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Transcranial acoustic holograms for arbitrary fields generation using focused ultrasound into the brain

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We present 3D-printed holographic lenses that correct the aberrations of the skull and produce arbitrary ultrasonic fields with the geometry of brain structures. Using experimental techniques on a human skull phantom (HSP), a multiple-point focusing lens is designed to focus at both hippocampi; a beam following a curved trajectory and a holographic plate producing a focus that overlaps the left hippocampus (LH). Skull and LH geometries and acoustic properties are obtained from CT-MRI scans. Time-reversal method is used to obtain the magnitude and phase of the back-propagated field. The holographic lenses are designed assuming each pixel of the lens vibrates as a Fabry-Pérot resonator. The resulting lenses are 3D-printed using SLA techniques. The three studied cases show similar results in simulation and experiment with and without the HSP: for the bi-focal beam, the reconstructed field matches the target foci; for the curved trajectory beam, the target acoustic image is reconstructed by the designed holographic lens; for the broad focus beam, results present the same qualitative performance providing a similar overall covering of the LH. The reported holographic lenses can be used to control the spatial features of ultrasonic beams inside the skull in an unprecedented manner using single-element ultrasonic sources.

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1. INTRODUCTION

Acoustic holographic lenses are complex surfaces that can modify the phase of the transmitted or reflected wavefront in such a manner that a complex image can be formed. Acoustic holographic lenses have demonstrated the ability to manipulate acoustic waves in free media, i.e., without inhomogeneities.[1–3] In the context of biomedical applications, when the target tissue lays behind high-impedance tissues, e.g., soft-tissue surrounded by bones, the beam experiences strong aberrations due to refraction, reflection and absorption processes.[4] In the particular case of transcranial propagation skull bones are always present in the path towards the central nervous system (CNS). In this way, the precise control of acoustic focus into the CNS is mainly limited due to the strong phase aberrations produced by the refraction and attenuation of the skull.[5] Only few works have tackled the problem of beam focusing through aberrating layers using metamaterials[7] or phase plates.[6] In Ref.[7] a 2D configuration was proposed theoretically using a metasurface based on membranes. Recently, the use of phase plates to generate simple focused sources have been reported to avoid beam aberrations in transcranial propagation.[6] However, the technique was limited to focus the beam into a single focal spot at the near field of the source. Besides, in some non-thermal transcranial ultrasound applications such as blood-brain barrier opening[8] or neuromodulation[9] the ultrasound beam might be set to fully-cover a geometrically complex CNS structure rather than focusing over a small focal spot.

This paper presents a summary of the work presented by our team in Ref.[10] Here, we propose the use of 3D-printed holographic phase plates to produce ultrasonic fields of arbitrary shape into the human brain. The holographic lenses designed in this work allow the reconstruction of complex diffraction-limited acoustic images including the compensation of the aberrations produced by a skull phantom, as shown in Fig. 1. In particular, we theoretically, numerically and experimentally demonstrate the generation of several holographic patterns, of increasing complexity, all with direct practical application to biomedical ultrasound: an arbitrary set of points, an arbitrary curved line, and an arbitrary volume.

