Supplementary Information for:

Simultaneous High Frame Rate Acoustic Plane Wave and Optical Imaging of Intracranial Cavitation in Polyacrylamide Brain Phantoms During Blunt Force Impact

Eric J. Galindo[1], Riley R. Flores[1], Ricardo Mejia-Alvarez[2], Adam M. Willis[2,3], Michaelann S. Tartis [1*]

[1] Department of Chemical Engineering, New Mexico Institute of Mining and Technology, Socorro, NM 87801

[2] Department of Mechanical Engineering, Michigan State University, East Lansing, MI 48824

[3] 59th Medical Wing, Office of the Chief Scientist, Lackland AFB, TX 78236
* Correspondence: Michaelann.Tartis@nmt.edu

Keywords:
Cavitation; plane wave imaging; traumatic brain injury (TBI); cranial phantoms; shockwaves; polyacrylamide

---

Section 3.2: Validation and comparison of cavitation behavior with a change of skull geometry to accommodate an ultrasound transducer

Supplementary Video 1

Description: Shadowgraph imaging of an original skull geometry filled with DI water revealing many pre-existing bubbles shown by minor speckled dark regions across the field of view. The impact generates cavitation, mainly localized in regions of pre-existing sites, leading to bubble collapse with shockwaves. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 100,000 FPS with a 0.20 μsec shutter speed.

Supplementary Video 2

Description: Shadowgraph imaging of an original skull geometry filled with DI water using a better sealing method drastically minimizes pre-existing bubbles. The impact decreases the number of cavitation bubbles compared to a head model with many pre-existing nuclei. Upon bubble collapse, the presence of shockwaves is visualized, propagating through the head model. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 100,000 FPS with a 0.16 μsec shutter speed.

Supplementary Video 3

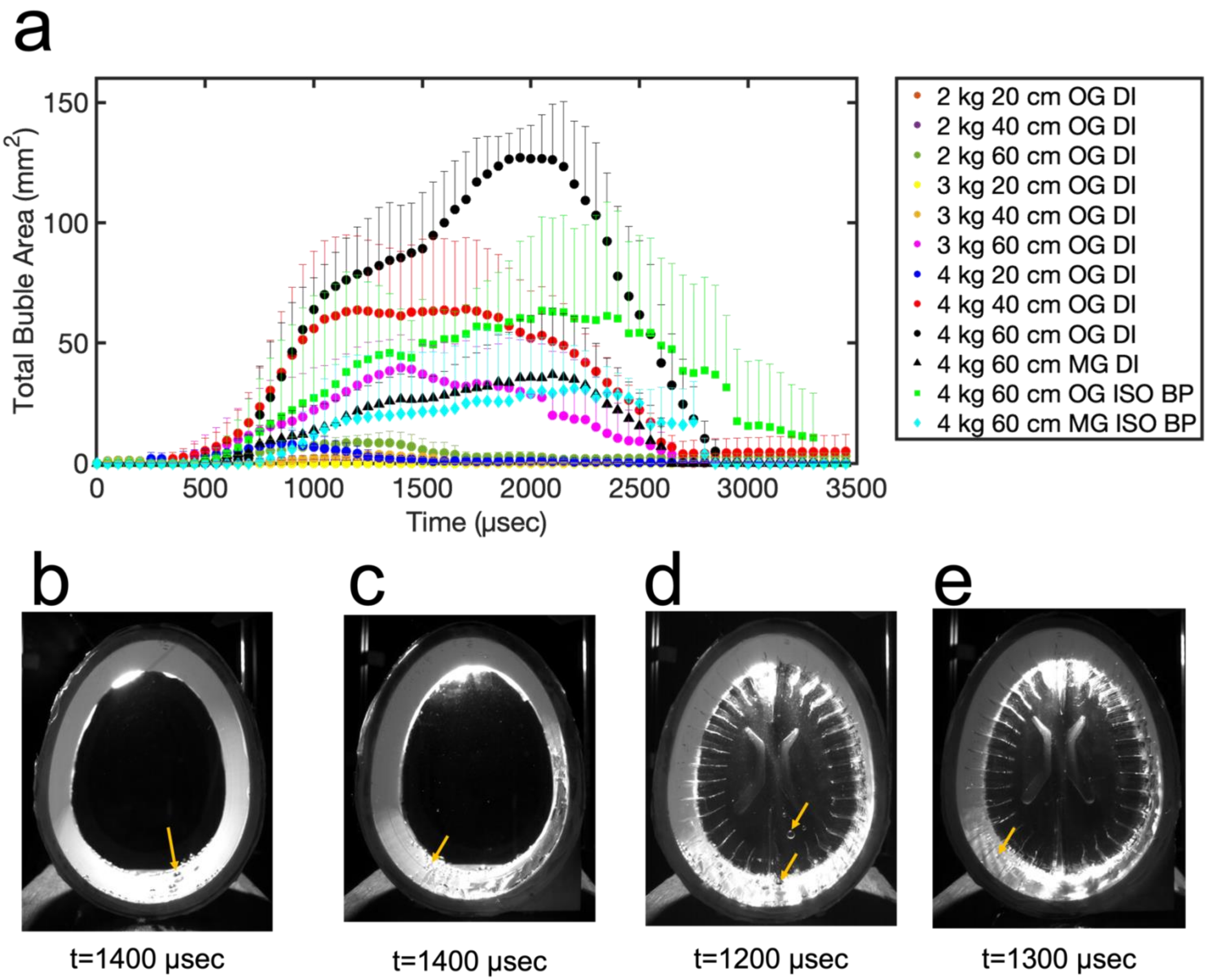
Description: Shadowgraph imaging of an original skull geometry filled with a single-layer polyacrylamide brain phantom and isotonic solution. Surface defects are present on the phantom, with major dark regions focused on the tissue-fluid interfaces. Cavitation is present at a reduced quantity where shockwaves are visualized upon bubble collapse. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 100,000 FPS with a 0.16 μsec shutter speed.

