Minimizing Invasiveness of Liver Resection Using an Integrated Tissue Ablation and Division Device With Blood Flow Sensing

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Liver cancer is the fifth most common cancer. Liver resection or hepatectomy has been performed to remove the cancerous portion of the liver organ. This paper reports an integrated surgical mechatronic device that minimizes blood loss during tissue resection and prevents excessive tissue ablation. The novel device integrates radio-frequency electrodes to induce coagulation to the blood vessels, a laser Doppler sensor to detect the stoppage of blood flow, and a retractable knife blade to divide the ablated tissue. Finite element simulation was used to improve upon the placement design of electrodes. Effectiveness of this device in reducing the invasiveness of tissue division was demonstrated with in vitro and in vivo animal experiments.
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1 Introduction

Liver cancer is the fifth most common cancer. Radio-frequency (RF) assisted methods are widely used in liver cancer treatments. Radio-frequency pulses (500 KHz) are used to induce ionic agitation and joule heating and, hence, coagulation to the liver tissue and cancerous cells [1]. Hepatectomy refers to the surgical procedure that removes partial liver tissue, which encapsulates the tumor, from the liver organ. These two processes are often performed separately. A new technique in liver resection was developed by Jiao et al. [2] to maximize the benefit of RF ablation for liver resection procedure with significant reduction in blood losses. Blood losses are associated with increased risk of postoperative complications and, hence, are undesirable [3]. The RF ablation was first performed on the desired line of resection followed by a manual resection with surgical scalpel. RF energy induces frictional heating causing coagulation for reducing blood loss while cutting.

This new technique combines the advantage of a reduction of blood loss and tumoricidal effect at the resection site without the use of sutures, surgical knots, clips, or glue. There are several advantages to the Habib technique in addition to blood loss reduction. The technique can be easily performed by a surgeon with good knowledge of liver anatomy. The technique also results in reduction of the length of the anesthetic time and the operating time.

Coagulative necrosis in liver tumor tissue takes a longer duration than that of normal tissue. According to the literature, a complete necrosis of liver tumor tissue will require about 20 min [4]. Based on our experience in the laboratory and from the literature, necrosis of normal liver tissue can be achieved in a shorter time [2]. The technique eliminates the need for intensive care unit facilities and reduces the need to employ Pringle's maneuver [4], which is often used for conventional tumor ablation for effective RF heating but results in ischemia-reperfusion hepatocellular injury. Ultimately, the technique results in less postoperative mortality and morbidity.

However, there are some limitations to Habib's technique. Firstly, radio-frequency energy should be applied carefully near the hilum or the vena cava because of its potential damaging effect on these structures. Secondly, healthy parenchymal tissue will be sacrificed for the resection procedure. Thirdly, it is not possible for the surgeon to be sure of the complete coagulation of the tissue along the cutting plane. Hence, occasional blood losses will be encountered during operation. This is evident in one of the cases done by clinical teams, and we will be offering a solution to this.

Several medical trials were done by many medical teams using the same technique. Dr. Habib and his team performed the technique on a 69-year-old gentleman with colorectal liver metastases who underwent a segment II/III liver resection following preoperative staging with spiral computed tomography (CT) scan. The segmental resection was then carried out according to the technique described above. The resection time was 45 min with a total blood loss of 30 ml during the division of the liver parenchyma. There was no morbidity in the patient and excellent recovery was observed in the patient who was discharged after 5 days.

Pellici et al. [5] conducted clinical trials on 17 patients (eight women and nine men with a mean age of 72-years-old) who underwent radio-frequency assisted liver surgery. Seven patients were affected by hepatocellular carcinoma; the other nine had colorectal liver metastases and one gastric metastases. There were no operative deaths from all 17 patients. Mean operative time was 220 min (ranging from 110 to 420 min). Mean blood loss was a very optimistic value of 53 ml (ranging from 5–150 ml) with no further devices involved (stitches, clips, tissue glue, and argon beam coagulator), but radio-frequency energy was required to get adequate hemostasis. No patient received blood transfusion, and Pringle maneuver was never required. One patient had an important intraoperative bleeding (total blood loss 150 ml) from an incompletely coagulated blood vessel, which was managed with manual compression and further RF sessions.

