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Ultrasonics 43 (2005) 265–269
Ultrasonics
www.elsevier.com/locate/ultras

# Intra-operative acoustic hemostasis of liver: production of a homogenate for effective treatment

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Accepted 5 July 2004
Available online 22 July 2004

**Abstract**

*Objective*: We have shown that High-Intensity Focused Ultrasound (HIFU) can effectively control bleeding from injuries to solid organs such as liver, spleen, and lung. Achievement of hemostasis was augmented when a homogenate of tissue and blood was formed. The objective of this study was to investigate quantitatively the effect of homogenate production on HIFU application time for hemostasis. Possible mechanisms involved in homogenate production were also studied.

*Methods*: Ten anesthetized rabbits had laparotomy and liver exposure. Liver incisions, 15–25 mm long and 3–4 mm deep, were made followed immediately by HIFU application. Two electrical powers of 80 and 100 W corresponding to focal acoustic intensities of 2264 and 2829 W/cm$^2$, respectively were used. Tissue and homogenate temperatures were measured. Smear and histological tissue sample analysis using light microscopy were performed.

*Results*: In treatments with homogenate formation, hemostasis was achieved in 76 ± 1.3 s (Mean ± Standard Error Mean: SEM) at 80 W. In treatments without homogenate formation (at 80 W), hemostasis was achieved in 106 ± 0.87 s. At 100 W, hemostasis was achieved in 46 ± 0.3 s. The time required for homogenate formation, at 80 and 100 W were 60 ± 2.5 and 23 ± 0.3 s, respectively. The homogenate temperature was 83 °C (SEM 0.6 °C), and the non-homogenate tissue temperature at the treatment site was 60 °C (SEM 0.4 °C). The smear and histological analysis showed significant blood components and cellular debris in the homogenate, with some intact cells.

*Conclusion*: The HIFU-induced homogenate of blood and tissue resulted in a statistically significant shorter HIFU application time for hemostasis. The incisions with homogenate had higher temperatures as compared to incisions without homogenate. Further studies of the correlation between homogenate formation and temperature must be done, as well as studies on the long-term effects of homogenate in achieving hemostasis.


*Keywords:* HIFU; Hemostasis; Liver; Rabbit

## 1. Introduction

High-Intensity Focused Ultrasound (HIFU) has been shown to provide an effective method of hemostasis for injuries to solid organs (e.g., liver and spleen), and major blood vessels [11]. The HIFU method is based on

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doi:10.1016/j.ultras.2004.07.002

concentrating a high level of ultrasound energy in an ellipsoidal focal volume approximately 1 mm by 10 mm. The high intensity at the focus, on the order of 1000 W/cm$^2$, can result in a rapid (less than 1 s) increase in tissue temperature to 70 °C, leading to coagulative necrosis and hemostasis at the focus. It has been reported that intra-operative application of HIFU results in the formation of a tissue and blood homogenate, which upon coagulation and hardening, appears to act as a plug aiding in hemostasis at the injured site [7,12]. The formation of this homogenate appeared to shorten the duration of the HIFU application required to achieve hemostasis. One objective of the current study was to determine whether the formation of the homogenate affected the HIFU application time. Another objective was to investigate the possible mechanisms involved in the formation of this homogenate and its effects on hemostasis.

## 2. Methods

Ten female New Zealand White Rabbits weighing approximately 4.5 kg each were used. The procedures were carried out according to the guidelines of the United States National Institutes of Health (NIH) for the use of laboratory animals. The animals were sedated using a subcutaneous injection of 0.25 ml Acepromizine® (10 mg/ml). Ear vein catheters were put in after initial pre-anesthesia took effect, and subsequent anesthesia was achieved using an 8:1 mixture of Ketamine and Xylezene, administered to effect. Additional injections of the same mixture were used to maintain adequate anesthesia. Prior to surgery, animals were heparanized.

A midline incision was made to open the abdomen from the xyphoid process to the level of the kidneys. The lobes of the liver were surgically exposed one at a time, at the time of HIFU treatment, beginning with the left middle lobe, then the right middle lobe, and finally the right lateral lobe. The lobes were exposed sufficiently to permit HIFU application, by retracting them from the abdomen using gauze-padded forceps. Incisions were made with a scalpel beginning at the most distal region of the liver lobe, and subsequently moving proximally towards the hilum. Incisions were approximately 15–25 mm long and 3–4 mm deep, spaced 1 cm apart. Bleeding began as soon as incisions were made. Each animal was used for treatment with and without homogenate production to eliminate inter-animal variability in hemostasis time. In each animal, separate lobes were randomly chosen for each type of treatment (with and without homogenate production).

The HIFU device was composed of a 5.47 MHz transducer, equipped with a solid titanium conical coupler [2,5]. The concave transducer had a focal point at 6.4 cm and a circular aperture of 3.7 cm, resulting in an f-number of 1.7. Two electrical drive powers (80 W for both homogenate and no homogenate production, and 100 W for homogenate production) were used. The acoustic intensities were 2264 and 2829 W/cm$^2$ for 80 and 100 W, respectively. Homogenate production was controlled by the HIFU application technique and scan speed of the HIFU transducer. For incisions in which homogenate production was desired, the transducer tip was held at the end of the incision until the homogenate began to appear. The tip was then scanned at an operator-controlled rate of approximately 1 mm/s along the incised region allowing homogenate to form in the path of the incision. For cases in which homogenate production was not desired, scanning at 1 mm/s across the incision began immediately at the start of HIFU treatment. Repeated scanning was conducted until hemostasis was achieved.

Temperature measurements were made in two animals with a thermocouple (Type K, Fluke 54 II Thermometer; Seattle, WA). The thermocouple was inserted in the region of HIFU treatment immediately after the HIFU transducer had made a pass over the region. If the thermocouple induced further bleeding to an area that was hemostatic by poking a hole in the tissue, the area was not retreated, and was considered to be hemostatic. Temperature measurements were performed for the homogenate formation and non-homogenate formation cases. For both homogenate and non-homogenate formation cases, approximately 4–5 temperature measurements per pass were made.

Samples of the homogenate were obtained for smear analysis using a small sterile spoon, immediately after the homogenate was formed. Representative tissue samples from each region were obtained for histological examination. The samples were fixed in formalin, embedded in paraffin, and stained with hematoxylin and eosin. Animals were euthanized with an overdose of the anesthetic. Histological analysis was performed on all samples. Homogenate remained in situ throughout histological processing, as confirmed by light microscopy that showed incisions with homogenate had a mass of blood products directly adjacent to recognizable intact liver tissue. Incisions without homogenate did not have the same mass present. Statistical tests were done using a two-sample t-test assuming unequal variances.

## 3. Results

The homogenate was formed only under certain conditions, including sufficient but not excessive bleeding (3–7 ml/min), and sufficient HIFU application duration (>15 s) in the region. Homogenate was first observed as a grayish, frothy substance that formed in the field of treatment, at the tip of the transducer. Quantification