Acoustic holograms for low-intensity ultrasound neuromodulation in non-human primates

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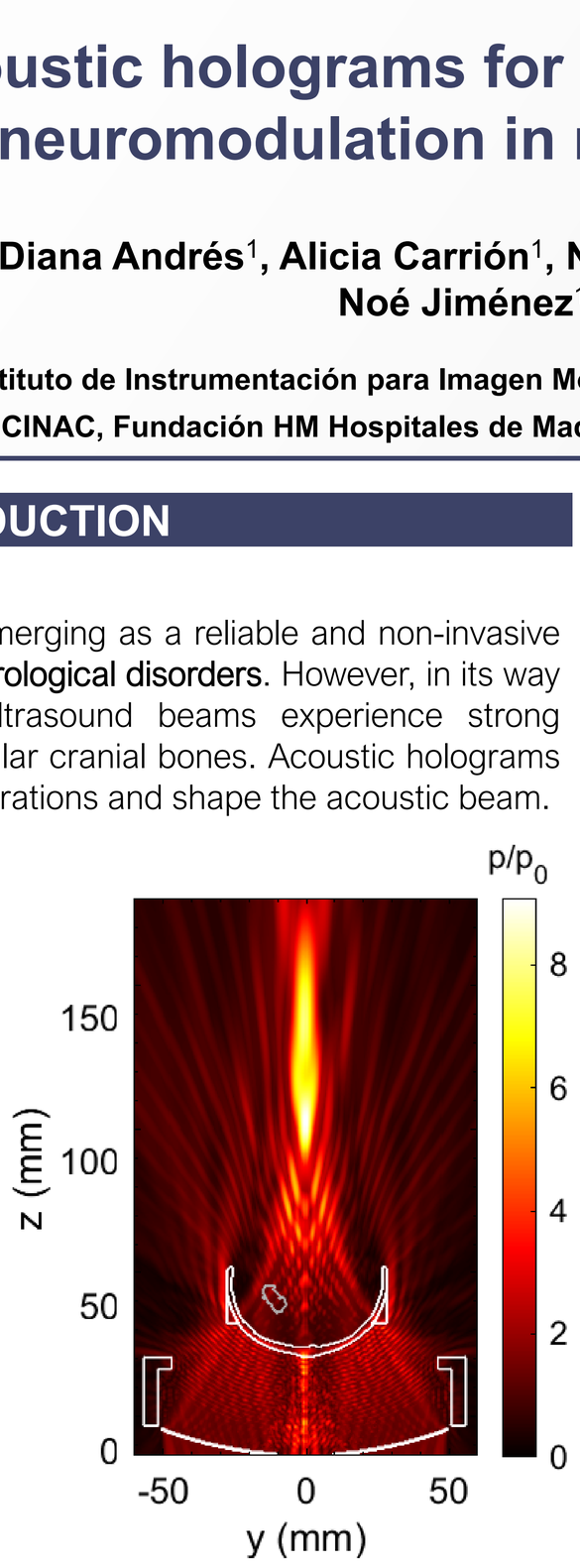
INTRODUCTION

Background

Transcranial focused ultrasound is emerging as a reliable and non-invasive therapeutical approach for many **neurological disorders**. However, in its way to the central nervous system, ultrasound beams experience strong aberrations due to the stiff and irregular cranial bones. Acoustic holograms have been used to correct these aberrations and shape the acoustic beam.

Our proposal

In this work we use **acoustic holographic lenses** coupled to a custom-made large aperture focused transducer (140-mm radius of curvature and 100-mm aperture) at 500 kHz for neuromodulation purposes in the left posterior putamen of rhesus macaques. We evaluate the system performance making direct measurements with an ex-vivo macaque skull. The focal region also was reconstructed by **holographic projection techniques** to avoid reflections between the skull and the hydrophone.



METHODS

Simulations

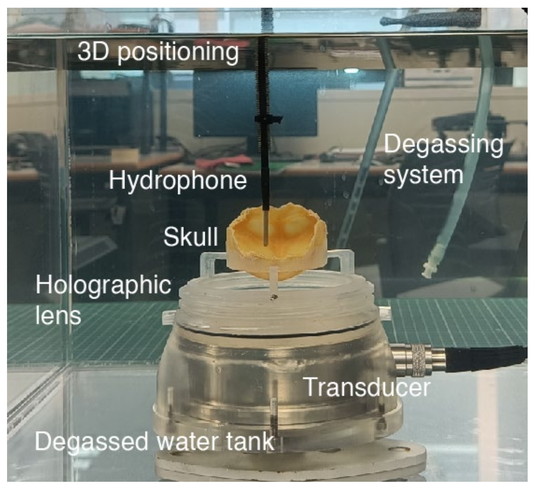
Pseudo-spectral (*k*-space) time-domain simulations of the constitutive relations for acoustic waves in heterogenous media including frequency-power law absorption and dispersion are used. The transducer was modelled as a quasi-rigid surface for a better approach to reality, and simulations ran during long time to capture multiple reflections in the skull and between the skull and the transducer.

