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Evaluation of Acoustic, Thermal, and Morphological Properties in the Egg White Phantom

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Abstract: The egg white phantom is a thermal lesion visualization phantom able to illustrate a thermal lesion. It is often used to evaluate the performance of HIFU and is less expensive than the BSA phantom. This study determined the optimal phantom composition for evaluated therapeutic ultrasound machines by varying the egg white concentration in the egg white phantom and demonstrated its utility as a therapeutic ultrasound phantom. The egg white phantom at varying egg white concentrations (10-40% in 10% intervals) was fabricated, and its thermal properties and acoustic properties were assessed. In addition, the size and shape of the formed lesion were compared between the egg white phantom and bovine liver tissue according to the electrical power. The results showed that 30% egg white phantom was optimal for the performance evaluation due to its thermal and acoustic properties. The generated thermal lesions formed sequentially as a cigar, ellipse, tadpole, and cone shapes according to the electrical power; a similar tendency was observed in the liver tissue. Hence, we conclude that the egg white phantom will prove useful in quantitatively evaluating the thermal effects of therapeutic ultrasound.

Key words: Egg white phantom, Acoustic property, Heat property, Focused ultrasound, Thermal lesion

I. Introduction

The thermal lesion visualization phantom is a transparent phantom that visually confirms a thermal lesion containing a heat-sensitive indicator using ultrasound. Initially, a polyacrylamide hydrogel (PAG) phantom was used as a support medium for protein electrophoresis and an intermediate mediator for ultrasonographic impedance matching [1,2]. Later, the bovine serum albumin (BSA) phantom was developed using a PAG phantom containing the protein derived from the bovine serum albumin, and it enabled thermal lesion assessment [3]. The BSA phantom was validated for the therapeutic ultrasound by characterizing the acoustic properties and the lesion formed during ultrasound [4,5]. However, the BSA phantom is difficult to fabricate because the bovine serum albumin is expensive and challenging to procure. Therefore, the egg white phantom was developed by using the egg white as an inexpensive protein alternative to BSA [6].

The egg white phantom has been applied primarily to in vitro studies for the performance evaluation of therapeutic ultrasonic devices such as High Intensity Focused Ultrasound (HIFU) and hyperthermia [7-14]. Unlike the tissue mimicking material (TMM) phantom [15], the production method of the thermal lesion visualization phantom is not standardized. As a result, the phantoms vary in protein concentration according to the specific methodology. The attenuation coefficient of the phantom was affected by the egg white concentration [6]; in addition, it is expected that a degree of thermal lesion would be changed by the amount of protein with a thermally-sensitive indicator. To ensure accurate measurements, the

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acoustic and thermal properties of the phantom should be evaluated based on the protein concentration. Also the optimal concentration should be selected for the performance evaluation of therapeutic ultrasound devices. Notably, the utility of egg white phantom as a therapeutic ultrasound phantom has not been quantitatively demonstrated because a detailed comparison between the estimated lesion and the actual lesion in tissue has not been performed.

In this study, the acoustic and thermal properties of the egg white phantom were evaluated according to the egg white concentration for use as a thermal visualization phantom. The most appropriate phantom concentration for the therapeutic ultrasound evaluation was determined. In addition, the utility of the egg white phantom as a therapeutic ultrasound phantom was determined using a liver tissue model, which is the main target of HIFU treatment.

II. Materials and Methods

1. Phantom preparation

The egg white concentration in the egg white phantom was adjusted from 10-40% in 10% intervals by mixing the egg white with polyacrylamide solution. The phantom was fabricated as previously described by Takegami et al [6]. Distilled water 1 M Tris, egg white, acrylamide/bis-acrylamide (19:1 ratio), 10% ammonium persulfate (APS), and 10% N,N,N',N'-Tetramethylethane-1,2-diamine (TEMED) were mixed sequentially. The mixture was hardened by polyacrylamide polymerization. The polyacrylamide introduced fiber crosslinking by copolymerization with N, N'-Methylenebisacrylamide; polymerization was initiated by the addition of APS, which generates the required free radicals in the presence of TEMED. Table 1 summarizes the phantom composition with increasing egg white.

Table 1. The phantom composition with increasing egg white.