We report a surgical device and method that incorporates both RF ablation and hepatectomy procedures. A laser Doppler flow (LDF) sensor was embedded in the device for blood flow sensing to firstly ensure minimal blood flow prior to resection and secondly prevent excessive tissue ablation. A user interface, which displays LDF sensor data graphically, provides the surgeon with real time blood flow readings from the flowmeter and visual and audio signals when the ablated tissue is ready for resection. Finite element simulations were used to justify design parameters of radio-frequency electrode placement.

In vitro experiments were conducted on an in vitro porcine liver model with a simulated fluid circulatory system attached to the portal vein for simulating perfusion. In vivo experiments were performed on live porcine models in a laparoscopic setting to measure the reduction in blood losses and efficiency of the device.

Section 2 provides an overview of the device. Section 3 describes the ablation mechanism and the derivation of optimal electrode placement using finite element method. Sections 4 and 5

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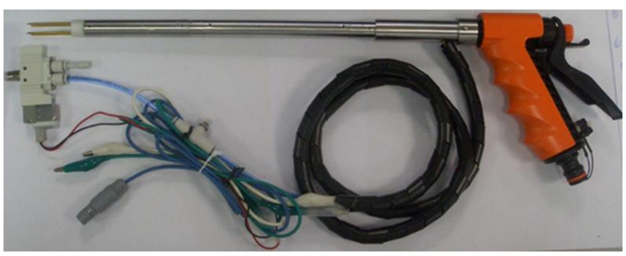
discuss the blood flow sensing and tissue division mechanism, respectively. Section 6 reports the experimental verification and validation of the prototype device. The paper is concluded with a discussion in Sec. 7.

2 Overview of Integrated Prototype Device

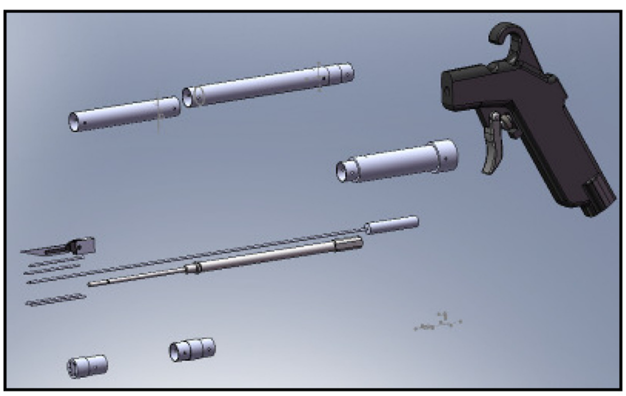
A device (Fig. 1(*a*)) was built to perform the Habib's technique in a single device. The prototype enables a laparoscopic surgical procedure and removes the need for switching of tools during surgery. A laser Doppler flow sensor was integrated for blood flow detection prior to cutting. The LDF sensor ensures minimal blood-flow in the target tissue and prevents unnecessary blood losses during resection. The sensor is connected to a computer via a data acquisition card and presents real time graphical information to the user.

A few design parameters were specified for the device. The device has to be small in diameter (15 mm) and long (30 cm) for laparoscopic surgery. A biocompatible material is required in preventing biological host response and, thus, plausible complications during surgery. Modular design was employed for the prototype, which consists of detachable components to ease the replacement of device parts. Components, which have a constant inner diameter for connection, are held down by set screws. This design allows efficient replacement of faulty or soiled parts for fast turnover time between servicing.

