3Pb5-10

Proceedings of Symposium on Ultrasonic Electronics, Vol. 32 (2011) pp. 549-550
8-10 November, 2011

Heating location control of gas exchanged microbubble enhanced HIFU

ガス置換超音波造影剤を用いた集束超音波治療における加熱領域制御手法の開発

Kiyoshi Yoshinaka[1]†, Ken-ichi Kajiyama[2], Hiroshi Utashiro[2], Takashi Azuma[2], Akira Sasaki[2], Shu Takagi[2], Yoichiro Matsumoto[2] ([1]AIST HTRI; [2]The Univ. of Tokyo)
葭仲 潔[1]† 梶山 賢一[2] 歌代 浩志[2] 東 隆[2] 佐々木 明[2] 高木 周[2] 松本 洋一郎[2]
([1](独)産業技術総合研究所ヒューマンライフテクノロジー研究部門 [2]東京大学)

1. Introduction

High-intensity focused ultrasound (HIFU) is widely used for therapeutic applications because it is an attractive and non-invasive tool by which to provide thermal therapy [1]. The sound pressure at the focal point reaches hundreds of megapascals, resulting in an increase in temperature, which necrotizes cells. Although HIFU treatment has been applied to prostate and breast tumors, for example, it is difficult to treat targets that lie behind bone (e.g., brain tumors) or that lie deep inside the body (e.g., liver tumors), because the ultrasound beam is reflected, refracted, and attenuated by the intervening tissue and/or bone. In order to resolve this problem, microbubble-enhanced HIFU has been developed [2-3]. Microbubbles are used as contrast agents for therapeutic applications of ultrasound imaging, and in a previous study, we used microbubbles to enhance the heating effect at the focal point of HIFU treatments. This enhancement of heating is caused by the generation of thermal energy based on the volume oscillation of microbubbles under the ultrasound irradiation. However, when microbubbles exist on the ultrasound pathway, they disturb the ultrasound propagation and distort the acoustic field. Distortion of the acoustic field leads to defocus and causes unexpected damage to tissue in the body.

In the previous study, we proposed a method by which to destroy microbubbles on the pathway of ultrasound and to focus the thermal energy only at the focal point in microbubble-enhanced HIFU treatment [4]. We developed a method for destroying microbubbles on the ultrasound pathway by irradiating repetitive high-intensity short-burst waves, where the durations of the intervals between burst waves are on the order of microseconds.

In this study we change the inner gas of the bubbles and evaluate our microbubble enhanced HIFU method.

----

k.yoshinaka@aist.go.jp

2. Method

The commercially available Levovist™ contrast agent was selected as a microbubble contrast agent. The average diameter of Levovist™ is 1.3 micrometer. In this study we use inner gas exchanged microbubble (C_3F_8-Levovist). An experiment was conducted with a polyacrylamide gel containing microbubbles in a uniform distribution having a void fraction on the order of 10^{-5}. The gel enables the positions of microbubbles, which have low solubility, to be fixed so that a stable uniform microbubble distribution can be maintained during the experiments. **Fig. 1** shows the experimental setup, which can measure the temperature distribution of the heating area. The piezoelectric (PZT) transducer generates ultrasound waves. The diameter and focal length of the PZT transducer are both 40 mm. The resonance frequency of the PZT transducer is 2.2 MHz. The ultrasound waves are irradiated to a gel in the water. The water is maintained at 37 deg C. The container filled with polyacrylamide gel is a cube having sides of 50 mm. A thermal liquid crystal sheet, the color of which changes with respect to temperature in the range of 50 to 60 deg C, is placed in the gel and positioned in the plane of the ultrasound beam axis.

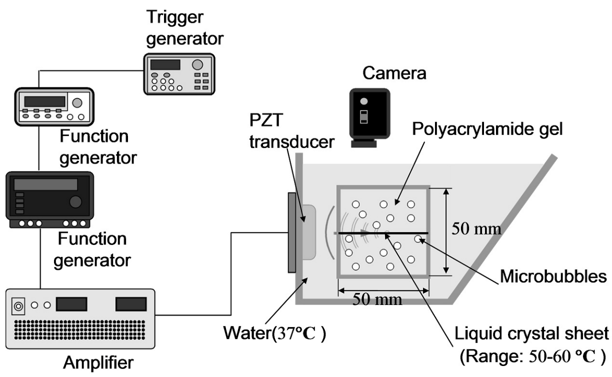

Fig. 1 Experimental apparatus.

3. Microbubble enhanced HIFU

Microbubble contrast agents have encapsulating shells because they are designed to be stable in order to be used in intravenous injection. The proposed method consists of two steps. The first step is repetitive high-intensity short-burst waves. In this step, burst waves destroy and fragment microbubbles on the ultrasound pathway, and the fragmented bubbles are then dissolved during the subsequent non-exposure time. In the second step, low-intensity continuous waves are irradiated in order to heat the focal point. **Fig. 2** shows the sequence of this method.