Components	Proportion (%, v/v)			
Egg white	10	20	30	40
Distilled water	54	48	42	36
40% Acrylamide	25.71	22.86	20	17.14
10% APS	0.64	0.57	0.5	0.43
TEMED	0.39	0.34	0.3	0.26
1M Tris	9.26	8.23	7.2	6.17
Total	100	100	100	100

2. Acoustic properties

The sound velocity, attenuation coefficient, density, and acoustic impedance were measured for each phantom, which is illustrated in Fig. 1. A water tank was filled with degassed water maintained at 37ºC, similar to the human body temperature. A single 3.5 MHz transducer was used to send and receive the ultrasonic signals (Technisonic Research, Inc., US). A function generator was used as an ultrasonic pulser/receiver (MKPR-1030, M.K.C Korea Inc., Korea). The received signal was stored in a digital oscilloscope (Waverunner 6100A, Lecroy, USA) and analyzed by Acqknowledge 3.7.5 (BIOPAC Systems, Inc., USA). The sound velocity in the fabricated phantom was calculated from the echo range by measuring Δt during a transmitted round trip; the attenuation coefficient was calculated using from the reflected signal as follows (1):

$$\alpha(f) = -20/(2d)log_{10}(A(f)/A_0(f)) \quad (1)$$

where α, in dB/cm is the attenuation coefficient of the phantom, d is the sample thickness, $A(f)$ is the reflected signal amplitude at the frequency f with the phantom, and $A_0(f)$ is the reflected signal amplitude at the frequency f without the phantom. The density of the phantom was calculated by measuring the volume and weight of specimen sized $5 \times 5 \times 5$ cm^3

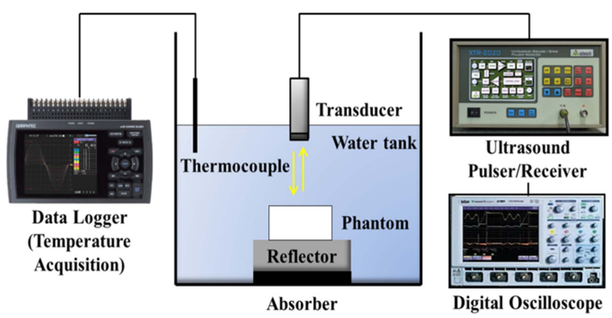

Fig. 1. The experimental setup for evaluating the acoustic properties of the phantom.

fabricated phantom. The acoustic impedance was measured by multiplying the sound velocity and density of each phantom. Ten samples per each egg white concentration were used for measuring the acoustic properties, and they were measured repeatedly 5 times. After measuring the acoustic properties of egg white phantom, the most similar tissue with the egg white phantom was confirmed by comparing the liver, breast, and soft tissue of human.

3. Thermal properties

To assess the thermal properties, the specific heat was measured in each phantom, and the thermal lesion was characterized by focused ultrasonication. The temperature change of the water and within the specimen was measured. The specific heat was then calculated based on the law of heat conservation as follows (2):

$$c_1 = (c_2 m_2 \Delta T_2)/(m_1 \Delta T_1) \quad (2)$$

where c_1 and c_2 are the specific heat of the phantom and water; m_1 and m_2 are the weights of the phantom and water; and ΔT_1 and ΔT_2 are the temperature changes of the phantom and water, respectively. The specific heat of the water, c_2 is generally 1 at 20°C.

To determine the lesion generated by a therapeutic ultrasound, a focused ultrasound was performed on the phantom specimen. A concave type single transducer (H-101, Sonic Concepts Co., USA) was used at a 1.1 MHz center frequency, a 100 μs period, 3.5 V_{p-p} burst wave, and 10 cycles. The electrical power was varied between 40 W, 60 W, and 80 W and lasted 60 s. The focal pressure obtained from each electrical power using a PVDF needle hydrophone in degassed water at 25°C. For the electrical powers of 40 W, 60 W, and 80 W, the focal pressures were 3.9, 4.70, and 6.2 MPa (acoustic intensity of 523.3, 737.6, and 1,298.8 W/cm^2), respectively. Fig. 2 shows the experimental setup for evaluating the thermal lesion by focused ultrasonication. After ultrasonication, the length of the resulting lesion was measured for each phantom according to the egg white concentration. Fig. 3 shows the mimetic diagram of thermal lesion after ultrasonication. (a) is the width of lesion that

