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● *Original Contribution*

TISSUE ABLATION ACCELERATED BY PERIPHERAL SCANNING MODE WITH HIGH-INTENSITY FOCUSED ULTRASOUND: A STUDY ON ISOLATED PORCINE LIVER PERFUSION

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Abstract—The aims of this study were to investigate the feasibility of accelerated tissue ablation using a peripheral scanning mode with high-intensity focused ultrasound (HIFU) and to explore the effect of flow rate on total energy consumption of the target tissues. Using a model of isolated porcine liver perfusion *via* the portal vein and hepatic artery, we conducted a scanning protocol along the periphery of the target tissues using linear-scanned HIFU to carefully adjust the varying focal depth, generator power, scanning velocity and line-by-line interval over the entire ablation range. Porcine livers were divided into four ablation groups: group 1, $n = 12$, with dual-vessel perfusion; group 2, $n = 11$, with portal vein perfusion alone; group 3, $n = 10$, with hepatic artery perfusion alone; and group 4, $n = 11$, control group with no-flow perfusion. The samples were cut open consecutively at a thickness of 3 mm, and the actual ablation ranges were calculated along the periphery of the target tissues after triphenyl tetrazolium chloride staining. Total energy consumption was calculated as the sum of the energy requirements at various focal depths in each group. On the basis of the pre-supposed scanning protocol, the peripheral region of the target tissue formed a complete coagulation necrosis barrier in each group with varying dose combinations, and the volume of the peripheral necrotic area did not differ significantly among the four groups ($p > 0.05$). Furthermore, total energy consumption in each group significantly decreased with the corresponding decrease in flow rate ($p < 0.01$). This study revealed that the complete peripheral necrosis barrier within the target tissues can defined using linear-scanned HIFU in an isolated porcine liver perfusion model. Additionally, the flow rate in the major hepatic vessels may play an important role in the use of the peripheral ablation mode, and this novel mode of ablation may enhance the therapeutic efficacy and tolerability of the treatment of large tumors using HIFU ablation. (E-mail: zoujz@haifu.com.cn)   © 2013 World Federation for Ultrasound in Medicine & Biology.

Key Words: **High-intensity focused ultrasound, Peripheral scanning mode, Therapeutic ultrasound, Hepatocellular carcinoma, Porcine liver perfusion, Thermal dose, Hepatic vessel, Flow rate.**

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most widespread solid malignancies in China. Generally, patients with advanced HCC, large-volume HCCs >5 cm in diameter or deep liver tumors (tumors at a depth of >12 cm from the surface of the skin) are not eligible for curative surgical resection by the time that they are definitively diagnosed (D'Agostino and Solinas 1995; Goldberg et al. 2000; Lin et al. 1997; Poon et al. 2009). In addition, patients with HCC in China often contract chronic type B or type C hepatitis and liver cirrhosis, which lead to a declining hepatic functional reserve and chronic liver failure. Although comprehensive measures have been undertaken for the treatment of advanced HCC, the overall survival rate of patients with HCC has not improved.

High-intensity focused ultrasound (HIFU) is a noninvasive technique that has been clinically used for conformal ablation of solid tumors without the insertion of any instrument into the lesions. The induction of coagulation necrosis by HIFU at a specific focal point can be predictably and accurately achieved by nesting lesions side-by-side without damaging the overlying tissues and structures within the acoustic path. The current results of HIFU ablation for HCC are greatly encouraging (Daum et al. 1999; Illing et al. 2005; Wu et al. 2004a,

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2004b). To date, the predominant application of HIFU therapy is based on ablation of the entire tumor to produce complete destruction and necrosis (ter Haar et al. 1991). However, the lengthy treatment time, which often increases adverse effects and potential complications for those patients with large HCCs, has become an obstacle. This dilemma presents a particular concern for the clinical application of HIFU (Wu et al. 2005).

