## Modeling of intensity-modulated ultrasound in pediatric brain tumors using acoustic holograms

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## **Background, Motivation and Objective**

Targeted drug delivery into the central nervous system is achieved by opening the blood-brain barrier in a non-invasive, transient, local and safe manner by using focused ultrasound (FUS) and microbubbles. This technique can be useful to enhance chemotherapy treatments in brain tumors. However, as brain tumors are large structures, conventional FUS methods do not allow a large volume covering, thus resulting a low-efficient procedure. In this work, we numerically show how 3D-printed acoustic holograms allow a large and localized FUS delivery along a pediatric brain tumor, as well as the correction of the skull aberrations. Several targeting configurations are numerically studied, aiming to increase the covered target volume but keeping a reduced out-of-target FUS delivery. The presented approach opens new paths for time- and cost-effective chemotherapeutical trials.

## Statement of Contribution/Methods

Simulations were done using the pseudospectral method implemented in the k-Wave Matlab toolbox. For the numerical hologram generation, we first extracted from CT-scan a pediatric patient's skull and from MRI the tumor geometry and location. Then, we back-propagated and phase-conjugated the recorded field to calculate the holographic acoustic wavefront. A phase-only lens was designed and excited with the single-element transducer to generate the target acoustic volume. We used a 250-kHz single-element transducer with different size depending on configuration (ROC=110 mm, OD=110 or 132 mm, ID=0 or 44 mm).

## **Results/Discussion**

A 16 % of tumor coverage is achieved with the best configuration, compared to a 5 % conventionally, and keeping a reduced 0.06 % of out-of-target delivery. However, as the focus spreads across a single section of the tumor, the focal amplitude decreases 1.6 times. The estimated duration of the sonication procedure and the number of microbubble injections can be reduced 3.2 times, defining a time- and cost-efficient approach. The reported acoustic holograms are a simple, low-cost, and feasible approach to considerably improve pediatric chemotherapeutical trials.

