

# Development and animal experiment of variable focusing HIFU system for prostate cancer treatment

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## Abstract

**Objective:** A prototype variable focal length array transducer system for a high-throughput HIFU (High Intensity Focused Ultrasound) has been developed and animal experiments have been carried out in order to demonstrate an ability to treat prostate through rectum.

**Methods:** Multi-elements linear array transducers with cylindrical acoustic lens are used to make the variable focal length system. The system consists of a therapy and imaging probe, a therapy control unit, an imaging and a power-generating unit, and a chiller unit. The therapy and imaging probe, that can scan the therapy beam in axial and liner direction mechanically in the rectum, consists of a couple of 48 elements 3.6MHz linear array therapy transducers with cylindrical acoustic lens for controlling focal length of high intensity ultrasound irradiation, and a 10mm diameter convex 6.5MHz diagnostic imaging array transducer centered on the couple of therapy transducers, that is used for aiming and monitoring the target region. For prostate cancer treatment, irradiation/rest time and region/pitch of irradiation position are designed through therapy control unit by monitoring diagnostic images.

**Results:** Lesions of coagulation necrosis are formed at the several focused depths 30 to 50mm from the transducer surface in the living prostate tissue of hound dogs by using this system.

**Conclusions:** By this study, a variable focusing HIFU system with acoustic lens for coagulation therapy was successfully demonstrated to coagulate prostate tissue by ultrasound beam focused at several distances in tissue from the rectum surface without exchanging probes.

## INTRODUCTION

We have developed the transrectal HIFU therapy system to treat benign prostate hyperplasia and prostate cancer, and demonstrated its operation through animal experiment, under five year scheme of NEDO (New Energy and Industrial Technology Development Organization of Japan) development project [1,2].

So far, at first, unification of an ultrasonic imaging transducer with a fixed focus ultrasonic therapy transducer is established for throughput improvement [3]. Secondly, a variable focusing HIFU system is constructed with an annular array divided spherical elements. This variable focusing system can enlarge the field of depth without exchanging many fixed focused probes [4]. Thirdly, a variable focusing HIFU system is developed with linear array and cylindrical lens [5,6].

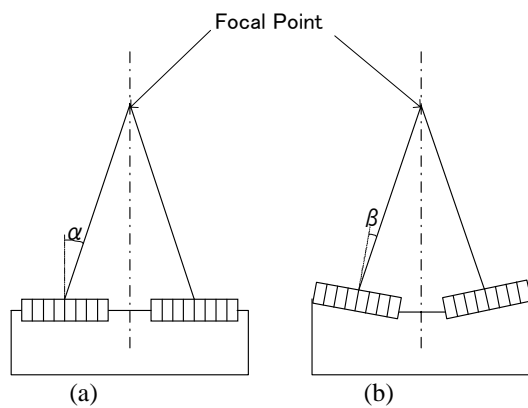
This time, we optimized a therapy transducer to increase the transmit efficiency and to improve the beam profile. In this paper, we describe our therapy system in detail, and report the experimental results applied to the dogs' prostate.

## MATERIAL AND METHODS

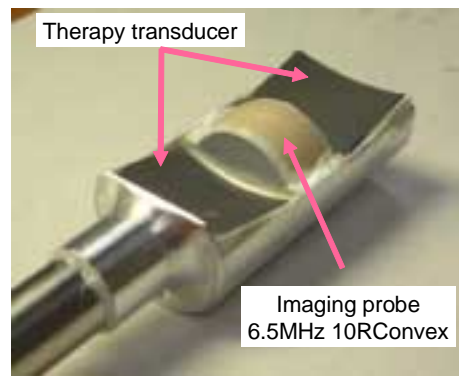
### Therapy head

Although the previous probe head [5] [6] had the pair of linear array therapy transducers arranged flat, this transducer pair is rearranged to incline to become inward looking in each other. This arrangement assures us to use the maximum ultrasonic power because of less beam deflection angle ( $\beta < \alpha$ ), as shown in the Fig. 1.