"Bubble destruction ultrasound parameters"

Frequency:2.2MHz, Intensity:5000W/cm^2, Peak to peak pressure 29.7MPa, Number of cycles:20, PRF(Pulse repetition frequency):0.5, 1, 2KHz, Number of pulses:100.

"Heating ultrasound parameters"

Frequency:2.2MHz, Intensity 400W/cm^2, Peak to peak pressure:11.8MHz, Exposure time: 60 sec(Continuous wave).

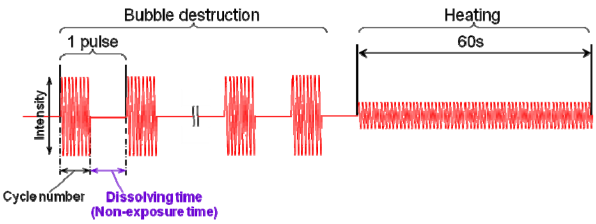

Fig. 2 Ultrasound sequence of microbubble enhanced HIFU

4. Result and discussion

Images of the temperature distribution for each non-exposed time are shown in **Fig. 3**. In the case of a nonexposed time of 0.5 ms, the heat-up region occurs at the edge of the container. This result suggests that at a non-exposed time of 0.5 ms, small number of microbubbles will be destroyed by the burst wave. For the non-exposed time of 1 ms, the heat-up region moves toward the focus. This occurs because the burst wave destroyed more microbubbles than the 0.5 ms non-exposed time. For the non-exposed time of 2 ms, the heat-up region occurs at the focus because the burst wave destroyed enough microbubbles to increase the temperature at the focus. As these results indicate, using a longer non-exposed time moves the heat-up region to the focus. This means that it is easier to destroy microbubbles at longer non-exposed times because there is more time for the fragmented microbubbles to diffuse.

5. Conclusion

We evaluated our microbubble enhanced HIFU method with gas exchanged microbubble. In the result, our method can use gas exchanged microbubble by adjustment of non-exposure time of bubble destruction wave.

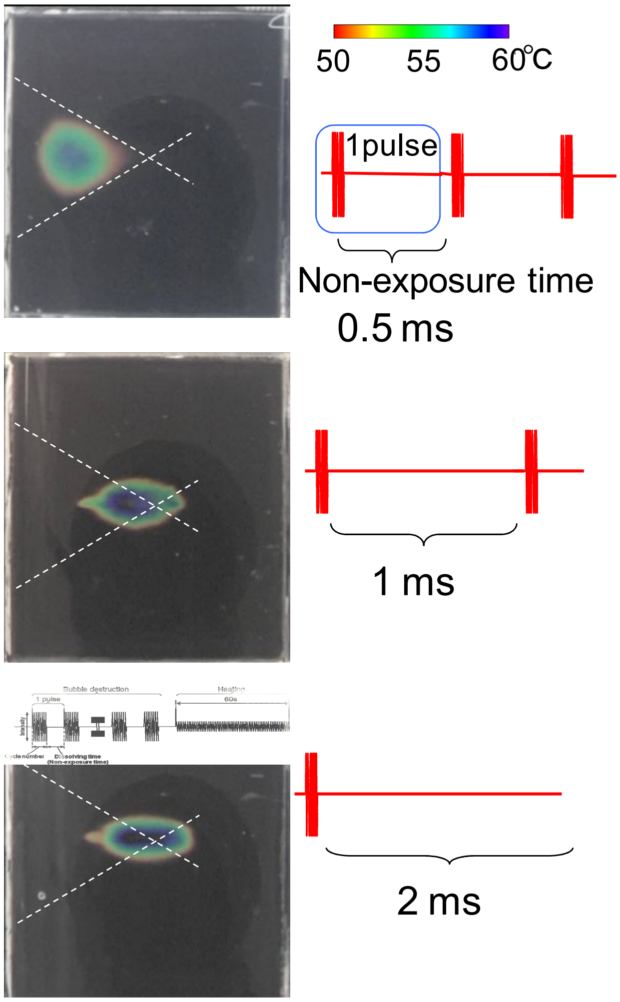

Fig. 3 Temperature distribution of microbubble enhanced HIFU (Comparison of non-exposed time)

Acknowledgment

The present study was partially supported by a Grant for Translational Systems Biology and Medicine Initiative (TSBMI) from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

References

1. G. T. Clement (2004) Perspectives in clinical uses of high-intensity focused ultrasound. Ultrasonics 42: 1087-1093.
2. Y. Matsumoto, J. S. Allen, S. Yoshizawa, et al. (2005) Medical ultrasound with microbubbles. Experimental Thermal and Fluids Science 29: 255-265 .
3. D. Razansky, P. D. Einziger, D. R. Adam (2006) Enhanced Heat Deposition Using Ultrasound Contrast Agent – Modeling and Experimental Observations. IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control 53(1):137-147.
4. K. Kajiyama, K. Yoshinaka, S Takagi, Y Matsumoto (2010) Microbubble enhanced HIFU. Physics Procedia, Vol. 3,1:305-314.