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Acoustic Holograms Allow the Generation of Complex Fields Inside the Central Nervous System

Sergio Jiménez-Gambín
Instituto de Instrumentación para Imagen Molecular (i3M)
Universitat Politècnica de València - CSIC
Valéncia, Spain

Noé Jiménez
Instituto de Instrumentación para Imagen Molecular (i3M)
Universitat Politècnica de València - CSIC
Valéncia, Spain
Corresponding Author, nojigon@upv.es

José M. Benlloch
Instituto de Instrumentación para Imagen Molecular (i3M)
Universitat Politècnica de València - CSIC
Valéncia, Spain

Francisco Camarena
Instituto de Instrumentación para Imagen Molecular (i3M)
Universitat Politècnica de València - CSIC
Valéncia, Spain

***Abstract*—Focused ultrasound is currently used in many emerging therapeutic applications for the non-invasive treatment of neurological disorders and pathologies inside the central nervous system. However, the accurate focusing of ultrasound beams at the central nervous system is mainly limited due to the strong phase aberrations produced by refraction and attenuation of the skull. We present 3D-printed acoustic holographic lenses for the generation of ultrasonic fields of complex spatial distribution inside the skull. Using holographic lenses with an aperture of 50 mm and working frequency of 1.1 MHz, we experimentally, numerically and theoretically produce acoustic beams whose spatial distribution match target structures of the central nervous system. In particular, we present three configurations of increasing complexity: a set of points, a curved trajectory and an arbitrary volume. Results show that, using low-cost 3D-printed lenses, ultrasonic beams can be focused not only at a single point, but overlapping at one or various target structures simultaneously, e.g., left and right hippocampi. These results open new paths to spread emerging therapeutic ultrasound applications including blood-brain barrier opening or neuromodulation using low-cost systems.**

***Index Terms*—Holograms, transcranial ultrasound, therapeutic ultrasound, blood-brain barrier opening, neuromodulation**

I. 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 and metasurfaces have demonstrated the ability to manipulate acoustic waves in free media, i.e., without inhomogeneities [1]–[5]. 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 [6]. 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 [7].

Only few works have tackled the problem of beam focusing through aberration layers using metamaterials [8] or phase plates [9]–[12]. In Ref. [8] 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 [9]–[11]. 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 [13] or neuromodulation [14] 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. [12]. Here, we propose the use of 3D-printed holographic phase plates to produce ultrasonic fields of arbitrary shape into the human brain, as sketched in Fig. 1. 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. 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.

II. Methods

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

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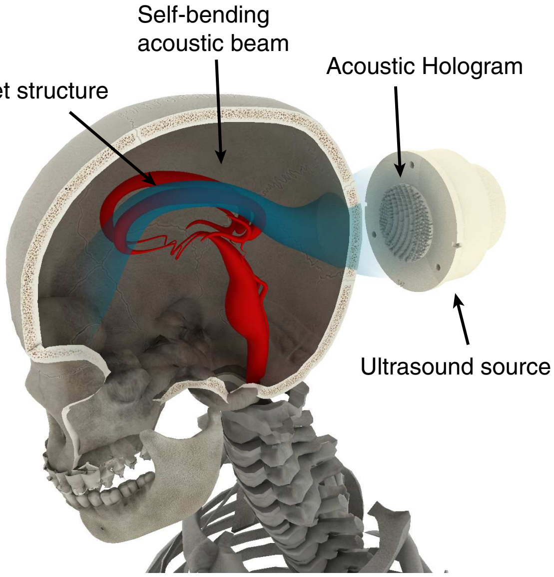

Fig. 1. Scheme of the holographic lens focusing over a target CNS structure.

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 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 were 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 were spatially distributed over a sagittal

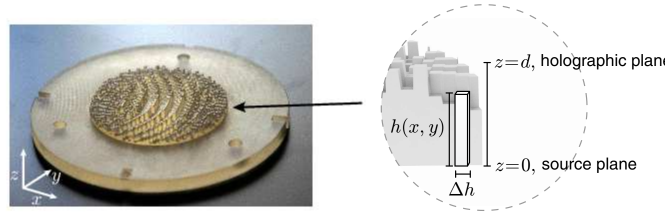

Fig. 2. Photograph and geometry of the holographic lens. The lens, of aperture $2a$ is subdivided in pixels of height h(x, y) and width Δh. The source is located at $z = 0$, while the holographic plane is located at $z = d$. Adapted from Ref. [11].