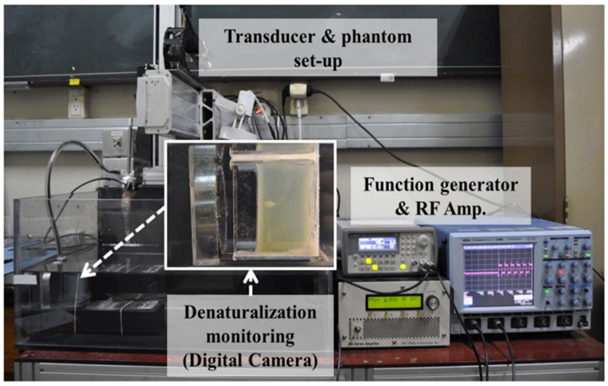

Fig. 2. The experimental setup for evaluating the thermal lesion by focused ultrasonication.

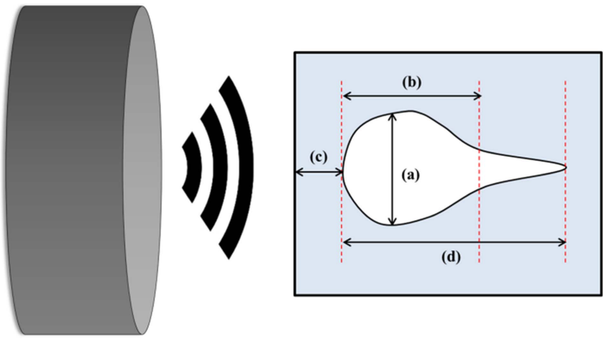

Fig. 3. The mimetic diagram of thermal lesion after ultrasonication. (a) width, (b) head-length, (c) distance from the surface, and (d) full-length.

was measured parallel to the lateral direction of ultrasound transducer. (b) is the length of head in a tadpole-shaped lesion, (c) is the distance between the front surface of the phantom to the lesion boundary, (d) is the full-length of lesion. (b), (c), and (d) were measured parallel to the axial direction of ultrasound transducer.

4. Tissue thermal lesion

The tissue morphology was compared between the bovine liver and the egg white phantom. The liver specimens were excised within 24 hours of slaughter to ensure freshness, cut to the size of 8.2 × 8.2 × 4 cm^3, and then fixed into an acrylic frame. A focused ultrasound was performed at conditions identical to those used to evaluate the phantom except the electrical power, which was varied at 10 W intervals between 10-100 W; For each electrical powers, the focal pressures were 2.1, 2.7, 3.4, 3.9, 4.3, 4.7, 5.3, 5.5, 6.2, and 6.4 MPa (acoustic intensity of 146.8, 242.2, 385.7, 523.3, 618.6, 737.6, 942.9, 1,002.9, 1,298.8, and 1,353.8 W/cm^2), respectively. To confirm the lesion formation and shape, the lesion in the egg white phantom was monitored in real-time continuously by digital camera (the maximum resolution is 1,230 megapixel). In the liver tissue, the middle of lesion was incised by monitoring with B-mode ultrasonic image to confirm the lesion formation and shape. Its image recorded using the same digital camera. The images of the lesions were traced by the same operator in ImageJ, and the lesion areas were calculated using a MATLAB program.

III. Results

1. Acoustic evaluation

Fig. 4 summarizes the acoustic property changes of the phantom according to the egg white concentration. The sound velocity decreased as the percentage of egg white increased between 10-30% (10% intervals); at a 40% concentration, the sound velocity was nearly identical to the velocity at 30% (logarithmic fit, coefficient of determination = 0.9526). The attenuation coefficient increased linearly (linear fit, coefficient of determination = 0.9057). Both the density and acoustic impedance increased as the egg white concentration increased, but the density plateaued at a 40% concentration (logarithmic and linear fit, coefficient of determination = 0.9764 and 0.9077, respectively).

Table 2 summarizes the acoustic property comparisons between the egg white phantom (10-40% egg white), liver tissue, and breast tissue. The sound velocity of the egg white phantom was 1,506-1,537 m/s, which differed from the liver tissues, but was similar to breast tissue. The acoustic impedance and density were 1.02-1.048 g/cm^3 and 1.567-1.579 MRayls, respectively, and were similar among all three tissues. The attenuation coefficient of the phantom was 0.06-0.106 dB/cm-MHz), which was 1/5 of the liver tissue coefficient. Overall, the acoustic properties of the phantom were most similar to those of breast tissue, except the attenuation coefficient.

