Multiphysics Framework for Modeling of FUS/HIFU and Induced Effects

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CO-ME
COMPUTER AIDED AND IMAGE GUIDED MEDICAL INTERVENTIONS

Outline

- Introduction
- Part I: FUS/HIFU Multiphysics Framework
- Part II: Applications
- Part III: US & Thermal Modeling of tcMRgFUS
- Conclusions & Future Work
- Acknowledgements & Funding

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- Part II: Applications
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Introduction: MRgFUS & Applications

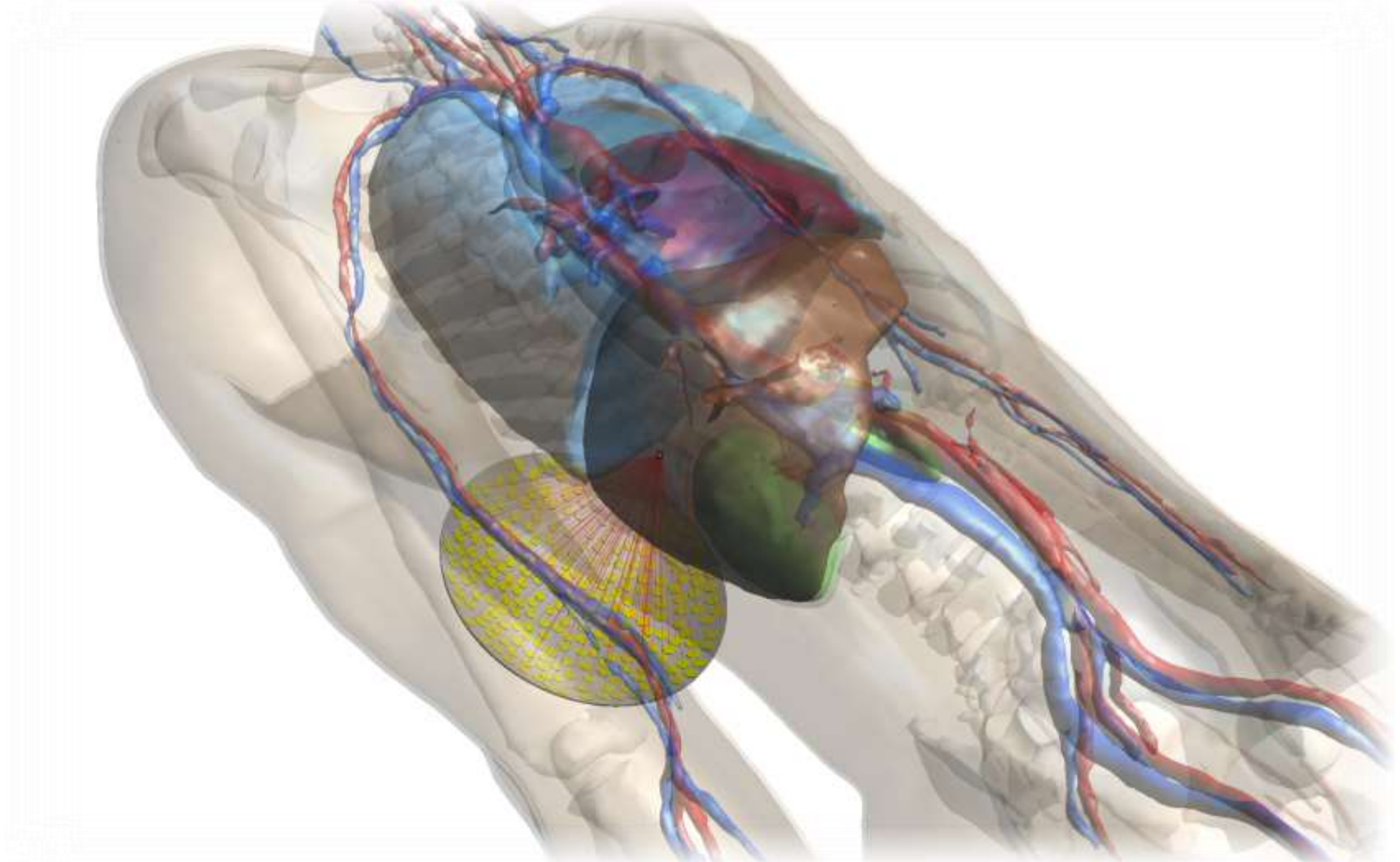
- advances in MR guided Focused Ultrasound (MRgFUS) allow use of US waves for therapeutic purposes
- modeling required for:
  - safety and efficacy assessment of ultrasonic devices (for therapeutic/diagnostic purposes)
  - device design and optimization
  - patient-specific treatment planning for acoustic therapies
  - outcome analysis & understanding of underlying mechanisms
- applications of interest to us:
  - evaluation and optimization of novel transducers/applicators for superficial and deep tumor ablation
  - modeling and treatment planning of FUS ablation (tumors and functional neurosurgery)
  - novel applications of FUS

Introduction: tcMRgFUS Neurosurgery

- clinical applications:
  - brain tumor ablation
  - functional neurosurgery:
    movement disorders (Parkinson's, essential tremor, dystonia…), neuropathic pain treatment, epilepsy, OCD
- pre-clinical applications:
  - reversible BBB disruption (focal drug delivery and activation to counter CNS diseases)
  - thrombolysis
  - neural stimulation
- special issues:
  - large number of transducer elements
  - distortion and focusing
  - skull heating, hot-spots

