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Weizhong Zhang
Graduate School of Beijing University of Chinese Medicine
Daibing Lv
Graduate School of Beijing University of Chinese Medicine
Shanfang Yuan
Graduate School of Beijing University of Chinese Medicine
Xi Meng
Graduate School of Beijing University of Chinese Medicine
Yang Ding
Graduate School of Beijing University of Chinese Medicine
Xiaoyu Wang
Graduate School of Beijing University of Chinese Medicine
Chaomeng Huang
Graduate School of Beijing University of Chinese Medicine
Daichuan Cheng
Third Affiliated Hospital of Beijing University of Chinese Medicine
Jianghua Yang
Third Affiliated Hospital of Beijing University of Chinese Medicine
Xiaoxing Liao
136613877390163.com

Third Affiliated Hospital of Beijing University of Chinese Medicine

Research Article

Keywords: Ureteral calculi, Holmium laser, Thermal damage, In vitro study, Prediction model

Posted Date: November 24th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11703078/v1

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Additional Declarations: No competing interests reported.

Prediction Model of Thermal Injury-Related Factors for Intraureteral Temperature Changes During Holmium Laser Lithotripsy : An In Vitro Study

Weizhong Zhang1, Daibing Lv1, Shanfang Yuan1, Xi Meng1, Yang Ding1, Xiaoyu Wang1, Chaomeng Huang 1, Daichuan Cheng2, Jianghua Yang2, Xiaoxing Liao 2

(1. Graduate School of Beijing University of Chinese Medicine, Beijing 100029; 2. Department of Urology, Third Affiliated Hospital of Beijing University of Chinese Medicine, Beijing 100029;)

Abstract: **Purpose:** To establish an in vitro porcine ureteral stone model, identify factors affecting ureteral inner-wall thermal injury during holmium laser lithotripsy, and construct a predictive model.
Methods: Fresh porcine urinary systems were used. A human stone (7–10 × 5–7 mm) was implanted into the upper ureter. A temperature sensor was fixed on the inner wall below the stone, and a 365 μm holmium laser fiber was placed below the stone. Perfusion was 20 or 40 mL/min; pulse width was long or short; power was 10 or 20 W (four modes). Activation lasted 10 or 20 s; each condition was repeated 3 times.
Results: Ninety-six measurements were obtained (53.18 ± 24.71 °C; range 27.28–105.10 °C). Perfusion rate was strongly negatively correlated with temperature ($r = -0.905$, $p < 0.001$); power was moderately positively correlated ($r = 0.210$, $p = 0.020$); pulse width showed no significant correlation ($r = 0.056$, $p = 0.295$). The model included time, perfusion rate, power, and pulse width ($R^2 = 0.874$; $F(4,91) = 157.407$, $p < 0.001$). At 20 mL/min, maximum temperatures exceeded 43 °C; at 40 mL/min, all remained below 43 °C.
Conclusion: Perfusion rate was the strongest negative factor. Increasing perfusion from 20 to 40 mL/min reduced temperature by 44.5 °C; each 10 W increase in power raised it by 10.3 °C; doubling activation time raised it by only 4.3 °C. Pulse width had no significant effect. Low power (10 W) is recommended; 40 mL/min maintained temperatures below 43 °C.

Keywords: Ureteral calculi, Holmium laser, Thermal damage, In vitro study, Prediction model

Funding Project: Capital's Funds for Health Improvement and Research(2024-3-7036)
Beijing University of Chinese Medicine Third Affiliated Hospital Medical-Engineering Cross-Disciplinary Project (2025-YJKT-YGJC-11)
Hebei Province Traditional Chinese Medicine Scientific Research Project Plan (B2025024)

