BASIC SCIENCE

Effects of water cooling on laser-induced thermal damage in rat hepatectomy

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Abstract

Purpose: High-powered lasers are commonly used for tissue resection in surgeries, including liver resection, medically known as hepatectomy; however, such lasers inevitably induce thermal damage that causes postoperative complications. This study aims to explore the effects of water cooling and different laser output modes on laser-induced thermal damage during hepatectomy.

Methods: To avoid the influence of superposition, a 980-nm diode laser was used for a single-point hepatectomy. Eighteen Sprague–Dawley rats were used to explore the effects of water cooling and different laser output modes. A constant energy 10-J laser was used to cut the liver tissue with a power of 10 W and time of 1 second. The rats were randomly divided into six groups. The first three groups were assigned as test subjects for different laser output modes. Group 1 was operated with a continuous laser output for a duration of 1 second. Groups 2 and 3 were operated with a pulsed laser output for a duration of 1 second and a pulse width of 0.5 and 0.25 seconds, respectively. Groups 4, 5, and 6 were assigned for the water cooling test. Water cooling was performed based on the parameters of the first three groups. Medical saline (0.9% NaCl) was used for water cooling. The main observation indicators were resection efficiency and thermal damage, including the area of the thermal damage zone. Resection efficiency is calculated by dividing the resection area by the total thermal damage area.

Results: In the three water cooling groups, the area of the resection, carbonized, sub-boiling coagulated, and total thermal damage zones were 0.0677, 0.00, 1.7293, and 2.2982 mm^2 in Group 4; 0.0465, 0.00, 1.3205, and 1.8414 mm^2 in Group 5; and 0.0565, 0.00, 1.4301, and 1.9650 mm^2 in Group 6, respectively. Compared with the first three groups, the water cooling groups exhibited significantly reduced thermal damage areas of in the carbonized, sub-boiling coagulated, and total thermal damage zones ($p < 0.001$ for all). In addition, there was no statistical difference in the resection area, vacuolated area, and resection efficiency. Furthermore, there was no statistical difference in the area of each thermal damage zone between the continuous and pulsed output groups. The resection efficiencies were 4.82%, 3.34%, 3.73%, 3.93%, 3.36%, and 3.01% in Groups 1 to 6, respectively. Moreover, there was no statistical difference ($p > 0.05$) in the resection efficiencies.

Conclusion: Water cooling can reduce the total laser-induced thermal damage area and prevent tissue carbonization. Therefore, this cooling method can be used as a simple and safe strategy for controlling thermal damage during hepatectomy.

INTRODUCTION

As a useful surgical equipment, lasers have been successfully employed in many surgical fields such as dermatology,[1–3] general surgery,[4–6] neurosurgery,[7,8] ophthalmology,[9,10] and urology.[11–13] Surgery for organ resection relies on high-power lasers, which cause corresponding thermal damage during various procedures, such as liver surgery.[6,14,15] Alagha et al.[6] demonstrated that thermal effects increased with increasing power for both laser modes, and histological evaluation revealed thermal effects, a narrow vacuolization zone, and negligible carbonization for higher power values. Andreas et al.[14] also revealed that thermal damage can occur when lasers are used for liver resection. Thermal damage behaves differently according to different parameters. At a 120-W laser power, the average vaporization zone and average solidification width were the largest (664.6 ± 5.9 and 375.6 ± 2.3 μm, respectively). Thermal injuries have been studied in other surgical procedures, such as vaporization of the prostate,[16] partial kidney resection,[17] and brain tissue ablation.[18]

Lasers can resect soft tissue mainly based on laser energy. They are among the most important means of surgical resection and are used in high-frequency electrosurgery and as ultrasonic scalpels. Laser-induced thermal liver damage may delay incision healing, cause blockage of liver blood flow, and cause partial liver necrosis.[19,20] In severe cases, it can cause liver necrosis, liver failure, and even death. Effective thermal damage control during liver surgery is of great importance. The focus of this study is on tissue resection and not on tissue ablation. Therefore, it is necessary to pay attention to the thermal damage. The principles of energy ablation and energy resection have always been considered to be similar. However, surgical resection requires the removal of the diseased tissue while minimizing damage to the remaining tissue to facilitate postoperative recovery.