Supplementary Video 4

Description: Shadowgraph imaging of an original skull geometry filled with a two-layer polyacrylamide brain phantom and isotonic solution. Visibility through the phantom is limited near the gray-and-white matter interface and tissue-fluid regions. The loss of visibility hinders the observation of cavitation; however, small bubbles are present. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 100,000 FPS with a 0.16 μsec shutter speed.

Supplementary Figure 1

Figure S1a shows that the total cavitation bubble area is less than the original geometry. This is shown in Figure S1c, where small-sized cavitation bubbles are present on the bottom surface (t=1400 μsec) of the skull and disappear near 2000 μsec without the presence of a distinct second round of cavitation. Cavitation is still present and more visible on the interfaces between the gel and 3D printed skull in the 2-layer phantom (Figure S1e), specifically at 1300 μsec, but attains a similar bubble area average compared to DI water.



Comparison of two skull geometries with various impact parameters for cavitation thresholds revealing (**a**) total bubble area of both original (OG) and modified (MG) geometries, (**b**) original and (**c**) modified geometry filled with DI water, (**d**) original and (**e**) modified geometry filled with a two-layer brain phantom (BP) and isotonic solution (ISO). Yellow arrows represent areas of bubble growth with respect to the cavitation phenomena (N=3).

Section 3.3: Comparison of acoustic plane wave imaging and optical imaging for intracranial cavitation detection with varying amounts of pre-existing scatterers

Supplementary Video 5

Description: High-speed optical imaging of an original skull geometry without a transducer port filled with DI water. This drop tower test does not involve an enhanced sealing method. The cavitation is out of focus but displays the formation of bubbles. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 20,000 FPS with a 48.4 μsec shutter speed.

