Laparoscopic High Intensity Focused Ultrasound: Application to Kidney Ablation


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Abstract. This work demonstrates the feasibility of using high intensity focused ultrasound (HIFU) for selective ablation of renal tissue through laparoscopic procedures. Two laparoscopic HIFU probe prototypes were developed and tested.

**Probe 1:** It is a hand-held probe with no integrated ultrasound imaging capability. It consists of two focused rectangular HIFU piezoceramic crystals mounted on a stainless steel tube for side and front firing configurations working at 4 and 5MHz respectively. During laparoscopic operation a separate video camera imaging channel is used for treatment monitoring.

**Probe 2:** It is a computer-controlled probe with an integrated ultrasound imaging working in conjunction with the Sonablate® HIFU system. It consists of a 4MHz focused rectangular HIFU piezoceramic transducer confocally coupled with a circular central element used for real-time pulse-echo imaging. Precise bi-plane mechanical movements of the transducer enable it to treat targeted tissue volumes under ultrasound imaging guidance.

Both prototypes were fully characterized for electrical impedances, acoustic fields, and total acoustic power outputs. They were then tested in an in vivo animal experimental study in which 20 pigs were treated through both open and sterile laparoscopic HIFU surgery procedures. Gross pathology and histology results demonstrated the feasibility of the laparoscopic HIFU to generate selective homogenous well-delineated necrotic lesions in a lobe of the kidney. Specifically, when treating under real-time ultrasound imaging guidance (probe 2) the ablated tissue region agrees with the planed lesion size and position within ±1mm. Moreover, it can be used as a hemostasis tool during standard partial nephrectomy to significantly reduce bleeding associate to these procedures.

INTRODUCTION

Nowadays, there is an increasing interest in laparoscopic techniques for performing different kinds of surgeries with significantly less morbidity and mortality [1, 2]. Among others, the urology surgery community is also investigating several laparoscopic surgery techniques. Notable examples are cryoaablation using extreme cold, radiofrequency ablation, and HIFU (high intensity focused ultrasound) ablation [3-5]. HIFU technology has demonstrated promising results in treating benign and malignant diseases in different organs including prostate, liver, kidney, breast, etc. [6-
Moreover, several recent studies have demonstrated the ability of the HIFU to control bleeding and to generate hemostasis (partial or total) in different tissues and vessels [10, 11].

Renal cell carcinoma is the third most common cancer in urology and is by far the most common malignant tumor of the kidney. After detection of the tumor, if the features are suggestive of malignancy or if it is growing rapidly, the patient is treated surgically with either partial or total nephrectomy depending on the size and location of the lesion and the preference of the physician. Since kidney is a highly vascularized organ, nephrectomy, as an invasive procedure, is usually associated with significant bleeding and high morbidity.

In the current feasibility study, we extended the application of the HIFU technology to laparoscopic surgery. To this end, two laparoscopic HIFU probe prototypes were developed and tested in porcine renal tissue treatments [12, 13]. Results of the in vivo porcine studies demonstrated the feasibility of HIFU in selective ablation of renal carcinoma through well-delineated contiguous necrosed lesion extending from the kidney’s pelvic system to the capsule. It was also demonstrated that laparoscopic HIFU could induce a circumferential disk-shaped necrotic tissue volume confined in a lobe of the kidney. This may be served as a hemostasis barrier prior to partial nephrectomy that leads to much less bleeding and lower morbidity.

