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Ultrasound Elasticity Imaging Lab
Columbia University



UNIVERSITAT POLITÈCNICA DE VALÈNCIA



Parametric Study of Transcranial Focused Ultrasound Propagation for Blood–Brain Barrier Opening

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- Acoustic Beam properties
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  - Gain effects
  - Beamwidth variations

Conclusions

Future Lines

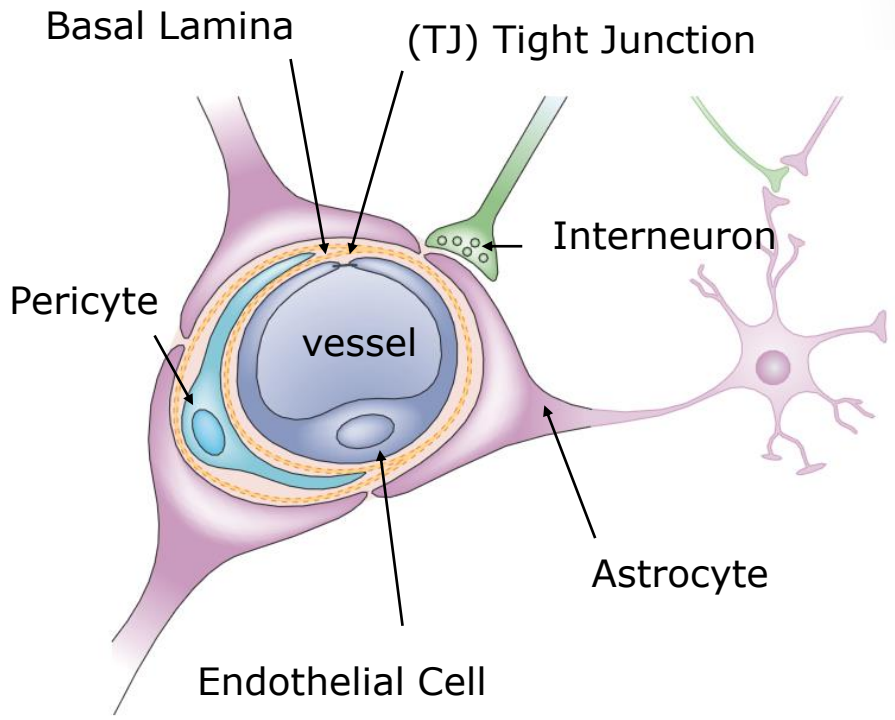
BLOOD-BRAIN BARRIER (BBB)

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- Allow passing oxygen and nutrients
- Block most useful therapeutic molecules (>500 Da)

- Isolation:
  - Virus, bacteria
  - Hormone, neurotransmitters
  - Drugs (95%)