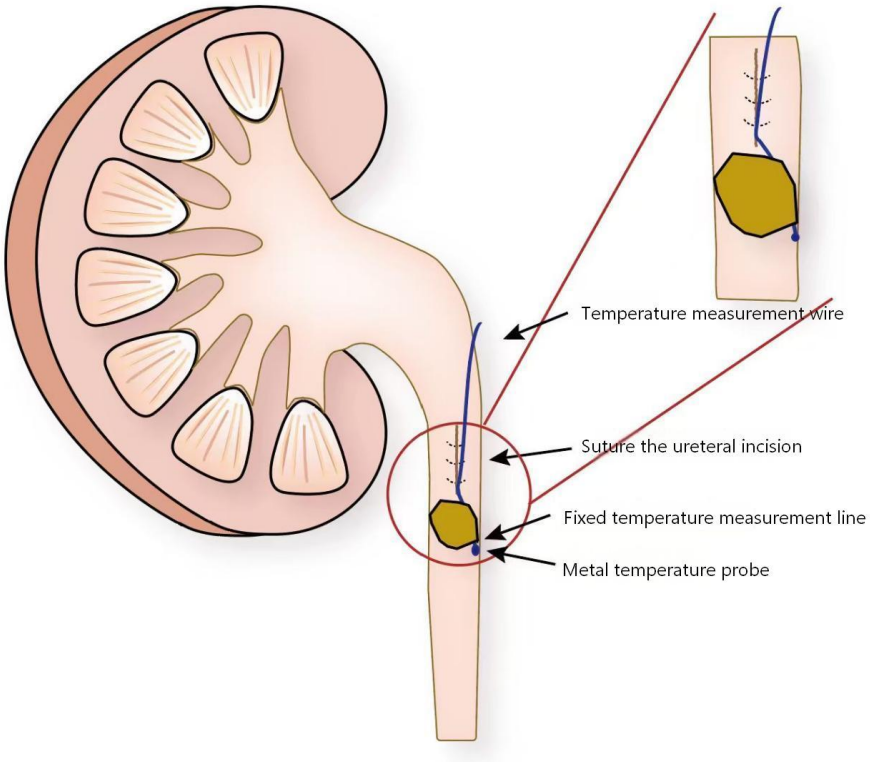
Author Affiliation: 1 Graduate School of Beijing University of Chinese Medicine, Beijing 100029
2 Department of Urology, Beijing University of Chinese Medicine Third Affiliated Hospital, Beijing 100029; Corresponding Author: Liao Xiaoxing, E-mail: 13661387739@163.com

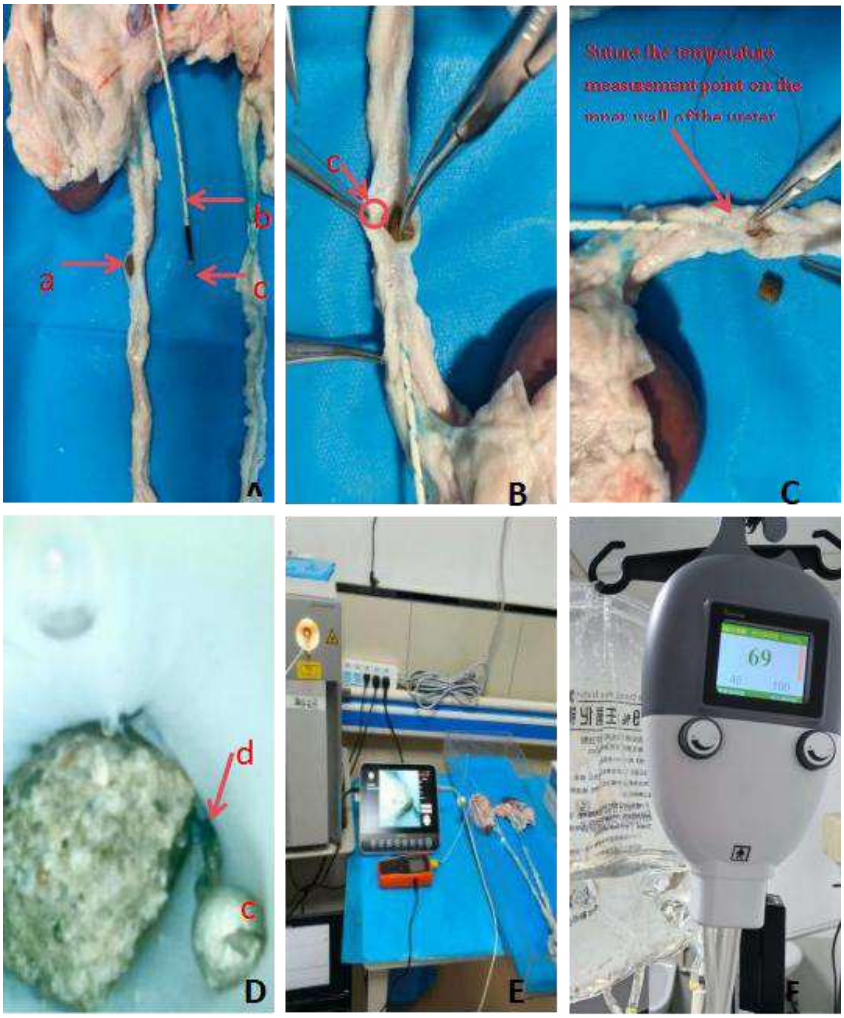
Holmium:YAG laser lithotripsy has become a standard treatment for ureteral calculi since the 1990s [1]. Unlike pneumatic lithotripsy, the holmium laser fragments stones primarily through photothermal effects [2]. Higher laser power improves fragmentation efficiency but also raises the temperature of surrounding fluid and increases the risk of thermal injury to the ureteral wall [3,4]. Perfusion rate, laser power, activation time, and pulse width all influence temperature elevation. In this study, we established an in vitro porcine ureteral stone model with a temperature sensor fixed directly on the ureteral inner wall, and we constructed a predictive model for thermal injury risk under different laser parameters.

