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Small Aperture Ultrasound Transducers for Intracavitary Tissue Ablation

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***Abstract*—Catheter directed ultrasound (US) transducer is capable of delivering high, focused acoustic power to the target tissue inside a body. The direct interaction with the tissue enables to minimize the concern of unintended tissue damages. Despite the potential advantages, the current therapeutic application of the intracavitary US device and literature is due to the inefficient delivery of the acoustic power from the small aperture and difficulty in fabrication. Therefore, we aim to develop a miniaturized intracavitary US transducer for tissue ablation. The proposed device is composed of double-layered PZT-5A, a matching layer, and a backing layer. Relatively high acoustic pressure (4.7 MPa) was generated by the small aperture (2 mm) prototypes. The therapeutic efficacy of the proposed method was validated through ex-vivo tests using porcine kidneys. Upon the sonification, the tissue temperature elevated to over 43 °C within 20 sec and the maximum temperature reached up to 53 °C at the five-minute sonification. The lesion volume after the US treatment was about 6.8 mm^3. The developed catheter US transducer can be used to ablate a tumor in deep organs of the body by guiding it through an endoscopic device.**

Keywords—small aperture, intracavitary, piezoelectric, tissue ablation.

I. Introduction

Focused ultrasound technique is increasingly used for non-invasive ablation of malignant tumors [1-2]. Heat energy induced by US energy ablates the target tissue, causing the coagulative necrosis with the elevated temperature [3]. The current configuration of the focused US device requires a careful attention to avoid unintended damage to healthy tissues. In addition, the noninvasive transducer usually delivers US waves via a surface probe which requires high power to transmit the US waves into the target that is deep inside the body [4]. To mitigate these issues, a minimally invasive US delivery may be considered, using small aperture intracavitary transducers inserted through endoscopes to target tissue (Fig. 1).

A variety of intracavitary modalities were introduced for therapeutic indications in the past. Nonetheless, the conventional intracavitary modalities, such as radio frequency (RF), microwave (MW), and cryoablation (CA), have their own limitations for the common therapeutic applications. For example, RF may result in the excessive damage to the normal tissue [5]. CA may cause complications such as fistulae to surrounding tissue [6]. For MW, it is hard to control the therapeutic zone and resolve the overheating issue [7]. In contrast, the intracavitary US would be relatively safe and reliable in comparison with the above existing technologies. Complications and negative side effects are rare with US as long as US waves direct and focus precisely on the target tissue [8]. Due to the potential advantages, the intracavitary US transducers have gained much attention in biomedical field. However, the therapeutic efficacy of current devices still requires substantial improvements due to the low acoustic power intensity level (< 5 W/cm^2), which severely limit its clinical application [9-10]. Our research group presented a forward-looking intravascular US transducer, generating a high acoustic pressure (> 2 MPa) with the aid of the multilayered piezoelectric elements [11-12]. However, the focal distance of the existing device is limited in around 1 mm due to the sub-megahertz operation condition.

The objective of this study is to develop a miniaturized intracavitary US device causing the necrosis of the target tissue with the hyperthermia effect inside the body. One big challenge would be to deliver a relatively high acoustic power from a small aperture (< ~2.8 mm) to the target volume. The developed device is validated through the ex-vivo test results with porcine kidney (Fig. 1). While the renal US therapy with noninvasive devices

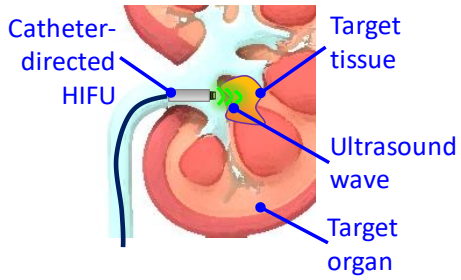

Fig. 1. Illustration of tissue ablation through the catheter-guided miniaturized intracavitary US transducer.

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has been introduced by many research groups [13-14], the intracavitary US for the kidney tissue has not been studied before.