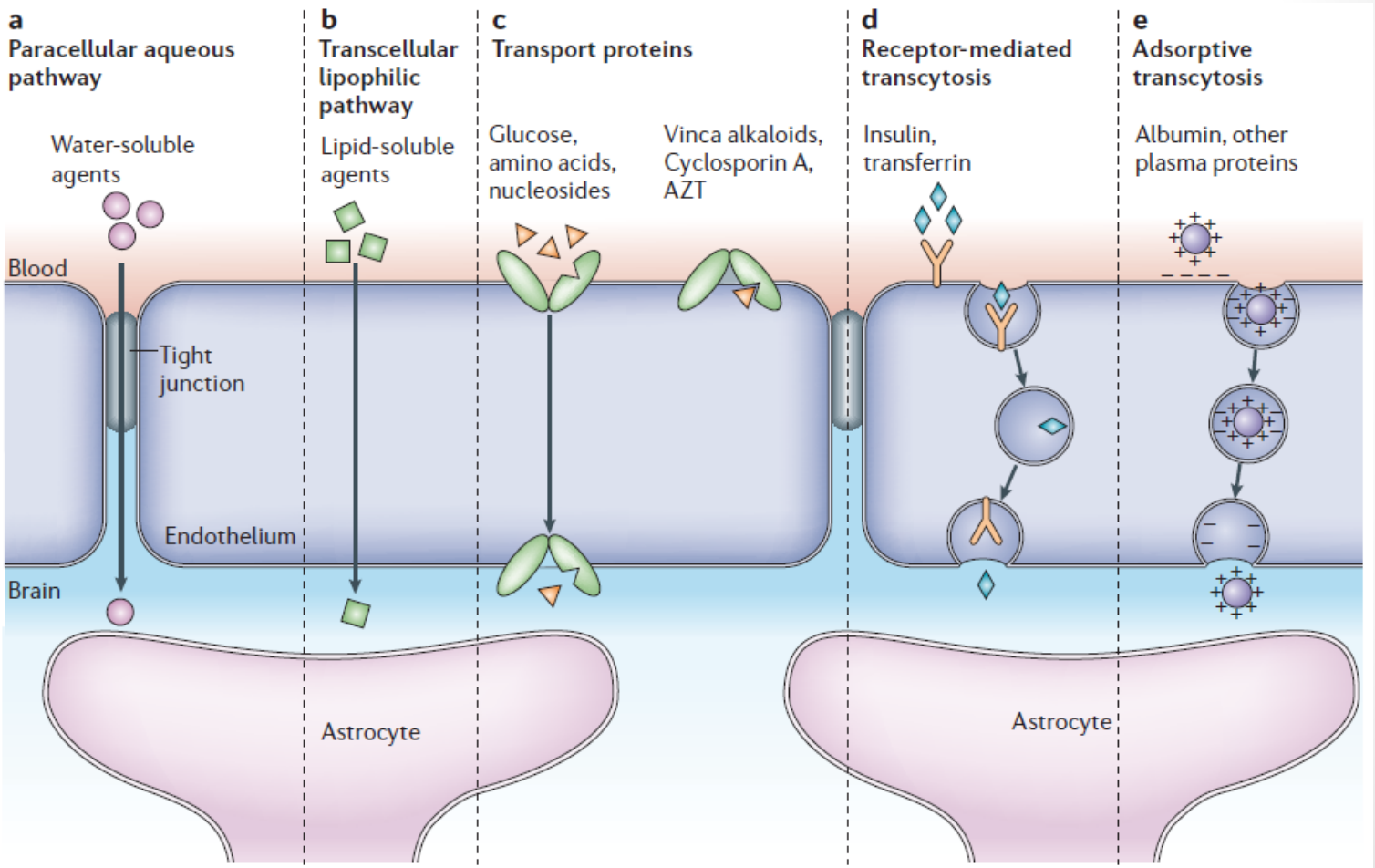


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Main pathways

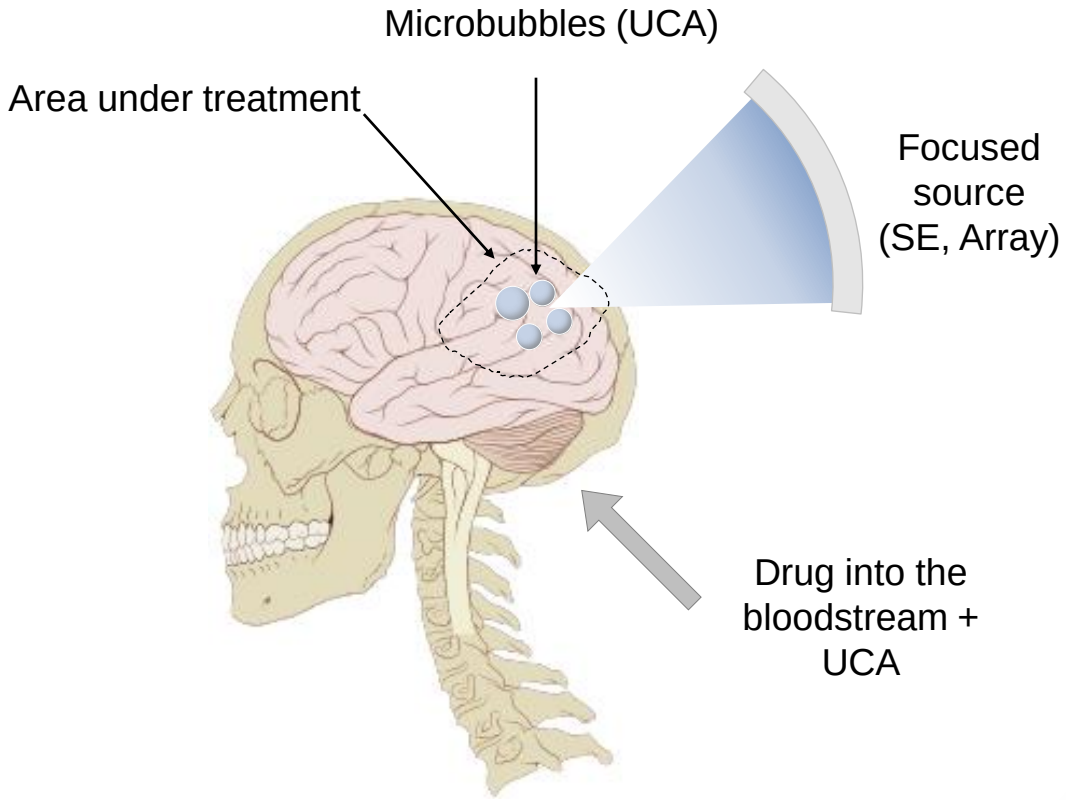


ULTRASOUND BBB OPENING

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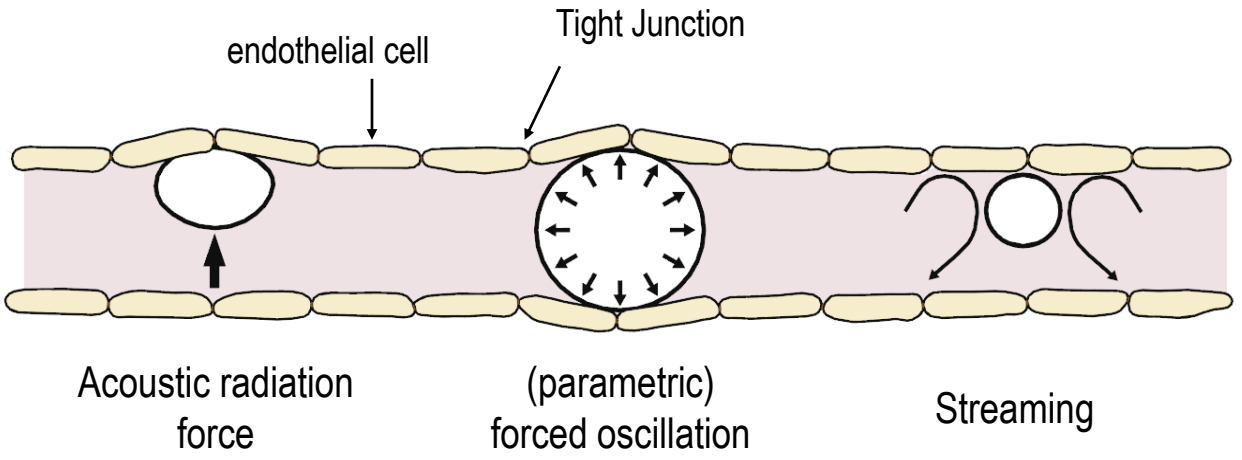
- Drugs administration to the central nervous system
- BBB opening:
  - Transient, Localized, Non Invasive, Safe