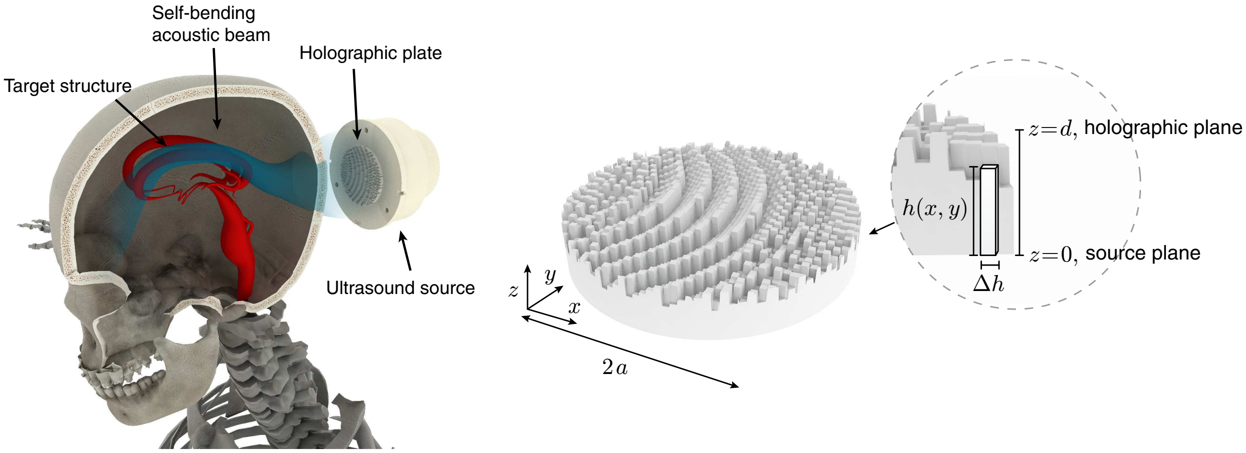

Figure 1: (a) Scheme of the holographic lens focusing over a target CNS structure. (b) Geometry of the holographic lens. The lens, of aperture $2a$ is subdivided in pixels of height $h(x,y)$ and width Δh. The source is located at $z = 0$, while the holographic plane is located at $z = d$. Adapted from Ref.[10]

2. METHODOLOGY

First, we provide the conditions to generate a simple holographic pattern, i.e., a set of diffraction-limited focal points. In particular, we extend the use of holographic lenses to generate bifocal beams, matching both foci simultaneously the location of left and right human hippocampus. Second, we demonstrate that ultrasonic beams with curved trajectory along the internal CNS tissues can also be produced. In this way, the acoustic beam can be bent following arbitrary paths producing a self-bending beam inside the CNS. Finally, we report the generation of a beam pattern that overlaps with the volume of a specific CNS structure in particular we target the right human hippocampus.

A. SKULL GEOMETRY AND ACOUSTIC PROPERTIES

In order to model the skull geometry, we used the CT Datasets of a female human head with an isotropic resolution of 1 mm (interpolated to 0.22 mm for the numerical simulation) from the National Library of Medicine's Visible Human Project available for general use by the University of Iowa. Experiments were conducted in a 3D printed skull phantom, while, in addition, we included full-wave simulations using the acoustical properties of the skull bones. Thus, for the skull phantom simulations we used homogeneous acoustical parameters matching those of the 3D printing material, while for the realistic skull simulations we used the same geometry but the inhomogeneous acoustical parameters of the skull were derived using the same the CT data, converting the apparent density tomographic data in Hounsfield units to density and sound speed distributions using the linear-piecewise polynomials.

B. LENS DESIGN

First, we set some virtual sources inside the skull phantom and the back-propagated field was estimated at a given surface outside the skull phantom. For the bifocal lens, two virtual sources were set as monopoles with same phase and amplitude, located at the center of mass of the two hippocampi (right and left). For the self-bending beam, a set of 50 virtual sources was located following an arbitrary curve, each source compensated by a phase factor accounting for the direction of arrival of the wavefront. Finally, for the volumetric hologram, a set of virtual sources was spatially distributed over a sagittal plane of the right human hippocampus. The recorded field was captured at a given surface, i.e, at a holographic surface, outside the skull phantom. Second, the recorded conjugated pressure distribution at the working frequency was used to design the physical lens. The lens surface was divided in squared pixels of different height,

