

Trans-fontanelle USgFUS Histotripsy for Intraventricular Clot Lysis in Neonatal Head Phantoms

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At-a-glance:
Trans-fontanelle Ultrasound guided Focused Ultrasound (USgFUS) is an effective means of non-invasive clot lysis in neonatal skull and brain phantom models.

Introduction

- Intraventricular hemorrhage (IVH) occurs in 3% of all live births in Canada, corresponding to 30% of neonates admitted to the neonatal intensive care unit (NICU) in vhevery year^{1,2}.
- Current treatments are invasive and often ineffective in alleviating the clot burden³.
- Complications due to IVH develop quickly, and infants, particularly those with very low birth weights often succumb to the condition³.
- There is an unmet clinical need to develop and test non-invasive methods to dissolve IVH clots.
- Our group is proposing USgFUS can be an effective way to non-invasively dissolve these clots.

Objective

This study demonstrates that trans-fontanelle ultrasound-guided focused ultrasound histotripsy is a feasible method for clot lysis within neonatal brain ventricles.

Methods

- Thermosensitive Polyacrylamide Gel**
- A thermosensitive polyacrylamide gel was formulated to match the acoustic properties of neonatal brains.
 - The formulation used can be seen in Table 1 below.
 - The speed of sound and attenuation at 1Mhz was found to be 1554.3 ± 16.4 m/s and 2.7 ± 0.34 Np/m respectively.
 - The values for speed of sound and attenuation are within the range listed for neonatal brain material found in literature⁴.
 - This gel was cast into a 3d printed neonatal skull phantom, and a blood clot was formed within the phantom.
 - All blood clots where left to clot at room temp for at least 3 hrs before being transferred to the fridge until use to avoid the blood going rancid.

Substance	Amount
Degasses DI Water	73.10% [v/v]
Acrylamide/Bis-acrylamide 40% (w/v)	24.80% [v/v]
Bovine Serum Albumin	15.00% [w/v]
MB60°C (Thermochromic Magenta Ink)	2.00% [v/v]
Silicon Dioxide (SiO2)	2.00% [v/v]
Ammonium Persulfate (APS)	0.50% [w/v]
TEMED	0.10% [v/v]

