3P5-3

Study on effectiveness of anti-infective system using a planar transducer irradiating low-intensity ultrasound to titanium dioxide particles

平面振動子を用いた酸化チタンへの超音波照射による抗感染システムの有効性評価

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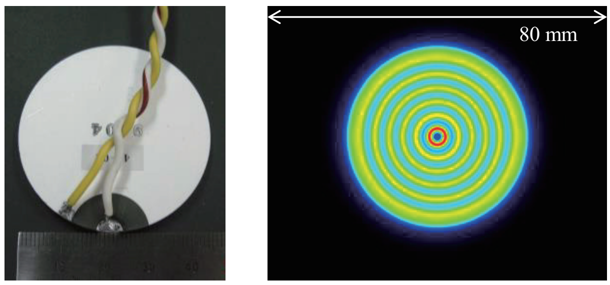
1. Introduction

Infection at the exit site of a catheter is a main cause of nosocomial infections. To overcome this problem, we have developed an anti-infection system utilizing the bioeffect of ultrasound that promotes the generations of the reactive oxygen species (ROS), by irradiating low-intensity focused ultrasound (LIFU) from a concave transducer to a cuff substrate coated with titanium dioxide (TiO_2) particles[1-3)]. The focused ultrasound used in this system has an advantage that the surrounding normal tissue is not exposed to unnecessary ultrasound irradiation because the required energy is provided to the only limited region. However, with respect to the transducer shape, since the concave transducer need a coupling material such as a water bag considering a focal depth, it might be inconvenient for daily clinical use.

On the other hand, if a planar transducer is used for the irradiation, the use of it matches the needs of clinical sites because it is easy to attach it on the skin. However, one concern when using the planar transducer is the lack of acoustic power for promoting the reaction and the unnecessary ultrasound exposure to normal tissues. Therefore, in this study, a prototype of a circular-planar transducer that was assumed to be attached on the skin was fabricated, and the performance evaluation with respect to the ROS generation under exposure of low-intensity ultrasound was conducted.

2. Preparation of a planar transducer

A custom-made circular-planar transducer with a center frequency of 500 kHz and a diameter of 45 mm was prepared. **Fig. 1**(a) shows a photograph of the circular-planar transducer. Electrodes are attached to both sides of the PZT and lead wires are connected. Assuming attachment to the skin, the ultrasound radiation surface is covered with a silicone sheet with a thickness of 0.1 mm. Fig. 1(b) shows the acoustic field calculated at a depth of 5 mm away from the transducer surface. **Fig. 2** shows the acoustical total power measured by a power meter (UPM-DT-1,Ohmic Instruments) when a voltage in the range of 5 to 60 V was applied to the transducer as a continuous wave. For example, the output per unit area at 2 W was equivalent to 0.1 W/cm^2. Needless to say, this output was lower than that of the focused ultrasound transducer used so far in this study[3)].



(a) (b)

Fig. 1 A custom-made circular-planar transducer (a) and its acoustic field at a depth of 5 mm from the transducer surface.

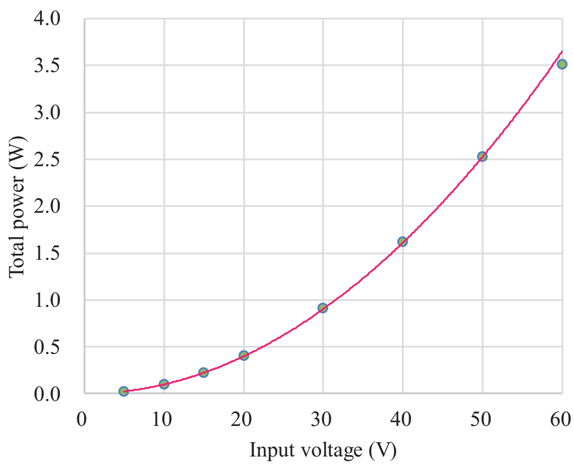


Fig. 2 Relationship the acoustical total power and the input voltage to the transducer.

