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Study on Changes in Shape of Denatured Area in Skull-mimicking Materials Using Focused Ultrasound Sonication

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***Abstract*:** Recently, ultrasound therapy has become a new and effective treatment for many brain diseases. Therefore, skull-mimicking phantoms have been developed to simulate the skull and brain tissue of a human and allow further research into ultrasound therapy. In this study, the suitability of various skull-mimicking materials(HDPE, POM C, Acrylic) for studies of brain-tumor treatments was evaluated using focused ultrasound. The acoustic properties of three synthetic resins were measured. The skull-mimicking materials were then combined with an egg white phantom to observe the differences in the ultrasound beam distortion according to the type of material. High-intensity polyethylene was found to be suitable as a skull-mimicking phantom because it had acoustic properties and a denatured-area shape that was close to those of the skull,. In this study, a skull-mimicking phantom with a multi-layer structure was produced after evaluating several skull-mimicking materials. This made it possible to predict the denaturation in a skull in relation to focused ultrasound. The development of a therapeutic protocol for a range of brain diseases will be useful in the future.

***Keywords*:** Focused ultrasound, Skull-mimicking material, Acoustic properties

1. Introduction

Ultrasound has been used in surgical therapeutic procedures for tumors associated with prostate cancer, liver cancer, pancreatic cancer, rectal cancer, kidney cancer, and breast cancer. In the case of brain tumors, however, ultrasound is strongly attenuated by the skull, and brain damage near the skull can result from the high temperatures caused by energy loss in the skull. An ultrasound beam can also be distorted by high the sound speeds and variations in thickness [1]. In addition, the technique of removing a piece of skull prior to sonication carries a high risk of complications. On the other hand, the recent development of new phased arrays and compensation methods for computed tomography (CT) imaging has enabled effective energy transfer through an intact skull [2] without destroying the organization outside. Therefore, the utility of non-invasive ultrasound surgery for the treatment of areas deep inside the brain has attracted considerable attention. In addition, brain tumor treatment is now possible using high-intensity-pulsed ultrasound. Moreover, ultrasound is for overcoming the blood–brain barrier, activation for drug delivery, and the treatment of functional disorders. Therefore, the possibility of treating brain diseases with ultrasound has increased, and noninvasive focused ultrasound for treating brain disorders is attracting increasing attention. If the market for brain treatments involving the use of ultrasound expands, the development of human head phantoms will become one of the main goals in the field of therapeutic ultrasound.

Hard tissues include cortical bone, trabecular bone, and dental hard tissues. The skull contains both trabecular bone and cortical bone. Therefore, it is important to determine the appropriate ranges for the acoustic properties to use in therapeutic ultrasound because cortical bone has a relatively higher sound velocity and attenuation coefficient. Cortical bone has a relatively isotropic and dense structure. Therefore, epoxy resin, acrylic, carbon fiber plastic, etc. can be used as mimic materials [3, 4]. Before clinical treatment, many studies have been conducted to evaluate the heating characteristics of focused ultrasound with the aim of developing various brain modeling and focused ultrasound techniques. On the other hand, there have been few studies on a comprehensive skull mimicking phantom to perform a performance evaluation and establish a treatment protocol using actual ultrasound therapy equipment. Considering the potential of the therapeutic ultrasound technology and the increase in the number of patients receiving treatment, a biological assessment has an influence on the performance. Therefore, for this evaluation, a quantitative phantom is urgently needed. In this study, to manufacture a skull-mimicking phantom, this study examined the acoustic and physical properties of the skull, and investigated the appropriate skull mimic materials. The suitability of three synthetic resins (HDPE, acrylic resin, POM C) as skull-mimicking materials was evaluated by measuring their acoustic properties. In addition, the thermal denaturation at the rear of each skull-mimicking material was observed using a tissue-mimicking material (TMM) phantom based on egg whites.

