-1上海瑞祥仪器厂）、温控水浴、生理盐水等核心手术器械。

该手术流程包括将结石精准置入肾盂，通过穿刺针插入温度探头，使其距离肾盂内的结石约2毫米。随后小心插入输尿管套管，并用结扎线固定于输尿管。使用同一根穿刺针将压力传感器分别置入上盏、下盏及肾盂。整个装置被置于恒温水浴中，温度维持在37°C以模拟人体环境温度。

实验步骤

实验室温度设定为25℃。激光碎石功率设置为10W（1.0焦耳×10赫兹，0.1焦耳×100赫兹）、15W（1.5焦耳×10赫兹，0.15焦耳×100赫兹）、20W（2.0焦耳×10赫兹，0.1焦耳×200赫兹）和25W（2.5焦耳×10赫兹，0.1焦耳×250赫兹）。
30 W（1.0 J×10 Hz，0.1 J×300 Hz）。灌注速度设置为10、15、20、25和30 ml/min（灌注液为生理盐水，温度为25°C）。连续激光激发时间为120秒。

对于20瓦（2.0焦耳×10赫兹）的激光碎石功率和10毫升/分钟的灌注速度（灌注液为生理盐水，温度为25°C），每个20秒构成一个操作周期。激光器采用ODC模式运行，通过设置10种不同ODC模式来模拟多种手术策略：ODC10%：激光激活2秒后关闭18秒。ODC20%：激活4秒后关闭16秒。ODC30%：激活6秒后关闭14秒。ODC40%：激活8秒后关闭12秒。ODC50%：激活10秒后关闭10秒。ODC60%：激活12秒后关闭8秒。ODC70%：激活14秒后关闭6秒。ODC80%：激活16秒后关闭4秒。ODC90%：激活18秒后关闭2秒。ODC100%：激光持续激活20秒，不设关闭周期。每个周期重复6次，形成大规模实验组。

温度探头和压力探头均以每秒一次的频率实时监测参数并记录变化。每组参数的上述实验重复5次，且每次重复均使用新肾脏。

数据收集和分析

实验至少重复五次，数据以平均值给出。使用R版本4.3.3中的ggplot2绘制数据图。数值以均值±标准差表示。采用配对t检验进行两组间比较，采用非参数秩和检验进行多组间比较。显著性差异设定为$p<0.05$。

结果

连续激光碎石术中肾内温度的变化

在10 W的碎石功率下，当冲洗速度分别为10 ml/min、15 ml/min、20 ml/min、25 ml/min和30 ml/min时，肾内温度达到稳态，稳态温度分别为38.6°C、35°C、33.1°C、31.7°C和30.7°C，均未超过安全阈值（图1）。在15 W的碎石功率下，当冲洗速度为10 ml/min时，肾内温度继续上升。然而，当冲洗速度为15 ml/min、20 ml/min、25 ml/min和30 ml/min时，肾内温度达到稳态，稳态温度分别为38.4°C、35.9°C、34.7°C和34.4°C，均未超过安全阈值（图2）。在20 W的碎石功率下，当冲洗速度为10 ml/min和15 ml/min时，肾内温度继续上升。然而，当冲洗速度为20 ml/min、25 ml/min和30 ml/min时，肾内温度

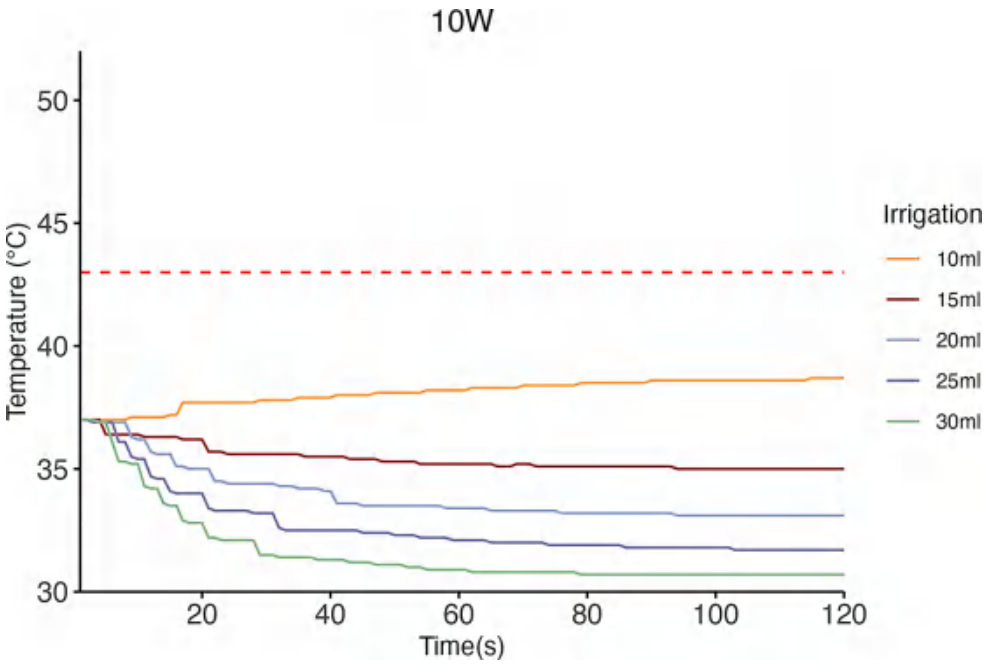


图1 10W碎石功率下各灌注速度的肾脏温度

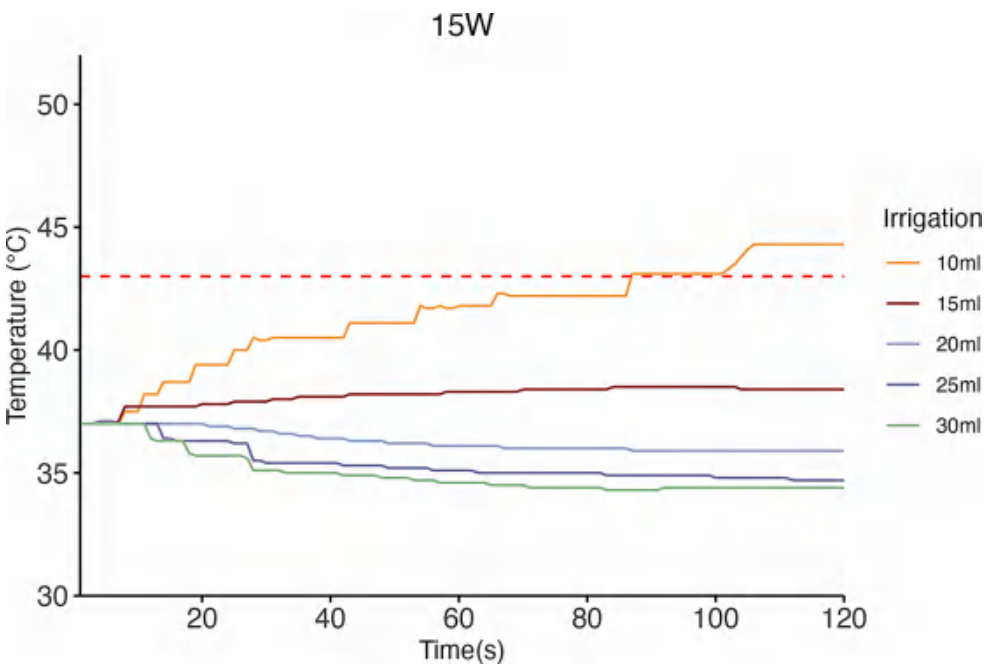


图2 15W碎石功率下各灌注速度的肾脏温度

达到稳态，稳态温度分别为38.7°C、36.3°C和34.2°C，均未超过安全阈值（图3）。在碎石功率为25W时，随着灌注速度为10ml/min、15ml/min和20ml/min，肾内温度持续上升。然而，在灌注速度为25ml/min和30ml/min时，肾内温度分别达到稳态，稳态温度为38.3°C和35.7°C，均未超过安全阈值（图4）。在碎石功率为30W时，随着灌注速度为10ml/min，肾内温度继续上升。min，15 ml/min，20 ml/min，和25 ml/min。然而，在30 ml/min的灌注速度下，肾内温度达到稳态，稳态温度为37.5°C，未超过安全阈值（图5）。在不同灌注速度下，肾内盆腔/盏压未超过30mmH $_2$O（表1）。

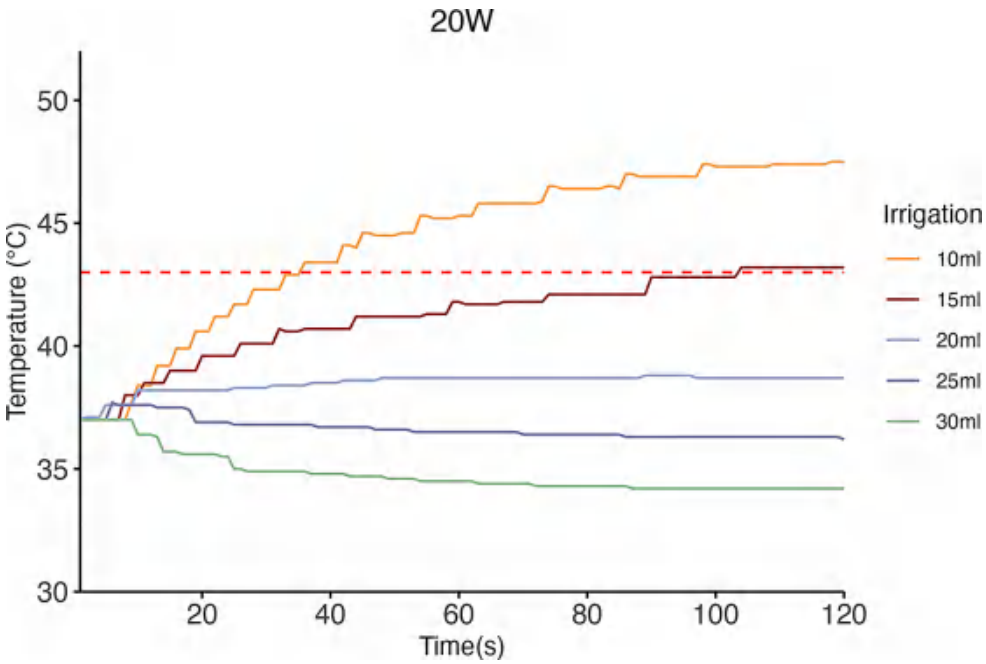


图3 20W碲石功率下各灌注速度的肾脏温度

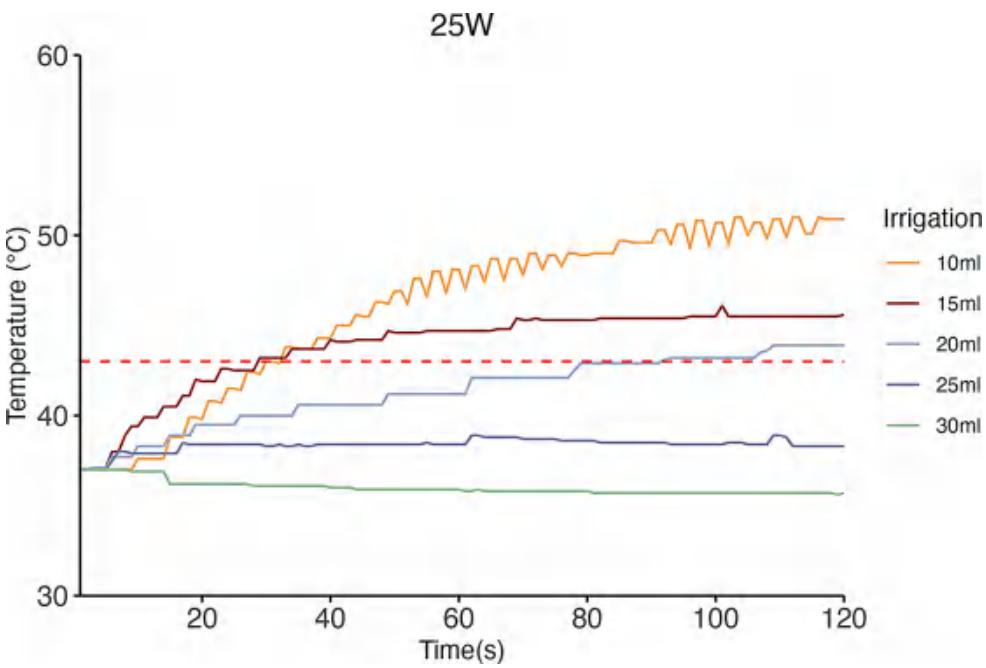


图4 25W碲石功率下各灌注速度的肾脏温度

不同ODC比值下的肾内温度变化

当工作循环率（ODC）维持在60%以下时，肾内稳态温度在达到某个临界值后趋于稳定，不会随时间推移继续升高。反之，当ODC超过70%时，后续稳态阶段的肾内温度会持续上升（图6）。随着ODC值的增加，最高肾内温度呈现显著上升趋势：ODC50%时为40.0±0.52°C；ODC 60%：41.6±0.38°C；ODC 70%：43.4±0.48°C；ODC 80%：44.8±0.73°C；ODC 90%：46.7±0.54°C（表2）。当ODC比率为70%、80%、90%和100%时，肾内温度达到安全阈值温度的时间分别为56.0±1.0s、51.8±1.48s、32.0±1.58s和20.6±1.14s（表3）。

图5 30W砾石功率下各灌注速度的肾脏温度

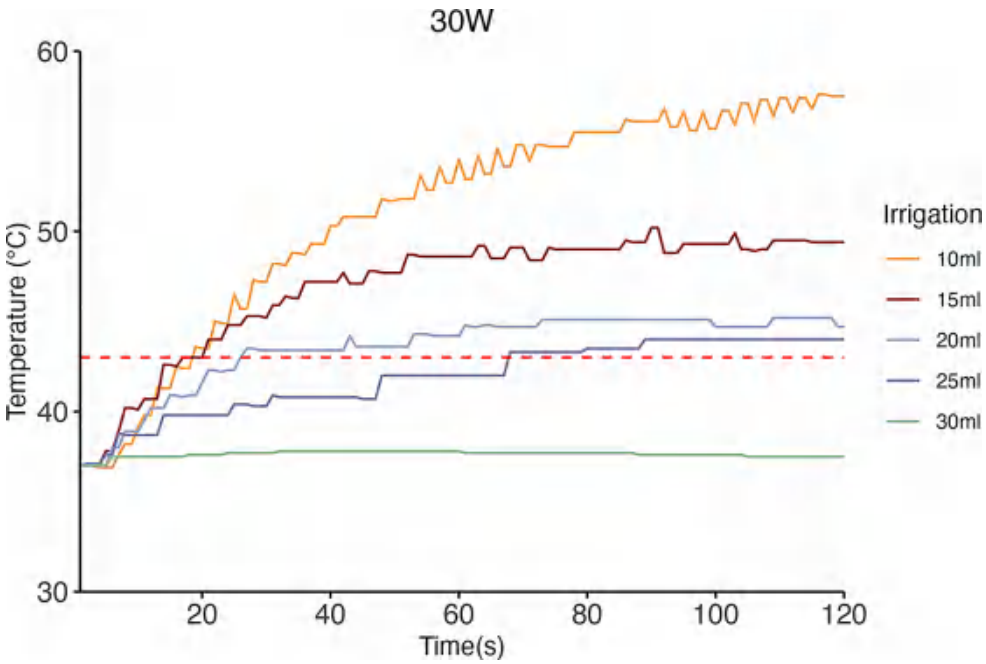


表1不同冲洗速度下的肾内压力条件（mmH_2O）

灌注速度	较高的花萼	向下花萼	肾盂	F	*p*
10 ml/min	4.2±0.07	3.85±0.23	4.83±0.09	33.46	<0.01
15 ml/min	4.6±0.19	4.88±0.08	5.48±0.15	28.27	<0.01
20 ml/min	5.96±0.04	6.08±0.15	6.35±0.12	10.05	<0.05
25 ml/min	6.18±0.04	6.50±0.28	9.08±0.15	215.68	<0.01
30 mlmin	7.95±0.54	8.65±0.53	11.55±0.15	54.82	<0.01

表3不同比例ODC达到安全阈值所需时间（秒）

乌氨酸脱羧酶 时间	70%	80%	90%	100%
到达安全区的时间阈值	56.0±1.0	51.8±1.48	32.0±1.58	20.6±1.14

图6 不同比例工作周期（ODC）下肾脏温度曲线（激光功率设定为20 W，冲洗速度为10 ml/min）

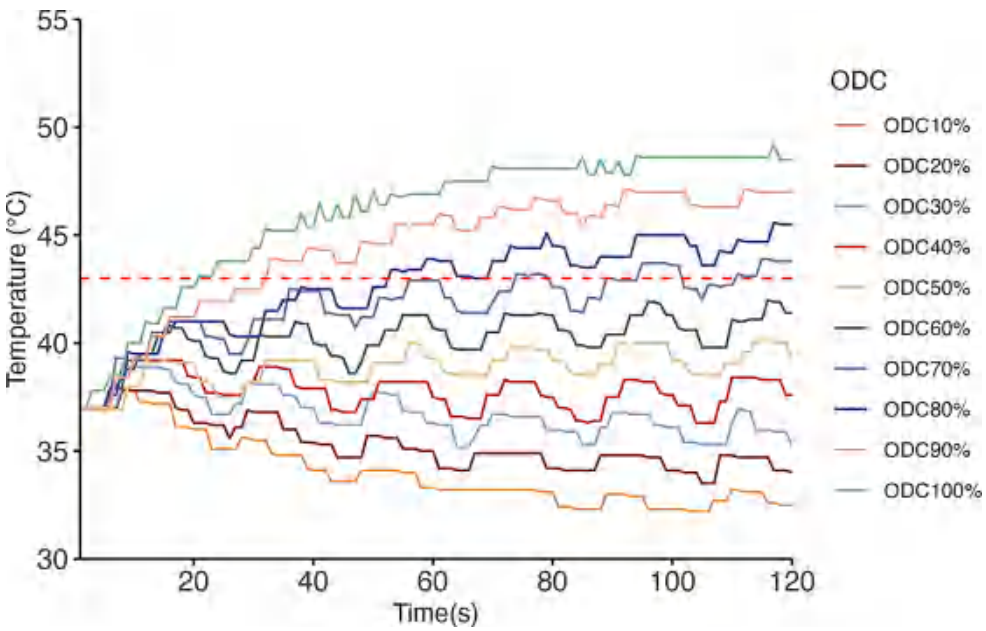


表2不同工作循环（ODC）会导致肾内温度不同（℃）

乌氨酸脱羧酶	50%	60%	70%	80%	90%
温度	40.0±0.52	41.6±0.38	43.4±0.48	44.8±0.73	46.7±0.54

讨论

早期研究显示，人体组织中存在大量细胞坏死现象。43 温度降至0°C时，细胞死亡率进一步上升至45°C[5]当温度达到60°C时，组织中的蛋白质会发生不可逆的变性，导致组织结构永久破坏、功能丧失。因此，43°C也被视为人体组织的温度临界值。在逆行肾内手术中，灌注速率是决定组织温度的关键因素。[6]采用较高的冲洗速率有助于避免肾脏内部温度升高。当冲洗速率达到100毫升/分钟时，即使激光连续工作一分钟，温度也不会超过38.5°C[7]。但若冲洗速率过高，肾内压力会增加，可能导致术后疼痛并提高感染风险[8-10]。反之，冲洗速率不足则可能引发术中体温升高，导致组织热损伤，同时因无法及时冲洗出碎石粉而影响视野，进而造成组织进一步损伤。因此，合理控制冲洗速率对确保手术安全至关重要。在本实验中，我们对激光碎石术中的温度调控进行了详细观察与分析。10瓦碎石功率和10 ml/min的灌注速率使肾脏温度在实验初期保持稳定，该恒定温度始终低于安全阈值。实验进行时，激光功率已提升至15瓦，但灌注速率保持不变。肾脏温度平台达到44°C，这超出了人体组织的安全限度。随后通过将灌注速率增加至15 ml/min，有效控制了损伤，使温度维持在安全水平以防止热损伤。实验结果表明，随着功率增加，肾脏温度会相应升高；反之，灌注速率增加会导致肾脏温度下降。我们的观察结果与Winship等人的研究发现一致。[11]该研究团队采用3.6W、6.4W、10W、16W和20W三种不同功率的激光器，配合0mmHg、100mmHg和200mmHg三种灌注压力开展实验。研究发现，肾脏温度与灌注流速共同决定传导温度：激光功率越高，肾脏温度就越高；灌注流速越快，肾脏温度就越低[11]。这项实验最引人注目的发现是研究表明，当碎石术的功率与冲洗速度按1：1比例同步调节时，肾脏的平台温度始终低于安全阈值。这种操作方式不仅显著提升了手术安全性，更为临床医生提供了创新参数调控方案——在确保碎石术疗效最大化的同时，有效降低肾脏热损伤风险。

在我们的研究中，考虑了20瓦的碎石机功率和10毫升/分钟的灌注流速，特别关注了50%至100%范围内ODC值的变化。这一现象与经典的锯齿状波动波完全一致，对应于激光周期性激活：当激光激活时，液体温度迅速上升，停用时则缓慢下降形成平台期。肾脏的ODC比在稳态下显著升高，这与Louters等人[的观察结果相似。12]因此，当ODC值升高时，温度和能量释放会显著增加。稳态肾温在达到某个数值后趋于稳定，若将ODC值维持在60%以下则不会继续上升。另一方面，当ODC值超过70%后，稳态肾温会持续升高，这可能反映了热蓄积效应的增强。研究还发现，当ODC值超过约70%时，显著降低ODC值会大幅延长肾温达到安全阈值所需的时间。这可能与Wanderling等人的研究结果相吻合。[13]现有理论得到实验结果的支持，这些结果表明，在对激光器连续激活时间进行最小化所需的ODC微调过程中，激光器可在不突破安全温度阈值的情况下持续工作更长时间。值得注意的是，本研究中存在一个关键点需要特别关注。

本实验采用固定超脉冲钬光纤激光器、光纤直径为1毫米的导管，以及配备柔性输尿管镜的输尿管导引鞘。光纤直径对软鞘温度及尺寸的影响仍是未来研究方向。此外，由于该实验为体外操作，无法体现肾灌注、尿液生成等生理因素对温度变化的影响。需要更多研究来验证动物实验能否解决这一问题。简而言之，研究结果表明，通过逆行肾内手术降低ODC比值可显著抑制肾温升，这为临床手术提供了安全有效的解决方案。

结论

因此，降低ODC比值能显著缓解超脉冲光纤铥激光碎石术中的肾温升高。当碎石功率与冲洗速度保持1：1比例时，可有效将肾温控制在安全范围内，避免肾组织热损伤。

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Rise in intraluminal temperature during ureteroscopy: Is this a concern?

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The global increase in urolithiasis prevalence has led to a shift towards minimally invasive procedures, such as retrograde intrarenal surgery, supported by advancements in laser technologies for lithotripsy. Pulsed lasers, particularly the holmium YAG and the newer thulium fiber laser, have significantly transformed the management of upper urinary tract stones. However, the use of high-power lasers in these procedures introduces risks of heat-related injury. Laser lithotripsy works through photothermal and photomechanical effects to fragment stones, but up to 96% of the laser energy is converted into heat, increasing the risk of thermal damage to the surrounding urothelial mucosa. Studies show that even at low-power settings, intrarenal temperatures can exceed the threshold for cellular injury, particularly in confined spaces like the ureter. This narrative review explores strategies to mitigate thermal injury, including optimizing laser settings, improving irrigation flow rates, and incorporating novel methods such as cold irrigation, controlling outflow resistance, and using suction. Understanding these approaches is crucial to enhancing patient safety during high-power laser lithotripsy procedures.

Keywords: Lasers; Peroperative complications; Temperature; Ureteroscopy; Urolithiasis

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INTRODUCTION

The prevalence of urolithiasis varies significantly across global populations and has seen a notable increase in recent decades [1]. Advances in technology have shifted surgical options toward minimally invasive endoscopic procedures, such as ureteroscopy and miniaturized percutaneous nephrolithotomy. The growing use of retrograde intrarenal surgery (RIRS), which utilizes flexible ureterorenoscopes, combined with innovations in laser technologies, has revolutionized the management of upper urinary tract stone disease [2,3].

Pulsed lasers are the primary and exclusive energy source used in flexible ureteroscopy across different energy sources for lithotripsy. The holmium YAG (Ho:YAG) laser has been the standard method for many years, evolving with high-power specs and modifiable pulse width. Thulium fiber laser (TFL) has recently emerged as a promising novel armamentarium for laser lithotripsy. TFL has a wide range of energy (0.025–6 J) and frequency (5–2,400 Hz), enabling less retropulsion and finer dusting [4,5]. A recent revisit of pulsed thulium YAG (Tm:YAG) gained attention for its specific characteristics as an alternative laser for lithotripsy, which awaits the accumulation of evidence [6].

Modern high-power lasers, with their higher frequency capabilities, have enabled faster surgeries. However, the use of high-power lasers in RIRS introduces heat-related challenges [7,8]. Lasers break down stones through two primary effects: photothermal and photomechanical. The photother-

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ⓒ The Korean Urological Association

mal effect, driven by electromagnetic radiation, heats the stone components, causing chemical decomposition through laser activation, boiling, or vaporizing surrounding water. The photomechanical effect occurs when water inside the stone's pores vaporizes, causing the stone to burst from within. When the pulse duration exceeds 10 μs, the photothermal effect dominates, while pulse durations beyond 200 μs render the photomechanical impact negligible [9]. During laser lithotripsy, the fluid surrounding the stones in the collecting system may experience a significant temperature rise, potentially leading to thermal injuries to the surrounding urothelial mucosa, as demonstrated in an *in vivo* porcine study [10].

METHODS

A literature search was conducted using the PubMed database from its inception to May 2024. The keywords used included 'ureteroscopy,' 'heat,' and 'temperature.' Boolean operators (AND, OR) were applied to refine the search results. The search included *in vitro*, human, and animal studies. Both original research and review articles were considered, along with additional articles identified through the references of selected works.

WHY DOES HEAT MATTER?

Concerns regarding potential indirect injuries to the urothelial mucosa during laser lithotripsy have grown as more stones are treated using high-power lasers (100–120 W), which may increase the risk of ureteral strictures or reduced renal function. While high-power laser systems enable higher frequencies, enhancing surgical efficiency, the energy levels have not changed significantly. However, not all pulses these systems generate are directed toward stone ablation. The primary advantage of high-power lasers lies in the dusting or pop-dusting techniques, which utilize higher frequencies. These strategies are increasingly favored over traditional stone fragmentation. Yet, as dusting becomes more prevalent, the predominant photothermal effect poses potential risks. Only 17% of laser pulses effectively strike the stone during high-power pop-dusting [11]. This not only reduces ablation efficiency but also raises the temperature inside the collecting system.

During laser lithotripsy, 91% to 96% of the laser energy is converted into heat, even during efficient stone ablation [10], which can potentially lead to tissue necrosis, as demonstrated in a pilot *in vivo* porcine study [12,13]. Both the peak temperature and the duration of exposure contribute to thermal cytotoxicity [14]. The potential for thermal cell injury can be estimated using the cumulative equivalent minutes at 43°C (CEM43°C) model, introduced by Sapareto and Dewey [15]. Thermal dose quantifies the biological risk of thermal injury from any time-temperature curve, with the threshold for injury and cell death set at 120 equivalent minutes. This corresponds to maintaining a temperature of 43°C for 120 minutes or shorter exposure times at higher temperatures: 44°C for 60 minutes, 45°C for 30 minutes, and 50°C for less than a minute. At 56°C, even one second of exposure can result in thermal injury. Animal studies have shown minor thermal damage at CEM43°C <20 minutes and significant damage at CEM43°C >70 minutes [16].

Studies have indicated that the threshold for cellular thermal damage is reached even at low-power settings (<30 W) [17]. A clinical study adjusting laser settings across different power levels (10–50 W) during ureteroscopy showed that intraluminal temperatures often exceeded 56°C, where thermal injury can occur within seconds at power levels above 15–20 W and, in all cases, above 25 W. Even at 10 W, temperatures of 43°C were reached at specific points [18]. Therefore, it is crucial to identify appropriate laser settings and develop strategies to minimize temperature-related complications.

WHAT FACTORS AFFECT TEMPERATURE DURING URETEROSCOPY

The thermal risk during laser lithotripsy is primarily influenced by two key factors: the amount of energy delivered and the heat capacity of the system. While laser power is the main determinant of energy delivery, the duration of laser activation and the operator duty cycle (ODC) also play critical roles. Heat capacity, on the other hand, is determined by the amount of heat the irrigation fluid can absorb. This is influenced by the volume of fluid present during laser activation—whether in the renal pelvis, calyx, or ureter—as well as the temperature and flow rate of the irrigation fluid. Additionally, the type of laser pulse used may contribute to temperature elevation.

1. Total power applied

Higher power settings result in more significant energy deposition, which increases the risk of thermal tissue injury. *In vitro* studies using different laser settings at a fixed flow rate show that the temperature rises proportionally to total power regardless of how pulse energy and frequency are combined [4,19-21]. Aldoukhi et al. [10] evaluated caliceal fluid temperature during high-power laser lithotripsy in an

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in vivo porcine model. At 40 W (0.5 J×80 Hz) for 60 seconds without irrigation, temperatures reached 60°C within 10 seconds of laser activation. The peak temperature was 84.8°C, and the mean time to reach the threshold for thermal injury (CEM43°C of 120 minutes) was 12.7 seconds [10]. In the same study, increasing irrigation rates to 15 mL/min and 40 mL/min reduced peak fluid temperatures to 58.5°C and 37.5°C, respectively. Teng et al. [22] investigated changes in calyceal irrigation fluid temperatures during Ho:YAG laser lithotripsy in a human trial. At 1 J×20 Hz without irrigation, the time required to reach 43°C was significantly shorter than at 0.5 J×20 Hz (8.84 seconds vs. 13.71 seconds) [22]. Both studies underscore the importance of adequate irrigation flow to mitigate temperature rises. Belle et al. [23], using a TFL in an *in vitro* silicone kidney-ureter model, demonstrated that high-power lasers are associated with an increased risk of thermal damage. They advocate for conservative laser settings during ureteroscopy laser lithotripsy to minimize this risk [23]. To avoid cellular thermal damage, temperature increases are proportional to power, with recommended limits of 20–30 W for the kidney and 10–15 W for the ureter [4,21,24].

2. Lasing time and pattern

The concept of "ODC" refers to the percentage of time the laser pedal is activated during a procedure. In an *in vitro* caliceal model, Aldoukhi et al. [25] measured thermal doses by applying 1,200 J of energy with different patterns of 50% ODC over 60 seconds. When 40 W was applied at 50% ODC with activation patterns of 30 seconds on/off and 15 seconds on/off, the thermal injury threshold was reached in 9 seconds. For a 10-second on/off pattern, the threshold was reached in 45 seconds, while shorter activation times did not reach the injury threshold. This suggests that, for equivalent energy delivery, more extended pedal activation patterns result in higher thermal doses [25]. Louters et al. [26] studied temperature changes related to escalating ODC by delivering 1,800 J of Ho:YAG laser energy at 30 W (0.5 J×60 Hz) to a fluid-filled glass bulb. Their findings showed higher ODCs increased maximum temperatures and thermal doses, with ODCs of 70% or more exceeding the thermal injury threshold. Comparatively, a 50% ODC required ten times longer to reach the thermal injury threshold and allowed for an eightfold increase in the maximal allowable energy compared to a 60% ODC [26]. However, caution is warranted when interpreting these results, as *in vivo* or *in vitro* studies may not fully reflect real clinical scenarios. For example, in actual practice, lasers are rarely activated continuously for 60 seconds. To better understand ODC in clinical settings, laser logs were analyzed from ureteroscopy cases, and it found that the mean ODC was 32%, meaning that during 1 minute of lasering, the laser was activated for approximately 20 seconds. During the minute of greatest energy delivery, the mean ODC reached 63% [25]. Awareness of these concepts is essential to reduce the risk of thermal injury during laser lithotripsy procedures. Effectively managing the ODC is one key strategy to control thermal dose and enhance patient safety.

3. Volume of fluid (renal pelvis/calyx/ureter)

Æsøy et al. [17] conducted a clinical trial involving ten patients to assess renal pelvis temperatures during sheathless RIRS. They observed that temperatures reached 43°C in three patients using 20 W and eight patients using 30 W. Their findings revealed an inverse correlation between intrarenal temperature and the anteroposterior diameter of the renal pelvis, underscoring the significance of fluid volume during laser activation [17]. Rezakahn Khajeh et al. [27] investigated fluid temperature elevation and thermal dose resulting from laser activation in fluid-filled glass bulbs simulating different calyx and renal pelvis volumes. At 40 W (0.5 J×80 Hz, short pulse [SP]), both temperature elevation and thermal dose were inversely related to the fluid volume and irrigation rate. In the smallest model (0.5 mL) without irrigation, the thermal injury threshold was reached in just 3 seconds, whereas in the largest model (60.8 mL), this threshold was not reached, regardless of irrigation. This suggests that the ureter, with its smaller fluid volume compared to the renal pelvis, is more prone to thermal injury.

Furthermore, the ureter is particularly vulnerable due to its lack of surrounding vasculature, which could otherwise provide a heat sink. Its narrow lumen also impedes irrigation flow, increasing the risk of circumferential injury and stricture formation [28]. Wang et al. [18] examined the thermal effects of laser lithotripsy within the ureter, increasing power from 10 to 50 W using a rigid ureteroscope with a 550 μm fiber. Across 30 datasets, the highest recorded temperatures exceeded 43°C in 100% of cases, with 63.3% of datasets showing peak temperatures above 56°C. As the power increased, the recorded temperatures generally rose in tandem [18]. For ureteral stones, a recommended approach involves (1) ensuring moderate irrigation, (2) limiting laser activation to 3- to 4-second bursts followed by 3- to 4-second pauses to allow temperature normalization, and (3) considering the use of lower power settings during prolonged procedures.

The risk of thermal injury is notably higher in cases of impacted ureteral stones, where irrigation flow is obstructed. In a 20 W dataset comparing seven cases of impacted stones

to four cases of non-impacted calculi, the mean intraoperative temperature of the irrigation fluid in the impacted stone group was significantly higher than in the non-impacted group (38.56℃±8.51℃ vs. 34.92℃±5.35℃, p<0.001). Given the ease of access to the renal pelvis with a flexible ureterorenoscope, a potential strategy is to reposition the stone from the proximal ureter into a broader, less thermally sensitive area, such as the calyx or renal pelvis [29,30].

4. Irrigation flow rate

Increasing the rate of continuous irrigation flow during laser lithotripsy is critical for reducing intrarenal temperature [1,31]. Thermography-based evaluations suggest that temperatures around the mucosa near stones can increase rapidly during laser lithotripsy, especially when irrigation is inadequate [32]. In an *in vitro* study, Villena et al. [33] demonstrated that each 20 mL/min increase in irrigation flow resulted in a significant reduction in intrarenal temperature by 4.7℃–9.2℃ (p<0.001) and a corresponding decrease in ureteral temperature by 2.6℃–8.8℃ (p=0.01). Experimental models further suggest that higher flow rates (50–100 mL/min) are necessary to maintain safe intrarenal temperature when using laser power settings of 20 W or higher. It is crucial to avoid laser activation without irrigation, as this can lead to temperatures exceeding 100℃, posing a serious risk of thermal injury [34]. Hein et al. [35] evaluated the thermal impact of laser power settings ranging from 5 to 100 W, in combination with various irrigation rates (0–100 mL/min at 37℃). Their findings indicate that even a low power setting of 5 W during RIRS can cause a harmful temperature increase if insufficient irrigation is applied. Based on their results, they developed a formula for estimating the temperature rise (ΔT) when using irrigation rates of ≥30 mL/min: ΔT=15 K×(power [W]/irrigation [mL/min]) [35].

In a human study, intrarenal temperature remained below 43℃ during 60 seconds of laser activation at both 1 J×20 Hz and 0.5 J×20 Hz, with irrigation flow rates of 15 mL/min or 30 mL/min. At an irrigation rate of 60 mL/min, the renal calyceal temperature was maintained within a safe range, even with continuous holmium laser activation up to 40 W. However, continuous activation of a Ho:YAG laser at 32 W or higher for more than 60 seconds with limited irrigation of 30 mL/min can lead to excessive local temperature elevation [36]. A thorough understanding of the relationship between laser power, irrigation rate, and intrarenal temperature is essential for safe and effective laser lithotripsy. In this context, Marom et al. [12] proposed thermal safety boundaries for ureteroscopy, offering a conceptual framework for selecting appropriate laser settings and irrigation rates to minimize the risk of thermal injury, based on findings from an *in vivo* porcine study.

5. Properties of laser

1) Laser type and mode

Although lasers share many similarities, they are not equivalent when it comes to laser-tissue interaction. They differ in key aspects such as temperature production, ablation depth, coagulation efficiency, and cutting speed [7].

The extent of high-temperature areas during laser activation was greater in long pulse (LP) mode and Moses mode (MM) compared to SP mode and virtual basket mode (VBM). In LP mode, high-temperature areas expanded primarily in an anterior direction during the early phase of laser irradiation, while in MM, they spread in a posterior direction during early laser activation [14].