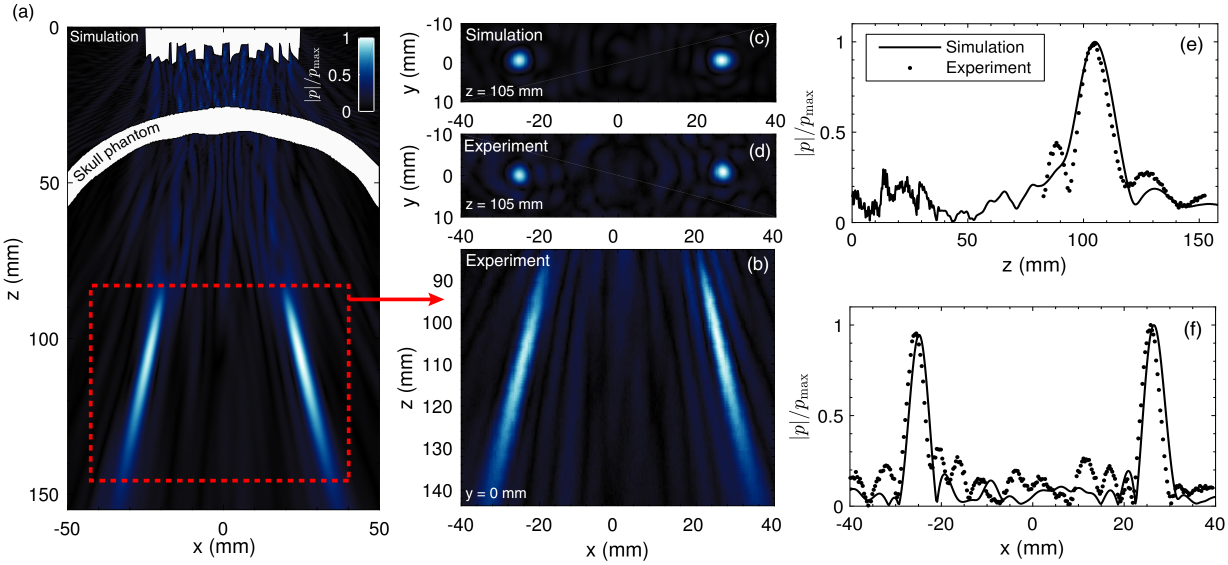

Figure 2: Axial field cross-section obtained for the bifocal lens using simulations (a) and experiments (b). (c-d) Corresponding transversal pressure field distributions. Colorbar in units normalized to the peak pressure. (e,f) Simulated and experimental normalized axial and transversal field cross-sections, respectively. Adapted from Ref.[10]

$h(x, y)$ and uniform. We assume each elastic column to vibrate longitudinally as a Fabry-Pérot resonator. Thus, for each column the field at the holographic plane is given by the analytical solution of the complex transmission coefficient of a slab of elastic material.

3. RESULTS AND DISCUSSION

A. MULTIPLE FOCAL-POINT HOLOGRAMS

First, two points located at the center of mass of both left and right human hippocampi are selected. The details about the hologram generation and the methods used can be found in Ref.[10] The field produced by the bifocal lens propagating through a human occipital/parietal skull phantom including the compensation for the aberrations of the skull is shown in Figs. 2 (a-f). First, Figs. 2 (a,b) show the axial field cross-section, $p(x, y = 0, z)$, using the pseudo-spectral simulation method and measured experimentally, respectively. We observe that the reconstructed field accurately matches the target foci, and the experimental results agree with the simulations. The corresponding transverse field distributions at $z = 105$ mm are shown in Figs. 2 (c,d) where sharp focusing is observed.

B. SELF-BENDING BEAMS

The previous results show that holographic phase plates can retain phase information of multiple foci. Using this idea, we can set more complex targets following the shape of functional structures found in the CNS. Here, we set the target holographic pattern to a beam following a curved trajectory. A sketch of the target trajectory is shown in Fig. 3 (a). The axial cross-sections of the forward propagated field in water is shown in Fig. 3 (a). We observe that using the TR method self-bending beams can be obtained, and the beam accurately follows the target trajectory. Using simulation and a lens made of elastic material a similar result is obtained, as shown in Fig. 3 (b). The experimental tests show a similar pressure field distribution in comparison with theory using the Rayleigh-Sommerfeld integral and simulations using pseudo-spectral methods. Finally, when the aberration layer of the skull phantom is included the corresponding holographic lens also reconstructs the target acoustic image with curved trajectory, as shown in Figs. 3 (c). A similar lateral shift of the peak pressure location in the experiments, of 0.25 mm in the x direction is observed at $z = 30$ mm and $y = 0$ mm. Both results demonstrate that using TR methods self-bending beams following a target curve can be obtained inside the skull phantom using acoustic holographic lenses.

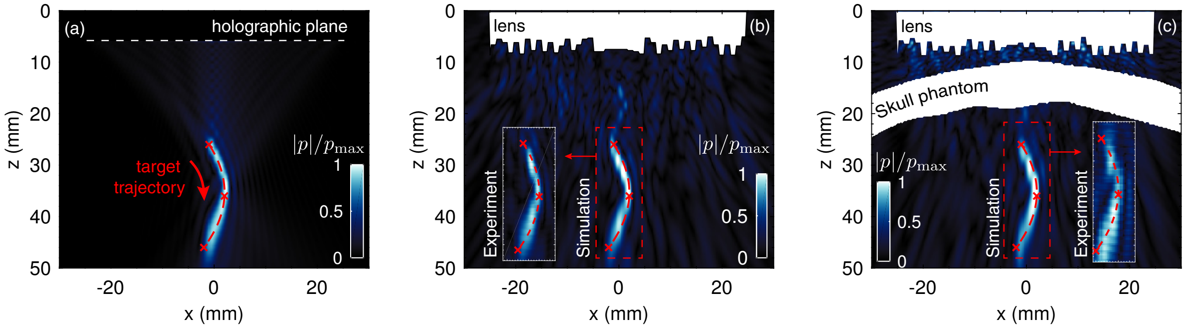

Figure 3: Theoretical (a) axial pressure field distribution for the self-bending beam in water. Simulated (b) axial pressure field distribution for the self-bending beam in water. Corresponding experimental results are shown in the insets in (b). (c) Simulated axial and transversal pressure field including the skull phantom. Corresponding experimental results are shown in the insets. Adapted from Ref.[10]

