

Blast-Induced Intracranial Cavitation Leading to Damage of the Blood-Brain Barrier

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Blast-Induced Traumatic Brain Injury (TBI)

Background

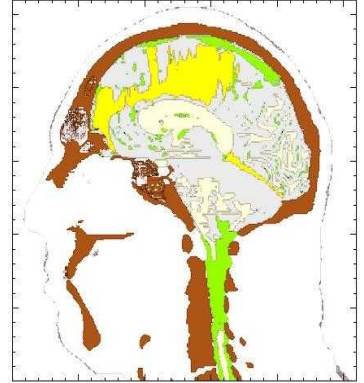
- **Closed-Head Blast Injuries** are leading cause of traumatic brain injury (TBI) in military personnel returning from combat [1]
 - Latest statistics show 352,000 US warfighters sustained TBI since 2000
- **Objective:** Primary Blast Injury (caused by direct blast exposure)
 - Investigate early-time intracranial wave mechanics leading to cavitation and traumatic brain injury
 - Previous work suggests shear stress and deviatoric shear energy correlate with localized brain injury identified in clinical TBI study
 - Separate work suggests intracranial cavitation may also cause brain injury
- **Hypotheses:** (1) Blast exposure induces intracranial fluid cavitation, (2) fluid cavitation, if it occurs, causes localized brain injury (3) the mechanisms of tissue damage, caused by cavitation bubble collapse, can be investigated on a microscale using a modeling & simulation approach
- **Significance:** Prediction, investigation, and identification of a new brain injury mechanism

[1] Defense & Veterans Brain Injury Center TBI numbers: DoD numbers for traumatic brain injury, 2015.

Modeling Approach

- Simulate blast exposure to a **macroscale** model of the head to identify regions of the brain exposed to cavitation [2]
 - Blast waves directed to the front, side and rear
 - Simulations predicted cavitation occurring in areas with high concentrations of CSF

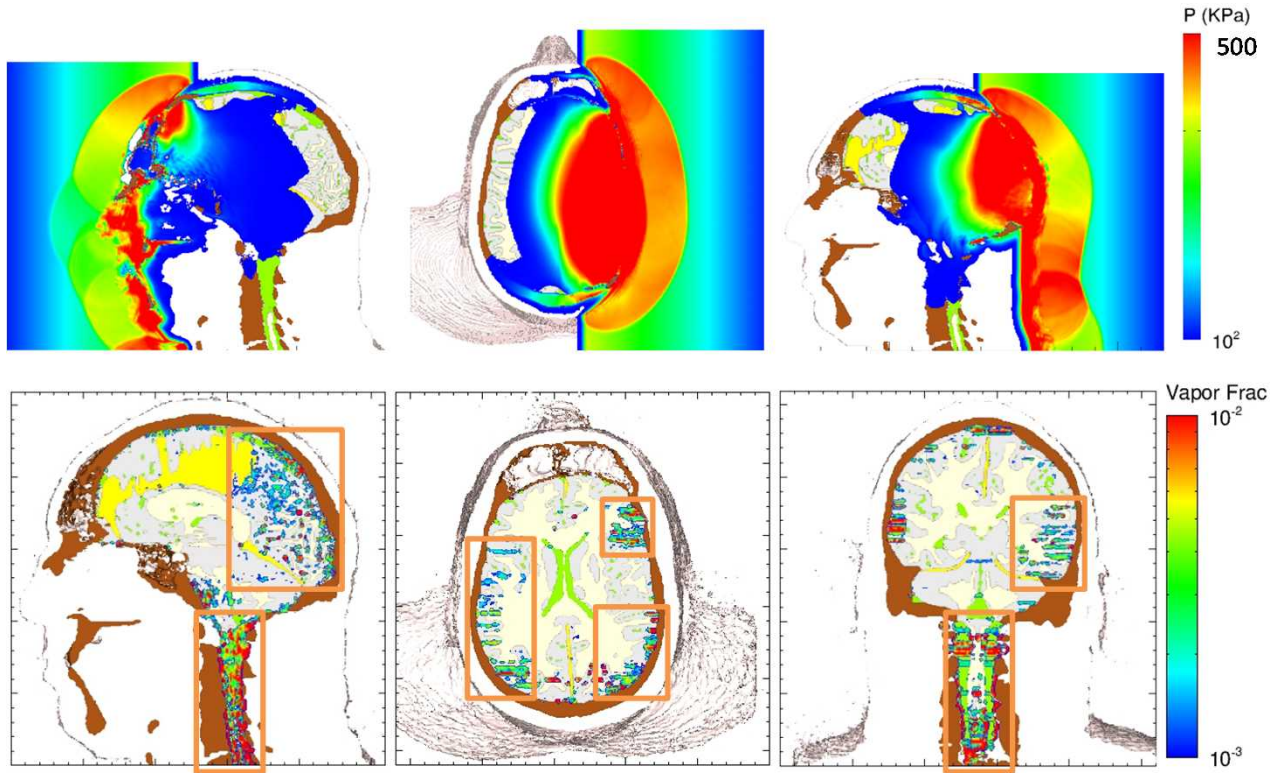
- Guided by the macroscale studies, conduct **microscale** investigations into the details of cavitation bubble collapse
 - Simulations assume the existence of cavitation bubbles
 - Investigate the tissue damaging mechanisms caused by bubble collapse near the blood brain barrier
 - Examine the effects of the compressive wave strength and bubble size