Supplementary Video 6

Description: Shadowgraph imaging of a modified skull geometry filled with DI water with the application of a better-selling method. The transmitted plane wave originating from the imaging sequence can be visualized before the cavitation event. The quantity of bubbles is drastically reduced from the enhanced sealing method with bubble collapse generating shockwaves. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 100,000 FPS with a 0.16 μsec shutter speed.

Supplementary Video 7

Description: High-speed optical imaging of a modified skull geometry filled with a two-layer polyacrylamide brain phantom and isotonic solution. This drop tower test does not involve an enhanced sealing method. The interface of the gray and white matter layers is visible before impact. The cavitation event is localized near the central sulcus, with several bubbles merging with one another. Motion in the brain is visualized upon impact and skull rebound. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 20,000 FPS with a 48.4 μsec shutter speed.

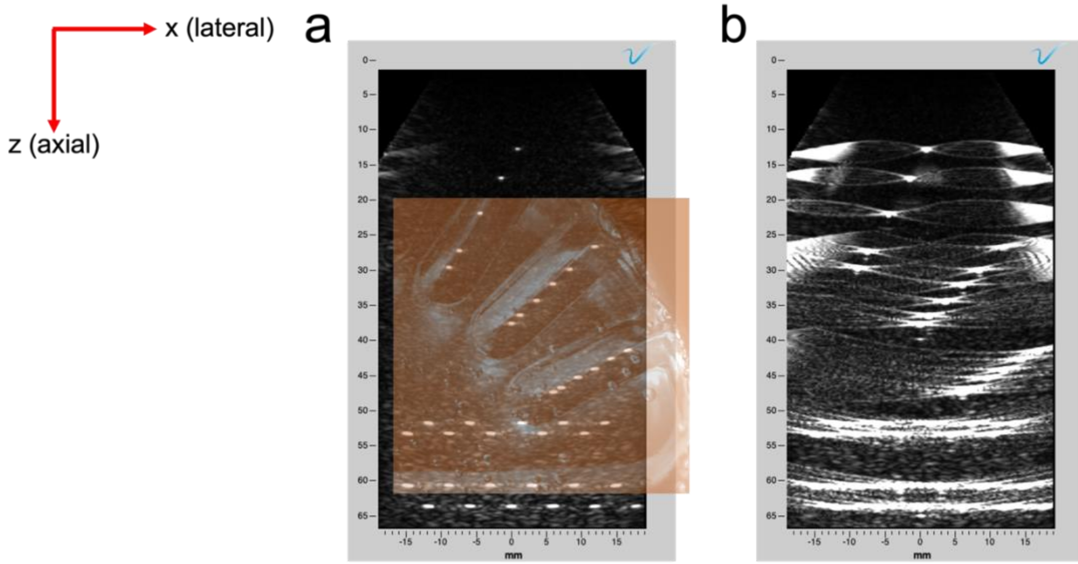
Supplementary Video 8

Description: Acoustic plane wave imaging of a two-layer phantom revealing pre-existing bright intensity from scatters trapped in the polyacrylamide gel. Upon impact, high-intensity regions are mainly visualized in the far field of the linear array transducer during cavitation. After the cavitation event, the high-intensity regions are diminished. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm.

The video is presented with a playback speed of 10 FPS based on an initial acquisition frame rate of 8,620 FPS (116 μsec/ acquisition).