2. Materials and Methods

2.1 Skull-mimicking Materials

The skull contains both trabecular bone and cortical bone. Therefore, a skull mimic material must have similar acoustic properties and thermal properties to the hard tissues (cortical bone, trabecular bone, dental hard tissues) found in the skull. The mimic material should be able to withstand long-term use in repeated experiments. In this study, the physical properties and acoustic properties of various polymeric synthetic resins were considered to develop a skull-mimicking phantom for the treatment of brain disease. On the other hand, the shape and structural characteristics were not considered.

Fig. 1 shows the macromolecule synthetic resin specimens used in this study, and Table 1 lists the physical properties of the specimens. Polyacetal (POM C) is used mainly for orthopedic implants and artificial hip joints.

High-density polyethylene (HDPE) has been used as a substitute material for bone in many studies [5, 6]. Acrylic resin is used as a simple alternative bone material.

The general features of the specimens used in this study are as follows:

① POM C: The material is extruded from a homopolymer acetal material or copolymer. Therefore, it has high crystallinity, fatigue resistance, rub resistance, and machinability.

② HDPE: The hardness is excellent even if the temperature rises rapidly. HDPE also has excellent chemical resistance and processability, and is avirulent.

③ Acrylic resin: The material has a high colorless transparency, as well as good workability and formability.

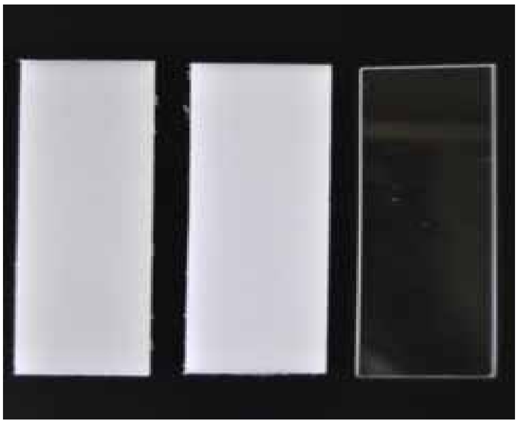


Fig. 1. Skull-mimicking materials: from left, HDPE, POM C, acrylic resin.

Table 1. Properties of the materials

Components		HDPE	POM C	Acrylic resin	ABS resin
Density (g/cm^3)		0.94	1.41	1.19	1.04
Thermal properties	Melting point (°C)	120	165	-	-
	Heat conductivity (W/(K·m))	-	0.31	-	0.25
	Heat deflection temperature (°C)	47	105	96	97
Mechanical properties	Tensile strength (MPa)	23	68	72	41
	1/2/5% deflection compression strength (MPa)	29	19/35/67	-	-

2.2 Evaluation of Acoustic Properties

Three skull mimic materials were used in this study: POM C, HDPE, and acrylic resin. Each of the samples had a width of 50 mm, length of 50 mm, and thickness of 6 mm. To measure the acoustic properties, a single 3.5-MHz transducer was used to send and receive the ultrasonic signals. A digital oscilloscope (Wave runner 6100 model, Lecroy Co., USA) was used to acquire and save the signal.

A function generator was used as an ultrasonic pulser/receiver (MKPR-1030 model, MKC KOREA Co., Korea). The sound velocity was measured using a pitch-catch method, instead of the echo-range method often used in non-destructive testing (Figs. 2 and 3). A single 1-MHz oscillator was used to generate an ultrasound pulse, and the signal was received using another single oscillator. The

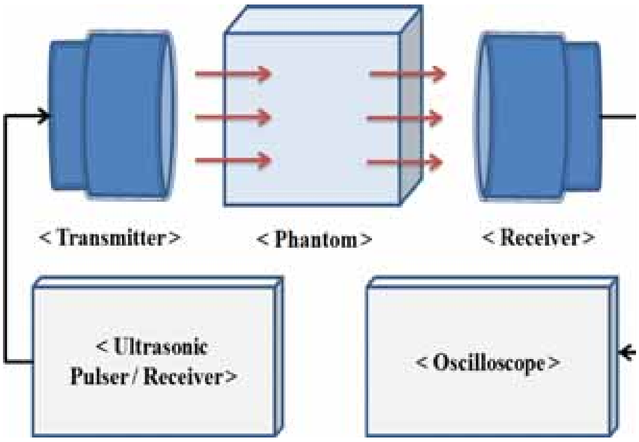


Fig. 2. Schematic diagram of pitch-catch method.

