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

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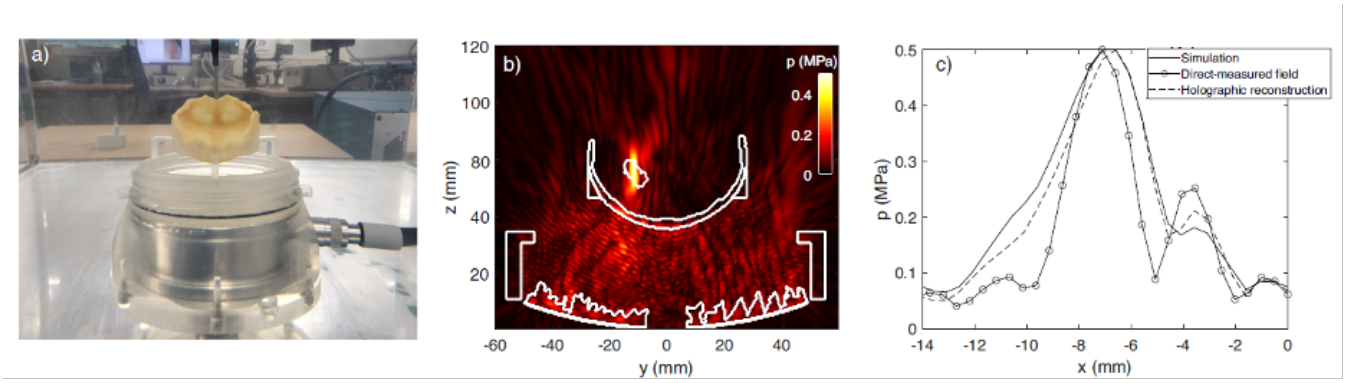
Abstract:

Focused ultrasound has gained relevance in neurological applications. However, to non-invasively focus inside the brain, ultrasound must pass through the skull, suffering from strong distortions. The aim of this work is to design and employ large-aperture focused transducers with holographic lenses to selectively sonicate deep-brain structures in non-human primates, such as the putamen, correcting skull aberrations and obtaining enough intensity at the focal spot for neuromodulation purposes.

We created acoustic holograms to focus on the left posterior putamen of a macaca mulatta using a focused transducer of 140-mm radius of curvature and 100-mm aperture, with 500-kHz central frequency. The hologram was designed with time-reversal methods and numerical simulations with a k-space pseudospectral method implemented in k-Wave. Its performance was experimentally evaluated with an ex-vivo macaque skull in a degassed water tank with direct measurements using a piezoelectric hydrophone. Due to the reduced anatomy of the skull, the focus appears close to the bone and reflections between the skull and the hydrophone might be captured. To avoid undesired artefacts, the focal region was also reconstructed by holographic projections of measurements taken at the far field.

Simulations, direct measurements and holographic projection results were in good agreement. Focus sizes in the simulation considering -3dB were 3 x 3 x 14 mm, while directly measured were 4.5 x 4.5 x 15.5 and with holographic projection were 4 x 4 x 14 mm. The maximum focal spot appeared in the same location for simulation and both measurements, generating 0.5 MPa rarefaction pressure, with 84% of the focus volume lying in the left putamen region. In conclusion, holographic lenses coupled to large-aperture focused transducers allow for precise targeting of small deep brain structures at sufficient amplitudes to generate neuromodulation.

Figure Caption: a) Experimental set-up. b) Simulated acoustic field with holographic lens and skull support. c) Comparison between simulation, direct measure and holographic reconstruction in a x-axis cut along the maximum of the focal spot.



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