2.1 Material Selection and Prototype Body Design. The two biocompatible materials selected for direct contact with the liver tissue are Delrin and 304 stainless steel. Delrin, also known as Polyoxymethylene, is an engineering thermoplastic plastic approved by US Food and Drug Administration (FDA) for surgical use. This light weight material, which has good wear and high temperature resistances is suitable for use at the distal end of the device that contacts the tissue. Type 304 (AISI) stainless steel was selected for the construction of the prototype body (Fig. 1(*b*)). Type 300 series are austenitic chromium-nickel alloys that consist of lower carbon content to ease forming. The 18/8 stainless steel contains around 18 wt. % Chromium and 8 wt. % Nickel and has generally good resistance to a corrosive environment. The resistance is improved by increasing the Nickel and Chromium content. Austenitic steels are prone to corrosion especially with the presence of chloride ions. Steel corrosion is reduced with high nickel austenitic alloys.



(a)



(b)

Fig. 1 (*a*) Tissue ablation and division prototype device. (*b*) Modular design of the prototype device.

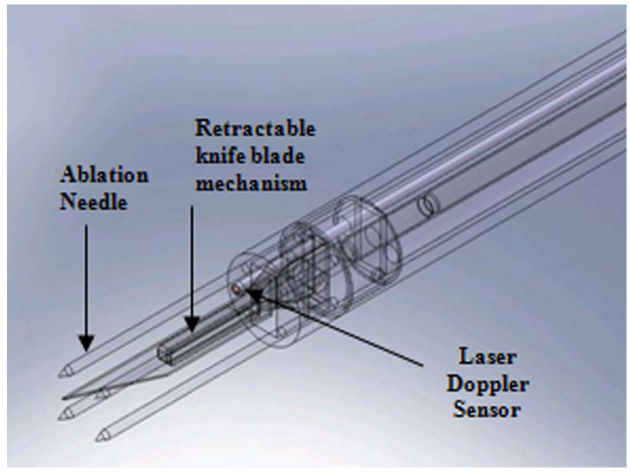


Fig. 2 Position of various parts

Design of connective steel lube is not trivial and design for assembly was done to effectively assemble all the parts without causing damage to individual components. The size of the parts also made design difficult as very small space is available for assembly.

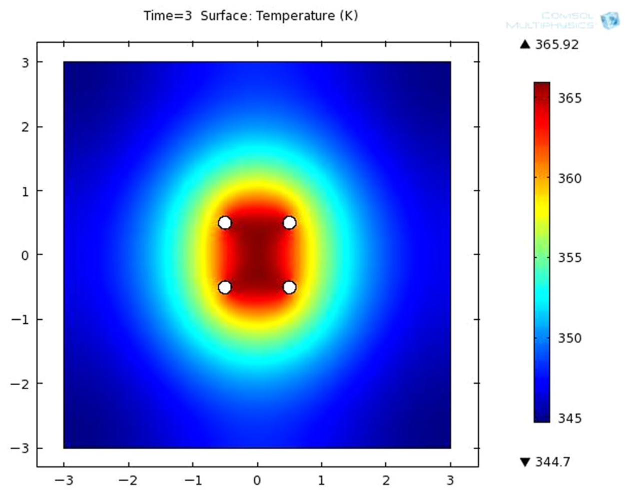
2.2 Assembly. The device was assembled into an integrated device with the three main functions: Ablation, resection, and blood flow sensing. Figure 2 shows a computer aided design 3D model of the device with various parts integrated into the laparoscopic device. A handle is attached to the prototype, which has a switch to toggle a pneumatic valve for knife blade actuation.

Sections of the tube were assembled with interference fitting as fasteners were deemed unsuitable due to their protrusion from tube surface. Interference fit also allows quick disassembly for part changes and maintenance. The laser Doppler sensor was mounted at the tip of the device with a rubber O-ring keeping it in position and providing protection. A retractable knife blade mechanism is attached to the foremost tube via a tapped screw thread. The knife blade will perform the resection in the ablation zone.