TFL has different properties from solid-state lasers like Ho:YAG and Tm:YAG. Since water absorption of TFL is four times higher than Ho:YAG, concern on higher temperature was proposed. Peteinaris et al. [37] demonstrated histopathological alterations in porcine kidneys resulting from continuous temperature increases above 43℃ when using TFL at 8 W. *In vitro* study by Peng et al. [38] showed that during TFL lithotripsy at power settings of 15W without irrigation, temperatures exceeded 43℃ after 20 seconds of laser activation. At 15 mL/min irrigation and 30 W, temperatures exceeded 43℃ after 45 seconds of laser activation. Temperatures did not exceed 43℃ at 25 mL/min and 50 mL/min irrigation rates, even at 30 W [38].

In an *in vitro* study by Belle et al. [23], TFL produced significantly higher intraureteral temperatures at all power settings (3.6, 10, 20, and 30 W), with an 11% increase in temperature compared to Ho:YAG. However, both laser technologies may remain within safe thermal limits at high energy settings, provided there is sufficient irrigation at a rate of 35 cc/min [23].

Æsøy et al. [20] investigated the temperature profile during TFL and Ho:YAG laser activation using an *ex vivo* porcine model. The lasers were activated for 180 seconds, followed by an additional 60 seconds after deactivation, using TFL (150 μm and 200 μm) and Ho:YAG (270 μm) fibers at power settings of 2.4, 8, 20, and 30 W. The threshold for thermal cell injury (43℃) was not reached at 2.4 W or 8 W, regardless of fiber size. However, a more pronounced rise in temperature was observed at 20 W and higher.

In an *ex vivo* study, Molina et al. [4] compared the rise in ureteral fluid temperature during laser lithotripsy using the 120 W Ho:YAG (P120; Lumenis Ltd.) and the 60 W SuperPulsed TFL (SPTF; SOLTIVE™). Laser lithotripsy

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was performed with a 200 μm core fiber at dusting settings (SPTF—0.1 J×200 Hz, SP; Ho:YAG—0.3 J×70 Hz, LP) and fragmenting settings (0.8 J×8 Hz, SP for both) for 5 seconds. The study showed that at the fragmenting setting, the median temperature increase was higher for TFL than for Ho:YAG (33.3℃ vs. 30.0℃). However, at dusting settings, the median temperature increase was not significantly different between the two lasers. At these settings, temperatures remained below 43℃ during ureteral lithotripsy [4]. A recent systematic review of experimental studies comparing Tm:YAG, TFL, and Ho:YAG revealed similar temperature changes across lasers, with all maintaining a safe temperature profile at power settings below 40 W [7].

MOSES technology is a laser delivery mode based on the "Moses effect," where an initial laser pulse creates a vapor bubble that enhances the energy transmission of a closely following second pulse. This effect has been shown in *in vitro* studies to reduce retropulsion, allowing higher power to be applied without the need to chase the stone. Winship et al. [39] evaluated the impact of different laser pulse types on heat production using a benchtop ureteral model. They compared SP, LP, Moses contact (MC), and Moses distance (MD) modes. LP produced significantly higher temperatures at 0.8 J×8 Hz and 1 J×10 Hz compared to MM [39]. The observed differences in heat production between pulse types are likely multifactorial and not fully understood. One explanation could be that total laser power output varies with pulse type, even when user-controlled pulse energy and frequency settings are identical. Additionally, for a fixed number of pulses at a fixed pulse energy, a longer pulse duration results in more active laser time, reducing cooling intervals between pulses. At lower pulse energies, no significant difference in heat production was observed between pulse types, which aligns with findings by Hardy et al. [40] that pulse energy and duration are correlated. Thus, at very low energies, pulse length differences may not be substantial enough to impact temperature rise.

More recently, Yamashita et al. [32] observed dynamic thermal changes among various pulse modes during laser activation using thermography. After 15 seconds and 30 seconds of activation at 0.4 J×60 Hz, water surface temperatures reached 44.7℃±1.2℃ and 46.5℃±0.5℃ for LP, and 42.2℃±0.7℃ and 44.3℃±0.6℃ for SP, respectively, demonstrating greater heat production with LP compared to SP [32]. LP and MM reached thermal thresholds faster and generated larger high-temperature areas compared to SP and VBMs. In the early phase of laser activation, most heat is produced in the forward direction with SP and LP, while in MM, the heat spreads backward, likely due to the water flow generated by laser shots in each mode. In VBM, which also uses Moses technology, the high-temperature area behind the laser fiber tip was relatively smaller compared to MM [14]. The MD mode delivers energy more efficiently through a vapor channel, resulting in more energy being directed toward stone comminution and less toward fluid heating. This is supported by previous studies showing that the single-pulse crater volume for MD was greater than for SP at a 0.5 mm distance [41].

However, *in vivo* studies have shown that MOSES pulse delivery technology does not result in a significant difference in maximal intrarenal fluid temperature compared to conventional pulse technology during flexible ureteroscopy at the same power settings, highlighting the need for further clinical research [42].

2) Fiber size

Larger laser fibers have been shown to generate significantly higher temperatures compared to smaller fibers when used at equivalent power settings. In an *ex-vivo* porcine study, Æsøy et al. [20] demonstrated a significant difference in mean temperature at 20 W between 150 μm and 200 μm fibers (39.6℃ vs. 44.9℃, p<0.001). Similarly, Butticè et al. [43] reported faster temperature elevation during laser activation in a kidney model when using a 272 μm fiber compared to a 200 μm fiber. However, it is important to note that even with consistent irrigation pressure, the irrigation flow rate decreases when larger laser fibers are introduced into the working channel, due to increased inflow resistance. This reduction in flow may limit the cooling capacity of the irrigation fluid [44].

3) Laser fiber to tissue distance

A study by Yang et al. [45] demonstrated significantly higher temperatures at shorter distances from the laser tip, attributed to the high concentration of laser energy at the fiber's activation point. The authors suggest that maintaining more than 0.05 cm between the tissue and the fiber can enhance safety [45]. Ventimiglia et al. [21] found a statistically significant positive correlation between average laser power and safety distance in an *in vitro* model, applying the thermal dose concept. They recommend limiting laser settings to below 20 W in the kidney, as thermal damage can occur even at a 5 mm distance from the laser fiber tip. In the ureter, laser settings should remain under 10 W, as tissue damage has been observed at 20 W, even at distances up to 1 mm from the fiber tip [21].

WAYS TO OVERCOME INTRARENAL TEMPERATURE ISSUES

1. Adjust irrigation temperature

Dau et al. [46] investigated the effect of irrigation fluid temperature on reaching the threshold for thermal injury during Ho:YAG laser activation at 0.5 J×80 Hz (40 W) for 60 seconds using an *in vitro* model. Compared to room temperature (19°C) and warmed irrigation (37°C), cold irrigation (1°C) significantly slowed the rate of temperature rise, reduced the plateau temperature, and lowered the thermal dose during laser activation. Without irrigation, the threshold for thermal injury was reached after 13 seconds of laser activation. With 12 mL/min irrigation, the threshold was reached in 46 seconds with room temperature irrigation, but it was not reached with cold irrigation. The same group also evaluated the effect of cold saline on caliceal fluid temperature *in vivo* using a porcine model. Consistent with the *in vitro* findings, cold irrigation effectively mitigated intrarenal temperature without impacting core body temperature, even at the maximum flow rate of 15 mL/min for 60 minutes [47].

2. Adjusting outflow resistance

As discussed, high irrigation rates have been shown to effectively control thermal dose in experimental settings [1,8,19,28,31,48]. Achieving higher irrigation rates requires minimizing outflow resistance, which refers to the friction and other factors affecting fluid dynamics as the irrigation fluid exits alongside the ureteroscope. This resistance can be reduced by using pressure-mitigating devices such as ureteral access sheaths (UAS) or catheters [49]. Larger UAS sizes further decrease outflow resistance, thereby increasing flow rates and cooling the fluid, with minimal impact on intrarenal pressure.

In an *ex vivo* porcine kidney model, Gallegos et al. [50] evaluated intrarenal temperatures under various conditions, including different irrigation heights (30, 40, and 50 cmH_2O), laser frequency (Hz), laser energy (J), and the presence or absence of a UAS. Using a 9.5 Fr flexible ureterorenoscope and a 275 μm fiber in the working channel, the application of a 12/14 Fr UAS reduced temperatures by 8.8°C compared to the no-UAS condition, in a multivariate model adjusted for energy, frequency, and irrigation rate [50].

However, larger UAS may increase the risk of ureteral injury. Considering the average size of the human ureter is approximately 10 Fr (3–4 mm), the risk of ureteral injury can reach up to 46.5% when using a 12/14 Fr UAS [51]. To minimize injury, the ideal UAS should strike a balance between being small enough to reduce trauma and large enough to ensure adequate irrigation flow and low intrarenal pressure. When UAS is inserted, the outer diameter of the ureteroscope directly impacts the outflow resistance. In this context, the concept of the "ratio of endoscopy-sheath diameter (RESD)" is vital for optimizing outflow resistance. Fang et al. [52] investigated the relationship between intrarenal pressure and RESD, concluding that maintaining an RESD below 0.75 is essential for preserving safe intrarenal pressure which translated to efficient irrigation fluid turnover, helping to regulate intrarenal temperature.

With the availability of slimmer flexible ureterorenoscope, various combinations of UAS and ureteroscopes can be tailored to specific clinical scenarios, even for patients with narrow ureters, while staying within the safe RESD range.

One promising approach to minimizing thermal injury during laser lithotripsy is the use of suction. Initially applied in percutaneous nephrolithotomy for over 25 years, the concept of suction has recently gained attention in ureteroscopy. Suction is now used not only to remove stone dust in pursuit of stone-free outcomes but also to reduce intrarenal pressure and temperature, which have become significant concerns in the high-power laser era. Current methods of utilizing suction in ureteroscopy include suction ureteral access sheath (SUAS), flexible and navigable sheath (FANS), and direct in-scope suction (DISS). Suction actively lowers intrarenal pressure, and by replacing warmed irrigation fluid with cooler fluid, it may theoretically reduce the risk of exceeding thermal dose thresholds [53,54]. At the same RESD, SUAS has demonstrated greater effectiveness in reducing intrarenal pressure and enhancing irrigation flow rate compared to conventional UAS. An RESD of <0.85 is recommended for RIRS procedures utilizing SUAS [55]. Other than active suction, the siphoning effect, which is a simple hydrodynamic created by the height difference between the two points, can also be easily applied to control the flow, eventually affecting the change in temperature [56]. However, preclinical and clinical evidence on the effect of suction and siphoning effect on intrarenal temperature remains limited, highlighting the need for further research.

FUTURE PERSPECTIVE

Human studies investigating 'safe' thresholds for intrarenal temperatures remain limited (Table 1). While numerous *in vitro* and *in vivo* studies have proposed strategies to reduce intrarenal temperatures, caution must be exercised when interpreting these findings, as preclinical results do not always directly translate to clinical outcomes [29]. Emerg-

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Table 1. Clinical studies on IRT change during laser lithotripsy

Study	Working space (No. of subjects)	Laser activation protocol	Inflow condition	Temperature measurement tool	Key findings
Æsøy et al. [17] (2024)	Renal pelvis (n=10)	• Laser power: 5, 10, 20, and 30 W • 120 s with continuous laser activation and for another 60 s after deactivation • Laser was deactivated whenever the IRT reached 43°C.	• Sheathless FURSL • Gravitational irrigation (23°C) at 60 cm • TFL/150 μm fiber	K-type thermocouple inserted through the nephrostomy tube	• IRT correlated directly to power settings • Temperatures reached 43°C in three patients applying 20 W and in eight patients applying 30 W. • The shortest activation-time until threshold was 12 s and 28 s with 30 W and 20 W settings, respectively. • There was a significant correlation between IRT and renal APD. • Using a sheathless approach, power settings of 20 W should be avoided, especially in the context of a nondilated renal pelvis.
Teng et al. [22] (2021)	Renal pelvis (n=32)	• Laser power: 1 J/20 Hz and 0.5 J/20 Hz 1) Laser activation for 60 s in the calices with irrigation → Temperature changes were documented every 5 s. 2) Laser activated without irrigation → Time needed to reach 43°C was recorded. • Laser was deactivated whenever the IRT reached 43°C.	• Storz fiberoptic flexible ureteroscope • Ho:YAG/200 μm fiber • Irrigation flow rate: 0 mL/min, 15 mL/min and 30 mL/min • 12/14 Fr UAS	K-type thermocouple attached to the scope (tip 5 mm from the distal end)	• With 15 mL/min or 30 mL/min irrigation, 43°C was not reached after 60 s laser activation at both 1 J/20 Hz and 0.5 J/20 Hz. • At the power setting of 1 J/20 Hz and irrigation flow rate of 15 mL/min, the temperature rise was significantly higher than other groups. • Without irrigation, the time needed to reach 43°C at 1 J/20 Hz was significantly shorter than that at 0.5 J/20 Hz (8.84±1.41 s vs. 13.71±1.53 s).
Wu et al. [36] (2023)	Renal pelvis (n=22)	• Laser power: 24 W, 80 Hz/0.3 J and 32 W, 80 Hz/0.4 J • 60-s laser activation	• Olympus fiber-optic flexible ureteroscope • Ho:YAG MOSES/200 μm laser fiber • Room temperature irrigation (25°C) • 12/14 Fr UAS	Thermocouple attached to the scope (its tip 5 mm from the distal end)	1) Room temperature irrigation (25°C) • With 30 mL/min or 60 mL/min irrigation, IRT did not reach 43°C in any patient after 60 s laser activation. 2) Warm irrigation (37°C), • At the setting of 32 W, 30 mL/min and 40 W, 30 mL/min after continuing laser activation, IRT reached close to or over 43°C.
Wang et al. [18] (2019)	Ureter (n=27) (30 sets)	Laser power: 10–50 W (setting unknown)	• Semirigid ureteroscope (WOLF 8.0/9.8 Fr) • Ho:YAG/550 μm laser fiber	Thermocouple temperature measurement wire	• Highest temperatures in the 30 sets of data all exceeded 43°C (100%), with 19 sets (63.3%) having peak temperatures higher than 56°C.

IRT, intrarenal temperature; FURSL, flexible ureteroscopic lithotripsy; TFL, thulium fiber laser; APD, anterior-posterior diameter; Ho:YAG, holmium YAG; UAS, ureteral access sheaths.

ing technologies are now being incorporated into flexible ureterorenoscope systems, enabling real-time temperature monitoring to maintain temperatures within safer limits [45]. These advancements may improve our understanding of the impact of temperature on clinical outcomes during ureteroscopy.

CONCLUSIONS

Intrarenal temperatures can rise significantly during laser activation, with irrigation playing a critical role in temperature control. Understanding the concept of thermal dose is essential when performing high-power laser lithotripsy, particularly in confined anatomical spaces. Implementing strategies to regulate energy delivery and optimize the system's heat capacity is key to maintaining safe temperature levels and minimizing the risk of temperature-related complications during ureteroscopy.

CONFLICTS OF INTEREST

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Research conception and design: Hyung Joon Kim and Sung Kyu Hong. Data acquisition: Hyung Joon Kim. Statistical analysis: Hyung Joon Kim. Data analysis and interpretation: Hyung Joon Kim. Drafting of the manuscript: Hyung Joon Kim and Sung Kyu Hong. Critical revision of the manuscript: Hyung Joon Kim and Sung Kyu Hong. Administrative, technical, or material support: Hyung Joon Kim. Supervision: Sung Kyu Hong. Approval of the final manuscript: Hyung Joon Kim and Sung Kyu Hong.

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输尿管镜检查过程中腔内温度的升高：这是一个问题吗？

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全球尿路结石患病率的上升趋势推动了微创手术的发展，例如逆行肾镜碎石术，这得益于碎石激光技术的进步。脉冲激光技术，尤其是钬YAG激光和新型铥光纤激光，已显著改变了上尿路结石的治疗方式。然而，高功率激光在这些手术中的应用会带来热损伤风险。激光碎石术通过光热效应和光机械效应来粉碎结石，但高达96%的激光能量会转化为热量，增加了对周围尿路上皮黏膜的热损伤风险。研究表明，即使在低功率设置下，肾内温度也可能超过细胞损伤的临界值，尤其是在输尿管等狭窄空间。这篇综述探讨了减轻热损伤的策略，包括优化激光参数、改善冲洗液流速，以及引入冷冲洗、控制流出阻力和使用负压吸引等创新方法。掌握这些技术要点，对提高高功率激光碎石术中的患者安全性至关重要。

关键词：激光；围手术期并发症；温度；输尿管镜；尿路结石

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介绍

尿路结石的患病率在全球范围内存在显著差异，且近几十年来呈现明显上升趋势[1]。随着技术进步，外科治疗方案已转向微创内镜手术，例如输尿管镜检查和微型经皮肾镜碎石术。逆行肾镜手术（RIRS）的广泛应用——该技术通过柔性输尿管肾镜配合激光技术革新，已彻底改变了上尿路结石的诊疗模式[2,3]。

在碎石术中，脉冲激光是不同能量源中用于输尿管镜检查的主要且唯一能量源。钬掺杂钇铝石榴石（Ho：YAG）激光该技术作为标准方法已沿用多年，其功率规格不断提升且脉冲宽度可调。铥光纤激光器（TFL）近期崭露头角，成为激光碎石术领域极具潜力的新利器。TFL具备宽能量范围（0.025—6焦耳）和高频段（5—2,400赫兹），能有效减少后坐力并实现更精细的碎石效果[4,5]。近期对脉冲式铥掺杂钇铝石榴石（Tm：YAG）的重新评估，因其作为碎石术替代激光器的独特性能而备受关注，目前仍在等待更多实证数据的积累[6]。

现代高功率激光器凭借其更高的频率性能，使得手术速度显著提升。然而，在RIRS治疗中使用高功率激光器会引发热相关问题[7,8]。激光器通过光热效应和光机械效应两种主要作用机制来粉碎结石。光热效应

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电磁辐射驱动的机械效应会使结石组件受热，通过激光激活、沸腾或周围水汽化引发化学分解。当结石内部孔隙中的水分汽化时，光机械效应就会发生，导致结石内部爆裂。当脉冲持续时间超过10μs时，光热效应会占据主导地位；而超过200μs的脉冲则会使光机械效应变得微不足道[9]。在激光碎石过程中，收集系统中结石周围的液体温度可能显著升高，正如一项*体内*猪实验所示[10]，这种高温可能对周围尿路上皮黏膜造成热损伤。

方法

我们使用PubMed数据库从建库至2024年5月期间进行了文献检索，检索关键词包括“输尿管镜检查”、“热”和“温度”，并采用布尔运算符（AND、OR）对检索结果进行细化，检索范围涵盖*体外*、人类和动物研究，既包含原始研究和综述文章，也包含通过选定文献的参考文献检索到的其他文献。

为什么热量很重要？

随着高功率激光（100-120瓦）在激光碎石术中的应用日益广泛，人们对输尿管黏膜可能遭受的间接损伤愈发担忧，这类技术可能增加输尿管狭窄或肾功能减退的风险。虽然高功率激光系统能实现更高频率、提升手术效率，但其能量水平并未显著改变。值得注意的是，并非所有脉冲都用于结石消融。高功率激光的主要优势在于其“粉尘消融”技术，该技术通过高频脉冲实现碎石效果，正逐渐取代传统碎石方式。然而随着粉尘消融技术的普及，其主导的光热效应也带来了潜在风险——在高功率粉尘消融中，仅有17%的激光脉冲能有效击中结石[11]。这不仅降低了消融效率，还会导致输尿管系统内部温度升高。

在激光碎石术中，91%至96%的激光能量转化为热能，即使在有效结石消融过程中[10]，这可能会导致组织坏死，*一项猪体内*预试验研究证实了这一点[12,13]。峰值温度和暴露时间都起着作用热细胞毒性[14]。热损伤的潜在风险可通过萨帕雷托和杜威提出的累积等效分钟数（43ºC，CEM43ºC）模型进行评估[15]。热剂量指标用于量化任何温度-时间曲线引发的热损伤生物学风险，其损伤阈值设定为120等效分钟。具体而言，当温度维持在43°C时需暴露120分钟，或在更高温度下分别暴露60分钟（44°C）、30分钟（45°C）及不足一分钟（50°C）。在热效应阈值（56ºC）下，即使仅暴露1秒也可能造成热损伤。动物实验表明，当暴露时间短于20分钟（CEM43ºC<20分钟）时仅产生轻微热损伤，而超过70分钟（CEM43ºC>70分钟）则会造成显著损伤[16]。

研究表明，即使在低功率设置（<30瓦）下，细胞热损伤的临界阈值也会被触发[17]。一项在输尿管镜检查过程中调整不同功率（10-50瓦）的临床研究显示，管腔温度常超过56ºC阈值——当功率超过15-20瓦时，热损伤可能在数秒内发生，而所有案例中功率超过25瓦时都会出现这种情况。即便在10瓦功率下，某些特定部位的温度也达到了43°C[18]。因此，确定合适的激光参数并制定策略以减少温度相关并发症至关重要。

URETEROSCOPY过程中哪些因素会影响温度？

激光碎石术中的热风险主要受两大因素影响：能量输送量和系统热容量。虽然激光功率是能量输送的主要决定因素，但激光激活时长和操作者工作周期（ODC）也起着关键作用。热容量则取决于冲洗液的吸热能力，这受激光激活时冲洗液的体积（无论是在肾盂、肾盏还是输尿管中）、温度及流速的影响。此外，所使用的激光脉冲类型也可能导致温度升高。

1. 总功率已应用

功率设置越高，能量沉积越显著，从而增加热损伤风险。*体外*研究显示，在固定流量条件下使用不同激光参数时，温度升高与总功率成正比，且不受脉冲能量和频率组合方式的影响[4,19-21]。Aldoukhi等[10]曾评估过高功率激光碎石术中膀胱体液的温度变化。

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*体内*猪模型。在40瓦（0.5焦耳×80赫兹）功率下未进行冲洗时，激光激活后10秒内温度达到60°C。峰值温度为84.8°C，达到热损伤阈值（CEM43°C为120分钟）的平均时间为12.7秒[10]。在同一研究中，将冲洗速率提高至15 mL/min和40 mL/min时，峰值液体温度分别降至58.5°C和37.5°C。Teng等人[22]在人体试验中研究了Ho：YAG激光碎石术期间盏状结构冲洗液温度的变化。在1焦耳×20赫兹未冲洗条件下，达到43°C所需时间显著短于0.5焦耳×20赫兹条件（8.84秒对比13.71秒）[22]。两项研究均强调了适当冲洗流量对缓解温度升高的重要性。Belle等人[23]使用*体外*硅胶肾输尿管模型中的TFL激光器，证明高功率激光与热损伤风险增加相关。他们建议在输尿管镜激光碎石术中采用保守的激光设置以降低该风险[23]。为避免细胞热损伤，温度升高与功率成正比，建议肾脏功率限制为20—30 W，输尿管功率限制为10—15 W[4,21,24]。

2. 激光时间和模式

“ODC”（热损伤阈值百分比）的概念指的是激光踏板在治疗过程中被激活的时间占比。在*体外*骨膜模型中，Aldoukhi等人[25]通过采用50%ODC的不同能量模式，以1200焦耳总能量持续60秒进行热剂量测量。当以50%ODC强度施加40瓦功率，采用30秒开/关+15秒开/关的激活模式时，仅需9秒即可达到热损伤阈值。若改为10秒开/关模式，阈值则需45秒才能触发，而更短的激活时间则无法达到损伤阈值。这表明在能量输出相同的情况下，延长踏板激活时间会导致更高热剂量[25]。Louters团队[26]通过向充液玻璃灯管输送30瓦（0.5焦耳×60赫兹）的Ho：YAG激光能量（1800焦耳总能量），研究了ODC值递增引发的温度变化。研究发现，随着热损伤阈值（ODCs）的升高，最大温度和热剂量也随之增加，当ODCs达到70%及以上时，即可突破热损伤阈值。相比之下，50%的ODC需要多出十倍时间才能达到热损伤阈值，且与60%的ODC相比，其允许的最大能量增幅可达八倍[26]。但需注意，这些结果在解读时需谨慎，因为*体内*或*体外*研究可能无法完全反映真实临床场景。例如在实际操作中，激光设备很少会连续工作60秒。为了更好地理解临床环境中的ODC，la-研究人员对输尿管镜检查病例的激光治疗记录进行分析，发现平均ODC值为32%，这意味着在1分钟的激光治疗过程中，激光器实际工作时间约为20秒。当能量输送达到峰值时，平均ODC值可飙升至63%[25]。掌握这些关键概念对于降低激光碎石术中的热损伤风险至关重要。有效控制ODC值是调节热剂量、提升患者安全性的核心策略之一。

3. 液体积（肾盂/肾盏/输尿管）

Æsøy等人[17]开展了一项涉及10名患者的临床试验，旨在评估无鞘激光肾消融术（RIRS）期间肾盂温度的变化。研究发现，使用20瓦功率的患者中有3人出现肾盂温度高达43°C，而使用30瓦功率的患者中这一比例为8人。研究结果表明，肾盂温度与肾盂前后径呈负相关，这突显了激光激活过程中液体容量的重要性[17]。Rezakahn Khajeh等学者[27] 本研究通过模拟不同肾盏和肾盂体积的玻璃球体，探究了激光激活引发的流体温度升高及热剂量变化。在40瓦功率（0.5焦耳×80赫兹，短脉冲[SP]）条件下，温度升高和热剂量均与流体体积及冲洗速率呈负相关。最小模型（0.5毫升）未冲洗时，仅3秒即达到热损伤阈值；而最大模型（60.8毫升）无论是否冲洗均未达到该阈值。这表明与肾盂相比，输尿管因流体体积较小，更容易发生热损伤。

此外，输尿管因缺乏周围血管网络而特别脆弱，这些血管本可提供散热功能。其狭窄的管腔还会阻碍冲洗液流动，增加环形损伤和狭窄形成的风险[28]。王等学者[18]研究了输尿管内激光碎石术的热效应，使用550μm光纤的刚性输尿管镜将功率从10瓦提升至50瓦。在30组数据中，所有案例记录的最高温度均超过43°C，其中63.3%的数据组峰值温度超过56°C。随着功率增加，记录的温度普遍同步上升[18]。对于输尿管结石，推荐的治疗方案包括(1) 确保适度灌溉，(2)将激光激活限制为3-4秒的脉冲，随后暂停3-4秒以使温度恢复正常，(3)在长时间操作过程中考虑使用较低功率设置。

当输尿管结石发生嵌顿导致冲洗液流动受阻时，热损伤风险显著升高。一项20 W研究通过对比七例嵌顿结石病例发现

在四例非嵌顿结石病例中，嵌顿结石组的术中冲洗液平均温度显著高于非嵌顿组（38.56°C±8.51°C vs.34.92°C±5.35°C，p<0.001）。鉴于柔性输尿管肾镜可轻松进入肾盂，一种潜在策略是将结石从近端输尿管重新定位至更宽广、热敏感性更低的区域，例如肾盏或肾盂[29,30]。

4. 灌注流速

在激光碎石术中提高连续灌注流速对于降低肾内温度至关重要[1,31]。基于热成像的评估表明，在激光碎石术过程中，结石附近的黏膜周围温度可能迅速升高，尤其是在灌注不足时[32]。在一项*体外*研究中，Villena等人[33]证明，灌注流速每增加20 mL/min，肾内温度就会显著降低4.7°C—9.2°C（p<0.001），输尿管温度则相应下降2.6°C—8.8°C（p=0.01）。实验模型进一步表明，当使用20 W或更高功率的激光时，需要更高的流速（50—100 mL/min）来维持安全的肾内温度。必须避免在无灌注的情况下激活激光，因为这可能导致温度超过100°C，造成严重的热损伤风险[34]。Hein等人[35]评估了5至100 W不同功率激光与各种灌注速率（0—100 mL/min，37°C）组合的热影响。他们的研究结果表明，即使在RIRS期间使用5 W的低功率设置，如果灌溉量不足，也会导致有害的温度升高。基于他们的研究结果，他们开发了一个用于估算使用≥30 mL/min灌溉速率时温度升高（ΔT）的公式：ΔT=15 K×（功率[W]/灌溉[ML/min]）[35]。

在一项人体研究中，当使用1 J×20 Hz和0.5 J×20 Hz两种激光激活模式时，即使在15 mL/min或30 mL/min的灌注流速下，肾内温度在60秒内仍保持在43°C以下。当灌注流速为60 mL/min时，即使持续使用高达40 W的钬激光激活，肾盏温度仍能维持在安全范围内。然而，若以32 W或更高功率的Ho：YAG激光持续激活超过60秒，且灌注流速仅为30 mL/min，可能导致局部温度过度升高。
[36]要实现安全有效的激光碎石术，必须全面掌握激光功率、冲洗速率与肾内温度之间的关系。在此背景下，Marom等学者[12]为输尿管镜检查制定了热安全边界，为选择合适的激光参数和冲洗速率提供了理论框架。

根据一项*体内*猪研究的结果，将热损伤风险降至最低。

5. 激光器属性

1) 激光类型和模式

虽然激光器具有许多相似之处，但在激光与组织的相互作用方面并不等同。它们在温度产生、消融深度、凝固效率和切割速度等关键方面存在差异[7]。

激光激活过程中，长脉冲（LP）模式和Moses模式（MM）的高温区域范围，明显大于SP模式和虚拟篮模式（VBM）。具体来说，在LP模式下，高温区域在激光照射初期主要向前方扩展；而MM模式下，高温区域则在激光激活初期向后方扩散[14]。

TFL与Ho：YAG和Tm：YAG等固态激光器具有不同的特性。由于TFL的水吸收率是Ho：YAG的四倍，因此提出了对更高温度的担忧。Peteinaris等人[37]展示了在使用8 W TFL时，当温度持续升高至43°C以上时，猪肾脏出现组织病理学改变。Peng等人[38]的体外研究显示，在15 W功率设置下进行TFL碎石术且未冲洗时，激光激活20秒后温度超过43°C。在15 mL/min冲洗和30 W功率下，激光激活45秒后温度超过43°C。即使在30 W功率下，25 mL/min和50 mL/min的冲洗速率下温度也未超过43°C[38]。

Belle等人[23]的*体外*研究表明，TFL在所有功率设置（3.6、10、20和30 W）下产生的输尿管内温度显著高于Ho：YAG，温度比Ho：YAG高11%。然而，只要以35 cc/min的速率进行充分灌洗，两种激光技术在高能量设置下可能仍处于安全的热限内[23]。

Æsøy等人[20]采用*离体*猪模型研究了TFL和Ho：YAG激光激活过程中的温度变化。实验中，研究人员分别使用功率为2.4、8、20和30瓦的TFL光纤（150μm和200μm）及Ho：YAG光纤（270μm），每次激活持续180秒，停机后继续加热60秒。结果显示：在2.4瓦和8瓦功率下，无论光纤尺寸如何，温度均未达到热细胞损伤阈值（43°C）。但当功率提升至20瓦及以上时，温度升高现象显著加剧。

在一项*ex vivo*研究中，Molina等人[4]比较了使用120 W Ho：YAG（P120；Lumenis Ltd.）和60 W SuperPulsed TFL（SPTF：soltive™）进行激光碎石术时输尿管液温度的升高。

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实验采用200μm光纤进行碎石，分别设置为碎石模式（SP-TF—0.1焦耳×200赫兹，SP；Ho：YAG—0.3焦耳×70赫兹，LP）和碎石模式（两种模式均采用0.8焦耳×8赫兹，SP）持续5秒。研究显示，在碎石模式下，TFL激光器的温度中位数增幅高于Ho：YAG激光器（33.3°C对比30.0°C）。但在碎石模式下，两种激光器的温度中位数增幅无显著差异。在此模式下，输尿管碎石术期间温度始终低于43°C[4]。近期一项系统综述对比了Tm：YAG、TFL和Ho：YAG三种激光器的实验数据，发现各激光器的温度变化趋势相似，且在功率低于40瓦时均能保持安全的温度曲线[7]。

摩西技术是一种基于“摩西效应”的激光输送模式，其原理是通过初始激光脉冲产生气泡，从而增强紧随其后的第二脉冲能量传输效率。*体外研究*表明，这种效应能有效减少反冲现象，使得无需追踪结石即可施加更高功率。Winship等人[39]使用台式输尿管模型评估了不同激光脉冲类型对产热的影响，对比了SP、LP、摩西接触（MC）和摩西距离（MD）四种模式。实验数据显示，当脉冲能量为0.8焦耳×8赫兹和1焦耳×10赫兹时，LP模式产生的温度显著高于MM模式[39]。脉冲类型间的产热差异可能由多重因素共同作用，目前尚未完全阐明。一种可能的解释是：即使用户设定的脉冲能量和频率相同，不同脉冲类型会导致总激光功率输出差异。此外，在脉冲能量固定且脉冲次数不变的情况下，延长脉冲持续时间会增加激光作用时间，从而缩短脉冲间的冷却间隔。在较低脉冲能量下，不同脉冲类型产生的热量无显著差异，这与Hardy等人[40]关于脉冲能量与持续时间存在相关性的研究结果一致。因此，在极低能量条件下，脉冲长度的差异可能不足以影响温度上升。

近期，山下等人[32]通过热成像技术观察到，不同脉冲模式在激光激活过程中会产生动态热变化。当采用0.4焦耳×60赫兹的参数进行15秒和30秒激活时，水表面温度分别达到44.7°C±1.2°C（LP模式）和46.5°C±0.5°C（SP模式），而SP模式的温度分别为42.2°C±0.7°C和44.3°C±0.6°C，这表明LP模式的产热量显著高于SP模式[32]。与SP模式和VBMs模式相比，LP模式和MM模式能更快达到热阈值，并形成更大的高温区域。在激光激活初期，SP模式和LP模式主要产生前向热传导，而MM模式的热量会向后扩散，这可能是由于水分子的热传导特性所致。

不同模式下激光脉冲产生的流动特性存在差异。采用Moses技术的VBM系统中，激光光纤尖端后方的高温区域比MM系统更为紧凑[14]。MD模式通过蒸汽通道实现更高效的能量传输，使得更多能量用于石料粉碎而非流体加热。此前研究证实，在0.5毫米距离下，MD模式的单脉冲坑体积显著大于SP模式[41]。

然而，*体内*研究表明，在相同功率设置下，与传统脉冲技术相比，moses脉冲输送技术在输尿管镜软镜检查期间不会导致最大肾内液体温度产生显著差异，这强调了进一步临床研究的必要性[42]。

2) 纤维尺寸

研究表明，当功率设置相同时，大直径激光光纤产生的温度显著高于小直径光纤。在一项*离体猪实验*中，Æsøy团队[20]发现150μm和200μm光纤在20瓦功率下的平均温度存在显著差异（39.6°C对比44.9°C，$p<0.001$）。类似地，Buttice团队[43]在肾脏模型中发现，使用272μm光纤时，激光激活过程中的温度上升速度比200μm光纤更快。但需注意的是，即使保持恒定的灌注压力，当大直径光纤进入工作通道时，由于流入阻力增大，灌注液流量会随之减少。这种流量下降可能会影响灌注液的冷却效果[44]。

3) 激光光纤到组织距离

杨等人[45]的研究表明，随着与激光尖端距离的缩短，温度会显著升高，这归因于光纤激活点处激光能量的高浓度。研究者建议，保持组织与光纤之间超过0.05厘米的间距可提升安全性[45]。文蒂米利亚团队[21]通过*体外*模型应用热剂量概念，发现平均激光功率与安全距离存在统计学意义上的正相关关系。他们建议在肾脏治疗中将激光功率限制在20瓦以下，因为即使距离激光光纤尖端5毫米仍可能引发热损伤。对于输尿管治疗，激光功率应控制在10瓦以内，因为在距离光纤尖端仅1毫米处，20瓦功率仍会导致组织损伤[21]。

克服肾内温度问题的方法

1. 调节灌溉温度

Dau等人[46]使用*体外*模型研究了在0.5 J×80 Hz（40 W）条件下激活Ho：YAG激光器60秒时，灌注液温度对达到热损伤阈值的影响。与室温（19°C）和温热灌注（37°C）相比，冷灌注（1°C）显著减缓了温度上升速率，降低了平台温度，并在激光激活期间降低了热剂量。未进行灌注时，热损伤阈值在激光激活13秒后达到。使用12 mL/min的灌注液时，室温灌注下阈值在46秒内达到，而冷灌注则未达到。同一研究团队还使用猪模型评估了冷盐水*体内*对肾盏液温度的影响。与*体外*结果一致，即使在最大流速为15 mL/min持续60分钟的情况下，冷灌注也能有效降低肾内温度而不影响核心体温[47]。

2. 调节出液阻力

如前所述，高灌注速率已被证实能有效控制实验环境中的热剂量[1,8,19,28,31,48]。要实现更高的灌注速率，需要最大限度降低流出阻力——即当灌注液随输尿管镜排出时，流体动力学中涉及的摩擦力及其他影响因素。通过使用减压装置（如输尿管通路鞘UAS或导管）可有效降低此类阻力[49]。增大UAS尺寸能进一步降低流出阻力，从而提升流速并实现液体冷却，同时对肾内压力的影响微乎其微。

