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Effects of crucial parameters on the freezing delivery in the cryosurgical system

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HIGHLIGHTS

- ► Study on key system parameters and their impacts on cryo-freezing performance.
- ► Pressure jump in freezing medium reduced initial freezing duration.
- ► Freezing medium flow rate markedly impacted initial freezing.
- ► Level of liquid nitrogen influenced the achievable minimum freeze temperature.

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ABSTRACT

Cryosurgery has been increasingly employed as an effective and affordable therapy to treat unresectable tumors. It is generally believed that rapid freezing, slow thawing and repeating freeze–thaw cycles improve surgical outcomes. A well-controlled freeze–thaw cycle requires the adequate regulation of these key parameters in the cryosurgical system. This study investigates key parameters that potentially enhance the temperature control of the cryoprobe. In conventional systems, the inlet pressure of the cryoprobe and the flow rate can be highly unstable under certain circumstances. These could induce significant difficulties in monitoring the real-time treatment response and analyzing their impacts on the system performance. We have proposed an enhanced system that stabilizes freezing medium's pressure and flow rate. With the enhanced system, the thermal impacts of critical parameters can be better processed and with greater accuracy. An orthogonal experiment analysis was also carried out to determine the optimal level of critical experimental factors. Key results showed that the cryoprobe freezing rate at the initial stage could be manipulated. In addition, the cooling medium flow rate was observed to be an influencing parameter on system performance. Results provided experimental evidence of parameters that promoted accuracy of the freezing delivery.

1. Introduction

Cryosurgery as an alternative therapeutic method has been known to be an effective and minimally invasive therapy to treat liver tumors by employing freezing at the cryogenic temperatures to destroy the tumorous tissue [1,2]. Compared to other treatments such as surgical excision, radiation therapy and chemotherapy, cryosurgery is relatively low cost, and induces less side effects and direct damage to the neighboring healthy tissue. Thus, it is widely applied to treat the cancerous cells of liver, lung, encephalon and bone [3–7]. Hepatic cryosurgery for the unresectable cancer treatment has been increasingly effective due to the presence of underlying disease, the presence of bilobar hepatic metastases, and anatomic location limits such as bifurcation of portal veins and confluence of hepatic veins.

Detrimental freezing does not always guarantee the complete tissue damage in the targeted area. The minimal invasive nature of cryosurgery may at times induces difficulties in controls, resulting in a large probability of recurrence [8]. To effectively apply the cryosurgical technique, it is not only essential to plan ahead of the procedure, but also to employ a reliable monitoring technique and perform the procedure with a reliable system. In this manner, cryosurgery can be employed to produces a predictable tissue response which in turns enhances the surgical success rate. The mechanism of the cellulous injury needs to be understood in order to connect the surgical process to the degree of cell destruction within the targeted region. It is generally believed that the intracellular ice plays an important role in cryoinjury by either electrical transient at the ice interface [9] or critical gradient in osmotic pressure across the membrane

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[10,11]. Many cryosurgeons consider the development of the critical temperature as the most important indicator to define the boundary of cryoinjury [12], with the conclusion that isotherm of either −50 °C or −40 °C can be taken as of the lethal temperature boundary [13–15]. Besides, the repetition of freeze–thaw cycles is well known to be effective in the treatment with a basic feature of rapid freezing and slow thawing [16–18]. Monitoring techniques in cryosurgery such as ultrasound [19] and MRI [12] are common tools in the cryosurgical process for the ice ball formation. The conventional way of determining the effectiveness of cryosurgical probes under laboratory conditions is to monitor the ice ball growth at the tip of the cryoprobe [20].

Cryoplanning involves determining essential operating parameters, adopting the appropriate monitoring technique, identifying the best positioning of the cryoprobe, and developing a well-controlled system to achieve the best surgical outcome. Although many efforts have devoted to cryoplanning [2,7,12,21], specific studies dedicated to investigating parameters that enhance the control of the cryosurgical system are limited. Basic thermal properties such as the flow rate, temperature, and pressures at essential locations in the common cryosurgical system can potentially affect the outcome of the surgery. The correlation between the system performance and the liquid level of the freezing medium ought to be judiciously investigated. Understanding these basic parameters ensures that the procedural guide of the cryoplan can be implemented with ease. Furthermore, the study of the temperature at the initial freezing is also useful to supplement accurate the initial conditions to many bioheat transfer models.