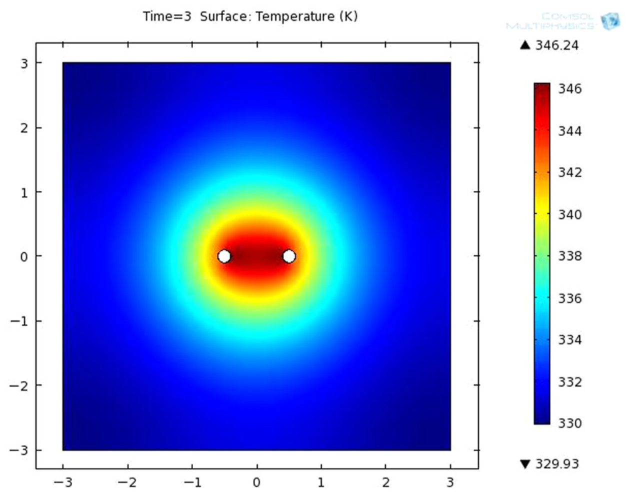
3 Ablation Mechanism and Optimal Electrodes Placement

3.1 Ablation Needles and Generator. Gold plated ablation needles were removed from an existing Habib 4x bipolar probe and fitted onto the prototype. Each ablation needle plated to reduce surface current formation and the sharp tip ensures minimal deformation prior to tissue break point. The ablation needles were connected to the Rita 1500X RF generator, a 100 W rated generator, and were set to an impedance-controlled mode during usage. Impedance controlled mode controls and stops the ablation process by sensing tissue impedance in between the RF needles.

3.2 Finite Element Simulation. Figures 3(*a*) and 3(*b*) present the temperature distribution from finite element analysis for four-electrodes and two-electrodes arrangement. The two arrangements were the only ones chosen for simulation due to the space constraint of the device. The simulation was done to investigate the optimum number of bipolar electrodes to be used. Comsol Multiphysics 4.1 was used to simulate the electric currents between the needles and, thus, the temperature distribution due to



(a)



(b)

Fig. 3 (*a*) Temperature distribution for four-electrodes RF ablation. (*b*) Temperature distribution for two-electrodes RF ablation.

RF ablation. The finite element analysis was performed as follows. Material properties were input into the program and an electric field was simulated according to the location of ablation needles and the electric power applied. The electric field generates heat in the tissue especially near the ablation needles and, hence, heat transfer to the other parts of the tissue. The joule bioheat equation was then used to simulate the temperature distribution of the tissue and its response in time. This gives us an understanding of how the burning zone will develop and aid in our placement of electrodes. The electric field distribution of the target tissue zone is governed by

$$\Delta \cdot E = \frac{\rho_c}{\varepsilon_0} \tag{1}$$

where ρ_c is the charge density, E is the electric field, and ε_0 the permittivity.

A modified Pennes bioheat equation was used for RF ablation simulation as

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot k \nabla T + J \cdot E - \rho_{bl} c_{bl} \omega_{bl} (T - T_{bl}) \tag{2}$$

where ρ is the density, c is the specific heat capacity of the material, T is the temperature, k is the thermal conductivity, J is the current density, E is the electric field, ρ_{bl} is the blood density, c_{bl} is the blood specific heat, ω_{bl} is the blood perfusion rate, and T_{bl} is the blood temperature.

Referring to the Fig. 3(*a*), the two circles on the left represent positively charged electrodes while the two on the right represent negatively charged electrodes. It can be observed that the zone of maximum temperature is between the needles and the plane perpendicular to it. This is highly desirable, as it serves as a justification for the placement and orientation of the knife blade. In addition, it aids in determining the maximum width of the knife blade. This will make sure that the cutting plane is experiencing the highest temperature and, hence, lower risk of blood flow. Higher temperature will result in higher probability of coagulation of blood. Taking into account the variability of tissue properties, a probability based finite element method was used to estimate the temperature distribution but will not be covered in detail in this paper. A general pattern of a vertical high temperature plane was observed. The four electrode design was a better choice, as it offers a larger hyperthermia area to allow a wider knife blade to be used.

