Micro-Receiver Guided Transcranial Beam Steering

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***Abstract*—A new method for focusing ultrasound energy in brain tissue through the skull is investigated. The procedure is designed for use with a therapeutic transducer array and a small catheter-inserted hydrophone receiver placed in the brain to guide the array's focus. When performed at high-intensity, a focal intensity on the order of several hundred watts per centimeter-squared is achieved, and cells within a target volume are destroyed. The present study tests the feasibility and range of the method using an ex vivo human skull. Acoustic phase information is obtained from the stationary receiver and used to electrically shift the beam to new locations as well as correct for aberrations due to the skull. The method is applied to a 104-element 1.1 MHz array and a 120-element 0.81 MHz array. Using these array configurations, it is determined that the method can reconstruct and steer a focus over a distance of 50 mm. Application of this minimally invasive technique for ultrasound brain therapy and surgery also is investigated in vitro with a 64-element 0.664 MHz hemisphere array designed for transskull surgery. Tissue is placed inside of a skull and a catheter-inserted receiver is inserted into the tissue. A focus intense enough to coagulate the tissue is achieved at a predetermined location 10 mm from the receiver, the maximum distance that this large element array can electronically steer the focus.**

I. Introduction

The concept of brain surgery and therapy performed through the intact skull [1]–[3] has an obvious appeal, because of the decrease in cost, risk, and recovery time associated with partial removal of the skull. A series of recent studies, both in vitro [4]–[6] and in vivo [7] demonstrate that such a technique is feasible using phased ultrasound transducer arrays. It has been proposed that skull models utilizing information derived from magnetic resonance imaging (MRI) and computed tomography (CT) scans could be used to focus through the skull. However, these theoretical methods need to be effectively tested. The threshold between laboratory results and clinical treatment is high, and a second minimally invasive method may be needed in the first patient treatments, even if the models are shown to be accurate in ex vivo testing. In addition, the models may not be effective for every tumor location and skull thickness. The present study proposes a minimally invasive focusing procedure that uses a small hydrophone inserted into a stationary position in the brain to provide information that can be used to focus through the beam to a target location through the skull.

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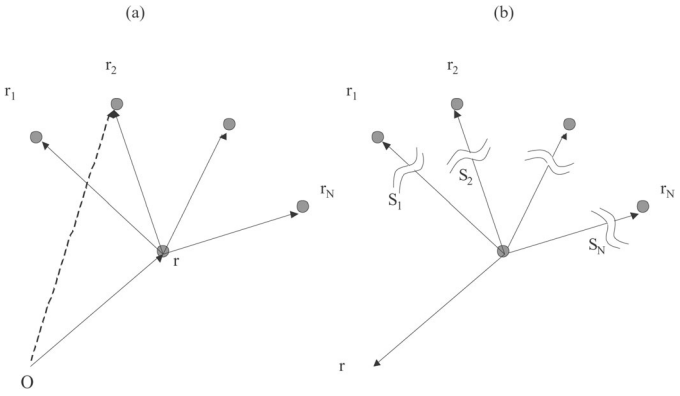

Fig. 1. (a) The acoustic phase at location r is the argument of an acoustic signal resulting from the summation of simple sources. (b) The skull is modeled as a thin phase screen is placed directly in front of each simple source. Although the phase of each acoustic signal is now spatially dependent, the change in phase for a point source is still the same everywhere.

In previous ex vivo skull studies, [7], a hydrophone was placed at the desired focal point to provide feedback for adjusting the driving phases of the array's elements. Using this method, the receiver must be moved to a new location and the phasing process repeated in order to produce a new focus. Similar drawbacks occur with using the acoustic time-reversal method suggested by Fink [8]. This procedure uses adiabatic phase-conjugation, which without modification will inherently focus upon a single source point [9]. Focusing away from this point requires moving the receiver or applying an analytical correction [10]. Another analytic corrective method for bone has been designed by Botros *et al.* for focusing through the ribcage [11]. However, this method treats the bone as impenetrable, producing an array of subaperture tissues that propagate between the bone.

The phasing process described here operates with a hydrophone placed in a single location and does not require precision placement. It is proposed that a flexible catheter-based hydrophone could be inserted into the brain via the blood vessel network, reaching the circle of Willis, and used to focus an array. The insertion would be similar to that used by existing cerebral catheters [12]. A related hydrophone phasing process was described by Seip *et al.* [13], [14], but for use in soft tissue as opposed to the present process applied entirely through bone.