[2] Taylor, P. A., Ludwigsen, J. S., and Ford, C. C., 2014, "Investigation of blast-induced traumatic brain injury," *Brain Inj.*, **28**(7), pp. 879–895

TBI Macroscale Modeling

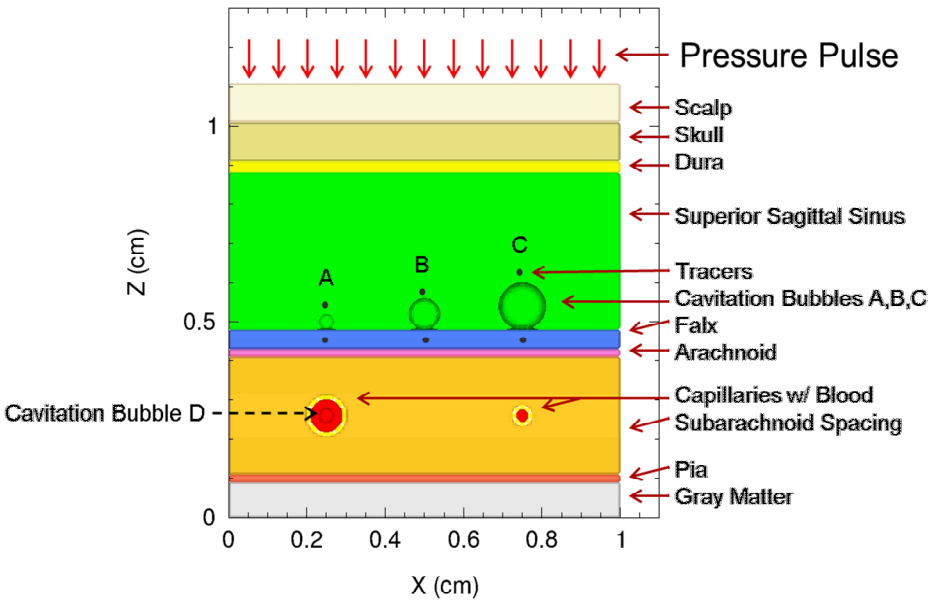
260 KPa Blast Exposure: Cavitation Vapor Volume Fraction



Note cavitation occurrence in white matter regions of the corpus callosum, cerebellum and brain stem

Past Microscale Models

Superior Sagittal Sinus



1 cm x 0.5 cm x 1.25 cm

Bubble Radii:

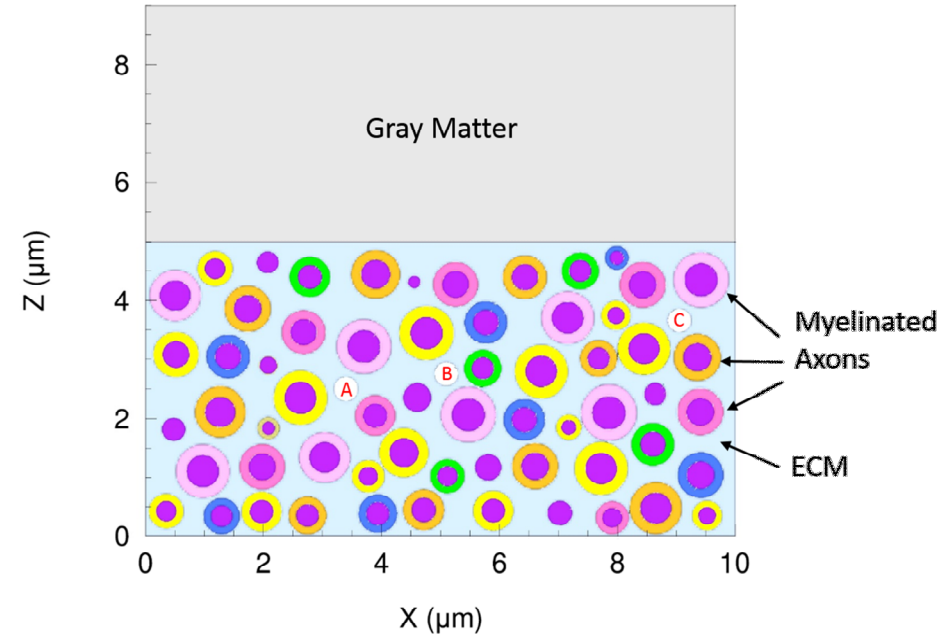
A: 0.2 mm

B: 0.4 mm

C: 0.6 mm

D: 0.2 mm

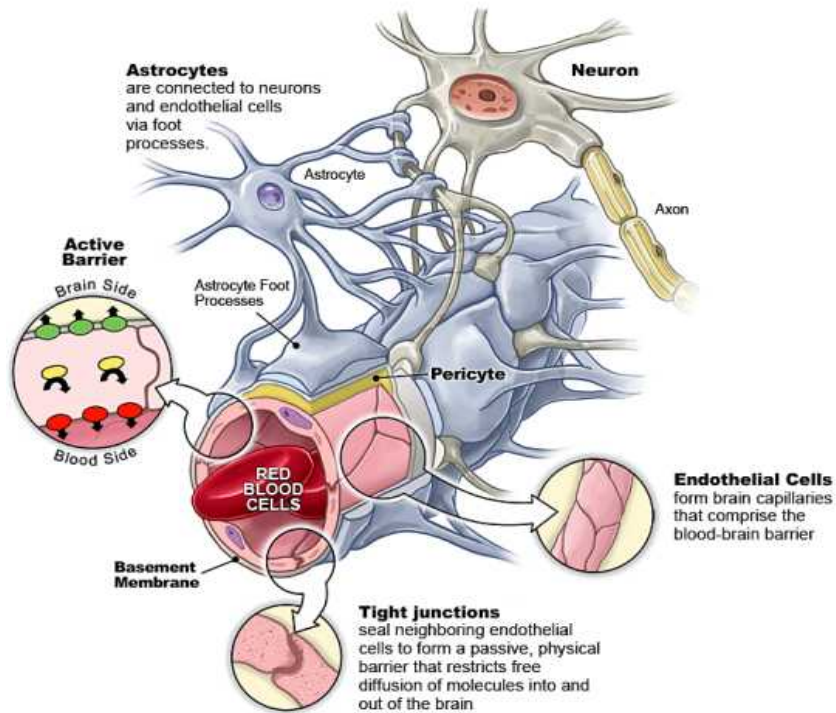
Axonal Fiber Bundles



10 μm x 10 μm x 9 μm

Bubble Radius of 0.3 μm

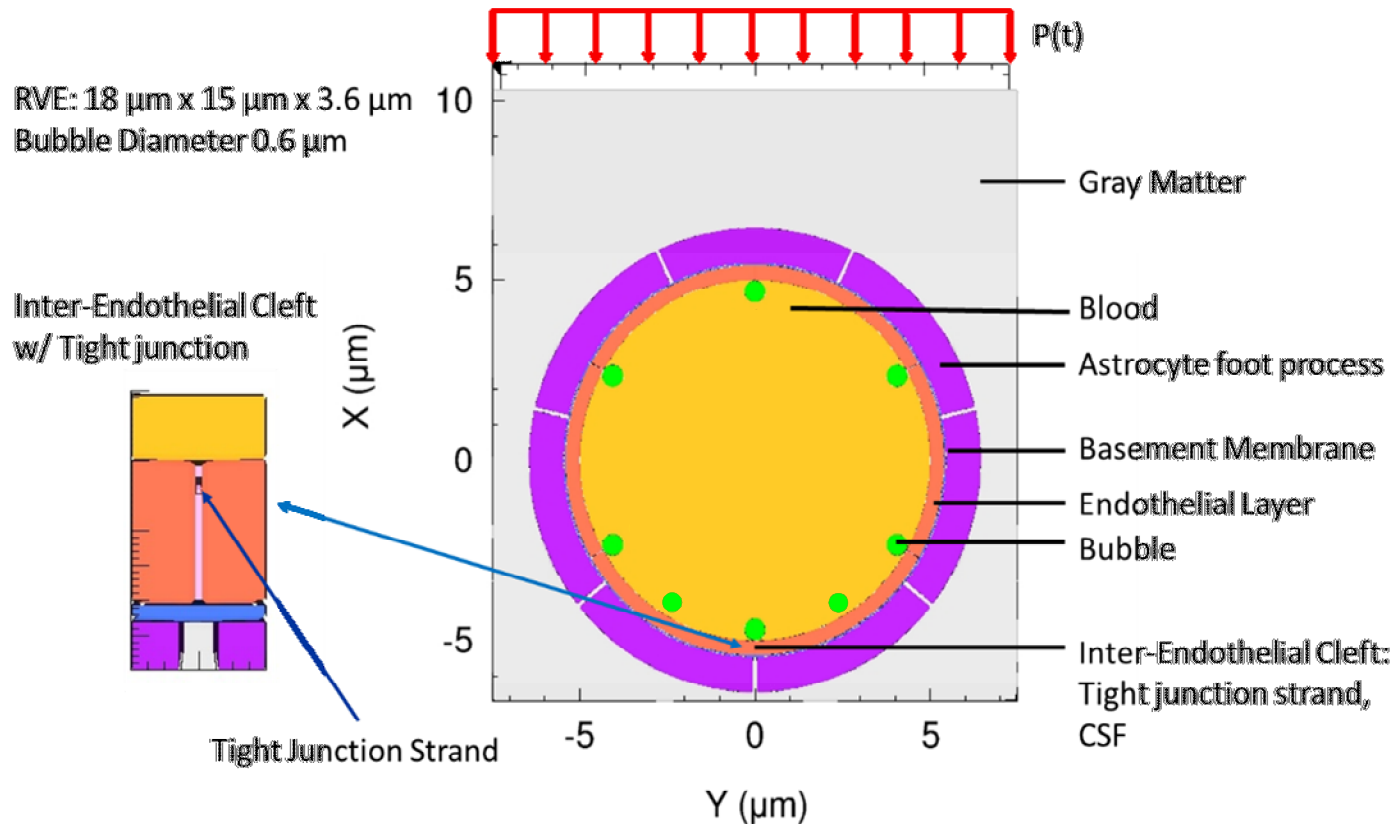
What is the blood brain barrier?



- Semi-permeable passageway between the circulating blood and the cerebrospinal fluid in the Central Nervous System (CNS) formed by endothelial cells connected by tight junctions
- Protects the CNS tissues, especially neurons, against harmful substances
- Allows the passage of water, some gases, and lipid-soluble molecules as well as molecules such as glucose and amino acids
- Astrocytes surrounding the endothelial cells provide support

<http://kollathdesign.com/portfolio/university-of-minnesota-college-of-pharmacy-duluth-blood-brain-barrier/>

Microscale Model of the Blood Brain Barrier



Parameters:

Compressive wave amplitude – 0, 400, 700 kPa

Bubble Diameter – $0.3 \mu\text{m}$, $0.6 \mu\text{m}$

If bubble collapse causes a member of the BBB to fail, the barrier breaks down, which could lead to neuroinflammation (meningitis) or neurodegeneration

Material Model

Material	Volumetric Response	Deviatoric Response
Gray Matter	Tillotson-Brundage	Swanson
Astrocyte	Tillotson-Brundage	Swanson
Basement Membrane	Tillotson-Brundage	von Mises
Tight Junction Strand	Mie-Gruneisen	Swanson
Endothelial Cells	Tillotson-Brundage	Swanson
Blood	Tillotson-Brundage	-
CSF	Tillotson-Brundage	-
Bubble contents	Sesame Tabular EOS	-