**MATERIALS AND METHODS**

**Probe 1: Hand-held Laparoscopic HIFU Probe**

A hand-held HIFU probe was developed to meet the main features required for sterile laparoscopic operations. The probe was built from a stainless steel tube with 11 mm outer diameter and 38 cm length (Figure 1). The probe consists of two focused rectangular HIFU piezoelectric crystals for side and front firing configurations. The crystals were made from a special high-power piezoceramic material (KEZITE NOVA 3B) capable of providing high acoustic powers required in HIFU applications (KERAMOS Inc., Indianapolis, IN). The parameters of the crystals are:

- Side firing crystal: Geometry = Truncated spherical concave, Radius of curvature = 30 mm, Aperture dimensions = 30×8 mm, Center frequency = 4.0 MHz.
- Front firing crystal: Geometry = Truncated spherical concave, Radius of curvature = 10 mm, Aperture dimensions = 10×7 mm, Center frequency = 5.0 MHz.

During HIFU procedure, the transducers are covered by a latex sheath filled with circulating water and supported by a backing sleeve. The backing support sleeve (Fig. 1-b), made from brass, has two functions: (1) protection of the coupling latex sheath, and (2) providing acoustic windows to allow the latex sheath to distend in the desired planes only in front of the crystals, i.e. in direction of the HIFU beam propagation for both the side and front firing crystals.

The laparoscopic HIFU probe was fully characterized by measuring its electrical impedance, acoustic field, and total acoustic power output. The probe was able to generate total acoustic power (TAP) levels of up to 35 W and 10 W for the side and front transducers respectively. These, in turn, correspond to maximum tissue focal...
intensities over 2000 W/cm² and 4000 W/cm² for the side and front transducers respectively. These intensity levels would be sufficient for tissue ablation through coagulation necrosis by rapid temperature rise (>90°C) and bubble activities initiated by superheating mechanisms.

Figure 2 shows the temperature response simulations of the front and side transducers in the kidney tissue. The temperature maps are shown at the end of a 3-s HIFU exposure time at the typical TAP values given in the figures. A full 3D solution to the linear acoustic field coupled to the bioheat transfer equation (BHTE) was used to calculate the temperature response [14]. However, since the HIFU fields are highly nonlinear, these simulations may give underestimation in the peak focal intensities and overestimation in the focus dimensions.

**Experimental Setup**

Figure 3 shows the block diagram of the experimental setup to control the HIFU exposure from the hand-held laparoscopic probe. The overall operation is controlled
by a laptop computer. The control programs were written in Matlab and C. The operator controls the HIFU shots using a foot switch. Each time the foot switch was pressed, 5 HIFU shots were fired each of 2 s on time followed by 2 s off time.

An active pump/chiller unit (SonaChill\textsuperscript{TM}, Focus Surgery Inc., Indianapolis, IN) was used in conjunction with the laparoscopic probe to ensure continuous circulation of cold water (~20°C) around the HIFU transducers. This led to application of high powers by increasing the efficiency of the transducer and reducing the risk of transducer overheating.

**FIGURE 3.** Experimental setup used for the hand-held laparoscopic probe.

**Probe 2: Computer-controlled Laparoscopic HIFU Probe**

The computer-controlled laparoscopic HIFU probe assembly (Figure 4-a) was designed based on modifications to the standard Sonablate\textsuperscript{®} transrectal probe (Focus Surgery Inc., Indianapolis, IN). While the electrical and mechanical components of the probe left unchanged, two major modifications were implemented into it.

- The probe tip was redesigned and built from stainless steel to make it adaptable to laparoscopic surgery requirements by making it narrower and longer.
- A new dual-element piezoelectric transducer (4.0 MHz center frequency for both therapy and imaging, and 30-mm focal length) was built with a geometry that was adaptable to the new tip. In the new design, therefore, the therapy element of the transducer was made narrower while the imaging element remained unchanged.

A supporting sleeve made from stainless steel is used to cover the probe tip (Figure 4-b). Similar to the hand-held probe, the sleeve is used for protection of the latex sheath, and to provide a window to allow the latex sheath to distend in the desired plane only in front of the crystal.