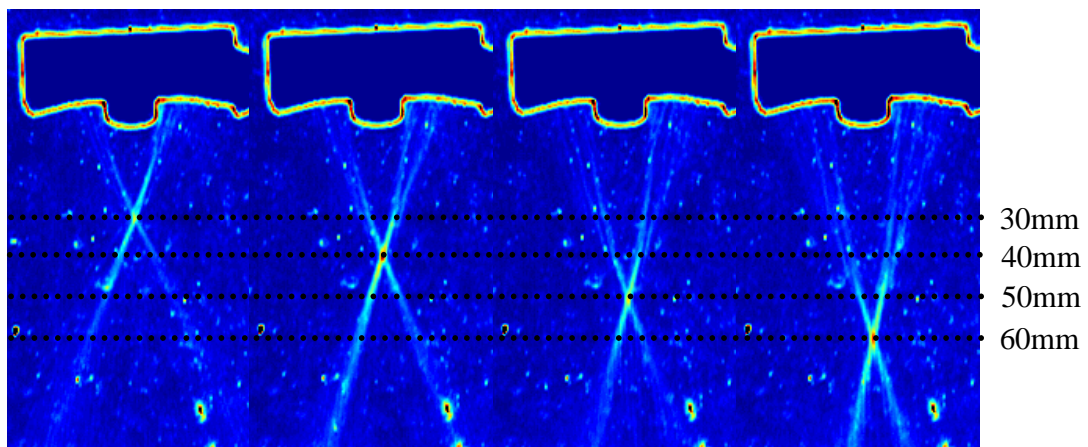
External view of the improved probe head is shown in the Fig. 2. In order to verify the system's variable focusing operation, beam pattern were measured by Schlieren method. The Schlieren images of variable focusing operation are summarized in Fig. 3. From these images, focal points are clearly observed to be controlled from 30mm to 60mm.



**FIGURE 1.** Schematic of (a) flat type therapy head and (b) inclined type therapy head.



**FIGURE 2.** External view of new head Therapy transducer has 96 (48+48) elements.



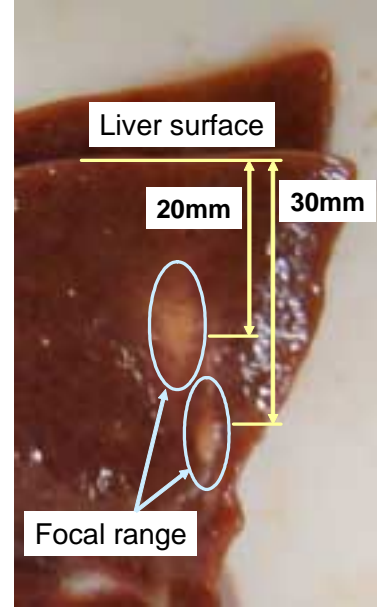
**FIGURE 3.** Schlieren images of the variably focused beam

## ***In vitro* study**

Irradiation experiment with extracted organ tissue was made using the above described probe. Extracted swine liver was fixed on stage in degassed water filled in the acrylic tank. The water temperature was 35 degree Celsius. The depth and position of irradiation region in the sample tissue are set according to the images given by the imaging transducer and the ultrasonic diagnostic device.

Immediately after the irradiation, the liver was removed from the tank, and the coagulated part of the liver was cut out and observed macroscopically. The irradiation condition is shown in Table 1. The photograph of the coagulated liver is shown in Fig. 4. The distance between the surface of probe and liver is adjusted 10mm.

As a result, in the case of the *in vivo* experiment, we may estimate the size of focus of ultrasonic therapy beam as 1 or 2mm in diameter and 10mm in length.



**FIGURE 4.** Lesion in swine liver by variable focusing HIFU

**TABLE 1. Irradiation condition**

Number	Focal length	Tissue depth	TAP
1	30mm	20mm	30W
2	40mm	30mm	25W

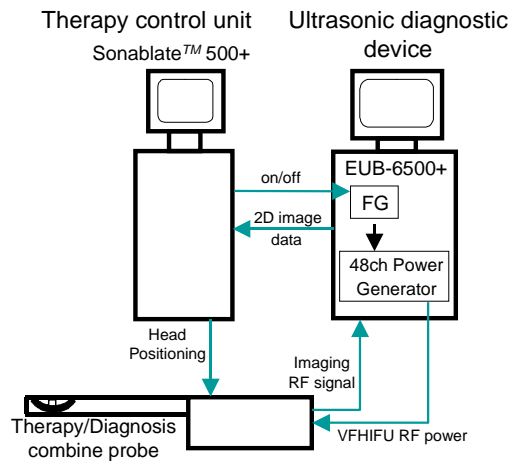
TAP: Total Acoustic Power

## **Total ultrasound therapeutic system**

Total ultrasound therapeutic system for *in vivo* experiment is necessary to control ultrasonic therapy beam and ultrasonic imaging beam simultaneously and cooperatively. This combination assures to improve aiming accuracy of the HIFU beam in the condition of real-time monitoring of the therapy region. Then, we can avoid the mismatch between the HIFU focal region and targeted region. Outline configuration and appearance of the integrated system are shown in the Fig. 5 and 6, respectively.

The system is constructed by combining 1) the variable focusing HIFU therapy head, 2) an ultrasonic therapy control unit of Sonablate<sup>TM</sup> 500 (therapy planning system and mechanical tool to move therapy head with head cooling system: Focus Surgery Inc.), and 3) an ultrasound diagnostic device EUB-6500 (Hitachi Medical Corporation).