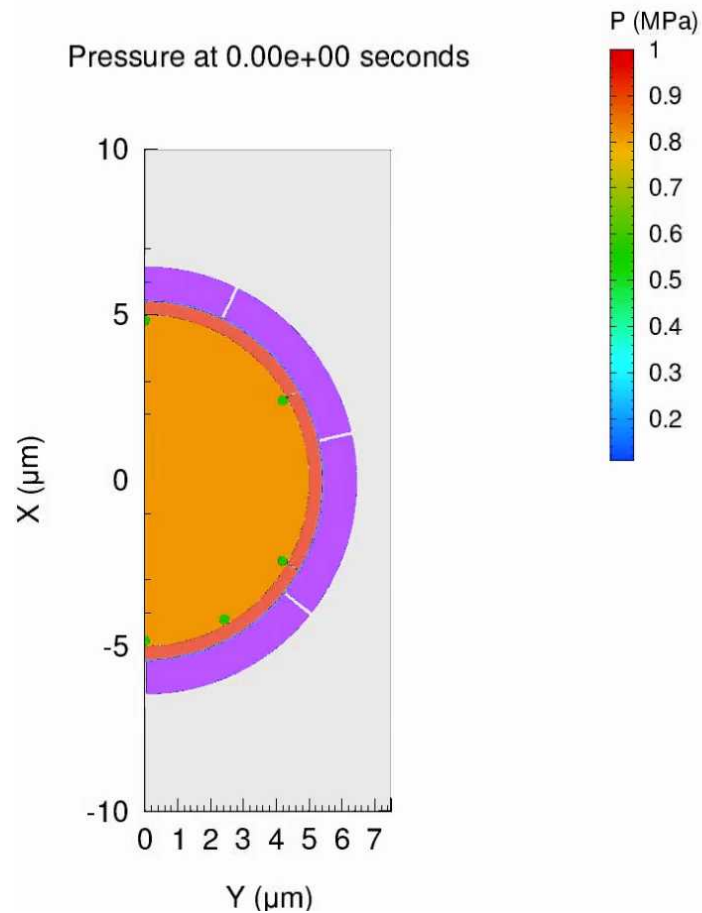
- EOS (volumetric response)
 - Equations relating pressure, volume, and temperature
 - The Tillotson-Brundage EOS accurately captures the respective bulk properties under compression and their susceptibility to fluid cavitation when subjected to isotropic tension (i.e. tensile pressure)
- Constitutive model (deviatoric response)
 - Use Swanson hyperelastic model for gray matter, astrocytes, endothelial cells, and tight junction strand [3]
 - Use von Mises for basement membrane

[3] Swanson, S. R., 1985, "A constitutive model for high elongation elastic materials," Trans. Am. Soc. Mech. Eng., **107**, pp. 110–114.