Because of the biological characteristics and natural course of malignant tumors, the infiltrative growth margins often possess a hypervasculature that is intricately developed, highly oxygenated and well nourished and, therefore, has a rapid heat transfer capacity (Chen et al. 1997; Marchal et al. 1985; Short and Turner 1980). Correspondingly, the marginal tumor tissues are the fastest-growing parts of a tumor and the most prominent contributors to the tumor's malignant behavior. By contrast, in the central region of a tumor, necrosis caused by poor nutrition is common, especially in large tumors, which exhibit an outgrowing blood supply, poor oxygenation, low metabolism and insufficient perfusion (Vaupel 1992). In fact, there is a strong evidence to support the notion that central necrosis of varying degrees is common in patients with large malignant tumors, even if no specific treatment is performed (Oquiñena et al. 2009). On the basis of this rationale, it is reasonable to hypothesize that the formation of a necrotic barrier at the periphery of a target tissue could induce secondary ischemic necrosis and hypoxic necrosis of the inner untreated tissue and effectively restrain tumor growth, ultimately leading to complete necrosis of the entire tumor.

The aims of our study were to explore whether the use of a peripheral scanning mode with HIFU could produce a complete necrotic barrier in an isolated porcine liver perfusion model and to investigate the influence of varying flow rates on the consumption of ultrasound energy for the sake of reducing the overall energy requirements for local tumor control.

METHODS

Organ harvesting

Forty-four porcine livers (mean weight, 1856 ± 137 g) were obtained immediately from a commercial slaughterhouse (the study was approved by the Institutional Care and Animal Use Committee of Chongqing Medical University), and the warm ischemia time was within 30 min. Each liver was immersed in 2 L heparinized perfusate (Table 1) and stored in a non-electric coolbox at 4°C. After storage for 2–4 h, the main hepatic artery and portal vein were cannulated and perfused with fresh, heparinized and heated perfusate using a heat exchanger to maintain the temperature at 37°C.

Table 1. Perfusate composition*

Component	Concentration (g/L)
Sodium chloride	6
Potassium chloride	0.3
Calcium chloride	0.2
Sodium citrate	3.1
6% Hydroxyethyl starch	30
Heparin	2000 IU

* The perfusate is composed of isotonic crystalloid and colloidal solution to maintain the relatively normal physiological status.

After ligation of the cystic duct, the proximal segment of the common bile duct was cannulated for the continuous drainage of bile by negative pressure.

Perfusion system

In total, 4 L perfusate was pumped from the perfusate reservoir using an extracorporeal circulation unit (Polystan, Copenhagen, Denmark). The portal vein and hepatic artery were used to track liver inflow, and the retrohepatic inferior vena cava was used to track liver outflow *via* three mono-head roller pumps, respectively (Fig. 1). The livers were placed in a cylindrical tank using Perspex board to contain the perfusate, with a 25-μm-thick Mylar membrane as an acoustic window on the bottom of the tank and with the liver hilus and hepatic vessel catheters oriented toward the top of the tank. The entire cylindrical tank was immersed in a large tank that was filled with degassed, deionized water (20°C). With this setup, the major proportion of the liver lobes could be exposed to the HIFU beam.

The fluid pressure in the major hepatic vessels was monitored using a PT-100 multichannel biological blood pressure sensor (Taimeng, Chengdu, China) and was recorded using the physiologic signal collecting and managing system software (2.0q version). The tip of the

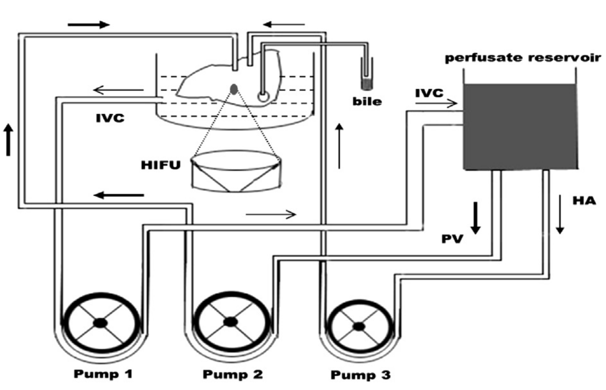

Fig. 1. Schematic diagram of the isolated porcine liver perfusion circuit. HA = hepatic artery, PV = portal vein, IVC = inferior vena cava, bile = bile drainage from the proximal portion of the common bile duct, Pump = mono-head roller pump of the extracorporeal circulation unit, HIFU = high-intensity focused ultrasound.