1.Materials and Methods

Experimental animals and materials. Fresh adult porcine kidneys, ureters, bladders, and urethras (2 sets, 4 sides) were obtained from a slaughterhouse in Tongzhou District, Beijing. Surrounding fat tissue was removed. The urinary system was placed in an acrylic water tank (80 cm × 30 cm × 10 cm) lined with sterile surgical towels.

Model establishment. A super-smooth guidewire was inserted through the urethra into the ureter and renal pelvis. A ureteral access sheath and a flexible ureteroscope were advanced into the upper ureter. The ureteral wall was longitudinally incised. A human kidney stone (7–10 mm × 5–7 mm) was placed inside the ureteral lumen. A K-type thermocouple temperature measurement line (KAIPUSEN, China; TT-K-44) was inserted approximately 1 cm above the stone. Under ureteroscopic guidance, the metal temperature probe was positioned parallel to the lower pole of the stone and sutured to the ureteral inner wall with a 5-0 needle. The ureteral incision was then closed [5]. (Figures 1 and 2)





Holmium laser lithotripsy. A 365 μm holmium laser fiber was inserted below the stone and connected to a holmium:YAG laser system (E.M.S. Electro Medical Systems S.A.). A disposable electrically controlled suction perfusion catheter (Nordson Medical Technology Co., Ltd.) was used to irrigate with normal saline at room temperature (24 °C). The laser was activated continuously for 10 or 20 s. Perfusion flow rates were set at 20 or 40 mL/min. Laser power was set at 10 W or 20 W using four modes: 1.0 J × 10 Hz, 2.0 J × 5 Hz, 2.0 J × 10 Hz, and 2.5 J × 8 Hz. Both long and short pulse widths were tested. The temperature sensor recorded real-time temperature every second. After each activation, the temperature was allowed to drop below 25 °C before the next measurement. Each condition was repeated 3 times, and the highest temperature was recorded .