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, $h(x, y)$ and constant width Δh, as shown in Fig. 2. 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, $T(x, y)$ of a slab of elastic material as:

$$T = \frac{2Z\mathrm{e}^{-ik_0[d-h(x,y)]}}{2Z\cos\left[k_L h\left(x,y\right)\right] + i\left(Z^2+1\right)\sin\left[k_L h\left(x,y\right)\right]}, \quad (1)$$

where d is the distance from the bottom of the lens to the holographic surface, the normalized impedance is given by $Z = Z_L/Z_0$, and $Z_0 = \rho_0 c_0$ is the impedance of water and $Z_L = \rho_L c_L$, $k_L = \omega/c_L$, ρ_L and c_L, are the impedance, wavenumber, density and sound speed of the lens material A detailed derivation of this expression can be found in Ref. [15].

III. Results

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. 3(a-f). Both holographic images present the same qualitative performance and provide a similar overall covering of the interest zone. In addition, both axial (Fig. 3 (a,b)) and transversal (Figs. 3 (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. 3 (e,f), show that the experimental and simulated acoustic holographic lens produces a field enhancement that matches the target distribution.

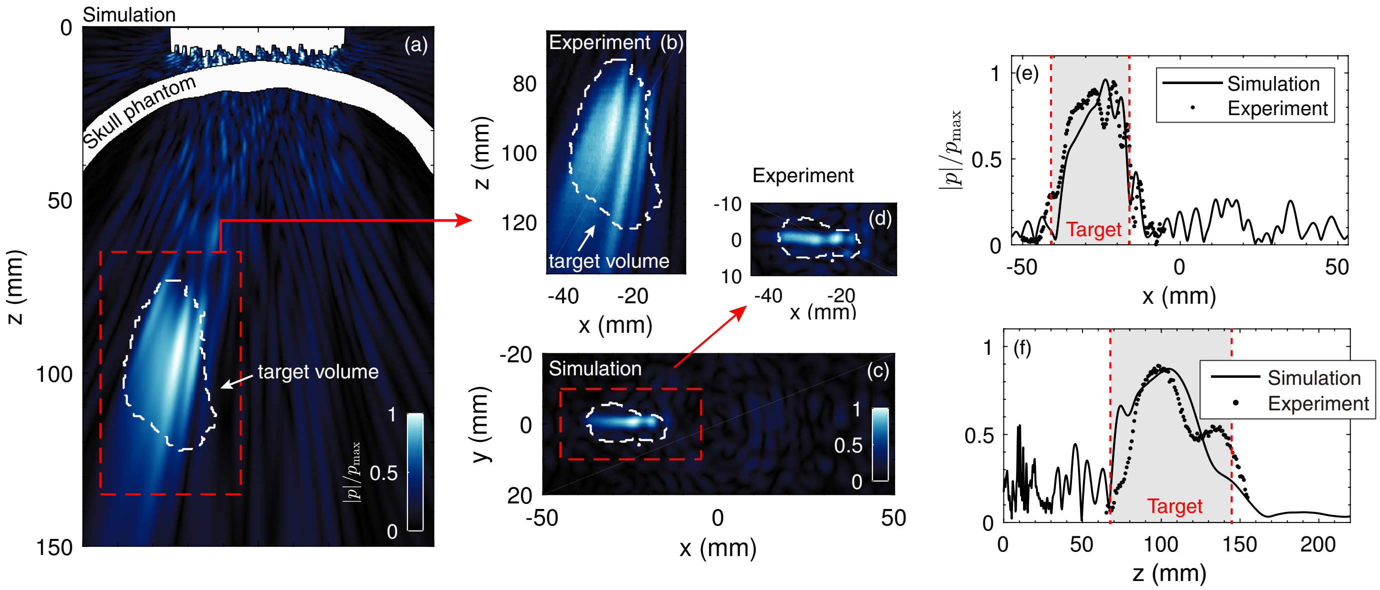

Fig. 3. Volumetric hologram results. (a,b) Simulated and experimental axial pressure distribution. (c,d) Transversal field cross-sections. (e) Simulated, experimental transversal field distribution. (f) Simulated and experimental axial pressure distribution. Adapted with permission from Ref. [11].

IV. Conclusions

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 [12] and their huge flexibility, we also advance incoming biomedical applications of active holographic metasurfaces for the generation of complex fields in the central nervous system.

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