ULTRASOUND BBB OPENING

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- Interaction micro bubble (UCA) ←→ endothelial tissue



ULTRASOUND BBB OPENING

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Limitations

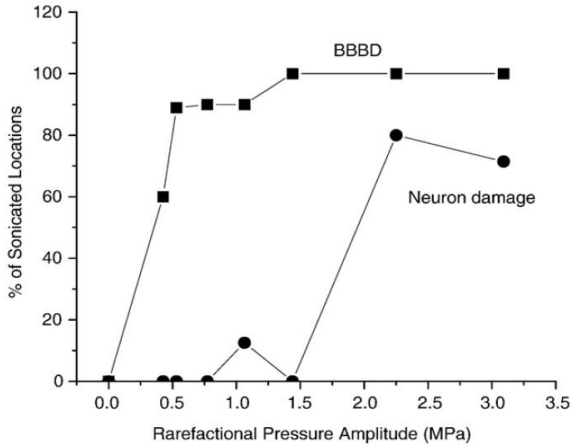
- **Amplitude**
  - Lower: >0,2 MPa

  Reach BBB opening

  - Upper: <1 MPa

  Brain tissue damage

    - *Heat effects, absorption*
    - *Inertial cavitation*



- **Frequency**
  - Lower: >200 kHz

  Beamwidth, focal area, intern resonances

  - Upper: <1 MHz

  Attenuation, beam control (phase aberrations)

GOALS

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How important are beam phase aberrations in real skull incidence angle?

Can nonlinear acoustics effects modify the area under treatment?

1. **Develop an acoustics computational method for lineal/nonlinear transcranial bone simulations.**
2. **Study the incidence angle and dependence with beam aberrations**
3. **Quantify nonlinear acoustics effects in transcranial propagation for BBB opening**

NONLINEAR MODEL

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Fluid dynamics conservative laws:

- Mass conservation:

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{v}) = 0$$

- Momentum conservation:

$$\rho\left(\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v}\nabla)\mathbf{v}\right) + \nabla p - \eta \nabla^2 \mathbf{v} - \left(\eta_B + \frac{1}{3}\eta\right)\nabla(\nabla \cdot \mathbf{v}) = 0$$

- Fluid's state equation (aprox. 2º order):

$$p' = c_0^2 \rho' + \frac{c_0^2}{\rho_0}\frac{B}{2A}\rho'^2$$

LINEAR MODEL

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- Continuity eq.:

$$\frac{\partial p}{\partial t} + \Omega p = -\rho_0 c_0^2 \nabla \cdot \mathbf{v}$$

- Momentum eq.:

$$\frac{\partial \mathbf{v}}{\partial t} + \Omega \mathbf{v} = -\frac{1}{\rho_0} \nabla p$$

- Where Ω are frequency independent losses → $\alpha \cdot f^0$
- Ω fitted to experimental bone attenuation data

COMPUTATIONAL METHOD

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- FDTD based simulations

- *Properties:*
  - Linear / nonlinear regime (Full wave)
  - Nonhomogeneous media
  - Included experimentally measured bone attenuation

  - No paraxial approximations
  - Backscattering
  - Arbitrary initial and boundary conditions

  - Validated: Ensured convergence to analytic solutions

BOUNDARY CONDITIONS

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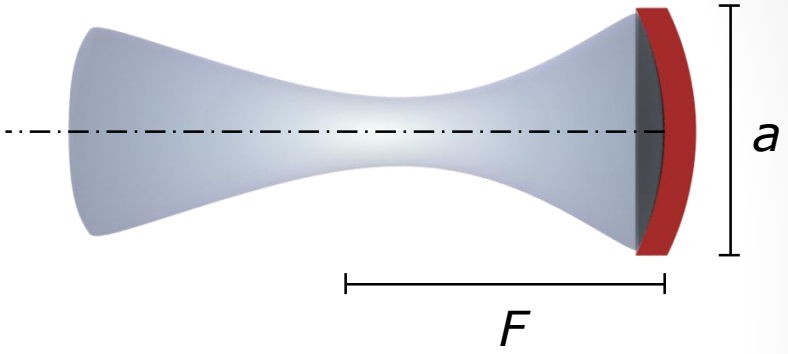
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Transducer design