2.Statistical Methods

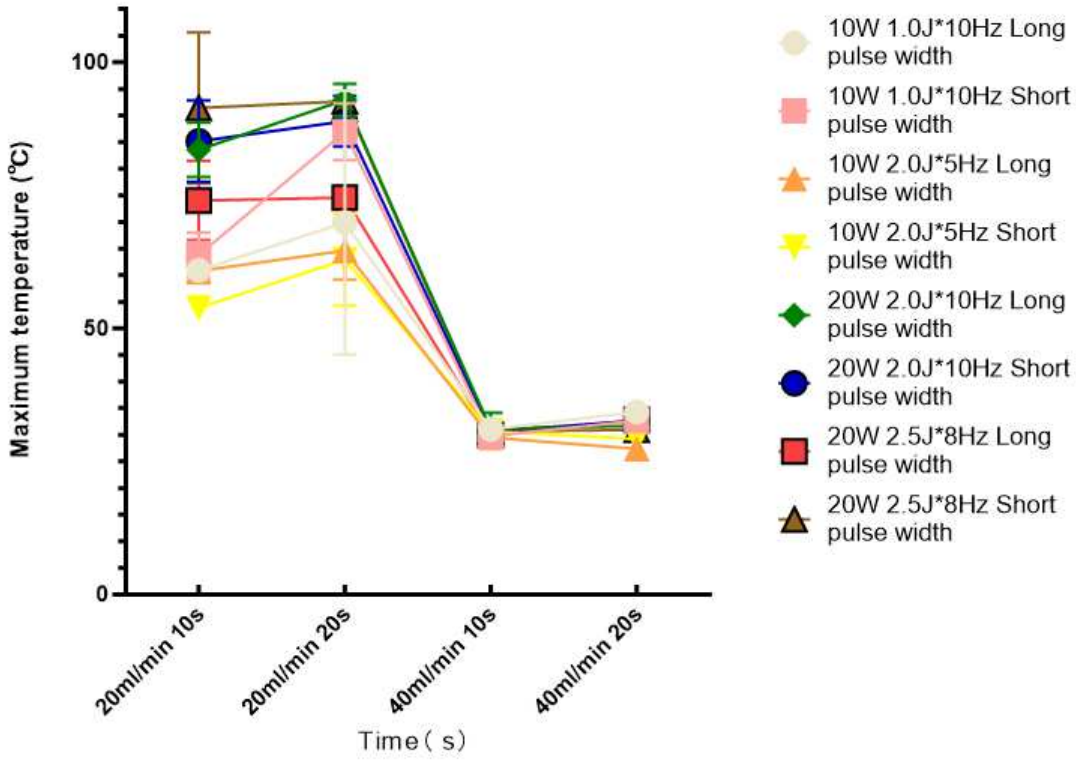
Data were analyzed using SPSS 24.0. Measurement data are expressed as mean ± standard deviation. Correlation analysis and multiple linear regression were performed. The laser energy and frequency were completely collinear; therefore, their product (laser power, 10 W or 20 W) was used as a variable. Model diagnostics included collinearity statistics, Durbin-Watson test, and residual analysis.

3.Results

Model validation. The ureteral stone was successfully implanted, and the temperature sensor was

fixed on the inner wall below the stone. Real-time temperature changes were reliably collected, confirming successful establishment of the model.

Temperature measurements. A total of 96 temperature measurements were obtained (53.18 ± 24.71 ° C). The highest temperature was 105.10 ° C, and the lowest was 27.28 ° C. At a perfusion rate of 20 mL/min, the maximum temperature in each group exceeded the 43 ° C safety threshold[6]. At 40 mL/min, the maximum temperature in all groups remained below 43 ° C (Figure 3).



Correlation and regression analysis. Perfusion rate was strongly negatively correlated with temperature ($r = -0.905$, $p < 0.001$). Laser power was moderately positively correlated ($r = 0.210$, $p = 0.020$). Pulse width showed a very weak, non-significant correlation ($r = 0.056$, $p = 0.295$). The regression model was:Temperature (°C) = 93.883 + 4.266 × (time) − 44.485 × (perfusion rate) + 10.348 × (power) + 2.739 × (pulse width).The model explained 86.8% of the variation in ureteral inner wall temperature ($R = 0.935$, $R^2 = 0.874$, adjusted $R^2 = 0.868$). ANOVA: $F(4,91) = 157.407$, $p < 0.001$. Durbin-Watson = 1.015, indicating slight positive autocorrelation, acceptable for an in vitro experiment. Collinearity diagnostics showed a maximum condition index of 14.795 (< 30) and a minimum eigenvalue of 0.021, suggesting no severe collinearity. Standardized residuals ranged from −2.816 to 2.816 (< ±3), with no abnormal outliers. Residual mean was close to 0, and the standard deviation was 0.979, consistent with normal distribution.Clinical interpretation. The regression coefficient for perfusion rate was −44.485 ($p < 0.001$), the strongest negative factor. When perfusion rate changed from 20 to 40 mL/min, temperature decreased by approximately 44.5 °C. The coefficient for power was +10.348 ($p < 0.001$), a significant positive factor; switching from 10 W to 20 W increased temperature by approximately 10.3 °C. The coefficient for activation time was +4.266 ($p = 0.022$); extending from 10 to 20 s increased temperature by approximately 4.3 °C. The coefficient for pulse width was +2.739

($p = 0.138$), not statistically significant, confirming no difference between long and short pulse widths.

