論 文 の 内 容 の 要 旨

論文題目　Development of US-guided Robotic HIFU System toward Non-invasive Tumor Treatment
（和訳　非侵襲腫瘍治療に向けた超音波援用ロボティックＨＩＦＵシステムの開発）

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This dissertation is about a development of a robotic HIFU system for non-invasive tumor treatment. In chapter 1, I introduce the advantages and limitations of the HIFU treatment. Compared to the conventional treatment methods, there are many advantages of HIFU treatment: non-invasive, less post-surgical complications, fast feedback, outpatient treatment, and so on. In particular, HIFU can concentrate an acoustic energy only on a focal spot and thermally ablate a tumor area. However currently available US-guided HIFU systems have also many limitations. In particular, to treat a moving tumor area by respiration, awake-operation is required; surgeon should control patient's respiration to position HIFU on the target every respiration cycle. This results in a long-time operation and be much burden to patient and surgeon as well. Moreover, target recognition by using US imaging is also very hard when the tumor area has similar acoustic impedance with surrounding normal tissues. Therefore, in this research, we focus to develop a robotic HIFU system equipped with US-guided target area detection to synchronize HIFU focus on the target motion.

In chapter 2, the research objectives are presented. Specifically, we define the treatment target as kidney tumors (RCC, Renal Cell Carcinoma). Conventionally, partial or radical nephrectomy has been recommended for the treatment of renal tumors. However to realize the non-invasive treatment of RCC by US-guided HIFU, we need to focus on the following issues,

(a)　Detection of unclearly observed tumor area by US imaging.
(b)　Compensation of kidney motion induced by respiration.
(c)　Integration of the US based target tracking and HIFU treatment.

To realize above, this research proposes novel target detection methods for motion compensation. Moreover, a US signal interlacing for simultaneous target tracking and HIFU irradiation is proposed. Here, the goal of the visual servoing accuracy was decided by

2.5 mm (RMS), considering 5 mm of unit treatment size for the moving target.

Chapter 3 introduces the system configurations of the developing robotic HIFU system. For three-dimensional target imaging and treatment, we devised an end-effector composed of two US imaging probes and a single-element HIFU transducer. Biplane US imaging is done by grabbing raw data from US diagnostic machine and conversion into 2.5-D B-mode image data in 'Visual servoing manager' software. The software also implements target detection, visual feedback error calculation, robotic part control, HIFU irradiation control, and so on. Robotic part includes a robot controller and a XYZ stage robot, to synchronize HIFU focus to detected treatment target. HIFU irradiation part is composed of pulse generator, amplifier, water circulation sub-system, and HIFU transducer. In particular, 3-D HIFU acoustic pressure distribution can be measured automatically by the scanning sub-system. This is for a performance management of currently using HIFU transducer. Moreover, a new phantom model was devised for the experiment. It is composed of a hydrogel-based tissue mimicking material and a renal-shaped BSA protein gel so that it can realize US imaging for kidney's boundary as well as a thermal response by HIFU irradiation. The phantom model is set in the lower aquarium and attached on the tip of linear actuator, moving phantom model as the captured cranio-caudal direction of human kidney. The magnitude of kidney motion is about 20 mm with maximum speed of 25 mm/s. Upper aquarium has enough space for moving end-effector, the water should be degassed. The US for both imaging and treatment are transmitted through a silicon membrane contacting on the phantom in lower aquarium, which will contact on the patient's skin in the future.

In chapter 4, I proposed a method of tumor area detection by using a preoperative 3-D model. As for the issue of unclear target area detection in US imaging, the key idea of the method is that the tumor area can be found from an alternative anatomical feature, kidney boundaries. In fact, the conventional methods have attempted to recognize the desired features from noisy US images. However most of them are very target specific, semiautomatic, or hard to be calculated in real time. Therefore we decided to employ an additional information (preoperative 3-D model) acquired from other imaging modalities, such as CT or MRI. These imaging modalities are hard to be used intraoperatively, however provide more information than US imaging, such as tumor area. Therefore the proposed method does not rely on US imaging only but uses preoperatively obtained patient's kidney and tumor models. By registering the preoperative 3-D kidney model in the US images, the unclearly observed tumor area can be identified in the US images indirectly. This method can be classified as one of the multi-modal registrations. However the conventional multi-modal registration methods, such as registering 2-D or 3-D US image with preoperative information from 2-D CT or MRI, are hard to be used to track a moving target due to its time-consuming calculation. Since we need to apply the detection method for tracking moving target, the calculation speed is very important. Biplane US imaging we adopted is another key to accelerate the target detection. 3-D model can be registered very fast with the 3-D boundary points which are provided from 2.5-D biplane US image. By the proposed method, single calculation to detect the target motion is very fast; it can be done in 20 ms approximately. It was used for the real-time motion tracking and also utilized in motion compensation. As a result, the visual servoing error for a respiratory-moving phantom model was about 1.7 mm (RMS), which satisfies the goal of visual servoing accuracy, 2.5 mm (RMS).