Part I: FUS/HIFU Multiphysics Framework

- Framework
- Validation
- Conclusions & Future Work



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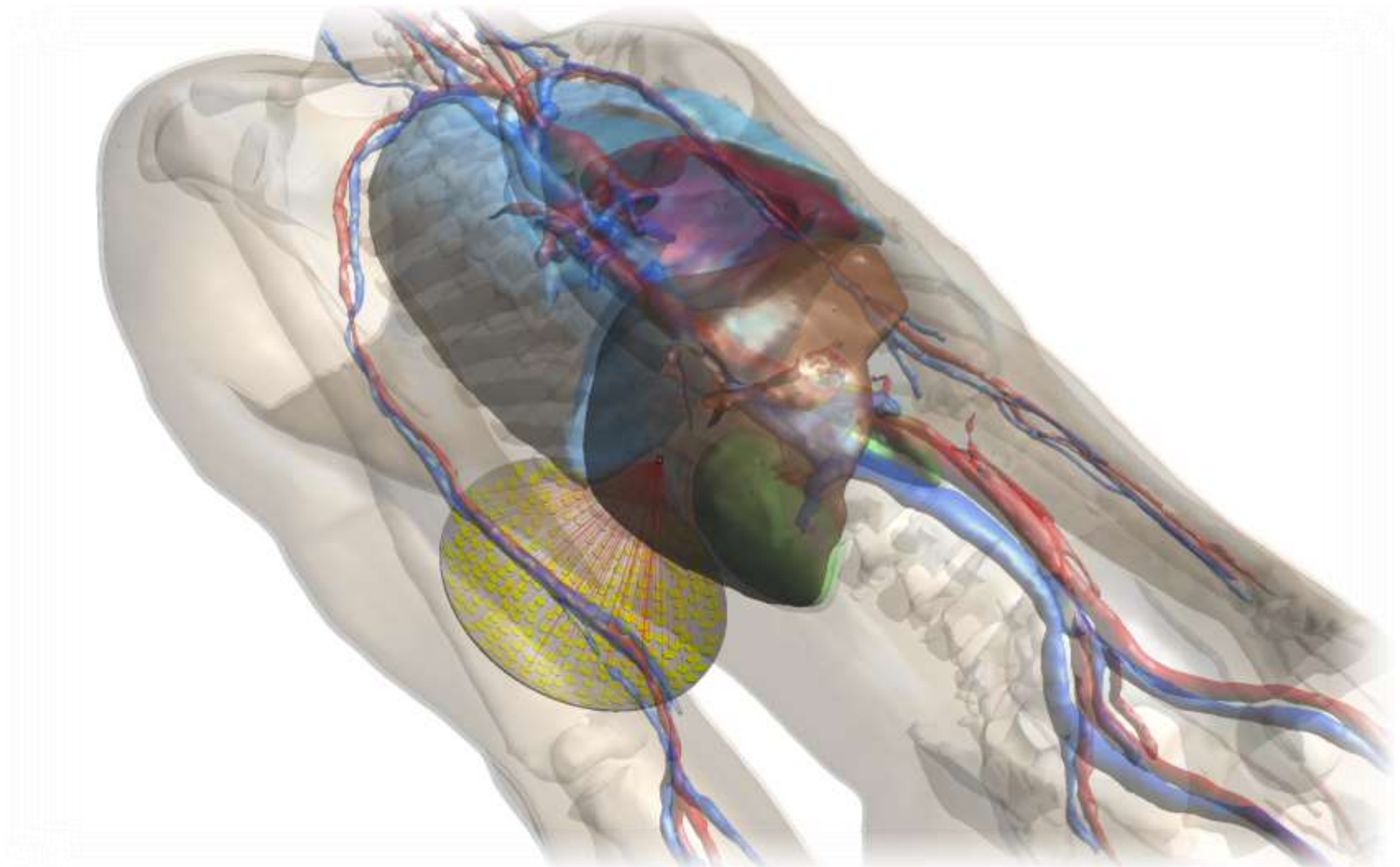
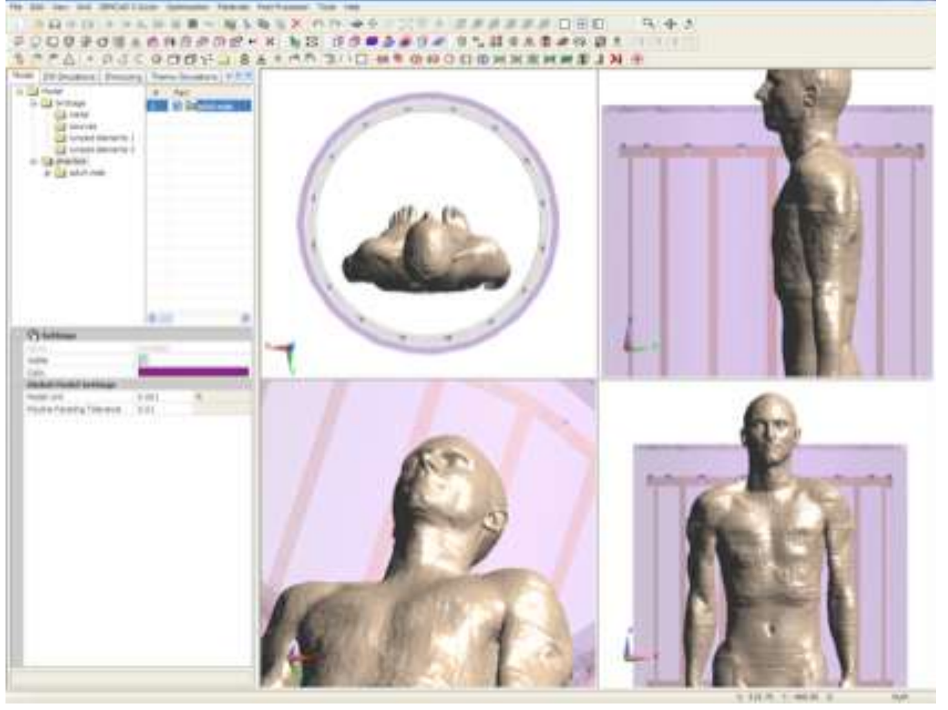