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3. Experiment

In order to investigate that the ROS production was promoted by ultrasonic irradiation to TiO_2 even at the low output as described above, an experiment using methylene blue (MB) solution was conducted. **Fig. 3** shows the experimental system. Degassed water for acoustic coupling was put into an acrylic container, and a small polystyrene cup poured with a suspension of 15 ml of diluted MB solution and 30 mg of TiO_2 particles with an average particle size of 250 nm was placed on the transducer. Subsequently, by using a power amplifier (HSA4001, NF) and a function generator (AFG3252, Tektronix), continuous wave (CW) of ultrasound with a frequency of 500 kHz and an acoustical total power of 2 W was irradiated for 15 minutes. From the suspension after ultrasound irradiation, only TiO_2 particles were removed by centrifugal separation, the absorbance of the MB solution was measured by using a spectrophotometer (VT650ST, Jasco), and then the efficiency of the ROS production was evaluated by the change in absorbance. In addition, comparison with the control groups was also conducted.

4. Results

Fig. 4 shows a result of comparing the absorbances of the four groups based on the combination of the presence or absence of ultrasonic irradiation and the presence or absence of TIO_2 particles. Here, #1 is a group that does not include both TiO_2 particles and ultrasonic irradiation (Ti-Us-), #2 is a group that includes TiO_2 particles but does not include the ultrasonic irradiation (Ti+Us-), #3 is a group that does not include TiO_2 particles but includes the ultrasonic irradiation (Ti-Us+), and #4 is a group that includes both TiO_2 particles and the ultrasonic irradiation (Ti+Us+). Among them, since the absorbance of #4 showed the largest change, it was assumed that the efficiency of ROS production in #4 was the largest.

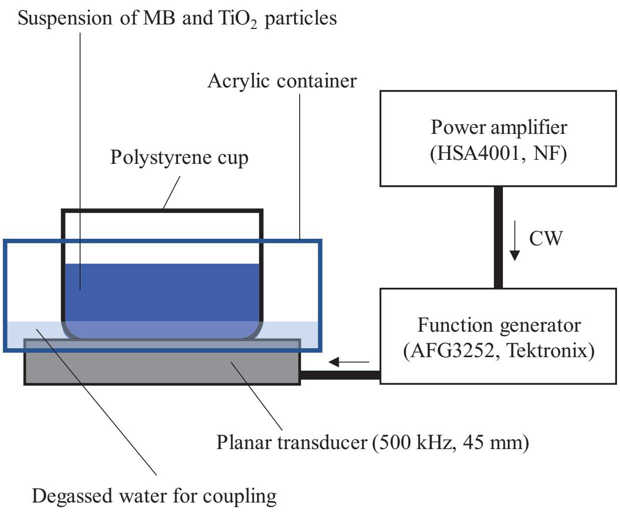

Fig. 3 An experimental setup using a circular-planar transducer.

5. Conclusions

From the result of experiment using MB solution, it was confirmed that the production of ROS was increased by ultrasound irradiation to TiO_2 particles even when using a planar transducer with lower intensity than the focused ultrasound transducer used previously in this study. In the future, we plan to investigate the relationship between the conditions of ultrasound irradiation, the size and quantity of TiO_2 particles, and the changes in absorbance. In addition, from the viewpoint of safety irradiation of ultrasound to the skin, we also plan to evaluate the temperature rise on the surface of the planar transducer.

References

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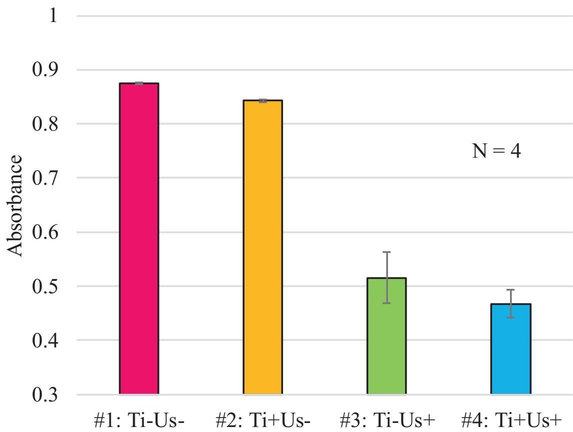

Fig. 4 A result of comparing the absorbances of the four groups. Here, #1: a group that does not include both TiO_2 particles and ultrasonic irradiation, #2: a group that includes TiO_2 particles but does not include the ultrasonic irradiation, #3: a group that do not include TiO_2 particles but includes the ultrasonic irradiation, and #4: a group that includes both TiO_2 particles and the ultrasonic irradiation.