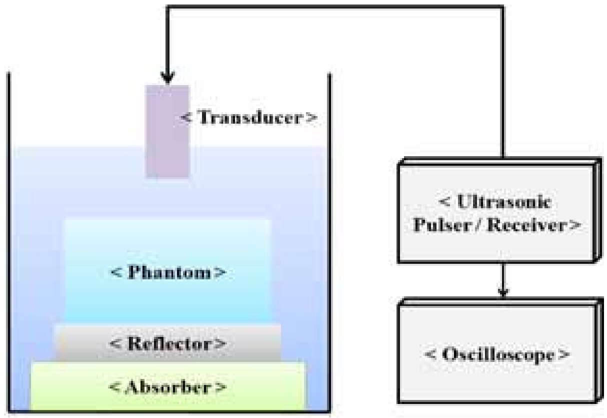


Fig. 4. Schematic diagram of the echo-range method.

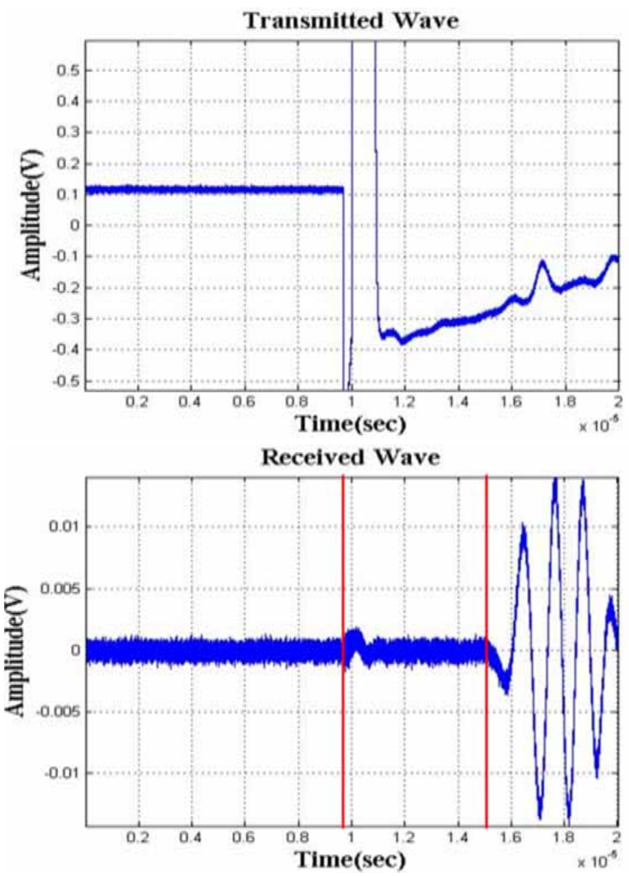


Fig. 3. Sound velocity calculation using the pitch-catch method.