2. Thermal property evaluation

As the egg white concentration increased (10%, 20%, and 30%), the specific heat of the phantoms de-

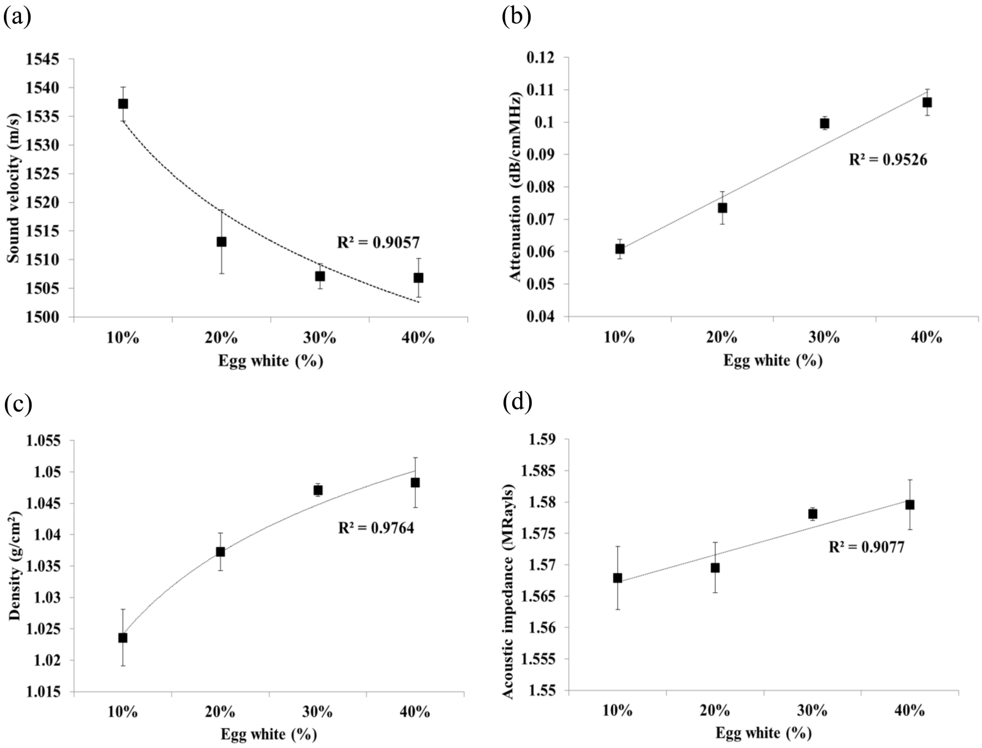

Fig. 4. The acoustic property changes of the phantom according to the egg white concentration; (a) sound velocity, (b) attenuation coefficient, (c) density, (d) acoustic impedance.

Table 2. The acoustic property comparisons between the egg white phantom (10-40% egg white), liver tissue, and breast tissue.

Acoustic Property	Phantom	Liver tissue[a]	Breast tissue[a]	Soft tissue[b]
Sound velocity (m/s)	1,506-1,537	1,595	1,510	1,561
Attenuation coefficient (dB/cm-MHz)	0.06-0.106	0.5	0.75	0.54
Density (g/cm^3)	1.02-1.048	1.06	1.02	1.043
Acoustic impedance (MRayls)	1.567-1.579	1.69	1.54	1.63

[a]ICRU 1998, [b]Mast et al. 2000.

creased to 1.79, 1.532, 1.505, and 1.448 cal/g°C, respectively (logarithmic fit, coefficient of determination = 0.9246). On visual examination, the lesion was tadpole-shaped at all concentrations performed at the same electrical power (80 W); the shape was most distinct in the 30% egg white phantom. Fig. 5 illustrates the lesion shapes identified by the focused ultrasound (80 W) at the varying egg white concentrations.

For quantitative analysis, the lesion length was measured parallel to the axial direction of ultrasound transducer, and the perpendicular dimension was designated as the width; the area was calculated at each point along the entire length and width. As the egg white concentration increased, the lesion length also increased until plateauing at a 40% concentration. However, the distance between the front surface of the phantom to the lesion boundary, directed towards the transducer, decreased as the egg white concentration increased; this confirmed that the lesion formed gradually directed towards the transducer. These dimensions in each phantom are illustrated in Fig. 6. In addition, the visual transparency of the phantom decreased as the egg white concentration increased. As a result, it was difficult to discern the lesion in the 40% egg white phantom, which had the lowest visual transparency. The color of the formed lesion was unclear due to the low concentration of thermal-sensitive indicator in the 10% egg white phantom; the lesion was easier to distinguish in the 30% egg white phantom compared to the 20% egg white phantom.