II. Materials and Methods

A. Theoretical Thermal Dose

Focused US waves result in frictional heat of the target tissue. The heat energy cumulated by the sonification elevates the tissue temperature, followed by coagulative necrosis. It is important to apply a proper degree of the acoustic energy to the target for the minimization of the potential damage of underlying tissue. One conventional approach for the estimation of the thermal dose is to consider the equivalent minutes at 43 °C (EM_{43}) based on the thermal profile measured from the target tissue upon the sonification [15]. Most soft tissues necroses under the exposure of a thermal dose of EM_{43} = 240 min [15]. The mathematical expression of the criteria is given by

$$EM_{43}(\mathbf{x},t) = \int_0^{\tau} R^{43-T(\mathbf{x},t)} dt, \tag{1}$$

$$R = \begin{cases} 0 & T < 37°C \\ 0.25 & 37°C \le T < 43°C \\ 0.5 & T \ge 43°C \end{cases} \tag{2}$$

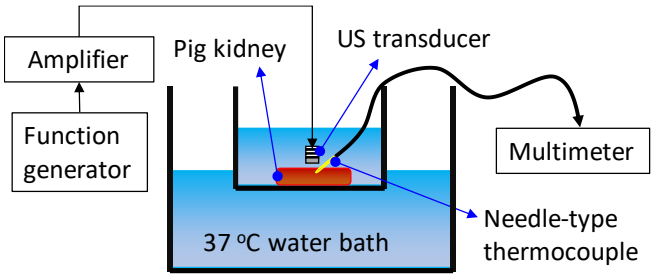
where τ is the total treatment duration; T is the temperature of the tissue; and $\mathbf{x}$ is the spatial position vector. Eq. (1) and (2) provide the required thermal dose causing the coagulative necrosis.

B. Transducer Fabrication and Characterization

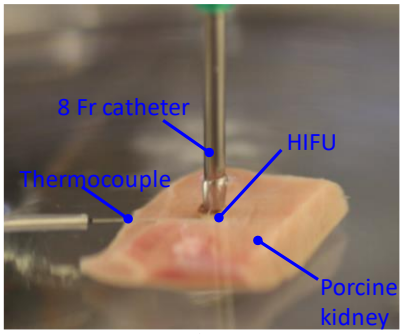
A dual-layer transducer is designed to efficiently transmit the US wave energy into a tissue media along the axial direction of the transducer. Two PZT-5A wafers, having the thickness of 500 μm and the lateral dimension of 2 mm × 2 mm, are stacked using a conductive bonding layer (E-Solder 3021, Von-Roll Inc., Cleveland, OH). Next, the matching layer, made of a composite of Al_2O_3 and epoxy were attached on the front side, followed by bonding the backing layer composed of air-microbubble (Blatek Industries Inc., State College, PA) and epoxy. The piezoelectric elements were connected by a coaxial cable (RG174U, Olympic Wire & Cable Corp., Fairfield, NJ). Parylene-C layer with the thickness of 10 μm was finally deposited on the outer surface of the transducer as the passivation layer. The details of the fabrication can be found in our previous work in [16]. The frequency characteristics of the fabricated transducer was measured by an impedance analyzer (4294A, Agilent Tech. Inc., Santa Clara, CA). Lastly, the acoustic pressure level, induced by the developed transducer, was measured by a hydrophone (HGL-0085, ONDA Corp., Sunnyvale, CA).

C. Ex-Vivo Ttest Set-Up

Fig. 2 illustrates the experimental set-up to demonstrate the temperature elevation and the ablation of animal tissue. Fresh porcine kidneys were used for the test specimen The cortex



(a)



(b)

Fig. 2. Schematic (a) and the photo (b) expressions of the ex-vivo test set-up.

portion of the kidney was cut to pieces with the approximate dimension of 30 mm × 60 mm × 10 mm. A piece of the kidney was placed inside water medium of a glass container. The temperature of the water was retained at around 37 °C by placing the glass container inside the hot water bath (Poly ProBath®, Revolutionary Science).

The miniaturized US device was located right above the kidney tissue to deliver the US wave to the tissue as illustrated in Fig. 2. The function generator (33250A, Agilent Tech. Inc., Santa Clara, CA) transmitted a pulsed sinusoidal signal (the duty rate of 20% and the pulse-repetition rate of 67 Hz) to the power amplifier (75A250A, AR, Souderton, PA). The amplified voltage signal was sent to the US device. Upon the sonification, the variation of the tissue temperature was measured for five minutes by using a needle type thermocouple which was inserted into the depth of about 1 mm of the tissue. The lesion volume induced by the sonification was observed on the surface and the section of the tissue, respectively.

III. Result and Discussions

A. Transducer Characterization

The resonance frequency of the fabricated device was found to be around 1.3 MHz from the electric impedance curve. The impedance value at the resonance was about 627 Ohm. Fig. 3 shows the acoustic pressure level produced by the device at the voltage input of 250 V_{pp}, which corresponds to a peak-to-peak pressure level of 4.72 MPa. The corresponding acoustic intensity was estimated to be 37 W/cm^2 for 20% duty cycle.

