35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Localized Elasticity Measurement for Detection of Coagulation during HIFU Therapy

Ryosuke Aoyagia[1], Hirohumi Nakamura[1], Takashi Azuma[1*], Kiyoshi Yoshinaka[2], Hideki Takeuchi[3], Keisuke Fujiwara[3], Kazunori Itani[3], Akira Sasaki[1], Shu Takagi[1], Yoichiro Matsumoto[1]

Abstract— **High intensity focused ultrasound (HIFU) treatment is one minimally invasive treatment method for cancer. Visualizing the internal treatment area of a body during HIFU treatment is required in order to achieve appropriate beam positioning and HIFU dosage. The objective of this work is to develop an ultrasound monitoring system for thermally induced coagulation. Localized motion imaging (LMI) is a monitoring method used to detect a localized mechanical response that is dependent on changes in tissue stiffness caused by thermal coagulation. In LMI, amplitude modulated HIFU causes oscillation of tissues in the HIFU focal area. The elastic modulus at a coagulated area increases and can be detected as an area with decreased oscillation amplitude., Localized control of the oscillation by changing the modulation frequency was conducted to increase the detection sensitivity for small coagulated areas in porcine liver. 2 and 7.5 MHz transducers were employed for HIFU and imaging, respectively. The amplitude modulation frequency was changed in the range from 50 to 200 Hz. The acoustic intensity of HIFU was 2.0 kW/cm2 at the focus and the exposure time was 45 s. The decrease in the amplitude of tissue oscillation at the focal point was detected within 5-10 s of HIFU exposure at the highest modulation frequency. The detected amplitude was decreased to 0.2, which indicates that for LMI, a high modulation frequency is suitable for the detection of small coagulation areas or areas of initial coagulation.**

I. Introduction

High intensity focused ultrasound (HIFU) treatment has been proposed as a minimally invasive treatment method for diverse applications, such as the treatment of cancerous tumors [1]. The high energy acoustic beam can create irreversible thermal damage at the focus of the transducer. The HIFU beam can be confined to the focal region without inducing irreversible thermal damage to the surrounding medium. The focal gain should be maximized to suppress adverse effects to normal tissue in the HIFU beam path. Therefore, typical HIFU focal spot sizes have a width of a few millimeters, which is smaller than typical tumor sizes treated in most cases. Multiple-exposure ablation is thus employed to treat a larger target volumes. The temperature elevation induced by in vivo ultrasound (US) depends on the local properties of the tissues that determine the energy absorption and heat transfer induced by thermal conduction and blood perfusion [2]. These properties can vary significantly between different tissues and within the target treatment volume. Even if the same treatment parameters are applied each time, the local properties of the tissue can lead to potential variation in the clinical results [3]. One method to avoid this uncertainty is to monitor the temperature elevation or lesion formation during treatment.

Until now, numerous imaging approaches have been established and implemented for HIFU lesion monitoring and treatment assessment in both magnetic resonance imaging (MRI) [4] and US [5]. MRI is currently held as the standard noninvasive guidance and monitoring method of HIFU, because it can provide quantitative spatial maps of induced temperature increase with high spatial resolution [6]. Nevertheless, the cost involved in MRI-controlled treatment is high; therefore, the search for lower-cost alternatives has become an important goal. US imaging to facilitate HIFU has advantages with respect to portability, low cost and spatiotemporal resolution. The potential role of US imaging for HIFU can be described as:

1. Planning to identify the location and spatial extent of the pathology to be treated,

2. guidance to predict the location, spatial extent and dose amount of the HIFU beam before treatment,

3. treatment monitoring to image the coagulated area during HIFU sonication,

4. treatment assessment to confirm the treated area after cooling down.

This paper addresses the third and fourth issues in this list. US coagulation imaging methods for monitoring and assessment based on various changes of tissue properties have been reported. From many physical properties, such as the US speed, attenuation, scattering properties, nonlinear B/A parameter and tissue stiffness, the change in tissue stiffness caused by coagulation is relatively larger than that of other parameters [7,8]. In a typical experiment with liver tissue, the stiffness after coagulation was approximately 10 times larger than that before coagulation [8].

The coagulation area per one shot of HIFU is small; therefore, the average change of the elastic modulus in the sample volume detected using elasticity imaging is small. To detect localized changes in stiffness, several groups have employed localized motion imaging (LMI) [9]. In this method, acoustic radiation is used as a driving force to deform tissue at the focal point. After coagulation, changes the tissue stiffness are detected as changes of deformation. LMI is a

[1]Facaulty of Engineering, The University of Tokyo
(e-mail: azuma@fel.t.u-tokyo.ac.jp)
[2]National Institute of Advanced Industrial Sci. and Tech.
[3]Hitachi Aloka Medical Co.,

radiation-force-based technique that induces vibration at the focal area for the detection of changes in localized stiffness, as shown in Fig. 1. The acoustic radiation force is modulated by changing the US intensity. A probe placed at the center of the transducer sends and receives back-scattered echo signals from the vibrating tissues at the focal area. The amplitude of the vibrating tissues can be measured by cross correlation between echo signals in consecutive frames. However, in these previous studies, detected contrast of the oscillation change was insufficient.