3. Morphologic comparison between the egg white phantom and tissue

The length, area, and shape of the lesions in the egg white phantom and bovine liver tissue identified

(a) (b) (c)

Fig. 5. The lesion shapes identified by focused ultrasound (80 W) at the varying egg white concentrations; (a) 10%, (b) 20%, (c) 30%, (d) 40%.

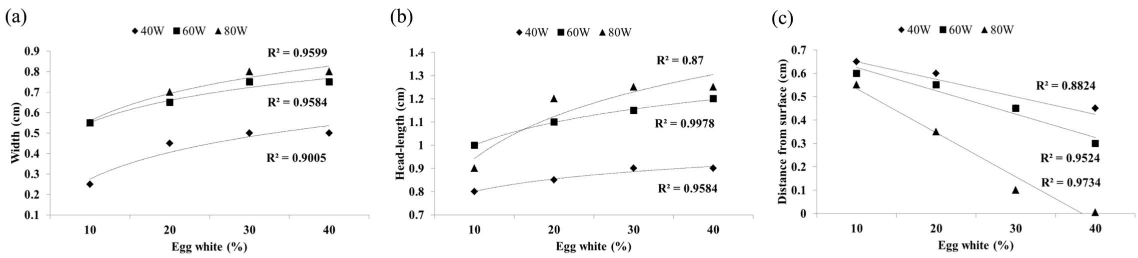

Fig. 6. The change of length in the formed lesion according to the egg white concentration by the focused ultrasound sonication.

