A novel method for estimating the focal size of two confocal high-intensity focused ultrasound transducers

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Estimating the focal size and position of a high-intensity focused ultrasound (HIFU) transducer remains a challenge since traditional methods, such as hydrophone scanning or schlieren imaging, cannot tolerate high pressures, are directional, or provide low resolution. The difficulties increase when dealing with the complex beam pattern of a multielement HIFU transducer array, e.g., two transducers facing each other. In the present study we show a novel approach to the visualization of the HIFU focus by using shockwave-generated bubbles and a diagnostic B-mode scanner. Bubbles were generated and pushed by shock waves toward the HIFU beam, and were trapped in its pressure valleys. These trapped bubbles moved along the pressure valleys and thereby delineated the shape and size of the HIFU beam. The main and sidelobes of 1.1- and 3.5 MHz HIFU beams were clearly visible, and could be measured with a millimeter resolution. The combined foci could also be visualized by observing the generation of sustained inertial cavitation and enhanced scattering. The results of this study further demonstrate the possibility of reducing the inertial cavitation threshold by the local introduction of shock wave-generated bubbles, which might be useful when bubble generation and cavitation-related bioeffects are intended within a small region *in vivo*. © 2005 Acoustical Society of America. [DOI: 10.1121/1.1904283]

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I. INTRODUCTION

The minimally invasive nature of high-intensity focused ultrasound (HIFU) has been a focus of several recent therapeutic applications, especially tumor ablation.^{1–5} The temperature of the target tissue at the focus of a HIFU transducer can increase to more than 65 °C within seconds, thus causing protein denaturing and cell death. However, the success of HIFU tumor ablation largely depends on the knowledge of the focusing properties of the treatment system, making techniques for quantitatively measuring the focal position and size essential.

Typical tools for measuring the position and size of a HIFU transducer are hydrophone scanning and schlieren optical imaging.⁶ A computer-controlled scanning system with

a needle or membrane hydrophone can accurately determine the position, size, and pressure amplitude of the main and sidelobes of a HIFU sound field. Although a very fine resolution can be achieved, the scanning process is time consuming and the alignment of the hydrophone to the HIFU transducer is critical to the accuracy of the measurements. Moreover, the hydrophone is fragile and quickly saturated at high pressures, and the calibration of a hydrophone in a multielement HIFU system becomes difficult due to the acoustic waves coming from several sources differing greatly in their incoming angles. Schlieren optic imaging provides an overview of the shape and location of a HIFU focus as well as sidelobes and secondary foci. However, the resolution is low and thus the obtained results are more qualitative than quantitative.

In this article we report a novel method for estimating the position and size of the focus of a 1.1 or 3.5 MHz HIFU transducer. The shapes and sizes of the main and sidelobes can be determined in a reasonably short time and with a high resolution. Furthermore, the changes in shape and pressures

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TABLE I. Simulation parameters.

Frequency (f)	1.1 MHz	3.5 MHz
Transducer radius	32 mm	17.5 mm
Geometric focus (data from the manufacturer)	62.64 mm	55 mm
Attenuation	0 Np/cm	0 Np/cm
Sound speed (c)	1500 m/s	1500 m/s
Wavelength (λ)	1.364 mm	0.429 mm
Grid size		
Field	0.1 mm	0.1 mm
Transducer (Δx and Δy)	0.164 mm	0.164 mm

where the foci of the two transducers intersect are also determined.

II. EXPERIMENTAL MATERIALS AND METHODS

A. Experimental setup

The experiments were performed in an acrylic tank (23 cm L×15 cm W×15 cm H) filled with tap water. The experimental system consisted of four transducers (1.1 and 3.5 MHz HIFU transducers; H-101 and SU-102, Sonic Concepts, Woodinville, USA), a shock wave transducer (Piezoston 100 with a FB7 G2 probe, Richard Wolf, Knittlingen, Germany) for producing bubbles, and a diagnostic B-mode scanner (Titan with a L38 probe, Sonosite, Bothell, USA) for imaging. The L38 is a 5–10 MHz broadband transducer with a central frequency of 7.5 MHz. The focus of the probe used with the shock wave generator was 1.7 mm in diameter and 6.7 mm in length, while the focal length was 20 mm from the edge plane of the probe (data from the manufacturer). The diameters and focal lengths of the 1.1 and 3.5 MHz transducers are listed in Table I. The 1.1 MHz HIFU and the shock wave transducers were positioned orthogonally on two adjacent walls of the water tank, as shown in Fig. 1. For experiments on the combined beam pattern of two HIFU transducers, the second HIFU transducer (3.5 MHz) was mounted on the wall

facing the 1.1 MHz HIFU transducer with their central axes parallel to each other but separated by about 4 mm. The B-mode probe scanned from the top of the water tank parallel to the axial direction of the shock wave transducer, i.e., cutting through the HIFU beam. The HIFU transducers were both mounted on 3-D positioners that allowed precise movement control.