The objective of this research is the optimization of oscillation localization to increase the detection sensitivity for coagulation using LMI. In the case of body tissue after coagulation, the acoustic velocity of the shear wave is considered to be approximately 3 m/s. The LMI oscillation change reflects the average change of the elastic modulus in the sampling volume. The width of the sampling volume is dependent on the wavelength of the shear wave. Therefore, it is expected that a decrease in the amplitude can be caused by changing the width of the sampling volume attributed to the AM frequency.

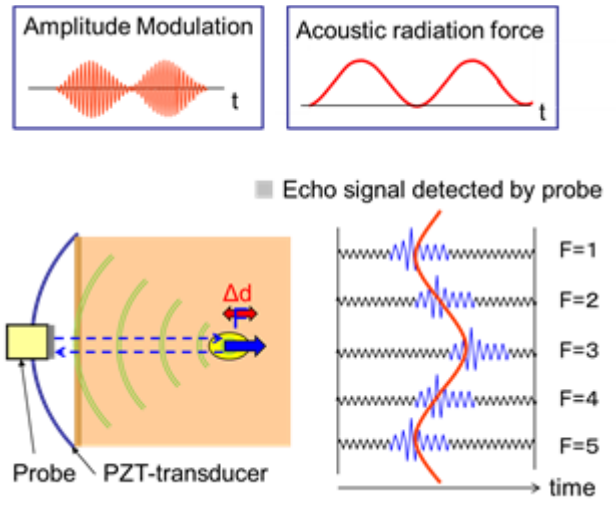

Fig. 1. Concept of localized motion imaging (LMI).

II. Material and Method

A custom-made, 56-element circular HIFU transducer (PZT5, 1-3 piezocomposite, Imasonic, Besançon, France) operated at a central frequency of 2 MHz was used for both localized motion and to create lesions in the tissue. The HIFU transducer was 100 mm in diameter with a central hole of 40 mm in diameter and a focal length of 100 mm. The intensity full width at half maximum (FWHM) of the transducer was 1.2 mm. A custom-made 96-element linear array transducer (Hitachi Aloka Medical, Japan) was mounted inside the central hole of the first HIFU transducer so that the beam axis of the two transducers overlapped. The diagnostic transducer had a central frequency of 7.5 MHz, a long axis width of 30 mm, a short axis width of 13 mm, and a bandwidth of 66%. To verify alignment and ensure that the US diagnostic transducer was effectively observing the HIFU focal point, the assembly was placed in a water tank and both beam axes were measured using a needle hydrophone (0.5 mm diameter, Type-80-0.5-4.0, Imotec, Germany).

The transducer assembly was mounted on an arm and introduced in a water tank facing the target liver tissue, which was mounted in polyacrylamide gel, as shown in Fig. 2. The HIFU transducer was excited at its central frequency by modulated bursts generated using 3 function generators (WF1974 and WF1946, NF Corp., Japan) and then amplified with a custom-made 56-channel RF amplifier (Hitachi Aloka Medical, Japan). The excitation was selected to modulate the HIFU burst with a frequency between 50 and 200 Hz.