In several studies, controlling the thermal damage has become the focus of laser surgery. Currently, there are several strategies to control thermal damage, including adjusting the laser output parameters, air flow, cryogen spray, and use of liquids such as glycerin and water, which are applied to different surgical scenarios. Alagha et al.[6] reported that the thermal damage can be reduced by the proper choice of laser wavelengths and laser parameter adjustment to prevent damage to healthy tissues. However, changing the wavelength is impractical for a particular laser. Aljekhedab et al.[21] demonstrated that ultrafast laser ablation of bone can be more efficient and has better surface qualities if assisted by a blowing air jet. In addition, water cooling during oral pulp and soft tissue surgery can reduce the temperature to avoid possible thermal damage and facilitate the spread of heat.[22,23] Similarly, Leung et al.[24] reported that the direct instillation of small volumes of cold liquid into the esophagus can effectively decrease the esophageal damage caused by atrial ablation. However, research and application of related cooling methods in hepatectomy are rare.

Based on professional theory and surgical techniques of hepatectomy, intraoperative changing of the laser output mode and water cooling may be used as a promising, safe, and fast thermal damage control method. Changing the laser output parameters involves adjustments of laser power, mode, pulse widths, and repetition frequencies in the pulsed mode. Water cooling is the continuous instillation of normal saline solution during a laser hepatectomy. Our previous studies demonstrated that thermal damage also increases with increasing laser output power.[25] Therefore, the output power should be adjusted to as low as possible to achieve similar cutting effects. At the same output power, the thermal damage caused by changes in the quasi-continuous wave (QCW) mode is not statistically significant, which may be due to the superimposed effect of the pulsed laser during the entire operation. To avoid the superimposing effect of the laser energy and more intuitively observe the effect of the two thermal damage control methods in liver resection, this study employs unit time in liver resection as the core surgical procedure, which is referred to as the single-point liver resection. The purpose of this study is to explore the effects of different laser output modes and water cooling on the thermal damage caused during laser single-point liver resection.

MATERIALS AND METHODS

This study was conducted based on relevant regulations for the Care and Use of Laboratory Animals in the Health Science Center of Xi'an Jiaotong University, China, and was approved by the Animal Experiment Ethics Committee of Xi'an Jiaotong University (No. XJTULAC2018-557). Figure 1 depicts a detailed schematic of the procedure followed in this study.

Hepatectomy procedure

Eighteen male Sprague–Dawley rats, weighing 280 ± 20 g, were procured from the Experimental Animal Center of Xi'an Jiaotong University, Xi'an, China. The rats were anesthetized via isoflurane inhalation after fasting for 12 hours, including anesthesia induction and maintenance. After fixation on the operation table, the rats were shaved and disinfected. After laparotomy along the midline, each larger lobe was sequentially exposed, and four cutting
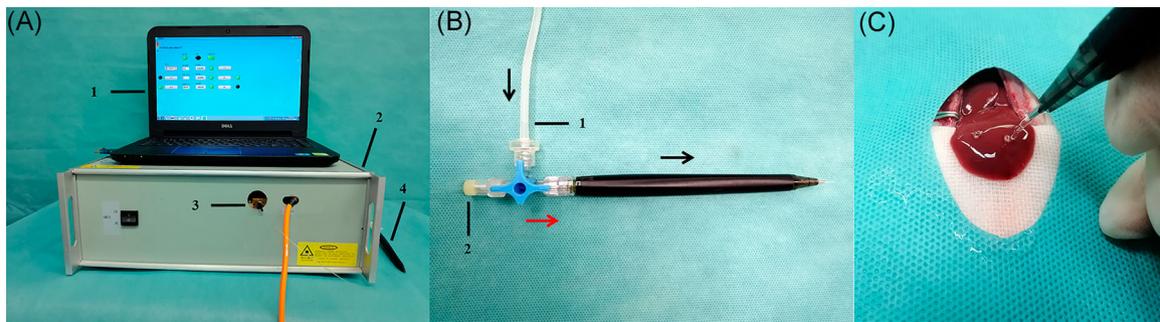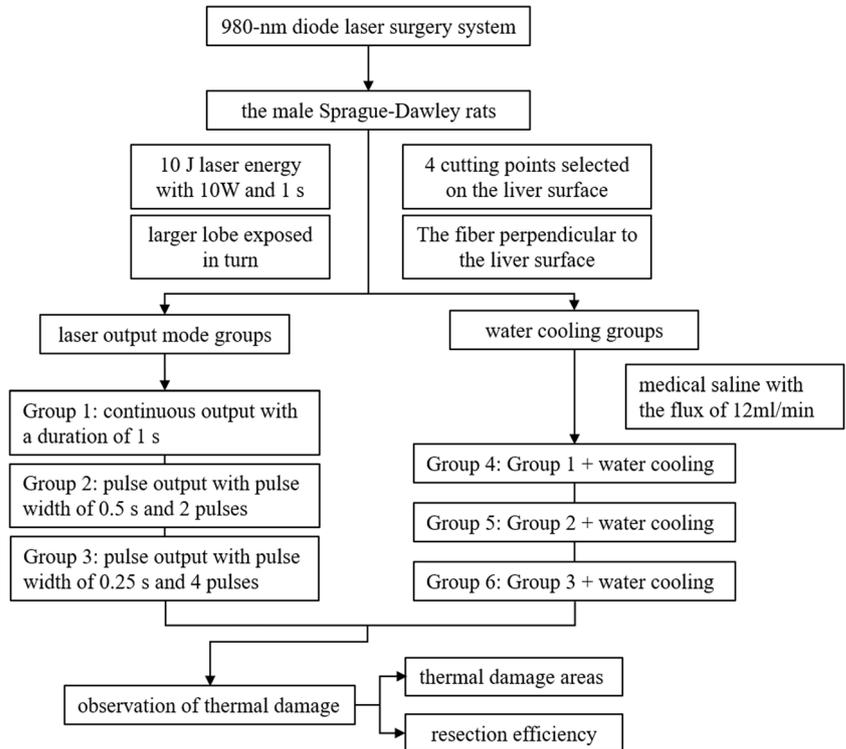
FIGURE 1 Detailed procedure schematic