在一项*离体*猪肾模型研究中，Gallegos团队[50]通过多变量模型评估了不同条件下的肾内温度变化，实验参数包括冲洗高度（30、40和50厘米$_2$水柱）、激光频率（Hz）、激光能量(J)以及是否使用UAS。研究采用9.5 Fr柔性输尿管肾镜配合275μm光纤作为工作通道，结果显示：当使用12/14 Fr UAS时，经能量、频率和冲洗速率校正后的温度降幅达到8.8°C，较未使用UAS的对照组显著降低[50]。

然而，较大的导管尺寸（UAS）可能增加输尿管损伤风险。考虑到人类输尿管平均直径约为10 Fr（3-4毫米），使用12/14 Fr UAS时输尿管损伤风险可达46.5%[51]。为降低损伤风险，理想的导管尺寸需在创伤最小化与尺寸适配性之间取得平衡。

该数值足以确保充足的灌注流量和较低的肾内压力。当插入UAS时，输尿管镜的外径会直接影响流出阻力。在此背景下，“内镜-鞘管直径比（RESD）”这一概念对于优化流出阻力至关重要。方等人[52]研究了肾内压力与RESD的关系，得出结论：保持RESD低于0.75对于维持安全的肾内压力至关重要，这能实现灌注液的高效循环，进而帮助调节肾内温度。

得益于更纤细的柔性输尿管肾镜问世，医生可针对不同临床情况灵活组合UAS与输尿管镜，即便面对输尿管狭窄患者，仍能确保安全的RESD范围。

在激光碎石术中减少热损伤的一种有效方法是采用负压吸引技术。这项技术最初应用于经皮肾镜取石术已有25年以上历史，近年来在输尿管镜检查领域也逐渐受到重视。如今，负压吸引不仅用于清除结石碎屑以实现无结石效果，还能有效降低肾内压力和温度——这在高功率激光时代已成为重要考量因素。目前输尿管镜检查中常用的负压吸引技术包括负压输尿管套管（SUAS）、柔性导航套管（FANS）以及内镜直吸（DISS）。负压吸引能主动降低肾内压力，通过用低温冲洗液替代温热冲洗液，理论上可减少超过热剂量阈值的风险[53,54]。在相同RESD值下，SUAS在降低肾内压力和提升冲洗流量方面比传统肾盂输尿管连接术（UAS）更有效。对于采用SUAS的输尿管结石碎石术（RIRS），建议将RESD值控制在0.85以下[55]。除了主动抽吸外，虹吸效应——这种由两点高度差产生的简单流体动力学现象——同样能有效调控血流，进而影响体温变化[56]。不过，目前关于抽吸和虹吸效应对肾内温度影响的临床前及临床证据仍显不足，这凸显了开展深入研究的必要性。

未来视角

目前针对肾内温度安全阈值的人体研究仍较为有限（表1）。尽管已有大量*体外*和*体内*研究提出了降低肾内温度的策略，但需谨慎解读这些研究结果，因为临床前研究结果并不总能直接转化为临床疗效[29]。Emerg-

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表1.激光碎石术中IRT变化的临床研究

研究	工作的空间（编号主题	激光激活方案	流入条件	温度测量工具	主要发现
Æsøy等人。[17] (2024)	肾盂 (n=10)	• 激光功率：5、10、20和30 W • 持续激光激活120秒，停用后继续60秒 • 当IRT达到43°C时，激光将被关闭。	• Sheathless FURSL • 重力灌溉（23°C），60 cm • TFL/150μm光纤	K型热电偶插入肾造瘘管	• IRT与功率设置相关 • 使用20W的三名患者和使用30W的八名患者的体温均达到43°C。 • 在30瓦和20瓦两种功率设置下，达到阈值所需的最短激活时间分别为12秒和28秒。 • IRT与肾APD存在显著相关性。 • 采用无鞘管技术时，应避免使用20瓦的功率设置，尤其在肾盂未扩张的情况下。
滕等人 [22] (2021)	肾盂 (n=32)	• 激光功率：1 J/20 Hz和0.5 J/20 Hz 1) 对花萼进行60秒激光激活并同步灌注——温度变化每5秒记录一次。 2) 激光激活无需冲洗——记录达到43°C所需时间。 • 当IRT达到43°C时，激光将被关闭。	• Storz纤维光导软性输尿管镜 • Ho：YAG/200μm光纤 • 灌注流速：0 mL/min、15 mL/min和30 mL/min • 12/14 Fr UAS	K型热电偶连接至内窥镜（尖端距离远端5 mm）	• 在15 mL/min或30 mL/min的灌溉条件下，无论是1 J/20 Hz还是0.5 J/20 Hz，60秒激光激活后均未达到43°C。 • 在功率设置为1 J/20 Hz和灌注流速为15 mL/min时，温度升高的幅度显著高于其他组。 • 在不进行灌溉的情况下，达到43°C所需的时间（1焦耳/20赫兹）显著短于0.5焦耳/20赫兹条件下的时间（8.84±1.41秒对比）。13.71±1.53 s).
Wu等人[36] (2023)	肾盂 (n=22)	• 激光功率：24 W，80 Hz/0.3 J和32 W，80 Hz/0.4 J • 60s激光激活	• Olympus光纤输尿管镜 • Ho：YAG moses/200μm激光光纤 • 室温灌注（25℃） • 12/14 Fr UAS	将热电偶连接至内窥镜（其尖端距离远端5 mm）	1) 室温灌注（25℃） • 使用30 mL/min或60 mL/min的灌注液，任何患者在60秒激光激活后，IRT温度均未达到43°C。 2) 温水冲洗（37℃）， • 在32瓦、30毫升/分钟和40瓦、30毫升/分钟的设置下，继续激光激活后，IRT温度接近或超过43°C。
王等人 [18] (2019)	输尿管（n=27）（30套）	激光功率：10-50 W（设置未知）	• 半刚性输尿管镜（WOLF 8.0/9.8 Fr） • Ho：YAG/550μm激光光纤	热电偶测温导线	• 30组数据中最高温度均超过43°C（100%），其中19组（63.3%）的峰值温度超过56°C。

IRT：肾内温度；FURSL：输尿管镜碎石术；TFL：钬光纤激光；APD：前后径；Ho：YAG：钬激光；UAS：输尿管套管。

如今，新技术已融入柔性输尿管肾镜系统，可实时监测温度，确保其保持在安全范围内[45]。这些技术进步有助于我们更深入地理解温度对输尿管镜检查临床效果的影响。

结论

在进行激光碎石术时，肾内温度可能显著升高，此时充分的冲洗液循环对控制温度至关重要。进行高功率激光碎石术时，特别是在解剖结构狭窄的部位，理解热剂量的概念尤为重要。通过优化能量输送策略并提升系统热容量，是维持安全温度水平、降低输尿管镜检查中温度相关并发症风险的关键所在。

利益冲突

洪承奎自2025年起担任《调查与临床泌尿学》主编，另一位作者无利益冲突。

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输尿管镜钬激光碎石术后输尿管狭窄的危险因素研究

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【摘要】 **目的：**分析输尿管镜钬激光碎石术后输尿管狭窄的独立危险因素。**方法：**选择 2021 年 1 月—2023 年 6 月在无锡第八人民医院接受输尿管镜钬激光碎石术治疗的 320 例输尿管结石患者，根据术后随访 1 年是否发生输尿管狭窄，将患者分为狭窄组（*n*=26）和未狭窄组（*n*=294）。采用单因素和多因素分析评价输尿管结石患者术后输尿管狭窄的独立危险因素。**结果：**单因素分析结果显示，狭窄组结石最大径≥2 cm、结石嵌顿、中重度肾积水和钬激光损伤黏膜的患者占比均高于未狭窄组，且手术时间长于未狭窄组，差异均有统计学意义（*P*<0.05）。logistic 回归分析表明，结石直径≥2 cm、结石嵌顿、中重度肾积水、手术时间和发生钬激光损伤黏膜是输尿管镜钬激光碎石术后输尿管狭窄的独立危险因素（*P*<0.05）；通过 ROC 曲线下面积来验证 logistic 回归模型。ROC 曲线结果显示，预测模型的敏感度为 84.6%，特异度为 85.7%，AUC 为 0.888。**结论：**结石直径、结石嵌顿、中重度肾积水、手术时间及钬激光损伤黏膜是输尿管镜钬激光碎石术后输尿管狭窄的独立危险因素。logistic 回归模型具有较高的预测敏感度和特异度，可有效预测术后输尿管狭窄的发生，为临床决策提供了有力支持。

【关键词】 输尿管结石 钬激光碎石术 输尿管狭窄 危险因素

Study on the Risk Factors of Ureteral Stricture after Ureteroscopic Holmium Laser Lithotripsy/XIA Tiancheng, GAO Mao, XU Guozheng, ZHANG Shuai. //Medical Innovation of China, 2025, 22(06): 116-120

[Abstract] **Objective:** To analyze the independent risk factors of ureteral stricture after ureteroscopic holmium laser lithotripsy. **Method:** A total of 320 patients with ureteral calculi who received ureteroscopic holmium laser lithotripsy treatment in Wuxi No.8 People's Hospital from January 2021 to June 2023 were selected. According to whether ureteral stenosis occurred during 1 year postoperative follow-up, the patients were divided into a narrow group (*n*=26) and a non-narrow group (*n*=294). Independent risk factors for postoperative ureteral stricture in patients with ureteral calculi were evaluated by univariate and multivariate analysis. **Result:** The results of univariate analysis showed that the proportions of patients with maximum stone diameter ≥2 cm, stone incarceration, moderate and severe hydronephrosis and holmium laser injury of mucosa in the narrow group were higher than those in the non-narrow group, and the operation time was longer than that in the non-narrow group, the differences were statistically significant (*P*<0.05). logistic regression analysis showed that stone diameter ≥2 cm, stone entrapment, moderate and severe hydronephrosis, operation time and the occurrence of holmium laser damage were independent risk factors for ureteral stenosis after ureteroscopic holmium laser lithotripsy (*P*<0.05). The logistic regression model was verified by the area under ROC curve. ROC curve results showed that the sensitivity of the prediction model was 84.6%, the specificity was 85.7%, and the AUC was 0.888. **Conclusion:** Stone diameter, stone incarceration, moderate to severe hydronephrosis, operation time and holmium laser lesion of the mucosa are independent risk factors for ureteral stricture after ureteroscopic holmium laser lithotripsy. logistic regression model has high predictive sensitivity and specificity, which can effectively predict the occurrence of postoperative ureteral stenosis, and provide strong support for clinical decision-making.

[Key words] Ureteral calculi Holmium laser lithotripsy Ureteral stricture Risk factors

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输尿管结石由肾结石下降，排入输尿管所引起，其发病率呈上升趋势[1-2]。输尿管镜钬激光碎石术因其微创、高效和安全等优点而成为治疗输尿管结石的主要方法[3-5]。尽管该技术应用广泛，但术后输尿管狭窄的发生仍然是一个不容忽视的并发症[6-9]，给患者带来了较大的痛苦和经济负担。输尿管狭窄不仅影响患者的生活质量，还可能导致严重的泌尿系统并发症，如肾积水和肾功能衰竭等[10]。因此，研究输尿管镜钬激光碎石术后输尿管狭窄的危险因素具有重要的临床意义。本研究旨在通过回顾性分析输尿管结石患者的临床资料，利用单因素和多因素 logistic 回归分析方法，系统评估术后输尿管狭窄的独立危险因素，以期为临床预防和治疗提供科学依据。

1 资料与方法

1.1 一般资料

选取 2021 年 1 月—2023 年 6 月在无锡第八人民医院接受治疗的 320 例输尿管结石患者作为研究对象。纳入标准：（1）首次接受输尿管镜钬激光碎石术治疗。（2）具备完整的临床资料。（3）符合钬激光碎石术适应证的输尿管结石。排除标准：（1）恶性肿瘤、肝肾功能障碍及免疫系统疾病。（2）术前已放置输尿管支架。（3）有输尿管手术史、输尿管息肉、肾结石及既往输尿管狭窄病史。（4）术前检查提示有输尿管狭窄。（5）手术过程中发生意外损伤。本研究已获本院医学伦理委员会的审查和批准。

1.2 方法

收集并记录患者基本资料和疾病资料，所有患者均接受输尿管镜钬激光碎石术。术后通过门诊或电话随访 1 年，以记录输尿管狭窄的发生情况。单因素分析用于评估各因素与输尿管狭窄发生的关系，设定 $P<0.05$ 为标准，将多变量纳入多元 logistic 回归分析，以筛选出影响输尿管镜下钬激光碎石术后并发输尿管狭窄的因素。

1.3 观察指标与评判标准

收集并比较患者的临床信息和基础数据。（1）病程：记录患者自诊断输尿管结石到手术的时间间隔；（2）体重、性别、年龄：记录患者的体重、性别和年龄；（3）钬激光对黏膜的损伤：在手术过程中记录钬激光对输尿管黏膜的损伤情况；（4）手术时间：记录从手术开始到结束的总时间；（5）肾积水程度：根据泌尿系 CT 扫描和超声检查结果进行判断，轻度肾积水为肾形态、肾实质厚度和回声正常、肾集合系统分离 2~3 cm，中度肾积水为肾柱显示不清、肾实质变薄、肾体积增大、肾集合系统分离 3~4 cm 并表现出明显的扩张，重度肾积水为肾柱出现放射状回声、肾实质明显变薄、区域位置为液性暗区、肾体积增大且形态异常；（6）结石大小：通过影像学检查（CT）测量并记录结石的最大直径。这些观察指标通过对比分析患者术后是否发生输尿管狭窄的组别差异，评估其对术后输尿管狭窄发生的影响，为临床预防和治疗提供依据。

1.4 统计学处理

本研究数据采用 SPSS 26.0 统计学软件进行分析和处理，计量资料以（$\bar{x} \pm s$）表示，组间比较采用独立样本 t 检验，组内比较采用配对 t 检验；计数资料以率（%）表示，采用 χ^2 检验。以 $P<0.05$ 为差异有统计学意义。使用 R 软件建立一般 logistic 回归模型，并通过 ROC 曲线下面积进行验证。ROC 曲线下面积 >0.7，表明模型具有良好的区分度。

2 结果

2.1 输尿管镜钬激光碎石术后输尿管狭窄的单因素分析

单因素分析结果显示，狭窄组结石最大径≥2 cm、结石嵌顿、中重度肾积水和钬激光损伤黏膜的患者占比均高于未狭窄组，且手术时间长于未狭窄组，差异均有统计学意义（$P<0.05$），见表 1。

2.2 输尿管镜钬激光碎石术后输尿管狭窄的多因素 logistic 回归分析

以是否发生输尿管狭窄为应变量（否 =0，是 =1），结石最大径（<2 cm 赋值为 0，≥2 cm 赋值为 1）、结石嵌顿（否赋值为 0，是赋值为 1）、肾积水程度（轻度赋值为 0，中度赋值为 1，重度赋值为 2）、钬激光损伤黏膜（否赋值为 0，是赋值为 1）和手术时间（赋值为实测值）为自变量，进行多因素 logistic 回归分析（引入水准为 0.05，剔除水准为 0.10）；结果显示，结石直径≥2 cm、结石嵌顿、中重度肾积水、手术时间和发生钬激光损伤黏膜是输尿管镜钬激光碎石术后输尿管狭窄的独立危险因素（$P<0.05$），见表 2。

2.3 输尿管镜钬激光碎石术后输尿管狭窄的 ROC 曲线

通过 ROC 曲线下面积来验证 logistic 回归模型。模型公式为 Logit（P）=−7.566+1.855 × 结石最大径 +1.949 × 结石嵌顿 +1.174 × 肾积水程度 +1.074 × 钬激光损伤黏膜 +0.034 × 手术时间。结果显示，该模型预测输尿管镜钬激光碎石术后输尿管狭窄的敏感度为 84.6%，特异度为 85.7%，约登指数为 0.703，AUC 为 0.888，95%*CI* 为（0.819，0.957），见图 1。

表1 输尿管镜钬激光碎石术后输尿管狭窄的单因素分析

组别	病程 [个月，($\bar{x}\pm s$)]	年龄 [岁，($\bar{x}\pm s$)]	性别 [例（%）]		受影响位置 [例（%）]		BMI [kg/m^2，($\bar{x}\pm s$)]
			男	女	左	右	
狭窄组（n=26）	5.36 ± 1.26	47.97 ± 4.34	16（61.54）	10（38.46）	14（53.85）	12（46.15）	23.69 ± 2.41
未狭窄组（n=294）	5.12 ± 0.97	47.64 ± 5.13	180（61.22）	114（38.78）	167（56.80）	127（43.20）	23.96 ± 2.28
t/χ^2 值	1.178	0.318	0.001		0.085		0.576
P 值	0.240	0.751	0.975		0.771		0.565

组别	血钙 [mmol/L，($\bar{x}\pm s$)]	手术时间 [min，($\bar{x}\pm s$)]	结石最大径 [例（%）]		结石嵌顿 [例（%）]	
			<2 cm	≥2 cm	是	否
狭窄组（n=26）	2.43 ± 0.30	56.28 ± 16.28	14（53.85）	12（46.15）	20（76.92）	6（23.08）
未狭窄组（n=294）	2.37 ± 0.33	48.94 ± 14.20	257（87.41）	37（12.59）	96（32.65）	198（67.35）
t/χ^2 值	0.895	2.496	20.758		20.258	
P 值	0.372	0.013	<0.001		<0.001	

组别	肾积水程度 [例（%）]			尿路感染并发症 [例（%）]		钬激光损伤黏膜 [例（%）]	
	轻度	中度	重度	是	否	是	否
狭窄组（n=26）	3（11.54）	8（30.77）	15（57.69）	22（84.62）	4（15.38）	13（50.00）	13（50.00）
未狭窄组（n=294）	140（47.62）	88（29.93）	66（22.45）	210（71.43）	84（28.57）	82（27.89）	212（72.11）
t/χ^2 值	18.686			2.083		5.594	
P 值	<0.001			0.149		0.018	

表2 输尿管镜钬激光碎石术后输尿管狭窄的多因素logistic回归分析

影响因素	B	SE	Waldχ^2 值	P 值	OR 值	95%CI
结石最大径	1.855	0.509	13.287	0.000	6.389	2.357，17.318
结石嵌顿	1.949	0.534	13.299	0.000	7.022	2.463，20.016
肾积水程度	1.174	0.325	13.040	0.000	3.236	1.711，6.120
钬激光损伤黏膜	1.074	0.492	4.768	0.029	2.927	1.116，7.674
手术时间	0.034	0.017	4.181	0.041	1.035	1.001，1.069
常量	−7.566	1.242	37.115	0.000	0.001	

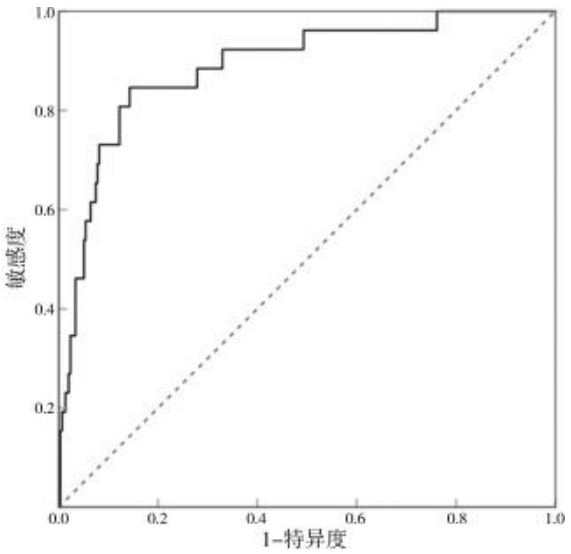


图1 输尿管镜钬激光碎石术后输尿管狭窄的ROC曲线

3 讨论

输尿管结石是泌尿系统中常见且高发的疾病，其主要表现为剧烈的腹痛、血尿和尿路梗阻，严重影响患者的生活质量[11-13]。随着微创手术技术的发展，输尿管镜钬激光碎石术因其创伤小、恢复快、疗效显著而成为治疗输尿管结石的首选方法[14-15]。然而，尽管该手术技术日益成熟，术后输尿管狭窄仍然是一个不可忽视的并发症，给患者带来了长期的健康风险和治疗挑战。术后输尿管狭窄的发生不仅影响患者的泌尿功能，还可能导致肾积水、感染等严重并发症，甚至危及肾功能[16-18]。研究表明，术后输尿管狭窄与术中操作、结石大小、结石嵌顿及肾积水程度等因素密切相关。Zheng 等[19] 的研究指出，结石嵌顿和肾积水是术后输尿管狭窄的重要风险因素，强调了术前和术中评估的必要性。此外，Wang 等[20] 的研究也发现，钬激光碎石术过程中产生的热效应可能导致黏膜损伤，进而增加狭窄的风险。基于此，明确术后输尿管狭窄的发生机制及其危险因素对提高手术疗效和预后具有重要意义。现有研究表明，结石大小、结石嵌顿时间、手术操作技术、术后护理等多种因素均可能影响术后输尿管狭窄的发生率。然而，这些研究多为单中心小样本

研究，结果尚存在争议，且缺乏系统的回归分析。本研究通过回顾性分析大量输尿管结石患者的临床数据，利用单因素和多因素 logistic 回归分析评估了输尿管镜钬激光碎石术后输尿管狭窄的独立危险因素，旨在为临床实践提供科学依据，并探索有效的预防和干预措施。通过本研究，希望能够进一步揭示术后输尿管狭窄的发病机制，优化手术操作流程，制定个体化治疗方案，从而降低术后并发症的发生率，提高患者的生活质量。

本研究结果显示，结石最大径、结石嵌顿、肾积水程度、手术时间和钬激光损伤黏膜是输尿管狭窄的相关因素。进一步的 logistic 回归分析则揭示，结石直径大、结石嵌顿、中重度肾积水、手术时间长和钬激光损伤黏膜是独立的危险因素。首先，结石的最大径是影响术后输尿管狭窄发生的一个重要因素。较大的结石在碎石过程中需要更长的时间和更高的能量，这可能导致输尿管黏膜的广泛损伤和炎症反应，从而增加术后狭窄的风险。此外，较大的结石也更容易嵌顿在输尿管内，进一步加重局部的机械性损伤和炎症反应，影响输尿管的正常愈合过程。其次，结石嵌顿是另一个显著的独立危险因素。嵌顿的结石不仅增加了手术操作的难度，还会导致局部组织的缺血和坏死，这些病理变化都会促使输尿管黏膜的纤维化和瘢痕形成，最终导致狭窄的发生。因此，在术前影像学检查中发现结石嵌顿的患者，需特别注意术后狭窄的预防和管理。而肾积水程度也是影响术后狭窄的重要因素之一。本研究发现，中重度肾积水的患者更容易发生术后输尿管狭窄。这可能是由于肾积水导致的肾盂压力增高和输尿管扩张，使得输尿管壁的结构和功能发生改变，增加了手术后的恢复难度。此外，肾积水本身也可能反映了结石存在较长时间，导致更严重的局部炎症和纤维化。手术时间长和发生钬激光对黏膜的损伤也显著增加了术后输尿管狭窄的风险。较长的手术时间通常意味着更复杂的手术操作和更高的手术难度，增加了输尿管损伤的可能性。此外，长时间的手术操作会导致局部组织的持续性压力和缺血，进一步加剧术后纤维化和瘢痕形成。钬激光损伤黏膜是影响术后狭窄的另一重要因素。钬激光在碎石过程中产生的高能量可以有效粉碎结石，但同时也可能对输尿管黏膜造成热损伤和机械损伤。这些损伤会引起局部炎症反应，导致黏膜下层的纤维化，最终形成狭窄。因此，在手术过程中，需尽量减少激光对黏膜的直接照射，以降低术后狭窄的风险。基于这些发现，本研究还使用 R 软件建立了预测模型，并通过 ROC 曲线对模型进行了验证。结果显示，预测模型的敏感度为 84.6%，特异度为 85.7%，AUC 为 0.888。这表明该模型在预测输尿管镜钬激光碎石术后输尿管狭窄方面具有较高的准确性，能够有效区分高风险和低风险患者，从而帮助临床医生在术前制定更有效的治疗策略。

综上所述，本研究明确了结石最大径、结石嵌顿和肾积水程度等是独立危险因素。临床上，对于具有这些高危因素的患者，应在术前进行充分评估，术中采取精细操作，并在术后密切随访，以降低术后输尿管狭窄的发生风险，提高患者的预后和生活质量。这些发现为进一步优化输尿管结石的治疗策略提供了科学依据，也为今后的相关研究指明了方向。

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RESEARCH

With great power comes great risk: High ureteral stricture rate after high-power, high-frequency Thulium fiber laser lithotripsy in ureteroscopy

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Abstract

Purpose To compare the safety and efficacy of Thulium Fiber Laser (TFL) using either manufacturer presets (MP) or individualized presets (IP) in ureteroscopy.

Methods Multi-institutional, retrospective analysis on the first patients treated with SOLTIVE® Premium (Olympus Medical Systems®) TFL in Switzerland in 2020. MP were used at the University Hospital of Geneva, while IP were used at the University Hospital of Zurich. Patient demographics, stone characteristics, and procedural details were collected. Primary outcome was postoperative ureteral stricture (US). Secondary outcome was stone-free rate (SFR).

Results A total of 158 patients were analyzed, 79 in each group. Demographics were similar between the two groups, except for a lower pre-stenting rate in the MP group (56% vs. 91%; $p<0.001$) and a higher rate of ureteral access sheath use in the MP group (65% vs. 44%; $p=0.011$). No significant differences in stone burden (median stone diameter 9 mm, median stone volume 267 mm^3), nor in the rate of impacted ureteral stones (29% vs. 34%; $p=0.49$). Mean power, maximal power, frequency settings, and energy consumption were significantly higher in the MP group. US rate was 11% in MP group compared to 1% in IP group ($p=0.009$). MP were a significant predictor of US on multivariable analysis (OR 12.4; $p=0.02$), independently from impacted ureteral stones. No difference in SFR between groups (85% and 84%; $p=0.67$).

Conclusion High-power, high-frequency laser settings from manufacturer laser presets increase the risk of US, without improving SFR. Future studies shall further evaluate optimal laser settings depending on patient characteristics and intraoperative situation.

Keywords Ureteroscopy · Lithotripsy · Thulium fiber laser · Ureteral stricture · Laser presets · Power

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Abbreviations

ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CI	Confidence Interval
CT	Computer Tomography
DJ	Double-J
HU	Hounsfield Units
IP	Individual Presets
MP	Manufacturer Presets
HUG	Hôpitaux Universitaires de Genève
OR	Odds Ratio
SFR	Stone Free Rate
TFL	Thulium Fiber Laser
UAS	Ureteral Access Sheath
US	Ureteral Stricture
URS	Ureteroscopy
USZ	Universitätsspital Zürich

Introduction

Ureteroscopy (URS) is currently the most widely used operative technique for the treatment of urolithiasis [1]. For ureteroscopic laser lithotripsy, a series of pulsed lasers can be used: the Holmium: YAG laser, the pulsed Thulium: YAG laser and the superpulsed Thulium Fiber Laser (TFL) [2–4]. The TFL has shown superiority over the Holmium: YAG in several aspects (e.g. higher stone ablation, smaller stone fragments, lower retropulsion, smaller laser fibers, higher stone-free rate (SFR), shorter operative time), but safety warnings and reports from urologists surfaced the concern if TFL is associated with a higher risk of ureteral stricture (US) [2, 5–7]. The proposed mechanisms are wide and not sustained by robust evidence, with conflicting findings between in vitro studies [7–11]. The question, then, is how far we can push laser settings during URS to maximize efficacy while ensuring the patient's safety. An analysis of a Twitter pool of experts from October 2021 resulted in a high degree of variability in preferred laser settings, with no consensus [12]. De facto, many urologists worldwide rely on laser presets provided by manufacturers, which show a high degree of variability too [13].

In this context, the first two hospitals using TFL in clinical routine in Switzerland followed different approaches for laser presets: the University Hospital of Geneva (Hôpitaux Universitaires de Genève, HUG) used manufacturer presets (MP), while the University Hospital Zurich (Universitätsspital Zürich, USZ) used individual presets (IP) based on recommendations from a fellowship-trained urologist who had established internal hospital guidelines on laser settings *(*Fig. 1*)* [14–16].

This difference in practice was the basis for a comparison between patients treated at the HUG and USZ for analysis of safety and efficacy of TFL laser lithotripsy.

Materials and methods

We conducted a multi-institutional and retrospective analysis of the first patients who underwent URS-lithotripsy with the SOLTIVE® Premium TFL (Olympus Medical Systems®, Tokyo, Japan) in Switzerland, namely at the HUG and USZ. The HUG discontinued the use of the TFL after 79 patients. Accordingly, the first 79 patients treated at the USZ were included for analysis. Patients with history of prior reconstructive ureteral surgery or pre-existing strictures were excluded, as well as patient who underwent URS with stone extraction, but no laser lithotripsy. Data was extracted from the hospital's medical information system. The following patient characteristics were collected: age, sex, BMI, diabetes mellitus history, ASA score, and prior history of ipsilateral URS. Data regarding characteristics and location of the stones were also collected, including their location within the kidney or ureter (proximal, mid and distal ureter), number of stones, maximal diameter of the largest stone, stone volume, maximal stone density measured in Hounsfield Units (HU), as well as presence of hydronephrosis at the time of diagnosis. To accurately estimate the stone volume, we employed the ellipsoid volume formula ($4/3\ \pi\ a*b*c$, where a, b, and c represent the radius of the stone in three dimensions, calculated from pre-operative Computer-Tomography (CT) scans in both axial and coronal views). In case of multiple stones, we summed up each stone volume [17]. The presence of an impacted ureteral stone was retrieved from the medical files. The general practice in both institutions was to consider a ureteral stone as impacted if at least one of the following criteria was met: (a) presence of ureteral dilation proximal to the stone and moderate to severe hydronephrosis (grade ≥ 2) [18]; (b) difficulty passing a guidewire or ureteral catheter beyond the ureteral stone at first attempt; (c) stone remaining in the same location on two separate imaging studies taken at least two months apart [19]. Regarding the surgical procedure, we collected data on unilateral vs. bilateral URS, pre- and postoperative Double-J (DJ) ureteral stenting (pre-stenting in both institutions usually for 10–20 days; post-operative DJ-stenting usually 5–14 days), and ureteral access sheath (UAS) use. *Detailed surgical procedure steps and instruments are provided in Supplementary Material*. Since all surgeries were performed in a university hospital setting, each patient was treated by either a urologist with >100 URS experience or by a urology resident under the supervision of an experienced urologist.

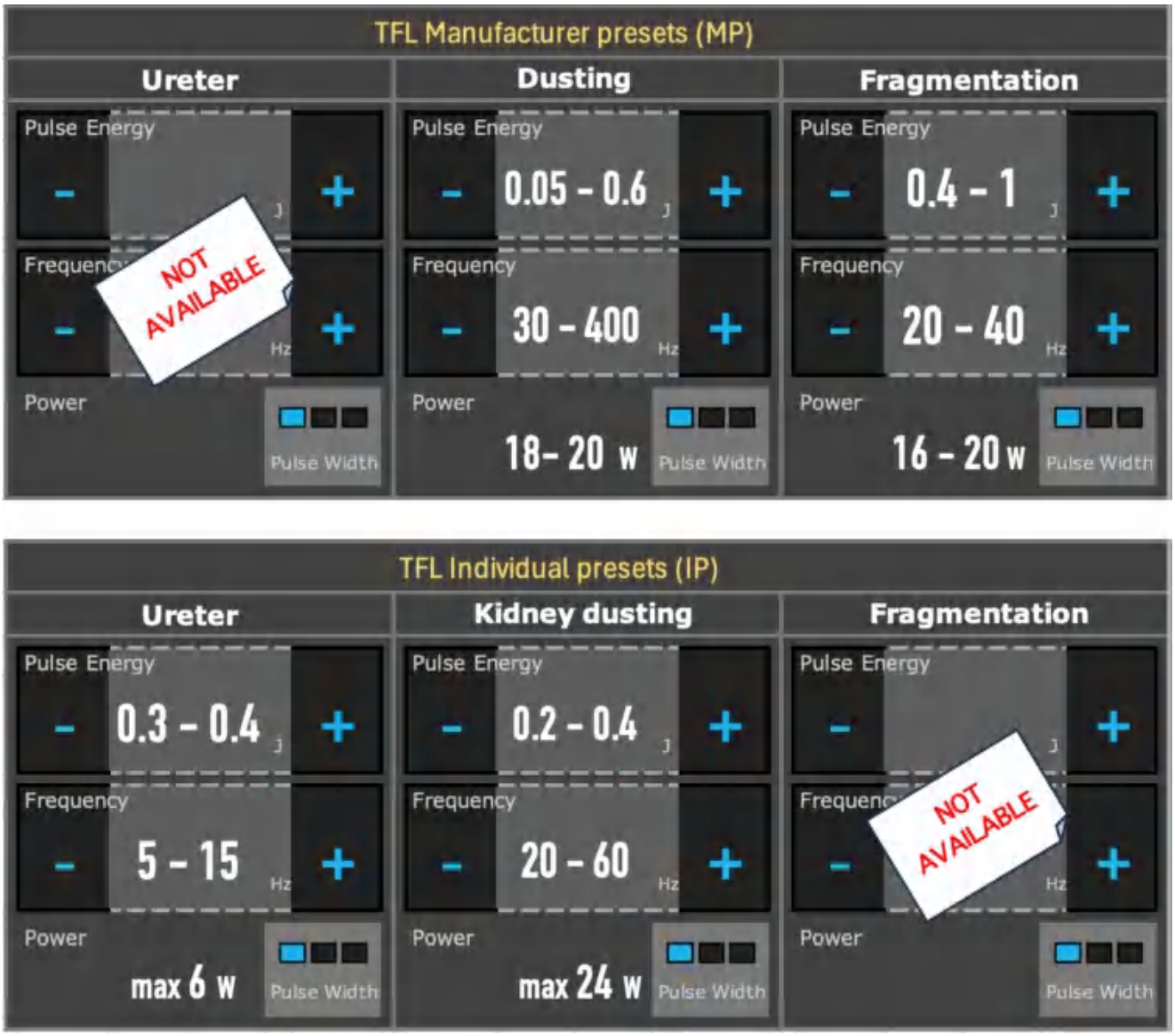


Fig. 1 Graphical user interface (GUI) comparison of manufacturer presets (MP) and individual presets (IP) for the Olympus SOLTIVE® Premium Thulium Fiber Laser (TFL) in 2020. Regarding manufacturer presets: Until July 2021, no manufacturer presets specifically intended for the ureter were available, nor was there any indication that the existing presets were designed for use in the kidney, but not the ureter. Regarding individual presets: Since the TFL was primarily introduced as a "dusting" laser, there were no individual presets dedicated to stone "fragmentation"

Laser settings were retrospectively extracted from the SOLTIVE® Premium laser generators, which have a record of the following parameters for each treated patient: type of laser fiber, active lasing time, total delivered energy, maximal power setting, as well as lowest and highest frequency settings. Mean power was calculated as total energy divided by lasing time. Mean laser energy consumption was calculated as total energy divided by stone volume (J/mm^3) [20].

Primary outcome was the presence of postoperative ureteral stricture (US). US was defined, according to Moretto et al., as signs of urinary flow impairment due to ureteral narrowing, associated with complications (such as pain, recurrent infections, or loss of renal function) and/or leading to re-intervention [21, 22]. In both institutions, patients underwent clinical evaluation and kidney-ultrasonography six weeks postoperatively. According to institutional guidelines, patients showing symptoms, impaired renal function, or hydronephrosis suggesting US were thoroughly evaluated. In such cases, the option of a retrograde ureteropyelography with diagnostic URS and/or dynamic scintigraphy was discussed. Other safety outcomes included intra-operative complications, as well as early (< 1 month) and late (≥ 1 month) postoperative complications, classified according to the Clavien-Dindo grading system [23, 24].

Secondary outcome was the SFR, defined as the endoscopic absence of fragments greater than 2 mm and absence of fragments greater than 2 mm in follow-up imaging (ultrasonography in all patients, with additional imaging (e.g. CT) based on the surgeon's discretion) [25].

Statistical analysis

Associations between categorical variables were analyzed with Chi Square tests or Fischer's exact tests, as appropriate. Differences between continuous variables were analyzed with independent t-tests or Mann-Whitney U tests, as appropriate. Correlations between continuous variables was analyzed with Pearson correlations tests or Spearman's rho test, as appropriate. Logistic regression was used for the analysis of predictors of dichotomic outcomes. Patients with bilateral URS were included in a per-patient analysis. All statistical tests were two-sided and p-values < 0.05 were considered significant. Statistical analysis and graph plotting were performed with IBM SPSS Statistics 29.0 (IBM Corp., Armond, NY, USA).

Results

A total of 158 patients were available for analysis, 79 patients in each group, all treated between June 2020 and May 2021. Mean age was 53 years.