The probe should be used in conjunction with the Sonablate\textsuperscript{®} HIFU device and the SonaChill\textsuperscript{TM} active pump/chiller unit. The Sonablate\textsuperscript{®} device was originally developed for computer-controlled image-guided HIFU treatment of prostate diseases including BPH (benign prostatic hyperplasia) and localized prostate cancer (Figures 4-c and 4-
d). Precise biplane mechanical movements of the transducer controlled by the Sonablate® device along with real-time ultrasound imaging during HIFU treatment and advanced treatment planning, make it a reliable and safe system for selective tissue ablation in order to treat solid tumors. Please refer to [15] for a more detailed description of the device.

**FIGURE 4.** (a) The computer-controlled laparoscopic HIFU probe and the supporting sleeve, (b) a close-up of the probe tip covered with the supporting sleeve and the water-filled latex sheath, (c) Sonablate® 200 HIFU device, and (d) Sonablate® 500 HIFU device.

Figure 5 shows the specifications of the dual-element transducer used in the laparoscopic probe for image-guided HIFU therapy. The transducer consists of two confocal elements (piezoelectric crystals). The central circular element is used for real-time ultrasound imaging of the target zone in the pulse-echo mode and the outer element is used to deliver HIFU energy to generate coagulation necrosis in the focal region.

The probe was fully characterized through a set of simulations and measurements similar to those performed for the hand-held laparoscopic probe.

**FIGURE 5.** Dual-element laparoscopic transducer. (a) Top view, and (b) side view.

**IN VIVO ANIMAL STUDY**

20 female Yucatan pigs with weights ranging from 40 to 55 kg were used in this study. The right kidney was treated in all the pigs under protocols approved by the
“Animal Experimental Usage Committee”, Indiana University School of Medicine, Indianapolis, IN. The animals were divided into 3 groups:

- Group 1 included 5 pigs, which were treated with the probe 1 (hand-held). The animals in this group were treated through sterile open and laparoscopic surgery procedures under a subacute 3-day survival study.
- Group 2 included 10 pigs, which were treated with the probe 2 (computer-controlled). The animals in this group were treated through sterile laparoscopic procedures under a subacute 3-day survival study.
- Group 3 included 5 pigs, which were treated with the probe 2. These animals were treated through sterile laparoscopic surgery procedures under a chronic 15-day survival study.

Table 1 below gives a summary of the protocols used for each group of animals.

**TABLE 1.** Summary of the protocols used for the *in vivo* porcine kidney experiments.

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Animals</th>
<th>Probe Type.</th>
<th>HIFU Exposure Parameters</th>
<th>Surgery Procedure</th>
<th>Applications</th>
</tr>
</thead>
</table>
| 1     | 5              | Hand held (Probe 1) | • TAP = 30 W  
• ON/OFF Times = 2/2 s  
• No. of Shots/Site = 5 | 3 open surgery  
2 lap. surgery  
Sterile  
Subacute (3-day survival) | Feasibility  
Hemostasis prior to partial nephrectomy |
| 2     | 10             | Computer controlled (Probe 2) | • TAP = 28 W  
• ON/OFF Times = 5/6 s  
• No. of Shots/Site = 1 | Lap. surgery  
Sterile  
Subacute (3-day survival) | Selective ablation of renal tissue |
| 3     | 5              | Computer controlled (Probe 2) | • TAP = 28 W  
• ON/OFF Times = 5/6 s  
• No. of Shots/Site = 1 | Lap. surgery  
Sterile  
Chronic (15-day survival) | Selective ablation of renal tissue |

All animals were treated under general anesthesia. Prior to surgery the animal received 1 g intravenous Cefazolin to prevent infection. Then it was anaesthetized with IM injection of Ketamine (100 mg/ml) and Xylazine (20 mg/ml) for induction followed by Sodium Pentothal (2.5% solution, 0.5 ml/lb) intubated and placed on isoflurane gas anesthesia throughout the procedure. For laparoscopic procedures, two laparoscopic trochars were inserted into the abdominal cavity to provide portals to introduce the HIFU probe as well as a separate video camera. The probe tip was then advanced under video camera guidance to the desired area close to the lower pole of the right kidney. Once the treatment was finished, the cannulas were removed and the openings in the abdominal wall were then closed with sutures and the animal returned to the cage when it recovered from anesthesia.
RESULTS