4.Discussion

Holmium laser lithotripsy has the characteristics of good directionality, excellent lithotripsy effect on various types of stones, and relative safety. It has become one of the commonly used lithotripsy methods in clinical practice [7]. However, the heat generated by the laser may cause protein denaturation, genetic damage, and ultimately lead to the death of urothelial cells [8]. Studies have found that the laser power setting during the operation and laser thermal damage are considered important risk factors for the occurrence of ureteral stenosis [9,10]. The thermal damage of holmium laser lithotripsy has attracted much attention in clinical practice.

This study and previous reports found: (1) During holmium laser lithotripsy, the perfusion speed is a crucial factor. In our study, we used perfusion speeds of 20 mL/min and 40 mL/min, and measured the temperature using different parameters and excitation times of holmium laser. We found that as the perfusion speed increased, the maximum temperature reached during the holmium laser excitation process decreased significantly. (2) The synergistic effect of power and frequency in holmium laser lithotripsy: Different energy and frequency combinations will significantly affect the lithotripsy volume. Generally, the “high energy low frequency” mode has higher pulse energy, and after laser focusing, it can generate a high-energy-density beam, causing rapid and intense thermal expansion and/or physical stress on local stones, resulting in local fragmentation and forming larger fragments, thus being more suitable for “fragmentation” lithotripsy. While the “low energy high frequency” mode has lower energy and produces smaller stone fragments, which is more suitable for “powderization” lithotripsy. Jiang Shuangjian et al. established an in vitro model of holmium laser thermal effect and set up low-frequency high-energy and high-frequency low-energy power configurations and measured the changes in water temperature in each group. They found that under the same power conditions, the energy output configuration of high-frequency low-energy would produce more heat than that of low-frequency high-energy [6]. Therefore, in ureteral lithotripsy, it is advisable to avoid using “high-frequency” laser parameters. (3) The amplification effect of obstruction (turbulence): The holmium laser pulse wave has peaks, a wide energy distribution, and larger bubbles, which have a significant impact on stone displacement. The displacement of stones will weaken the laser response and reduce the thermal effect. In the obstruction model, due to the obstruction of water flow and turbulence, the temperature rise caused by the same laser parameters is much higher than the results of previous non-obstruction models. This directly explains why the risk is higher when dealing with incarcerated stones in clinical practice. Similar studies in the past have shown that Winship B et al. found that if the lithotripsy reaches a high temperature during laser lithotripsy, as the laser stops, the temperature will quickly return to a safe level [11]. (4) Increasing the perfusion flow rate: The perfusion flow rate should be sufficient to maintain clear vision and reduce local temperature. Increasing the irrigation fluid flow rate is a commonly used clinical method, but it is necessary to note that the irrigation fluid flushing pressure will increase accordingly with the flow rate.

Although the academic community has recognized that laser activation can cause an increase in liquid temperature and there are records of ureteral thermal damage [12,13,14], there is still a lack of clear guidance on how to select safe laser parameters. Most previous studies focused on measuring the temperature of the fluid in the lumen [15]. Although this detection method is relatively simple in

experimental operation, it should be noted that the actual temperature in the ureteral tissue is the key factor that triggers complications and pathological changes. According to the principle of heat conduction, the heat generated in the lumen by laser activation will cause the temperature on the inner side of the ureteral wall to reach a peak, while the temperature on the outer side will be relatively lower. And previous experimental studies were mostly non-animal models, which could not well reflect the true situation of holmium laser thermal effect. We have proposed some feasible suggestions to reduce thermal damage during ureteroscopic holmium laser lithotripsy. (1) Under the premise of ensuring the efficiency of lithotripsy, it is recommended to use a low-power setting for the lithotripsy. Generally, a low-power setting is sufficient to crush most of the stones. It is recommended that the power setting of most equipment should not exceed 20 watts. (2) Avoid excessive laser excitation time: Experimental results show that when the irrigation fluid is insufficient to completely remove the heat generated by holmium laser lithotripsy, the temperature will increase with the increase of laser excitation time, thereby increasing the risk of ureteral thermal damage. In this study, an in vitro pig ureteral stone model was established for holmium laser lithotripsy experiments to evaluate the thermal effect of holmium laser in ureteroscopic laser lithotripsy and the protective effect of liquid irrigation perfusion. Based on the experimental results, the temperature increase caused by holmium laser excitation is affected by multiple factors such as laser power, excitation duration, liquid perfusion flow rate, and laser pulse width type. High-power lasers can cause a rapid increase in temperature. The longer the holmium laser excitation time, the higher the temperature. A high liquid perfusion flow rate can better remove the heat generated by the holmium laser thermal effect and control the temperature of the ureteral inner wall. Under the same conditions, the thermal effect of holmium laser in the short pulse width mode is more significant.