All patients underwent preoperative CT scan to assess stone burden. The majority of procedures were performed for kidney stones rather than ureteral stones. Specifically, 70% of patients had kidney stones (with/without concomitant ureteral stones), while 53% had ureteral stones (with/without concomitant kidney stones). There was a significant correlation between maximal stone size and stone volume (Spearman's rho 0.92; $p < 0.001$; Supplementary Fig. 1). Table 1 provides comprehensive patient characteristics.

Among baseline patient characteristics, diabetes mellitus was less prevalent in the MP group compared to the IP group (9% vs. 20%; $p = 0.04$). Additionally, the MP group had a significantly lower proportion of pre-stented cases (56% vs. 91%; $p < 0.001$). No other baseline variables showed significant differences between the two groups. Specifically, stone burden was comparable (median maximal stone size: 9 mm in both groups; $p = 0.39$; median stone volume 269 mm³ in the MP group and 264 mm³ in the IP group; $p = 0.67$). Similarly, the rate of impacted ureteral stones did not differ significantly between the MP and IP group (29% vs. 34%, respectively; $p = 0.49$).

Significant differences in procedural characteristics were observed between the two groups. The MP group demonstrated higher rate of UAS use, shorter active lasing times, higher energy consumption (J/mm³), higher mean power, higher maximal power settings, and higher laser frequency settings (applicable to both lowest and highest frequency settings) compared to the IP group *(*Table 1*and* Fig. 2*)*.

No patient was lost to follow-up, and all patients underwent at least one first postoperative control within 3 months after surgery. Nine cases of US occurred in the MP group (11%) compared to one case (1%) in the IP group ($p = 0.009$). Impacted stone status, absence of pre-stenting, manufacturer laser presets, increasing total laser energy as well as increasing mean power were found as predictors of US on univariable analysis *(*Table 2*)*. On multivariable analysis, two independent variables emerged as predictors of US: impacted stone status (OR 7.10 (CI 1,67–30,1); $p = 0.008$) and manufacturer laser presets (OR 12,4 (CI 1,48–104); $p = 0.02$) *(*Table 2*)*.

Detailed patient characteristics and management of the 10 patients with US are presented in *Supplementary Table 1*. All patients had ureteral stones at initial diagnosis. All patients underwent retrograde ureteropyelography to locate and measure the US. The location of the US corresponded to the original stone location in 4 from 10 patients (40%), while further distally to the stone location in 4 patients (40%) and more proximally in the remaining 2 patients (20%). Most cases were managed with laparoscopic DaVinci-assisted ureteroplasty (using buccal mucosal graft or appendix flap) or ureteral reimplantation (50%) or balloon dilation and ureteral stenting (33%). Additionally, one case required nephrectomy, while another resolved spontaneously. Patients who underwent reconstruction were followed-up with clinical, ultrasound and renal function assessments for a minimum of 2 years with no loss of follow-up, showing excellent outcomes after reconstructive surgery, with no evidence of recurrence.

As for intraoperative, early postoperative, and late postoperative complications, no significant differences were observed between the MP and IP groups.

SFR did not significantly differ between groups (85% and 84% in the MP and IP group; $p = 0.67$).

Discussion

To the best of our knowledge, this is the first clinical study confirming the risks associated with the use of high-power, high-frequency settings from manufacturer laser presets in the context of ureteroscopic lithotripsy. Specifically, manufacturer laser presets led to a significantly higher risk of postoperative US (OR = 12.4; $p = 0.02$ on multivariable analysis), compared to more conservative, individualized laser presets, with no difference in SFR between both groups. Most cases of US required major surgical intervention. What

Table 1 Patient characteristics

Baseline characteristics					Procedural characteristics				
Variable	**Overall (*n* = 168)**	**Manufacturer laser presets (*n* = 79)**	**Individual laser presets (*n* = 79)**	p-value	**Variable**	**Overall (*n* = 168)**	**Manufacturer laser presets (*n* = 79)**	**Individual laser presets (*n* = 79)**	p-value
Age (mean, SD)	53 (17)	52 (19)	54 (15)	0.48*	**UAS use**	86 (54%)	51 (65%)	35 (44%)	**0.011****
Male : female ratio	2.1: 1	2.0: 1	2.2: 1	0.87**	**Postoperative DJ-stenting**	156 (99%)	79 (100%)	77 (98%)	0.16**
BMI (mean, SD) (kg/m^2)	26 (5)	26 (5)	26 (5)	0.76*	**Laser fiber core diameter**				**< 0.001****
					150 µm	84 (53%)	5 (6%)	79 (100%)	
					200 µm	68 (43%)	68 (86%)	0 (0%)	
					365 µm	6 (4%)	6 (8%)	0 (0%)	
Diabetes mellitus	23 (15%)	7 (9%)	16 (20%)	**0.04****	**Active lasing time (mm: ss) (median, IQR)**	06:28 (01:56–16:36)	04:38 (01:37–09:37)	13:05 (02:42–23:33)	**< 0.001*****
ASA score				0.65**	**Total energy (KJ)**	6.26 (1.63–17.1)	6.50 (2.28–16.38)	5.98 (9.03–17.50)	0.41***
1	17 (11%)	9 (11%)	8 (10%)						
2	94 (59%)	50 (63%)	44 (56%)						
3	41 (26%)	17 (22%)	24 (30%)						
4	6 (4%)	3 (4%)	3 (4%)						
Prior history of URS	44 (28%)	22 (28%)	22 (28%)	1.00**	**Energy consumption (J/mm^3) (median, IQR)**	18 (7–32)	20 (11–44)	17 (7–26)	**0.031*****
Stone location				0.94**	**Mean power (W) (median, IQR)**	19 (8–20)	20 (20–25)	8 (6–15)	**< 0.001*****
Kidney	67 (43%)	33 (42%)	34 (43%)						
Ureter	48 (30%)	25 (32%)	23 (29%)						
Both	43 (27%)	21 (26%)	22 (28%)						
Ureteral stones' location				0.18**	**Maximal power setting (W) (mean, SD)**	21 (13)	27 (13)	15 (9)	**< 0.001***
Proximal	54 (59%)	54 (59%)	31 (69%)						
Mid	25 (28%)	25 (28%)	8 (18%)						
Distal	9 (10%)	9 (10%)	4 (9%)						
Multiple	3 (3%)	3 (3%)	2 (4%)						
Number of stones (median, IQR)	1 (1–3)	1 (1–3)	2 (1–3)	0.28***	**Lowest frequency setting (Hz) (median, IQR)**	40 (10–200)	200 (100–200)	14 (5–30)	**< 0.001*****
Maximal stone size (mm) (median, IQR)	9 (7–13)	9 (7–13)	9 (7–13)	0.39***	**Highest frequency setting (Hz) (median, IQR)**	100 (40–400)	400 (200–400)	40 (30–100)	**< 0.001*****
Stone volume (mm^3) (median, IQR)	267 (110–751)	269 (117–565)	264 (110–857)	0.67***	**Postoperative outcomes**				
Maximal stone density (HU) (mean, SD)	1142 (391)	1108 (382)	1177 (399)	0.27*	**Variable**	**Overall (*n* = 168)**	**Manufacturer laser presets (*n* = 79)**	**Individual laser presets (*n* = 79)**	p-value
Impacted stone	50 (32%)	23 (29%)	27 (34%)	0.49**	**Intraoperative complications**	Total: 8 (5%)	Total: 3 (4%)	Total: 2 (3%)	0.15**

Table 1 (continued)

Baseline characteristics					Procedural characteristics				
Variable	**Overall (*n* = 168)**	**Manufacturer laser presets (*n* = 79)**	**Individual laser presets (*n* = 79)**	p-value	**Variable**	**Overall (*n* = 168)**	**Manufacturer laser presets (*n* = 79)**	**Individual laser presets (*n* = 79)**	p-value
					Ureteral perforation	6 (4%)	2 (3%)	1 (1%)	
					Renal pelvis perforation	1 (1%)	1 (1%)	0 (0%)	
					Priapism	1 (1%)	0 (0%)	1 (1%)	
Preoperative hydronephrosis ≥ Grade 2	47 (30%)	21 (27%)	26 (33%)	0.38**	**Early postoperative complications**	Total: 8 (5%)			
	Total: 9 (11%)	Total: 5 (6%)	0.47**						
					CD I				
					Hematuria	2 (1%)		0 (0%)	
					CD II		2 (3%)		
					UTI	4 (3%)		3 (4%)	
					Delirium	1 (1%)	1 (1%)	1 (1%)	
					CD IV		0 (0%)		
					TIA	1 (1%)	0 (0%)	1 (1%)	
Bilateral URS	9 (6%)	4 (5%)	5 (6%)	0.73**	**Late postoperative complications**	Total: 10 (6%)	Total: 9 (11%)	Total: 1 (1%)	**0.009****
					CD IIIb				
					Ureteral stricture	10 (6%)	9 (11%)	1 (1%)	
					Others	0 (0%)	0 (0%)	0 (0%)	
Pre-stenting	116 (73%)	44 (56%)	72 (91%)	**<0.001****	**Stone free status**	132 (84%)	65 (82%)	67 (85%)	0.67**

*T-test, **Chi-square, ***Mann-Whitney U Test

SD = standard deviation; IQR = interquartile range; BMI = body mass index; ASA = American Society of Anesthesiologists; URS = ureteroscopy; HU = Hounsfield units; UAS = ureteral access sheath; TIA = transient ischemic attack; CD = Clavien-Dindo

had been previously hypothesized in several in vitro studies [7, 26] and highlighted by safety complaints [27–33], is now supported by compelling evidence provided by this study. It serves as a crucial caveat to all urologists performing ureteroscopic laser lithotripsy, underscoring the need for careful evaluation and adjustment of laser settings.

Recent systematic reviews have reported an overall 3% rate of US after URS [22, 23]. In the present study, the US rate in the MP group was 11%, arguably exceeding the safety threshold for this procedure. Understandably, the hospital involved (HUG) opted to discontinue the use of the TFL within less than a year after its acquisition. In contrast, use of IP resulted in a 1% US rate, indicating that ureteroscopic laser lithotripsy can be performed safely with the TFL when using IP.

Two critical factors likely explain the association between laser settings and US formation: high-power and high-frequency. High-power can result in excessive and rapid local energy delivery, potentially causing thermal tissue damage, which may ultimately lead to US formation [34–36]. Similarly, high-frequency is associated with suboptimal energy delivery to the stone surface, increasing the likelihood of inadvertent targeting of ureteral wall rather than the ureteral stone [26, 37].

Ultimately, high-power is mostly associated with high-frequency, and vice versa, because of the relatively narrow range of pulse energy used for laser lithotripsy (predominantly 0.4–1.5 J) [38]. In the present study, mean power, maximal power, lowest and highest frequency settings were all significantly higher in the MP group, compared to the IP group. Additionally, mean power was revealed as a significant predictor of US on univariable analysis (OR = 1.03 for each additional increase of 1 W; $p = 0.046$). Finally, laser energy consumption was significantly higher in the MP group compared to the IP group: 20 J/mm^3 vs. 17 J/mm^3 ($p = 0.031$) (the lower, the better, as highlighted by recent reports) [39, 40]. This difference in laser energy consumption is likely attributed to less precise targeting of the stone surface with high-frequency settings. This hypothesis is supported by the findings of two in vitro studies where higher frequency settings were associated with a less effective delivery of laser energy to the stone surface [41, 42].

Poor stone targeting due to impaired visibility during stone dust production and delayed human reaction time when off-target further exacerbates the hazards associated

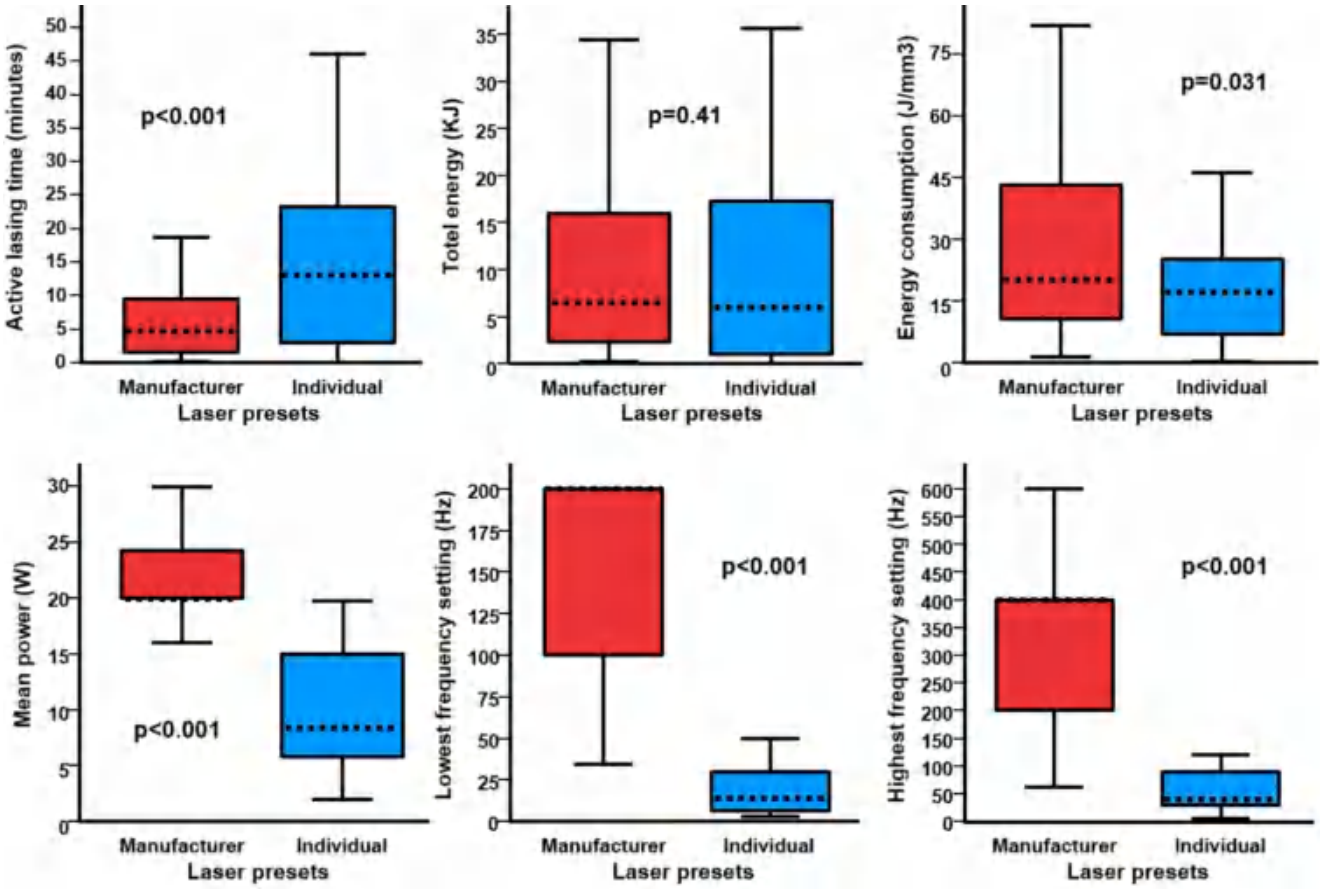


Fig. 2 Distribution of laser settings retrieved from the laser generators. Boxplots with median as dotted lines, boxes as 25th to 75th percentiles, and whiskers as 10th to 90th percentiles

with high-frequency lithotripsy [38]. In our study, most patients with US had laser frequency settings ranging from 100 to 400 Hz. Given a mean visual reaction time of at least 250 ms [43], most surgeons would likely release the laser pedal only after delivering 25 to 100 laser pulses in case of poor stone targeting or reduced visibility. These excessive, uncontrolled laser pulses not only possibly account for the observed differences in laser energy consumption, but might also have contributed to the formation of US in this study.

Presence of an impacted ureteral stone emerged as the second significant and independent predictor of US on multivariable analysis (OR = 7.10; $p = 0.008$). This finding aligns with a recent systematic review and meta-analysis, which confirmed impacted stone as an established predictor of US (OR = 7.47; $p = 0.01$, based on 5 studies including 13550 patients) [22]. In the present cohort, seven out of ten patients who developed US (70%) had impacted stones. However, 43 other patients with impacted stones did not develop US, underscoring the influence of competing risk factors such as high-power, high-frequency laser lithotripsy.

All cases of US occurred in patients with stones located in the ureter at initial diagnosis. Noteworthy, strictures occurred at the same location as the original stone in only 40% of all cases with US. This observation suggests that either stones were displaced between initial diagnosis and ureteroscopic laser lithotripsy, or that thermal tissue damages may have occurred distantly from the site of local laser energy delivery. Consequently, and until proven otherwise, high-power high-frequency laser lithotripsy should be considered hazardous for both ureteral and kidney stones. Future studies shall verify the hypothesis of distant heat-generated tissue damages by protocolling the site of laser emission in a prospective manner.

Interestingly, pre-stenting significantly reduced the risk for US on univariable analysis (OR = 0.2; $p = 0.022$). Although this finding may partly reflect practice differences between the two hospitals (56% pre-stenting in the MP group vs. 91% in the IP group; $p < 0.001$), it is plausible to hypothesize that pre-stenting contributes to US prevention by dilating the ureter and improving irrigation flow, therefore minimizing risks of ureteral trauma and optimizing conditions of laser lithotripsy [44]. Overall, pre-stenting is associated with higher SFR and fewer intra- and post-operative complications [45]. Further studies are needed to

Table 2 Logistic regression analysis for predictors of ureteral stricture

Variable	Univariable		Multivariable*	
	OR (95% CI)	***p***	**OR (95% CI)**	***p***
Age (continuous)	0.98 (0.94–1.02)	0.32		
Male vs. female	4.59 (0.57–37.3)	0.15		
BMI (kg/m2) (continuous)	1.03 (0.91–1.17)	0.64		
Diabetes mellitus	1.4 (0.3–7.6)	0.62		
Maximal stone size (mm) (continuous)	1.04 (0.94–1.15)	0.44		
Stone volume (mm^3) (continuous)	1.00 (1.00–1.00)	0.92		
Impacted ureteral stone	5.70 (1.41–23.1)	**0.015**	7.10 (1.67–30.1)	**0.008**
Preoperative hydronephrosis≥Grade 2	1.63 (0.44–6.06)	0.47		
Failed primary URS attempt	1.6 (0.3–8.1)	0.57		
Pre-stenting	0.2 (0.06–0.8)	**0.022**		
UAS use	0.8 (0.2–3.0)	0.77		
Manufacturer (MP) vs. individual laser presets (IP)	10.0 (1.24–81.2)	**0.031**	12.4 (1.48–104)	**0.02**
Laser fiber core diameter				
150 µm	1.00 (Ref.)			
200 µm	4.71 (0.94–23.5)	0.059		
365 µm	8.20 (0.63–106.6)	0.11		
Active lasing time (s) (continuous)	1.00 (1.00–1.00)	0.64		
Total energy (KJ) (continuous)	1.02 (1.00–1.04)	**0.026**		
Laser energy consumption (J/mm^3)	1.00 (0.99–1.02)	0.60		
Mean power (W)	1.03 (1.00–1.06)	**0.046**		
Maximal power setting (W)	1.02 (0.98–1.07)	0.28		
Lowest frequency setting (Hz)	1.00 (0.99–1.01)	0.12		
Highest frequency setting (Hz)	1.00 (0.99–1.01)	0.16		
Intraoperative ureteral or pelvic perforation	3.18 (0.34–30.2)	0.31		

*Only variables retained in a forward conditional multivariable analysis with an entry level at ≤0.05 and removal cut-off at ≥0.1 were retained in the model

OR = odds ratio; 95% CI = 95% confidence interval; BMI = body mass index

explore the impact of pre-stenting on reducing the risk of US.

Regarding the use of UAS, it was more frequently employed in the MP group (65% vs. 44% in the IP group; $p = 0.011$). Nevertheless, UAS use was not identified as a predictor of US. These findings are consistent with previous studies, which suggest that there is no established association between UAS placement during URS and the development of US [19, 46].

Neither stone size (maximal diameter) nor stone volume emerged as predictors of US in our study. Conversely, total delivered energy was identified as significant predictor of US on univariable analysis (OR = 1.02 for each additional 1 kJ; $p = 0.026$). This finding underscores that all laser parameters (power, frequency and cumulative delivered energy) should be cautiously selected and monitored during URS.

This study has several limitations. First, its retrospective design inherently introduces potential biases, limits retrieval of some information such as details on irrigation settings (pressure, manual pump, volume, rate, etc.) and does not warrant a follow-up longer than provided for by institutional guidelines. Second, the laser system does not provide detailed information regarding the mean frequency applied during the operation. This lack of granularity restricts our ability for analysis. Additionally, the study is based on data collected from two institutions, each employing different approaches to URS technique. A difference in surgeons' expertise between the two institutions cannot be formally excluded. Nevertheless, both are university hospitals from the same country with a urologist with >100 URS experience present in each surgery, suggesting a minimal impact of possible differences in expertise. Another limitation is the relatively small sample size of 158 patients, which, while sufficient for preliminary observations and findings, may lack statistical power needed to detect subtle associations or rare complications. Despite these limitations, we consider the results of the present study to be robust, as all other significant variables that could influence the rate of US (such as age, ASA score, prior URS history, stone localization and burden, rate of impacted stones) were equally distributed between the two groups. The significant correlation between stone burden parameters (maximal stone size and stone volume) further underscores the quality of the data that was available for analysis. Of note, SFR was not based on systematic postoperative CT scan, potentially leading to an overestimation of success rates. The SFR shall be

interpreted accordingly. Larger prospective studies are warranted to confirm our findings and establish safety thresholds for laser settings in lithotripsy.

Conclusions

High-power, high-frequency settings from manufacturer laser presets significantly increase the risk of US formation, independently from impacted ureteral stones, and without improving SFR. Our findings underscore the importance of careful selection of laser settings during TFL lithotripsy, advocating for individualized laser presets with more conservative settings tailored to each patient and clinical scenario. Future research should prioritize prospective studies to evaluate the specific effects of individual laser parameters, such as power, frequency, cumulative delivered energy and laser energy consumption, in order to identify optimal settings, which can maximize efficacy while minimizing the risk of tissue damage. Additionally, the development of dynamic, real-time adjustable presets based on intraoperative feedback (irrigation flow and temperature, targeting of the stone, laser fiber working distance, stone particle size, stone type, stone ablation rate, etc.) represents a promising avenue for improving patient outcomes.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The local ethics committees approved the study protocol (Study ID: BASEC 2023 − 00660 and 2024 − 00272).

Competing interests The authors declare no competing interests.

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研究

大功率带来大风险：输尿管镜下高频钬光纤激光碎石术后输尿管狭窄率高

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摘要

目的：比较输尿管镜检查中使用钬光纤激光（TFL）制造商预设（MP）或个性化预设（IP）的安全性和有效性。

方法本研究为多中心回顾性分析，针对2020年瑞士首例使用Soltive® Premium（奥林巴斯医疗系统公司）TFL治疗的患者。其中MP组在日内瓦大学医院实施治疗，IP组在苏黎世大学医院实施治疗。研究收集了患者人口统计学特征、结石特性及手术细节等数据。主要结局指标为术后输尿管狭窄（超声检查），次要结局指标为结石清除率（SFR）。

研究结果显示，共纳入158例患者进行分析，每组79例。两组患者的人口学特征基本一致，但金属探头组（MP组）的术前置入率较低（56%对比91%；$p<0.001$），输尿管套管使用率较高（65%对比44%；$p=0.011$）。结石负荷（中位结石直径9毫米，中位结石体积267 ^{3}毫米）和输尿管结石阻塞率（29%对比34%；$p=0.49$）均无显著差异。金属探头组的平均功率、最大功率、频率设置及能量消耗均显著高于普通探头组。金属探头组的超声检查率高达11%，而普通探头组仅为1%（$p=0.009$）。多变量分析表明，金属探头组是影响超声检查率的显著预测因素（比值比12.4；$p=0.02$），且该因素独立于输尿管结石阻塞存在。两组的超声检查率差异无统计学意义（85%对比84%；$p=0.67$）。

结论制造商激光预设的高功率、高频激光设置会增加超声检查风险，但未改善SFR。未来研究应根据患者特征和术中情况进一步评估最佳激光设置。

关键词输尿管镜检查·碎石术·钬光纤激光器·输尿管狭窄·激光预设值·功率

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缩写

ASA美国麻醉医师协会
BMI体重指数
西 置信区间
CT计算机断层扫描
流行音乐播音员 双J
HU Hounsfield单位
冰点 个人预设
MP制造商预设
日内瓦大学医院HUG
OR比值比
SFR石头免费费率
TFL钇光纤激光器
UAS输尿管通路鞘
美国输尿管狭窄
URS输尿管镜检查
USZ苏黎世大学医院

介绍

输尿管镜碎石术（URS）目前是治疗尿路结石最常用的技术[1]。在输尿管镜激光碎石术中，可采用多种脉冲激光器：钬：钇铝石榴石激光器、脉冲钬：钇铝石榴石激光器以及超脉冲铥光纤激光器（TFL）[2–4]。TFL在多个方面优于钬：钇铝石榴石激光器（如更高的结石消融率、更小的碎石颗粒、更低的后弹力、更细的光纤、更高的无结石率（SFR）、更短的手术时间），但泌尿科医生的安全警示和报告指出，TFL可能增加输尿管狭窄（US）的风险[2，5–7]。目前提出的致病机制范围广泛且缺乏有力证据支持，体外研究结果也存在矛盾[7–11]。因此，关键问题在于如何在确保患者安全的前提下，最大限度地提升输尿管镜碎石术的疗效，同时合理调整激光参数设置。对2021年10月Twitter专家库的分析显示，首选激光设置存在高度可变性，且无共识[12]。事实上，全球许多泌尿科医师依赖制造商提供的激光预设，这些预设也存在高度可变性[13]。

在此背景下，瑞士前两家在临床常规中使用TFL的医院在激光预设方面采用了不同的方法：日内瓦大学医院（HopitauxUniversitairesdeGeneve，HUG）使用制造商预设（MP），而苏黎世大学医院（Universitatsspitalzurich，USZ）使用个体预设（IP），这是根据一位接受过专科培训的泌尿科医生的建议而制定的，该医生已建立了医院内部的激光设置指南(图1）[14-16]。

这种临床实践差异为比较HUG和USZ两家医院接受治疗的患者提供了基础，用于分析TFL激光碎石术的安全性和有效性。

材料和方法

我们对瑞士日内瓦大学医院（HUG）和洛桑大学医院（USZ）使用溶剂® Premium TFL（奥林巴斯医疗系统公司，日本东京）进行上尿路碎石术（URS）的首批患者进行了多机构回顾性分析。HUG在完成79例患者治疗后停止使用TFL设备，因此本研究纳入了USZ医院前79例接受治疗的患者。排除标准包括：既往接受过输尿管重建手术或存在狭窄的患者，以及仅进行URS取石但未实施激光碎石术的患者。数据采集自医院医疗信息系统，收集的患者特征包括：年龄、性别、体重指数（BMI）、糖尿病病史、ASA分级评分及同侧输尿管URS既往治疗史。同时记录结石特征与位置信息，包括肾脏或输尿管近端、中段、远端的分布情况、结石数量、最大结石直径、结石体积、以亨氏单位（HU）表示的最大结石密度，以及诊断时是否存在肾积水。为准确估算结石体积，我们采用椭球体体积公式（4/3 π a*b*c，其中a、b、c分别代表结石在三维空间中的半径，数据来源于术前CT扫描的轴位和冠状位图像）。对于多发结石的情况，我们对每颗结石的体积进行累加[17]。通过查阅病历记录确认输尿管结石是否发生梗阻。两家医疗机构的常规诊疗标准是：若满足以下任一条件，则判定为输尿管结石梗阻：(a)结石近端存在输尿管扩张，且伴有中度至重度肾积水（分级≥2级）[18] (b)首次尝试时导丝或输尿管导管难以通过输尿管结石；(c)在至少间隔两个月的两次影像学检查中，结石仍位于原位[19]。关于手术操作，我们收集了单侧与双侧输尿管碎石术（URS）的数据，术前术后双J（DJ）输尿管支架置入情况（两家机构通常术前支架留置10-20天，术后支架留置5-14天），以及输尿管套管（UAS）使用情况。*详细手术步骤和器械信息详见补充材料*。由于所有手术均在大学附属医院完成，每位患者均由具有>100例URS经验的泌尿科医生或在资深泌尿科医生指导下进行的住院医师操作。

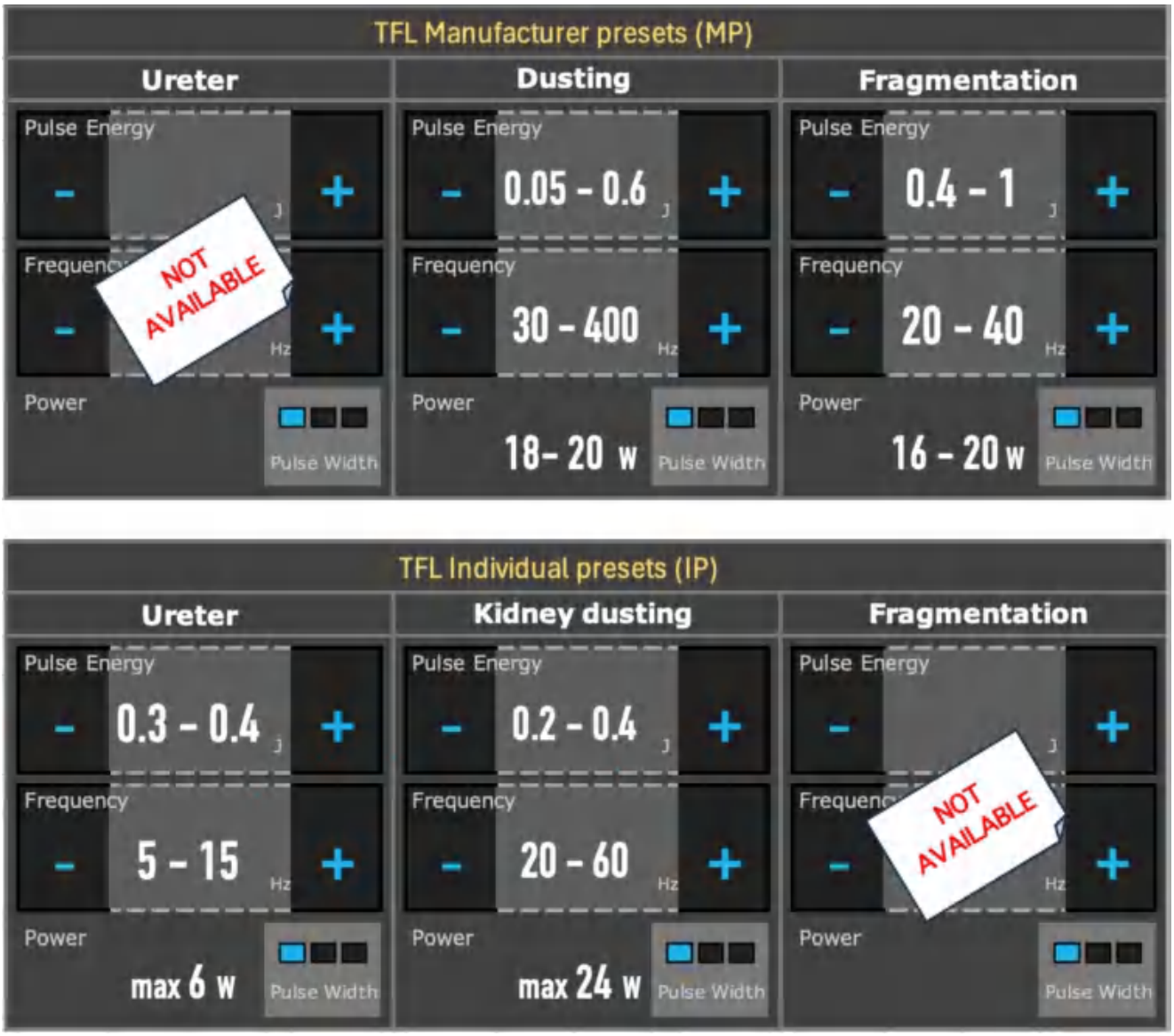


图1展示了2020年奥林巴斯Soltive® Premium钬光纤激光器（TFL）制造商预设（MP）与用户自定义预设（IP）的图形界面对比。关于制造商预设：截至2021年7月，市场上尚未出现专为输尿管设计的制造商预设方案，也未见相关技术指标的明确记载。现有预设模式专为肾脏设计，不适用于输尿管。关于单个预设模式：由于TFL最初主要作为碎石激光器推出，因此未提供专门用于结石碎石的预设模式。

我们从soltive ® Premium激光治疗仪中回溯提取了治疗参数，该设备可记录每位患者的以下参数：激光光纤类型、有效激光时间、总能量输送量、最大功率设置以及最低和最高频率设置。平均功率计算方法为总能量除以激光时间。平均激光能量消耗则通过总能量除以结石体积（焦耳/立方毫米^3）得出[20]。

主要结局指标为术后输尿管狭窄（US）的存在。根据Moretto等人的定义，输尿管狭窄是指因输尿管变窄导致的尿流障碍，常伴随疼痛等症状。（复发感染或肾功能丧失）和/或导致再次手术干预[21，22]。两家医疗机构均要求患者在术后六周接受临床评估和肾脏超声检查。根据机构诊疗指南，出现症状、肾功能受损或超声提示肾盂积水的患者需进行全面评估。对于此类病例，将讨论采用逆行输尿管肾盂造影结合诊断性尿路逆行扫描和/或动态显像检查方案。其他安全性指标包括术中并发症，以及根据Clavien-Dindo分级系统[23，24]分类的早期（<1个月）和晚期（≥1个月）术后并发症。

次要结局指标为SFR，定义为内镜检查未见大于2 mm的碎片，且随访影像（所有患者均进行超声检查，根据外科医生的判断可进行额外影像检查，如CT）中亦无大于2mm的碎片[25]。

统计分析

分类变量间的关联性分析采用卡方检验或费希尔精确检验，具体视情况而定。连续变量间的差异性分析采用独立样本t检验或曼-惠特尼U检验，视情况而定。连续变量间的相关性分析采用皮尔逊相关检验或斯皮尔曼rho检验，视情况而定。二分类结局预测因子的分析采用逻辑回归模型。双侧上尿路梗阻患者纳入个体患者分析。所有统计检验均为双侧检验，p值<0.05视为具有统计学意义。统计分析与图表绘制使用IBM SPSS Statistics 29.0软件（美国纽约州阿蒙德市IBM公司）完成。

结果

共有158名患者可供分析，每组79名，均在2020年6月至2021年5月期间接受治疗，平均年龄为53岁。

所有患者均接受术前CT扫描以评估结石负荷。多数病例为肾结石而非输尿管结石。具体而言，70%的患者患有肾结石（伴/不伴输尿管结石），而53%的患者为输尿管结石（伴/不伴肾结石）。结石最大尺寸与结石体积存在显著相关性（斯皮尔曼相关系数0.92；p <0.001；补充图1）。表1列出了患者的详细特征。

在基线患者特征方面，与IP组相比，MP组的糖尿病发病率较低（9%vs.20%；p=0.04）。此外，MP组的术前置入支架比例显著低于IP组（56%vs.91%；p <0.001）。两组在其他基线变量方面未见显著差异。具体而言，结石负荷相当（两组最大结石中位尺寸均为9毫米；p=0.39；MP组结石体积中位数269 mm³，IP组264 mm³；p=0.67）。同样，输尿管结石阻塞率在MP组和IP组间也无显著差异（分别为29%vs.34%；p=0.49）。

两组在操作特征上存在显著差异。MP组的UAS使用率更高，主动激光时间更短。与IP组相比，能量消耗更高（J/mm³）、平均功率更高、最大功率设置更高、激光频率设置更高（适用于最低和最高频率设置）（表1和图2）。

所有患者均保持随访无失访，且术后3个月内均完成至少一次首次术后复查。MP组发生9例碎石（11%），而IP组仅1例（1%）（p=0.009）。单因素分析显示，结石阻塞程度、未置入支架、激光器预设参数、总激光能量递增及平均功率提升是碎石的预测因素（表2）。多因素分析中，结石阻塞程度（OR7.10（CI1.67–30.1）；p=0.008）和激光器预设参数（OR12.4（CI 1.48–104）；p=0.02）（表2）成为碎石的独立预测因素。

患者的详细特征及管理

10例US患者见*补充表*

1. 所有患者在初次诊断时均存在输尿管结石。所有患者均接受逆行输尿管尿路造影以定位并测量结石。超声显示的结石位置与10例患者中4例（40%）的原结石位置相符，另有4例（40%）显示结石位置更远端，其余2例（20%）显示结石位置更近端。多数病例采用腹腔镜达芬奇辅助输尿管成形术（使用颊黏膜移植片或阑尾瓣）或输尿管再植术（50%）或球囊扩张联合输尿管支架术（33%）进行治疗。此外，1例需行肾切除术，另1例结石自行消退。接受重建手术的患者至少随访2年，期间未出现失访情况，术后恢复良好，无复发迹象。