Supplementary Figure 2

A simulation of the high frame rate plane wave script was run through the Verasonics hardware, predicting areas of acoustic contrast and artifacts that may occur during impact. Before running the simulation, stationary scatterers (media points) were placed in the approximate locations of the white and gray matter boundaries within the phantom, and sulcal regions exposed to the CSF simulant with attenuation values of -0.5 dB/cm/MHz to mimic biological tissue as presented by Figure S2a. A pre-defined speckle pattern was also integrated to increase its comparability to experimental data. The simulation revealed several acoustic scatterers as areas of high contrast in the lateral direction in both the soft matter tissue and sulci regions, where media points near each other produce more contrast (Figure S2b). Acoustic artifacts such as side lobes, are present on each scatterer. In the near field, the location of the scatterer can be distinguished, whereas sidelobes produce immense contrast localized on the outer boundaries of the reconstructed frame when placed near the center (x=0 mm). If the media points are placed away from the center lateral position, the side lobe generates contrast opposite of the location of the scatterer. Side lobes are still present in the mid-field of the transducer (z=35-50 mm) with a reduced effect even though the media points are near each other. However, the contrast is centered around the scatterer merging with other nearby points. A small degree of reverberation is visualized between vertically closely spaced media points; however, this acoustic artifact should be more prominent in tissue simulants as presented through clinical ultrasound [1]. In the far field of the transducer, the side lobes are still distinguishable, but contrast has been merged across all scatterers in the lateral direction of the transducer, limiting the chance of deciphering the location of each source.

