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A Control Framework for the Non-Invasive Ultrasound Theragnostic System

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***Abstract*—The non-invasive ultrasound theragnostic system, we propose, tracks and follows movement in an affected area —kidney stones here—, while High-Intensity Focused Ultrasound (HIFU) is irradiated onto the area. In this paper, the concept of the novel medical support system, which integrates the therapy and diagnostics, is illustrated at first. Secondly, structuring the required functions for the proposed system is discussed. Third, the overview of the constructed system configuration is illustrated. Fourth, the problem of the stone motion tracking by ultrasonography is clarified. To cope with this problem, the respiratory motion of a human kidney is analyzed and a controller, by utilizing the quasi-periodical motion of the respiratory kidney motion, is proposed. Finally, the result of the servoing and HIFU irradiation experiments of the model stone, which moves based on the real human kidney motion data, is reported to confirm the effectiveness of the proposed controller and the constructed system.**

I. INTRODUCTION

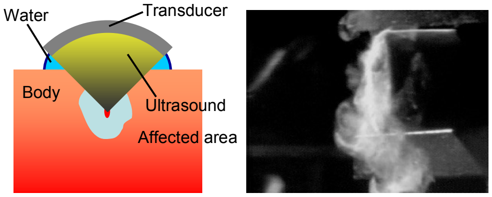
AREAS can be selectively diagnosed and treated non-invasively by using high-intensity focused ultrasound (HIFU), based on the same principle as conventional ultrasound. It propagates harmlessly through living tissue. If the ultrasound beam is focused too tightly, however, energy in the focal volume may raise temperature locally [1].

It is thus possible to treat affected area in focal volume without damaging surrounding or overlying tissues, which is a promising alternative to current abdominal and endoscopic surgeries thanks to its non-invasiveness (Fig.1 (a)).

A number of reports have been made since Lynn, et al. demonstrated the potential medical application of HIFU [1][2]. e.g., the non-invasive destruction of kidney stones (Fig.1 (b)) by energy generated by cavitation. One advantage is that debris from such stones is small enough to avoid problems with adjacent organs [3].

JC HIFU is widely used in clinical practice [4][5]. Some 19 devices in clinical use were used to treat 1050 patients with a variety of tumors [6][7]. Compensation was not made, however, for movement in the affected area, mainly due to respiration. The need to prevent such movement when irradiating focused ultrasound on the affected area thus conventionally places a large burden on the physician and patient.

In the integrated system we propose for non-invasive ultrasound diagnosis and treatment. Movement is compensated by tracking and following the affected area through stereo ultrasound imaging, while simultaneously irradiating the affected area.



(a) (b)

Fig. 1. (a) High Intensity Focused Ultrasound (HIFU), (b) Destruction of kidney stone by HIFU

The concept behind our proposal focuses on destroying tumors and stones. Using focused ultrasound directly without damaging healthy tissue while tracking and following the affected area —kidney stones in this case— during movement due, for example to the patient's respiration.

Pernot et al., Nakamura et al., Thankral et al., and Ginhoux et al. have studied how to compensate for organ movement[8-12]. Pernot et al. proposed 3-dimensional (3D) motion canceling using multiple ultrasound transducers on a spherical surface but servoing performance is insufficient[8]. Nakamura proposed synchronization between organ movement and slave manipulator operation using a 955 fps high-speed CCD camera and robot controlled based on H_∞ control theory[9][10]. Thankral et al. proposed modeling physiological movement based on a Fourier linear combiner (FLC) algorithm [11]. But did not shown how to apply the algorithm to actual robotic servoing.

Ginhoux et al. proposed model predictive control (MPC) with an adaptive observer [12]. as applied to a living pig, and verified the proposal's effectiveness. Their system is based on a 500 fps high-speed CCD camera.

Such a camera cannot be used for non-invasive diagnosis and treatment, however, due to the need to avoid damaging healthy tissue.

Abolmaesumi et al., Krupa et al. have studied the motion tracking using image speckle information[13][14]. Abolmaesumi proposed a controller utilizing diagnostic image features for carotid artery[13]. Krupa proposed an estimation and control method to automatically synchronize the 6-DOF motion of an ultrasound probe with a moving 3D ultrasound volume[14].