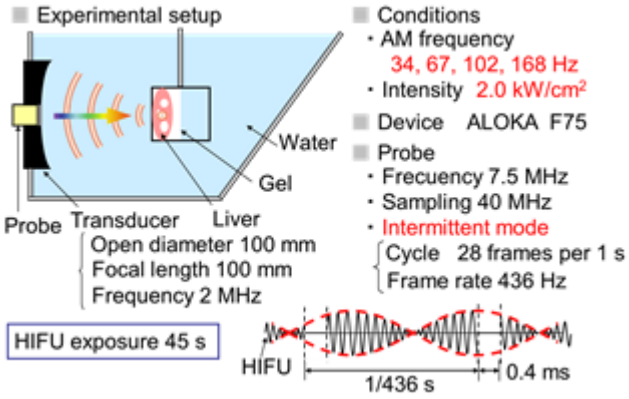

Fig. 2. Experimental setup and conditions

III. Results and Discussion

Figure 3 shows the normalized amplitude of oscillations as a function of time. The results indicate that the oscillation change is highly dependent on the AM frequency. At 168 Hz, coagulation was detected with sufficiently high contrast after 5 s exposure. Figures 4-7 show the amplitude at each depth on the focal line during exposure. The focal point in the propagation direction is located at a depth of 10 mm. The large amplitudes observed over the entire depth after 35 s at both 34 and 67 Hz, after 25 s at 102 Hz, and after 20 s at 168 Hz indicated correlation errors caused by cavitation. Oscillations at the deep areas were due to correlation errors from the tank water. The liver tissue or polyacrylamide gel was located at lower depths, in the upper area of the figures. In these areas, oscillations were localized near the focal area and the amplitudes decreased over time. The durations of these oscillations were short at high modulation frequencies. In contrast, the oscillating area was narrow at high AM frequency. Therefore, AM frequency optimization is essential for LMI with high sensitivity and a large imaging area.
To detect the initiation of coagulation, the cross section of the target sample was observed optically during exposure. To visualize the cross section at the focal area, a mixed target sample consisting of polyacrylamide gel and liver tissue was fabricated. The boundary between both materials was set at the focal plane of HIFU. The results indicated that the beginning of coagulation under this experimental condition

was 5 s after initial HIFU exposure, which is consistent with the results shown in Fig. 3.

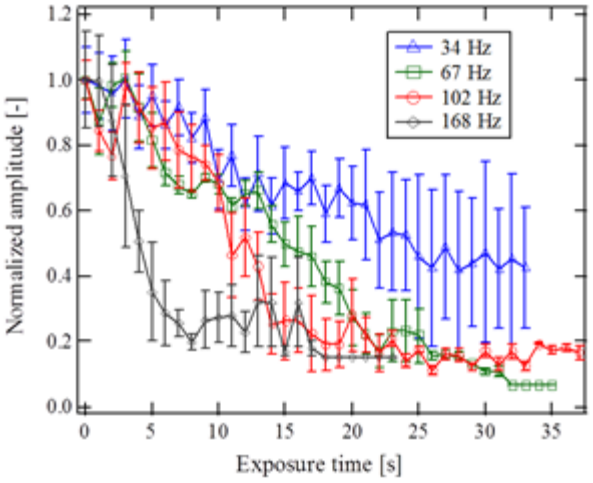

Fig. 3. Normalized amplitude change during HIFU exposures at modulation frequencies of 34, 67, 102, 168 Hz.

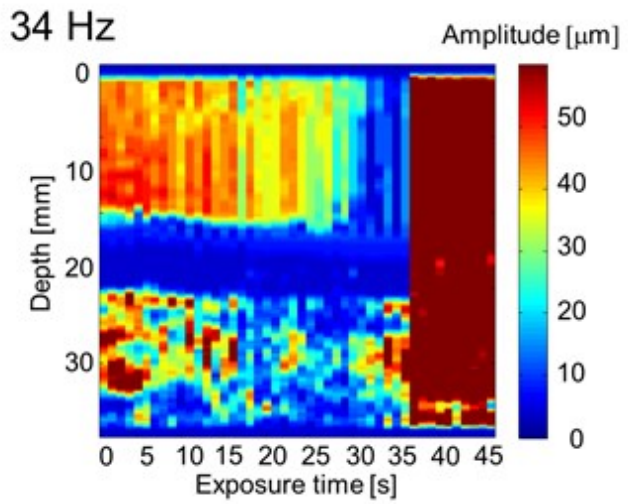

Fig. 4. Amplitude of LMI at the focal line with a modulation of 34 Hz.

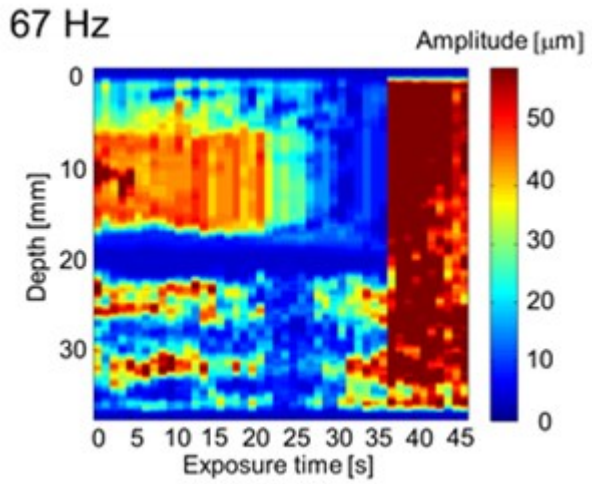

Fig. 5. Amplitude of LMI at the focal line with a modulation of 67 Hz.