在术中、术后早期和术后晚期并发症方面，MP组和IP组之间未观察到显著差异。

SFR在两组间无显著差异（MP组和IP组分别为85%和84%；p=0.67）。

讨论

据我们所知，这是首项证实使用制造商预设的高功率、高频激光参数进行输尿管镜碎石术存在风险的临床研究。具体而言，与更为保守的个性化激光参数设置相比，制造商预设参数显著增加了术后超声检查风险（多变量分析显示比值比OR=12.4，p=0.02），但两组的碎石成功率（SFR）无显著差异。多数术后超声病例最终需要进行重大手术干预。

表1患者特征

基线特征					程序特征				
变量	全面的（*n*=168）	制造商 turer激光预设（*n*=79）	个人 激光预设值（*n*=79）	p值	变量	全面的（*n*=168）	制造商 turer激光预设（*n*=79）	个人 激光预设值（*n*=79）	p值
年龄（平均值，SD）	53 (17)	52 (19)	54 (15)	0.48*	UAS使用	86 (54%)	51 (65%)	35 (44%)	**0.011****
雄性：雌性比率	2.1: 1	2.0: 1	2.2: 1	0.87**	术后DJ支架植入术	156 (99%)	79 (100%)	77 (98%)	0.16**
BMI（均值，标准差）（kg/m ^{2}）	26 (5)	26 (5)	26 (5)	0.76*	激光光纤芯径				**<0.001****
					150 µm	84 (53%)	5 (6%)	79 (100%)	
					200 µm	68 (43%)	68 (86%)	0 (0%)	
					365 µm	6 (4%)	6 (8%)	0 (0%)	
糖尿病混音	23 (15%)	7 (9%)	16 (20%)	**0.04****	有效激光时间（mm：ss）（中位数，IQR）	06:28 (01:56–16:36)	04:38 (01:37–09:37)	13:05 (02:42–23:33)	**<0.001*****
ASA评分				0.65**	总能量（KJ）	6.26 (1.63–17.1)	6.50 (2.28–16.38)	5.98 (9.03–17.50)	0.41***
1	17 (11%)	9 (11%)	8 (10%)						
2	94 (59%)	50 (63%)	44 (56%)						
3	41 (26%)	17 (22%)	24 (30%)						
4	6 (4%)	3 (4%)	3 (4%)						
既往尿路结石病史	44 (28%)	22 (28%)	22 (28%)	1.00**	能耗（J/mm ^{3}）（中位数，IQR）	18 (7–32)	20 (11–44)	17 (7–26)	**0.031*****
石头位置				0.94**	平均功率(W)（中位数，IQR）	19 (8–20)	20 (20–25)	8 (6–15)	**<0.001*****
肾脏	67 (43%)	33 (42%)	34 (43%)						
输尿管	48 (30%)	25 (32%)	23 (29%)						
都	43 (27%)	21 (26%)	22 (28%)						
输尿管结石地点				0.18**	最大功率设置(W)（平均值，标准差）	21 (13)	27 (13)	15 (9)	**<0.001***
近端	54 (59%)	54 (59%)	31 (69%)						
在...中间	25 (28%)	25 (28%)	8 (18%)						
远端	9 (10%)	9 (10%)	4 (9%)						
多选	3 (3%)	3 (3%)	2 (4%)						
数量结石（中位数，IQR）	1 (1–3)	1 (1–3)	2 (1–3)	0.28***	最低频率设置-滴答声（Hz）（中位数，IQR）	40 (10–200)	200 (100–200)	14 (5–30)	**<0.001*****
最大结石尺寸（mm）（中位数，IQR）	9 (7–13)	9 (7–13)	9 (7–13)	0.39***	最高频率组-滴答声（Hz）（中位数，IQR）	100 (40–400)	400 (200–400)	40 (30–100)	**<0.001*****
石体积（mm ^{3}）（中位数，Iqr)	267 (110–751)	269 (117–565)	264 (110–857)	0.67***	术后结局				
最大结石密度（HU）（平均值，SD）	1142 (391)	1108 (382)	1177 (399)	0.27*	变量	全面的（*n*=168）	Manufac-激光扫描仪预先布置（*n*=79）	Individ-紫外激光预先布置（*n*=79）	p值
受影响的石头	50 (32%)	23 (29%)	27 (34%)	0.49**	术中困难	总计：8（5%）	总计：3（4%）	总计：2（3%）	0.15**

表1（续）

基线特征					程序特征				
变量	全面的（*n*=168）	制造商turer激光预设（*n*=79）	个人激光预设值（*n*=79）	p值	变量	全面的（*n*=168）	制造商turer激光预设（*n*=79）	个人激光预设值（*n*=79）	p值
					输尿管穿孔肾盂穿孔阴	6 (4%)	2 (3%)	1 (1%)	
						1 (1%)	1 (1%)	0 (0%)	
					茎异常勃起	1 (1%)	0 (0%)	1 (1%)	
外科手术前的肾积水sis≥2级	47 (30%)	21 (27%)	26 (33%)	0.38**	术后早期并发症	总计：8（5%）			
	总计：9 (11%)	总计：5（6%）		0.47**					
					CD I血尿	2 (1%)		0 (0%)	
					CD II		2 (3%)		
						4 (3%)		3 (4%)	
					UTI谵妄	1 (1%)	1 (1%)	1 (1%)	
					CD IV		0 (0%)		
					TIA	1 (1%)	0 (0%)	1 (1%)	
双侧尿路结石	9 (6%)	4 (5%)	5 (6%)	0.73**	术后晚期并发症	总计：10（6%）	总计：9 (11%)	总计：1（1%）	**0.009****
					CD IIIb				
						10 (6%)	9 (11%)	1 (1%)	
					输尿管狭窄其他	0 (0%)	0 (0%)	0 (0%)	
支架植入前	116 (73%)	44 (56%)	72 (91%)	**<0.001****	石头空闲状态	132 (84%)	65 (82%)	67 (85%)	0.67**

T检验，**卡方检验，***曼-惠特尼U检验

SD=标准差；IQR=四分位距；BMI=体重指数；ASA=美国麻醉医师协会；URS=输尿管镜检查；HU=豪斯菲尔德单位；UAS=输尿管导管鞘；TIA=一过性脑缺血发作；CD=克拉维恩-丁多分类

这一假设此前已在多项体外研究[7，26]中被提出，并因安全投诉[27-33]而备受关注，如今这项研究提供的有力证据为其提供了支持。对于所有实施输尿管镜激光碎石术的泌尿科医生而言，这都是一条至关重要的警示，强调了在评估和调整激光参数时必须谨慎操作。

近期系统综述显示，输尿管镜碎石术后发生输尿管狭窄（US）的总体发生率为3%[22，23]。本研究中，机械碎石组（MP组）的输尿管狭窄发生率达11%，这一比例显然已超过该手术的安全阈值。可以理解的是，相关医院（HUG）在引进TFL设备不到一年后便决定停用。相比之下，采用内镜碎石术（IP）的病例中输尿管狭窄发生率仅为1%，这表明使用内镜碎石术时，通过TFL进行输尿管镜激光碎石术是安全可行的。

激光参数与超声波形成之间的关联可能主要由两个关键因素决定：高功率和高频。高功率会导致局部能量传递过快过强，可能引发组织热损伤，从而最终形成超声波[34–36]。同样，高频参数会降低能量传递到结石表面的效率，增加了治疗风险。非故意靶向输尿管壁而非输尿管结石[26，37]。

总体而言，高功率通常与高频相关联，反之亦然，这主要归因于激光碎石术中使用的脉冲能量范围相对狭窄（主要为0.4–1.5焦耳）[38]。本研究显示，MP组的平均功率、最大功率、最低频率和最高频率设置均显著高于IP组。此外，单变量分析表明平均功率是超声波能量的重要预测因子（每增加1瓦，比值比OR=1.03；p=0.046）。最后，MP组的激光能量消耗显著高于IP组：20焦耳/毫米^{3}对比17焦耳/毫米^3（p=0.031）（如近期研究所强调的，数值越低效果越好）[39，40]。这种能量消耗差异可能源于高频设置对结石表面的靶向精度较低。该假设得到两项体外研究的支持：高频设置会导致激光能量向结石表面的传递效率降低[41，42]。

结石定位不佳，因结石粉尘生成时能见度降低，且当偏离目标时人体反应时间延迟，这会进一步加剧相关危害。

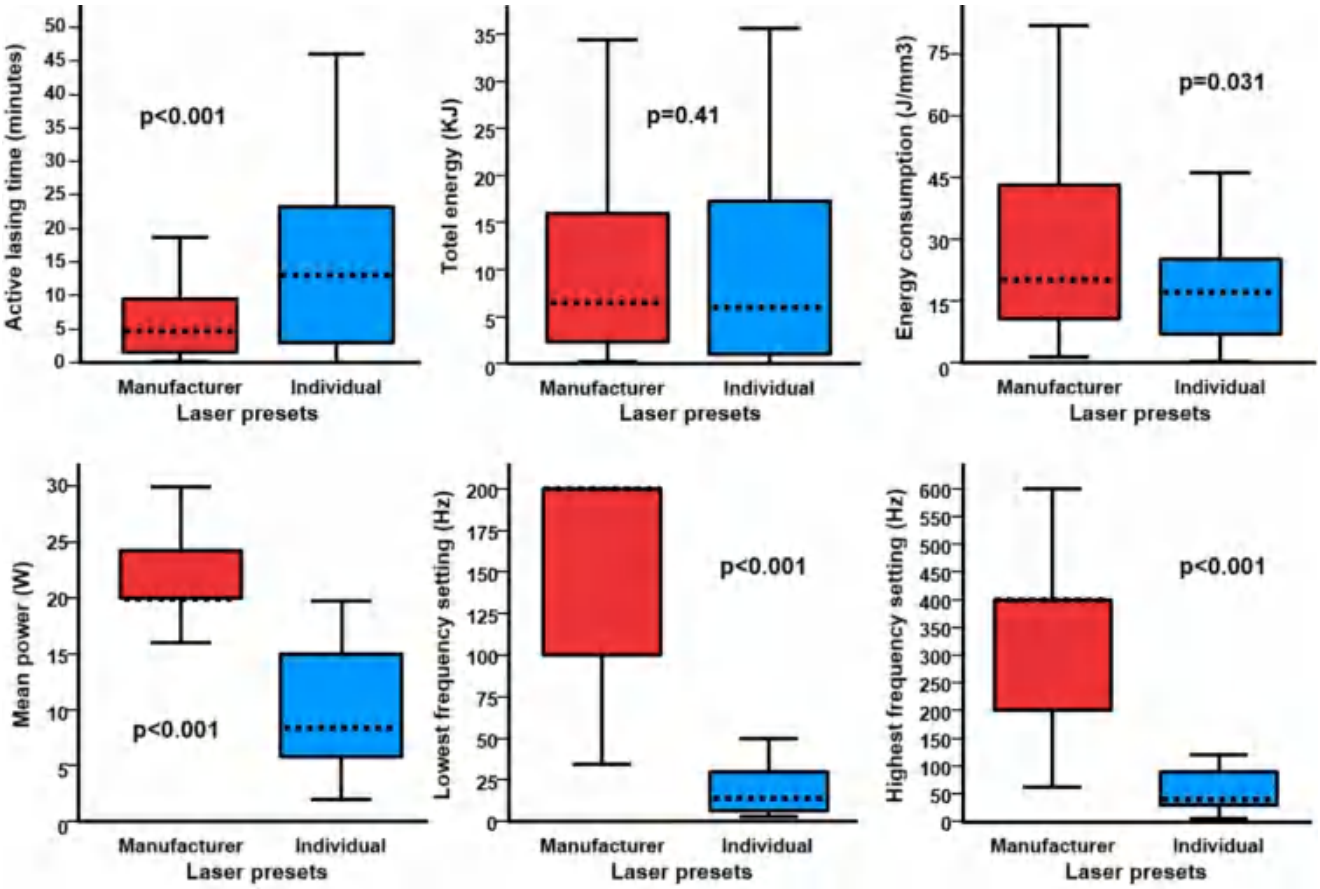


图2激光发生器获取的激光设置分布。箱线图中，中位数用虚线表示，箱体代表25%至75%百分位数，须线代表10%至90%百分位数。

采用高频碎石术[38]。本研究显示，多数接受超声碎石术的患者激光频率设置在100至400赫兹之间。根据平均视觉反应时间至少250毫秒[43]，多数外科医生在结石定位不佳或视野受限时，通常会在发射25到100个激光脉冲后才松开激光踏板。这些过度且不受控的激光脉冲，不仅可能导致观察到的激光能量消耗差异，还可能
本研究还对美国的形成作出了贡献。

多变量分析显示，输尿管结石嵌顿是超声检查的第二重要独立预测因素（比值比=7.10；p=0.008）。这一发现与近期系统综述和荟萃分析结果一致，该研究基于5项研究（共纳入13550名患者）证实嵌顿结石是超声检查的明确预测指标（比值比=7.47；p=0.01）[22]。在本研究队列中，出现超声检查的患者中有70%（7例/10例）存在结石嵌顿。然而，另有43例结石嵌顿患者未出现超声检查，这凸显了其他竞争性风险因素的影响，例如高功率高频激光碎石术等技术手段。

所有尿路结石病例均发生在初次诊断时输尿管已有结石的患者中。值得注意的是，这些病例均伴有输尿管狭窄。在采用超声检查的病例中，仅有40%的患者结石位置与最初发现时完全一致。这一发现表明，结石可能在初次诊断与输尿管镜激光碎石术之间发生位移，或者热损伤可能发生在激光能量作用区域之外。因此，在缺乏确凿证据证明之前，高功率高频激光碎石术对输尿管结石和肾结石都可能存在风险。未来研究应通过前瞻性方案，对激光发射部位进行标准化操作，以验证“远端热损伤”的假设。

值得注意的是，单变量分析显示术前置入支架可显著降低输尿管结石（US）风险（比值比=0.2；p=0.022）。尽管这一发现可能部分源于两家医院的诊疗差异（MP组术前置入支架56%vs.IP组91%；p<0.001），但可以合理推测：术前置入支架通过扩张输尿管并改善冲洗液流动，从而降低输尿管损伤风险，优化激光碎石术条件，进而预防结石形成[44]。总体而言，术前置入支架与更高的结石碎石率（SFR）及更少的术中术后并发症相关[45]。未来仍需进一步研究以验证这一结论。

表2输尿管狭窄预测因子的逻辑回归分析

变量	单变量		多变量*	
	或（95%置信区间）	***p***	**或（95%置信区间）**	***p***
年龄（连续）	0.98 (0.94–1.02)	0.32		
男性vs.女性	4.59 (0.57–37.3)	0.15		
BMI（kg/m2）（连续）	1.03 (0.91–1.17)	0.64		
糖尿病	1.4 (0.3–7.6)	0.62		
最大结石尺寸（mm）（连续）	1.04 (0.94–1.15)	0.44		
石方体积（mm^3）（连续）	1.00 (1.00–1.00)	0.92		
输尿管结石	5.70 (1.41–23.1)	**0.015**	7.10 (1.67–30.1)	**0.008**
术前肾积水≥2级	1.63 (0.44–6.06)	0.47		
主URS尝试失败	1.6 (0.3–8.1)	0.57		
支架植入前	0.2 (0.06–0.8)	**0.022**		
UAS使用	0.8 (0.2–3.0)	0.77		
制造商（MP）与激光光纤芯径的个体激光预设（IP）	10.0 (1.24–81.2)	**0.031**	12.4 (1.48–104)	**0.02**
150 µm	1.00 裁判员			
200 µm	4.71 (0.94–23.5)	0.059		
365 µm	8.20 (0.63–106.6)	0.11		
实际激光时间(s)（连续）	1.00 (1.00–1.00)	0.64		
总能量（KJ）（连续）	1.02 (1.00–1.04)	**0.026**		
激光能量消耗（J/mm^3）	1.00 (0.99–1.02)	0.60		
平均功率(W)	1.03 (1.00–1.06)	**0.046**		
最大功率设置(W)	1.02 (0.98–1.07)	0.28		
最低频率设置（Hz）	1.00 (0.99–1.01)	0.12		
最高频率设置（Hz）	1.00 (0.99–1.01)	0.16		
术中输尿管或骨盆穿孔	3.18 (0.34–30.2)	0.31		

在前向条件性多变量分析中，仅保留进入标准≤0.05且剔除阈值≥0.1的变量，最终纳入模型。

OR=比值比；95%CI=95%置信区间；BMI=体重指数

研究支架植入前的干预措施对降低溃疡性结肠炎（US）风险的影响。

关于UAS的使用，MP组的使用频率更高（65%vs.IP组的44%；*p*=0.011）。然而，UAS的使用并未被确定为US的预测因素。这些发现与既往研究一致，既往研究表明URS期间放置UAS与US的发展之间没有明确的关联[19，46]。

在我们的研究中，无论是石块尺寸（最大直径）还是体积，均未被证实为超声波能量（US）的预测因子。相反，在单变量分析中，总能量传递量被确定为超声波能量的重要预测因子（每增加1 kJ，比值比OR=1.02；*p*=0.026）。这一发现强调，在尿路结石（URS）治疗过程中，所有激光参数（功率、频率和累积能量传递量）都应谨慎选择和监测。

本研究存在若干局限性。首先，其回顾性研究设计本身存在潜在偏倚，导致部分信息难以获取，例如灌注参数（压力、手动泵、体积、流速等）的详细数据，且未遵循机构指南要求的随访时长。其次，该激光系统未能提供所用平均频率的详细信息。在手术过程中，这种缺乏细节的局限性制约了我们的分析能力。此外，本研究数据来自两家采用不同URS技术方案的医疗机构，两家机构外科医生的专业水平差异无法完全排除。不过，两家均为同国的大学附属医院，且每家手术室都配备有超过100次URS手术经验的泌尿科医生，这表明专业水平差异对结果的影响微乎其微。另一个局限是样本量相对较小（158例患者），虽然足以进行初步观察和得出结论，但可能缺乏检测细微关联或罕见并发症所需的统计效力。尽管存在这些局限，我们认为本研究结果具有可靠性，因为所有可能影响超声检查率的其他显著变量（如年龄、ASA评分、既往URS病史、结石位置及数量、结石阻塞率）在两组间分布均等。结石负荷参数（最大结石尺寸和结石体积）之间的显著相关性进一步凸显了可用于分析的数据质量。值得注意的是，SFR未基于系统性的术后CT扫描，这可能导致成功率被高估。SFR应

因此应相应地进行解释。有必要开展更大规模的前瞻性研究，以验证我们的发现，并为碎石术中激光参数的安全阈值提供依据。

结论

制造商预设的高功率、高频激光参数会显著增加超声碎石形成的风险，这种风险与输尿管结石本身无关，且无法提升碎石成功率。我们的研究结果强调了在TFL碎石术中谨慎选择激光参数的重要性，建议采用个体化激光预设方案，根据每位患者的具体情况和临床场景选择更为保守的参数设置。未来研究应优先开展前瞻性试验，评估功率、频率、累积能量输送量及激光能耗等具体参数对疗效的影响，从而确定既能最大化治疗效果又能最大限度降低组织损伤风险的最佳参数组合。此外，基于术中实时反馈（如冲洗液流量与温度、结石定位、光纤工作距离、结石粒径、结石类型、碎石速率等）开发动态实时可调预设方案，是提升患者治疗效果的极具潜力的研究方向。

补充信息在线版本包含补充材料，可在https://doi.org/10.1007/s00345-0 25-05553-0上找到。

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可控脉冲掺铥光纤激光器碎石特性实验研究

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摘　要: 利用峰值功率 600 W 的掺铥光纤激光器, 用 Labview 程序外控激光脉冲参数进行体外碎石实验, 研究脉冲铥激光碎石规律, 为临床应用提供参考。结果表明, 脉冲铥激光具有较好的碎石能力, 设置能量 0.3 J 的脉冲铥激光冲击草酸钙结石时碎片颗粒大部分直径小于 0.5 mm, 具有较好的粉末化能力; 当脉冲能量较小时, 碎石效率随脉冲能量变大快速提高, 对于峰值功率 600 W 的铥激光, 双脉冲组合并不能产生明显的“摩西效应”使碎石效率提升; 另外掺铥光纤激光碎石时为提高碎石效率可能设置较大脉宽, 此条件下激光在水中的穿透距离较大, 实验中达到 5.4 mm, 因此, 手术中要充分考虑光纤端与周围组织的安全距离, 避免造成周围组织的损伤。

关键词: 激光碎石; 掺铥光纤激光器; 双脉冲组合; 组织损伤
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Experimental study on the characteristics of pulse controlled thulium fiber laser lithotripsy

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Abstract: Using the peak power of 600 W thulium-doped fiber laser, the laser pulse parameters were controlled by Labview program to carry out the extracorporeal lithotripsy experiment, and the law of pulsed thulium laser lithotripsy was studied to provide reference for clinical application. The results show that the pulsed thulium laser has good lithotripsy ability. When the pulsed thulium laser with an energy of 0.3 J is set to impact calcium oxalate stones, most of the debris particles are less than 0.5 mm in diameter, which has good pulverization ability. When the pulse energy is small, the gravel efficiency increases rapidly with the increase of pulse energy. For the thulium laser with a peak power of 600 W, the double pulse combination does not produce obvious ‘Moses effect’ to improve the gravel efficiency. In addition, a large pulse width may be set to improve the efficiency of thulium-doped fiber laser lithotripsy. Under this condition, the penetration distance of laser in water is large, reaching 5.4mm in the experiment. Therefore, the safe distance between the fiber end and the surrounding tissue should be fully considered in the operation to avoid damage to the surrounding tissue.

Key words: laser lithotripsy; thulium-doped fiber laser; dual-pulse combination; tissue damage

1　引言

近年来, 软镜技术快速发展, 激光可通过光纤传导经输尿管进行肾盂内碎石从而避免了穿刺损伤, 激光碎石的优势得到充分发挥。激光碎石设备中, 1 940 nm 波长的脉冲铥光纤激光器(TFL)作为一种新兴技术备受关注, 与钬激光相比, 具有光纤芯径小、脉冲频率高、碎石粉末化好及反冲小等优点[1-5]。

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2021 年,Panthier 等人[6]体外研究比较了 TFL 和 Ho:YAG 在不同激光设置下用 150 μm 光纤和 272 μm 光纤的消融率,研究表明在相同的环境和光纤下,TFL 消融率至少是 Ho:YAG 消融率的两倍,比 Ho:YAG 产生更高的烧蚀体积。同年,Jones 等人[7]初步临床研究表明,超脉冲光纤铥激光碎石术因其能改善手术中的能见度,可以治疗结石类型范围大等优点,具备成为新一代碎石工具的潜力。2022 年,Ulvik 等人[8]对比了铥激光和钬激光碎石疗效差异,铥激光肾结石清除率要高于钬激光,术中出血发生率也低于钬激光。然而,在 2023 年许力为等人[9]的一项研究中,TFL 组与 HL 组比较患者术后并发症发生率略高,同年 Ahmad Para Sajad 等人[10]在临床研究指出,尽管 TFL 在输尿管镜激光碎石术中展现出显著优势,但其在术后输尿管狭窄的发生率与钬激光碎石相比却较高,这些发现给提出了新的挑战,需要进一步深入研究铥激光碎石特性,以降低并发症风险。通过实验研究不同脉冲形式下的铥激光碎石作用特性,研究不同参数铥激光碎石效率及效果,为临床应用提供参考。

2 铥激光碎石分析

铥激光碎石机制与钬激光相似,主要是光热效应以及光机械效应,即激光能量被结石中的水、有机物、矿物质吸收,结石孔隙间的水瞬间温度升高汽化,形成微爆使结石分解,另外被照射结石部分若温度高于物质阈值温度,可导致结石的热分解[11-13],因此,铥激光碎石是一个复杂的物理化学过程,其特性直接决定了碎石效率及组织损伤。根据铥激光在水中的吸收系数分析,其穿透深度应该只有 0.1 mm,但通常碎石用的激光脉宽有几百微秒,其作用过程包含了空泡产生、膨胀、坍塌及冲击等多个过程,激光脉冲峰值功率、脉冲形式等参数决定了此过程特性。文献[14]研究了脉冲钬激光与水作用的微爆过程,其微爆空化气泡约 300 μs 时开始坍塌,脉冲宽度大于 300 μs 时,空化气泡进入混乱多泡状态。

激光作用过程特性直接决定了碎石效率和损伤范围[15-17],提高单位能量碎石效率需要尽可能多的激光能量作用于结石或结石内空隙间的水,因此,理想的状态是合适的铥激光能量瞬时形成一个小空泡,让更多的激光能量穿过空泡作用到结石上。如双脉冲钬激光的“摩西效应”就是利用小能量脉冲产生气泡将水分开,然后使大能量脉冲激光作用于结石而提高碎石效率。

3 实验装置和方法

3.1 结石模型

不同的人体结石样本内外形貌、成分都有较大差异,不容易标定不同参数铥激光碎石效率及特性。肾结石成分主要为磷酸钙和草酸钙,其中草酸钙结石是较硬的一种,实验中制作草酸钙结石模型,分析铥激光碎石特性,同时用人体草酸钙结石样本(图 1b)验证铥激光碎石的有效性。

草酸钙结石的主要形成机制是钙、草酸盐结晶,而钙离子、草酸离子、尿酸离子和磷酸盐离子是晶体形成的主要促进剂,它们可以通过几种机制的激活来促进石材成分的结晶或聚集[18]。组织成分是影响激光与组织作用的最重要因素,根据草酸钙结石的主要成分,同时考虑结石硬度等特点,实验中结石模型是用一水草酸钙($CaC_2O_4 \cdot H_2O$)和石膏粉($CaSO_4 \cdot 2H_2O$)加清水凝结所形成的固体,结石中的羟基(-OH)是铥激光碎石的主要作用群体[12]。具体制作方法为:(1)将一水草酸钙、石膏粉和清水按 1∶2∶1 的比例混合加入到容器中;(2)搅拌至一水草酸钙和石膏粉混合均匀;(3)将混合物缓慢地倒入正方体模具中,静置待形成草酸钙结石样本模型(图 1 a)。



(a)结石模型



(b)人体草酸钙结石样本

图 1 结石模型及人体结石样本

3.2 实验装置及方法

如图 2 所示,实验装置由激光器、医疗光纤、脉冲驱动系统、信号检测示波器、双轴显微镜和方形石英烧杯等组成。其中激光器为峰值功率 600 W 的脉冲铥光纤激光器(上海科乃特激光科技有限公司产品),工作波长为 1 940 nm,光纤为芯径 370 μm 的低氢氧医疗光纤。脉冲驱动系统通过 Labview 软件自行编程

设置,并通过计算机串口连接驱动卡(型号:NI USB-6211,采样率:100 kHz)实现输出参数控制,改变方波的占空比以及相位大小实现任意脉冲波形驱动(图 3),同时信号由示波器实时检测,保证光脉冲的准确性。

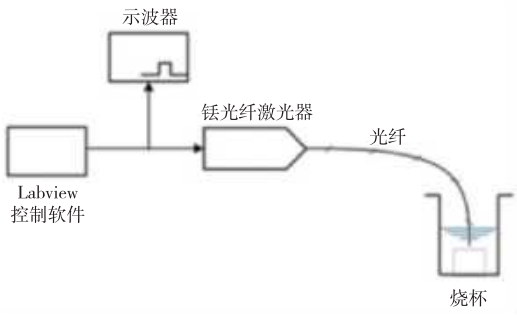


图 2 实验装置示意图

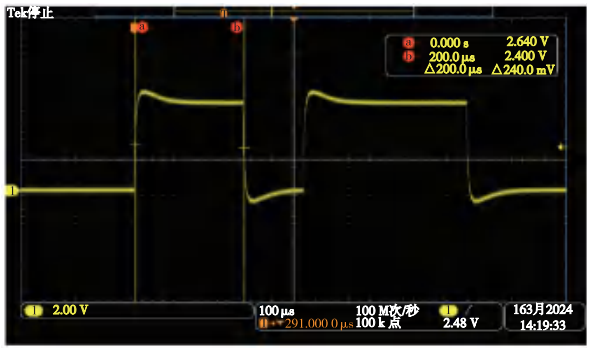


图 3 双脉冲波形

测量铥激光在水中的穿透深度时,将光纤浸入到方形烧杯的水中,调整光纤端部到水底部的距离,用黑色相纸观察到激光传出烧杯底部时,记录光纤端部到水底的距离标定激光脉冲穿透水的深度。激光穿透深度的数据通过多组实验,去掉误差较大的值,取 5 组一致性较好的平均值得出实验结果。另外设置不同的激光参数在水环境下进行碎石特性和碎石效率实验,通过多次重复减小随机误差,同时用内窥镜观察碎石过程(图 4)。

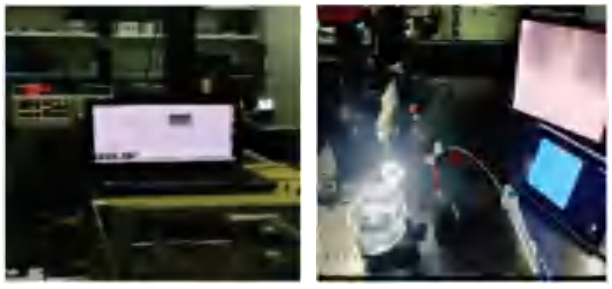


图 4 实验装置

激光碎石数据通过电子天平(型号:YJ-DTF-300,精度:0.001 g)称重获得,因为粉末化结石在水中不易收集,实验时先用电子天平称已经充分浸泡过水的结石质重,记录数据,碎石后再进行称重,实验前后的质量相减得到消融质量。经过多组实验后,去掉误差较大的值,取 5 组一致性较好的平均值得出结果。

4 实验结果及分析

4.1 不同参数的铥激光脉冲在水中的穿透深度

1 940 nm 的铥激光根据辐射波长水吸收系数计算在水中的穿透深度不足 0.1 mm,被视为一种安全的碎石激光,但实验中发现脉冲铥激光作用于水时,脉冲能量产生汽化空泡而使激光穿透更深的距离[20]。使用峰值功率为 600 W 的 TFL,设置脉宽从 100 μs~3 000 μs,测量激光脉冲穿透水的深度,结果如图 5 所示。

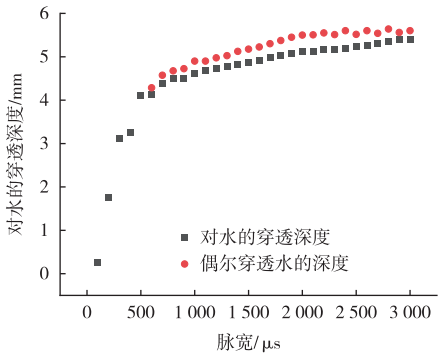


图 5 脉冲激光穿透水的深度

可以看出单脉冲铥激光在峰值功率 600 W 不变的情况下,激光在水中的穿透深度随脉宽增大(能量增大)而快速增大,但当脉宽达到 550 μs 后,穿透深度随脉宽变大趋势变缓。铥激光脉冲在 500 μs 时,其在水中的穿透深度为 4.1 mm,继续增大脉宽穿透深度达到 5.4 mm。另外一个明显特征是当激光脉宽小于 500 μs 时,固定脉宽的激光脉冲穿透水的深度基本保持一致,但当脉宽继续增大时,同样脉宽的激光脉冲在水中的穿透深度在一定范围内随机变化,推断此功率的铥激光作用时气泡的第一次坍缩和崩塌发生在大约 500 μs,对激光的吸收开始产生不确定性。

鉴于实验中铥激光脉冲小于 500 μs(能量 0.3 J)时,应该处于一次气泡形成过程,因此我们以 0.3 J 能量大小设置不同的双脉冲形式,分析峰值功率 600 W 的 TFL 产生的“摩西效应”特性,实验中分别以 100 μs+400 μs 和 200 μs+300 μs,300 μs+200 μs 和 400 μs+100 μs 四种组合测量不同脉冲间隔情况下双脉冲组合穿透水的特性,结果如图 6 所示。其中 100 μs+400 μs 的双脉冲组合在间隔 200 μs 时,穿透深度明显降低,在间隔 400 μs ~ 500 μs 时,穿透深度较大,略小于单脉冲情况的穿透深度,200 μs+300 μs 的双脉冲组合在水中的穿透深度一直较小。

以上实验可以看出脉冲参数对铥激光与水作用规律产生巨大影响,因为激光器峰值功率只有 600 W,作用过程中膨胀冲击和持续能量注入交织在

一起,无明显瞬态微爆特征,因此,高峰值能量的钬激光所能产生的明显“摩西效应”在低峰值功率的铥激光作用时并不明显,因为峰值功率低,不能在短时间内集中足够能量产生微爆形成明显分水孔洞,但长脉冲条件下产生的持续空泡使铥激光具有较大的水穿透深度,一定程度影响手术安全性。

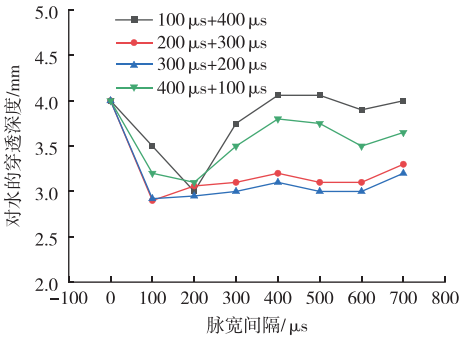


图 6　双脉冲组合穿透水的深度

4.2　不同参数的铥激光脉冲碎石效率

将结石模型置于水中进行碎石实验,完成后使用电子天平进行称重,得到碎石质量,用以分析不同参数的激光碎石效率。实验过程中通过内窥镜观察,可以看到当激光照射到结石表面,瞬间会出现大量白色粉末扩散到周围的水中,同时会有一些粉末被吸引至消融凹坑附近,表明碎石时不断重复微爆冲击和气泡塌陷回吸等过程(图 7)。



图 7　激光碎结石模型

使用峰值功率为 600 W 占空比 5 %(平均功率 30 W)的脉冲铥激光进行碎石,分析不同单脉冲能量的碎石效率,图 8 为碎石 1 分钟情况下不同脉宽参数的碎石质量。可以看出随着脉宽增大,碎石效率有明显提高。当单脉冲脉宽为 1 ms(能量 0.6 J)时,继续增大脉宽碎石效率增加变慢,当单脉冲脉宽为 2 ms(能量 1.2 J),继续增大脉宽碎石效率不再有明显变大。可以分析在小能量脉冲情况下,激光能量损失在水中的较多,作用到结石内部能量不足,形不成高效率的冲击作用,实验结果显示脉冲能量至少超过 0.6 J。

根据理论分析,“摩西效应”可以产生更高的碎石效率,通过前面分析气泡塌陷的临界脉宽 500 μs(能量 0.3 J),继续延长脉宽微爆过程本身进入混乱状态,已经不能体现“摩西效应”的原理及结果,因此,选择总脉冲宽度 500 μs 进行碎石实验,为方便过程观察,设置较低频率(20 Hz,占空比 1%),在 100 μs+400 μs 和 200 μs+300 μs,300 μs+200 μs 和 400 μs+100 μs 四组双脉冲组合形式和不同双脉冲间隔情况下进行碎石实验,碎石时间为 3 min,碎石结果如图 9 所示。可以看出,激光与脉冲作用规律复杂,脉冲形式对碎石效率会产生较大影响,对于峰值功率 600 W 的铥激光脉冲组合,100 μs+400 μs 双脉冲组合效率相对较高,碎石效率最高点为双脉冲间隔 400 μs。

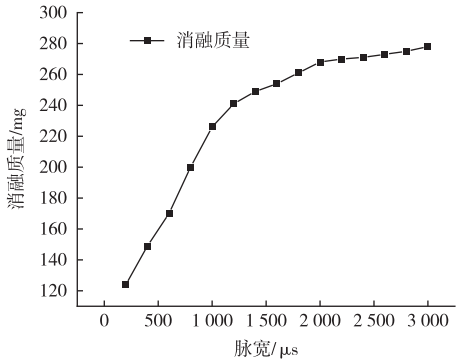


图 8　不同脉宽情况下碎石效率

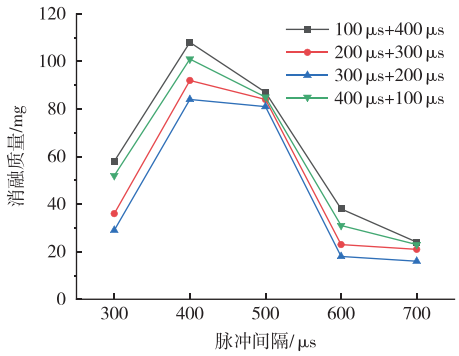


图 9　双脉冲组合的激光消融质量

使用峰值功率为 600 W 占空比 5%(平均功率 30 W),设置 100 μs+400 μs 双脉冲组合形式(总能量 0.3 J),设置最佳效率状态即双脉冲组合间隔为 400 μs 进行碎石,1 min 碎石质量为 165.5±5 mg,与 500 μs 的单脉冲碎石质量 158 mg 比较(图 8),碎石效率略有提高,因此双脉冲组合产生的“摩西效应”并不明显,同时根据图 9 可以判断,在此峰值功率情况下,大部分双脉冲组合形式低于单脉冲的碎石效率。可以分析“摩西效应”是高峰值功率双脉冲激光碎石时,前置小脉冲形成有效微爆,延迟一段时间使水有时间分开,避免更多的能量被吸收,从而提高碎石效率,因此,低峰值功率情况下进行双脉冲组合,不能起到相应作用。

随后,以同样激光参数对人体草酸钙结石样本进行碎石的操作,总能量仅 0.3 J 的铥激光脉冲具有一定碎石能力。如图 10 所示,实验中最小的碎片约为 50 μm,碎片颗粒大部分小于 0.5 mm,可以看出小能量脉冲铥激光碎石具有较好的粉末化能力。



图 10 人体草酸钙结石样本碎石

5 讨论

肾盂内激光碎石避免了穿刺损伤,但因输尿管细长而灌注液流量小,激光热量不易带走而容易引起肾盂烫伤,同时因输尿管及肾盂区域狭窄而容易损伤周围组织,因此,如何提高单位能量碎石效率,减小热冗余,如何避免或减小激光对周围组织的损伤变得尤为重要。通过实验可以得出,对于峰值功率 600 W 的 TFL 具有较强的碎石能力,在脉冲小于 1 ms(能量 0.6 J)时,随着脉宽变大,单位能量碎石效率快速提高,因此铥激光碎石脉冲能量不宜太小。但对于峰值功率不是很高的 TFL,提高脉冲能量要加大脉宽,此长脉宽激光脉冲与水作用会产生多次坍缩的微爆过程,使铥激光脉冲在水中具有大的穿透深度(实验中达到 5.4 mm),且穿透能力具有一定随机性,这在肾结石激光手术中容易损伤周围组织,因为部分损伤手术中并不容易直接观察到,最新研究 TFL 术后输尿管狭窄的较高发生率[10-11]应该与此相关。因峰值功率不高,通过双脉冲控制的 TFL 产生的“摩西效应”不明显。通过实验分析,TFL 具有较好的碎石潜力,但目前仍存在不足,随着峰值功率进一步提高,可实现良好的碎石应用。

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RESEARCH

Evaluating safe irrigation rates for Tm fiber laser lithotripsy to prevent thermal injury: an in vitro and numerical simulation

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Abstract

Purpose To evaluate temperature changes and thermal injury during thulium fiber laser (TFL) lithotripsy in the urinary tract and identify the safe irrigation rate, providing a reference for optimal parameter settings in clinical practice.