II. Theory

The basis of the beam-steering method is illustrated by considering a series of N radiating point sources located in a homogeneous medium at positions r_n. Each source is harmonically driven at the same frequency and amplitude but varying phases. The acoustic pressure at position r resulting from the sources is given by:

$$P(r) = \sum_{n=1}^{N} Pn \frac{e^{i(k|r-r_n|-\omega t+\phi_n)}}{|r-r_n|}, \tag{1}$$

where ϕ_n is the relative phase of each source. Without loss of generalization, the source at r_1 can be chosen to possess a relative phase of $\phi_n = 0$ radians. In this case, the maximum pressure amplitude at location r will occur when:

$$\phi_n = k\left(|r-r_1| - |r-r_n|\right). \tag{2}$$

As illustrated in Fig. 1(a), under these conditions all waves arrive in phase and r may be defined as a phase-controlled focal point. Additional adjustment of the driving phase of any source will lower the overall amplitude. A random phase, θ_n, added to each source in (1) will in general destroy this focus.

Ultrasound propagation through the skull, in a simplified model, is approximated as a phase screen [15] placed close to the radiating sources as shown in Fig. 1(b). The screen distorts the phase of the waveform by an amount θ_n as a function of position on the screen. Such models have been reported in relation to the skull [9] and other organs [16]. For the present example, which considers an array of point sources, introduction of a phase screen S between the sources modifies the field at r so that:

$$P = \Sigma \alpha_n P_n e^{i(kr_n-\omega t)+\phi_n+\theta_n}. \tag{3}$$

The phase screen introduces an additional phase shift θ_n to each element and shades the amplitude by a factor of $\alpha_n < 1$. For the generalized case of a continuous source, the change in phase from the unperturbed signal P_0 is a function of r, r_n, and the amplitude factor α_n. However, the phase of a single point-source element is considerably less complicated. When the driving element is just a point source, the phase shift in the field is simply θ_n and is independent of the location of r. That is, changing the driving phase by θ_n shifts the phase of the field by this same amount at all spatial locations past the screen. Thus, measurement of the phase at any location past the phase screen then provides the phase distortion caused by the screen for the nth source at any other point. By powering each source by itself, a receiver at point r_a could be used to calculate phase correction necessary to restore a focus at point r_b:

$$\Delta\phi(r_b) = \arg\left(\frac{P(r_a)}{P_0(r_a)}\, P_0(r_b)\right), \tag{4}$$

where measurement or calculation of the field without the screen S is given by P_0 and the field with the screen in place is P.

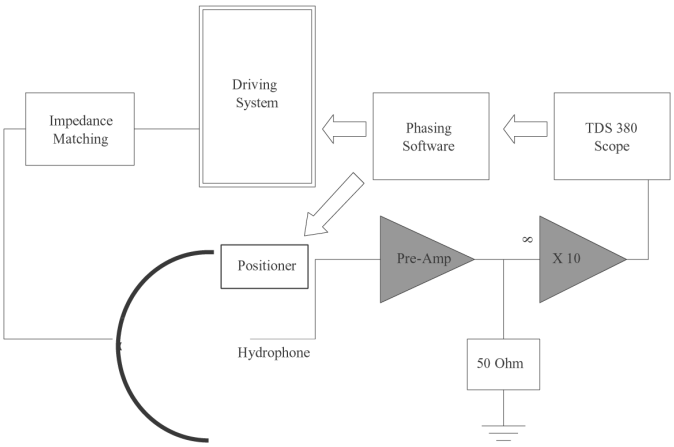

Fig. 2. Diagram of the experimental setup used for phase correction through an ex vivo human skull. The brain cage of a skull is placed between the transducer and the hydrophone. Phase-correction is performed automatically using feedback from the oscilloscope. A stepping-motor-controlled positioner guides the hydrophone to precise locations.

III. Experiment Procedures

A. Single-Element Study

Application of the phase screen as a model of the skull is, of course, an approximation due to finite size of the acoustic beamwidth incident upon the skull and finite thickness of the skull. To test the validity of the approximation for transcranial propagation, the field from a single element of a transducer array (used later in beam steering experiments) is measured after it propagates through an ex vivo human skull. The phase of the field provides a means of evaluating the range of the beam guidance method. This evaluation examines the range of validity of (4) for the relevant frequency and transducer geometry described here.