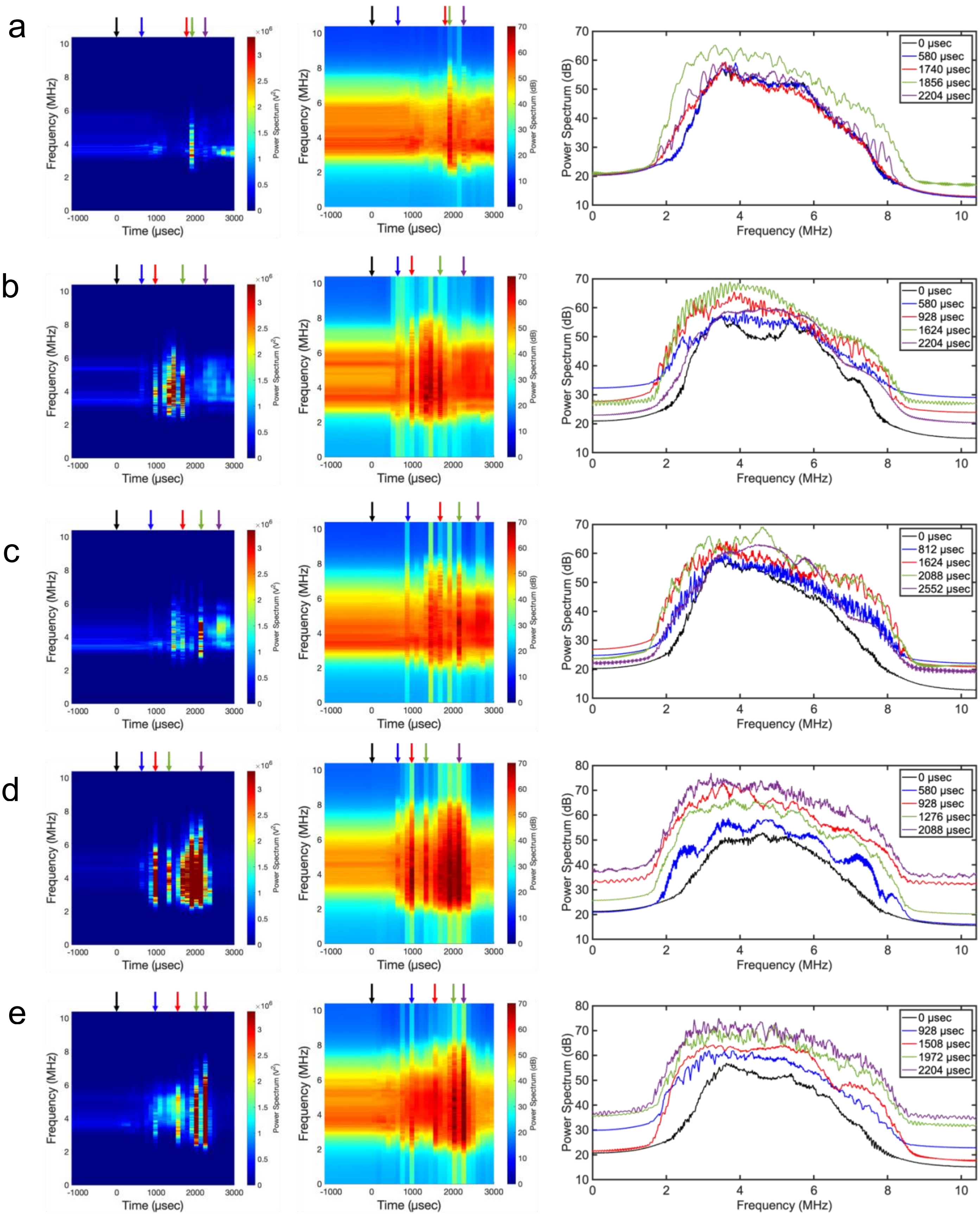


A Verasonics acoustic plane wave simulation of 128 transmit and 64 receive channels with acoustic scatterers was placed in areas where cavitation was predicted to occur. Acoustic scatterers are placed in the (**a**) sulci and central sulcus regions, revealing (**b**) high-intensity regions in the lateral direction.

[1] Baad, M., Lu, Z. F., Reiser, I., & Paushter, D. (2017). Clinical significance of US Artifacts. *Radiographics*, *37*(5), 1408–1423. https://doi.org/10.1148/rg.2017160175