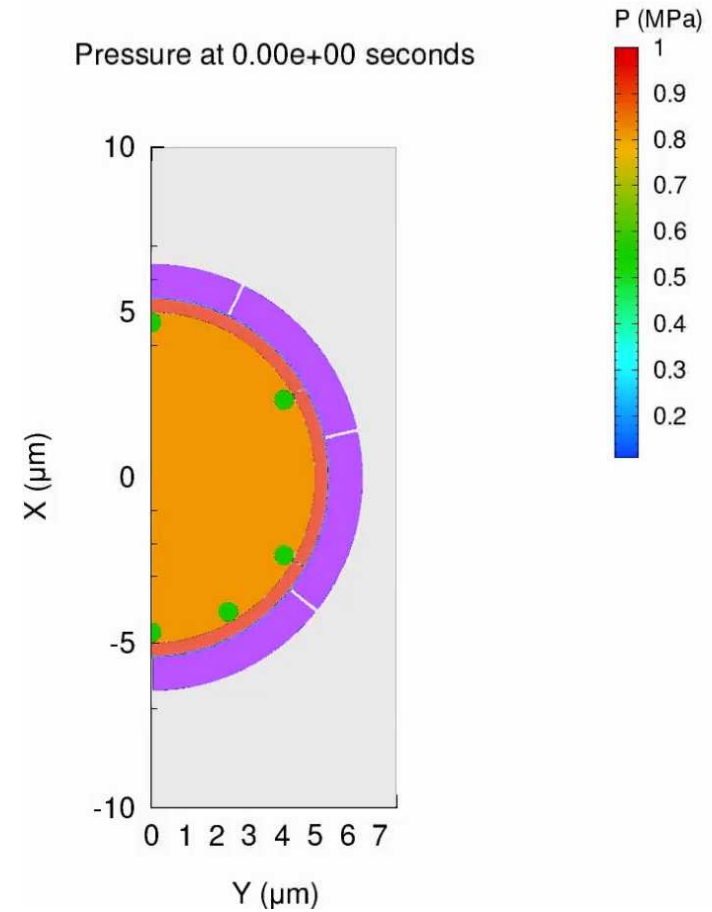
Effect of Bubble Diameter

Spontaneous bubble collapse

0.3 μm diameter bubble



0.6 μm diameter bubble



Effect of Compressive Wave Amplitude

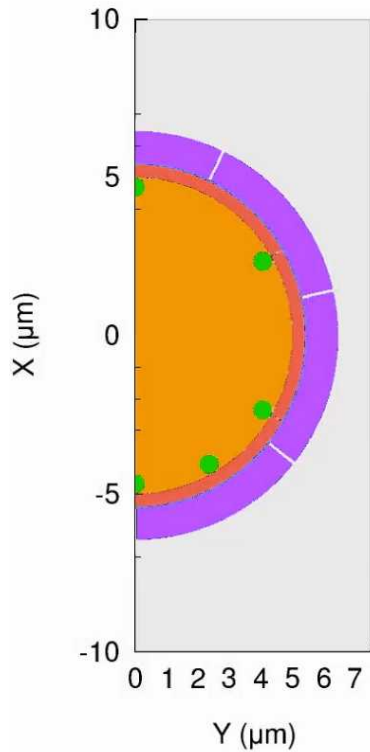
0.6 μm diameter bubbles

Spontaneous bubble collapse

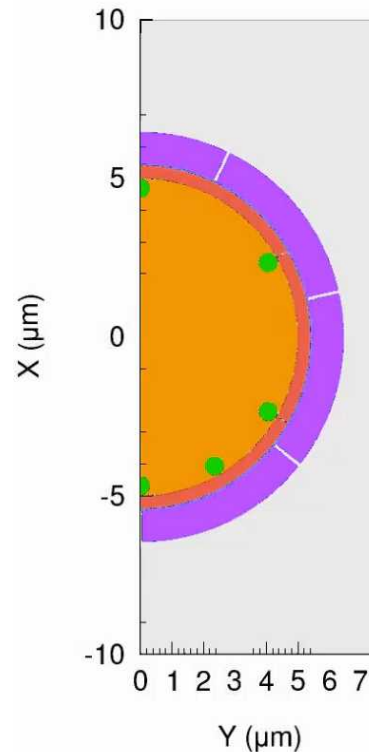
400 kPa wave

700 kPa wave

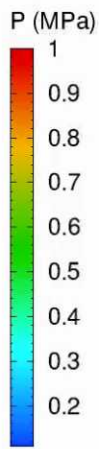
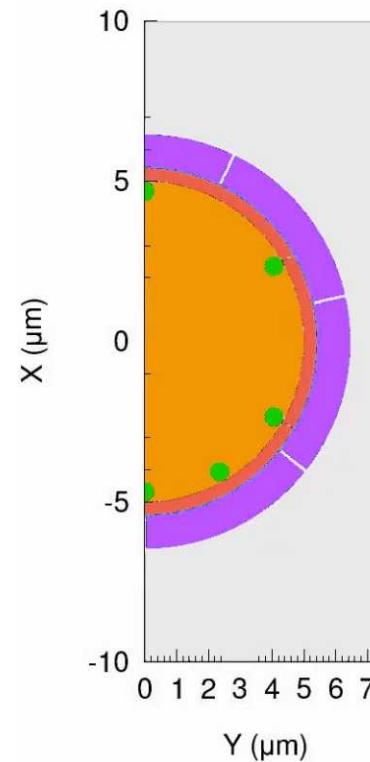
Pressure at 0.00e+00 seconds



Pressure at 0.00e+00 seconds



Pressure at 0.00e+00 seconds



Hypotheses:

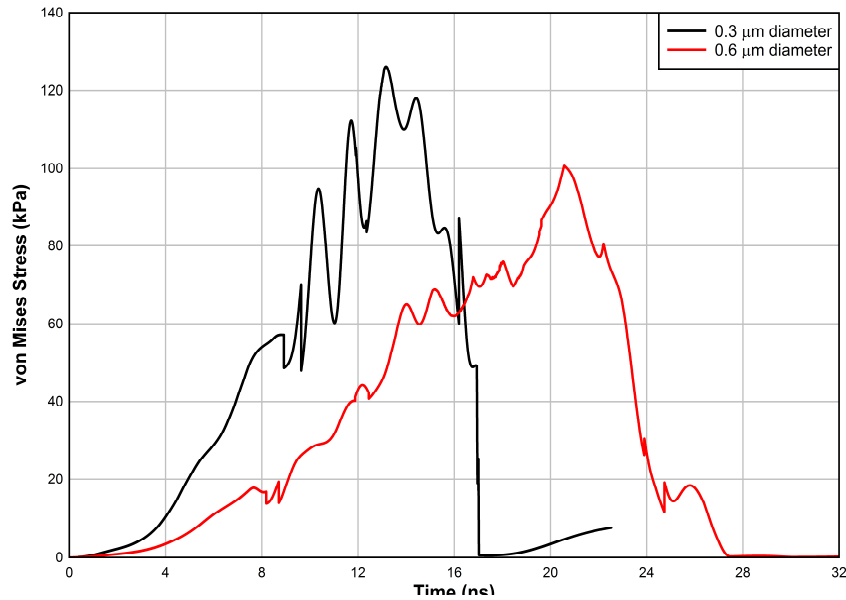
- Cavitation bubble collapse dependent on:
 - Bubble diameter
 - Strength of intracranial stress wave (related to blast strength)

- Effects of cavitation bubble collapse:
 - Microjetting of fluid surrounding bubble in downstream direction for scenarios with a follow-on compressive wave of 400 or 700 kPa
 - Increase in pressure and von Mises stress in tight junction strand downstream of the bubbles after collapse

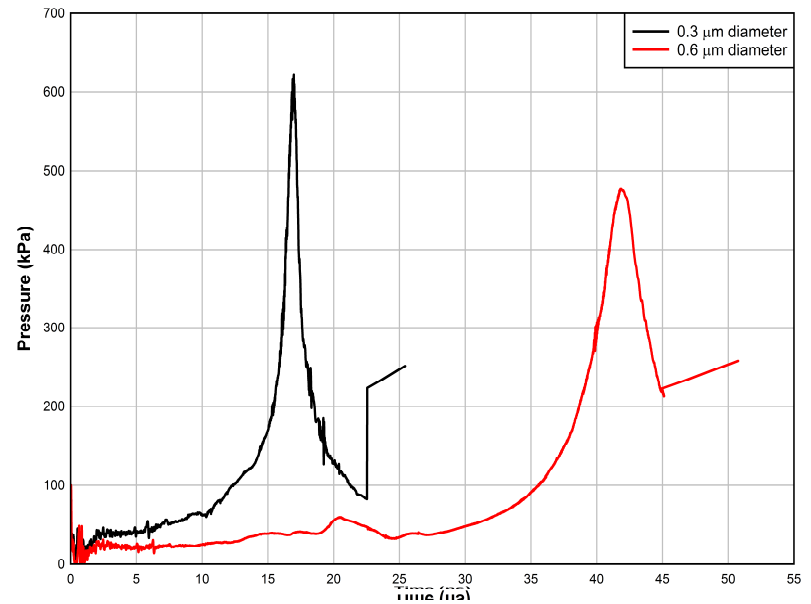
Effect of Bubble Diameter

- As the bubble diameter increases, the downstream von Mises stress and pressure decrease