Methods An in vitro thermal injury experiment was conducted using a home-made TFL operating at 40 W. The experiment utilized a glass tube simulating the urinary tract. A peristaltic pump circulated 25 °C saline at irrigation rates ranging from 10 to 40 mL/min. Real-time temperature measurements were recorded using thermocouples, and thermal injury was assessed by calculating the thermal dose threshold. Additionally, a validated numerical simulation model was developed to analyze temperature distributions and predict safe irrigation rates at 20 and 30 W.

Results In the in vitro experiment, at 40 W, severe thermal injury occurred in the urinary tract when the irrigation rate was below 30 mL/min, particularly in the ureter and renal calyx. The numerical simulation model demonstrated a high degree of consistency with the experimental results. According to the simulation, at 30 W, thermal injury occurred in the renal calyx when the irrigation rate was below 20 mL/min. At 20 W, thermal injury was observed in the renal calyx when the irrigation rate was below 10 mL/min.

Conclusions The increase in temperature and the extent of thermal injury were strongly dependent on laser power and irrigation rate, with a lesser dependence on anatomical location. The accuracy of the numerical simulation was validated through experiments, demonstrating its capability to reliably predict temperature variations and thermal injury under different laser power settings and irrigation rates.

Keywords Thermal injury · Tm fiber laser lithotripsy · Numerical simulation · Irrigation rate · Urinary tract

Introduction

Laser lithotripsy (LL) has become one of the mainstream methods for treating urinary calculi [1]. Compared to traditional lithotripsy techniques, such as shockwave lithotripsy and pneumatic ballistic lithotripsy, LL combined with flexible ureteroscopy offers advantages in efficiency, precision, and versatility. However, the laser-induced photothermal effects [2] can potentially cause thermal injury to urinary tissues, leading to complications such as ureteral stricture [3] and thermal injury of the renal pelvis and calyx [4], which in turn may result in impaired renal function [5].

Ho: YAG LL has long been considered the gold standard for retrograde ureteroscopy procedures. In Ho: YAG LL, factors such as laser parameters, irrigation rate, and location within the urinary tract significantly affect fluid temperature and the extent of thermal injury [6, 7]. Recently, thulium fiber laser (TFL) lithotripsy has emerged as a strong alternative to Ho: YAG LL [8–10]. TFL has a water absorption coefficient four times higher than the Ho: YAG laser. It also features broader parameter ranges, including higher pulse repetition frequencies (up to 2400 Hz), wider pulse energies

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(0.025–6 J), a flatter pulse waveform, and a peak power of 500 W [11]. These characteristics give TFL distinct advantages, such as faster stone ablation, finer stone dust, reduced retropulsion, and greater procedural flexibility, making it highly effective for lithotripsy [12]. Due to differences in the parameters of the two lasers, several studies have compared the thermal effects of TFL and Ho: YAG LL, with conflicting conclusions. Some studies have reported that TFL results in faster temperature rise and more pronounced thermal effects [13–15], while others have shown that the temperature profiles of TFL and Ho: YAG lasers are similar [16–18]. Consequently, it is essential to evaluate the safety parameters of TFL independently, as applying Ho: YAG laser parameters and irrigation rates directly may pose significant safety risks. Additionally, the use of high-power LL can result in higher stone ablation efficiency [19–21], but it also increases the risk of thermal injury [22]. Therefore, greater attention should be given to the thermal injury associated with high-power LL.

This study investigates temperature variations and thermal injury risks during thulium fiber laser (TFL) lithotripsy in the urinary tract, aiming to identify safe irrigation rates to mitigate these risks. A custom-designed glass tube model, which simulates the size and shape of the ureter, renal calyx, and renal pelvis, was used to provide a more accurate in vitro representation of the urinary tract. Advanced numerical simulation techniques were employed to model the temperature distribution and predict safe irrigation rates. Our findings provide a reliable method for assessing the thermal safety of TFL lithotripsy and propose an optimal irrigation rate to enhance the safety of LL procedures.

Materials and methods

Experimental setup

A testing apparatus was constructed to evaluate the extent of thermal injury during LL. This setup was designed to simulate the thermal effects induced by TFL lithotripsy at various locations within the urinary tract. A custom glass tube was used to replicate the anatomical structure of the urinary tract, with its upper, middle, and lower sections mimicking the shape and dimensions of the ureter, renal pelvis, and renal calyx, respectively (Fig. 1a). The tube, filled with physiological saline, was submerged in a water bath maintained at 37 °C. A homemade quasi-continuous-wave TFL (Table S1) was used in this study to deliver laser energy through an delivery fiber (diameter of 272 μm) positioned within the tube (Fig. 1b). Concurrently, a peristaltic pump delivered 25 °C saline from a reservoir through a syringe needle to the fiber tip for irrigation. The upper end of the glass tube was sealed with a rubber stopper, through which a long needle (irrigation inlet) extended into the test section of the glass tube. The delivery fiber was threaded through the needle to reach the test area. Additionally, a short needle (irrigation outlet) passed through the rubber stopper and was positioned at the upper end of the glass tube (Fig. S1). This setup simulates the irrigation system comprising a ureteral access sheath and a flexible ureteroscope. A K-type thermocouple, temperature sensing module, and data acquisition system were connected sequentially, with temperature recorded at a sampling rate of 1 Hz. The thermocouple was positioned flush with the fiber tip on the inner wall of the tube, allowing for accurate temperature measurements near the tube wall, which were then transmitted to a computer for storage.

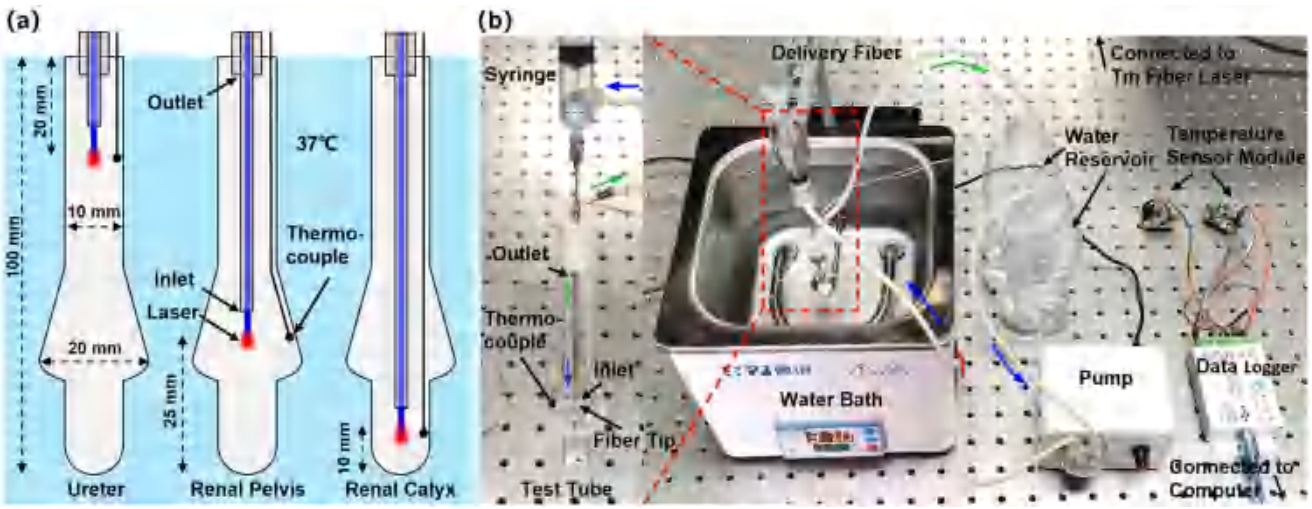


Fig. 1 Experimental setup: **a** Schematic of the glass tube simulating different regions of the urinary tract, **b** Laser thermal effect testing system, where the blue and green arrows represent the directions of inflow and outflow, respectively

Laser-induced thermal injury experiments were conducted at the upper (ureter), middle (renal pelvis), and lower (renal calyx) sections of the tube. The laser operated at an average power of 40 W (2 J × 20 Hz), with irrigation rates set at 10, 20, 30, and 40 mL/min. Once the temperature within the tube stabilized at 37 °C, the micro-pump was activated to initiate irrigation, and temperature data collection began. After 20 s, the laser was activated and operated continuously for 60 s. Following laser deactivation, irrigation and temperature recording continued for an additional 40 s.

Numerical simulation model

Numerical simulations were employed to calculate the temperature and flow fields during LL, enabling a better understanding of the mechanisms underlying laser-induced thermal injury and aiding in the prediction of optimal LL parameters. To ensure simulation accuracy and improve computational efficiency, an axisymmetric model was developed based on the experimental setup. The fiber tip was positioned at three specific locations within the simulated urinary tract regions: 20 mm from the top of the tube (ureter), 25 mm from the bottom (renal pelvis), and 10 mm from the bottom (renal calyx). Temperature probes were placed on the tube wall at each location to calculate inner wall temperatures. To provide a clearer description of the numerical simulation process, the supplementary materials include the thermal properties (Table S2) of the materials used in the simulation, the boundary conditions (Table S3 and Fig. S2), and the governing equations (Equations S1–S4). Additionally, simulations were conducted to analyze the temperature distribution and thermal injury in the renal calyx under 30 W and 20 W laser power settings.

Thermal dose

Thermal injury to biological tissue depends on both temperature elevation and exposure duration, and thermal dose is commonly used to quantify the extent of thermal injury in tissues. A standard method for calculating thermal dose involves converting the time-temperature profile into an equivalent exposure time at 43 °C, according to the following Eqs. [23],

$$TD_{43} = \int_0^{t_{end}} R^{43-T(t)} dt \tag{1}$$

where

$$R = \begin{cases} 0, & T \le 37°C \\ 0.25, & 37 < T < 43°C \\ 0.5, & T \ge 43°C \end{cases} \tag{2}$$

In Eqs. (1–2), T represents temperature, t is time, and R is a coefficient that varies with temperature. The thermal dose at 43 °C, denoted as TD_{43}, is expressed in minutes. Any temperature above 43 °C causes an exponential increase in the thermal dose. The time threshold for tissue injury is typically set at $TD_{43} = 120$ min. When TD_{43} exceeds 240 min, the tissue is considered to be denatured [24].

Results

In vitro experiments on thermal injury

At a laser power of 40 W, temperature variations were measured at three distinct urinary tract locations under different irrigation rates. Figure 2a-c presents the time-dependent inner wall temperature profiles for three distinct urinary tract regions. For each location, the maximum temperature (T-Max) decreased as the irrigation rate increased. The T-Max data for each urinary tract location are presented in Table 1. Under the low irrigation rate of 10 mL/min, the highest T-Max was observed in the renal calyx (60.2 °C), followed by the ureter (58.8 °C) and the renal pelvis (45.2 °C). At moderate irrigation rates of 20 and 30 mL/min, T-Max was highest in the ureter (51.2 and 45.2 °C), followed by the renal pelvis (49.4 and 43.8 °C) and renal calyx (48.6 and 44.5 °C). Under high irrigation rate of 40 mL/min, the T-Max values at the three sites were relatively similar, ranging from lowest to highest as follows: ureter (38.9 °C), renal pelvis (39.4 °C), and renal calyx (39.5 °C). As the irrigation rate increased, T-Max values for the three locations converged. Notably, at the high irrigation rate of 40 mL/min, T-Max for all locations remained below 43 °C, whereas at low and moderate irrigation rates, T-Max exceeded 43 °C in all locations.

The temperature curves were converted into thermal dose curves using Eq. 1 to evaluate the extent of thermal injury in urinary tract tissues. Figure 2d-f presents the time-dependent thermal dose curves. The laser is activated at 20 s, and the thermal dose increases rapidly over time. After the laser action ends at 80 s, the thermal dose reaches its maximum and remains constant. For a given location, higher irrigation rates delayed the time required to reach $TD_{43} = 120$ min. At low irrigation rates, the thermal doses at all three locations greatly exceeded the 120-minute and even 240-minute thresholds, indicating severe thermal injury in all regions. The risk of thermal injury was higher in the ureter and renal calyx compared to the renal pelvis. At an irrigation rate of 10 mL/min, the thermal doses for the renal pelvis, ureter, and renal calyx were 7.12×10^5, 3.60×10^4, and 2.03×10^6 min, respectively. At an irrigation rate of 20 mL/min, the thermal doses at the three locations were 7.20×10^3,

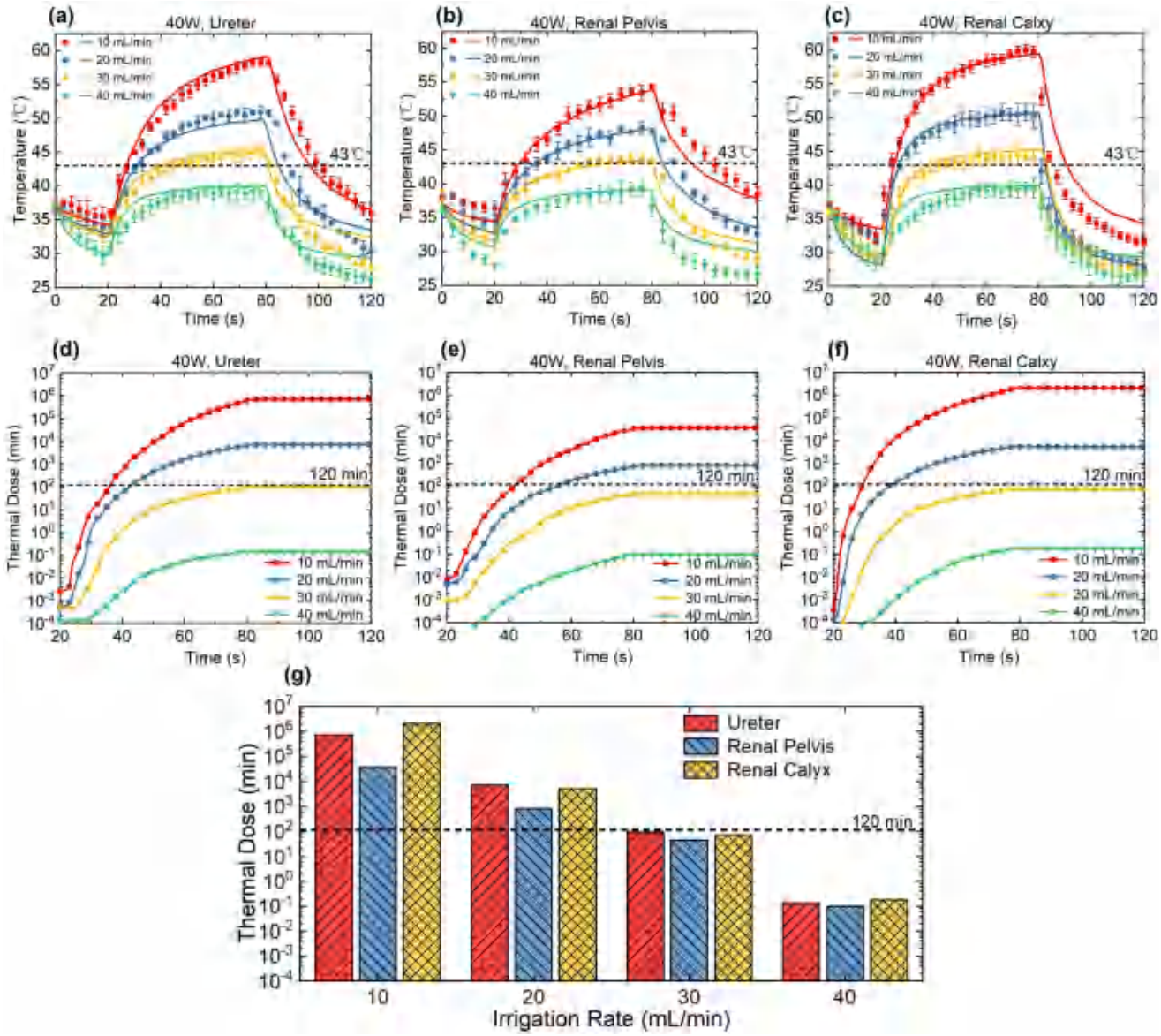


Fig. 2 Temperature and thermal dose at 40 W laser power, **a-c** measured temperatures (dots) and simulated temperatures (lines), **d-e** thermal dose calculated based on the temperatures, **g** total thermal dose after 120 s

Table 1 Maximum temperatures at different locations in the urinary tract

Urinary tract	T-Max (°C)			
	Irrigation rate (mL/min)			
	10	20	30	40
Ureter	58.8	51.2	45.2	38.9
Renal Pelvis	54.3	48.6	44.5	39.4
Renal Calyx	60.2	49.4	43.8	39.5

8.19×10^2, and 5.22×10^3 min, respectively. When the irrigation rate increased to 30 mL/min, the thermal doses at the ureter, renal calyx, and renal pelvis decreased significantly to 99.13, 46.07 and 73.59 min, respectively. These values were below the injury threshold, and no thermal injury was observed at any location. At the highest irrigation rate of 40 mL/min, the thermal dose at all locations was two orders of magnitude lower than the injury threshold, ensuring safe conditions across all regions.

Simulation of thermal injury

The numerical simulation model was employed to calculate temperature profiles and temperature field distributions at a laser power of 40 W. As shown in Fig. 2(a)-(c), the simulated data (lines) closely matched the experimental data (dots) across three urinary tract locations and four irrigation rates, demonstrating the model's high accuracy. Due to the smaller volume of the renal calyx, which makes it

more susceptible to thermal injury, the numerical simulation model was further used to analyze thermal injury in the renal pelvis at lower laser power settings (20 and 30 W) and to predict safe irrigation rates, as shown in Fig. 3. At a power of 30 W, the maximum temperatures at irrigation rates of 10, 20 and 30 mL/min were 47.4, 43.3 and 39.6 °C, respectively. Severe thermal injury occurred only at 10 mL/min, where the thermal dose reached 624.94 min, exceeding the injury threshold. At a power of 20 W, the maximum temperature at all irrigation rates remained below 43 °C, and no thermal injury was observed.

Figure 4 (a)-(c) show the temperature field distribution in different urinary tract regions at 79 s under high power 40 W. At a high irrigation rate of 40 mL/min, no significant heat accumulation was observed in any of the regions. In the ureter, the area affected by laser-induced heating displayed a spindle-like shape. At irrigation rates of 10 and 20 mL/min, substantial heat accumulation occurred, with a large high-temperature zone concentrated below the irrigation outlet in the ureter. At 30 mL/min, a slight degree of heat accumulation was observed. The laser-induced thermal effect zone in the renal pelvis forms an inverted triangle, with thermal accumulation mainly concentrated in the lower part of the renal pelvis and the upper part of the renal calyx. In contrast, the thermal effect in the renal calyx forms a triangle, with the highest temperature zone primarily located in the lower part of the renal calyx. Compared to the other sites, thermal accumulation in the renal pelvis was relatively lower. Furthermore, Fig. 4(d) and (e) present the temperature distributions in the renal calyx under 30 and 20 W laser power, respectively. Compared to 40 W, the thermal effect significantly weakened with reduced power. Notably, at 30 W power and an irrigation rate of 10 mL/min, distinct thermal accumulation was observed at the bottom of the renal calyx. However, at 20 W power, no significant thermal accumulation was observed within the renal calyx, consistent with the temperature trends shown in Fig. 3.

Discussion

As the use of high-power lasers increases, the risk of laser-induced thermal injury to the urinary system also rises [25, 26]. Understanding and controlling temperature elevations caused by laser application have become increasingly important for ensuring the safety of LL. An appropriate irrigation rate can effectively reduce the risk of thermal injury to tissues. However, laser-induced thermal injury varies across different regions of the urinary tract. Therefore, urologists must balance laser parameters, irrigation rate, and temperature control based on the specific region of the urinary tract being treated.

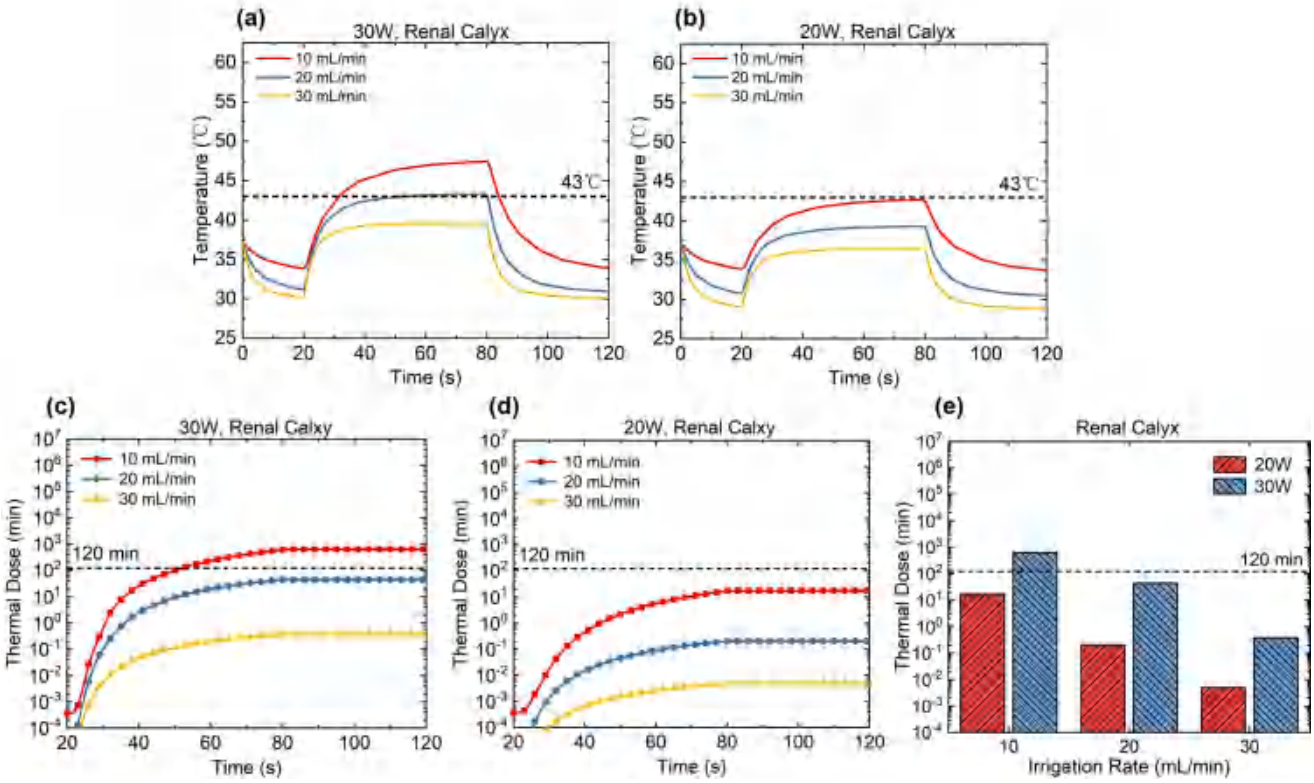


Fig. 3 Temperature profiles and thermal dose in the renal calyx obtained through simulation. **a-b** temperature profiles, **c-d** thermal dose, **e** total thermal dose after 120 s

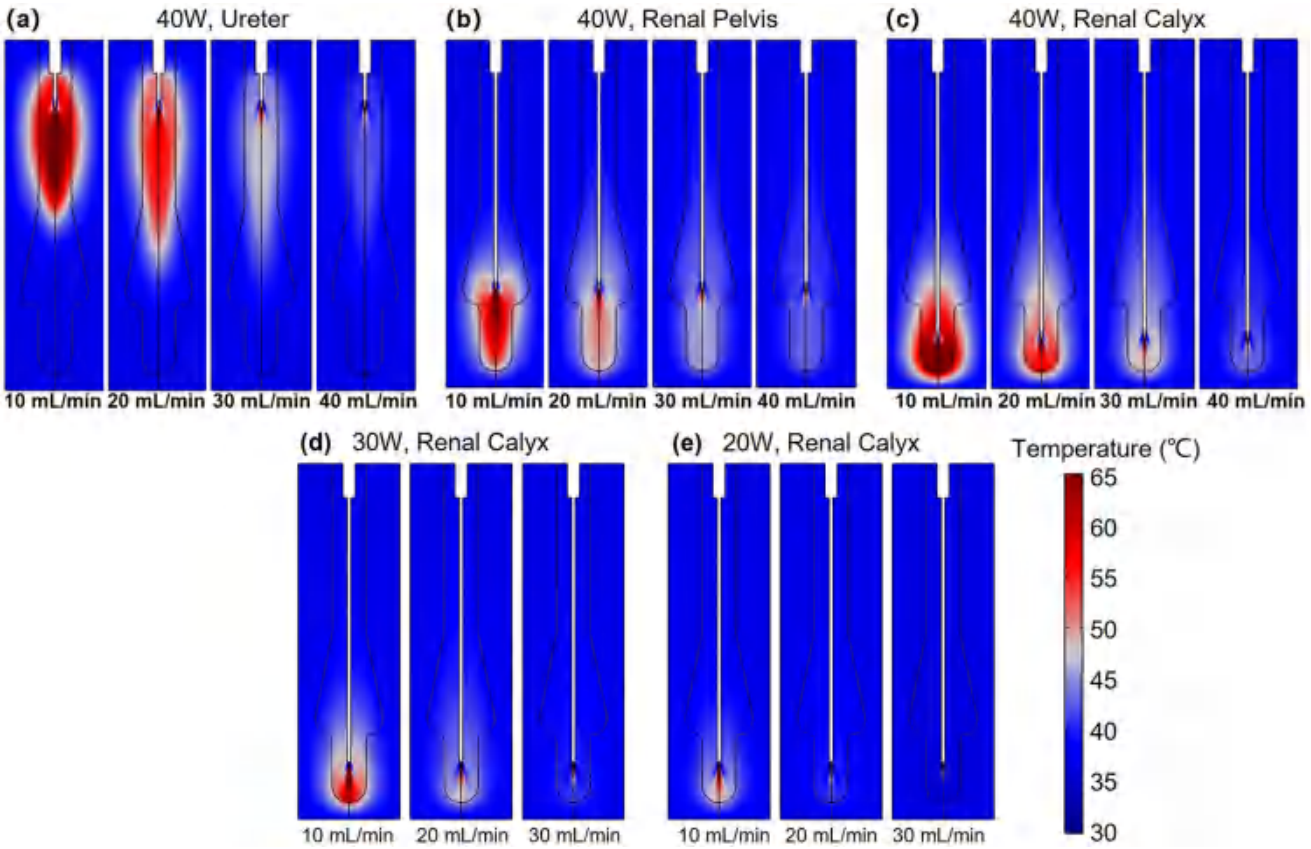


Fig. 4 Temperature field distribution from simulation, **a-c** 40 W in different urinary tract regions, **d** 30 W in the renal calyx, **e** 20 W in the renal calyx

Thermal injury in different regions of the urinary tract is closely related to their volume and shape. Under low irrigation rates, there is some space below the laser heating zone in the ureter and renal pelvis, which facilitates heat dissipation and results in relatively lower inner wall temperatures. The funnel-shaped structure of the renal pelvis further aids in the effective dispersion of heat within its cavity. In contrast, thermal injury is most pronounced in the renal calyx. Due to the narrow and enclosed structure of the calyx, heat generated in the laser heating area tends to accumulate, potentially causing thermal injury to the renal papilla. Therefore, increasing irrigation rates or adopting intermittent laser activation [14, 27], particularly in narrow spaces with limited heat diffusion, such as obstructed ureters or narrow renal calyces, is essential for safely reducing temperature thresholds during lithotripsy. Increasing the irrigation rate can effectively reduce the temperature and minimize the risk of thermal injury in the stone treatment area. This effect is attributed to the increased convective heat transfer coefficients at higher irrigation rates, which enhance cooling efficiency [28]. However, excessively high irrigation rates may lead to elevated intrarenal pressure, potentially causing pyelovenous backflow [29] or stone retropulsion. Therefore, to prevent thermal injury while minimizing the risk of elevated intrarenal pressure, a lower irrigation rate should be selected as the safe flow rate. Based on the in vitro experimental results, the safe irrigation rate for 40 W power was identified as 30 mL/min. According to the numerical simulation results, the safe irrigation rates for the renal calyx at 30 and 20 W were 20 and 10 mL/min, respectively. Since the renal calyx is the smallest of the three anatomical regions, its safe irrigation rate can also be considered a conservative reference for other urinary tract locations.

This study has several limitations. The experimental setup and simulation model represent a simplified version of the actual urinary tract structure, which cannot fully replicate its complex anatomical features. A three-dimensional simulation model based on CT data could provide greater precision and reliability in predicting thermal injury. Additionally, the rigidity of the glass material used in this study differs from the elasticity of the actual urinary system, so future research will focus on expanding TFL thermal injury experiments using silicone-based models or ex vivo porcine urinary tract models to better simulate real-life conditions. These advancements will provide a stronger scientific basis

for optimizing clinical LL techniques and enhancing safety assessments.

Conclusions

This study investigated the impact of irrigation rates on thermal injury in different regions during TFL lithotripsy. The results indicate that the increase in temperature and the extent of thermal injury were strongly dependent on laser power and irrigation rate, with a lesser dependence on anatomical location. The accuracy of the numerical simulation was validated through experiments, demonstrating its capability to reliably predict temperature variations and thermal injury under different laser power settings and irrigation rates. This study provides an effective method for assessing the risk of thermal injury during TFL lithotripsy and identifies a safe irrigation rate, offering valuable insights for enhancing the safety of LL procedures.

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Author contributions R.Z.: data analysis, data collection or management, and manuscript writing/editing; D.W.: supervision, project development and manuscript editing; C.W.: data collection, manuscript editing; Y.L.: data collection and analysis; X.M.: data collection and analysis; Z.L.: data analysis; S.L.: project development; C.L.: supervision, project development; X.W.: project development. All authors reviewed the manuscript.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval No ethical approval as the study does not involve any human or animal participants.

Competing interests The authors declare no competing interests.