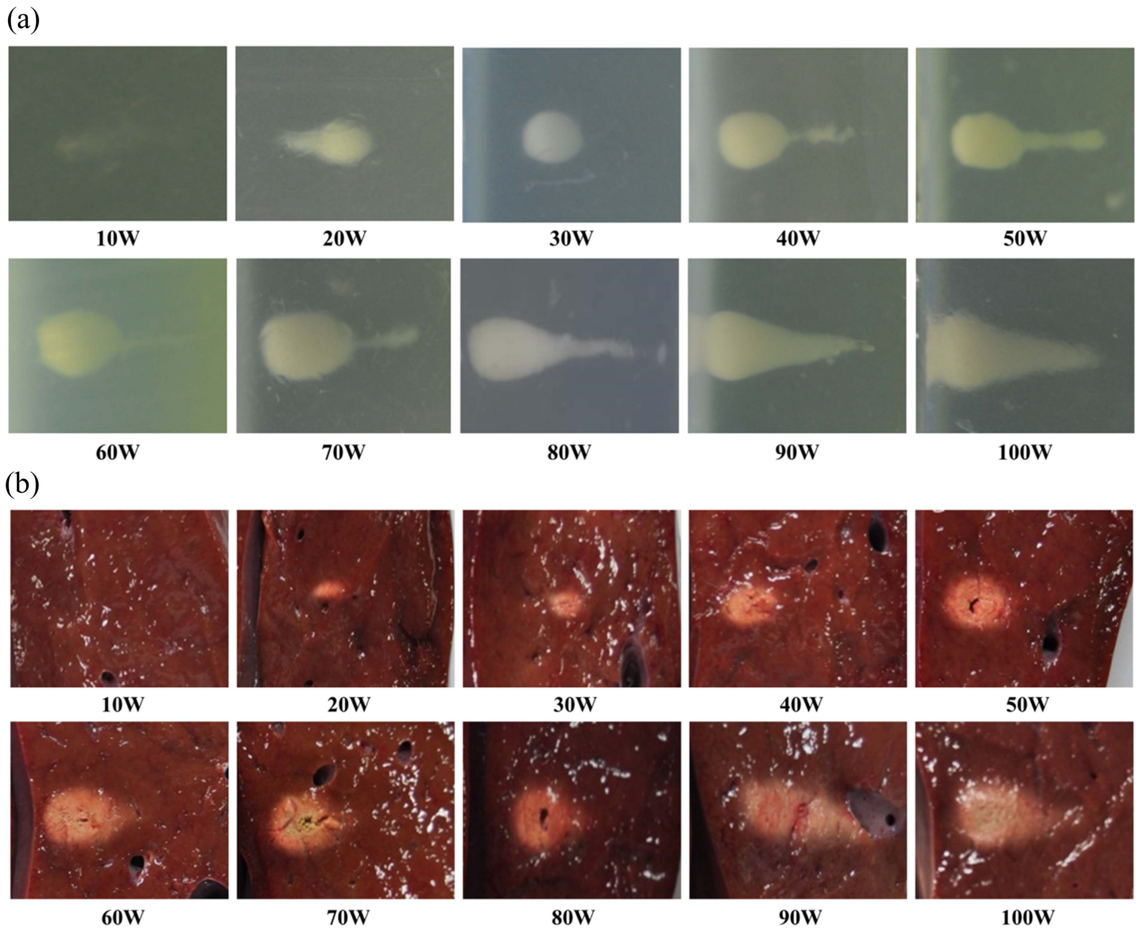

Fig. 7. The changing lesion shape in the egg white phantom and liver tissue according to the electrical power; (a) egg white phantom, (b) Liver tissue.

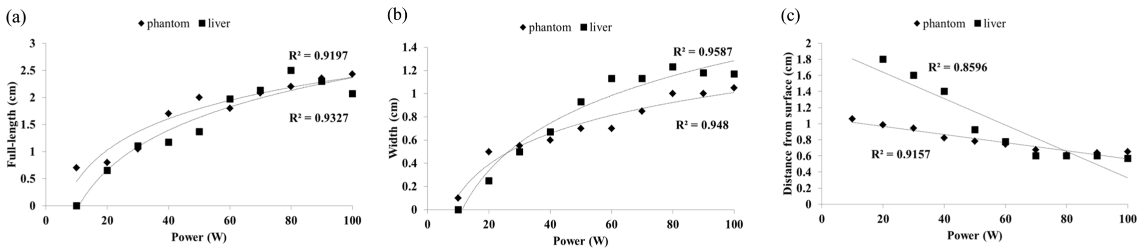

Fig. 8. The change of the length of the formed lesion in the phantom and liver tissue according to the electrical power; (a) The full-length of lesion, (b) width of lesion, (c) the distance between the front surface of the phantom to the lesion boundary.

by focused ultrasonication were measured and compared. Based on these measurements, the 30% egg white phantom had the most easily distinguished lesion and the most similar acoustic properties to liver tissue. Fig. 7 shows the changing lesion shape in the egg white phantom and liver tissue according to the electrical power. In the 30% egg white phantom, the cigar-shaped lesion formed at 10 W, while the small tadpole-shaped lesion with a tail directed towards the transducer occurred at 20 W. At 30 W, an elliptical lesion formed, and at 40-80 W, a tadpole-shaped lesion with a head directed towards the transducer formed. A cone-shaped lesion appeared at 90-100 W. By contrast, in liver tissue, the lesion did not form at 10 W, and a cigar-shaped lesion was observed at 20 W. Further, while the elliptical lesion appeared between 30-50 W, the tadpole and cone-shaped lesions formed at 60-80 W and 90-100 W,

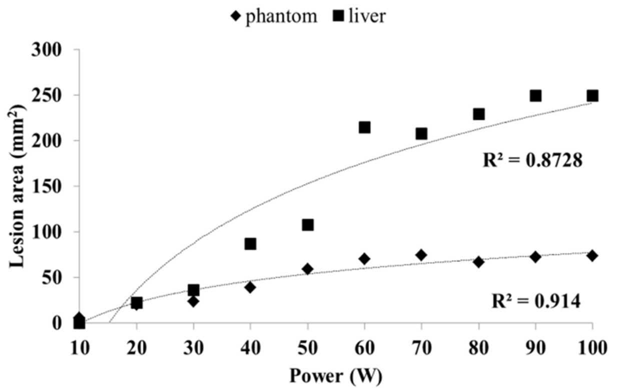

Fig. 9. The area of the formed lesions in the phantom and liver tissue according to the electrical power.

respectively. This morphologic trend of cigar, elliptical, tadpole, and cone-shaped lesions occurred sequentially as the electrical power increased from 10 W to 100 W, confirming that the lesion shapes in the phantom and liver tissue were similar. Fig. 8 and 9 summarize the length and area of the formed lesions in the phantom and liver tissue.