A transducer is placed approximately 5 cm from the skull surface and the acoustic pressure waveform is measured at a point using a 0.075 mm PVDF needle hydrophone (Precision Acoustics, Dorchester, UK) as the receiver. A 20-cycle sinusoidal signal is generated by an arbitrary waveform generator (Wavetek, model 305, Everett, WA) and fed to a power amplifier (ENI, model 3100L, Rochester, NY). Hydrophone response is sent through a pre-amp (Precision Acoustics, model HA1) into an amplifier (Preamble Instruments Model 1820, Beaverton, OR) and recorded by a digital oscilloscope (Textronix, model 380, Beaverton, OR).

A stepping motor positioner (Parker, Irwin, PA) then moves the hydrophone to a new location, and the process is repeated. Measurements are performed about the transducer's geometric focus over an area normal to transducer axis of symmetry. An area 40 cm × 40 cm is measured at 0.8 mm intervals. Waveform data are transferred to a computer that calculates the phase at each position. The measurement area is assumed to be large enough to apply a previously described [17] angular spectrum approach [18]

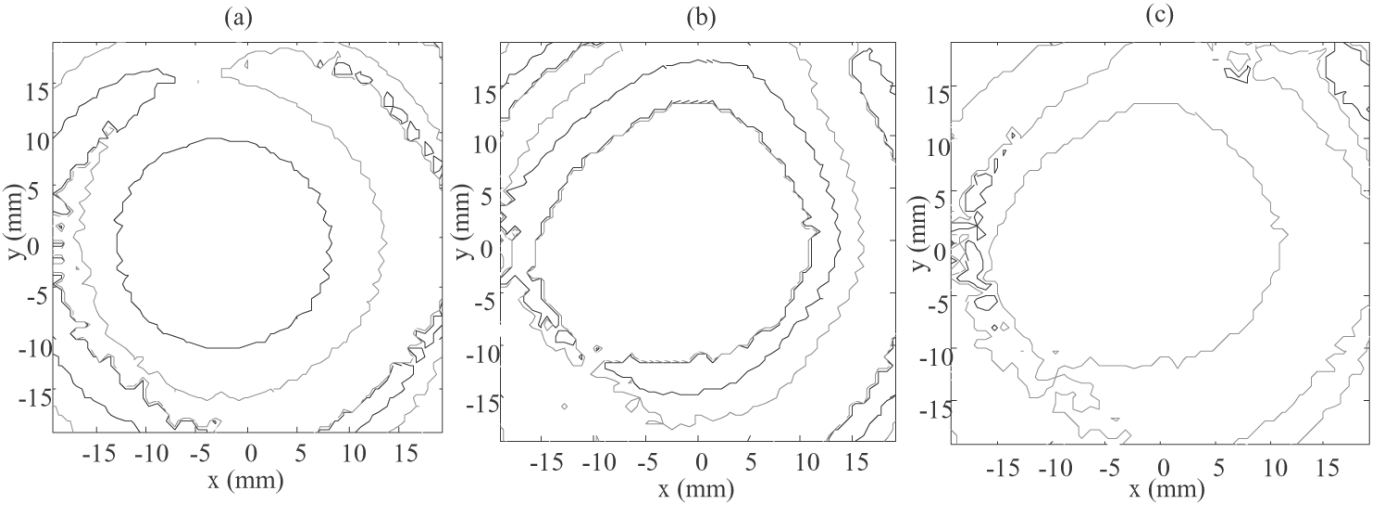

Fig. 3. Contour plots of (a) the phase of the acoustic pressure measured about the geometric focus of a 19-mm-diameter 0.81 MHz focused element. (b) Phase of the same element after a human skull is placed between the element and the receiver. (c) The argument of the division of the field with the skull in place by the field without the skull. Contour intervals are at pi/2 radians.

for finding the ultrasound phase in additional locations in front of and behind the measurement plane. The transducer is a single element of a 0.81 MHz, 120-element array used in the ensuing hydrophone-guidance experiment. The elements span a diameter of 19.2 cm and are made of a 1-3 PZT composite. The element is circular with a diameter of 19 mm. All measurements are taken in a test tank filled with deionized, degassed water and padded with rubber to inhibit reflections from the tank walls.