In this work, a common cryosurgical system with liquid nitrogen was experimentally studied using *in-vitro* porcine liver samples. The performance of the two cryosurgical systems was presented and several key parameters were compared. The new system incorporating thermal stabilization devices was tested under constant flow rate and of passive control conditions.

2. Methods

2.1. Experimental setup

A schematic diagram of the experimental setup is shown in Fig. 1. The pressurized liquid nitrogen was stored in a nitrogen cylinder (SOXAL) and controlled by a liquid use valve at the top of the cylinder. The liquid withdrawal steel tube was connected to the liquid use valve outlet on the liquid cylinder and connected to a pressure regulator (REGO, RG125), a safety relief valve (REGO 9400), a needle valve and a pressure transmitter (Huba control Type 500, 0–16 bar) accordingly. A lab-designed cryoprobe of 6 mm in diameter has two ports: one inlet and one outlet. The inlet was connected to a homocentric inner steel tube inside of the cryoprobe with the end near the tip, while the outlet was connected to the interlayer of the inner tube and the out wall at the upper side of the cryoprobe. When the liquid use valve and needle valve were open, liquid nitrogen entered the cryoprobe by the inner tube until the tube end for vaporization when its pressure drop. It then returned back via an interlayer between the out wall of the cryoprobe and inner tube to the exhaust copper tube. The exhaust copper tube was measured by another pressure transmitter (P2) (Huba control Type 500, 0–8 bar) before connecting to a pressure stabilizer which comprised of a large cylinder container. To ensure full vaporization prior to discharging to the environment, the nitrogen flow was passed into a water temperature controlled bath (Thermo Fisher Scientific SAHARA S49) using a copper helix tube. The single-phase outflow was measured by a gas flow meter (Malema flow sensor MTF4130-D-01) and a pressure gage at downstream. Three T-type thermocouple probes (OMEGA Engineering SCPSS-040U-6) were employed to measure sample temperatures while a thermocouple wire was used to measure the tip temperature of the cryoprobe. Data of temperatures, pressures and flow rates were periodically logged by a data logger (Agilent, 34970A) and then transferred to an external computer for a real-time investigation. Porcine livers

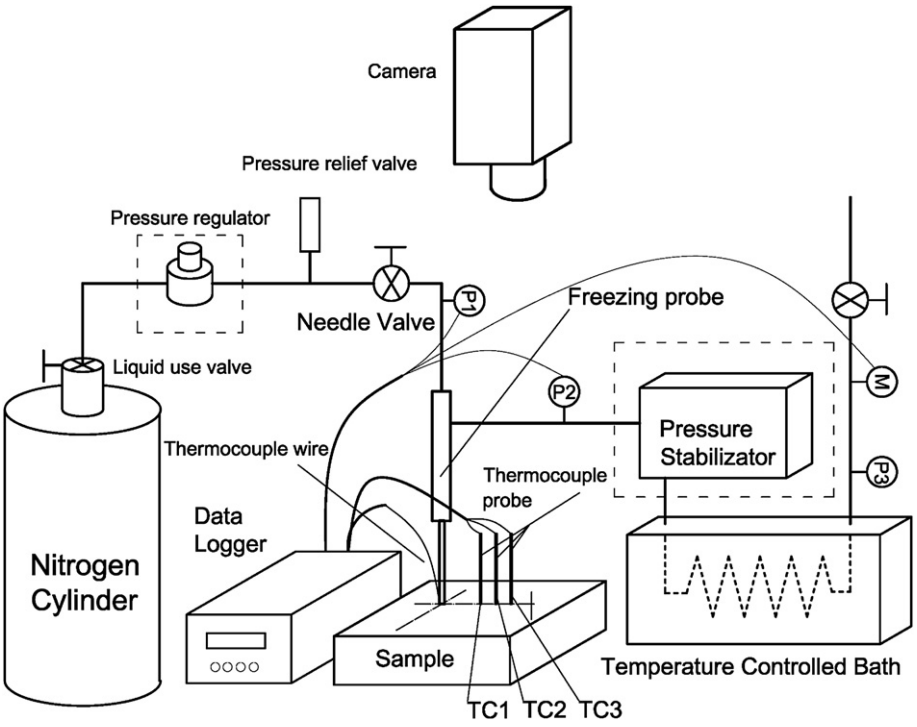

Fig. 1. Schematic diagram of the experimental setup with key devices (marked with dotted boxes) to stabilize the pressure and flow rate.