Tracking and following organ movement —kidney stones here— while simultaneously irradiating the affected area

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raises a problem mainly due to ultrasound imaging, its dead time, and bubbles generated by HIFU irradiation. Especially, bubbles generated by HIFU irradiation make the image quality worse and this increases image tracking error. This differs from the abovementioned studies. To solve this problem, we propose a novel control framework using quasi-periodical kidney movement, focusing on enhancing servoing performance for this special non-invasive ultrasound theragnostic system.

We proceed by presenting the concepts, required functions and the system configuration of ultrasound theragnostic system, then discuss the required servoing precision and the problems in the visual motion tracking by ultrasound images. We then analyze kidney movement mainly due to respiration, and propose a controller by utilizing regular movement in the affected area to enhance servoing performance. We then review experimental results demonstrating the effectiveness of our proposed controller and the constructed system.

II. NON-INVASIVE ULTRASOUND THERAGNOSTIC SYSTEM

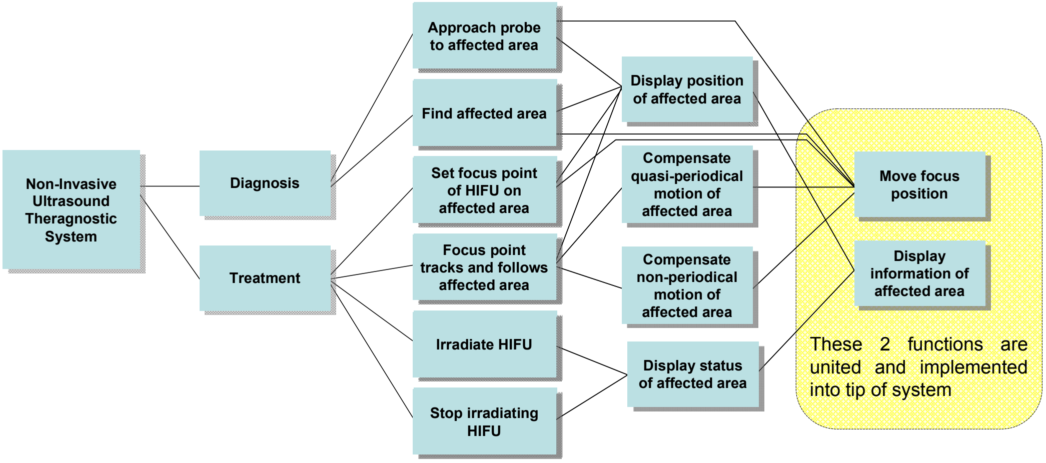
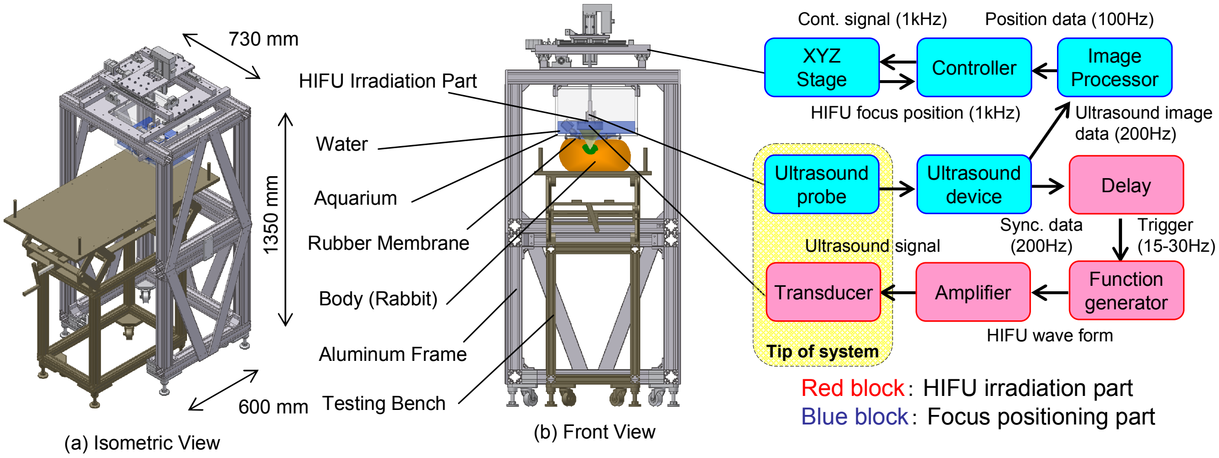