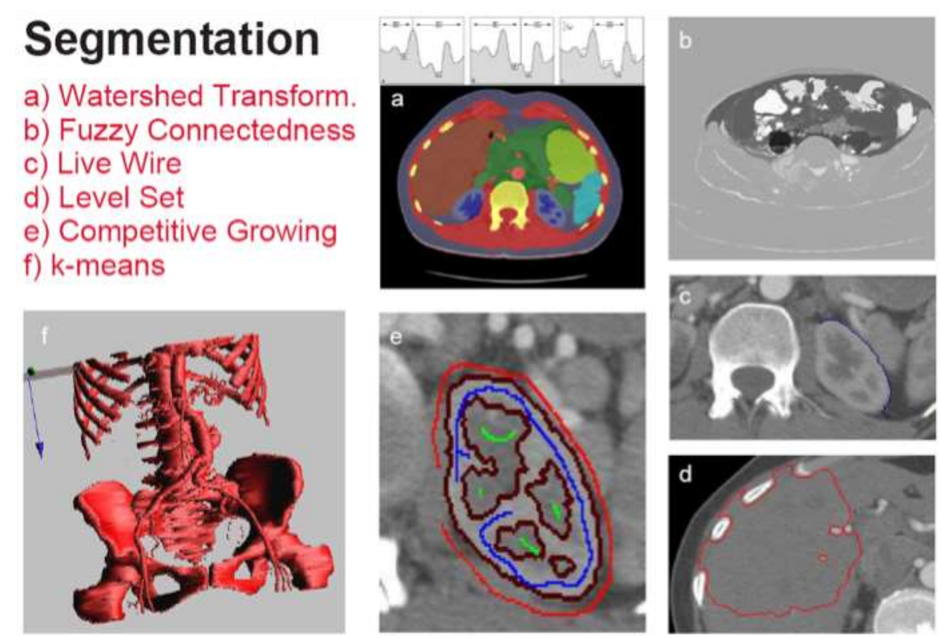
Framework: Overview

- simulation platform
  - 3D modeling, anatomical models
  - simulation setup (parameters, gridding, voxeling…)
  - scripting, visualization, post-processing
- segmentation platform
  - segmentation of MRI/CT image data
- solvers:
  - acoustic solver
  - µ-Bubble solver
  - thermal solver
  - flow solver