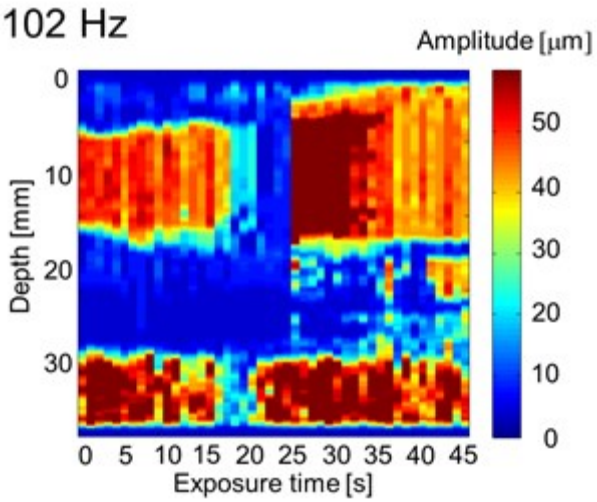

Fig. 6. Amplitude of LMI at the focal line with a modulation of 102 Hz.

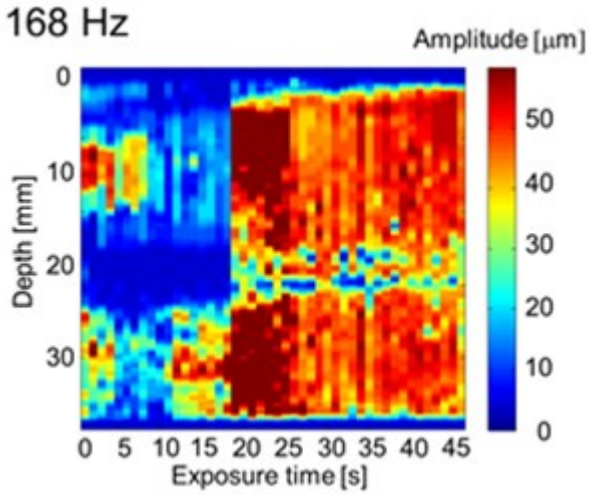

Fig. 7. Amplitude of LMI at the focal line with a modulation of 168 Hz

IV. IV. CONCLUSION

Visualizing the internal treatment area of a body during non-invasive HIFU treatment is required to control the HIFU dosage. We have developed an US monitoring system for thermally induced coagulation using LMI, which is a monitoring method to detect a localized mechanical response, specifically, the change in tissue stiffness caused by thermal coagulation. To increase the detection sensitivity for a small coagulated area, localized control of the oscillation by changing the modulation frequency was conducted in experiments with porcine liver. Initial coagulation was detected with sufficient contrast at a modulation frequency of 168 Hz. The results indicate that a high modulation frequency is suitable for the detection of a small coagulation area or initial coagulation using LMI

REFERENCES

[1] Ter Haar G, Sinnett D, Rivens I, 1989, "High-intensity focused ultrasound–A surgical technique for the treatment of discrete liver-tumors," Phys. Med. Biol. 34, p. 1743.

[2] Billard BE, Hynynen K, Roemer R B, 1990, "Effects of physical parameters on high temperature ultrasound hyperthermia," Ultrasound Med. Biol. 16, p. 409.

[3] Poissonnier L, Chapelon JY, Rouviere O, Curiel L, Bouvier R, Martin X, Dubernard JM, Gelet A, 2007, "Control of prostate cancer by transrectal HIFU in 227 patients," Eur. Urol. 51, p. 381.

[4] Hynynen K, Pomeroy O, Smith DN, Huber PE, McDannold NJ, Kettenbach J, Baum J, Singer S, Jolesz FA, 2001, "MR imaging-guided focused ultrasound surgery of fibroadenomas in the breast: A feasibility study," Radiology, 219, p. 176.

[5] Vaezy S, Shi X, Martin RW, Chi E, Nelson PI, Bailey MR, Crum LA, 2001, "Real time visualization of high-intensity focused ultrasound treatment using ultrasound imaging," Ultrasound Med. Biol. 27, p. 33.

[6] Ishihara Y, Calderon A, Watanabe H, Okamoto K, Suzuki Y, Kuroda K, Suzuki Y, 1995, "A precise and fast temperature mapping using water proton chemical shift," Magn. Reson. Med. 34, p. 814.

[7] Choi MJ, Gunter SE, Lee JM, Paeng DG, Lee KI, Coleman A, 2011, "Changes in ultrasonic properties of liver tissue in vitro during heating-cooling cycle concomitant with thermal coagulation," Ultrasound Med. Biol., 37, p. 2000.

[8] Brosses ES, Gennisson JL, Pernot M, Fink M, Tanter M, 2010, "Temperature dependence of the shear modulus of soft tissues assessed by ultrasound," Phys. Med. Biol. 55, p. 1701.

[9] Hoh GY, Luo J, Mmarquet F, Maleke C, Vappou J, Konofagou EE, 2011, "Performance Assessment of HIFU Lesion Detection by Harmonic Motion Imaging for Focused Ultrasound (HMIFU)," Ultrasound Med. Biol., 37, , p. 2013.