Fig. 2. Decomposing and reconstructing (structuring) functional requirements for non-invasive ultrasound theragnostic system



(a) Isometric View

(b) Front View

Fig. 3. Constructed system configuration of non-invasive ultrasound theragnostic system

A. *Structuring Required functions*

It is required to be made clear the required functions for the system to realize the efficient system. An overview of the decomposing and reconstructing (structuring) functions is shown in Fig.2. First, the required function of the integrated system for non-invasive ultrasound theragnostic system is decomposed into these 2 functions as mentioned below.

(FR-1) Function to diagnose
(FR-2) Function to treat

Among those, We broke (FR-1), above, into 2 sub functions:

(FR-1.1) Function to approach the probe to the affected area.
(FR-1.2) Function to find the affected area.

(FR-2) is broken into these 4 sub functional requirements.

(FR-2.1) Function to set the focus of HIFU on the affected area.
(FR-2.2) Function for the focus of HIFU to track and follow the affected area
(FR-2.3) Function to irradiate HIFU to the affected area.
(FR-2.4) Function to stop irradiating HIFU.

Next, functional requirements are reconstructed, considering the implementation of the system. Among those, the functional requirements (FR-1.1), (FR-1.2), (FR-2.1), and (FR-2.2) are combined as the function (R-FR-1.1) to display position of the affected area to the medical doctor. Same as this, (FR-2.3) and (FR-2.4) are combined as the function (R-FR-1.4) to display the states of the affected area to the medical doctor. (R-FR-1.1) and (R-FR-1.4) are combined as the function (R-FR-2) to display information of the affected area.

For (FR-2.2), these 2 functions below should be realized.

(R-FR-1.2): Compensate the quasi-periodical motion of the affected area.

(R-FR-1.3): Compensate the non-periodical motion of the affected area.

(R-FR-1.2), (R-FR-1.3), (FR-1.1), (FR-1.2), and (FR-2.1) are combined as the function (R-FR-1) to move the focus position. Considering the method to implement (R-FR-1) and (R-FR-2), we propose the novel united hardware mechanism, where the ultrasound transducer and the ultrasound probes are united and implemented into the tip of the hardware system. This makes it possible to acquire diagnostic images and treat the affected area at the same time. To diagnose and treat the affected area at the same time, a function below is required.

(i) HIFU and the diagnostic ultrasound don't interfere with each other.

To adopt the robotic system, these functions as follows are also required.

(ii) Secure safety.

(iii) Lessen uneasiness.

(iv) Secure ultrasound paths to the affected area.

B. *Implementation of System*

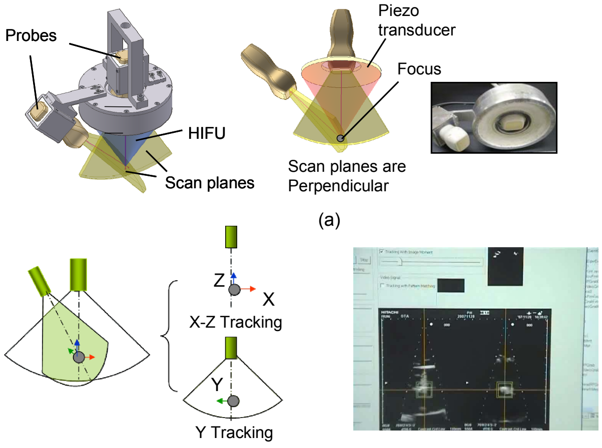
The non-invasive ultrasound theragnostic system is constructed based on the structured functional requirements (Fig.3). Stereo diagnostic images are acquired using 2 diagnostic probes. Based on stereo images, 3D positioning data of the affected area, the relative value to the focused position of the HIFU, is obtained. In control, the focus tracks and follows the kidney stone by using 3D positioning data. HIFU is irradiated onto the kidney stone using the function generator, amplifier, and transducer. The specification of irradiation of HIFU is detailed in reference [13].