- f_0 = 500 kHz
- Focal (F) = 90 mm
- Aperture (a)= 80 mm

Gain = 18,1

f_{number} = 1,125



In the limit for paraxial aproximations

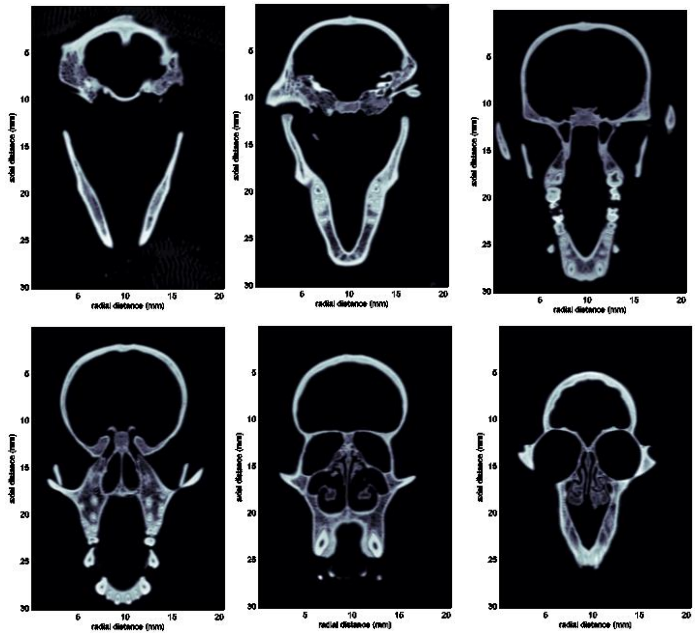
BOUNDARY CONDITIONS

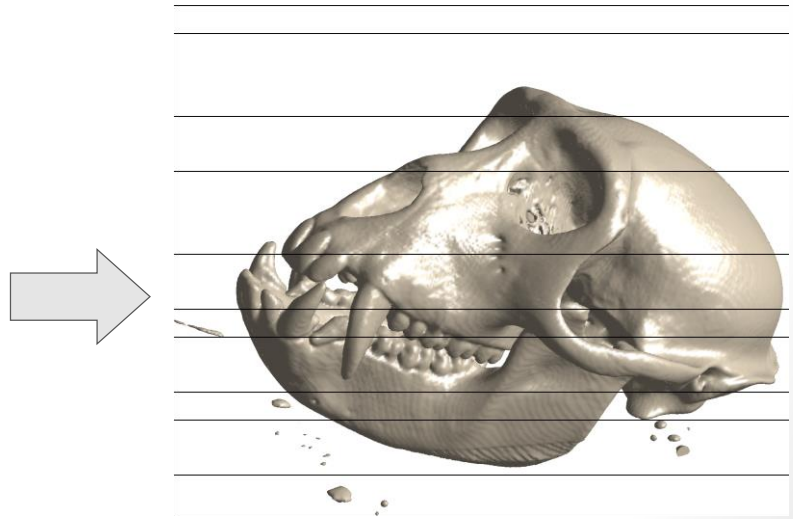
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- **Nonhomogeneus**: Rhesus primate (*Macaca mulatta*)
- CT-imaging

  E. E. Konofagou and T. Deffieux, *IEEE T Ultrason. Ferr.* **57**(12) 2637 - 2653 (2010)





resolution : 488-μm, slice 625 μm.

BOUNDARY CONDITIONS

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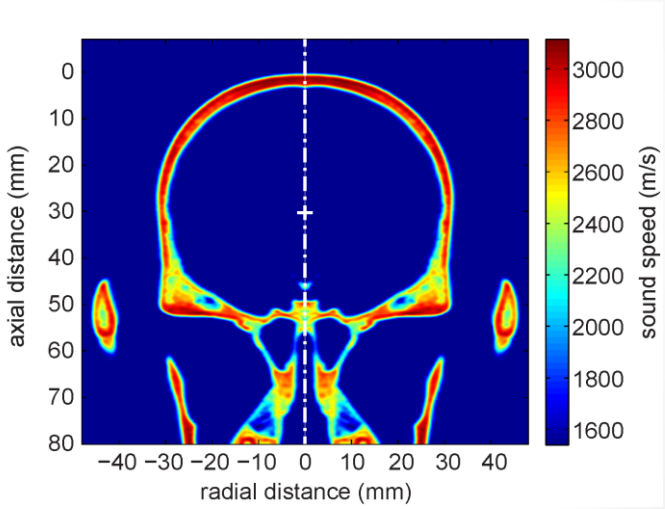
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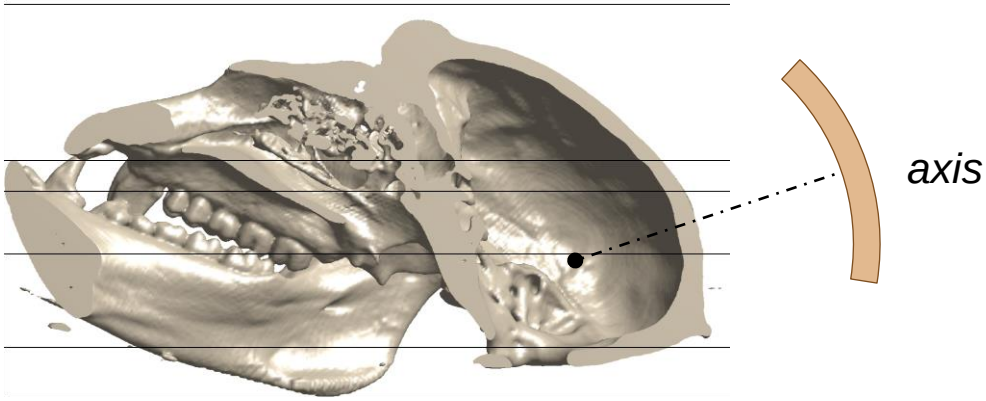
Mapping for sound speed, density and absorption (locally homogeneous)