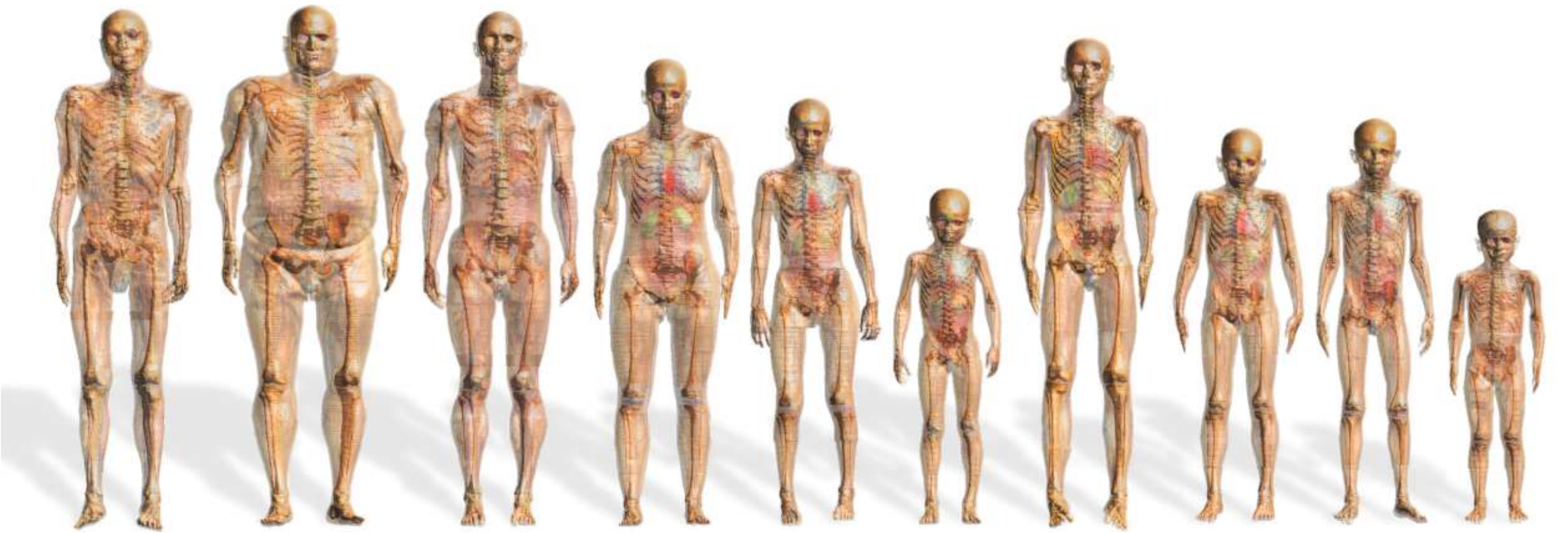
Framework: Image Segmentation

- custom software
- tool box with many, flexibily combinable segmentation methods
  - robust techniques ranging from:
    highly interactive (e.g., live wire, interactive watershed transform, brush) ↔ highly automatic (e.g., improved k-means-based clustering, competitive fuzzy connectedness, competitive growing)
  - method specific user interactions paradigms
  - novel techniques (e.g., Gamma method based clustering, image based adaptation)
  - routines for noise reduction, hole/gap/island removal, smoothing, skin adding, connected component analysis
- live-wire based method for vascular tree extraction (vessel wall extraction to be improved)
- topologically flexible interpolation
  - not every slice has to be segmented
  - image based adaptation based on fuzzy logic