The system is designed so that the two devices operate cooperatively. That is, in Fig. 5, high quality images obtained by the diagnostic device are transferred into the therapy control unit, and these images are redisplayed with therapy protocol GUI on the monitor of the unit. The ON/OFF (irradiation/rest) control of power generator is performed by the therapy unit following the protocol. Moreover, HIFU mode and Monitoring mode work in timesharing fashion (quasi real-time).



**FIGURE 5.** Construction of the therapy system      **FIGURE 6.** Outline view of the therapy system

### ***In Vivo* Animal study**

By the developed variable focusing HIFU system, animal experiments were conducted for the prostate gland of dog. The purpose of the experiment is as follows.

- 1) Carry out coagulation of the internal-organ tissue of prostate in each focal setting, and check medical treatment capability for living body.
- 2) Check the timesharing operation of HIFU and Monitoring mode with total ultrasonic therapy system.

The protocol of the experiment consists of following steps.

1. Measurement of position and size of prostate gland with the imaging transducer
2. Transfer of the results to Sonablate™ 500
3. Treatment Planning
  - Setup irradiation time and treatment scan pitch
  - Setup irradiation position and power
4. Operation of a chiller unit
5. Irradiation (Fig.7)
6. Euthanasia after the operation
7. Removal of a prostate and rectum
8. Formalin immersion, sectioning, and comparison with the treatment plan (Fig. 8)

The irradiation condition is shown in Table 2.

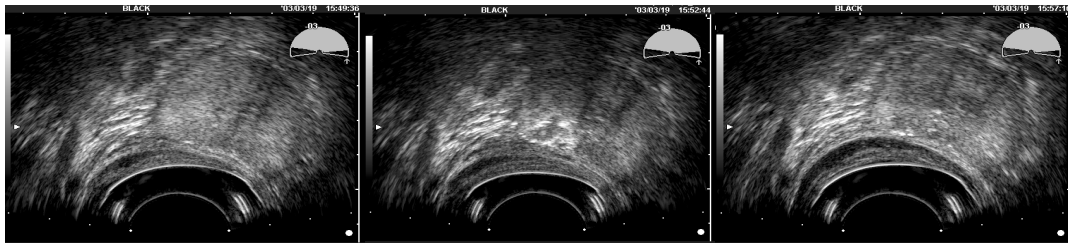
Fig. 7 shows real-time ultrasonic images in HIFU therapy (a) before, (b) just after, and (c) 5 minutes after the irradiation. After the irradiation, the ultrasonic image at a focal point is observed to be hyperechoic.

Fig. 8 shows the cross-sections of the prostate fixed in formalin. It is confirmed clearly that the outline of irradiated region has denatured.

**TABLE 2. Summary of the protocols used for the *in vivo* animal experiment**

Number	No. of sector	No. of linear	Focal length	TAP
1	5	3	30mm	55W
2	5	3	35mm	62W
3	4	3	40mm	68W
4	4	3	45mm	75W

On/Off time=4/8 s    Sector pitch = 3deg. Linear Pitch = 3mm



**FIGURE 7.** Real Time US Images in HIFU Therapy (a) Before irradiation (b) Just after irradiation (c) After 5 minutes



**FIGURE 8.** Cross-section of the prostate fixed with formalin

## RESULTS & DISCUSSION

It was confirmed that we successfully enlarge the irradiated area up to at least 25mm from the former 10mm (fixed focus case). This is due to movement of the focal depth from 30mm to 45mm by electrically variable focusing HIFU system.

According to our experimental result, in order to coagulate living tissue, more total acoustic power was needed with variable focusing system in comparison with fixed focusing one. We suppose that beamwidth of variable focusing system is more broad than of fixed focusing system. Therefore, element pitch of the array transducer is smaller than that previously reported, number of array elements is increased up to 48 from 32, and pair of arrays is set inclined inward symmetrically. As a results, less total acoustic power from

the newly developed probe realises enough irradiation than the conventional one without unnecessary hotspots.

Of course, the depth of focus of elevetioal beam has to be improved because it is determined by the curvature of the acoustic lens and not be optimized to the depth of therapy region. This requests us to select the best aperture size in lateral dimension and some other parameters of this system. This issue will be reported elsewhere in the near future.

## CONCLUSIONS

Our variable focusing HIFU system with acoustic lens for coagulation therapy was successfully demonstrated to coagulate prostate tissue by ultrasound beam focused at several distances in tissue from the rectum surface without exchanging probes. Our solution to improve efficiency of HIFU system (to narrow beam width and to reduce total acoustic power) is also reported.

## ACKNOWLEDGMENTS

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