B. Beam Steering

The second experiment directly applies the beam steering method. Two arrays are used, one optimized for axial beam steering, and the other for radial steering. The first array, designed for axial steering, is a 1.1 MHz 104-element transducer [19] with a 16-cm radius of curvature. The array is constructed from a custom 1-3 Piezocomposite (Imasonic, France). The second array is the 0.81 MHz, 120-element array described in the previous section. The arrays were not specifically designed for the correction of aberrations in the skull.

Signals to the transducers are generated by two phased array driving systems manufactured in-house [20]. The two systems are similar, except one is designed to operate from 1 to 2 MHz, the other from 0.5 to 1 MHz. The amplifiers are equipped with phase feedback for increased control, and individual array elements are matched to electrical resonance at 50Ω. The 0.075 mm hydrophone receiver is affixed to the positioning system and positioned at locations in the test tank where the ultrasound is to be focused. Because the array is designed to have a large steering range along its axis of propagation, points are located near the axis. A separate continuous wave signal is delivered at 0.5 W electrical power to each transducer element, and the waveform at the hydrophone is recorded. The driving phase of each signal is evaluated and adjusted so that every element arrives at the receiver in phase. The magnitudes of the phase adjustments are then saved to a data file. The element-by-element phasing process is controlled as illustrated in Fig. 2. The receiver is next moved to a new location near the axis and the process is repeated. This phasing is performed in seven locations ranging from 12 cm to 18 cm from the array face at 1 cm increments.

The skull is now placed between the hydrophone and the transducer. The receiver is returned to the position 16 cm from the transducer, and the phasing process is repeated. Phase measurements at this location with and without the skull are entered into (4) to calculate the driving phases for all seven positions. The hydrophone is returned to each of the positions with the skull still in place, and the receiver response is recorded with all 104 elements driven simultaneously. The response also is measured for two additional phasing scenarios: the driving phases that focus the array at the relevant position in water without the skull in place, and using the driving phases that are obtained by directly applying the phasing process at the relevant positions.

C. High Intensity Operation

To demonstrate the utility of the method, a third experiment is performed using low intensity phase information at one location past the skull in order to produce a high intensity focus in a second location. Low intensity signals are below 0.5 W/cm^2; high power operation can exceed 500 W/cm^2. A tissue sample is placed inside the skull with the goal of producing a lesion at the intended focus by coagulation. Degassed bovine muscle stored in a 0.9% saline solution is used as the tissue sample. A 0.8 mm PVDF hydrophone receiver, manufactured in our laboratory, is used as a receiver for the experiment. Unlike the Precision Acoustics needle hydrophone described earlier, the in-house design is flexible, and it has an encapsulated tip for increased durability allowing it to be inserted into tissue. The receiver is inserted into the tissue sample using

a catheter, and its output is amplified with the Preamble amplifier set at X10 gain.

A 64-element, 30-cm-diameter hemisphere array (manufactured in-house) is used at its resonant frequency of 0.665 MHz [7]. The PVDF receiver is inserted into the tissue and placed in the water tank without the skull. Using the positioning system, the phase of each element is recorded in a location near the geometric center of the array as well as in a second location 10 mm radially outward from the geometric center. Next, the skull is placed around the tissue sample, and the phasing process is repeated at the position 10 mm from the center. A maximum power of 0.5 W electrical is used in the phasing process. The driving phases are then calculated using (4). Using these calculated phases, the power is increased to nearly 30 W per channel for a total electric power of about 1900 W, as monitored by internal power meters located on each channel of the driving system. The tissue is sonicated for 30 seconds at this power. The entire process is repeated for a new position 8 mm in front of the receiver and toward the array.

IV. Results

A. Single-Element Measurement

Phase measurements over a planar area are performed both with and without the skull and entered into (4) as described in the previous section. Fig. 3(a) shows the phase, $\arg(P_0)$, as a function of position without the skull and Fig. 3(b) shows the phase, $\arg(P)$, when the skull is inserted between the transducer and the receiver. According to the model, division of the two fields, $\arg(P/P_0)$, should produce a uniform phase. The actual result is shown in Fig. 3(c), which is found to be relatively uniform about the geometric center. The mean phase is found to vary by less than $\pi/8$ radians over an area of 474 mm^2. If perfectly symmetric, this would correspond to a circular area with a diameter of 29 mm.