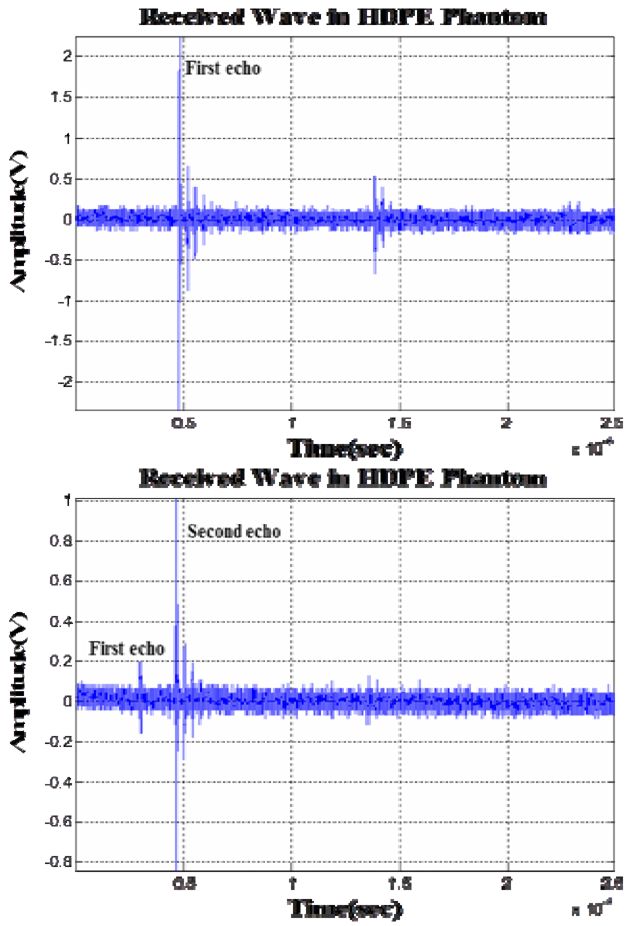


Fig. 5. Reflected signal for the attenuation coefficient calculation using the echo-range method; in water(up), in phantom(down).

attenuation coefficient was measured using spectral finite difference schemes. In the spectral difference method, the amplitude of the reflected signal was obtained in the frequency domain using a fast Fourier transform (FFT). After connecting the peak points of the center frequencies of the signals and obtaining a slope, the attenuation coefficient was determined (Figs. 4 and 5). The density was calculated using the mass and volume of the material, and the acoustic impedance was calculated using the sound speed and density.

2.3 Observation of the Changes in Focusing Using an Egg White Phantom

The status distortions and propagation shapes at the rear sides of the skull mimicking materials during focused ultrasound exposure were compared. The egg white

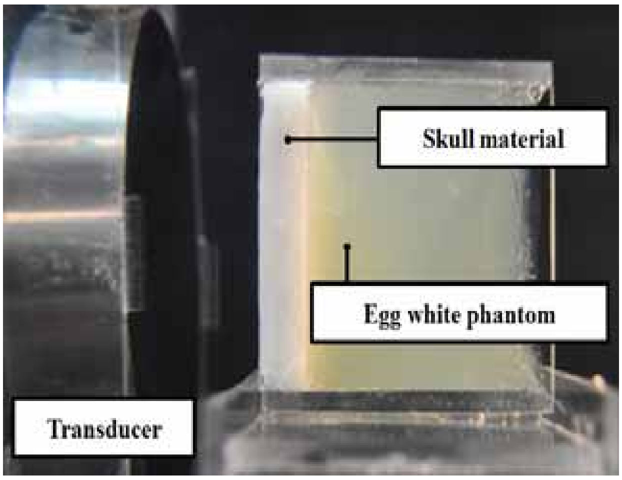


Fig. 6. Experimental set up for denaturation observation.

phantom, which had similar thermal and electrical properties to biological tissue, could effectively visualize the increases in temperature. A skull-mimicking phantom and a 30% egg white phantom were used. The center frequency of the transducer (H-101, Sonic Concepts Co.) was 1.1 MHz, and 60-s sonications were delivered with acoustic intensities between 20 and 90 with 3.5 $V_{p\text{-}p}$. The levels of thermal denaturation were compared in accordance with the presence or absence of a material similar to the skull. The focal point was formed within the egg-white phantom to compare the denaturation sizes and sites. A digital camera (D90 from Nikon, Japan) was also used to perform real-time recording and observe the time of the initial denaturation. Fig. 6 shows the denaturation observation experiment.