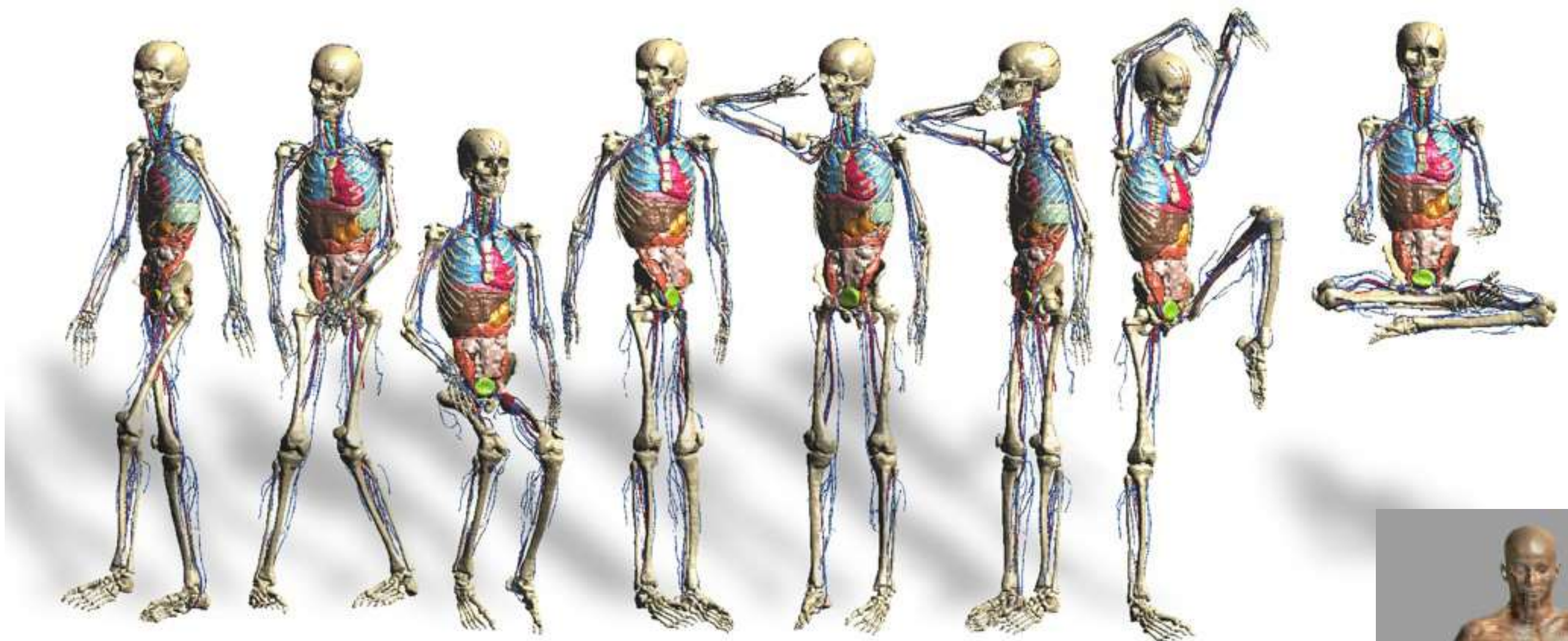


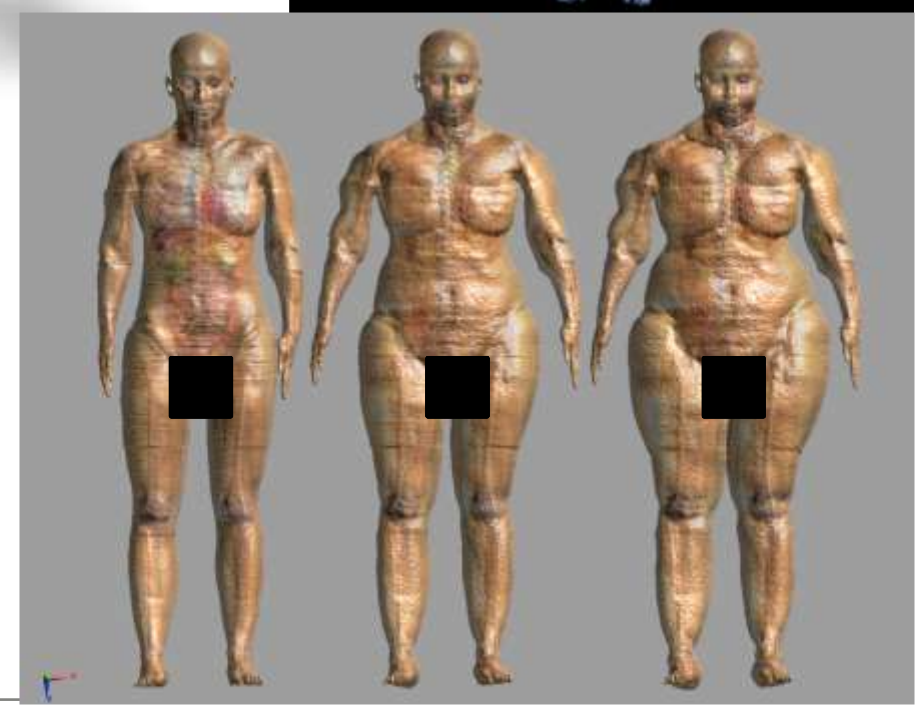
Framework: Virtual Population

- CAD models, >200 distinguished organs/tissues
- extensive literature-based tissue parameter database (online)
- pregnant women, animal models (dog, mice, rats, pig)



Framework: Posing / Morphing





- volume preserving influence region based deformation fields
- physics-based morphing

Framework: Acoustic Solver: Models

- selected numerical models:
  - linear propagation: linear acoustic pressure wave equation

$$\rho \nabla \frac{1}{\rho} \nabla p - \frac{1}{c^2} \frac{\partial^2 p}{\partial t^2} - \frac{\widetilde{a}}{c^2} \frac{\partial p}{\partial t} = 0$$

  - non-linear propagation: Westervelt-Lighthill equation:

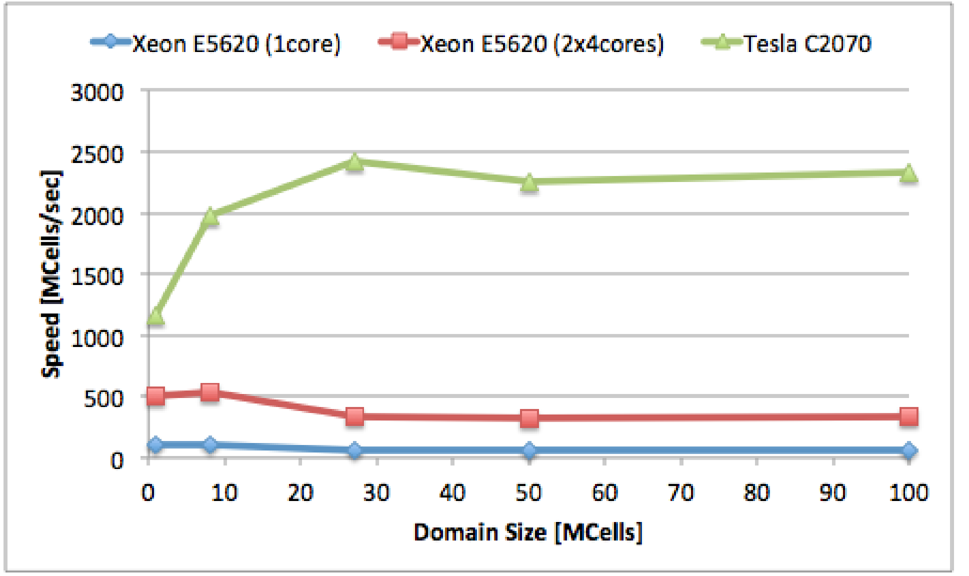
$$\rho \nabla \frac{1}{\rho} \nabla p - \frac{1}{c_0^2} \frac{\partial^2 p}{\partial t^2} + \frac{\delta}{c_0^4} \frac{\partial^3 p}{\partial t^3} + \frac{\beta}{2\rho_0 c_0^4} \frac{\partial^2 p^2}{\partial t^2} = 0$$

p : pressure, c : equilibrium speed of sound in medium, ρ : equilibrium density of medium

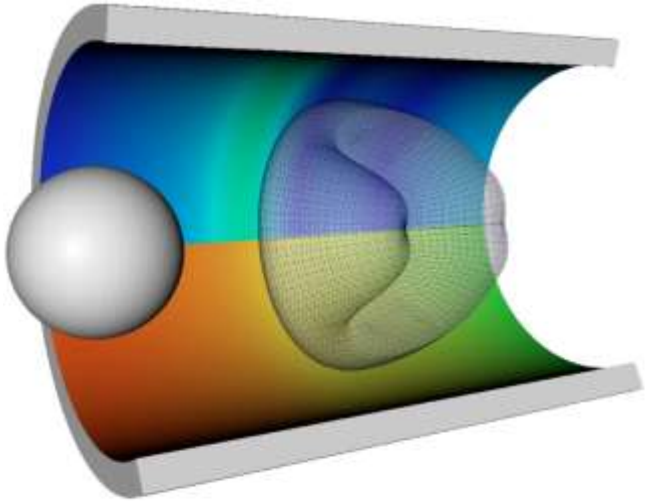
α : attenuation coefficient of medium, δ : diffusivity of medium, β : nonlinearity parameter