$$\rho_0(r,z) = \rho_{water} + (\rho_{\max} - \rho_{water})\rho_{CT}(r,z)$$

$$c_0(r,z) = c_{water} + (c_{\max} - c_{water})\rho_{CT}(r,z)$$

$$\alpha(r,z) = \alpha_{skull}$$



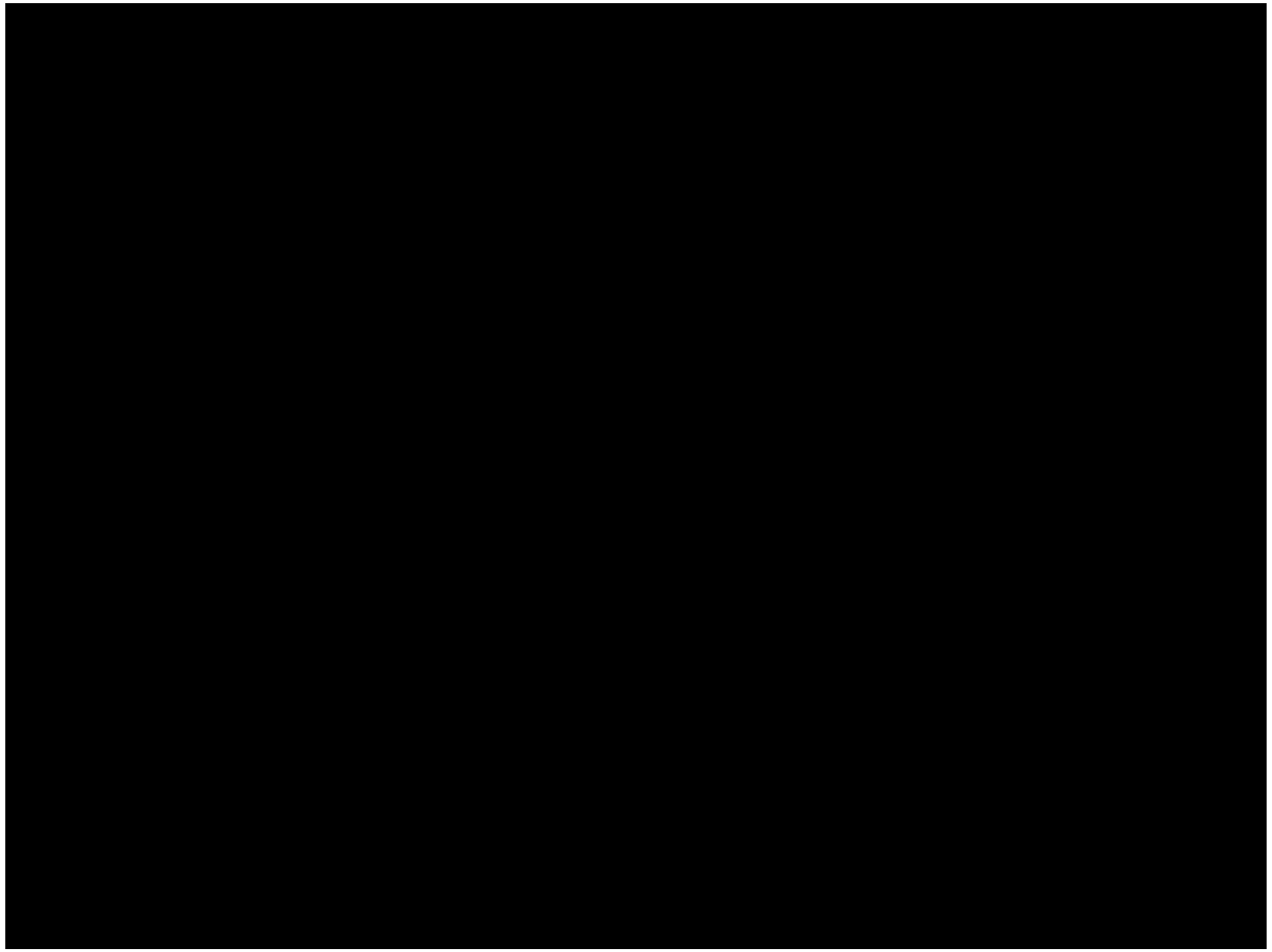


RESULTS (linear)