FIGURE 2 Laser system and surgical procedure. (A) Laser system used in this study: "1" laser control panel; "2" 980-nm diode laser; "3" laser output and transmission fiber; "4" device for fixing the fiber; (B) device for fixing the fiber used in this study: "1" tube for medical saline; "2" transmission fiber; "red arrow" laser output direction; "black arrow" saline flow direction; (C) Intraoperative laser single-point hepatectomy with water cooling

points were selected for each liver lobe. The positions of the four cutting points were relatively fixed. Two cutting points were evenly selected on the transverse line of the distal quarter perpendicular to the liver lobe, and the other two points were at the corresponding positions of the transverse line of the proximal quarter.

Laser surgery device

Liver resection was performed using a 980-nm diode laser (FL-JGRZ01-30-976-400; Focuslight Technologies Inc.). The maximum peak power of the laser device is 30 W. The system, working in continuous wave (CW) and QCW

modes, was equipped with a 3-m flat-cut bare-ended quartz fiber (FL-FP03-SH/B-400/440-0.22-S-3M-N; Focuslight Technologies Inc.) to transmit the laser, with a core diameter of 400 μm. Before each laser application, the distal end of the fiber was checked for irregularities (in case of being broken or burned) and polished when necessary. Figure 2 displays the laser system used, water cooling device, single-point liver resection procedures, with a power of 10 W in CW mode, and the water cooling procedure. The water cooling device was specially designed for this study, as shown in Figure 2B. The red arrow indicates the insertion direction of the silica fiber, and the black arrow indicates the water flow direction. The flux was set to 12 ml/min.

Study design

To explore different laser-induced thermal damage control methods in liver resection, this study used a constant energy 10-J laser, with a power of 10 W and a time of 1 second, to cut liver tissues by adjusting the laser output mode or adding water during the operation. To observe the effects more clearly, a single point of resection and a unit time of 1 second were selected. The rats were randomly divided into six groups. Group 1 was assigned as the laser continuous output group (CW group) with a duration of 1 second. Groups 2 and 3 were assigned as the laser pulse outputs (QCW group) with a total time of 1 second. The pulse width used on the CW group was 0.5 seconds with two pulses. For the QCW group, the pulse width was 0.25 seconds with four pulses. Groups 4, 5, and 6 were assigned as the water cooling groups, to which water cooling was applied on the basis of the first three groups. Medical saline (0.9% NaCl) at a flow rate of 12 ml/min, controlled by a medical micro-infusion pump, was used for cooling. The specific groups and thermal damage control methods used in this study are listed in Table 1.