The pressure values of the HIFU transducers were calculated from hydrophone (Onda, Sunnyvale, USA) pressure measurements performed in water at low output amplitudes that were linearly extrapolated to higher outputs. The peak negative pressures at the focus of the 1.1 MHz transducer were 1.62 and 5.88 MPa for outputs of 100 and 400 mV from the function generator, respectively. The peak negative pressure of the 3.5 MHz transducer was around 3 MPa at the focal point. Two arbitrary function generators (33120A, Agilent, Palo Alto, USA; and DS345, Stanford Research Systems, Sunnyvale, USA) and two power amplifiers (150A250B and 150A100B, Amplifier Research, Souderton, USA) were used to drive the 3.5 and 1.1 MHz HIFU transducers, respectively. The pulse repetition frequency (PRF) was 500 Hz, and the pulse length was 100 cycles for both transducers. A clinical shock wave generator was used to induce inertial cavitation and generate bubbles, and was set to its highest output level (20, the corresponding peak negative pressure provided by the manufacturer was 19.0 MPa) and the highest PRF (4 Hz) for maximal bubble production. The beam-pattern images obtained by the diagnostic B-mode scanner were recorded on a VCR and off-line processed frame-by-frame using commercial software (Premiere Pro 1.5, Adobe Systems, San Jose, USA; Matlab, The MathWorks, Natick, USA).

B. Experimental procedures

1. Series 1. Beam pattern of a single HIFU transducer

In order to test the feasibility of using shock wave-generated bubbles to visualize the beam pattern of HIFU transducers, the 1.1 and 3.5 MHz transducers were first tested individually. The 1.1 MHz HIFU transducer was driven at either 100 or 400 mV and moved along its axial direction at a step size of 1 or 2 mm, respectively. The shock wave generator produced and pushed bubbles toward the HIFU beam while B-mode images were taken continuously. After finishing “slicing” along the HIFU beam, the B-mode imaging plane was aligned with the HIFU focal plane again, and B-mode and color Doppler images were both taken. The output of the 1.1 MHz HIFU transducer was increased until enhanced scattering due to inertial cavitation at the center of the HIFU beam was induced. The beam pattern of the 3.5 MHz transducer was determined in a similar way.

2. Series 2. Simulation

To understand the beam profiles obtained in the above experiments, simulations were performed by modeling the 1.1 MHz HIFU transducer as a collection of point sources in a grid. For any point on the destination plane (fixed z value),

FIG. 1. Setup of the experimental apparatus: top and side views.

the following Rayleigh–Sommerfeld integral⁷ was used to calculate the relative pressure amplitude contributed by each grid point of the source transducer:

$$p(x, y, z) = i \frac{\rho c k}{2\pi} \int_S \frac{u e^{-ik(r-r')}}{r-r'} dS, \quad (1)$$

where $i = \sqrt{-1}$, ρ = tissue density, c = sound speed, k = wave number ($k = 2\pi/\lambda$, λ is the wavelength, and $c = f\lambda$, where f is sound frequency), u = complex surface velocity of source, and $r - r'$ = distance between a certain point on the transducer surface to a certain point in the acoustic field. For more efficient and convenient calculations, the above equation was simplified to

$$p(x, y, z) = i \text{ AMP} \frac{\Delta x \Delta y}{2\pi} \sum \sum \frac{e^{-ik(r-r')}}{r-r'}. \quad (2)$$

The amplitude of the simulated pressure field is relative when AMP is set to 1, and Δx and Δy are the step sizes in the x and y directions. The parameters used in the simulation program are listed in Table I. The simulated results were then compared with the experimental results (see Sec. III).

3. Series 3. Combined beam pattern of two HIFU transducers

The major challenge in beam-pattern plotting is encountered during the testing of a multielement transducer (especially when the elements are at large angles to each other). To demonstrate the advantages of our newly developed method, two HIFU transducers (one 1.1 and the other 3.5 MHz) were arranged facing each other, but with a 4 mm distance between their parallel central axes on purpose. The 3.5 MHz transducer was turned on first since its focal pattern was small and difficult to determine. The obtained B-mode images of the overlapping beam pattern were recorded and analyzed offline.