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Incidence angle study

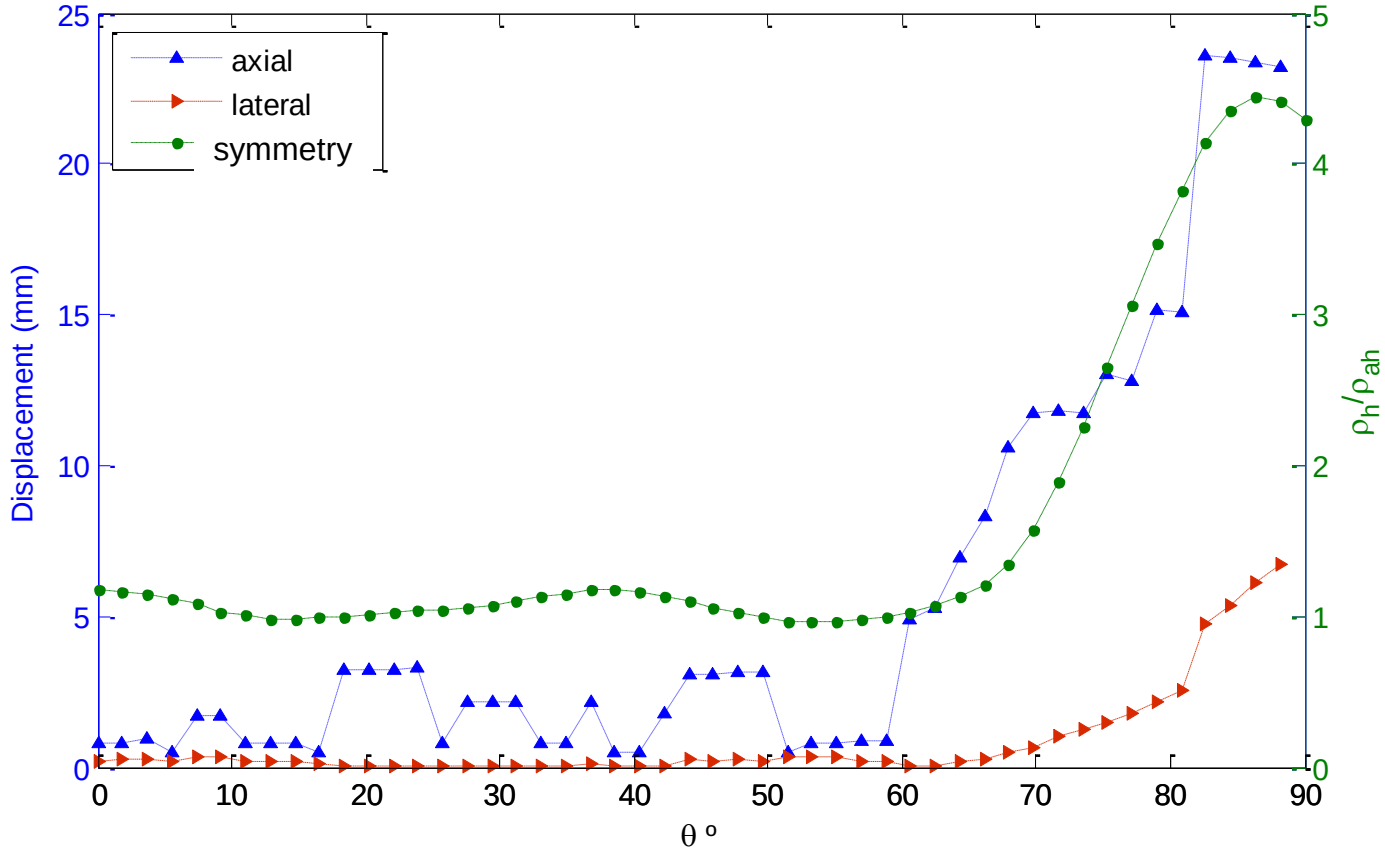


RESULTS (linear)

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Incidence angle study



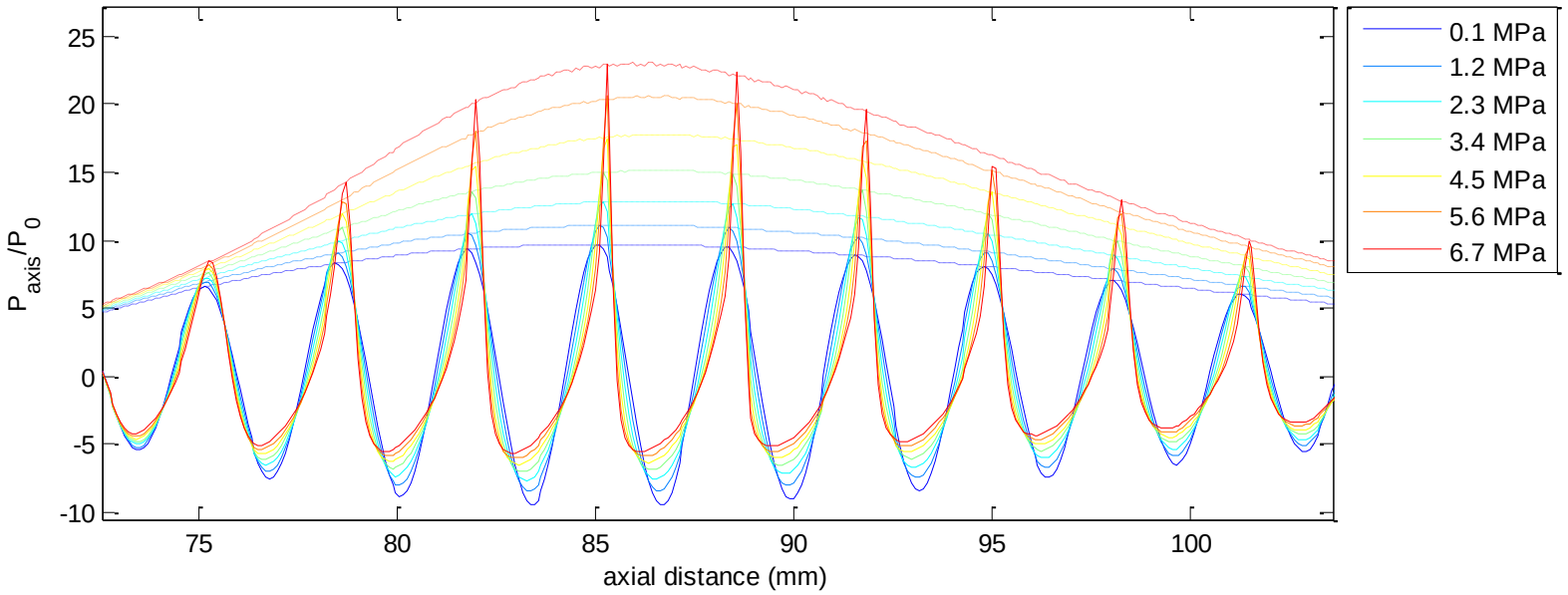
RESULTS (Nonlinear)

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Axial profiles:

- Asymmetry due to nonlinear effects

Normalized axial pressure for different input amplitude



RESULTS (Nonlinear)

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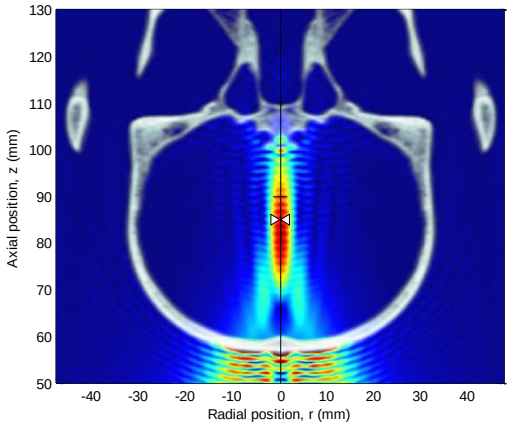
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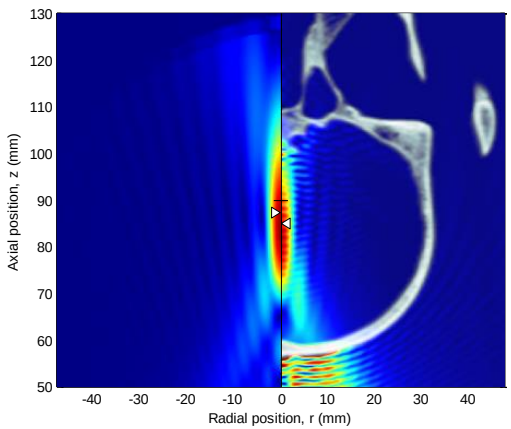
Pressure (Abs)