3. Results

3.1 Evaluation of the Acoustic Properties

In this study, the acoustic properties of three synthetic resins were measured to evaluate their suitability as a skull-mimicking material. Table 2 lists the acoustic properties of the skull-mimicking materials. The sound velocity was used to emulate the structure of a real human skull, which is 2,700-4,300 m/s. The attenuation coefficient was 4.6–12.5 dB/cm-MHz, and the acoustic impedance was 7.8 × 10^6kg/㎡/s, as reported elsewhere [7]. In this study, among the skull-mimicking materials, the sound speed was highest for HDPE (2,713 m/s). The sound speed was the lowest for POM C. The speed for POM-C was generally lower than those reported in the literature. The attenuation coefficient was highest for POM C (7.239 dB/cm-MHz), which was similar to the attenuation coefficient of the human skull. The density and acoustic impedance were also highest. The acrylic resin had a similar attenuation coefficient to that of a skull, but that of HDPE was not included in the range. The acoustic impedances of all the materials tested showed no significant differences.

Table 2. Acoustic properties of the skull-mimicking materials.

Acoustic parameters	*Skull	HDPE	POM C	Acrylic
Sound velocity (m/s)	2,740 - 4,300	2,713.1	2,485.6	2,549.7
Attenuation coefficient (dB/cm-MHz)	4.6 - 12.5	2.948	7.239	4.308
Density (g/㎤)	-	0.958	1.407	1.214
Acoustic impedance (×10^6 kg/㎡/s)	7.8	2.581	3.481	3.096

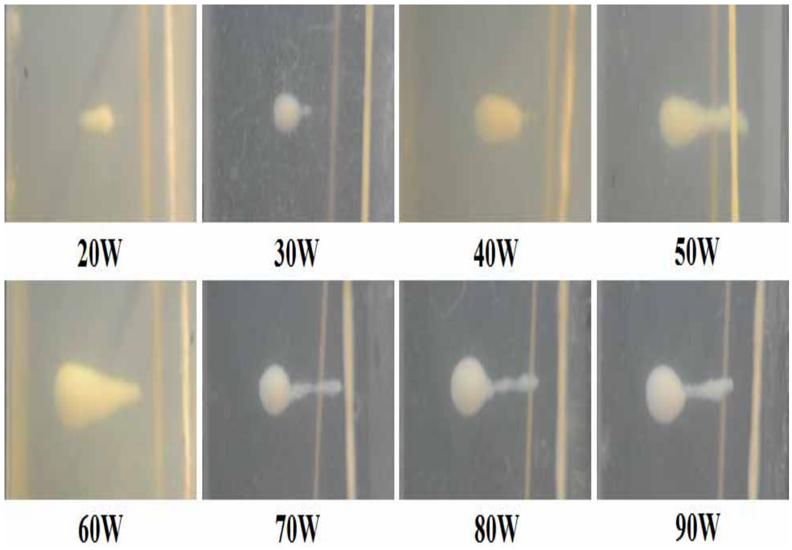
3.2 Observation of Changes in Focusing by Using Egg White Phantom

This study compared the shapes of the areas of denaturation at the rear sides of three synthetic resins during focused ultrasound exposure. A single egg phantom not combined with the skull phantom was used as the control group. The denaturation changed from an oval shape to a tadpole shape after increasing the intensity (20-90 W/㎠). In addition, the head and tail lengths of the denaturation increased. In the case of POM C, cigar- and oval-shaped denaturation shapes were generally observed, and no consistent pattern occurred as the intensity increased. The denaturation area observed for HDPE had a cigar shape for 20–30 W/㎠ and a tadpole shape for 40–90 W/㎠. HDPE appeared to be most similar to the control group, with a delay in the first degeneration formation time. Therefore, this skull-mimicking material appears to be suitable. The acrylic resin was excluded as a candidate skull-mimicking material because of surface deformation caused by repeated exposure. Fig. 7(a) shows the changes in the denaturation shape of the egg-white phantom of the control group according to the intensity. Fig. 7(b) shows how an intensity increase changed the denaturation of the egg-white phantom at the back of the POM C. Fig. 7(c) shows how an increase in intensity altered the denaturation of the egg-white phantom at the back of the HDPE. Fig. 8 presents the denaturation form of a phantom structure.