von Mises Stress in Tight Junction Strand, Adjacent to Lowest Bubble



Pressure in Tight Junction Strand, Adjacent to Lowest Bubble

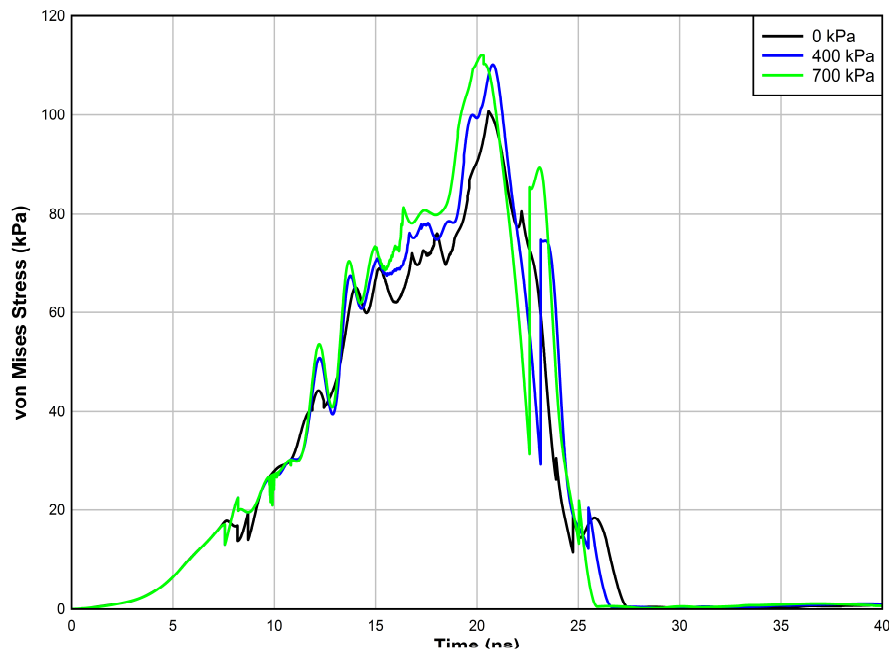


Spontaneous bubble collapse

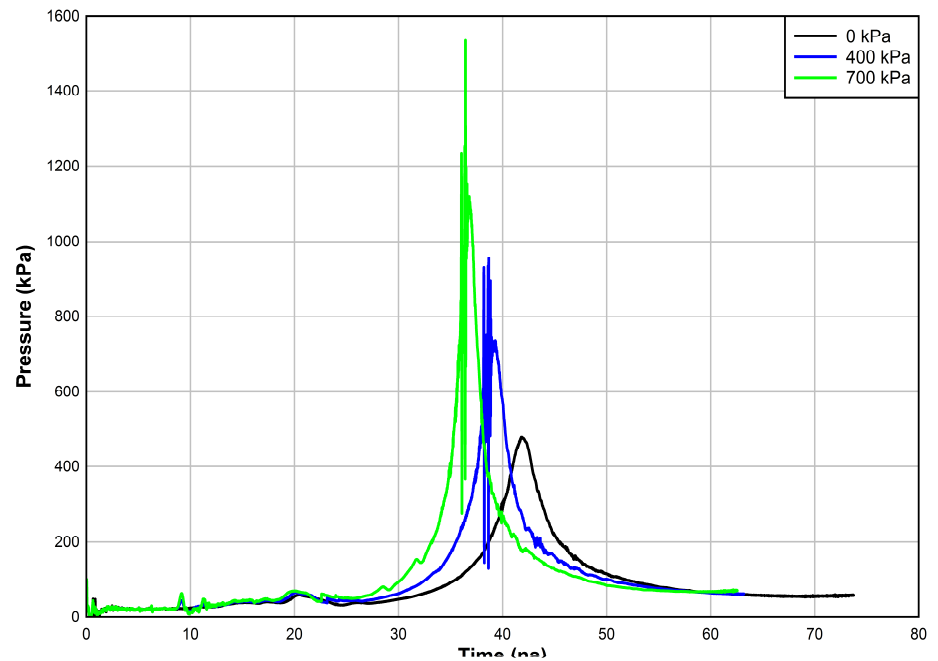
Effect of Compressive Wave Amplitude

- As the compressive wave amplitude increases, the downstream von Mises stress increases slightly
- Downstream pressures increase with increasing compressive wave strength

von Mises Stress in Tight Junction Strand, Adjacent to Lowest Bubble



Pressure in Tight Junction Strand, Adjacent to Lowest Bubble



0.6 μm diameter bubble

Concluding Remarks

- Modeled 3 microscale scenarios within the blood brain barrier to investigate effects of cavitation bubble size in the presence of intracranial compressive waves of various magnitudes: 1) bubbles at ambient pressure and the passage of a compressive wave of 2) 400 kPa or 3) 700 kPa
 - Measured von Mises stress and pressures experienced by the tight junction strand, endothelial cells, basement membrane, and astrocytes adjacent to bubble
- Simulations predict an increase in downstream von Mises stress with increasing compressive wave amplitude and decreasing bubble size
- Future work includes fine tuning material models and using more accurate dimensions of the blood brain barrier
- The inter-endothelial cleft can be considered a weak point in the vascular wall that, if damaged, would constitute a functional breach of the blood-brain barrier that could lead to neurological diseases such as meningitis, epilepsy, or multiple sclerosis

Questions?