Framework: Acoustic Solver

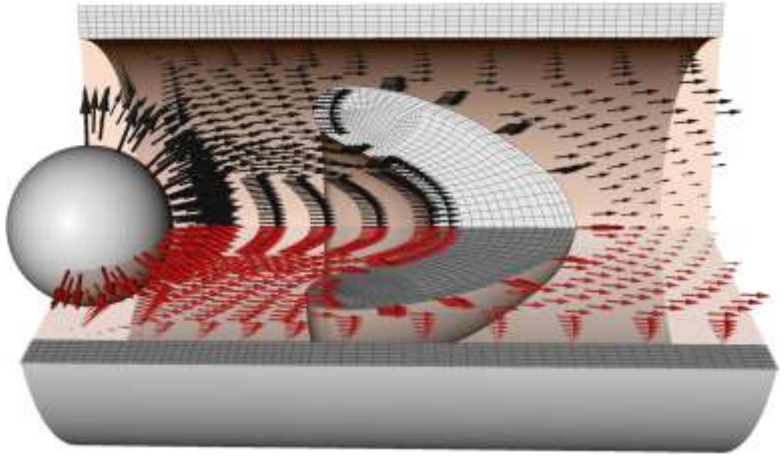
- acoustic Solvers:
  - 3D FDTD solvers for highly inhomogeneous anatomies (accounting for air-tissue and bone-tissue interfaces)
  - linear & non-linear variants
  - parallelization
  - CPU: OpenMP, up to 9x speed-up on 12 cores
  - GPU: CUDA, up to 36x speed-up on single GPU
  - Perfectly Matched Layer (PML) absorbing boundary conditions (allowing for domain truncation along inhomogeneous interfaces)



Framework: µ-Bubble Solver



- effect of µ-bubble sonication on BBB disruption (LTNT, ETH Zurich):
  - encapsulated µ-bubble in capillary
  - sonication by incident FUS field
  - cavitation
- implementation:
  - FVM simulation using FSI
  - bubble motion with modified Rayleigh-Plesset ODE accounting for confinement in vessel and viscoelastic lipid shell

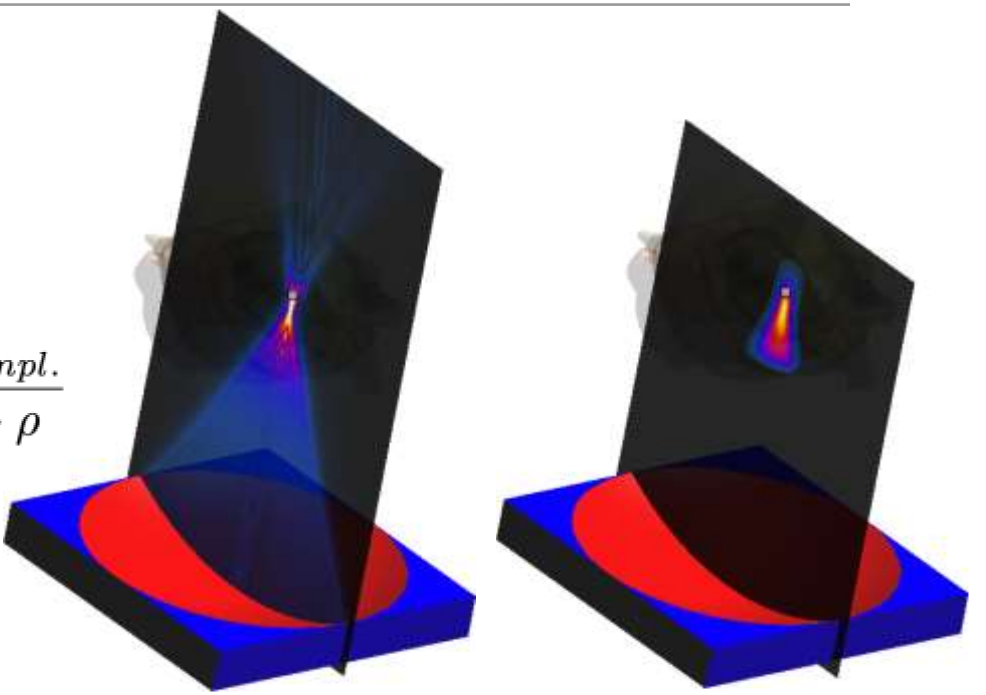


- lumped parameter model:
  - UCA concentration -> modified effective tissue properties -> modified macroscopic pressure -> (shear) stresses on vessel wall

Framework: Thermal Solver I

- Pennes Bioheat Equation, widely used in thermal modeling:

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + \rho Q_{acoust.} + \rho Q + \rho_b c_b \rho \omega (T_b - T) \text{ where } Q_{\text{acoust.}} = \alpha \frac{p_{ampl.}^2}{c \cdot \rho}$$