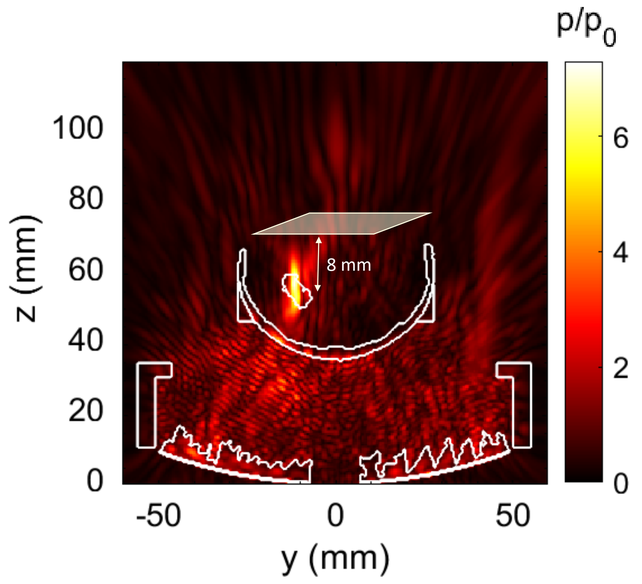
Holographic lens design

The **holographic lens** was designed with time reversal methods, setting a virtual source at the target location. Resulting holographic lens is designed assuming each pixel of the lens vibrates as a Fabry-Pérot resonator, encoding the phase of the wave. The resulting lens is 3D printed with photo-sensitive polymers.

Experiments

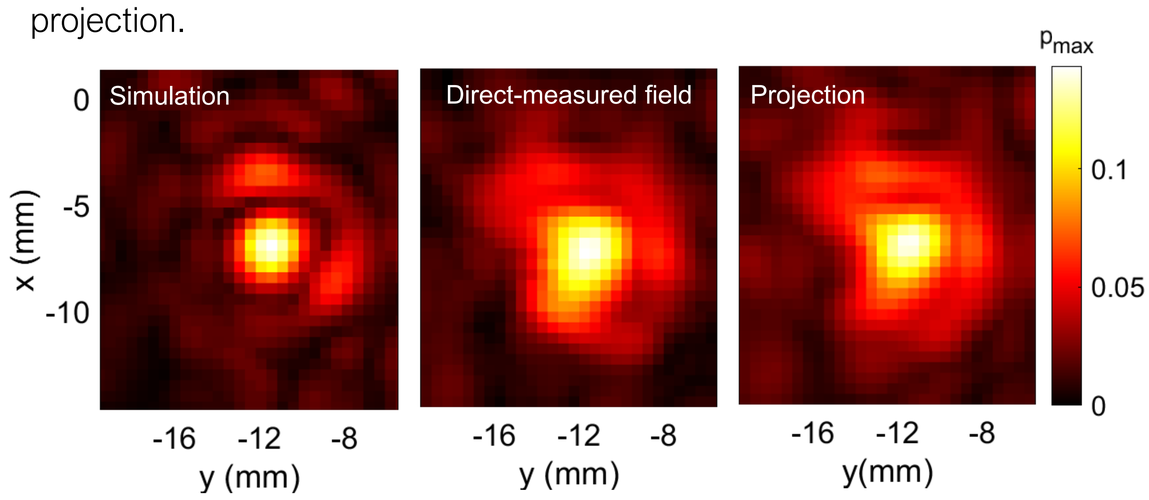
Direct acoustic measurements were done with a piezoelectric hydrophone in a degassed water tank. **Holographic projection techniques** were also applied to retrieve the whole focus shape. To do this, an XY-plane located 8 mm above the focus is measured. The plane dimensions (30x30 mm^2) must ensure retrieving all the information coming from the transducer and the formed focus.