Table 1: Formulation for Brain Phantom Gel

USgFUS System

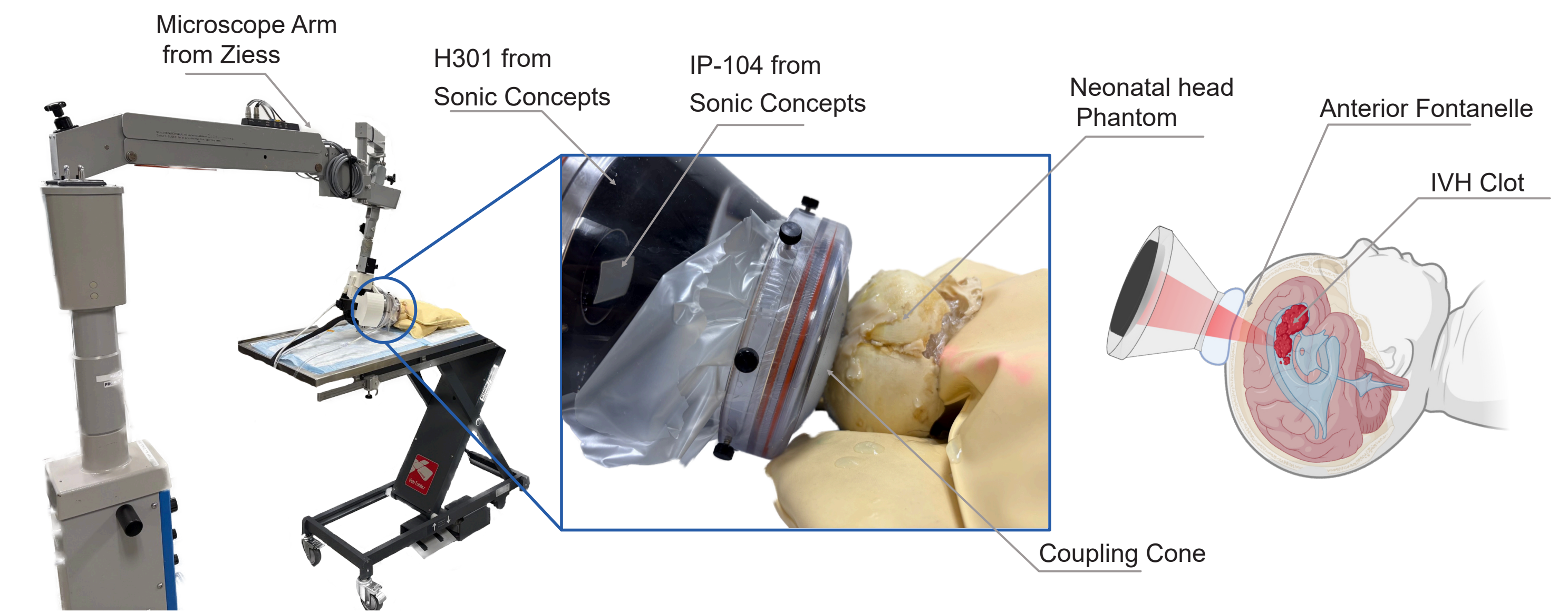


Figure 1: USgFUS system used for Trans-fontanelle clot lysis. Not depicted here is the beamformer, the Vantage System from Verasonics, Inc.

Clot Lysis Measurement

- To measure the amount of clot that was lysed, pre and post treatment MR Images where taken of the phantom.
- The clot volume was then measured by manually segmenting the images in slicer 3d.

Ultrasound Parameters

- 1.1-MHz, 60-second pulsed sonication was applied with a 10-msec pulse duration and a 1.0-Hz pulse repetition frequency; the power was ramped up until clot lysis was observed (max 1645 w of electrical power).
- These sonication parameters are consistent with boiling histotripsy.
- The maximum peak negative pressure measured from this system at operating powers (<1700 w input power) is 5.5 Mpa.
- The beam profile and calibrated axial pressure plots for the H301 FUS transducer can be seen below in Figure 2.