Section 3.4: Acoustic spectral analysis and cavitation mapping

Supplementary Figure 3



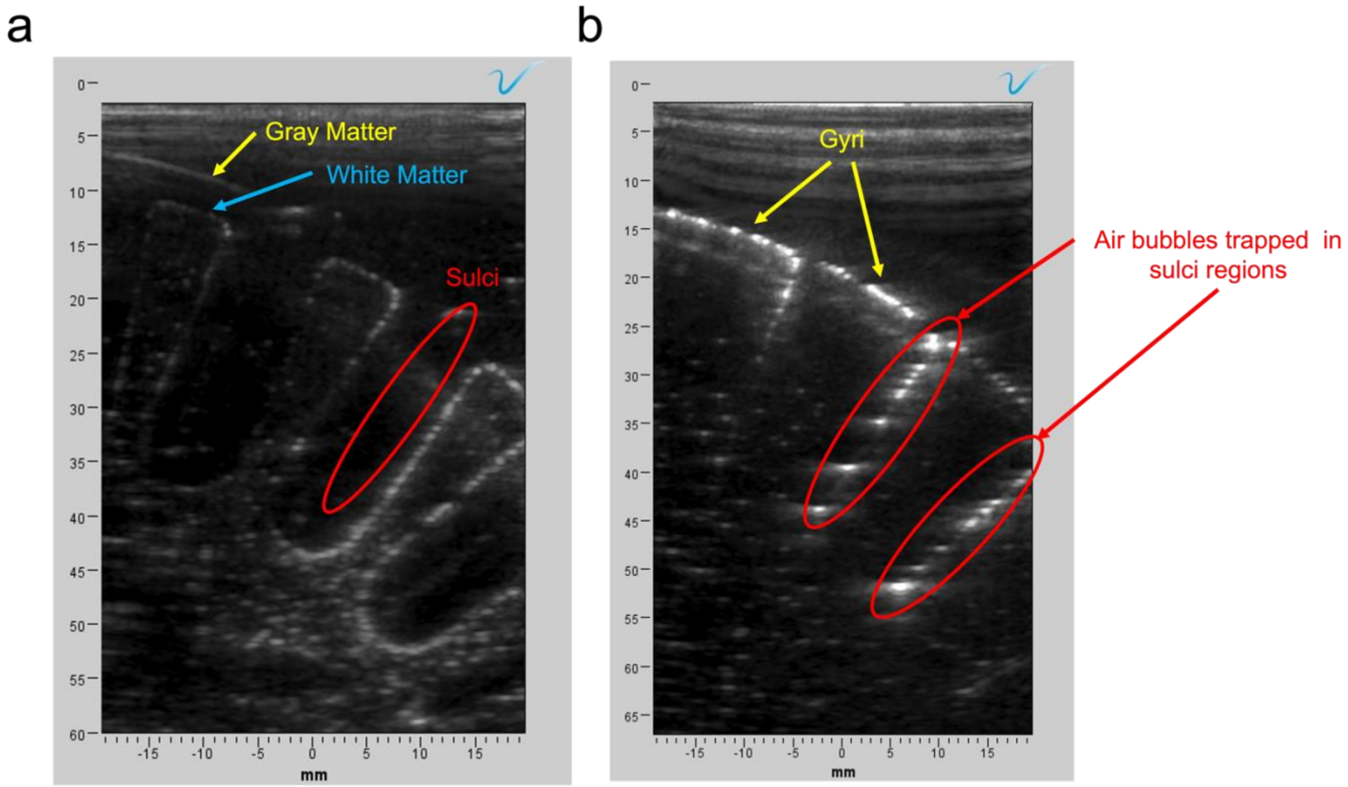
Acoustic spectral analysis regarding averaged 64 channels revealing linear and log power spectrograms and time-dependent logarithmic spectra. The following tests involve a better sealing method and go as follows: (**a**) of a single-layer brain phantom, (**b**) a two-layered phantom, and (**c**) DI water. Both tests regarding (**d**) a two-layered phantom and (**e**) DI water correspond to tests with more pre-existing bubbles.