4 Blood Flow Detection

Almond and Wheatley [6] investigated the performance of LDF with changes in flow characteristics in the hepatic microcirculation. Red blood cell flux measured by LDF sensor is sensitive to alterations in red blood cell velocity and concentration. It was concluded that the value of continuous real-time monitoring without perturbation of circulation is extremely valuable compared to other techniques. LDF sensor incorporates such advantages and, hence, is preferred to other blood flow monitoring technologies. The reliability, noninvasiveness, and simplicity of LDF application are also major advantages. In addition, small dimensions of

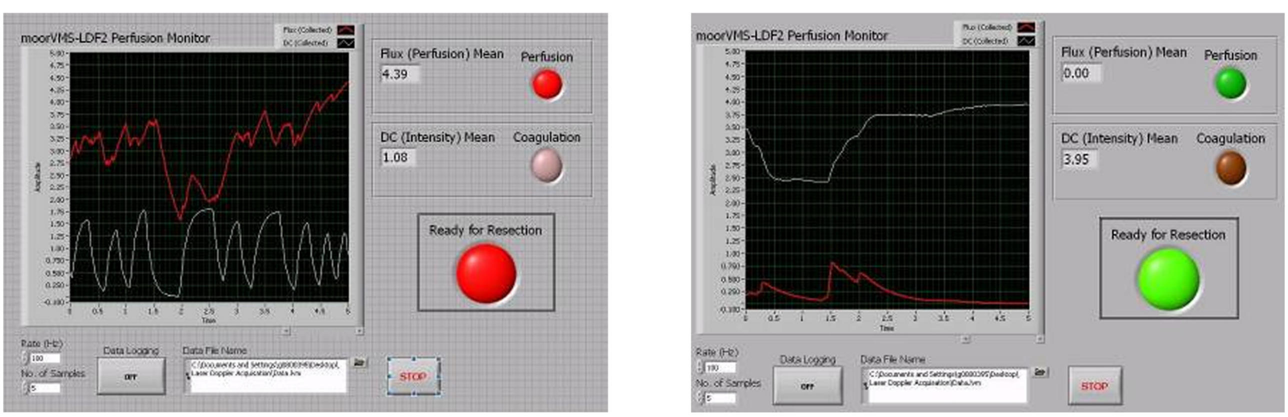


Fig. 4 User interface for LDF information display

the probe also make it suitable for our application to be integrated into a laparoscopic device.

MoorVMS-LDF2 laser Doppler blood flow meter [7] from Moor Instruments was selected for the integrated LDF. The meter has a dual channel input for two LDF optical fiber sensors to be used at any one time. The LDF optical fiber sensor is 1.5 mm in diameter with a sensing volume of 5 mm in radius. Sensor outputs low power monochromatic laser, which is safe without the need for additional protective kit. The sensor is able to sense capillary diameter of 10 μm with a flow spectrum of between 0.01 and 10 mm/s. The sensor is placed adjacent to the knife blade for blood flow detection in the cutting plane.

A data acquisition card was used to collect real time data from the laser Doppler bloodflow meter, and a computer user interface was built using LabVIEW 8.6 (Fig. 4). Real time data is presented to the surgeon with a graphical plot of the Flux and the DC value. Flux value represents the red blood cell velocity and concentration while the DC value represents the intensity of reflected laser beam. The DC was found to be able to distinguish between surfaces of different color due to the different amount of laser adsorption for each color. Hence, the DC value was used as a second confirmation of a well ablated tissue.

4.1 Calibration of Sensor. Prior to integration of the sensor, experiments were done to calibrate the sensor and relate it to fluid flow velocity. This helps the surgeon to better visualize blood flow in terms of velocity instead of the more unconventional flux unit. In addition, it will help us to decide on a value as benchmark for interface to decide if a resection action should be performed.