Observation of thermal damage

In our previous study, we explored the effects of different 980-nm diode laser parameters in hepatectomy.[25] Based on this, the main observation indicators of the study were resection efficiency and thermal damage in different methods, including each area of the thermal damage zone, seeking a more reasonable and safe thermal damage control strategy. Thermal damage was evaluated using a histological specimen, hematoxylin-eosin (HE) stain, to obtain the thermal damage area of each zone. Resection efficiency was calculated using the following formula: resection area/ total thermal damage area, where area is in mm^2. The thermal damage caused by the laser liver resection comprises three areas: the carbonized, vacuolated, and subboiling coagulated zones, with the deeper area being normal tissue.

Data analysis

Continuous data were tested using the Kolmogorov −Smirnov test for normality. Normally and abnormally distributed variables are expressed as mean ± standard deviation (SD) and median (interquartile range) and were compared using Student's t test and Mann −Whitney rank-sum test, respectively. Statistical significance was set at $p < 0.05$, and all hypothesis tests were two-sided. All statistical analyses were performed using the SPSS Statistics software (version 25.0; IBM Corporation).

RESULTS

In this study, Sprague–Dawley rats were used to explore the effects of different laser output modes and water cooling in reducing the thermal damage caused by lasers. The results presented herei include a comparison of the resection efficiency and different areas of thermal injury in the different models.

Overall manifestations of thermal damage

Figure 3 displays two examples of HE-stained sections under Group 1 and Group 4 settings. The thermal damage caused by laser single-point ablation is depicted in the slice as follows: "1" resection zone, "2" carbonized zone, "3" vacuolated zone, "4" subboiling coagulated zone, and "5" normal liver tissue. The classic pathological stratification of thermal damage is shown in Figure 3A, however, an obvious carbonized area is not shown in Figure 3B, probably because of the addition of water cooling to stop the appearance of the carbonized zone.

Changing the laser output mode

The mean values of the thermal damage areas for different laser output settings are depicted in Figure 4.

TABLE 1 The specific groups and the methods of controlling thermal damage used

Groups	Energy (J)	Peak power (W)	Pulse width (s)	Frequency (Hz)	Total duration (s)	Water cooling
1	10	10	-	-	1	No
2	10	10	0.50	1	2	No
3	10	10	0.25	2	2	No
4	10	10	-	-	1	Yes
5	10	10	0.50	1	2	Yes
6	10	10	0.25	2	2	Yes

