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Estimation of sonodynamic treatment region with chemosonoluminescence in gel phantom

ゲルファントムを用いたケモソノルミネッセンスによる音響化学治療の治療領域評価

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1. Introduction

High-intensity focued ultrasound (HIFU) treatment is a less invasive treatment by focusing ultrasound on the target tissue from outside the body and heating to coagulate the tissue. Sonodynamic treatment is another type of ultrasonic cancer treatment genrating reactive oxygen species by combining cavitation and a sensitizer. When a microbubble is subjected to ultrasound at its resonant frequency, its oscillation amplitude increases to an extreme. This is followed by its catastrophic collapse, at which the gas inside it may receive virtually adiabatic compression causing temperarure rise to thousands of degrees in centigrade. At such high temperature, the senstizer can be activated and water molecules can be thermally decomposed, generating active oxygen species which will attack cancer cells.

"Trigger HIFU" sequence, consisiting of an extremely high intensity short "Trigger" pulse followed by a moderate intensity long "Sustaining" burst, should be effective for sonodynamic treatment as well as cavitation enhanced HIFU heating because the acoustic pressure needed for generating cavitation is much higher than that for utilizing it. In this study, we conducted experiments using chemosonoluminescence phenomennon with luminol in a gel to invesitage both localization and efficiency of generating reactive oxygen species by such Trigger HIFU exposure. Reactive oxygen speices mediating chemosonoluminescence with luminol and sonodynamic treatment with a sensitizer may be different, but the elementary process of sonochemically effective cavitation is thought to be similar.

2. Materials and Methods

2.1 Experimental procedure

Experiments were performed in a water tank containing degassed water at room temperature with a therapeutic transducer and a gel, as shown in **Fig. 1**. The acrylamide gel was degassed in 0.7 mM luminol for 4 hour. The 128-channel 2D-array therapeutic transducer (Imasonic) with a focal length of 120 mm and a diameter of 147 mm was driven by a staircase driving system (Microsonic) at a frequency of 1 MHz. In this study, we used five irradiation patterns shown in **Table. 1**. All patterns were at a pulse repetition frequency of 3 Hz for 30 cycles. During the irradiation, images were acquired with the shutter of the DSLR camera always opened. All experiments were done in the darkroom.

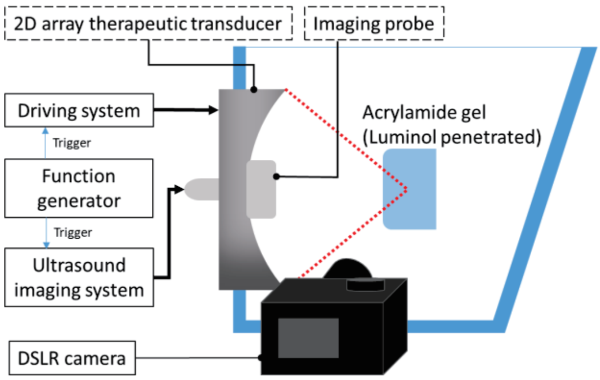

Fig. 1 Schematic of experimental setup

Table. 1 Irradiation pattern

No.	Focus point	Waveform	Conditions
1	1 point		Triggered Pulse – 1 MHz, 100 µs, 46 kW/cm² Sustaining Burst – 1 MHz, 10 ms, 237 W/cm²
2	1 point	Rest – 100µs	Triggered Pulse – The same condition as Sequence 1 **Rest – 100 µs** Sustaining Burst – The same condition as Sequence 1
3	2 point		1st point – TP : 100 µs, SB : 25 µs × 200 = 10 ms 2nd point – TP : 100 µs, SB : 25 µs × 200 = 10 ms
4	1 point		TP – offset 4 mm SB – The same condition as Sequence 1
5	2 point		TP – offset 4 mm SB – The same condition as Sequence 3

2.2 Date processing

Since the luminance of luminol is blue, the blue component of the image obtained by the DSLR camera was extracted, normalized by the maximum value, and binarized with the threshold of the half value, as shown in **Fig. 2**. The volume of chemosonoluminescence was estimated as follows. The length of a line with a binarized value of one