skull

water skull

Linear

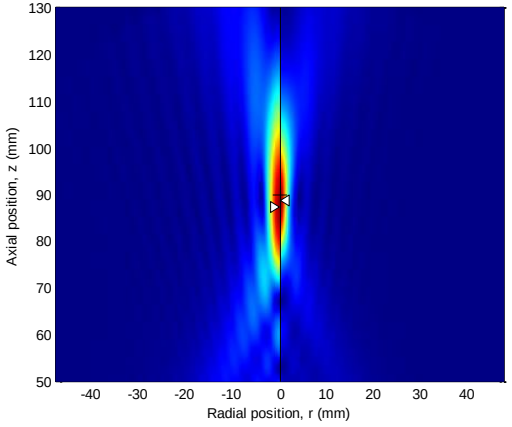


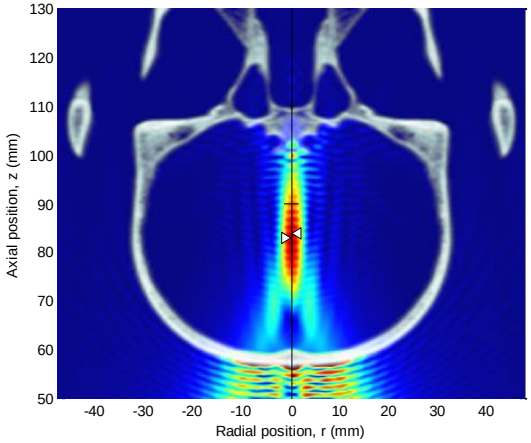


Linear water **Nonlinear**

Linear skull **Nonlinear**

Nonlinear





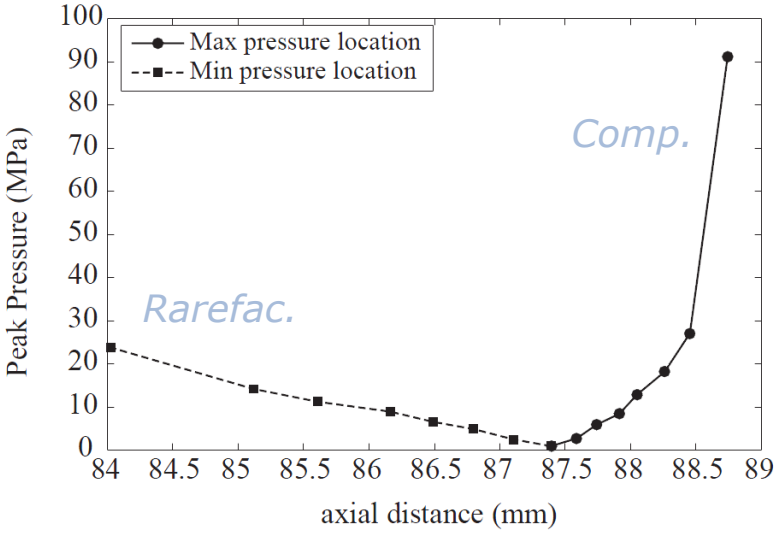
RESULTS (Nonlinear)

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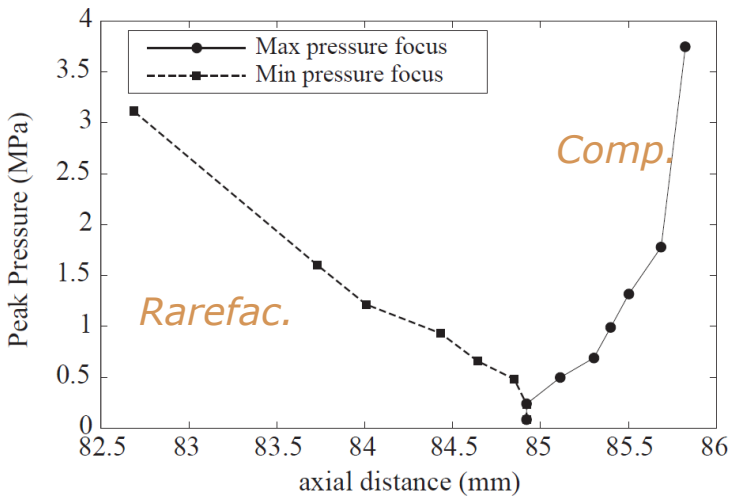
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Focal displacements

Water



Skull



Linear	- 2.6 mm shift	- 5.1 mm focal change
Comp.	+ 1.35 mm nonlinear shift	+ 0.90 mm nonlinear shift
Rarefac.	- 3.37 mm nonlinear shift	- 2.24 mm nonlinear shift

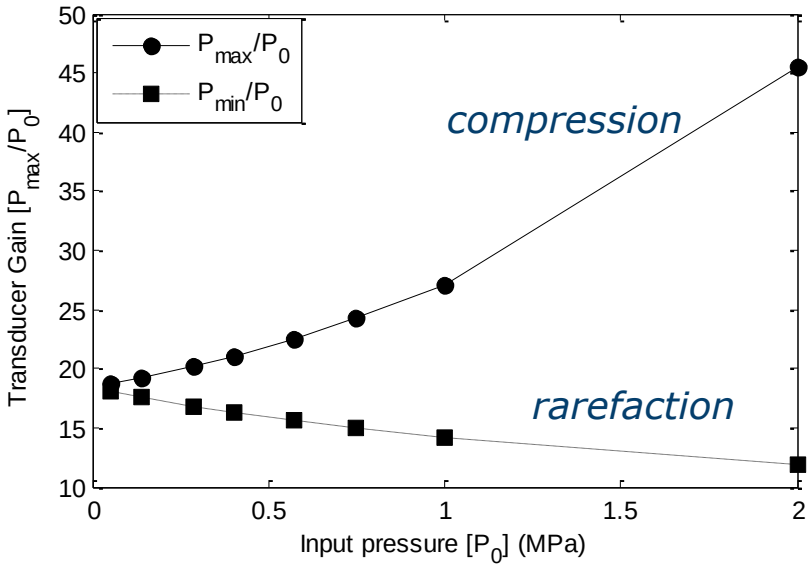
RESULTS (Nonlinear)