Section 4.1: Benefits and limitations of PAA in mimicking brain tissue

Supplementary Table 1: Shore OO hardness values for 10% (w/v) 60-1 PAA brain phantoms

Phantom Number	Figure Number	10% (w/v) 60-1 PAA Shore OO Hardness
1	S1d	13.2 ± 0.4
2	S1d	10.4 ± 0.5
3	4b	12.6 ± 0.5
4	4c	11.8 ± 0.8
5	6a	12.4 ± 0.5
6	6b	12.8 ± 0.4
7	6c	12.7 ± 0.7

Supplementary Figure 4



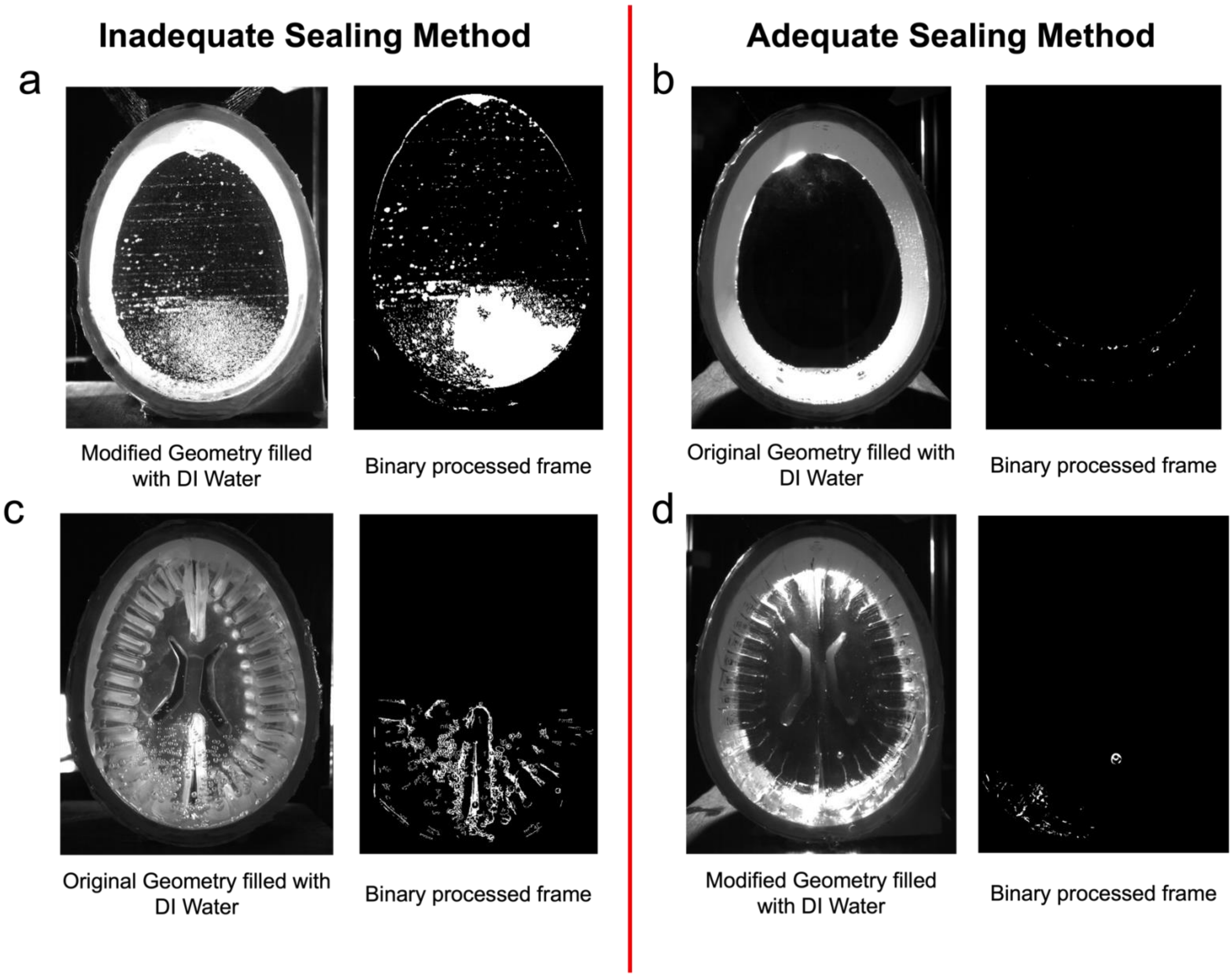
A high-quality wide-beam image of a (**a**) two-layer brain phantom reveals the gray and white matter where the interface is illuminated as high-intensity regions from trapped pre-existing bubbles during the polyacrylamide polymerization process. A (**b**) single-layer brain phantom displays trapped air bubbles in the sulcal regions after swelling for more than 24 hours in an isotonic solution. Both acoustic images were taken before impact and are caused by sealing and hydrogel fabrication methods.

Section 4.4: Minimizing pre-existing bubbles during the assembly process

Supplementary Video 9

Description: High-speed optical imaging of an original skull geometry filled with DI water. Pre-existing bubbles are visualized on the surface of the acrylic plates before impact. Upon impact, a large quantity of cavitation is present in the contrecoup region of the skull, translating to the coup. DI water is visualized leaking upon impact caused by an inadequate seal. The generated impact comprises a mass of 4 kg and an impactor drop height of 60 cm. The video is presented with a playback speed of 10 FPS based on an initial recording of 20,000 FPS with a 48.4 μsec shutter speed.

Supplementary Figure 5



Comparison of sealing methods and their effect on the segmentation of cavitation bubbles through MATLAB image processing. An inadequate sealing method for (**a**) a modified skull geometry filled with DI water creates cavitation throughout the entire head model. A better sealing method is applied to a (**b**) an original skull geometry where fewer cavitation bubbles are present and localized towards the bottom of the head model. Implementing a brain phantom into the head models complicates bubble segmentation by attaining the same pixel intensity for both (**c**) inadequate and (**d**) adequate sealing methods. All tests involve impacts comprised of a mass of 4 kg and an impactor drop height of 60 cm.