The field measured at the geometric center of the transducer was numerically projected forward and backward in space using an angular spectrum approach [17], [18]. The relative phase, $\arg(P/P_0)$, is calculated along the acoustic axis and is observed to deviate by less than 0.12 radians over a distance of 20 cm in front of, and behind, the geometric center.

B. Beam Steering

Using phase information from the hydrophone placed near the geometric center of the 104-element array, the beam is steered through the skull to seven locations on-axis over a 60-cm range. Voltage response is recorded and used to calculate acoustic intensity, assuming a hydrophone sensitivity of 10 mV/MPa and an acoustic impedance of water equal to 1.5×10^6 kg m^{-1} s^{-1}. At each of the target locations, three measurements are performed, each the result of a different driving phase. The first driving phase steers the beam to the target location in water when the skull is not present. The second is obtained "invasively," using feedback from the hydrophone to phase the array. The third uses the hydrophone-guided method, with feedback coming from only a single location at the geometric center of the transducer. Results are summarized in Fig. 4. In all positions, a significant gain occurs between the intensity from steering the beam without further correction and the intensity when using the hydrophone-guided method. Over a range of 50 mm about the geometric center this gain ranges from 7X to greater than 13X. The intensity measured using the hydrophone-guidance method differs from the direct phasing method by less than 10% between the geometric focus and a distance of 20 mm beyond the focus. As the beam is steered closer to the transducer, this error becomes larger, reaching a 50% dropoff near 30 mm from the geometric center.

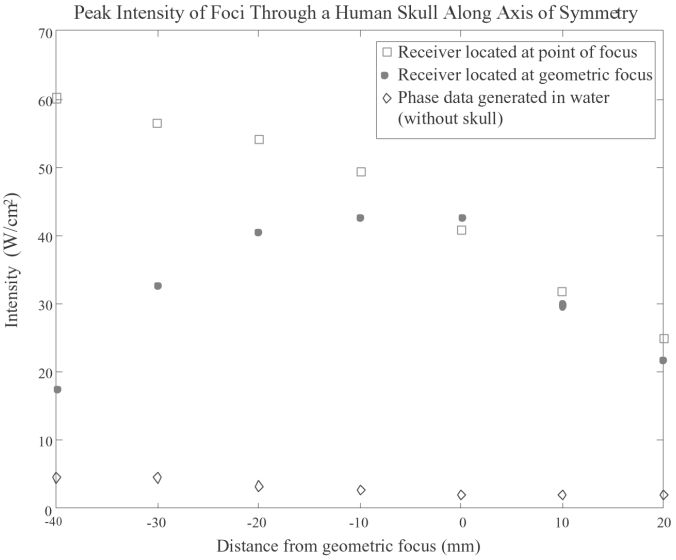

Fig. 4. Intensity as a function of focal location on-axis using three different focusing methods: phasing through direct feedback from a hydrophone placed at the focal locations in water (diamonds); phasing through direct feedback from a hydrophone placed at the focal locations inside the skull (squares); and phasing using the hydrophone guidance method, with a stationary hydrophone located inside the skull at the geometric center of the transducer (circles).

To examine changes in the ultrasound beam shape, hydrophone measurements are taken with the precision acoustics needle hydrophone at positions z = 20 mm, z = 0 mm, and z = −20 mm over 10 mm × 10 mm areas at intervals of 0.2 mm. Fig. 5 provides intensity plots taken at these locations before and after application of the phasing procedure. Without correction, the primary effect of the skull is observed to be a shifting away from the intended focal location, as well as some degradation of the beam. After the hydrophone-guidance method is applied in each position, the focus is shifted to its intended location, and a more uniform focus is produced.

Similar measurements are made using the 120-element 0.81 MHz hemisphere array, but with the beam now shifted in the radial direction. Intensities at the intended focal points are given in Fig. 6. Considerable gain occurs when