III. RESULTS

A. Beam pattern of a single HIFU transducer

To rapidly determine the focal size and location of a HIFU beam, the HIFU transducer was moved along its axial direction while B-mode images were taken sequentially. Figure 2(a) shows one of the recorded images near the focus of a 1.1 MHz HIFU beam. When bubbles produced by the shock wave transducer were pushed toward the HIFU beam, a few concentric rings (white rings) appeared where bubbles were trapped and moved along the rings, which clearly visualized the locations of the pressure valleys around the HIFU focus (Fig. 3). The diameter of the central dark region was smaller for the 3.5 MHz transducer than for the 1.1 MHz transducer (Fig. 4). The radius of the first ring, which can be easily measured, was the radius of the first zero of the acoustic beam, and thus was larger than the focal radius (usually defined as being 6 dB below the maximum pressure) of the HIFU beam. In other words, the focal radius should be smaller than the diameter of measured radius of the first ring, 1.6 mm in Fig. 5(a). The number of visible rings increased with the pressure level [Fig. 2(b) and Fig. 5], whereas the diameter of the first ring was the same for low [Fig. 5(a)] and

FIG. 2. (a) A B-mode image of the beam pattern of a 1.1 MHz HIFU transducer near its focus. The output from the function generator is 100 mV (producing a peak negative pressure of 1.62 MPa). The vertical white line was produced by a shock wave pulse. (b) A B-mode image of the beam pattern of a 1.1 MHz HIFU transducer at the same position as (a), but for a higher voltage output from the function generator (400 mV, 5.88 MPa). More rings are clearly evident.

high [Fig. 5(b)] pressures. The minimum diameter of the central dark region occurred 48 mm from the edge plane of the 1.1 MHz HIFU transducer [Figs. 5(a) and 5(b)]. At a low-pressure condition, “radius steps” were seen at a few positions, e.g., 40–41, 42–45, 46–50, 50–54, and 55–59 mm [Fig. 5(a)]. At the transition from one step to the next one, the measured radii could be either at the upper “step” (case 2) or the lower “step” (case 1). The radius of the second ring (white triangle) for case 1 coincided with that of the first ring for case 2 (gray square).

Bubbles for visualizing the beam pattern of a HIFU transducer can be provided by means other than a shock wave transducer. Figure 6 shows the bubbles generated at the center of the HIFU focus by inertial cavitation at higher pressure levels (frame 3) that visualize the first and second rings of the HIFU beam when they moved outward. However, compared to the bubbles generated by a shock wave trans-

FIG. 3. A group of bubbles (white solid arrow) is moving along the third pressure valley (the third ring) of the 1.1 MHz HIFU beam. The acoustic parameters used in this test was 100 mV output from the function generator, pulse length=100 cycles, and PRF=500 Hz. The B-mode imaging slice cut through the focal plane of the HIFU transducer (48 mm from the transducer's edge plane). In this figure, only frames 5, 7, 10, 14, 18, and 26 are shown for simplicity.

ducer, bubbles from the HIFU focus lasted for a shorter time and thus were probably smaller. Figure 7 shows a Doppler image of the bubbles generated by a HIFU transducer. An oscillating ball with rapidly changing color was evident at the focus of the HIFU transducer, which is indicative of the fast phase change in backscattered signals due to the generation and collapse of bubbles by inertial cavitation. This phenomenon was sometimes called the pseudo-Doppler shift and has been used to produce images of “stimulated acoustic emission.”⁸

B. Matching experimental and simulated results

In order to elucidate the physical meaning of the experimental results, the beam patterns of both 1.1 and 3.5 MHz HIFU transducers were simulated and compared to the rings evident on the B-mode images. In Fig. 8, it is clear that the white rings of the 1.1 MHz HIFU beam matched well with the location of the pressure valleys measured using a needle hydrophone. It is worth noting that the pressures at the valleys were not zero. The measured pressure might be the sum

FIG. 4. The focal beam patterns of (a) 1.1 MHz and (b) 3.5 MHz HIFU transducers. The B-mode imaging slice cut through the focal planes of both HIFU transducers. Comparing (a) and (b), the focal beam size of the 3.5 MHz transducer is smaller than that of the 1.1 MHz one.

FIG. 5. The radii of each ring at (a) low- (100 mV) and (b) high-pressure (400 mV) output are shown. The minimum diameter of the 1.1 MHz HIFU transducer occurred 48 mm from the edge plane. At a low-pressure condition, "radius steps" were seen at a few positions, e.g., from 46 to 50 mm and from 50 to 54 mm. At the transition between two steps, e.g., at 50 mm, the measured radii could be either at the upper "step" (case 2, gray square) or the lower "step" (case 1, black circle). The radius of the second ring (white triangle) for case 1 coincided with that of the first ring for case 2 (gray square). The error bar indicates the size of the standard deviation. At least 3 measurements were performed for each data point.

of transmitted and reflected waves from all directions. Furthermore, for the 1.1 MHz HIFU transducer, the locations of the dark rings in the images match well the locations of the simulated pressure peaks [Fig. 9(a)]. Similarly, the locations of the first white ring coincide well with the location of the second pressure valley for the 3.5 MHz HIFU transducer. The tiny inner ring in the simulation results cannot be seen in the experiment, probably because of the resolution limitations of B-mode images [Fig. 9(b)].