The experiment was performed using a PH800 Dymax aquarium pump, which was connected to a 1/4 in. valve and the outlet pressure measured with a pressure gauge. Fluids used for calibration were water (less viscous) and milk (viscosity closer to blood) pumped through a thin transparent polymer pipe of 3 mm diameter. The LDF sensor was mounted to sense for flux and DC readings with different flow velocity. Results for both water and milk were recorded and plotted (Figs. 5(*a*) and 5(*b*)).

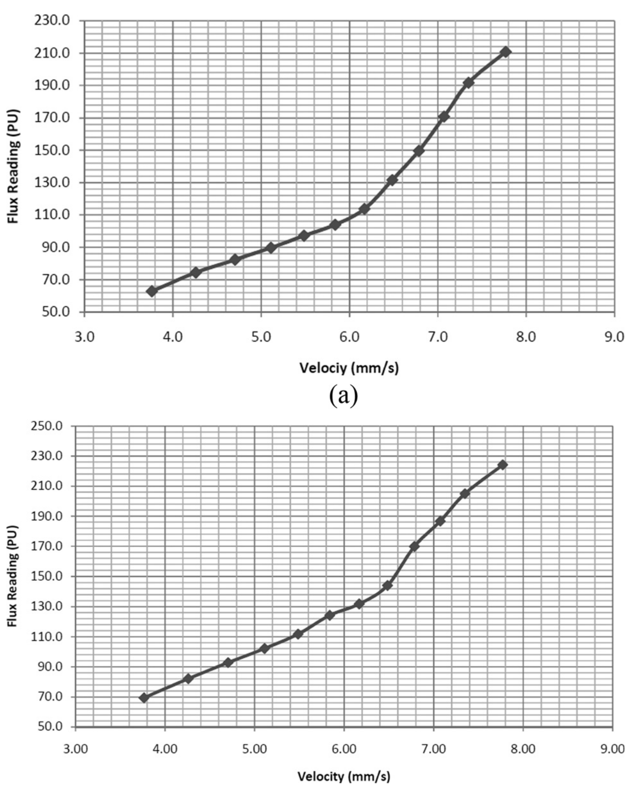


Fig. 5 (*a*) Calibration of LDF sensor with water. (*b*) Calibration of LDF sensor with milk.

Results obtained in both cases shows piecewise linear behavior between flow velocity and flux values. Piecewise linear curves can be explained due to pipe wall resistance and varying fluid boundary layers with different velocities. It was observed that the slope of the curve for milk is steeper compared to that of water due to higher viscosity.

Comparison with results obtained by Almond and Wheatley [6] done on rats hepatic perfusion of varying concentration showed consistency in the relationship between viscosity and steepness of curve. Hence, the calibration results can be used as a preliminary guideline for the LDF sensor integrated and will aid in more accurate calibration during in vivo studies.

5 Resection Mechanism

Pneumatic cylinder actuator from SMC, CDJ2B6-60SR-B, was identified as suitable for our usage. It is a single acting spring return air cylinder. The cutting blade was mounted onto the air cylinder with a blade holder. A pneumatic valve was connected to the air cylinder for the control of the actuation stroke while the return stroke is spring actuated. Pneumatic actuation was chosen as it provides the fastest actuation speed at the smallest possible size. Other alternatives such as electromagnetic actuators, spring loaded actuators, and motor driven actuators were explored and concluded to be unsuitable. A pistol handle was integrated for optimal comfort for the user with knife blade actuation lever mounted on it.

Experiments were done to investigate the effects of blade shape and thickness on cutting. Several different blades were tested, ranging from surgical blades to self-fabricated and sharpened blades. Feedback from medical staff suggests that knife cut opening visibility is an important issue during surgery, as it will facilitate placement of the device for the next cut. Tests were done on a mechanical loading setup to investigate the force required for ablated tissue penetration. Surgical blades require the least force for penetration while self-fabricated square blades require three times the force required for penetration.