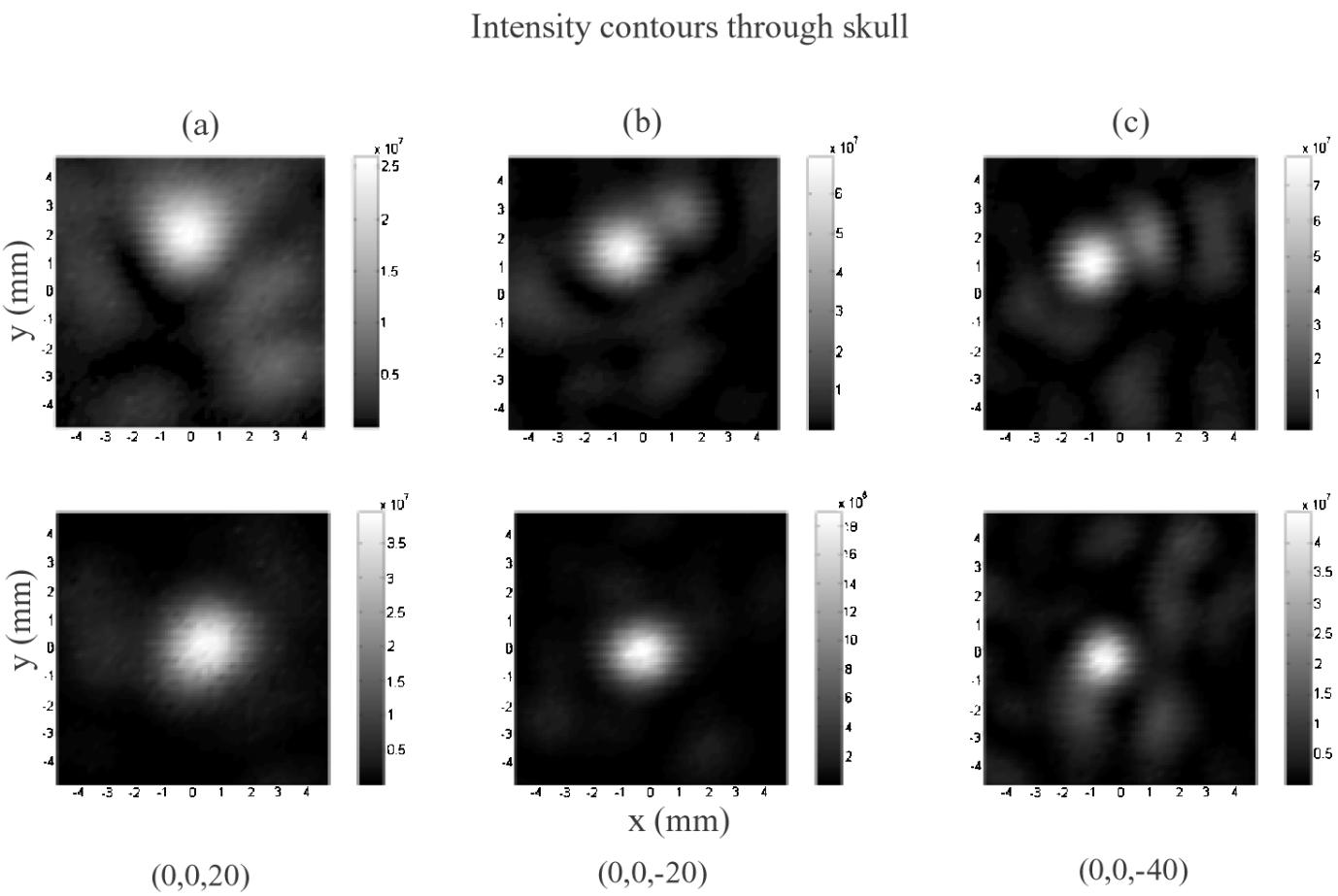

Fig. 5. Area measurements performed through phased beam steering alone (top) and using the hydrophone guidance method (bottom) measurements are taken (a) 20 mm from the geometric center, toward the transducer; (b) at the geometric center; and (c) 20 mm from the geometric center, away from the transducer.

using the hydrophone-guided method is applied between −10 mm and 10 mm away from the geometric center, where a gain greater than 10X is recorded at each position. The intensity of the hydrophone-guidance method differs from the direct phasing method by less than 25% in this range and by less than 7% within 5 mm from the transducer axis.