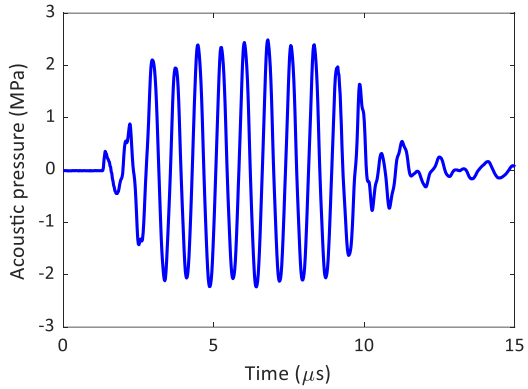


Fig. 3. Acoustic pressure of the fabricated US transducer at 250 V_{pp} sinusoidal input of 1.3 MHz.

B. *Ex-Vivo Test*

The temperature elevation of the kidney tissue induced by the insonation was investigated as shown in Fig. 4. The tissue was heated up to over 43 °C just within 20 sec and the maximum temperature was 53.3 °C after the five minute sonification. There was no significant dissipation of the temperature during the US exposure. Right after powering off at five min., the tissue temperature decreased exponentially. Fig. 5 shows the ablated portion due to the US exposure. Discolored portions of the tissue were observed at the horizontal surface (Fig. 5(a)) and the vertical section (Fig. 5(b)). To make sure the irreversible change, the US-exposed tissue was left in the atmosphere for 20 min. The volume of the lesion by the sonification was about 2.6 × 2.6 × 1.0 mm^3.

The test results show that the applied US intensity (37 W/cm^2) was sufficient to result in the irrevocable thermal necrosis of the tissue. In addition, the time to achieve the equivalent thermal dose (EM_{43}) of 240 min was estimated to be about 2.5 minutes from the thermal profile obtained from Fig. 4; this indicates that the applied US dose for five minutes was enough to cause the coagulative necrosis. In this study, none of the additional agents, such as microbubbles or nanodroplets,

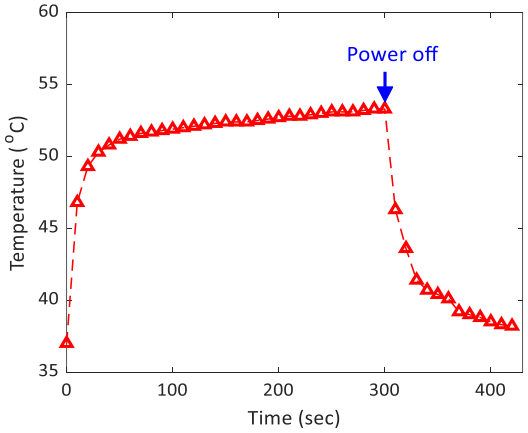


Fig. 4. Temperature variation of the kidney tissue upon the sonification by the US device.

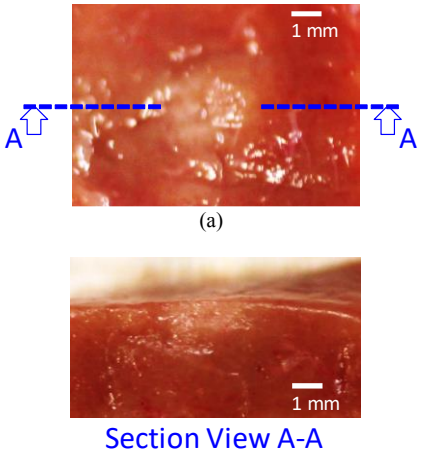


Fig. 5. Tissue with the ablated lesion by the miniaturized US transducer; (a) the horizontal view and (b) the section view.

were introduced [17-19]. Yet the US combined with the special fluidic media is worth studying for the expedited treatment. While the US device used in this study has double layers only, more layers could be integrated in the transducer to empower the acoustic power [20].

IV. Summary and Conclusion

This paper proposed a miniaturized intracavitary US transducer for tissue ablation. The acoustic intensity of the fabricated US transducer was estimated to be 37 W/cm^2 at 250 V_{pp} excitation. Under this operation condition, the temperature elevation and the ablation of the porcine kidney were successfully demonstrated. The temperature was increased up to 53.3 °C for the five minutes sonification. The lesion volume after the US treatment was about 6.8 mm^3. The ex-vivo test results validated the therapeutic effectiveness of the proposed device, showing the irreversible tissue ablation within a relatively short treatment time (< 5 min.).

The proposed transducer may penetrate into the deep organ through an endoscopic device and deliver high acoustic power to the target. This technique is expected to minimize the potential, unintended damage to surrounding tissue by accurate targeting.

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