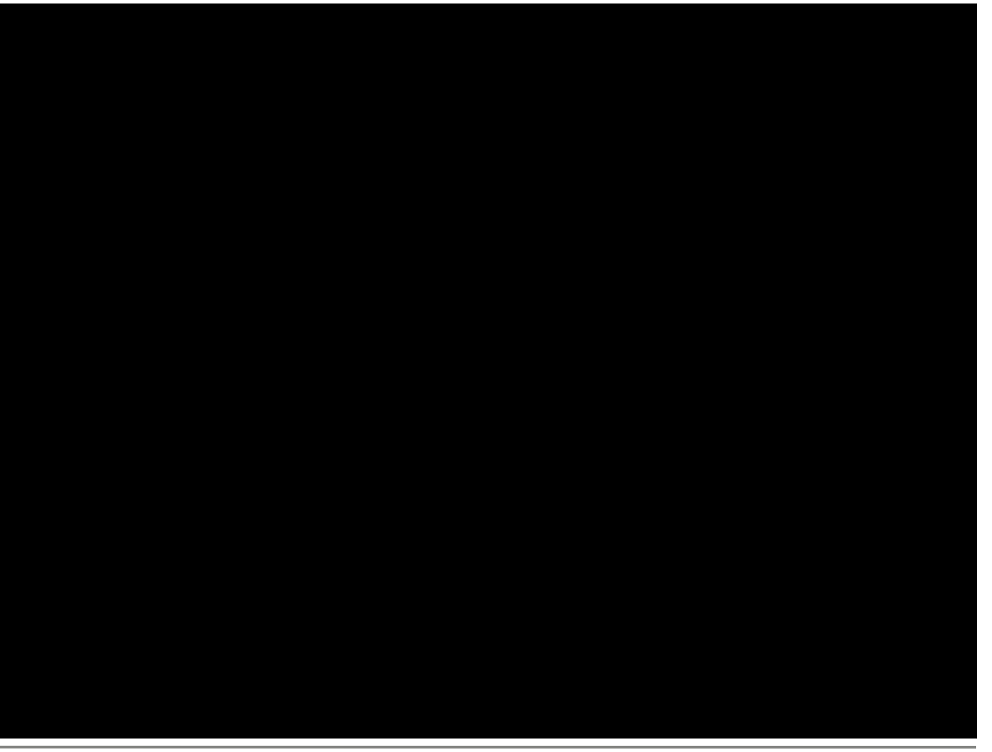
- common caveats of most implementations
  - not accounting for directivity of blood flow
  - not accounting for the discreteness of vessels
  - assumption of local equilibrium between blood and environmental T (only true for small capillaries / arterial bleed-off)
  - not considering temperature dependence of tissue parameters
- sophisticated thermal solver modeling the complex thermal phenomena required to accurately simulation ablation

Framework: Thermal Solver II

- high performance explicit & implicit FD solvers
  - conformal schemes to reduce staircasing effects
  - thin structure models (accuracy & speed)
- temperature dependent tissue parameters
  - thermoregulation, vascular shut-down
- perfusion modeling
  - DIVA (Lagendijk), effective tensorial thermal conductivity, convection based on CFD simulation for major vessels
    - coupling of the 3D simulation to a pseudo-1D simulation of the vessel network
    - blood flow directivity (improved accuracy and over 100x acceleration)
  - support for MR perfusion maps
- thermal dose (CEM43) and tissue damage (Arrhenius) modeling

Framework: Flow Solver

- acoustic streaming
- microbubble concentration
- flow solver:
  - incompressible Navier-Stokes equation
  - coupled with the acoustics solver through Reynold stresses term
  - GMRES with a Schur complement preconditioning method
  - parallelized through MPI & PETSc