As the electrical power increased, the length of the lesion also increased in both the tissue and phantom, however, this trend plateaued at an 80-90 W. This trend was also observed in the lesion area of both the liver tissue and phantom. The area of the lesion increased beginning at the focal point and moving towards the transducer, indicating that the distance between the specimen front surface to the lesion boundary decreased with increasing electrical power. The lesion is generated towards the transducer as the electrical power increases. Notably, the changing width of lesion was in the liver tissue larger than in the phantom.

IV. Discussion

This study determined the optimal composition for a therapeutic ultrasound phantom by evaluating the acoustic and thermal properties in the phantoms comprising variable egg white concentrations. In addition, the utility of egg white phantom was confirmed by comparing the thermal lesion morphology to that obtained in tissue by therapeutic ultrasonication.

As the egg white concentration increased, the sound velocity of the phantom decreased, and the attenuation coefficient, density, and acoustic impedance increased. However, the sound velocity, density, and acoustic impedance plateaued at 40% egg white phantom, though this trend was not observed in the attenuation coefficient. In previous study, the sound velocity and attenuation coefficient of the phantom increased as the egg white concentration increased [6]. This trend in the attenuation coefficient is similar to our result, but the sound velocity is opposed. They were adjusted the egg white concentration by changing the combination the degassed water with an egg white in order to increase the egg white concentration in the phantom. However, in this study, all materials of phantom decreased except an egg white. Accordingly, the sound velocity of phantom in this study may decrease because the amount of the materials affecting stiffness of the phantom such the acrylamide, TEMED reduced. The density and sound velocity of the phantom in this study were similar to the properties in soft tissue, including breast tissue, but the attenuation coefficient was 0.06-0.106 dB/cm-MHz, which corresponds to only 1/5 of the attenuation coefficient in soft tissue. The differing attenuation coefficient may reflect scatter and acrylamide.

The specific heat was decreased as the egg white concentration and the lesion length increased. Similar to the acoustic properties, this trend in the lesion length plateaued in the 40% egg white phantom. The egg white concentration appears to affect the acoustic and thermal properties of the phantom. There is an upper limit of the sound velocity, density, acoustic impedance, and the lesion size changes above a certain protein proportion. These results, combined with the ease of lesion identification illustrated by visual transparency, indicate that the 30% egg white phantom is the optimal therapeutic ultrasound phantom. A focused ultrasound generated cigar, elliptical, tadpole, and cone-shaped lesions similarly in both the 30% egg white phantom and bovine liver. However, the initial electrical powers for lesion formation were 10 W in the phantom and 20 W in the liver, which indicates that this phenomenon is caused by non-uniformity or attenuation in the tissue. Furthermore, the elliptical lesion formed over a wider range in the liver tissue than in the phantom, but the resulting lesions in both were tadpole and cone-shaped.

The coagulation temperature in 10% egg white phantom was reported to be at 67°C [11], but we measured the coagulation temperature of 59°C in 30% egg white phantom in the previous study [18]. This result is similar to the critical temperature of 60°C for thermal destruction of biological tissue [19]. Therefore 30% egg white phantom is appropriate to confirm the thermal destruction of tissue. However, as the electrical power increased, the increasing width of lesion in the liver tissue was higher than in the phantom. The specific heat in the liver tissue was reported to be 1.001 cal/g°C at 83.5°C, it is lower than the value of the egg white phantom [20]. This difference may affect to the increasing temperature in the around of focal region, and it requires further experimental work.

V. Conclusion

The egg white phantom is a thermal lesion visualization phantom, and it is widely applied in the performance evaluation. In this study, we confirmed that egg white concentration affected the properties of the egg white phantom. The acoustic and thermal properties of the egg white phantom were changed according to its egg white concentration. Also the acoustic properties as well as the thermal properties were also saturated at the specific protein concentration. The present study is expected to contribute to a standard therapeutic ultrasound phantom. The results revealed the 30% egg white phantom as the optimal concentration for the therapeutic ultrasound phantom. We surmise that egg white phantom is useful to quantitatively evaluate the thermal effects of therapeutic ultrasound. However, a mismatch of thermal lesion in the egg white phantom and soft tissue will be solved by adjusting the attenuation coefficient, which will obtain through further study.

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