# Estimation of thermal coagulation region induced by bubble-enhanced ultrasonic heating using numerical simulation

Gen Miura<sup>1‡</sup>, Shohei Mori<sup>1</sup>, and Shin Yoshizawa<sup>1,2,3\*</sup>

(<sup>1</sup>Grad. School of Eng., Tohoku Univ.; <sup>2</sup>Grad. School of Biomed. Eng., Tohoku Univ.; <sup>3</sup>SONIRE Therapeutics)

## 1. Introduction

High-intensity focused ultrasound (HIFU) treatment is a non-invasive cancer treatment that delivers high-intensity ultrasound from outside the body. The temperature in the target region increases by HIFU and cancer tissue is coagulated. One of the problems in HIFU treatment is long treatment time due to the small focal region compared to the volume of cancer tissue. Therefore, we have proposed an efficient treatment method using "Trigger HIFU sequence" that uses cavitation bubbles generated by negative pressure of ultrasound<sup>1)</sup>. Bubbles are generated by a high-intensity, short-duration "trigger pulse", and continuously oscillate by a mediumintensity, long-duration "heating burst". Although it is known that the coagulated region of tissue depends on the bubble generation region, further study is required to predict the thermally coagulated region  $^{2)}$ . In this study, we purpose accurately estimation of coagulated region after HIFU sonication with cavitation bubbles by using numerical calculations.

# 2. Materials and Method

## 2.1 Experimental setup

**Fig. 1** shows the experimental setup used in this study. A 256-element array transducer with a diameter of 12 cm and a focal length of 12 cm was used to generate HIFU at a frequency of 1.0 MHz. Experiments were conducted in degassed water (dissolved oxygen saturation 20-25%). To prevent the influence of dissolved bubbles, the chicken breast tissue was soaked in 0.9% physiological saline and degassed using a deaerator for 3 hours. After HIFU sonication, the chicken was taken out of the water and quickly frozen for 1 hour. The chicken was cut along the XZ-plane and the short and long diameter of the coagulated region were measured.

## 2.2 Trigger HIFU sequence

**Fig. 2** shows the trigger HIFU sequence. Trigger pulses with 0.025 ms at 30 kW/cm<sup>2</sup> and heating bursts with 9.95 ms at  $1.0 \text{ kW/cm}^2$  were used in the sequence. The HIFU intermission was set to

> E-mail: <sup>‡</sup>miura.gen.r1@dc.tohoku.ac.jp, \*shin.yoshizawa.e7@tohoku.ac.jp

0.010 and 0.015 ms after the trigger pulse and the heating burst, respectively. An external trigger was input using function generator, and the duty ratio was set to 1/3.5 or 1/3, for 30 s of sonication.

## 2.3 HITU simulator

The coagulated region was estimated using the "HITU simulator", which is an axisymmetric acoustic field / temperature field simulator that considers the nonlinear propagation of ultrasound waves<sup>3)</sup>. Based on the results of other temperature measurement experiments outside the focal region, we made the layer model shown in **Fig. 3** and **Table I** and calculated<sup>4,5)</sup>. In this numerical calculation, the part where cumulative equivalent minutes at 43 °C (CEM43) calculated using the temperature field is 240 minutes or more was defined as the coagulated region, and the short and long diameter were estimated.







Fig. 2 Trigger HIFU sequence.

	Layer1	I Lay	/er2	Layer3 Lay	er4 <mark>I</mark> La I	yer5
	Water	Chic	ken 0	26000 260000		
			¦B	ubbles I		
Trans	ducer	i	i	i	i.	Z
0(cm)		10	11	13	14	
Fig. 3	Laver mod	el used	in HI	ΓU simula	ator.	

 Table I
 Materials and parameters of layer.

		-			
Material	Water	Chicken	Bubbles	Chicken	Water
Layer	1	2	3	4	5
Sound speed (m/s)	1520	1520	1520	1520	1520
Mass density (kg/m <sup>3</sup> )	1000	1000	1000	1000	1000
Attenuation at 1 MHz (dB/m)	0.22	58	133	58	0.22
Fraction of attenution due to absorption	0	0.85	0.85	0.85	0
Exponent in attenuation power law	2	1	1	1	2
Nonlinear parameter	3.5	4.5	4.5	4.5	3.5
Heat capacity (J/kg/K)	4180	4180	4180	4180	4180
Thermal conductivity (W/m/K)	0.55	0.55	0.55	0.55	0.55

#### 3. Result and Discussion

Fig. 4 shows the results of the experiment and numerical calculations. Regarding the experimental results, the short and long diameter of the coagulated region were measured by converting the image into grayscale, setting a brightness threshold, and performing binarization. Only when the duty ratio was 1/3, traces of tissue destruction were observed in the thermally coagulated region. The reason is thought to be that the temperature became higher and boiling bubbles were generated as the duty ratio increased. Table II shows a comparison of results with each duty ratio. The difference in the short and long diameter were within 5%, and that the estimation was accurate. Fig. 5 shows the results of comparing the color map image of the grayscale tissue image and the border of CEM43 obtained from the numerical calculation. When the duty ratio is 1/3.5, the estimated area corresponds to the high brightness area, although qualitatively. It can be seen that when the duty ratio is 1/3, the vertical length of the part far from the transducer is smaller than in the numerical calculation. This is thought to be due to the excessive generation of bubbles near the focal point, which shields the propagation of the ultrasonic waves, reducing the heating effects of the heating burst.

#### 4. Conclusion

From the results of experiments and numerical calculations, we were able to estimate the coagulated region in bubble-enhanced HIFU treatment with high accuracy. Using this numerical calculation, it is possible to accurately estimate the treatment region before HIFU treatment, which is expected to lead to improvements in treatment safety and efficacy. In addition, numerical calculations using temperature fields can also be applied to multifocal HIFU sonication, and further application are expected.



Fig. 4 Comparing images with each duty ratio.

Table II Comparison of diameter.

		Short diameter	Long diameter	n
Duty ratio 1/3.5	Simulation(mm)	2.82	11.86	—
	Experiment(mm)	2.81	11.91	3
	Difference(%)	0.38	0.44	—
Duty ratio 1/3	Simulation(mm)	3.17	13.55	_
	Experiment(mm)	3.13	13.78	3
	Difference(%)	1.38	1.66	_



Fig. 5 Color map image and border of CEM43.

#### References

- R. Takagi, S. Yoshizawa, and S. Umemura, Jpn. J. Appl. Phys. 49, 07HF21 (2010).
- S. Kannoto, S. Yoshizawa, Jpn. J. Appl. Phys. 63, 03SP71 (2024).
- 3) J. Soneson, "HITU\_Simulator v2.0 User's Manual", FDA (2019).
- A. Asai, H. Okano, S. Yoshizawa, and S. Umemura, Jpn. J. Appl. Phys. 52, 07HF02 (2013).
- 5) K. Ueda, S. Ito, S. Umemura, S. Yoshizawa, Jpn. J. Appl. Phys. **60**, SDDE13 (2021)