FIGURE 3 Examples of an HE-stained section induced by a power of 10 W in CW mode with or without water cooling. Thermal damage zone of a single-point liver section (magnification, ×40). "1" resection zone, "2" carbonized zone, "3" vacuolated zone, "4" subboiling coagulated zone, and "5" normal liver tissue. Sample (A) without and (B) with water cooling. HE, hematoxylin-eosin
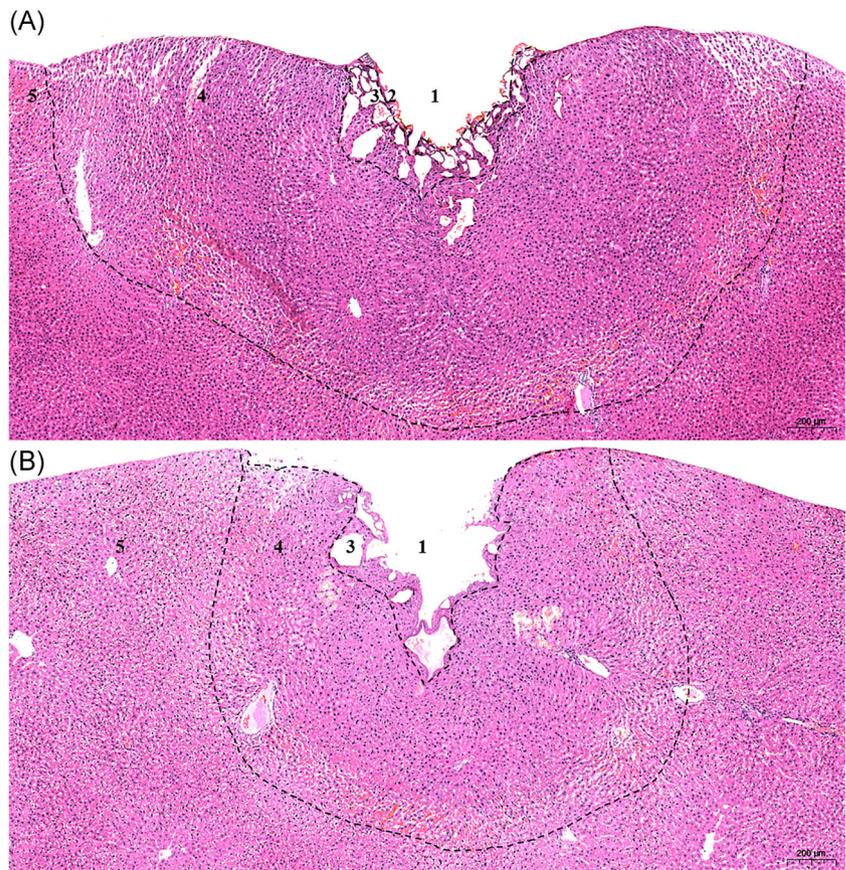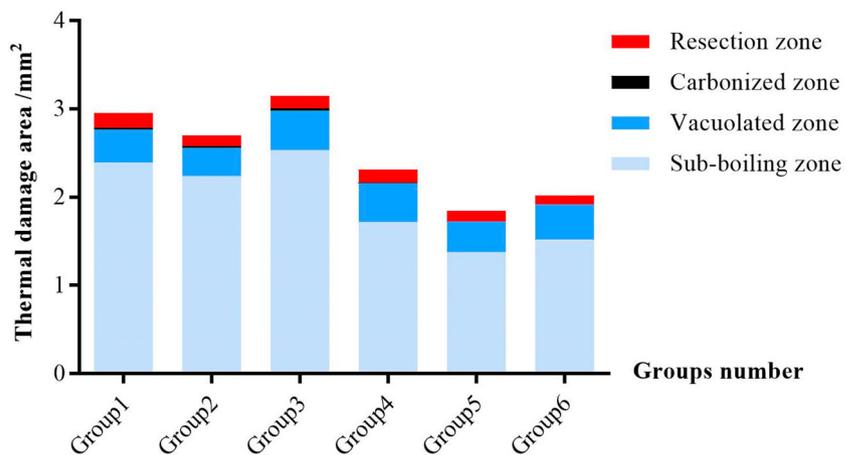

FIGURE 4 Thermal damage control by changing the laser output mode and water cooling during operation. Groups 1 to 3 had different laser output modes. Groups 4 to 6 applied water-cooling based on parameter adjustment during operation.

The median areas of the resection zone, carbonized zone, vacuolated zone, subboiling coagulated zone, and total thermal damage were 0.1545, 0.0234, 0.3567, 2.3094, and 2.9559 mm^2 in Group 1; 0.0851, 0.01651, 0.3091, 2.3012, and 2.8400 mm^2 in Group 2; and 0.1041, 0.0211, 0.3977, 2.4330, and 3.0474 mm^2 in Group 3, respectively. There was no statistical difference in the area of each thermal damage zone between Groups 1 and 2 ($p > 0.05$) or between Groups 1 and 3 ($p > 0.05$). The resection efficiency was 4.82% (0.53%, 8.22%), 3.34% (0.30%, 6.92%), and 3.73% (0.50%, 6.84%), respectively, and there was no statistical difference between Groups 1 and 2 ($p = 0.397$) and between Group 1 and Group 3 ($p = 0.509$). Therefore, it may be unreasonable to control the degree of thermal damage by changing the laser output mode in single-point resection.