This study has several shortcomings due to the design and conditions of the experiment: (1) Although we used fresh pig renal ureter disarticulated tissues, the isolated tissues lack blood perfusion and are at the environmental temperature, so the tissue temperature cannot represent the actual value in the human body; (2) The pig ureter and the human ureter have inherent differences in anatomy and physiology; (3) In this study, the temperature measurement point was fixed on the ureteral inner wall. Although it can almost represent the laser effect on the ureter during lithotripsy from the measurement position, the actual heat is unevenly distributed.

Based on the results and limitations of this study, if the relevant verification can be further conducted in live animal models, it can truly reflect the laser thermal effect problem in clinical practice; in addition, in clinical work, it is hoped to have an intraoperative real-time temperature monitoring system to protect against ureteral damage. Currently, temperature monitoring devices for surgical control have been clinically applied in ureteral soft scopes. Wang Xiaofu et al. [16] retrospectively analyzed the perioperative bleeding and inflammatory indicators, stone clearance rate, complication rate, and renal function of the control group and the conventional surgery group in the temperature-controlled pressure surgery group, and found that for upper urinary tract stones with a diameter of ≤ 2.5 cm, the intelligent temperature-controlled pressure ureteral soft scope combined with negative pressure suction sheath lithotripsy had satisfactory stone clearance rate and fewer postoperative complications; the next step of the study will conduct a correlation analysis of intraoperative laser parameters, perfusion volume, and the incidence of ureteral stenosis after surgery to obtain the safe mode of lithotripsy parameters, which is also our future research goal.

In conclusion, we found that high power, long holmium laser excitation time, low perfusion flow rate, and short pulse width mode can cause a significant increase in the temperature of the ureteral inner wall. The regression model constructed in this study can predict the temperature under different parameter combinations and provide a reference for clinical parameter setting. A perfusion rate of 40 mL/min maintained temperature below the 43 °C safety threshold in all tested conditions. A low-power (10 W) setting is recommended, with escalation to 20 W only if needed. Long or short pulse width can be selected based on fragmentation efficiency without concern for thermal damage.

Declarations

Funding: This work was supported by the Capital's Funds for Health Improvement and Research (2024-3-7036), the Beijing University of Chinese Medicine Third Affiliated Hospital Medical-Engineering Cross-Disciplinary Project (2025-YJKT-YGJC-11), and the Hebei Province Traditional Chinese Medicine Scientific Research Project Plan (B2025024).

Conflict of interest: The authors declare no competing interests.

Ethics approval: Not applicable. This in vitro study used slaughterhouse-derived porcine organs; no live animals or human participants were involved.

Informed consent: All authors have given their consent for the publication of this article.

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

Author contributions:WZ and XL were responsible for the study's conceptualization and design. DL and SY performed the in vitro model establishment and data acquisition. XM and YD conducted the temperature measurements and data curation. XW and CH performed the statistical analysis and interpretation. DC and JY provided technical support and resources. WZ drafted the manuscript. XL critically revised the manuscript for important intellectual content and supervised the entire study. All authors have read and approved the final manuscript.

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Figure Legends

Fig. 1 Schematic diagram of the holmium laser lithotripsy model for ureteral calculi

Fig. 2 Experimental images of the model for holmium laser lithotripsy of ureteral calculi. A Incision placement of the stone: (a) the stone; (b) the temperature measurement line; (c) the metal temperature measurement point at the end of the temperature measurement line. B Position of the stone and the temperature measurement point. C Suturing and fixation of the temperature measurement point. D Position of the stone and the temperature measurement point under the ureteroscope: (d) the suturing point at the temperature measurement point. E Holmium laser lithotripsy model for ureteral stones. F One-time electrically controlled suction perfusion catheter

Fig. 3 Maximum temperature under different laser modes and perfusion flow rates. The dashed line indicates the 43 °C safety threshold