C. The combined beam pattern of two HIFU transducers

To understand the beam pattern of two facing transducers, the focal location of each transducer was determined first. The focus of the 1.1 MHz transducer was then moved by adjusting the 3-D positioner to make the focal planes of both the 1.1 and 3.5 MHz beams coincide. The two foci were separated by 4 mm distance on purpose.

The pressure levels of the 1.1 and 3.5 MHz HIFU transducers were both below the pressure threshold to induce inertial cavitation of bubbles provided by shock waves. There-

fore, before turning both transducers on, no bubble was generated near the confocal plane of both transducers after the bubbles from the shock waves passed or dissolved. When two transducers were turned on simultaneously, the pressures of both transducers summed up and thus the peak pressure level near the focus of the 3.5 MHz transducer increased. The bubbles from the shock wave transducer probably acted as seeds of inertial cavitation and induced bubble generation. Continuous bubble generation was seen at the intersecting area and could persist up to a few minutes when bubbles from the shock wave generator disappeared for a long time. The enhanced scattering signals of the generated bubbles then clearly demonstrated the location of the intersecting area (Fig. 10).

IV. DISCUSSION

In this report we describe the results of a simple and novel method to determine the size and location of HIFU beams. The new method is particularly useful when analyzing a transducer array with a complex arrangement, for example, as used in the noninvasive ablation of a brain tumor

FIG. 6. The beam pattern of a 1.1 MHz HIFU transducer was visualized by bubbles generated by inertial cavitation (frame 3). Two rings are clearly evident in frames 5–11 (550 mV or $P=8.09$ MPa, 100 cycles, 500 Hz PRF). The vertical white lines in each frame were produced by the HIFU transducer itself. Only frames 1, 3, 5, 7, 9, and 11 are shown.

FIG. 7. The bubbles generated by inertial cavitation at the focus of a 1.1 MHz HIFU transducer looks like a ball changing in color rapidly (mosaic pattern) in a directional color power Doppler image (550 mV, 100 cycles, 500 Hz PRF).

FIG. 8. The white rings of the 1.1 MHz HIFU beam compared with the location of the pressure valleys measured by a needle hydrophone.

using a transcranial ultrasound array. Arranging two transducers from the bilateral temporal area of the skull—where the bone is thinner—may be preferable because the output from each transducer decreased and the possibility of overheating the brain tissue outside the target reduced. Unfortun-

nately, the resulting beam pattern cannot be measured by a traditional needle hydrophone system. Furthermore, our proposed method can also be used to rapidly construct a 3-D beam pattern, in contrast to 3-D measurements with a needle hydrophone system usually taking many hours to complete. The proposed method is able to perform beam plotting of two facing transducers, and can construct a 3-D beam pattern in a relatively shorter time. However, the proposed method is not able to determine the absolute peak pressure or intensity, or the pressure profile of the focus. In addition, the resolution is limited by the frequency of the diagnostic ultrasound probe (in our case, a 7.5 MHz central frequency), and thus is not adequate for a focal size smaller than 1 mm. To clearly show a whole ring (the first pressure valley) in the B-mode images, an area of about $1 \times 1 \text{ mm}^2$ (or about 5×5 pixels) is necessary. The use of a diagnostic probe with a higher frequency would increase the resolution.

Before turning on both transducers, the output of each transducer was lower than the inertial cavitation threshold of the bubbles from the shock wave generator, and hence no enhanced scattering was seen. When the foci of two transducers intersected, the peak pressure increased and exceeded these bubbles' inertial cavitation threshold. Therefore, before introducing bubbles to the intersecting area, no inertial cavitation or enhanced scattering was detected. Seeding some

FIG. 9. The comparisons between the simulation and experimental results are shown for (a) the 1.1 MHz and (b) the 3.5 MHz HIFU transducers. For both transducers, the B-mode imaging planes were set at their focal planes. The scale of the simulation and experimental results are the same. For (a), dashed circles indicate the locations of the second and third pressure valleys for both simulation and experimental results. For (b), white dashed circles indicate the second and fourth pressure valleys.