In chapter 5, I proposed the other tracking method by using intraoperative information induced by HIFU treatment. Thermal ablations by HIFU irradiation can cause a tissue coagulation which also brings an echo enhancement in US image. In the present research, my idea is that the coagulated lesion (CL) by HIFU thermal ablation is not only the result of treatment but also a tracking landmark. CL in US image is very good tracking landmark inasmuch as non-invasively created, distinctive US speckle change, three-dimensional, and existing during operation. Initial CL position is defined by the preoperative model registration method. After CL generation, biplane imaging of CL facilitates the three-dimensional tracking, moreover the stochastic US speckle pattern tracking was applied for the high-speed and robust tracking. By using the proposed method, visual servoing for moving phantom model was experimented too. As a result, the motion compensation error was about 1.7 mm (RMS) which is same accuracy with the previously proposed method in chapter 4.

Based on the proposed target-tracking methods, 3-D visual feedback errors between current HIFU focus and the desired treatment position can be calculated. Since the end-effector with imaging probes and HIFU transducer moves together, moreover the 3-D target position (x, y, z) is directly calculated, hand-eye position-based visual servoing is applied. Moreover biplane US imaging speed is not very fast (20Hz, considering HIFU irradiation) as an optical video imaging, time-delay can cause unstable visual servoing. Therefore time-delay compensation was applied in the visual servoing.

Chapter 6 presents the integration of US-guided visual servoing and HIFU irradiation. If the HIFU treatment considers only static targets, US imaging is not necessarily required in the mid-treatment. However for a moving target, we should overcome an intervention in

US imaging due to the HIFU irradiation. At this time, we built a sophisticatedly designed time-line strategy so that the system can selectively grab non-HIFU-interfered US images. Therefore, I propose an optimized thread model to realize both target feature detection and HIFU irradiation; it is referred to as US signal interlacing. I applied the US signal interlacing in the robotic HIFU system, and also experimented the HIFU treatment with the moving phantom model. More specifically, for moving target treatment, treatment and imaging are equally important. Therefore, we decided that 50 % is the maximum duty cycle for HIFU irradiation and also the remaining 50 % was set for US imaging. As a result, during target motion compensation, the developed system can generate about 827,000 pulses a second with 1.685 MHz of HIFU transducer, which achieved about 50 % of duty cycle for HIFU. In the experiment, virtual tumor model was set in the upper center of phantom kidney. By the preoperative 3-D model based target-tracking method, the moving target was ablated by HIFU. As a result, the proposed robotic HIFU system successfully compensated the motion of kidney phantom and also generated a denaturalization in the desired position. Different size of coagulated lesion could be produced according to the total irradiation time. Additionally, we could know that the HIFU irradiation during the motion compensation makes a spherical lesion while the HIFU irradiation for static target creates cigar-shaped lesions.

In Chapter 7, I discuss merits and demerits of the proposed methods. For the preoperative model based tracking method, we need to take into account a deformation of kidney. Concerning to the renal deformation, a simple experiment was performed to estimate the effect of the deformation on the visual servoing accuracy. Additionally, we discussed about US imaging error from the sound speed change or acoustic distortion for more precise target detection. Toward the future clinical use of this system, I proposed some ideas in terms of high-speed US imaging, enhancement accuracy, incorporating with external sensors, HIFU treatment protocol for moving targets, large-area ablation by preoperative planning, and so on.

In chapter 8, I conclude this research, reminding the developed system and proposed methods with experimental results. Novel target-tracking methods using preoperative and intraoperative information were introduced. In this research, motion compensation was realized by robotic system based on real-time calculation of the proposed target detection methods. Moreover, by US signal interlacing, HIFU treatment for moving target was also available. Although the developed system is still very prototype, this research showed that the developed US-guided robotic HIFU system can be an alternative and reinforcement for the conventional non-invasive HIFU treatment of moving tumors.