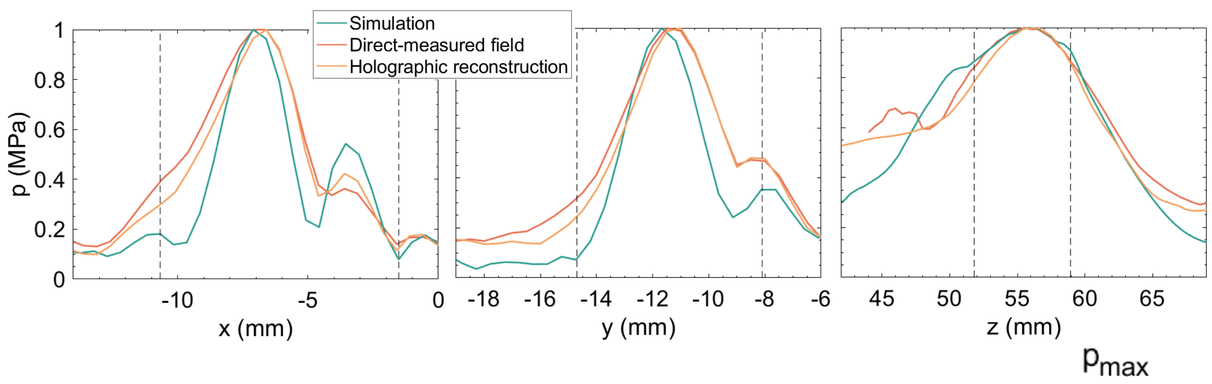


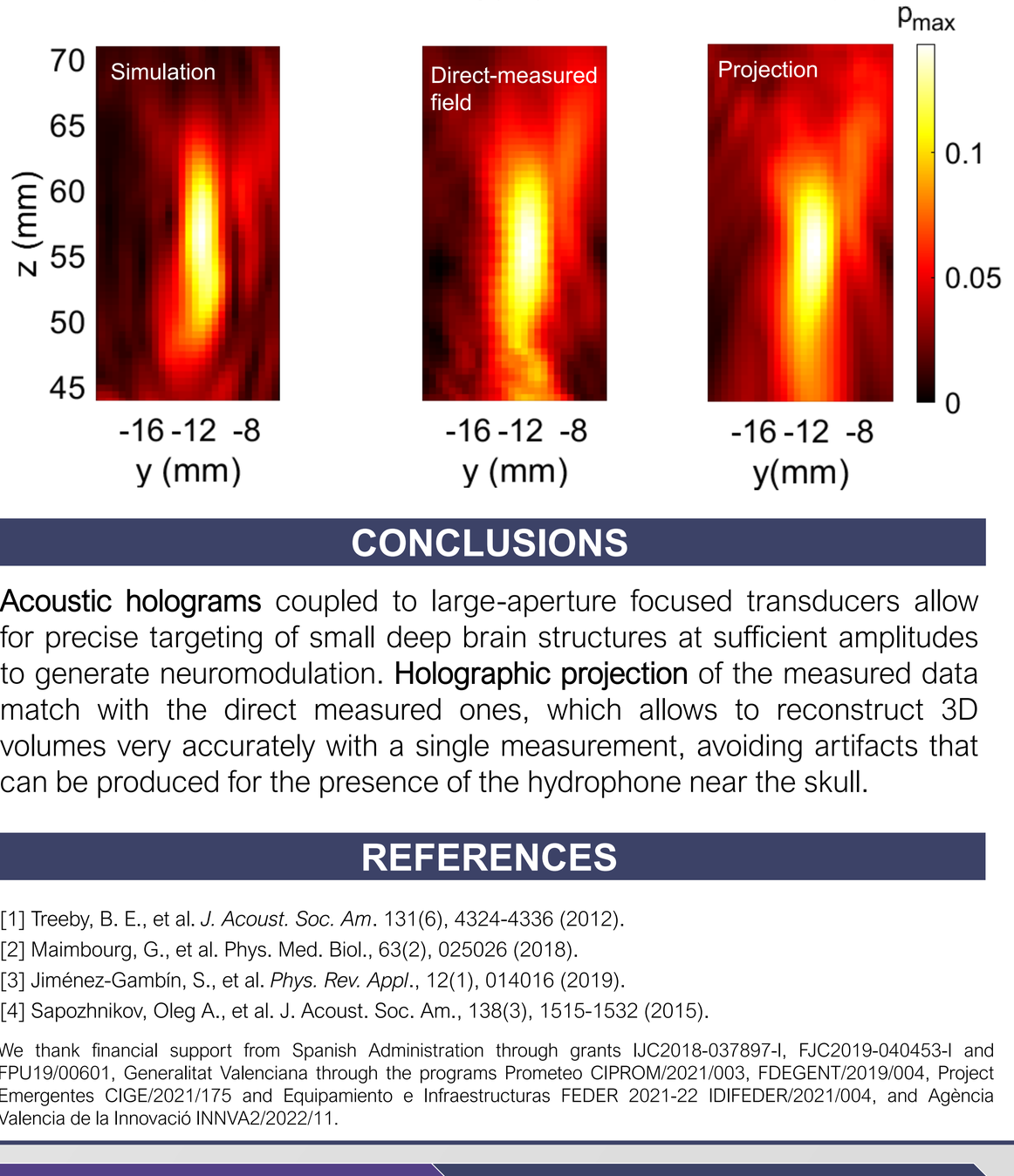
RESULTS

Acoustic fields obtained by simulation, direct measurement, and holographic projection were in good agreement. Focus sizes considering a -3 dB threshold were 3 x 3 x 14 mm^3 in the simulation, 4.5 x 4.5 x 15.5 mm^3 in direct measurements and 4 x 4 x 14 mm^3 using the holographic projection.



The focal spot appeared at the target location for simulation and both measurements, generating 0.5 MPa rarefaction pressure, with 55% and 40% of the focal volume lying in the left putamen region for simulation and holographic reconstruction, respectively. A 14% of the target volume was sonicated in the simulation results, while 38% of this volume was actually sonicated, measured using **holographic reconstruction**.





CONCLUSIONS

Acoustic holograms coupled to large-aperture focused transducers allow for precise targeting of small deep brain structures at sufficient amplitudes to generate neuromodulation. **Holographic projection** of the measured data match with the direct measured ones, which allows to reconstruct 3D volumes very accurately with a single measurement, avoiding artifacts that can be produced for the presence of the hydrophone near the skull.

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