The robot has a spherical piezoelectric transducer and two ultrasound probes (Fig.4 (a) and (b)) —one in the center of the piezoelectric transducer and the other is located in the lateral side of the piezoelectric transducer. These two probes meet two conditions:

(i) Image planes, acquired by probes, are mutually perpendicular (Fig.4(b)).

(ii) The focus of HIFU, irradiated by piezoelectric transducers, is on both image planes acquired by probes (Fig.4(b),(c)).

The two ultrasound image planes are shown in Fig.4 (c). The stone is shown as bright regions in left and right ultrasound images. The left ultrasound image is acquired by the probe in the center of the piezoelectric transducer and that at right by the probe on the lateral side of the piezoelectric transducer.



(a)

(b) (c)

Fig. 4. (a) Tip of system with 2 ultrasound probes for diagnosis and a transducer for HIFUtreatment (b) Ultrasound image planes, which are perpendicular to each other, (c) Ultrasound image planes which are acquired by ultrasound probes

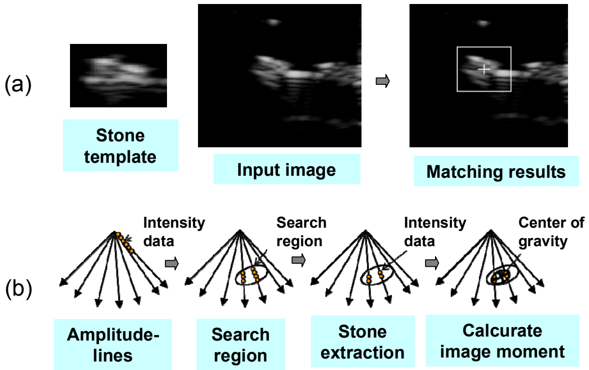


Fig. 5. Visual motion tracking method, (a) Conventional analog template matching method, (b) Image moment method

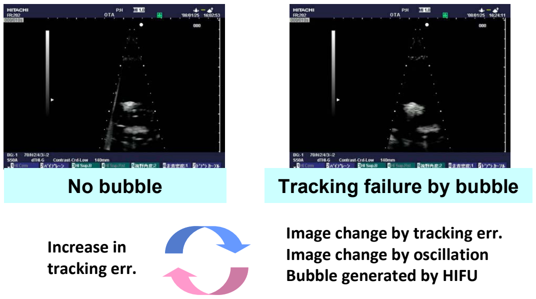


Fig. 6. Problems in visual motion tracking by ultrasound images

The kidney stone is tracked by imaging left and right ultrasound images based on the Matrox Imaging Library (MIL8.0) processing cycle, which involves 5 steps: 1: Grabbing ultrasound images. 2: Processing grabbed images to enhance image quality for tracking the kidney stone. 3: Detecting the 3D location of the stone. 4: Finding and updating the target by blob analysis if the kidney stone is lost during tracking.

In the conventional prototype system, we applied template matching method to detect the 3D location of the stone by using analog video signal (Fig.5 (a)). However, this has 2 problems: 1: The sampling time is 30 ms by using analog video signal. 2: The shape change of the stone in the ultrasound images increases the visual tracking error. To cope with these problems, we developed the novel image moment method (Fig.5 (b)). We could also enhance the sampling time (10 ms) by utilizing the Radio Frequency signal (raw data of the ultrasound device). The robustness against the shape change could be enhanced by utilizing the center of gravity of the intensity data of the search region in the ultrasound image.

C. Required Servoing Precision and Problems in Visual Motion Tracking by Ultrasound Images

In this section, we discuss the required servoing precision and the problems in the visual motion tracking by ultrasound images. First, we discuss the required servoing precision. Desired servoing precision in the presented system is within the radius of the irradiated object.

$$e_d < k_r \bar{r}_{stone} \qquad (1)$$

Here,

$\bar{r}_{stone}$: The average radius of the irradiated object. k_r : proportionality constant. In the present work, the irradiated object is the model stone [13], whose diameter is about 5mm. Therefore, the target tracking precision is set as 0.5mm ($k_r = 10$). The irradiated region of HIFU (lesion) is ellipsoidal form, whose long axis is about 2mm and the short axis is about 1mm. The graphic resolution of the ultrasound diagnostic image is about 0.3mm when the 3MHz probe is applied.