Hand-held Laparoscopic HIFU Probe

The hand-held laparoscopic probe was used to induce a cross-sectional disk-shaped necrotic lesion in the lower pole of the right kidney in the group 1 animals (n=5) through open and laparoscopic surgery procedures. During laparoscopic procedures, a separate laparoscopic video camera was used to guide the operator in positioning the probe. On autopsy (3-day post treatment) a coagulated area appeared as a whitish circumferential rim about 1 cm wide on the surface of the kidney (Figure 6-a). A drastic change in color of the lower pole was also observed within the circumferential HIFU lesion. This is believed to be due to the depletion of arterial blood supply resulting in gangrene of the lower pole. This indeed supports the hypothesis that the HIFU-induced lesion may act as hemostasis barrier which significantly blocks the blood flow to the lobe of the kidney. Both gross pathology and histology results revealed contiguous well-delineated necrotic disk-shape lesion extending from the kidney’s pelvic system to the capsule (Figures 6-b and c). The average treatment time for a circumferential lesion of about 30cc was approximately 45 minutes.

Computer-controlled Laparoscopic HIFU Probe

Fifteen pigs, divided in two groups (subacute and chronic), were treated using the computer-controlled laparoscopic HIFU probe. The entire operation was controlled by the Sonablate® 200 HIFU system. To obtain an adequate positioning, the kidney was imaged in the transverse and longitudinal planes under the Sonablate® 200 imaging. Then, through the Sonablate® 200 treatment planning, a target zone of dimensions $2.0 \times 1.6 \times 1.5$ cm$^3$ were planned in the lower pole of the kidney. The overall treatment time to create a contiguous lesion of about 5cc was around 30 minutes. Gross pathology (Figure 7) and histology (Figure 8) examinations revealed well-delineated contiguous necrosed lesions with excellent agreement in location and size (within ± 1
mm) with the planned treatment zone. Moreover, Figure 8-b clearly demonstrates a very sharp demarcation of only a few cells wide (<20 cells) between the treated and the intact kidney tissue.

DISCUSSION AND CONCLUSION

This study shows the feasibility of laparoscopic HIFU to create repeatable well-delineated selective necrotic lesions in a highly vascular organ such as kidney. In this technique the HIFU applicator comes in direct contact to the organ which leads to a more efficient delivery of the HIFU dosage. Specifically, it was shown that the delivery of the HIFU dosage under real-time ultrasound imaging guidance (probe 2) led to an accurate selective tissue ablation with an accuracy of ±1 mm in lesion size and position. Moreover, when applied properly, the laparoscopic HIFU can be used as a hemostasis tool during standard partial nephrectomy to significantly reduce bleeding associate to these procedures.

Acoustic field and temperature response measurements and simulations in the kidney tissue as well as the histo-pathologic examination of the lesions suggest that the tissue ablation was obtained through both thermal (coagulation necrosis) and non-thermal (bubble-related activities) mechanisms. Indeed, within the range of powers (TAP) we used in this study the temperature at the focal point may rise to above 90°C in less than a second. Moreover, the appearance of a hyperechoic region (usually
observed in the real-time ultrasound B-mode images during treatment) around the focus supports that cavitation/bubble activities may have a significant role in this mode of tissue ablation.

Work is under progress to develop the next generation of the laparoscopic HIFU probe. This new design combines a HIFU source and a confocal phased array imaging transducer into a flexible hand-held laparoscopic probe. The phased array imaging allows for real-time monitoring of the target zone during HIFU treatment. Besides, a manually-controlled hinge design gives the flexibility in movement and positioning which is required during laparoscopic operations.

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