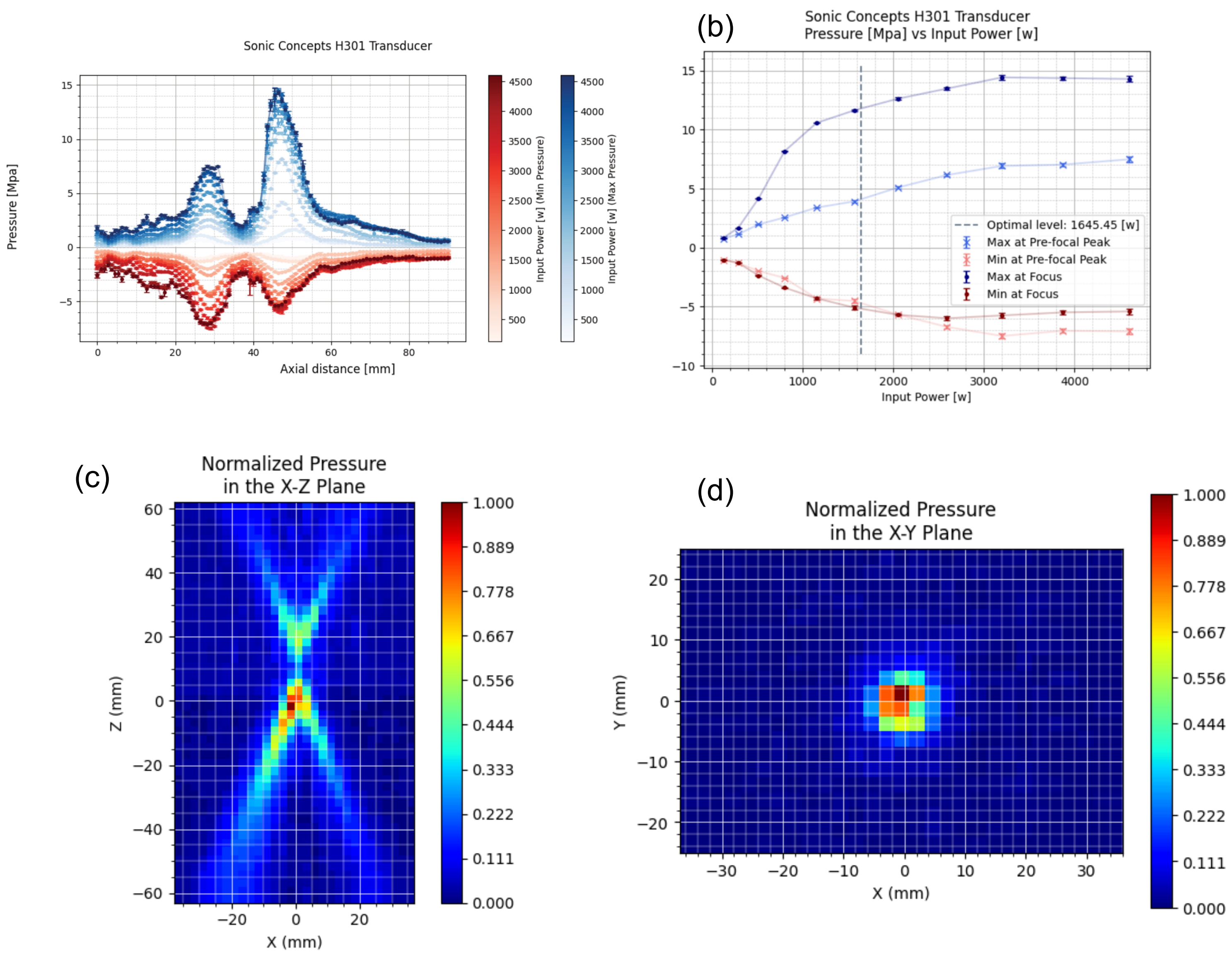


Figure 2: (a) Axial pressure plots for input powers ranging from 128 w to 4608 w, (b) Pressure (peck positive and negative) at the focus, and the prefocal peak over the input power range of 128 w to 4608 w. (c) X-Z normalized pressure beam profile though the focus. (d) X-Y normalized pressure beam profile though the focus.

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Results

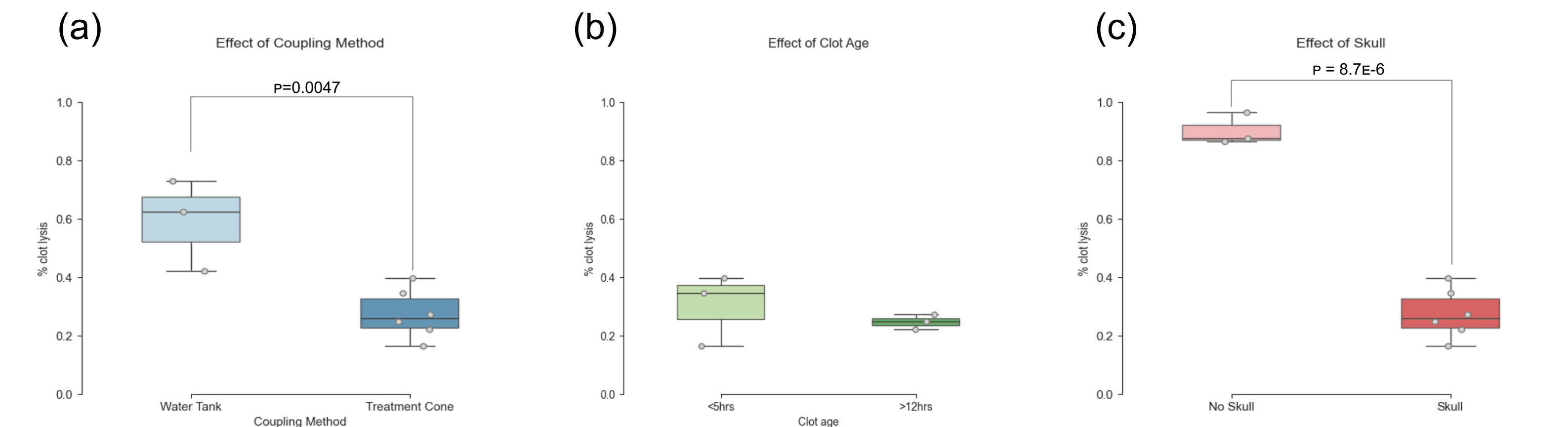


Figure 3: (a) Shows the effect of the coupling media on ultrasound-mediated clot lysis. (b) Shows the effect of the clot age on ultrasound-mediated clot lysis for clots <12hrs and >5hrs. (c) Shows the effect of the skull on ultrasound-mediated clot lysis within the phantom models. Both groups used the treatment cone as the coupling medium.