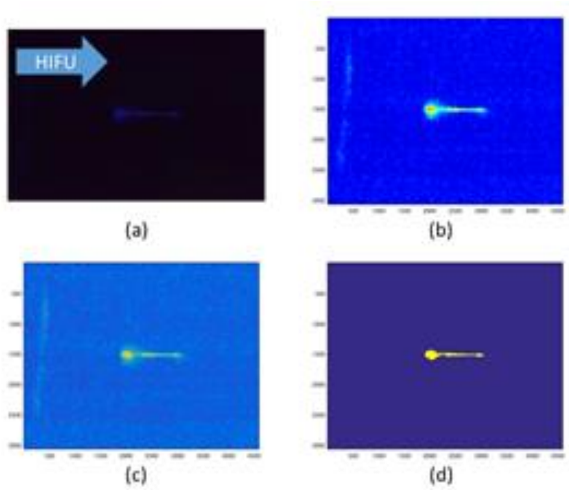

Fig. 2 Flow of date processing.
(a) Raw data, (b) Blue component,
(c) Normalized, and (d) Binarized.

was detected on all lines perpendicular to the ultrasound irradiation axis. Calculate the volume of the disk with a diameter of the length on each line. By summing up the disk volumes the approximate volume of chemosonoluminescence was obtained. In this way, possible overestimation of the volume can be avoided although the center of the disk may change for each line.

3. Results and Discussion

The calculated light emitting volume of each irradiation sequence for 30 seconds is shown in **Fig. 3**. Comparison between Sequences 1 and 2 shows the tendency that the reactive oxygen generation region decreases with the intermission time after Tigger pulse. In Sequence 3, the volume was smaller than Sequence 1, although the irradiated acoustic energy was twice more. These indicate that the intermission reduced the bubble size to that less effective for the generation of reactive oxygens.

The length of the light emitting region in the focal zone is compared in **Fig. 4**. By giving a 4 mm axial offset between the focal points of Trigger pulse, the axial expansion of the length emitting region was reduced. This indicates that the reactive oxygen generation can be better localized by the offset.

4. Conclusion

For sonodynamic therapy, in which the localization and high efficiency of generating reactive oxygen are the subjects to be pursued, the results obtained from the experiments in the gel suggests that a certain axial offset between the focal points of Trigger pulse makes the localization better and closer to the intended point.

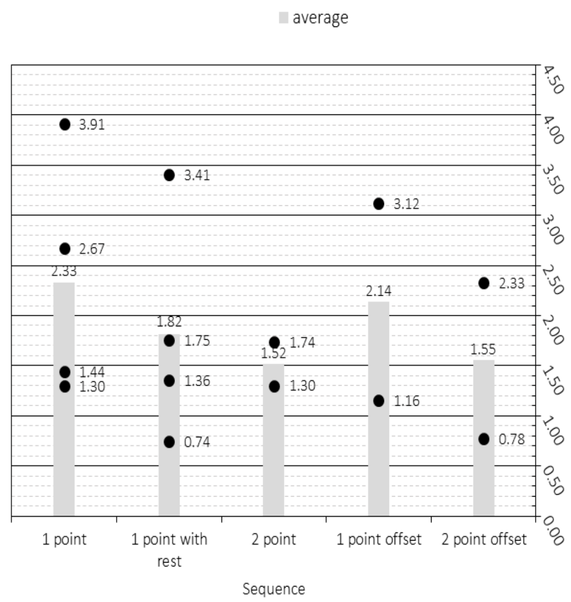

Fig. 3 Approximate volume

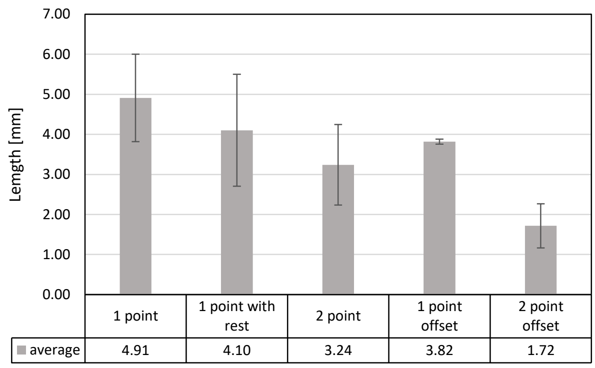

Fig.4 Length of light emitting region

References

1. Prevenslik TV: Ultrasonics. **42**(1-9). P. 313. 2003
2. P. Riesz: Enveronmental Health Prespectives. **64**(1985) p. 233.
3. H. N. McMurray: Journal of Physical Chemistry. **103**(1999). No. 20. p. 3955.
4. J. Yasuda: Japanese Journal of Applied Physics. **55**(2016).

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