Water cooling during operation

Figure 4 displays the thermal damage control results via the addition of water, which are listed in the different zones in terms of their respective areas. In the three groups, the areas of the resection, carbonized,

TABLE 2 Resection efficiency of changing output mode and water cooling by laser

Groups	Resection efficiency, median (IQR)	p Values
1	4.82% (0.53%, 8.22%)	0.962
4	3.93% (0.00%, 10.21%)	
2	3.34% (0.30%, 6.92%)	0.207
5	3.36% (0.91%, 11.23%)	
3	3.73% (0.50%, 6.84%)	0.792
6	3.01% (0.39%, 8.41%)	

Abbreviation: IQR, interquartile range.

vacuolated, subboiling coagulated, and total thermal damage zones were 0.0677, 0.00, 0.3941, 1.7293, and 2.2982 mm^2 in Group 4; 0.0465, 0.00, 0.3185, 1.3205, and 1.8412 mm^2 in Group 5; and 0.0565, 0.00, 0.3772, 1.4301, and 1.9650 mm^2 in Group 6, respectively. There were statistically significant differences in the areas of the carbonized zone ($p < 0.001$), subboiling coagulated zone ($p < 0.001$), and total thermal damage zone ($p < 0.001$) between Groups 1 and 4. These differences in the three zones were also statistically significant between Groups 2 and 5 and between Groups 3 and 6 ($p < 0.001$ for all). In the comparison of these groups, there was no statistical difference between the resected and vacuolated areas. The resection efficiency, as listed in Table 2, is 3.93% (0.00%, 10.21%) in Group 4, 3.36% (0.91%, 11.23%) in Group 5, and 3.01% (0.39% and 8.41%) in Group 6. There was no statistical difference between Groups 1 and 4 ($p = 0.962$), Groups 2 and 5 ($p = 0.207$), and Groups 3 and 6 ($p = 0.792$). In other words, adding water while performing laser surgery does not reduce the resection efficiency by controlling thermal damage.

In summary, there is no evidence in the current study that changing the laser output mode during surgery can control thermal damage. Water cooling during the operation can reduce the thermal damage without reducing the efficiency of single-point ablation.

DISCUSSION

Lasers have been successfully used in liver surgeries, whether in animal experiments or clinical trials, mainly because of their high selectivity and precision.[4,5,14,26–28] However, for laser surgery, certain thermal effects can result in resection or ablation of the tissue, and excessive thermal damage may cause serious clinical consequences. Therefore, it is necessary to strictly control the thermal damage caused by lasers during surgeries. Based on the results of this study, intraoperative water cooling has proven to be a promising thermal damage control method, which is of great significance for the clinical application of lasers in hepatectomy.

Histological analysis is an accepted method for assessing the status of cells and tissues during thermal damage. The resection area is expressed as the defect area in the slice. Slice quality issues, such as image distortion, can be avoided or reduced using the following process: first, ensure the normal shape of the sample during sample acquisition, fixation, and wax block embedding; second, the wax tape should be naturally flattened during slicing and patching, and there should be two wax tapes on the same section; finally, the quality of the slices should be checked when sealing the slices after HE staining, and unqualified slices should be discarded. The entire process was performed according to the standard pathological section process. During the slice-reading process, incomplete or folded slices were discarded. The reading process was completed under the guidance of a Pathology Professor from Xi'an Jiaotong University. The built-in module of the microscope was used to delineate the resection area to ensure the authenticity and reproducibility of the data. It was necessary to select the densest points possible according to the edge of the resection area to completely delineate the area. Each area was delineated three times to obtain the average area.

The five common thermal damage reduction methods mentioned previously have their own advantages, disadvantages, and application scenarios, which are mainly divided into two categories: internal control methods and external cooling methods. Stephan et al.[29] demonstrated that in the chosen settings, the pulsed Tm:YAG laser created less carbonization than the CW Tm:YAG laser, less trauma than the Ho:YAG laser, and it featured the most controllable behavior with an evenly increasing incision depth and laser damage zone with increasing laser power. This indicates that the pulsed mode mitigates thermal damage to some extent. For the internal control methods, changing the laser output mode is preferred. Traditionally, there has been less thermal damage in the QCW mode. The theory is based on the fact that higher peak powers, such as the megawatt level, and narrower pulse-widths, such as the femtosecond level in the QCW mode, will be sharper when used as surgical instruments. In this way, if the acting time on the same part of the tissue is shorter, naturally, the thermal damage will be smaller, which has a unique advantage in terms of lack of blood supply to organs or tissues. For the blood-rich liver, appropriately increasing the pulse width and decreasing the sharpness is helpful in achieving hemostasis during the operation to ensure a safe procedure. In terms of basic research, we also performed liver resection in rats using a femtosecond laser and discovered no thermal damage. Liver cross-sections bleed easily. This is because the laser has a high single-pulse energy at the pulse output, similar to a sharp scalpel. The results of this study indicate that changing the laser output mode does not reduce thermal damage. These results depend on the pulse interval as well as the pulse width. Therefore, cooling through pulse pauses was

not sufficient to reduce the thermal damage. If this interval is extended, thermal damage reduction can be achieved. However, for complex liver resections, the operation time is longer, thus, extending the pulse interval is impractical.