The image showing the various cuts are available in Fig. 6. It is evident that the square blades (in left and center circles) give more visible cuts to the ablated liver tissue. The surgical blade, which requires less force, gives a cut with very low visibility. The square blade was chosen to be more suitable due to its better cut visibility. Cutting force is of least importance, as we are able to provide it in abundance from the pneumatic actuator.

6 Experiments

6.1 In Vitro Experiments. In vitro experiments were conducted with a liver harvested from the abattoir. An external circulation system was used to mimic the flow of blood through the liver. The circulator system comprised a fluid pump to ensure fluid

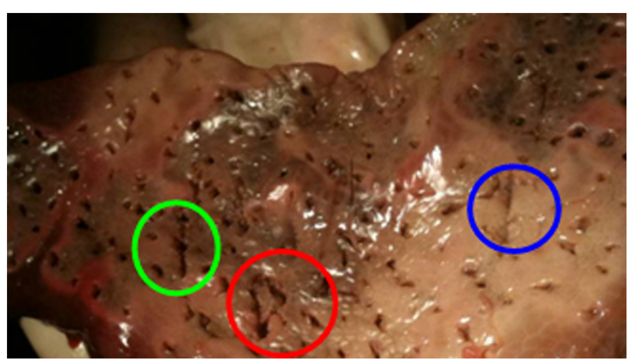


Fig. 6 Knife blade visibility. (L to R) Small square blade, large surgical blade, large square blade.

Fig. 7 Device in use during in-vivo testing

circulation through the liver test sample via the hepatic portal vein. This enables flow in the vessel of the liver specimen to better reproduce actual in vivo conditions. However, the fluid is a mixture of blood and water of a lower temperature as compared to actual blood at body temperature. Naturally occurring blood coagulation was not replicable during the device testing. Results from the device testing were satisfactory, and a good resection with minimal fluid loss was achieved. The in vitro setup lacks the actual laparoscopic environment, elements of space constraint, a pressurized interior, and actual physiological condition.

6.2 In Vivo Experiments. Animal experiment was conducted to test the new device [8]. The experiment was conducted in the Advance Surgical Training Centre (ASTC), National University Hospital of Singapore. The facility has state-of-the-art surgical setup for testing of the device (Fig. 7). Comparative study with conventional devices was performed. A left lateral liver resection was performed on a 45 kg live adult pig using the described device, and a similar procedure was performed on another porcine model using a commercially available device. A CT opaque dye gel was injected to simulate a tumor in the liver. Intraoperative blood loss and duration of resection were compared. The new device took a total of 20 min for the resection with a blood loss of 100 ml while the commercial device took 25 mins with a blood loss of 150 ml. The integrated device was sufficient for full resection with no other tool required for complete resection. Results were encouraging as the prototype managed to perform its intended task by completing the surgery in the intended time. The blood flow sensor proved to be valuable as the sensor readings encouraged the surgeon to increase the application of RF energy.

7 Discussion and Conclusion

This paper reports the design, development, and evaluation of a new surgical device for hepatectomy. An effort was made to incorporate the Habib method of liver resection using radio-frequency ablation for hepatectomy into a single device. A blood sensing laser Doppler sensor was also integrated for confirmation of blood flow stoppage. The maximum 5 mm sensing depth of the laser Doppler sensor is a limitation to the device and should be addressed in future prototypes. Several design parameters were reviewed and computer simulation was employed for better device design. Design process involves material selection for the device body, part design for mechanisms and mountings, components selection for actuator and sensors, and finally design for assembly for all the parts. Computer simulation using finite element was used to refine the design for radio-frequency electrode placement. Device testing was done in vitro on a liver sample with a fluid circulatory system connected. Good results from the device were achieved. In vivo animal experiment was conducted on two live porcine model comparing the new device to existing devices available in the market. Result from the new device was satisfactory, as it met the target for the surgical time while minimizing blood losses.

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