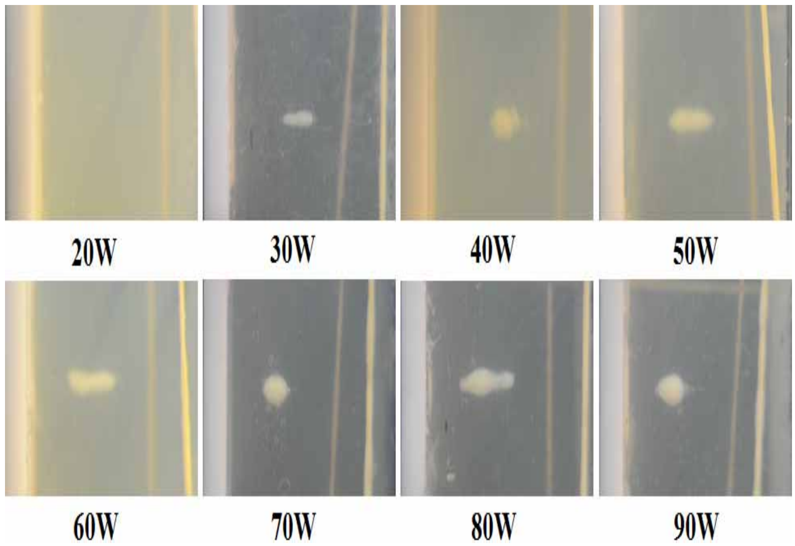
Figs. 9 and 10 show the distance from the surface, and the lateral length of denaturation according to the intensity, respectively. The distance from the surface decreased gradually and the lateral length increased with increasing intensity. These results suggest that when the site of the focal point is close to the transducer, the energy transferred to the focal point increases with increasing acoustic intensity.

4. Discussion and Conclusion

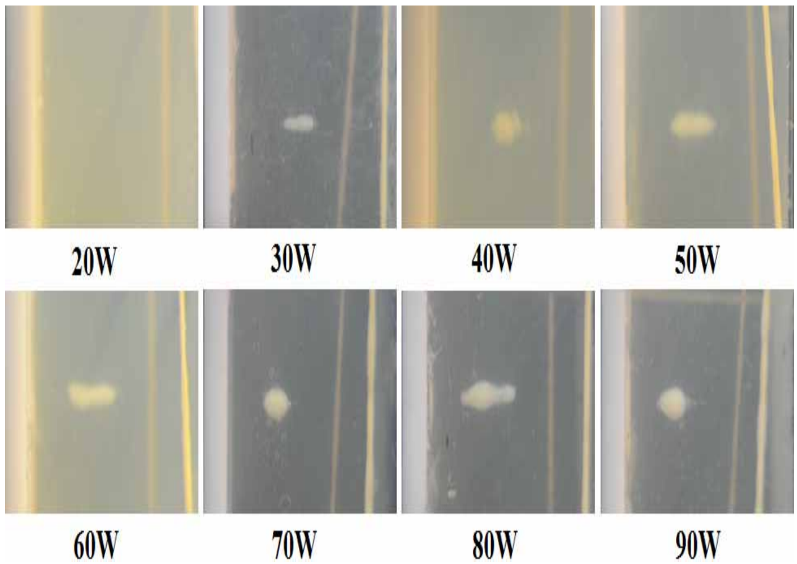
This study examined the acoustic and physical properties of the skull reported in the literature, and proposed suitable synthetic skull-mimicking materials. The thermal resistance of the skull-mimicking materials was evaluated using ultrasound. Acrylic resin was excluded as a candidate skull-mimicking material due to surface



(a) Control



(b) POM C



(c) HDPE

Fig. 7. Denaturation of an egg white phantom (a) Control, (b) POM C, (c) HDPE.