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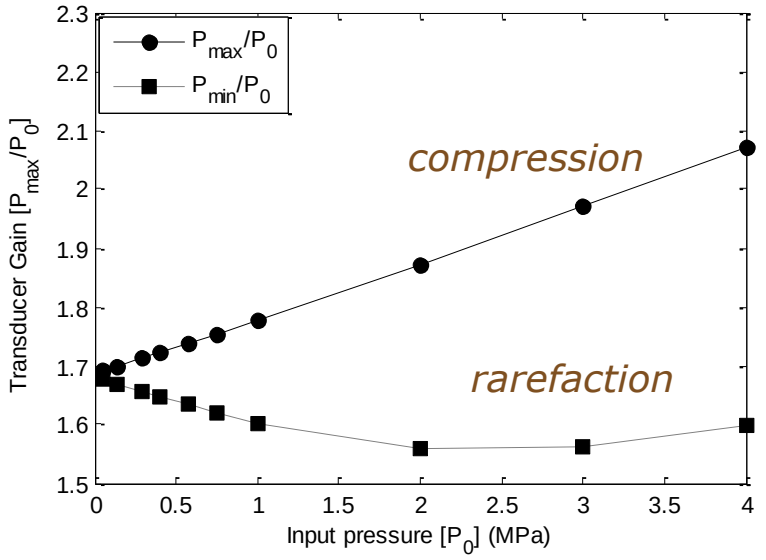
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Effective Gain

Water



Skull

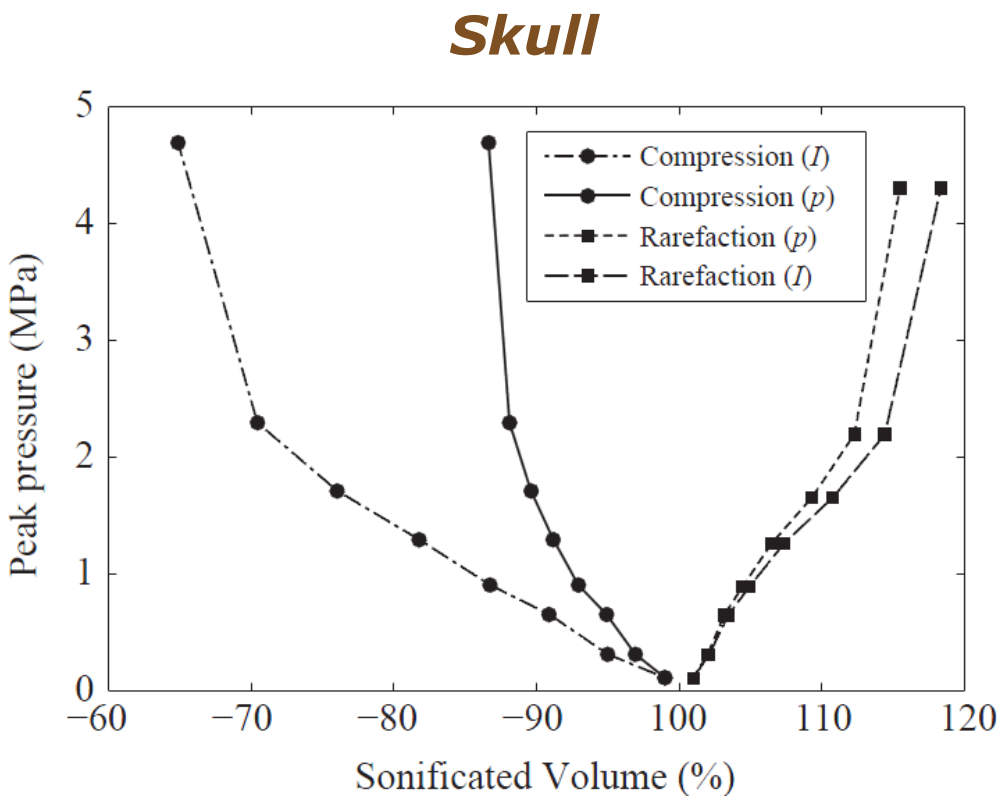


RESULTS (Nonlinear)

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Beamwidth and area under treatment



CONCLUSIONS

- Linear/Nonlinear acoustics simulations for transcranial bone propagation for BBB Opening in a Rhesus primate.

- Linear:
  - Estimation of focal displacements and angle dependence / symmetry
  - Focal displacements agree with experimental data

- Nonlinear:
  - Treatment area (Focal position and Beamwidth)
  - Effective Gain

  - Different behavior for compression and rarefaction profiles

(NEAR) FUTURE LINES

- *Experimental:*
  - CT-imaging including soft tissue
- *Modeling:*
  - Bone models
  - Soft tissue (brain/muscle) attenuation models
  - Ultrasound Contrast Agents effects: (dispersion/acoustic emission/cavitation/Nonlinear)
  - Bio-Heat diffusion models
- *Optimization:*
  - Patient specific beam propagation → treatment area
    - Incidence angle transducer position → focal / beamwidth

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Thanks for your attention

Noé Jiménez