C. High Intensity Operation

Two thermally induced lesions are created inside a degassed porcine tissue sample placed within the skull. These lesions demonstrate high power (1900 W) focusing at locations approximately 1 cm from the receiver. Sonications at low power (0.5 W) are first performed with the hydrophone located 8 mm behind the planned high power focus in order to obtain phase information. The phased 1900 W signal is focused into the tissue for 30 seconds. Lesion dimensions are determined by sectioning the tissue, which is measured radially along two orthogonal axes and along the lesion axis. The lesion is found to be nearly spherical in shape with $D_{max} = 6.5$ mm, $L_{max} = 7.5$ mm. The lesions are found to be reproducible in a subsequent sonication. Next, a lesion is created 10 mm radially outward from the hydrophone. The lesion is found to have

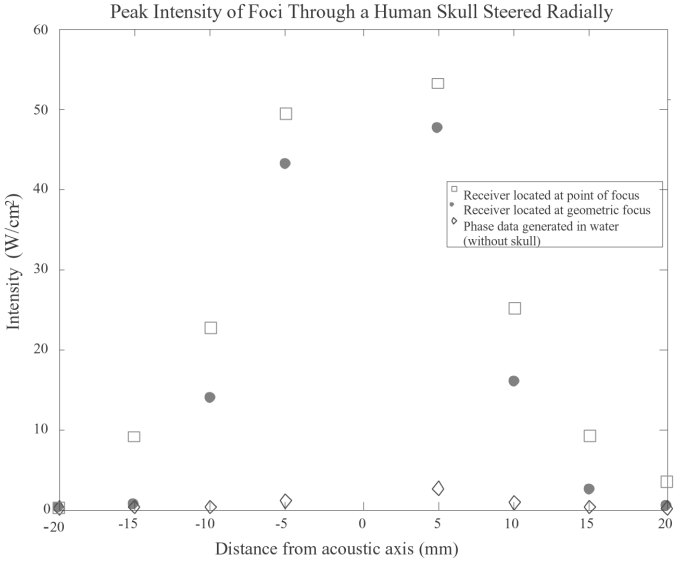

Fig. 6. Intensity as a function of focal location on-axis using three different focusing methods: phasing through direct feedback from a hydrophone placed at the focal locations in water (diamonds); phasing through direct feedback from a hydrophone placed at the focal locations inside the skull (squares); and phasing using the hydrophone guidance method, with a stationary hydrophone located inside the skull at the geometric center of the transducer (circles).