Second, we discuss the problems in the visual motion tracking by ultrasound images (Fig.6). When the bubbles are generated (or image change occurred by tracking error / oscillation of the mechanical system), the tracking error increases. This tracking error causes the image change. This image change causes the tracking error. This is the negative spiral. This negative spiral makes the tracking performance worse and worse. In contrast, this fact shows the possibility that the tracking performance could be enhanced dramatically. Then, we propose a controller by utilizing the quasi-periodical motion of the respiratory kidney motion.

III. FEED-FORWARD CONTROL

Based on the discussion on the required servoing precision and problems in the motion tracking by ultrasound images in Section II C, a novel controller is proposed by utilizing the quasi-periodical kidney motion by respiration.

A. Semi-Periodical Organ Motion by Respiration

Fig.7 show a quasi-periodical kidney motion in a body, which is acquired by an ultrasound probe. It is confirmed that [Feature 1] the motion path of the kidney in a period is similar to the one in another period, as shown in Fig.7. It is also confirmed that [Feature 2] Similar during in the high speed motion area, [Feature 3] Less similar during in the low speed motion area.

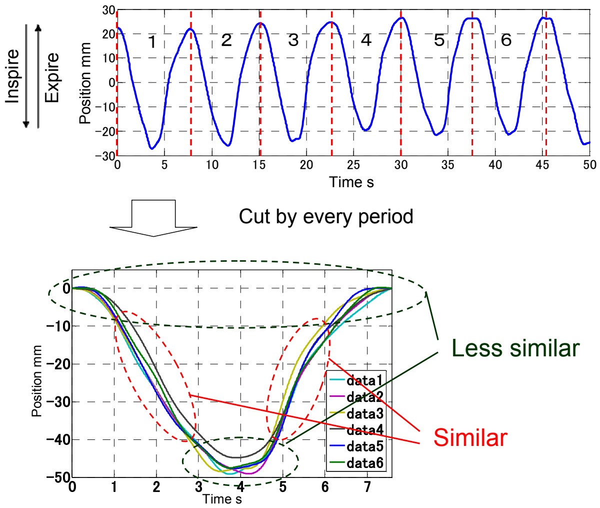


Fig. 7. Quasi-periodical kidney motion

B. Control Methodology

The block diagram of the controller is shown in Fig 8. Here, r : Target position, e : Servoing error, $\hat{e}'$: Referred servoing error (100Hz), $\hat{r}$: Presumed target position, $\hat{e}''$: Presumed servoing error (1kHz), u : velocity command value, y :Focus position of HIFU, $\hat{y}$: Presumed focus position of HIFU. Our system is composed of position acquisition part $O(s)$, Controller part $C(s)$, motor driving part of XYZ stage $P(s)$, Oscillation part of the hardware mechanism $M(s)$, The presumed value $\hat{O}(s)$ of $O(s)$. Those mathematical model are expressed below.

$$O(s) = \hat{O}(s) + d_o \qquad (2)$$

$$M(s) = -\frac{s^2}{s^2 + 24s + 3.1\times 10^3} + d_m \qquad (3)$$

$$P(s) = \frac{s + 7.5\times 10^{-4}}{s(s + 2.2\times 10^{-3})}\exp(-0.003s) \qquad (4)$$

Here, d_o is the disturbance, which is mainly caused by the noize of the ultrasound image, tracking error, etc. d_m is the mechanical disturbance, which cannot be expressed in $M(s)$. Target position is acquired by the ultrasound machine at the limited sampling rate of 100Hz. While, the XYZ stage is controlled at the rate of 1kHz in the presented system.