C. VOLUMETRIC HOLOGRAMS

Going further, we designed a holographic lens which produces an acoustic image that fits the right human hippocampus volume. The holographic surface was placed near the occipital/parietal bones to adapt the acoustic image to the elongated geometry of the human hippocampus. However, we locate the lens at the center of the skull symmetry plane in order to demonstrate the steering capabilities of this holographic lens. The field distribution produced by acoustic holographic lenses including the skull phantom is shown in Figs. 4. Both holographic images present the same qualitative performance and provide a similar overall covering of the interest zone. In addition, both axial (Fig. 4 (a,b)) and transversal (Figs. 4 (c,d)) field distributions are similar of those produced in water without the skull phantom, showing that, first, limited-diffraction holographic volumes can be reconstructed and, second, the aberrations produced by the skull phantom on these complex beams can be compensated at the source plane by the acoustic holographic lenses. Finally, the transversal and axial cross-sections, shown in Figs. 4 (e,f), show that the experimental and simulated acoustic holographic lens produces a field enhancement that matches the target distribution.

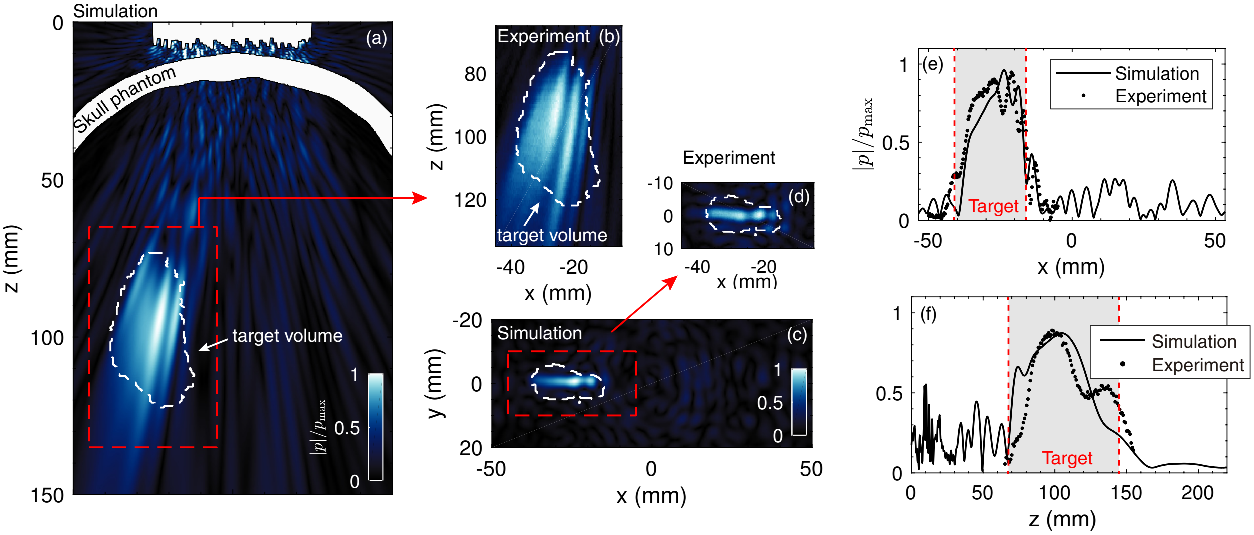

Figure 4: Volumetric hologram results. (a,b) Simulated and experimental axial pressure distribution. (c,d) Transversal field cross-sections. (e) Simulated, experimental transversal field distribution. (f) Simulated and experimental axial pressure distribution. Adapted from Ref.[10]

4. CONCLUSION

We have shown that using 3D printed acoustic holograms it is possible to conform diffraction-limited ultrasonic fields of arbitrary shape compensating the aberrations of the human skull. In particular, experimental tests using a 3D printed skull phantom and numerical simulations using a realistic skull were performed to accurately generate multiple focal holograms, self-bending beams and volumetric holographic fields overlapping a target CNS structure. The proposed approach using holographic lenses represents a step forward when compared with the existing solutions using phase arrays, since it opens new venues to develop reliable and cost reduced ultrasonic applications. The concept shown in this work opens new doors to optimize and widespread incoming therapy treatments such as ultrasound-assisted blood-brain barrier opening for drug delivery and neuromodulation, or ultrasonic imaging of the central nervous system using low-cost devices. Considering the emergence of metamaterials[11–13] and their huge flexibility, we also advance future biomedical applications of active holographic metasurfaces for the generation of complex fields in the central nervous system.

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