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研究

评估Tm光纤激光碎石术的安全灌注率以防止热损伤：体外和数值模拟

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摘要

目的：评估铥光纤激光（TFL）碎石术中尿路温度变化及热损伤情况，确定安全冲洗速率，为临床实践中的最佳参数设置提供参考。

方法使用自制的40瓦TFL进行体外热损伤实验。实验采用模拟尿路的玻璃管，无蠕动泵以10至40 mL/min的冲洗速率循环25°C的生理盐水。通过热电偶记录实时温度测量值，并通过计算热剂量阈值评估热损伤。此外，还开发了一个经过验证的数值模拟模型，用于分析温度分布并预测20瓦和30瓦下的安全冲洗速率。

结果在体外实验中，当功率为40瓦时，若冲洗速率低于30毫升/分钟，尿路会发生严重热损伤，尤其在输尿管和肾盏中。数值模拟模型与实验结果高度一致。根据模拟结果，在30瓦功率下，当冲洗速率低于20毫升/分钟时，肾盏会发生热损伤。在20瓦功率下，当冲洗速率低于10毫升/分钟时，肾盏中可观察到热损伤。

结论温度升高和热损伤程度与激光功率和冲洗速率密切相关，与解剖位置的依赖性较弱。数值模拟的准确性通过实验得到验证，证明其能够可靠地预测不同激光功率设置和冲洗速率下的温度变化和热损伤。

关键词热损伤·Tm光纤激光碎石术·数值模拟·冲洗率·尿路

介绍

激光碎石术（LL）已成为治疗尿路结石的主流方法之一[1]。与传统的碎石术技术相比，如冲击波碎石术而气压弹道碎石术与LL联合应用的柔性输尿管镜技术，在效率、精准度和适用性方面具有显著优势。但激光诱导的光热效应[2]可能对尿路组织造成热损伤，引发输尿管狭窄[3]、肾盂及肾盏热损伤[4]等并发症，进而可能导致肾功能受损[5]。

Ho：YAGLL技术长期以来被视为逆行输尿管镜手术的金标准。在Ho：YAGLL过程中，激光参数、冲洗速率及尿路内定位等因素会显著影响液体温度和热损伤程度[6，7]。近年来，铥光纤激光（TFL）碎石术已崭露头角，成为Ho：YAGLL的有力替代方案[8–10]。TFL的水吸收系数是Ho：YAG激光的四倍，其参数范围也更为宽泛，包括最高可达2400赫兹的脉冲重复频率和更宽的脉冲能量范围。

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（0.025–6焦耳）、更平缓的脉冲波形以及500瓦的峰值功率[11]。这些特性赋予TFL独特优势，例如更快的碎石速度、更细腻的碎石粉尘、更低的后向冲击力以及更高的操作灵活性，使其成为碎石术中的高效选择[12]。由于两种激光器参数存在差异，多项研究对比了TFL与Ho：YAG激光的热效应，但结论存在分歧。部分研究指出TFL会导致更快的温度升高和更显著的热效应[13–15]，而另一些研究则表明TFL和Ho：YAG激光的温度分布曲线相似[16–18]。因此，必须独立评估TFL的安全参数，因为直接套用Ho：YAG激光的参数和冲洗速率可能带来重大安全隐患。此外，使用高功率LL确实能提高碎石效率[19–21]，但同时也增加了热损伤风险[22]。因此，应更加重视高功率LL引发的热损伤问题。

本研究通过分析铥光纤激光（TFL）碎石术中温度波动与热损伤风险，旨在确定安全冲洗速率以降低相关风险。我们采用特制玻璃管模型模拟输尿管、肾盏及肾盂的尺寸与形态，从而在体外更精准地还原泌尿道结构。运用先进的数值模拟技术对温度分布进行建模，预测安全冲洗速率。研究结果为评估TFL碎石术的热安全性提供了可靠方法，并提出最佳冲洗速率方案以提升腔镜手术的安全性。

材料和方法

实验设置

为评估激光碎石术（LL）过程中热损伤的程度，我们研制了一套测试装置。该装置旨在模拟TFL碎石术在泌尿道不同部位引发的热效应。实验采用特制玻璃管模拟泌尿道解剖结构，其上、中、下三段分别对应输尿管、肾盂和肾盏的形态与尺寸（图1 a）。玻璃管内注入生理盐水后，置于37℃恒温水浴中。本研究使用自制的准连续波TFL系统（表S1），通过管内直径272μm的光纤传输激光能量（图1 b）。同时，蠕动泵将储液罐中的25℃生理盐水通过注射器针头输送至光纤尖端进行冲洗。玻璃管顶端用橡胶塞密封，一根长针（冲洗入口）穿过橡胶塞延伸至测试段。光纤通过针头穿线，直达测试区域。此外，一根短针（用于冲洗出口）穿过橡胶塞并定位在玻璃管的上端（图S1）。该装置模拟了包含输尿管套管和柔性输尿管镜的冲洗系统。K型热电偶、温度传感模块和数据采集系统依次连接，以1赫兹的采样率记录温度。热电偶与光纤尖端齐平地安装在管壁内侧，确保在管壁附近进行精确的温度测量，随后将数据传输至计算机进行存储。

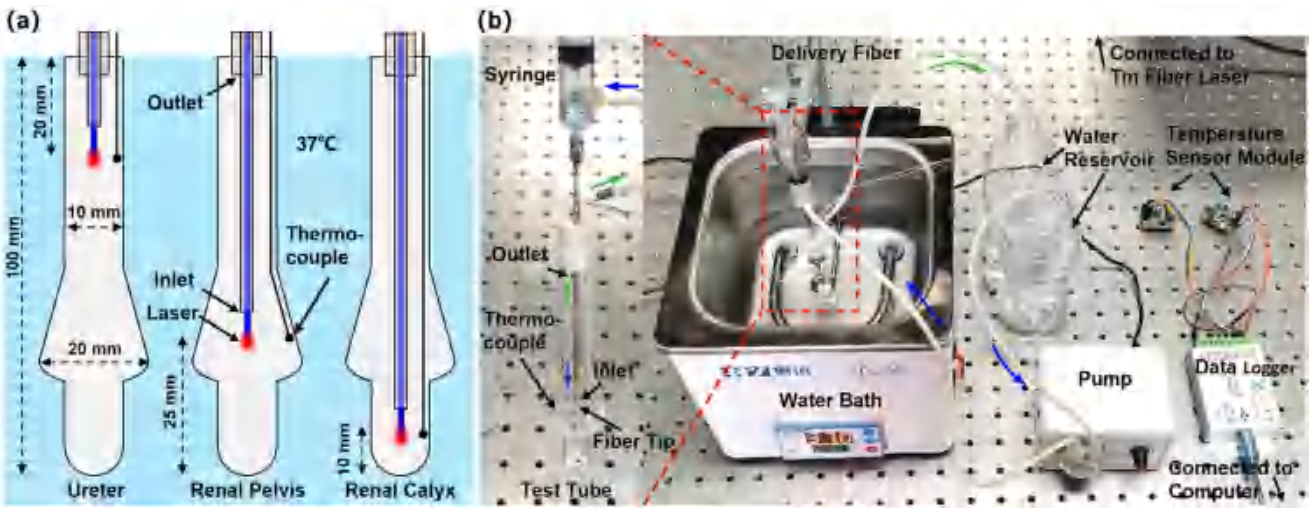


图1实验装置：**a**模拟不同尿路区域的玻璃管示意图，**b**激光热效应测试系统，其中蓝色和绿色箭头分别代表流入和流出方向

激光诱导热损伤实验在导管的上段（输尿管）、中段（肾盂）和下段（肾盏）进行。激光以平均功率40 W（2 J×20 Hz）运行，灌注速率设置为10、20、30和40 mL/min。当导管内的温度稳定在37°C时，激活微泵以启动灌注，并开始收集温度数据。20秒后，激光被激活并连续运行60秒。激光关闭后，灌注和温度记录继续进行40秒。

数值模拟模型

为精确计算激光乳化术（LL）过程中的温度场与流场分布，我们采用数值模拟技术，从而深入解析激光热损伤的形成机制，并为确定最佳LL参数提供理论依据。为确保模拟精度与计算效率，我们基于实验装置构建了轴对称模型。模拟尿路区域内的光纤尖端分别设置在三个关键位置：输尿管管口上方20毫米处、肾盂底部25毫米处及肾盏底部10毫米处。通过在管壁各点安装温度探头，实时监测管壁内部温度。为便于理解数值模拟流程，补充材料中详细列出了模拟材料的热学参数（表S2）、边界条件（表S3及图S2）以及控制方程（方程S1-S4）。此外，我们还针对肾盏区域开展了温度分布与热损伤分析，分别测试了30瓦与20瓦两种激光功率下的热效应。

热剂量

生物组织的热损伤程度取决于温度升高幅度和暴露时间，常用热剂量来量化组织损伤程度。标准计算方法是将时间-温度曲线转换为43°C等效暴露时间，具体计算公式如下：23],

$$TD_{43} = \int_0^{t_{end}} R^{43-T(t)} dt \tag{1}$$

在哪里

$$R = \begin{cases} 0, & T \le 37°C \\ 0.25, & 37 < T < 43°C \\ 0.5, & T \ge 43°C \end{cases} \tag{2}$$

在公式（1–2）中，T表示温度，t为时间，R是随温度变化的系数。43°C时的热剂量（记作TD_{43}）以分钟为单位。当温度超过43°C时，热剂量会呈指数级增长。组织损伤的时间阈值通常设定为TD_{43}=120分钟。当TD_{43}超过240分钟时，组织即被视为发生变性[24]。

结果

热损伤的体外实验

在40 W的激光功率下，测量了不同冲洗速率下三个不同尿路位置的温度变化。图2 a-c展示了三个不同尿路区域随时间变化的内壁温度分布。对于每个位置，最大温度（T-Max）随着冲洗速率的增加而降低。每个尿路位置的T-Max数据见表1。在10 mL/min的低冲洗速率下，肾盏的T-Max最高（60.2°C），其次是输尿管（58.8°C）和肾盂（45.2°C）。在20和30 mL/min的中等冲洗速率下，输尿管的T-Max最高（分别为51.2°C和45.2°C），其次是肾盂（分别为49.4°C和43.8°C）和肾盏（分别为48.6°C和44.5°C）。在40 mL/min的高冲洗速率下，三个部位的T-Max值相对接近，从低到高依次为：输尿管（38.9°C）、肾盂（39.4°C）和肾盏（39.5 °C）。随着冲洗速率的增加，三个位置的T-Max值趋于一致。值得注意的是，在40毫升/分钟的高灌溉速率下，所有位置的T-Max均保持在43°C以下；而当灌溉速率较低或中等时，所有位置的T-Max均超过43°C。

温度曲线通过公式1转换为热剂量曲线，以评估尿路组织的热损伤程度。图2 d-f展示了随时间变化的热剂量曲线。激光在20秒时激活，热剂量随时间迅速增加。激光作用在80秒结束时，热剂量达到最大值并保持恒定。对于给定位置，较高的冲洗速率会延迟达到TD_{43}=120分钟所需的时间。在低冲洗速率下，三个位置的热剂量均显著超过120分钟甚至240分钟阈值，表明所有区域均出现严重热损伤。与肾盂相比，输尿管和肾盏的热损伤风险更高。在10 mL/min的冲洗速率下，肾盂、输尿管和肾盏的热剂量分别为7.12×10^{5}、3.60×10^{4}和2.03×10^{6}分钟。在20 mL/min的冲洗速率下，三个位置的热剂量为7.20×10^{3}、

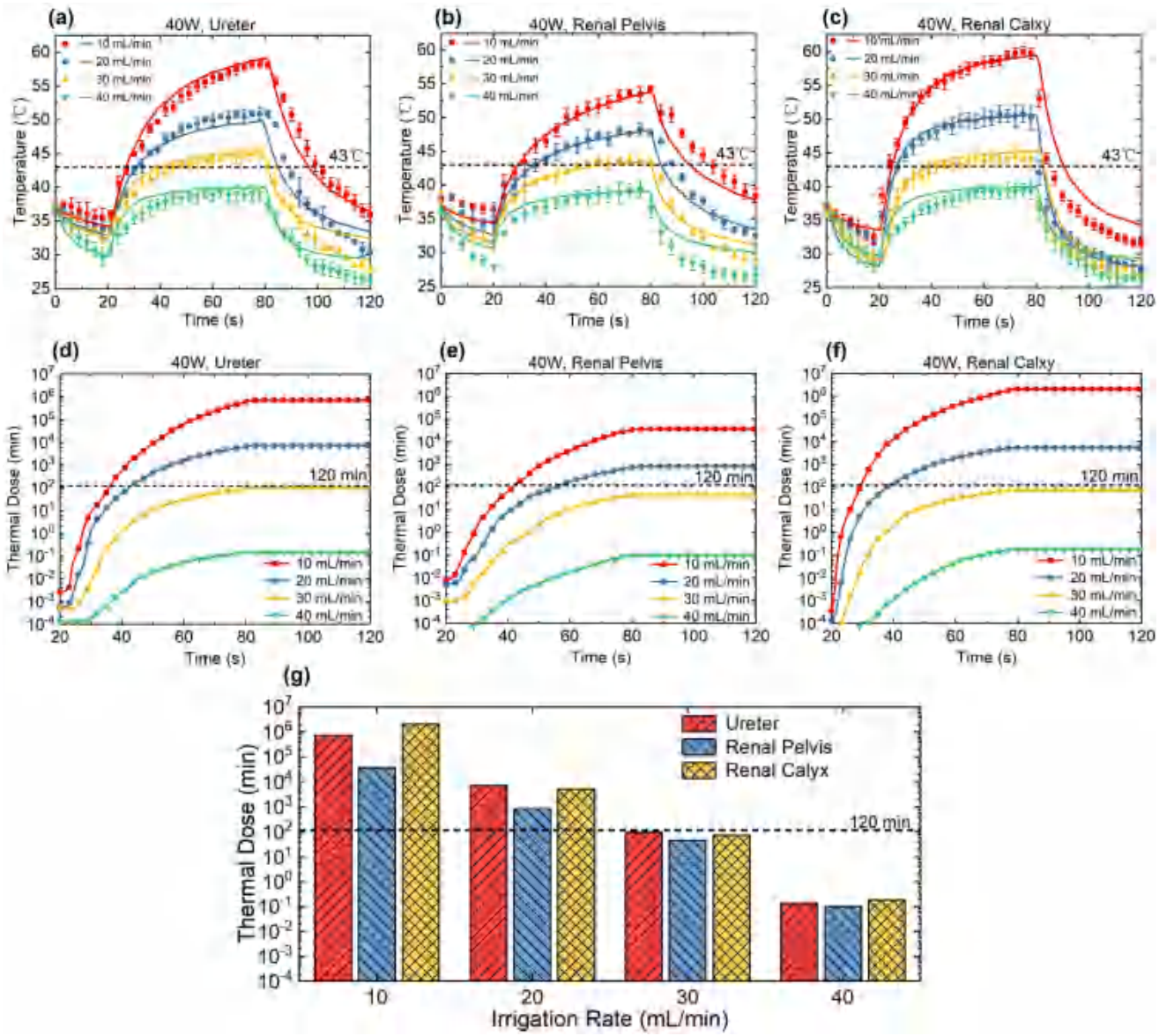


图2 40W激光功率下的温度和热剂量，**a-c**测量温度（点）和模拟温度（线），**d-e**根据温度计算的热剂量，**g** 120s后的总热剂量

表1尿液不同部位的最高温度

大片土地

尿路	T-Max（℃）			
	灌注率（mL/min）			
	10	20	30	40
输尿管	58.8	51.2	45.2	38.9
肾盂	54.3	48.6	44.5	39.4
肾盏	60.2	49.4	43.8	39.5

8.19 当灌注速率增加到30 mL/min时，输尿管、肾盏和肾盂的热剂量分别显著降低至99.13、46.07和73.59分钟。这些数值均低于损伤阈值，且未出现热损伤。

在任何位置观测到的结果显示，在最高灌溉速率40 mL/min时，所有位置的热剂量比损伤阈值低两个数量级，确保了所有区域的安全条件。

热损伤模拟

本研究采用数值模拟模型，在40瓦激光功率条件下计算温度分布曲线及温度场分布。如图2(a)-(c)所示，模拟数据（曲线）与实验数据（散点）在三个尿路部位和四种冲洗速率下均高度吻合，充分验证了模型的高精度。由于肾盏体积较小，这使得

由于更易受到热损伤，数值模拟模型进一步用于分析较低激光功率设置（20和30 W）下肾盂的热损伤，并预测安全灌注速率，如图3所示。在30 W功率下，灌注速率分别为10、20和30 mL/min时的最大温度分别为47.4、43.3和39.6°C。仅在10 mL/min时发生严重热损伤，此时热剂量达到624.94 min，超过损伤阈值。在20 W功率下，所有灌注速率的最大温度均低于43°C，且未观察到热损伤。

图4(a)-(c)展示了在40 W高功率下79秒时不同尿路区域的温度场分布。在40 mL/min的高冲洗速率下，所有区域均未观察到显著的热量积聚。在输尿管中，激光诱导加热影响的区域呈现纺锤状。当冲洗速率降至10和20 mL/min时，出现明显的热量积聚，输尿管冲洗出口下方形成了一个大面积高温区。在30 mL/min时，观察到轻微的热量积聚。肾盂中的激光诱导热效应区呈倒三角形，热量积聚主要集中在肾盂下部和肾盏上部。相比之下，肾盏中的热效应呈三角形分布，最高温度区主要位于下部。

肾盏的一部分。与其他部位相比，肾盂中的热积累相对较低。此外，图4(d)和(e)分别展示了在30 W和20 W激光功率下肾盏内的温度分布。与40 W相比，功率降低时热效应显著减弱。值得注意的是，在30 W功率和10 mL/min的灌注速率下，肾盏底部观察到明显的热积累。然而，在20 W功率下，肾盏内未观察到显著的热积累，这与图3中所示的温度趋势一致。

讨论

随着高功率激光应用的日益普及，激光引发的泌尿系统热损伤风险也随之上升[25，26]。掌握并控制激光治疗导致的温度升高，已成为保障激光治疗安全的关键所在。适当控制冲洗速率能有效降低组织热损伤风险。但需注意，不同泌尿道区域对激光热损伤的敏感度存在差异。因此，泌尿科医生需根据具体治疗部位，灵活调整激光参数、冲洗速率及温度控制策略。

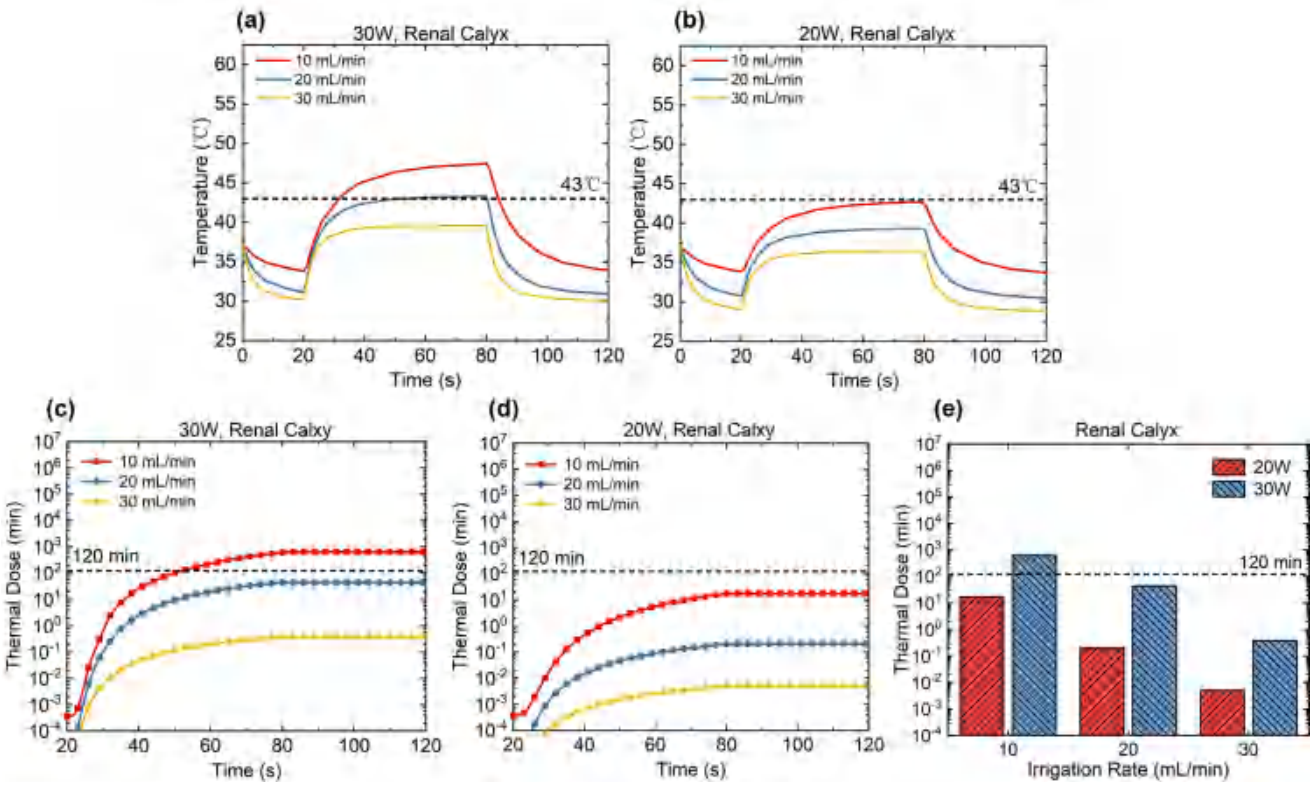


图3通过模拟获得的肾盏温度曲线和热剂量。**a-b**温度曲线，**c-d**热剂量，**e** 120秒后的总热剂量

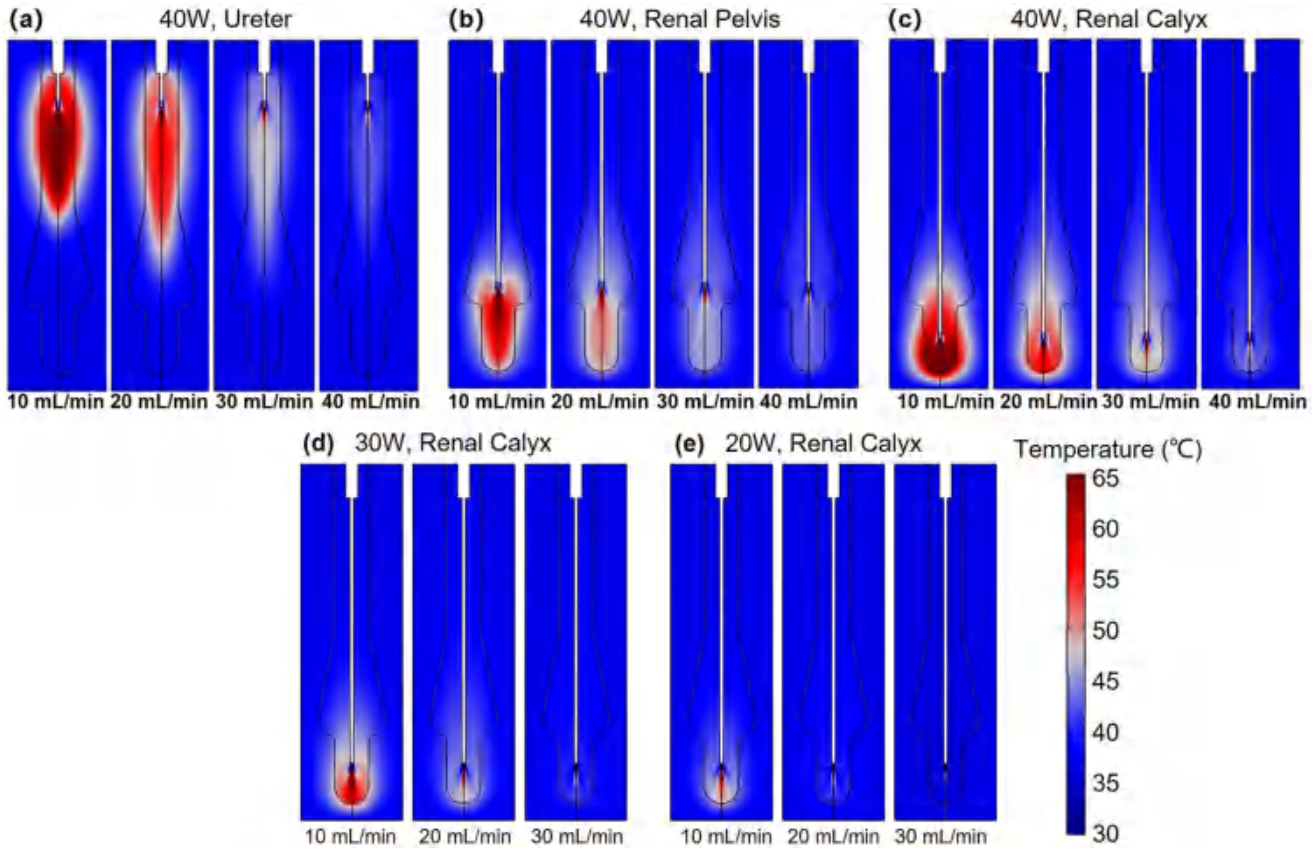


图4模拟温度场分布，**a-c**不同尿路区域40W，**d**肾盏30W，**e**肾盏20W

尿路不同部位的热损伤程度与其体积和形态密切相关。当冲洗速率较低时，输尿管和肾盂在激光加热区下方存在一定空间，这有利于热量散发，使内壁温度相对较低。肾盂漏斗状结构还能有效促进腔内热量扩散。相比之下，肾盏的热损伤最为显著。由于肾盏结构狭窄且封闭，激光加热区产生的热量容易积聚，可能对肾乳头造成热损伤。因此，在输尿管梗阻或肾盏狭窄等热扩散受限的狭窄空间进行碎石时，提高冲洗速率或采用间歇性激光激活[14，27]，对于安全降低温度阈值至关重要。增加冲洗速率能有效降低结石处理区域的温度，最大限度减少热损伤风险。这种效应归因于较高灌溉率时对流热传递系数的增加，从而提高了冷却效率[28]。然而，过高灌溉率可能导致肾内压力升高，从而可能引起肾盂静脉逆流[29]或结石后退。

因此，为了在最小化肾内压力升高的风险的同时防止热损伤，应选择较低的冲洗速率作为安全流速。根据体外实验结果，40瓦功率的安全冲洗速率被确定为30 mL/min。根据数值模拟结果，肾盏在30瓦和20瓦下的安全冲洗速率分别为20 mL/min和10 mL/min。由于肾盏是三个解剖区域中最小的，其安全冲洗速率也可作为其他尿路部位的保守参考。

本研究存在若干局限性。实验装置与模拟模型虽是对真实尿路结构的简化呈现，但无法完全复现其复杂的解剖特征。若采用基于CT数据的三维模拟模型，将能更精准可靠地预测热损伤。此外，本研究使用的玻璃材料刚性与真实尿路系统的弹性存在差异，因此未来研究将重点拓展TFL热损伤实验，通过硅胶基模型或离体猪尿路模型来更真实地模拟实际环境。这些改进将为相关研究奠定更坚实的科学基础。

用于优化临床LL技术并提升安全性评估。

结论

本研究探讨了TFL碎石术中不同灌注速率对热损伤的影响。研究结果表明，温度升高和热损伤程度主要取决于激光功率与灌注速率，而解剖位置的影响相对较小。通过实验验证了数值模拟的准确性，证明其能可靠预测不同激光功率设置和灌注速率下的温度变化及热损伤情况。本研究为评估TFL碎石术中的热损伤风险提供了有效方法，并确定了安全灌注速率，为提升LL手术安全性提供了重要参考依据。

补充信息在线版本包含补充材料，可在https://doi.org/10.1007/s00345-0 25-05614-4上找到。

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声明

伦理审批本研究不涉及人类或动物受试者，因此无需伦理审批。

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RESEARCH

High-power Ho:YAG lithotripsy increases subclinical renal stress: a prospective randomized KIM-1 study

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Abstract
This study aimed to compare the safety profile of high-power (HPL) and low-power (LPL) Holmium:YAG lasers in retrograde intrarenal surgery (RIRS), using urinary Kidney Injury Molecule-1 (KIM-1) as an early biomarker for acute kidney injury (AKI). Sixty patients with renal stones (1.5–2.5 cm) were prospectively randomized into HPL and LPL groups. Urinary KIM-1 and KIM-1/creatinine ratios were measured preoperatively and at 4 and 24 h postoperatively. Intraoperative parameters, stone-free rates (SFR), complications, and renal function (eGFR, serum creatinine) were also assessed. Intrarenal temperatures were recorded before and after lithotripsy. Operative time, SFR, complication rates, and renal function parameters were similar between groups ($p > 0.05$). However, KIM-1 levels were significantly higher in the HPL group at 24 h postoperatively (278.8 ± 239.6 pg/mL vs. 170.3 ± 172.9 pg/mL, $p = 0.003$), and the KIM-1/creatinine ratio was also elevated (5.5 ± 4.5 vs. 3.1 ± 2.0, $p = 0.035$). No significant differences were observed in postoperative serum creatinine or eGFR. Intraoperative renal temperatures increased slightly in the HPL group, but the difference was not statistically significant. While high-power laser lithotripsy does not adversely affect global renal function, it is associated with elevated levels of renal injury biomarkers, suggesting greater subclinical renal stress.

Keywords Kidney stone · Retrograde intrarenal surgery · High-power laser · Low-power laser · KIM-1 · Urinary KIM-1

Introduction

Urolithiasis is a major global health issue, affecting 10 to 15% of the population and representing a prevalent urological condition that contributes significantly to morbidity [1]. Nephrolithiasis, a specific form of urolithiasis, refers to the presence of stones in the kidneys and is associated with a multifactorial etiology that includes genetic factors, obesity, and dehydration [2]. Retrograde intrarenal surgery (RIRS), shockwave lithotripsy (SWL), and percutaneous nephrolithotomy (PCNL) are the primary treatment modalities for managing kidney stones [3].

Retrograde intrarenal surgery (RIRS) is a minimally invasive procedure that employs a flexible ureteroscope (fURS) along with laser energy, commonly utilizing a holmium laser, for the treatment of renal stones [4]. Flexible ureteroscopy and laser lithotripsy (FURSL) particularly effective for stones that are small to medium-sized (typically < 2 cm) or located in anatomically challenging areas [5]. Due to advancements in technology and training, FURSL is now frequently used for stones up to 2 cm, achieving high stone-free rates and lower complication rates than PCNL [6]. The holmium:YAG (Ho:YAG) laser is regarded as the gold standard for laser lithotripsy in flexible ureteroscopy, offering efficient treatment for various kidney stone compositions [7].

Ho:YAG lithotripsy, utilizing a Holmium laser that emits light at a wavelength of 2100 nm, is highly absorbed by water, which results in minimal thermal injury to adjacent renal and ureteral tissues [8]. Ho:YAG lasers are commonly classified into two categories: low-power (LPL) and high-power lasers (HPL) [9]. Lasers with a single cavity that

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produce up to 30 W of power are classified as LPL, while lasers with multiple cavities that produce over 30 W are categorized as HPL [10]. Previous similar studies have shown that the use of HPL significantly reduces operation time and hospitalization compared to LPL [11, 12]. Although, concerns have been raised regarding the short-term effects such as acute kidney injury (AKI) and long-term effects of high-power laser on the kidneys due to the high pressure and temperature generated [12].

Recently, new biomarkers for acute kidney injury (AKI) have been found. Key examples include NGAL, IL-18, KIM-1, and TIMP-2, which may help diagnose AKI early [13, 14]. Of the new biomarkers, urinary KIM-1 (KIM-1) stands out as a reliable indicator for detecting acute kidney injury (AKI). It has also been approved by the US Food and Drug Administration (FDA) for use in preclinical drug development [15]. KIM-1 is a specific marker of kidney tubule injury that is released into urine after acute kidney damage and is one of the first indicators of such injury. KIM-1 has been shown to be an effective biomarker for comparing the kidney damage caused by RIRS techniques [16].

In this study, we aimed to compare the safety of high-power and low-power laser lithotripsy using KIM-1, an early marker for acute kidney injury (AKI).

Materials and methods

This study was approved by the Ethics Committee of Necmettin Erbakan University Faculty of Medicine on July 7, 2023 (2023/4402). Written and verbally informed consent was obtained from all participants. The study was designed prospectively and funded by the Necmettin Erbakan University Scientific Research Projects Coordination Unit (Project No: 24TU18007).

Patient selection and study criteria

The study was conducted on patients aged 18–65 years who presented with kidney stones at the Urology Clinic of Necmettin Erbakan University Faculty of Medicine and underwent Retrograde Intrarenal Surgery (RIRS) between October 1, 2023, and May 1, 2024. A total of 60 patients were included, following strict inclusion and exclusion criteria to ensure a homogeneous patient group and enhance result reliability.

Eligible participants were healthy adults aged 18–75 years with CT-confirmed kidney stones (1.5–2.5 cm) and an eGFR of≥60. Exclusion criteria included pyuria, ureteral stones, positive urine culture, renal parenchymal thinning, recent surgery, kidney malformations, chronic kidney disease, solitary kidney, or nephrotoxic agent use. Patients who had undergone stone surgery in the past three months or were unable to undergo ureterorenoscopy due to ureteral strictures were also excluded.

Preoperative prophylaxis

All patients received antibiotic prophylaxis before surgery. A third-generation cephalosporin (ceftriaxone) was administered an hour preoperatively, while patients with allergies received an alternative antibiotic, such as ciprofloxacin or amikacin.

Urine sample collection and analysis

Urine samples were collected at three time points: preoperatively, 4 h postoperatively, and on the 24th hour postoperative. Samples were centrifuged at 3000 rpm for 10 min, separated into Eppendorf tubes, and stored at -80 °C until analysis. On the study day, the samples were thawed, and urinary KIM-1 levels (Elabscience Biotechnology Inc, USA) were measured. Urinary KIM-1/creatinine ratios were then calculated and compared across groups.

Devices and settings

A Redpine® RP-U-C12 Single-Use Video Flexible Ureteroscope (Guangzhou, China) was used for all procedures. For LPL used 272 µ fiber with Dornier® 30 W Laser (Germany) and for HPL used 272 µ fiber with Jenna Surgical® 150 W Laser (Germany). Laser technique chosen by block randomization.

Randomization method

Patients were randomized into High Power (HPL) or Low Power (LPL) groups using a block randomization method to ensure balanced group sizes. A total of 60 patients were assigned in blocks of four (15 blocks in total), with each block including 2 patients for HPL and 2 for LPL. The random sequence was computer-generated by an independent statistician and kept in sealed opaque envelopes, opened only at the time of enrollment. Both surgeons and patients were blinded to group assignment until allocation.

Intraoperative procedure and surgical technique

All procedures were performed by an experienced surgeon with a minimum of 60 RIRS cases. Surgeries were conducted under general anesthesia, with patients positioned in the dorsal lithotomy position. A sterile surgical field was

established, and all steps of the procedure followed strict aseptic protocols.

Intrarenal temperature measurement

Intrarenal temperature was measured at the beginning and end of lithotripsy using aspirated intrarenal fluid through the flexible ureterorenoscope channel.

Postoperative management

Patients were closely monitored for complications such as fever, hematuria, and urinary infections. Vital signs and hemodynamic stability were assessed regularly. On postoperative day 1, a plain abdominal X-ray was taken to evaluate residual stones and double-J stent positioning.

Outcome measures

The primary outcome measure was the stone-free rate, assessed by standard care imaging at three months post-procedure. Secondary outcome measures included intraoperative and postoperative complications, operative time, hospitalization time, postoperative fever, and DJ stent requirement. Operation time was defined as the total duration of the procedure in minutes. Postoperative fever incidence was recorded as a binary outcome (yes/no). Hospitalization time was inferred from perioperative management, although not explicitly stated in the data. The presence of residual stone and postoperative complications were evaluated and classified according to the Modified Clavien grading system.

In terms of biochemical markers, preoperative and postoperative serum creatinine, hemoglobin levels, and estimated glomerular filtration rate (eGFR) were measured and compared. Urinary Kidney Injury Molecule-1 (KIM-1) levels were recorded at baseline, 4th hour, and 24th hour postoperatively. Additionally, the ratio of KIM-1 to serum creatinine (KIM-1/Cr) was calculated at each of these time points to provide normalized values. Intraoperative thermal changes were evaluated by measuring intrarenal temperature before and after lithotripsy, with the difference noted in °C. Perioperative management parameters, including the presence or absence of pre- and postoperative DJ stents, were also documented as part of the outcome analysis.

Statistical analyses

Statistical analysis of the data obtained from the study was conducted using IBM SPSS Statistics software (Version 27, IBM Corp., Armonk, NY, USA) [17]. The normality distribution of continuous variables was evaluated using Kolmogorov–Smirnov and Shapiro–Wilk tests. Data with normal distribution were expressed as mean ± standard deviation (mean ± SD), while data without normal distribution were expressed as median (minimum–maximum) values. Independent Samples t-test was used to compare normally distributed continuous variables between groups, whereas Mann–Whitney U test was used for variables not showing normal distribution. Changes within a single group between preoperative and postoperative periods were assessed using Paired Samples t-test or Wilcoxon signed-rank test depending on the distribution. Categorical variables were summarized as frequencies and percentages, and comparisons between groups were conducted using Chi-square (χ^2) test or Fisher's exact test depending on expected cell counts. A multivariate logistic regression analysis was performed to determine the effect of independent variables on the dependent variable. For analyzing the changes in renal injury biomarkers (KIM-1 and KIM-1/creatinine ratios) over time, Repeated Measures ANOVA or Friedman test was used depending on distribution. In analyses where significant differences were identified, pairwise comparisons with Bonferroni correction were applied for post-hoc comparisons. In all statistical analyses, a p-value of <0.05 was considered statistically significant.

Results

The mean age of the 60 patients included in the study was 52.3 ± 12.4 years. Among the High Power laser group, the mean age was 51.5 ± 13.3 years, whereas it was 53.1 ± 11.6 years in the Low Power group. There was no significant difference between the groups (p = 0.636). Stone size averaged 16.5 ± 4.5 mm in the High Power group and 14.7 ± 4.0 mm in the Low Power group (p = 0.057). The stone density was 918 ± 266 HU in the High Power group and 961 ± 303 HU in the Low Power group, with no significant difference (p = 0.571). Preoperative double J (DJ) stent placement was performed in 43.3% (n = 26) of patients, with 36.7% (n = 11) in the High Power group and 50.0% (n = 15) in the Low Power group (p = 0.417) (Appendix Table 3).

The mean operative time for all patients was 70.7 ± 14.47 min, with 71.4 ± 13.6 min in the High Power group and 70.0 ± 15.5 min in the Low Power group, showing no significant difference (p = 0.202). Postoperative DJ stenting was performed in 88.3% (n = 53) of patients, with 83.3% (n = 25) in the High Power group and 93.3% (n = 28) in the Low Power group, showing no significant difference (p = 0.228). The residual stone rate in the study population was 20.0% (n = 12). These cases were equally divided between the groups, with 6 patients in the High Power group and 6 in the Low Power group (p = 1.00).

Table 1 Perioperative and Postoperative Outcomes

Parameters	Total (n=60)	High Power (n=30)	Low Power (n=30)	P-value
Operation Time (min)	70.7±14.47	71.4±13.6	70.0±15.5	0.202
Postoperative DJ stent	53 (88.3%)	25 (83.3%)	28 (93.3%)	0.228
Residual Stone	12 (20%)	6 (20%)	6 (20%)	1.000
Modified Clavien Grade 1	56 (93.3%)	29 (96.7%)	27 (90.0%)	0.301
Modified Clavien Grade 2	4 (6.7%)	1 (3.3%)	3 (10.0%)	
Modified Clavien Grade 3	0 (0%)	0 (0%)	0 (0%)	
Modified Clavien Grade 4	0 (0%)	0 (0%)	0 (0%)	
Modified Clavien Grade 5	0 (0%)	0 (0%)	0 (0%)	
Postoperative Fever	11 (18.3%)	6 (20%)	5 (16%)	0.556

Table 2 Comparison of Urinary KIM-1 and Creatinine Levels in Study Groups

Parameters	High Power (n=30)	Low Power (n=30)	P-value
KIM-1 Pre-op	66.0±52.9	62.5±42.1	0.807
KIM-1 Post-op 4th hour	186.2±237.0	95.9±63.9	0.114
KIM-1 Post-op 24th hour	278.8±239.6	170.3±172.9	0.003
Creatinine Pre-op (mg/dL)	41.09±24.6	42.49±35.7	0.450
Creatinine Post-op 4th hour (mg/dL)	50.86±35.4	42.86±25.4	0.549
Creatinine Post-op 24th hour (mg/dL)	62.82±35.1	58.54±31.5	0.626
KIM-1/Creatinine Pre-op	2.6±3.0	2.7±4.2	0.935
KIM-1/Creatinine Post-op 4th hour	4.9±7.1	3.0±3.1	0.287
KIM-1/Creatinine Post-op 24th hour	5.5±4.5	3.1±2.0	0.035

This equal distribution indicates that the laser power setting did not have a significant impact on stone-free outcomes in our study. Complications were classified using the Modified Clavien Classification, with Grade 1 complications observed in 93.3% (n=56) of cases, including 96.7% (n=29) in the High Power group and 90.0% (n=27) in the Low Power group (p=0.301). Grade 2 complications were found in 6.7% (n=4) of cases, with 3.3% (n=1) in the High Power group and 10.0% (n=3) in the Low Power group. No Grade 3–4-5 complications were observed (Table 1).

Preoperatively, there was no significant difference in KIM-1 levels between the Low Power (62.5±42.1 pg/mL) and High Power (66.0±52.9 pg/mL) groups (p=0.807). However, postoperative KIM-1 levels increased significantly in both groups, with a more pronounced elevation in the High Power group at both 4th (186.2±237.0 pg/mL vs. 95.9±63.9 pg/mL, p=0.114) and 24th hours (278.8±239.6 pg/mL vs. 170.3±172.9 pg/mL, p=0.003). Similarly, the KIM-1/Creatinine ratio was significantly higher at the 24th hour in the High Power group (5.5±4.5 vs. 3.1±2.0, p=0.035), indicating increased renal stress (Table 2). These findings suggest that higher laser power is associated with greater postoperative renal injury biomarker elevation, although no acute renal dysfunction was observed based on serum creatinine and eGFR levels (Table 2) (Fig. 1).