PID Feedback control is applied, at first, by error between the target and the focus position. The integral part is implemented in $P(s)$. PD part is expressed as $C(s) = K_P(1 + T_D s)$. Here, we applied Ziegler-Nichols ultimate sensitivity method to determine proportional

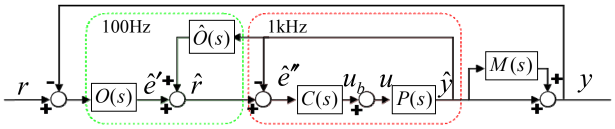
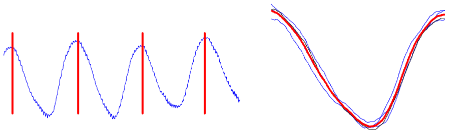
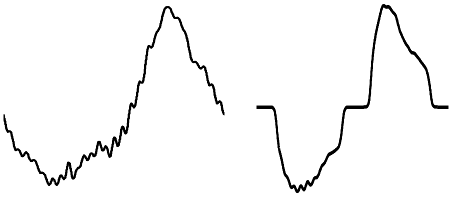


Fig. 8. Block diagram of the conventional controller



(i) Data segmentation (ii) Standard motion model generation



(iii) Velocity value transformation (iv) Velocity command value generation

Fig. 9. Block diagram of the controller, (i) Data segmentation, (ii) Standard motion model generation, (iii) Velocity value transformation, (iv) Velocity command value generation

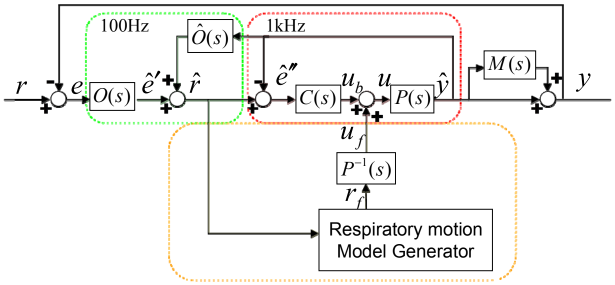


Fig. 10. Block diagram of the proposed controller by utilizing the quasi-periodical motion of the respiratory kidney motion

gain $K_P = 19.4$ and derivative time $T_D = 0.014$. The controller is designed $C(s) = (19.4 + 0.26s)F(s)$.

In the kidney motion tracking by utilizing ultrasound image, there exist some problems and difficulties. First, due to the effect of dead time, servoing error increases with feedback control alone. The shape changes when the servoing error becomes large and the quality of the ultrasound image becomes worse for visual tracking. Second, the visual tracking error occurs promptly during the HIFU irradiation. This is mainly caused by the bubbles generated by HIFU around the crushed pieces of the kidney stone.

To solve this problem, we propose feed-forward control method by utilizing the quasi-periodical motion of the organ due to respiration. The procedures for the feed-forward term generation is shown in Fig.9. The block diagram of the feed-forward control is shown in Fig.10.

The period and the amplitude fluctuates, while the kidney motion is quasi-periodical. Then, (i) the kidney motion is segmented into each period at first. Second, (ii) the standard motion model r_f is generated based on the last several segments. Third, (iii) the standard motion model is transformed into the velocity data and (iv) the velocity command value u_f is generated by $P^{-1}(s)$.

Then, the u_f is input to $P(s)$ with the feedback term u_b.

IV. EXPERIMENT

Servoing and HIFU irradiation experiments of the model stone are conducted to confirm the effectiveness of the proposed controller by utilizing the quasi-periodical motion of the kidney. The tracking and following target is the artificial model stone[15]. The model stone and its motion mechanism is shown in Fig.11. Here, these parameters as follows are set by considering the position and motion of the human kidney.

$d_1 = 55$ [mm]: Distance from the water surface

$d_2 = 10 \sim 50$ [mm]: Motion range

The moving direction of the stone model is the translational axis that corresponds to the axis of the human body. The real kidney motion data (Fig.7) is input to the stone model. Specifically, we compared the tracking and following performance of the model stone under these 2 conditions.

[FB] Servoing only by the feedback control.

[FB+FF] Servoing not only by the feedback control but also by the proposed feed-forward control by utilizing the quasi-periodical motion of the kidney.