For external cooling methods, air, water, and cryogen spray are more commonly used as opposed to glycerol. Kirschbaum et al.[30] achieved thermal injury mitigation via local perfusion of the lungs. Heat emission to the environment surpasses heat reduction via perfusion in nonanatomically laser-resected lung lobes. This method enables a longer time to reach a tissue damage temperature of greater than 42°C as a surrogate marker for tissue damage. This is a promising topical cooling method. In addition, to prevent such thermal damage, sufficient time should be provided for spontaneous tissue cooling before additional laser application. The most effective cooling strategy against heat accumulation is submerging the target area in ice-cold water for at least 5 seconds during lung resection.[31] In laser dermatology, cryogen spray cooling has been used to protect the epidermis from unwanted thermal damage.[32–35] Chang et al.[36] demonstrated that glycerol can improve the energy deposition in the endopelvic fascia to reduce unnecessary thermal damage during laser treatment of female stress urinary incontinence. These methods are more effective for liquid cooling. The liver is located in the abdominal cavity. For liver resection, the liquid material for liquid cooling must be carefully selected to avoid adverse effects on the surrounding tissues. Water cooling is a thermal damage control method that is worth exploring. The results indicate that regardless of the laser output mode, water cooling can reduce thermal damage, which is mainly reflected in the areas of the carbonized, subboiling coagulated, and total thermal damage zones, and does not change the resection area and resection efficiency. Compared to changing the laser output mode, water cooling is an instant cooling method. Therefore, intraoperative water cooling can be used as a reliable thermal damage control strategy, which not only conforms to human physiological rules but is also easy to operate. Water cooling can reduce the thermal damage while absorbing energy to increase the water temperature, which may cause further damage to the surrounding tissue. In this study, no thermal damage to the surrounding tissue was observed, except for thermal damage to the laser-cut surface. Monitoring and controlling the water temperature are also very important. Therefore, surgical safety should be ensured.

This study has some limitations. The study demonstrated that water cooling is effective in controlling the overall thermal damage through the carbonized and subboiling coagulated zones. However, the vacuolated area was not affected. Reducing the vacuolated area may further control thermal damage, but it would require further research. Our future research will focus on the specific thermal damage reduction performance of water cooling, including the time effect of water cooling, flow rate changes, concentration changes, and water temperature. However, this method has limitations in that it assesses the status of cells and tissues. To a certain extent, the thermal damage calculation may be inaccurate. We minimize this inaccuracy as much as possible with the procedure presented in the Methods section and, at the same time, appropriately increasing the sample size. In addition, to determine whether this water cooling method is effective, a single-point resection method was used to avoid the heat superposition effect in the liver resection mode. The comprehensive effects of liver resection need to be clarified further.

CONCLUSION

This study aimed to explore the effects of changing the laser output power and water cooling on the thermal damage caused during laser single-point liver resections. The results indicated that controlling thermal damage by changing the laser output mode during laser liver resection was not effective. Water cooling could obviously reduce the carbonized layer and total thermal damage area, which can be used as a simple and safe strategy for thermal damage control during operation. Methods to reduce the vacuolated area should be further studied to further reduce thermal damage.

AUTHOR CONTRIBUTIONS

The authors confirm contribution to the paper as follows: *conceptualization*: Tao Ma and Yi Lv; *methodology*: Dinghui Dong and Shasha Wei; *experiment implementation*: Liyu Shan, Huan Chen, and Rongfeng Wang; *data analysis*: Liyu Shan and Tao Ma; *writing - original draft preparation*: Liyu Shan, Yue Wang, and Rongfeng Wang; *writing - review and editing*: Yue Wang and Huan Chen; *supervision*: Tao Ma and Yi Lv.

CONFLICTS OF INTEREST
The authors declare no conflicts of interest.

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