There was no significant difference between preoperative and postoperative eGFR values in both groups. In the Low Power group, eGFR increased from 73.0±20.7 to 75.5±21.1 (p=0.295), while in the High Power group, eGFR increased from 73.3±19.2 to 76.5±16.5 (p=0.188). Similarly, serum creatinine levels showed a slight but non-significant postoperative decrease in both groups (p>0.05), indicating that renal function remained stable postoperatively. Hemoglobin

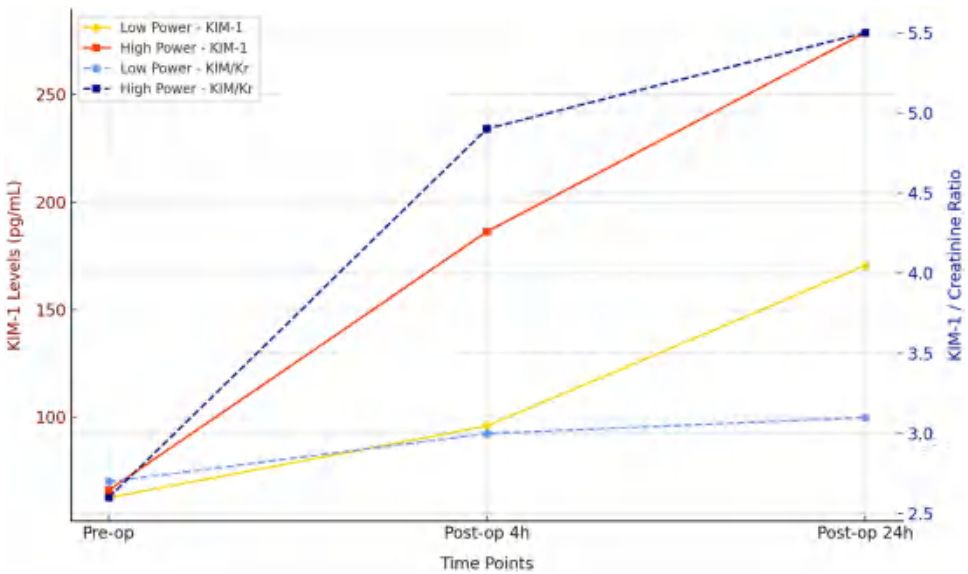


Fig. 1 KIM-1 And KIM-1/Creatinine Levels Over Time

levels also showed no significant changes, suggesting that blood loss was minimal. These results confirm that despite elevations in renal injury biomarkers, overall renal function was not significantly impaired, and no major postoperative complications related to renal dysfunction were observed (Appendix Table 5).

KIM-1 levels showed a steady increase in both groups postoperatively, but the High Power group exhibited significantly higher values at the 24th hour (278.8±239.6 pg/mL vs. 170.3±173 pg/mL, p=0.003). Similarly, the KIM-1/Creatinine ratio was higher in the High Power group at 24 h (5.5±4.5 vs. 3.1±2.0, p=0.035). These findings indicate that higher laser power correlates with greater renal stress and potential injury, despite stable renal function parameters. This suggests that subclinical renal stress may be more pronounced with high-power laser lithotripsy (Table 2) (Fig. 1).

Preoperatively, intra-renal temperatures were comparable in both groups (p=0.867). By the end of lithotripsy, temperatures increased slightly more in the High Power group (28.7±2.4 °C) compared to the Low Power group (28.2±2.4 °C), but the difference was not statistically significant (p=0.135). The mean temperature difference was also similar (2.56±1.4 °C vs. 2.49±1.5 °C, p=0.860) (Appendix Table 4) (Fig. 2).

Discussion

In our study, the effects of different laser power settings applied during retrograde intrarenal surgery (RIRS) on renal tissue were examined using biochemical markers. The demographic, clinical, and radiological parameters were similar in both groups, indicating that the findings were obtained from a homogeneous patient population. However, in the postoperative period, significant increases were observed in renal injury markers KIM-1 and KIM/spot urine creatinine ratios, particularly in patients treated with high-power laser. This suggests that high-power laser use may induce micro-level damage in renal parenchyma due to thermal and mechanical stress. The absence of significant differences between groups in operative time, stenting rates, complications, and residual stones further supports that these biomarker changes are directly related to laser power. Additionally, the lack of significant changes in glomerular filtration rate (eGFR), serum creatinine, and hemoglobin levels suggests that overall renal function was preserved, and that the increase in KIM-1 levels reflects the laser's tissue effects with high sensitivity. These findings highlight the potential of high-power lasers to cause renal tissue damage, emphasizing the importance of optimizing laser parameters in clinical practice.

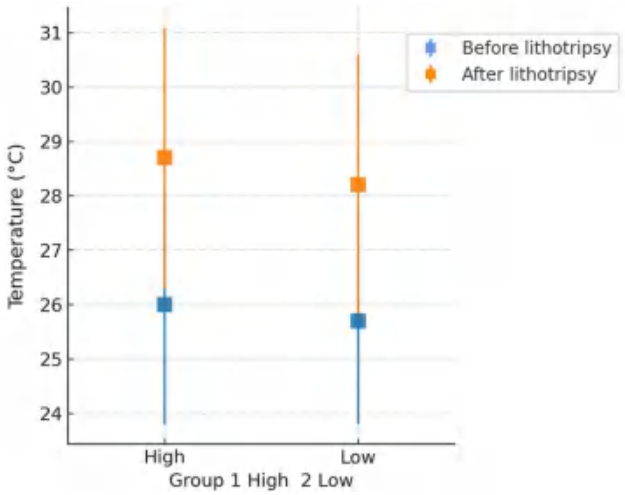


Fig. 2 Intrarenal temperatures were slightly higher in the high-power group, aligning with KIM-1 trends

Several studies in the literature have demonstrated that the use of high-power holmium lasers positively influences surgical efficiency. Rojo et al. [18] reported that in the pediatric population, high-power laser use resulted in shorter operative times and higher stone-free rates compared to low-power lasers. Similarly, Peretti et al. [19] found that low-energy but high-frequency laser settings significantly reduced operative time while achieving comparable stone-free rates to standard settings. Pietropaolo et al. [11] also reported that, in the treatment of lower pole stones, high-power laser use was associated with significantly higher stone-free rates and shorter operative times compared to low-power lasers. Additionally, Mekayten et al. [20] demonstrated that high-power laser significantly reduced stone dusting time regardless of stone density. Collectively, these studies suggest that high-power laser settings improve stone fragmentation efficiency, thereby leading to shorter operative durations and higher success rates in achieving stone-free status. Unlike previous studies, our findings revealed no significant differences in stone-free rates or operative times between the High Power and Low Power groups.

Shestha et al. [21] and Erol et al. [12] reported comparable success and complication rates between high-power and low-power laser groups. While Erol et al. found shorter operative time, hospital stay, and fluoroscopy duration with high-power lasers, our study confirmed similar success rates but observed no significant differences in hospital stay or fluoroscopy time between groups.

In light of our findings, low-power laser use may be particularly appropriate in patients with higher susceptibility to renal stress—such as those with solitary kidneys, early-stage renal dysfunction, or advanced age. Conversely, high-power laser settings may be more suitable for patients with adequate renal function, especially when maximizing

surgical efficiency and minimizing operative time are key considerations. Individualized laser parameter selection based on renal reserve and surgical goals is recommended to optimize both safety and efficacy.

While KIM-1 is a valuable and sensitive marker for detecting early subclinical kidney injury, its routine use in clinical practice is currently limited due to factors like high cost, limited availability, and lack of integration into standard care. At this stage, it may be more suitable for research purposes or in selected high-risk patients—such as those with impaired kidney function, a solitary kidney, or undergoing repeated endourological procedures—where closer renal monitoring could impact clinical decisions.

This study has several limitations, including its single-center design, small sample size (n = 60), and short follow-up period, which may limit the generalizability and long-term interpretation of the results. The exclusion of patients with renal stones < 1.5 cm restricts applicability to a broader population. Additionally, reliance on KIM-1 alone may be insufficient to fully assess renal injury, highlighting the need for more comprehensive biomarker panels and histopathological evaluation. The intrarenal temperature measurement method used was indirect and may not reflect real-time thermal dynamics. Finally, the lack of significant differences in some parameters may reflect limited statistical power. Despite these limitations, the study provides valuable insights into laser power, stone-free rates, and postoperative renal injury biomarkers in RIRS. Further validation of our findings requires multicenter, randomized controlled trials.

Conclusion

Our study demonstrates that although high-power laser lithotripsy provides comparable operative times and stone-free rates to low-power lasers, it is associated with significantly higher levels of renal injury biomarkers such as KIM-1 and KIM-1/creatinine ratio in the early postoperative period. These findings suggest a higher degree of subclinical renal stress in the high-power group. Despite stable serum creatinine and eGFR levels, the increased biomarker levels highlight the potential tissue-level effects of high-power laser usage. Further multicenter, randomized trials are needed to validate these results and guide safe laser parameter selection in RIRS.

Appendix

See Tables 3, 4, 5.

Table 3 Demographic and Baseline Clinical Characteristics

Parameters	Total (n = 60)	High Power (n = 30)	Low Power (n = 30)	P-value
Age (mean ± SD)	52.3 ± 12.4	51.5 ± 13.3	53.1 ± 11.6	0.636
Gender—Male	36 (60.0%)	19 (63.3%)	17 (56.7%)	0.598
Gender—Female	24 (40.0%)	11 (36.7%)	13 (43.3%)	
Comorbidity—DM	30 (42.0%)	12 (40%)	18 (60.0%)	0.121
Comorbidity—HT	9 (12.4%)	5 (16.7%)	4 (13.3%)	0.718
Comorbidity—CAD	17 (23.6%)	7 (23.3%)	10 (33.3%)	0.390
Comorbidity—COPD	2 (2.7%)	1 (3.3%)	1 (3.3%)	1.000
Comorbidity—Hyperlipidemia	2 (2.7%)	1 (3.3%)	1 (3.3%)	1.000
Opacity—Radiopaque	50 (83.3%)	26 (86.7%)	24 (80.0%)	0.488
Opacity—Radiolucent	10 (16.7%)	4 (13.3%)	6 (20.0%)	
Stone size (mm)	15.6 ± 4.3	16.5 ± 4.5	14.7 ± 4.0	0.057
Stone density (HU)	940 ± 284	918 ± 266	961 ± 303	0.571
Hydronephrosis—Yes	24 (41.4%)	15 (50%)	9 (32.1%)	0.168
Hydronephrosis—No	34 (58.6%)	15 (50%)	19 (67.9%)	
Stone side—Right	23 (38.3%)	8 (26.7%)	15 (50.0%)	0.063
Stone side—Left	37 (61.7%)	22 (73.3%)	15 (50.0%)	
Preoperative DJ stent—Yes	26 (43.3%)	11 (36.7%)	15 (50%)	0.417
Preoperative DJ stent—No	34 (56.7%)	19 (63.3%)	15 (50%)	

Table 4 Intrarenal Thermal Effect of Study Groups

Parameters	High Power (n = 30)	Low Power (n = 30)	P-value
Intrarenal temp before lithotripsy (°C)	26.0 ± 2.2	25.7 ± 1.9	0.867
Intrarenal temp after lithotripsy (°C)	28.7 ± 2.4	28.2 ± 2.4	0.135
Temperature difference (°C)	2.56 ± 1.4	2.49 ± 1.5	0.860

Table 5 Preoperative and Postoperative Biochemical Parametersc

Parameters	Low Power Pre-op	Low Power Post-op	P value	High Power Pre-op	High Power Post-op	P value
eGFR	73.0±20.7	75.5±21.1	0.295	73.3±19.2	76.5±16.5	0.188
Serum Creatinine	1.11±0.4	1.06±0.4	0.152	1.08±0.3	1.02±0.2	0.071
Hemoglobin	13.5±2.2	13.2±2.2	0.136	13.3±1.8	17.3±23.7	0.797

Author contributions HA: project development, manuscript writing, data managing, laboratory analysis, collection and storage of samples. FG: data analysis, manuscript Editing, editing of figures and tables. MGS: data analysis, manuscript editing, editing of tables. CT: laboratory analysis, sample collection and storage.SG: manuscript editing. MB: project development, manuscript editing, surgical application.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

Ethics approval Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects". The study was performed in the Clinical Ethic Committee of Necmettin Erbakan University Faculty of Medicine (No: 2023/4402). Consent to participate All participants give their consent to participate in the study. Consent for publication All participants give permission to publication.

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研究

高功率Ho：YAG碎石术增加亚临床肾应激：一项前瞻性随机KIM-1研究

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摘要

本研究旨在比较高功率（HPL）和低功率（LPL）钬：钇铝石榴石激光在逆行肾内手术（RIRS）中的安全性，使用尿液肾损伤分子-1（KIM-1）作为急性肾损伤（AKI）的早期生物标志物。60名肾结石患者（1.5–2.5厘米）被前瞻性随机分为HPL组和LPL组。术前及术后4小时和24小时分别测量尿液KIM-1水平和KIM-1/肌酐比值。同时评估术中参数、无结石率（SFR）、并发症及肾功能（eGFR、血清肌酐）。记录碎石术前后肾内温度。两组的手术时间、SFR、并发症发生率及肾功能参数无显著差异（p>0.05）。然而，术后24小时HPL组的KIM-1水平显著升高（278.8±239.6 pg/mL vs.170.3±172.9 pg/mL，p=0.003），KIM-1/肌酐比值也升高（5.5±4.5 vs.3.1±2.0，p=0.035）。术后血清肌酐或eGFR未见显著差异。HPL组患者术中肾温度略有升高，但差异无统计学意义。虽然高功率激光碎石术不会对整体肾功能造成不良影响，但其伴随的肾损伤生物标志物水平升高提示存在更严重的亚临床肾功能压力。

关键词肾结石·逆行肾内手术·高功率激光·低功率激光·KIM-1·尿KIM-1

介绍

尿路结石症是全球范围内的重大公共卫生问题，影响着全球10%-15%的人口，作为常见的泌尿系统疾病，对发病率具有显著贡献[1]。肾结石症作为尿路结石症的一种特殊类型，特指肾脏内结石的存在，其病因复杂多样，涉及遗传因素、肥胖和脱水等多重因素[2]。目前治疗肾结石的主要方式包括逆行肾镜取石术（RIRS）、体外冲击波碎石术（SWL）和经皮肾镜取石术（PCNL）[3]。

逆行肾镜手术（RIRS）是一种微创治疗方案，通过柔性输尿管镜（fURS）配合激光能量（通常采用钬激光）来清除肾结石[4]。在处理中小型结石（通常<2 cm）或位于解剖结构复杂区域的结石时，柔性输尿管镜联合激光碎石术（FURSL）效果尤为显著[5]。随着技术进步和专业培训的提升，如今FURSL已广泛应用于直径达2厘米的结石治疗，其结石清除率高且并发症发生率低于传统碎石术（PCNL）[6]。在柔性输尿管镜碎石术中，钬：钇铝石榴石（Ho：YAG）激光被公认为激光碎石的金标准，能高效处理各类肾结石成分[7]。

Ho指出：采用波长2100纳米钬激光的YAG碎石术，由于水分子对其光波具有高吸收特性，可将热损伤控制在肾脏及输尿管邻近组织的最小范围[8]。Ho进一步说明：YAG激光器主要分为低功率（LPL）和高功率（HPL）两类[9]。单腔结构的激光器

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功率不超过30瓦的激光设备被归类为LPL级，而具有多个腔体且功率超过30瓦的激光器则被归类为HPL级[10]。先前类似研究表明，与LPL级相比，使用HPL级设备能显著缩短治疗时间并减少住院需求[11，12]。不过，由于高强度激光会产生高压高温，学界对急性肾损伤（AKI）等短期影响以及高功率激光对肾脏的长期危害提出了担忧[12]。

近期，医学界发现了急性肾损伤（AKI）的新型生物标志物。其中，白细胞介素-18（NGAL）、白细胞介素-18（IL-18）、肾小管上皮细胞生长因子1型（KIM-1）和血管紧张素II受体拮抗剂2（TIMP-2）等指标，为早期诊断AKI提供了重要依据[13，14]。在这些新发现的生物标志物中，尿液中的KIM-1（肾小管上皮细胞生长因子1型）尤为突出，已成为检测急性肾损伤（AKI）的可靠指标。该标志物已获得美国食品药品监督管理局（FDA）批准，可用于临床前药物研发[15]。KIM-1作为肾小管损伤的特异性标志物，会在急性肾损伤发生后随尿液排出，是此类损伤最早出现的预警信号之一。研究还表明，KIM-1可作为有效生物标志物，用于评估不同透析技术（如血液透析、腹膜透析、血液滤过、血液透析滤过等）对肾脏造成的损伤程度[16]。

本研究旨在通过急性肾损伤（AKI）早期标志物KIM-1，对比高功率与低功率激光碎石术的安全性差异。

材料和方法

本研究于2023年7月7日获得内杰梅廷·埃尔巴坎大学医学院伦理委员会批准（编号：2023/4402）。所有参与者均签署了书面知情同意书并接受了口头说明。研究采用前瞻性设计，由该校科学研究项目协调单位资助（项目编号：24TU18007）。

患者选择和研究标准

本研究在2023年10月1日至2024年5月1日期间，于内杰梅廷·埃尔巴坎大学医学院泌尿科诊所开展，对象为18-65岁肾结石患者。通过严格筛选纳入标准和排除标准，最终筛选出60例患者，确保研究对象同质性，从而提升结果可靠性。所有患者均接受了逆行肾镜手术（RIRS）。

符合入选标准的受试者为18-75岁健康成年人，需经CT确诊的肾结石（1.5-2.5厘米）且估算肾小球滤过率（eGFR）≥60。排除标准包括：尿脓症、输尿管结石、尿培养阳性、肾实质变薄、近期接受过手术、肾脏畸形或慢性排除标准包括肾病、单侧肾或使用肾毒性药物。此外，过去三个月内接受过结石手术或因输尿管狭窄无法进行输尿管肾镜检查的患者亦被排除。

术前预防

所有患者术前均接受抗生素预防治疗。术前1小时给予第三代头孢菌素（头孢曲松），对有过敏史的患者则改用环丙沙星或阿米卡星等替代抗生素。

尿液样本采集和分析

尿液样本在三个时间点采集：术前、术后4小时及术后24小时。样本经3000转/分钟离心10分钟后，分装至Eppendorf离心管中，于-80℃冷冻保存待测。实验当天解冻样本后，使用美国Elabscience生物技术公司试剂盒测定尿液KIM-1水平，随后计算尿液KIM-1/肌酐比值，并进行组间比较分析。

设备和设置

所有手术均采用Redpine®RP-U-C12一次性视频输尿管镜（中国广州）完成。LPL手术使用272μ光纤搭配Dornier®30 W激光（德国），而HPL手术则采用272μ光纤配合Jenna Surgical®150 W激光（德国）。具体激光技术选择通过区组随机化确定。

随机化方法

为确保两组样本量均衡，采用区组随机化方法将患者随机分配至高功率组（HPL）或低功率组（LPL）。研究共纳入60名患者，按四人一组进行分组（共15个区组），每个区组包含2名HPL组患者和2名LPL组患者。随机序列由独立统计学家通过计算机生成，并密封在不透明信封中，仅在入组时开封。在分组完成前，外科医生和患者均不知晓具体分组情况。

术中操作和手术技术

所有手术均由一位拥有至少60例RIRS病例经验的资深外科医生完成。手术在全身麻醉下进行，患者采取背部截石位。手术区域保持无菌状态。

该程序已建立，且所有步骤均严格遵循无菌操作规范。

肾内温度测量

在碎石术开始和结束时，通过输尿管肾镜的柔性通道抽取肾内液体，以此测量肾内温度。

术后管理

密切监测患者发热、血尿、尿路感染等并发症，定期评估生命体征和血流动力学稳定性。术后第1天行腹部平片检查，评估残留结石及双J支架置入位置。

结果测量

主要结局指标为术后3个月通过标准影像学检查评估的无结石率。次要结局指标包括术中及术后并发症、手术时间、住院时间、术后发热情况以及是否需要植入DJ支架。手术时间定义为整个手术过程的总耗时（以分钟为单位）。术后发热发生率记录为二元结局指标（是/否）。住院时间根据围手术期管理情况推算得出，尽管数据中未明确说明。残留结石的存在及术后并发症均依据改良Clavien分级系统进行评估和分类。

在生化指标方面，研究团队对术前术后血清肌酐、血红蛋白水平及估算肾小球滤过率（eGFR）进行了检测与对比。尿肾损伤分子-1（KIM-1）水平分别在术前基线、术后4小时及24小时进行记录。此外，通过计算各时间点KIM-1与血清肌酐的比值（KIM-1/Cr）获得标准化数值。术中热变化通过测量碎石术前后肾内温度差值（以°C为单位）进行评估。围手术期管理参数（包括术前术后双侧肾动脉支架置入情况）也被纳入结果分析范围。

统计分析

采用IBM SPSS Statistics软件（版本27，IBM公司，美国纽约州阿蒙克）[17]对研究数据进行统计学分析。通过该软件评估连续变量的正态分布情况。采用柯尔莫哥洛夫-斯米尔诺夫检验和夏皮罗-威尔克检验。正态分布数据以均值±标准差（均值±SD）表示，非正态分布数据则以中位数（最小值-最大值）呈现。对于组间正态分布连续变量的比较，采用独立样本t检验；对于非正态分布变量则使用曼-惠特尼U检验。同一组患者术前与术后的变化情况，根据数据分布采用配对样本t检验或威尔科克森符号秩检验进行评估。分类变量以频数和百分比形式汇总，组间比较根据预期单元格数采用卡方（χ^2）检验或费舍尔精确检验。通过多变量逻辑回归分析评估自变量对因变量的影响。针对肾损伤生物标志物（KIM-1及KIM-1/肌酐比值）的动态变化分析，根据数据分布采用重复测量方差分析或弗里德曼检验。在发现显著差异的分析中，采用Bonferroni校正进行两两比较以进行事后检验。所有统计分析中，p值<0.05均视为具有统计学意义。

结果

本研究纳入的60例患者平均年龄为52.3±12.4岁。高功率激光组的平均年龄为51.5±13.3岁，低功率组为53.1±11.6岁，两组间无显著差异（p=0.636）。结石平均大小方面，高功率组为16.5±4.5毫米，低功率组为14.7±4.0毫米（p=0.057）。结石密度方面，两组分别为918±266 HU和961±303 HU，差异无统计学意义（p=0.571）。术前双J型支架置入率方面，高功率组为36.7%（n=11），低功率组为50.0%（n=15），两组差异无统计学意义（p=0.417）（详见附表3）。

所有患者的平均手术时间为70.7±14.47分钟，其中高功率组为71.4±13.6分钟，低功率组为70.0±15.5分钟，两组间无显著差异（p=0.202）。术后进行DJ支架置入术的患者比例为88.3%（n=53），高功率组为83.3%（n=25），低功率组为93.3%（n=28），两组间无显著差异（p=0.228）。研究人群的残留结石率为20.0%（n=12），两组间病例数均等分布，各6例（p=1.00）。

表1术中和术后结局

参数	总计（n=60）	高功率(n=30)	低功率（n=30）	概率值
操作时间（分钟）	70.7±14.47	71.4±13.6	70.0±15.5	0.202
术后DJ支架	53 (88.3%)	25 (83.3%)	28 (93.3%)	0.228
残留石	12 (20%)	6 (20%)	6 (20%)	1.000
改良型克拉一年级	56 (93.3%)	29 (96.7%)	27 (90.0%)	0.301
改良型克拉二年级	4 (6.7%)	1 (3.3%)	3 (10.0%)	
改良型克拉三年级	0 (0%)	0 (0%)	0 (0%)	
改良型克拉五年级	0 (0%)	0 (0%)	0 (0%)	
改良型克拉五年级	0 (0%)	0 (0%)	0 (0%)	
术后发热	11 (18.3%)	6 (20%)	5 (16%)	0.556

表2研究中尿KIM-1和肌酐水平的比较组

参数	高功率（n=30）	低功率（n=30）	概率值
KIM-1 Pre-op	66.0±52.9	62.5±42.1	0.807
术后第4小时KIM-1	186.2±237.0	95.9±63.9	0.114
术后24小时的KIM-1	278.8±239.6	170.3±172.9	0.003
肌酐术前（mg/dL）	41.09±24.6	42.49±35.7	0.450
肌酐术后4小时（mg/dL）	50.86±35.4	42.86±25.4	0.549
肌酐术后24小时（mg/dL）	62.82±35.1	58.54±31.5	0.626
KIM-1/Creatinine Pre-op	2.6±3.0	2.7±4.2	0.935
术后第4小时的KIM-1/肌酐	4.9±7.1	3.0±3.1	0.287
术后24小时的KIM-1/肌酐	5.5±4.5	3.1±2.0	0.035

这种均衡分布表明，在本研究中，激光功率设置对结石清除率没有显著影响。我们采用改良克雷文分类法对并发症进行分级，其中1级并发症发生率为93.3%（n=56），高功率组为96.7%（n=29），低功率组为90.0%（n=27）（p=0.301）。2级并发症发生率为6.7%（n=4），高功率组为3.3%（n=1），低功率组为10.0%（n=3）。未观察到3-4-5级并发症（见表1）。

术前，低功率组（62.5±42.1 pg/mL）与高功率组（66.0±52.9 pg/mL）的KIM-1水平无显著差异（p=0.807）。然而，术后两组的KIM-1水平均显著升高，其中高功率组在第4小时（186.2±237.0 pg/mL vs.95.9±63.9 pg/mL，p=0.114）和第24小时（278.8±239.6 pg/mL vs.170.3±172.9 pg/mL，p=0.003）的升高更为明显。同样，高功率组在第24小时的KIM-1/肌酐比值显著更高（5.5±4.5 vs.3.1±2.0，p=0.035），表明肾应激增加（表2）。这些结果表明，更高的激光功率与术后肾损伤生物标志物的升高相关，尽管根据血清肌酐和eGFR水平未观察到急性肾功能障碍（表2）（图1）。

两组患者术前与术后估算肾小球滤过率（eGFR）均无显著差异。低功率组eGFR从73.0±20.7提升至75.5±21.1（p=0.295），而高功率组则从73.3±19.2增至76.5±16.5（p=0.188）。血清肌酐水平在术后两组均出现轻微下降（p>0.05），但未达统计学显著性，表明术后肾功能保持稳定。血红蛋白

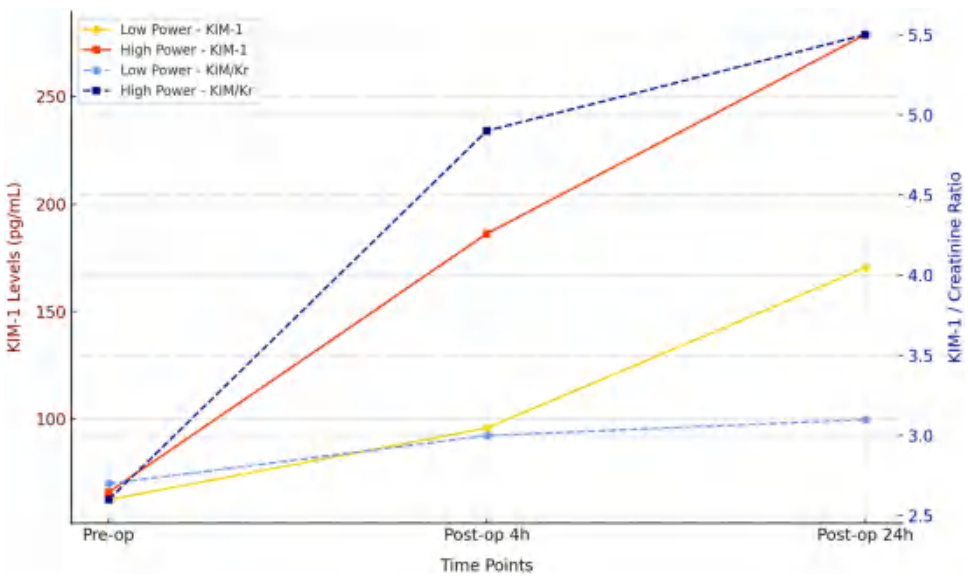


图1 KIM-1和KIM-1/肌酐水平随时间的变化

水平也未显示任何显著变化，这表明失血量极小。这些结果证实，尽管肾损伤生物标志物升高，但整体肾功能未出现显著损害，且未观察到与肾功能障碍相关的重大术后并发症（附表5）。

两组术后KIM-1水平均呈现稳定上升趋势，但高功率组在24小时时的数值显著更高（278.8±239.6 pg/mL vs.170.3±173 pg/mL，p=0.003）。同样，高功率组在24小时时的KIM-1/肌酐比值也更高（5.5±4.5 vs.3.1±2.0，p=0.035）。这些发现表明，尽管肾功能参数稳定，但更高的激光功率与更大的肾应激和潜在损伤相关。这提示亚临床肾应激在高功率激光碎石术中可能更为显著（表2）（图1）。

术前，两组的肾内温度相当（p=0.867）。碎石术结束时，高功率组的温度（28.7±2.4°C）比低功率组（28.2±2.4°C）略高，但差异无统计学意义（p=0.135）。平均温度差也相似（2.56±1.4°C vs.2.49±1.5°C，p=0.860）（附表4）（图2）。

讨论

本研究通过生化标志物检测，系统评估了逆行肾内手术（RIRS）中不同激光功率设置对肾组织的影响。两组患者的人口学特征、临床表现及影像学参数均无显著差异，表明研究结果具有普适性。

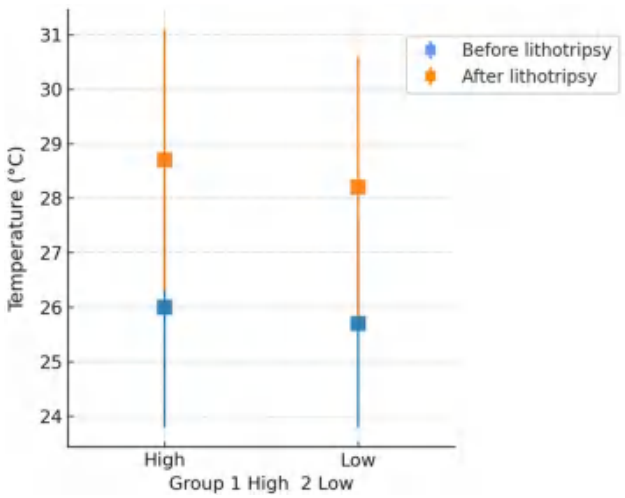


图2高功率组的肾内温度略高
与KIM-1趋势一致的组

研究数据来源于同质化患者群体。然而在术后阶段，高功率激光治疗组的肾损伤标志物KIM-1及尿液中KIM-1与肌酐比值出现显著升高，这表明高功率激光可能因热机械应力导致肾实质微损伤。各组在手术时间、支架置入率、并发症及残留结石方面未见显著差异，进一步证实这些生物标志物变化与激光功率直接相关。此外，肾小球滤过率（eGFR）、血清肌酐和血红蛋白水平未见明显变化，说明整体肾功能保持稳定，KIM-1水平升高反映了激光对组织的高敏感性损伤效应。这些发现凸显了高功率激光可能引发肾组织损伤的潜在风险，强调了临床实践中优化激光参数的重要性。

多项研究表明，使用高功率钬激光器可显著提升手术效率。Rojo等人[18] 研究显示，在儿童患者群体中，高功率激光治疗相较于低功率激光，能缩短手术时间并提高无结石率。Peretti等学者[19] 研究发现，采用低能量但高频的激光设置，不仅显著缩短了手术时间，其结石清除率也与标准设置相当。Pietropaolo等[11] 研究还指出，在治疗下极结石时，与低功率激光相比，高功率激光能显著提高无结石率并缩短手术时间。此外，Mekayten等人[20] 研究证实，无论结石密度如何，高功率激光都能显著缩短碎石时间。综合来看，这些研究结果表明，高功率激光参数能有效提升碎石效率，从而缩短手术时间并提高结石清除成功率。与以往研究不同，我们的数据显示高功率组与低功率组在结石清除率和手术时间上均无显著差异。

谢斯塔等人[21] 以及Erol等人[12] 研究显示高功率激光组与低功率激光组的手术成功率及并发症发生率具有可比性。尽管Erol等学者发现高功率激光组的手术时间、住院时长及透视检查时间较短，但本研究证实两组成功率相当，且未发现住院时间或透视检查时间存在显著差异。

根据我们的研究结果，低功率激光治疗可能特别适合肾功能易受损伤的患者，例如单侧肾脏患者、早期肾功能不全或高龄人群。相反，高功率激光治疗可能更适合肾功能正常患者，特别是在需要最大化治疗效果时。

手术效率和缩短手术时间是关键考量因素。建议根据肾功能储备和手术目标进行个体化激光参数选择，以优化安全性和有效性。

尽管KIM-1作为检测早期亚临床肾损伤的敏感指标具有重要价值，但由于成本高昂、供应有限且尚未纳入标准诊疗流程等因素，其临床常规应用目前仍受限。现阶段该指标更适合用于科研研究或特定高危人群——例如肾功能不全患者、单侧肾脏患者或需反复接受泌尿系统手术的患者——这些情况下更密切的肾脏监测可能对临床决策产生重要影响。

本研究存在若干局限性，包括单中心设计、样本量较小（n=60）以及随访周期较短，这些因素可能限制研究结果的普适性和长期解读价值。排除肾结石直径小于1.5厘米的患者，限制了研究适用人群的广泛性。此外，仅依赖KIM-1指标可能不足以全面评估肾损伤，这凸显了构建更全面的生物标志物组合及组织病理学评估的必要性。研究采用的肾内温度测量方法为间接法，可能无法真实反映实时热力学动态。最后，部分参数未呈现显著差异，可能与统计效力不足有关。尽管存在这些局限，本研究仍为激光功率、无结石率及RIRS术后肾损伤生物标志物提供了重要参考。未来需通过多中心随机对照试验进一步验证研究结果。

结论

我们的研究表明，虽然高功率激光碎石术在手术时间和无结石率方面与低功率激光相当，但术后早期阶段的肾损伤生物标志物（如KIM-1和KIM-1/肌酐比值）水平显著升高。这些发现表明高功率组存在更高程度的亚临床肾功能压力。尽管血清肌酐和估算肾小球滤过率（eGFR）水平稳定，但生物标志物水平的升高凸显了高功率激光可能对组织产生的影响。未来需要开展更多多中心随机对照试验来验证这些结果，并指导RIRS治疗中安全的激光参数选择。

附录

见表3、4、5。

表3人口统计学和基线临床特征

参数	总计（n=60）	高功率 (n=30)	低功耗 (n=30)	概率值
年龄（平均值±SD）	52.3±12.4	51.5±13.3	53.1±11.6	0.636
性别—男性	36 (60.0%)	19 (63.3%)	17 (56.7%)	0.598
性别—女性	24 (40.0%)	11 (36.7%)	13 (43.3%)	
合并症—糖尿病	30 (42.0%)	12 (40%)	18 (60.0%)	0.121
合并症—HT	9 (12.4%)	5 (16.7%)	4 (13.3%)	0.718
合并症—CAD	17 (23.6%)	7 (23.3%)	10 (33.3%)	0.390
合并症—COPD	2 (2.7%)	1 (3.3%)	1 (3.3%)	1.000
合并症—高脂血症	2 (2.7%)	1 (3.3%)	1 (3.3%)	1.000
不透明-显影	50 (83.3%)	26 (86.7%)	24 (80.0%)	0.488
混浊-透光	10 (16.7%)	4 (13.3%)	6 (20.0%)	
石料尺寸（mm）	15.6±4.3	16.5±4.5	14.7±4.0	0.057
结石密度（HU）	940±284	918±266	961±303	0.571
肾积水-是	24 (41.4%)	15 (50%)	9 (32.1%)	0.168
肾积水-无	34 (58.6%)	15 (50%)	19 (67.9%)	
石侧—右	23 (38.3%)	8 (26.7%)	15 (50.0%)	0.063
石侧—左	37 (61.7%)	22 (73.3%)	15 (50.0%)	
术前DJ支架—是	26 (43.3%)	11 (36.7%)	15 (50%)	0.417
术前DJ支架—否	34 (56.7%)	19 (63.3%)	15 (50%)	

表4研究组的肾内热效应

参数	高权力 (n=30)	低权力 (n=30)	概率值
碎石术前肾内温度（℃）	26.0±2.2	25.7±1.9	0.867
碎石术后肾内温度（℃）	28.7±2.4	28.2±2.4	0.135
温差（℃）	2.56±1.4	2.49±1.5	0.860

表5术前和术后生化参数c

参数	低功率预操作	术后低功率	P值	高功率预操作	术后高功率	P值
eGFR	73.0±20.7	75.5±21.1	0.295	73.3±19.2	76.5±16.5	0.188
血清肌酐	1.11±0.4	1.06±0.4	0.152	1.08±0.3	1.02±0.2	0.071
血红蛋白	13.5±2.2	13.2±2.2	0.136	13.3±1.8	17.3±23.7	0.797

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