CCL(Cavitation Cloud Lithotripsy [3]) is applied to crush the model stone. Irradiation time is set 30 minutes.

The experimental result is shown in Table 1. The transition of the position of the model stone, the focus, the motion tracking error between the stone and the focus in each condition, is shown in Figs.12(a) and (b). The maximum tracking error is 1.5mm, the average tracking error is 0.38mm, only by the feedback control. In contrast, the maximum tracking error is 1.2mm, the average tracking error is 0.24mm, with the feed-forward control.

The distribution of the motion tracking error during 120 s with the sampling rate 1kHz (Total amount 120,000 points) is shown in Figs.13(a)(b). The standard deviation of the tracking error is (a) 0.44mm, (b) 0.29mm in the experiment. The crushed model stone after the 30 minutes is shown in Figs 14(a)(b)(c). In the figure, (a) is under the condition [FB], (b) is under the condition [FB+FF], and (c) is under the condition where the kidney stone is still.

It is confirmed that the servoing performance could be enhanced by the proposed the proposed feed-forward control by utilizing the quasi-periodical motion of the kidney. I think the improvement of the phase delay, which is mainly caused by dead times, is effective. Phase delay between the target position and the focus position of HIFU is calculated as (a) 56ms, (b) 26ms. Concerning the destruction of the model stone,

Table 1 Stone motion tracking performance

	FB	FB+FF
Avg. Error mm	0.38	0.24
Max. Error	1.5	1.2
Stand. Dev. mm	0.44	0.29

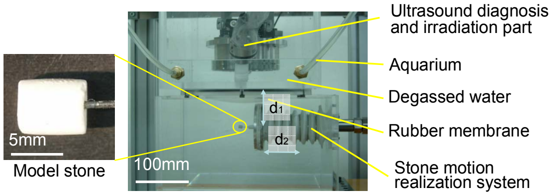
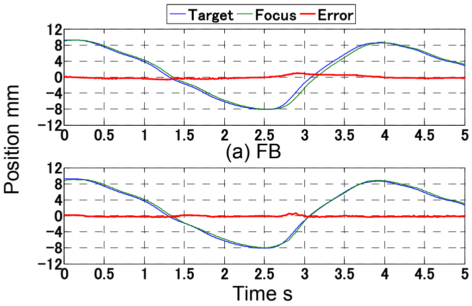
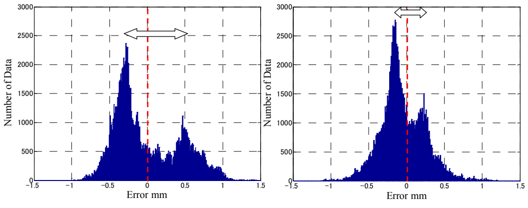


Fig. 11. Overview of tip of experimental system



(b) FB+FF

Fig. 12 Motion tracking error between stone and focus



(a) FB (b) FB+FF

Fig. 13 Distribution of the motion tracking error

(a) FB (b) FB+FF (c) Still

Fig. 14 Destruction results of model stones by HIFU

the crushed shape is almost circle within the 5mm diameter model stone among in the condition (a)-(c). This is the sufficient results for the purpose to crush the stone. Usual stones in the human body is about 20-30mm in diameter. Stones within the diameter 4mm could be emitted out of the body with the unine.

V. CONCLUSION

In this paper, a control framework for a non-invasive ultrasound theragnostic system is proposed. The concept of the proposed "non-invasive ultrasound theragnostic system" is to destroy tumors or stones. The proposed system tracks and follows the motion of the affected area (kidney stones in the presented system). High Intensity Focused Ultrasound (HIFU) is irradiated to the affected area at the same time.

Specifically, the functional requirements for the system are made clear at first. Second, the non-invasive ultrasound theragnostic system is constructed based on the introduced functional requirements. Third, the required servoing precision and the problems in the motion tracking by ultrasound images are discussed. Fourth, the controller by utilizing the quasi-periodical motion of the affected area, which is mainly caused by respiration, is proposed and implemented to enhance the servoing performance. Fifth, the result of the servoing experiment for the model kidney stone is reported and the effectiveness of the proposed control method and constructed system were confirmed.

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