FIG. 10. The combined effect of the 1.1 and 3.5 MHz HIFU transducers is shown. The left column (a1, b1, and c1) is the original B-mode images taken at the confocal plane of the two transducers. Locations of the first rings of both transducers are shown by thick (3.5 MHz) and thin (1.1 MHz) dashed rings. When the 3.5 MHz HIFU transducer is on but the 1.1 one is off, the first ring of its beam pattern is clearly seen (thin arrow in a1 and a2). After turning on the 1.1 MHz transducer and supplying the focal area with shock wave-generated bubbles, the focus of the 3.5 MHz transducer filled with high-scattering signals, most likely bubbles (thick arrow in b1 and b2). The bubbles were generated and destroyed repeatedly at the focus of the 3.5 MHz beam. The moving direction of the shock wave-generated bubbles is indicated by the arrow heads (b1 and b2). The bubble-like signals at the focus of the 3.5 MHz transducer can sustain for up to a few minutes after supplying “seed” bubbles generated by shock waves once. The c1 and c2 plots were taken after about a minute after stopping supplying bubbles from shock waves.

bubbles by the shock wave transducer to the combined focus induced inertial cavitation, and the enhanced scattering was sustained for longer periods of time (up to a few minutes). In our case, the focal pressure of the 3.5 MHz transducer increased by summation with the pressure of the first sidelobe of the 1.1 MHz transducer, and exceeded the inertial cavitation threshold at 3.5 MHz. We believe that bubbles were generated, grew, and collapsed continuously at the intersecting area.

The schlieren imaging uses light to form images, which will not alter the sound field of the target transducer, and is pretty fast. However, the schlieren imaging method is basically a semiquantitative measurement of the pressure profile of the ultrasound beam. The bright and dark patterns projected on a screen can be used to determine the relative positions of the focus and sidelobes. Moreover, an absolute value of the beam size cannot be easily obtained. Furthermore, the schlieren imaging could be distorted easily at the presence of bubbles from inertial cavitation. The laser light diffracted while passing through moving bubbles and thus reduced the quality of the generated images. The new imaging method using bubbles can be used to perform measurement quantitatively. The obtained image quality even improves at the presence of bubbles from inertial cavitation.

The “step” behavior seen in Fig. 5 represented the true pressure profile around the HIFU focus. As seen in Fig. 11(a), the bright parts represent the pressure crests (peaks and saddles) while the dark parts are the pressure valleys. This background beam plot was created using the simulation equations described above. Bubbles tended to move to the low-pressure area and thus accumulated in the dark regions. The measured radii of the beam profile represented the inner most pressure valleys which bubbles could reach at different distances from the transducer surface. When the transducer’s output was low, the pressure at the saddle part [A in Fig. 11(b)] was low enough to allow bubbles to climb over it and stayed in the first pressure valley, the lowest “step” (46–50 mm). The pressure gradually increased while the distance to the transducer increased, and prevented bubbles from further climbing over. Bubbles stayed in the second pressure valley and formed a higher step (B, 50–54 mm). Ambiguity occurred at the transition between two steps. That is, bubbles can stay either in the lower or the higher pressure valley. Figure 11(b) shows the relative pressure amplitudes of the first pressure valley, the pressure crest, and the second pressure valley. However, when the output pressure was high enough [Fig. 5(b)], bubbles were more and more difficult to

(a)

(b)

FIG. 11. (a) Simulated pressure profile of the 1.1 MHz HIFU transducer near the transducer focus. "X" represents the positions where focal sizes were measured (see Fig. 5). "A" is the lowest pressure step at position 46 to 50 mm. The pressure "crest (peak and saddle)" outside A is low and bubbles can climb over and enter "A" to form the first ring. "B" is where the second pressure "step" locates (50 to 54 mm). The detailed pressure profiles of slice C (through step "A"), D (through first pressure crest), and E (through step "B") are shown in (b).

enter the inner pressure valleys and the measured radii thus increased rapidly.

Our observations indicate that shock waves can be used to provide nuclei to reduce the cavitation threshold and to locally induce inertial cavitation activity. The focal size of a shock wave is small ($1.7 \times 1.7 \times 6.7$ mm), and thus a large amount of energy can be directed to a small region *in vivo*.

The negative pressure of the shock wave was sufficiently low to induce cavitation and create bubbles in the intrahepatic vessels and bile.^{9,10} It is also possible for bubbles to be generated in loose tissue such as liver parenchyma. The shock wave-generated bubbles can be used to provide bubble seeds for further cavitation activity, and thus may be used to facilitate ultrasound-related bioeffects, such as drug delivery or

gene transfection, when used with a therapeutic ultrasound transducer.

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