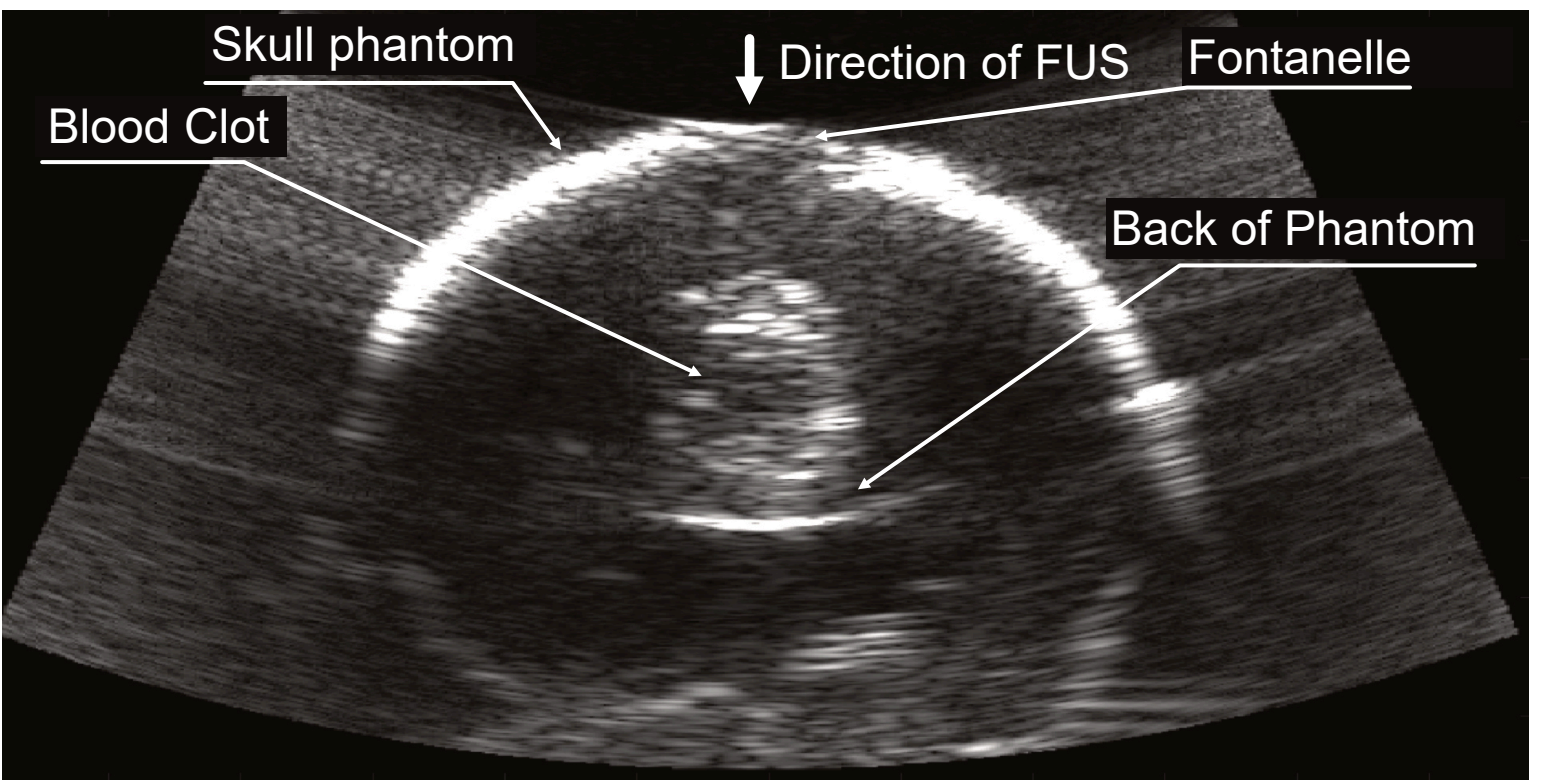
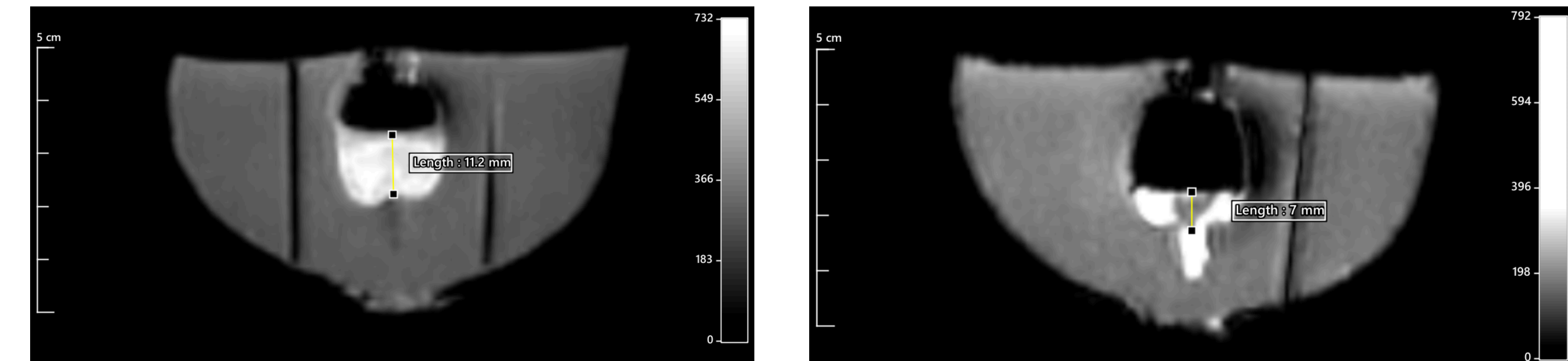


Figure 4: Intra-treatment Image of the neonatal head phantom



Discussion

Intra-treatment Images

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Conclusion

References

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