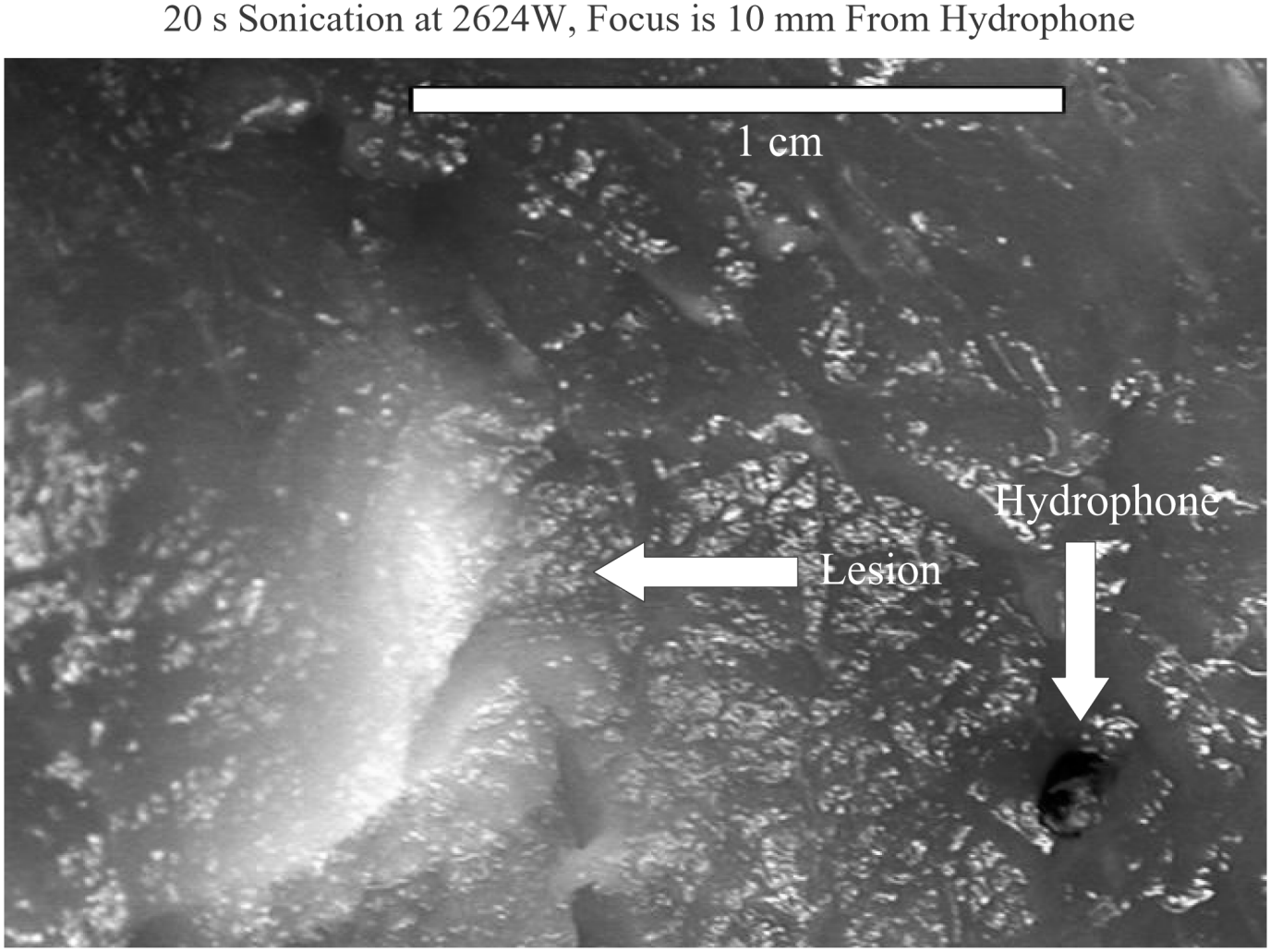

Fig. 7. Lesion produced in ex vivo porcine muscle placed inside a human skull focused using a hydrophone located 10 mm from the point of sonication (a 10 mm white scale bar is added for reference). A 30 second sonication was performed at 1900 W.

dimensions of $D_{max} = 9.0$ mm, $L_{max} = 8.0$ mm. A section of the lesion is presented in Fig. 7, sliced approximately normal to the ultrasound axis, showing the location of the lesion relative to the hydrophone.

V. Discussion

Experiments demonstrate that a receiver placed at a single stationary location inside a human skull may be used to produce a focus at locations away from the receiver. The study also shows that the transducer driving phases necessary for this process may be obtained at low ultrasound intensities then used for high power operation. Similar techniques have been proposed to correct for aberrations in soft tissue [13]; to our knowledge this in vitro study is the first to correct for tissue surrounded by bone. The method may have application in minimally invasive ultrasound brain surgery and other therapies applied through bone.

The spatial range of the method is dependent on the transducer array geometry. Investigations of the fields from individual elements of a given array can provide detail on the range of that particular transducer. For example, the present study measured the field of a focused 0.81 MHz, 283-mm^2 element before and after propagation through the skull (Fig. 3). Using (4), the radial range was predicted in Section IV-A to be approximately 29 mm as determined by the 50% intensity drop-off point. When the method is directly applied to the array, a range of approximately 24 mm is achieved (Fig. 6).

The choice of arrays used in the experiments was based on selecting the most relevant pre-existing transducers in our laboratory. The arrays are not necessarily optimal for the hydrophone guidance method, and significant improvements could potentially be achieved with an array designed to maximize the experimental agreement with (4).

High power application of the procedure was performed using a 64-element therapeutic transskull array. Tissue coagulation was achieved a distance of 10 mm radially outward from the hydrophone and 8 mm axially. The hemisphere-shaped array is configured to restore the focus at the geometric center of the transducer. The beamwidths of the 64 individual elements are too tight to permit beam

steering. It is expected that a significant improvement in the steering range would occur using a similar array with more elements.

VI. Conclusions and Future Work

Results of this preliminary study are encouraging and promote further investigation in two areas. The first is the development of an array configuration that optimizes the range of the single-receiver beam steering method. Second is the design of a catheter-inserted micro-receiver capable of uncomplicated insertion into the brain via the blood vessel network. A finalized beam steering device could then be applied alone as a minimally invasive surgical technique, or used as a quality assurance device for the testing of proposed noninvasive transskull surgery. In practice, the position of the receiver in the brain relative to the transducer array could be located using MRI. Although the present study concentrates on application in the brain, it also is possible that the technique could be applied to other organs, such as the liver, that are currently difficult to reach due to scattering by bone.

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