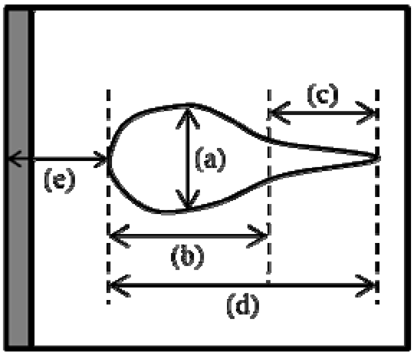


Fig. 8. Form of a Tadpole denaturation in the Phantom (a) Width, (b) Head, (c) Tail, (d) Full-length, (e) Distance from the surface.

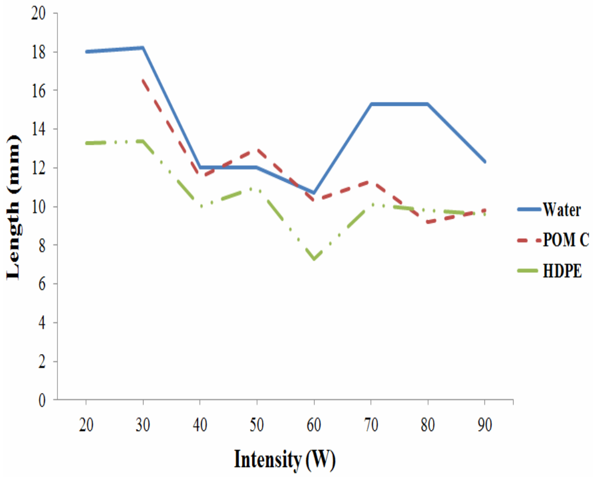


Fig. 9. Distance from the surface of denaturation.

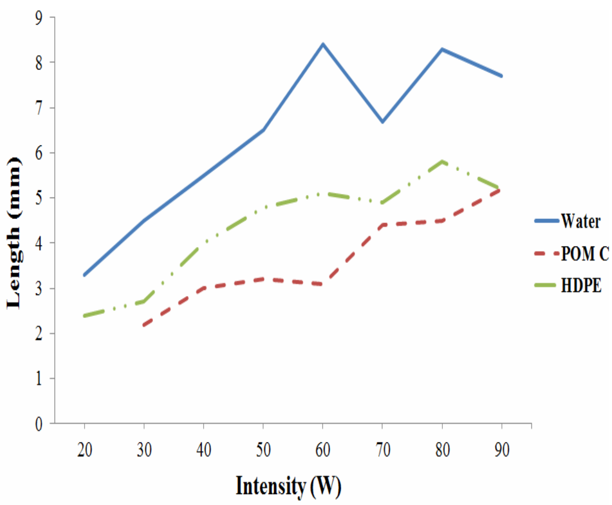


Fig. 10. Width of denaturation.

deformation caused by repeated exposure. In an evaluation of the acoustic properties, POM C was found to have the highest attenuation coefficient among the skull mimic materials, but the degeneration was difficult to verify when increasing the intensity. Therefore, it was also excluded from the skull-mimicking materials. HDPE had a relatively high attenuation coefficient, sound velocity, and acoustic impedance. Moreover, considering that the density of HDPE was most similar to that of the skull, it appeared to be a suitable skull-mimicking phantom. On the other hand, it showed the disadvantage of having a lower actual sound velocity than that of the skull (approximately 85%–90%). On the other hand, HDPE caused the least distortion in the ultrasound beam, and the denaturation was the closest to the original form. Therefore, HDPE could be a useful skull-mimicking material for evaluating ultrasound brain surgery. In this study, a skull-mimicking phantom with a multi-layer structure was produced and the denaturation in the skull by focused ultrasound was predicted. The development of a therapeutic protocol for a variety of brain diseases will be useful in the future.

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