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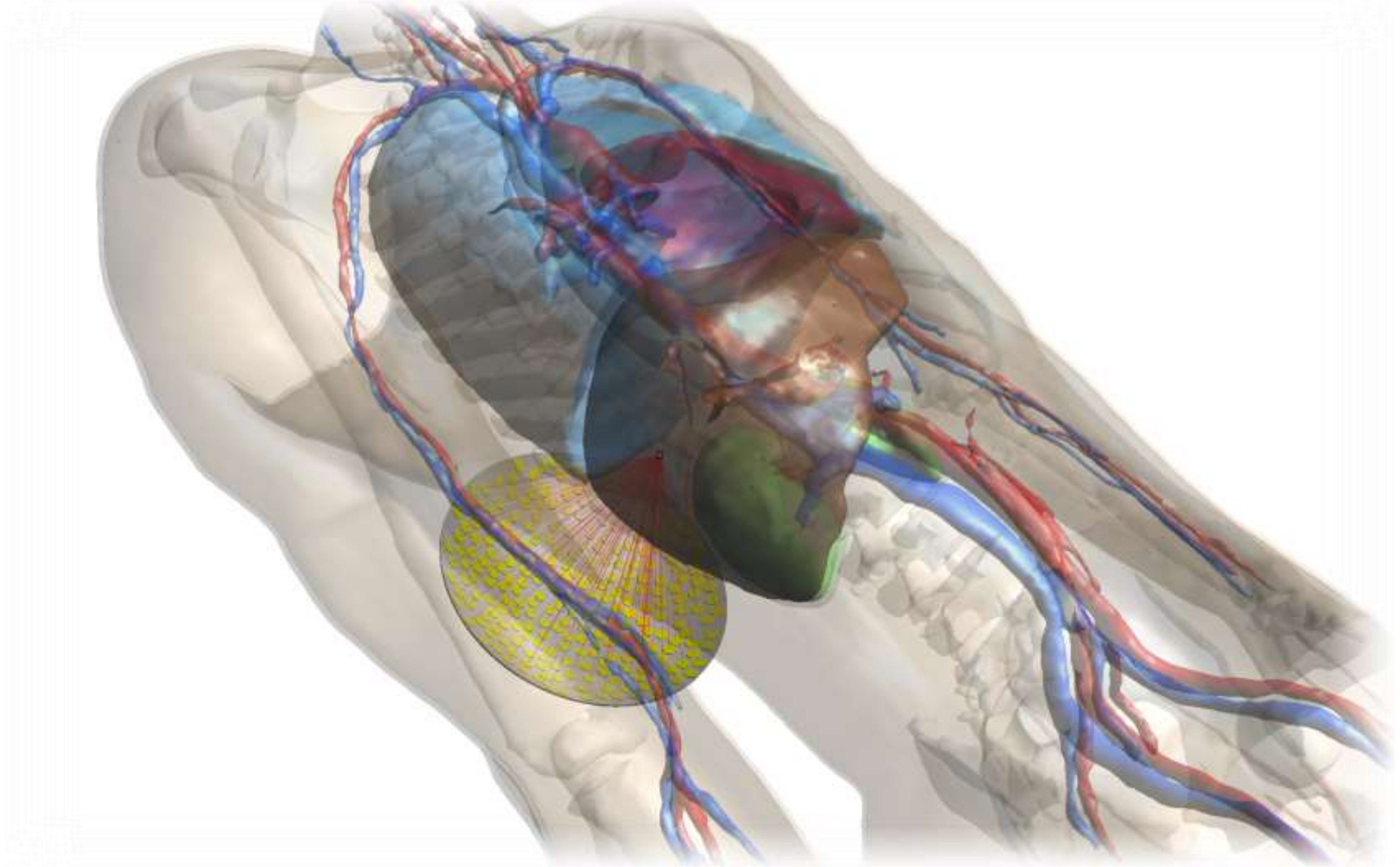
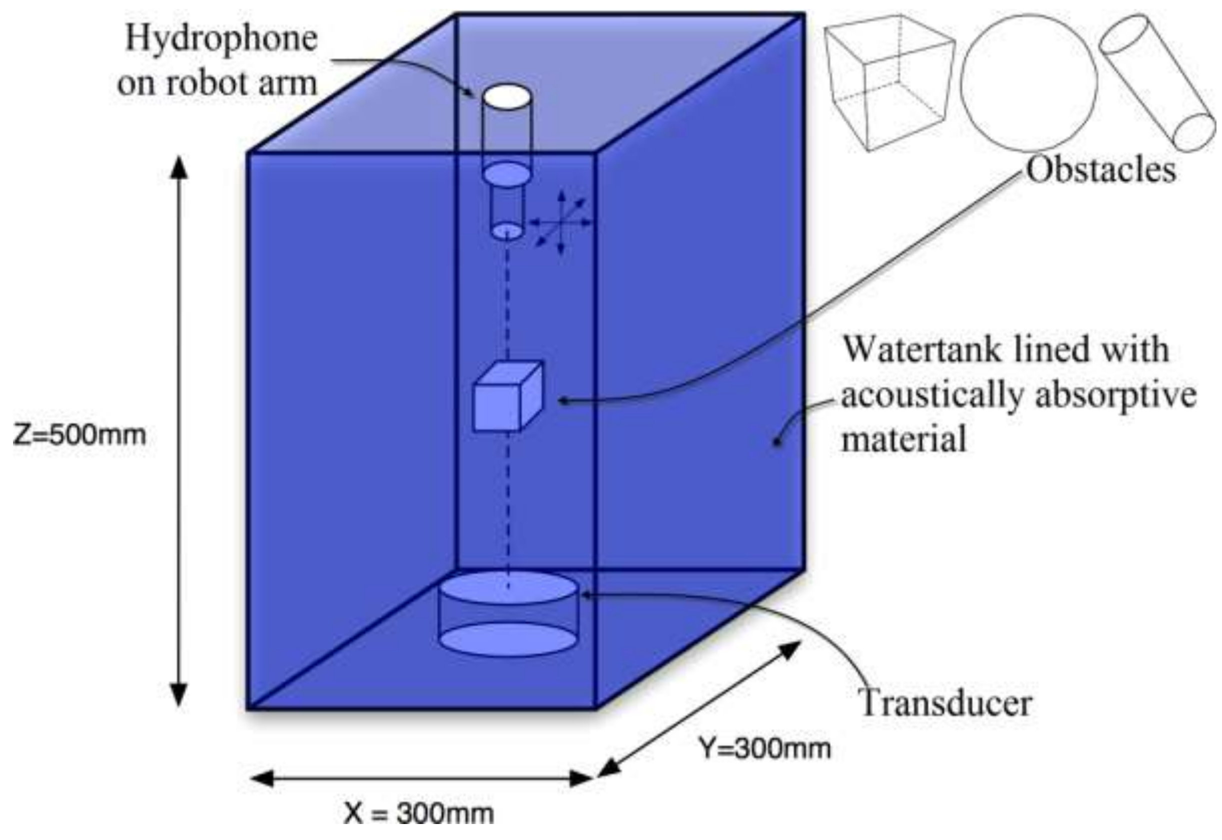
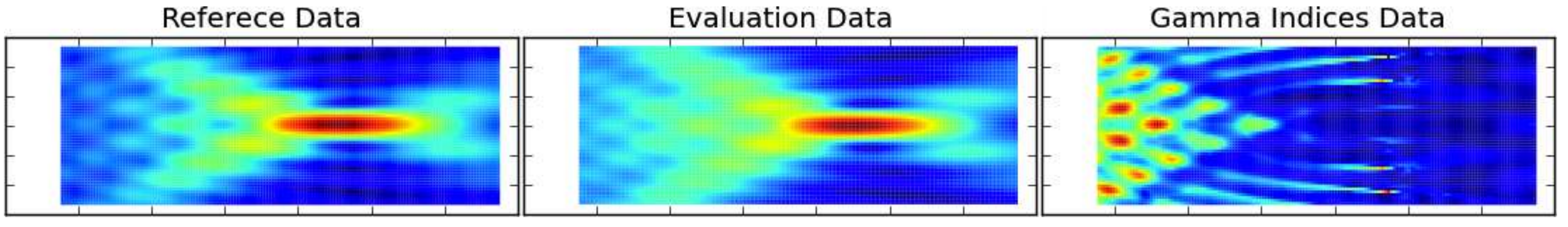


Validation: Approaches

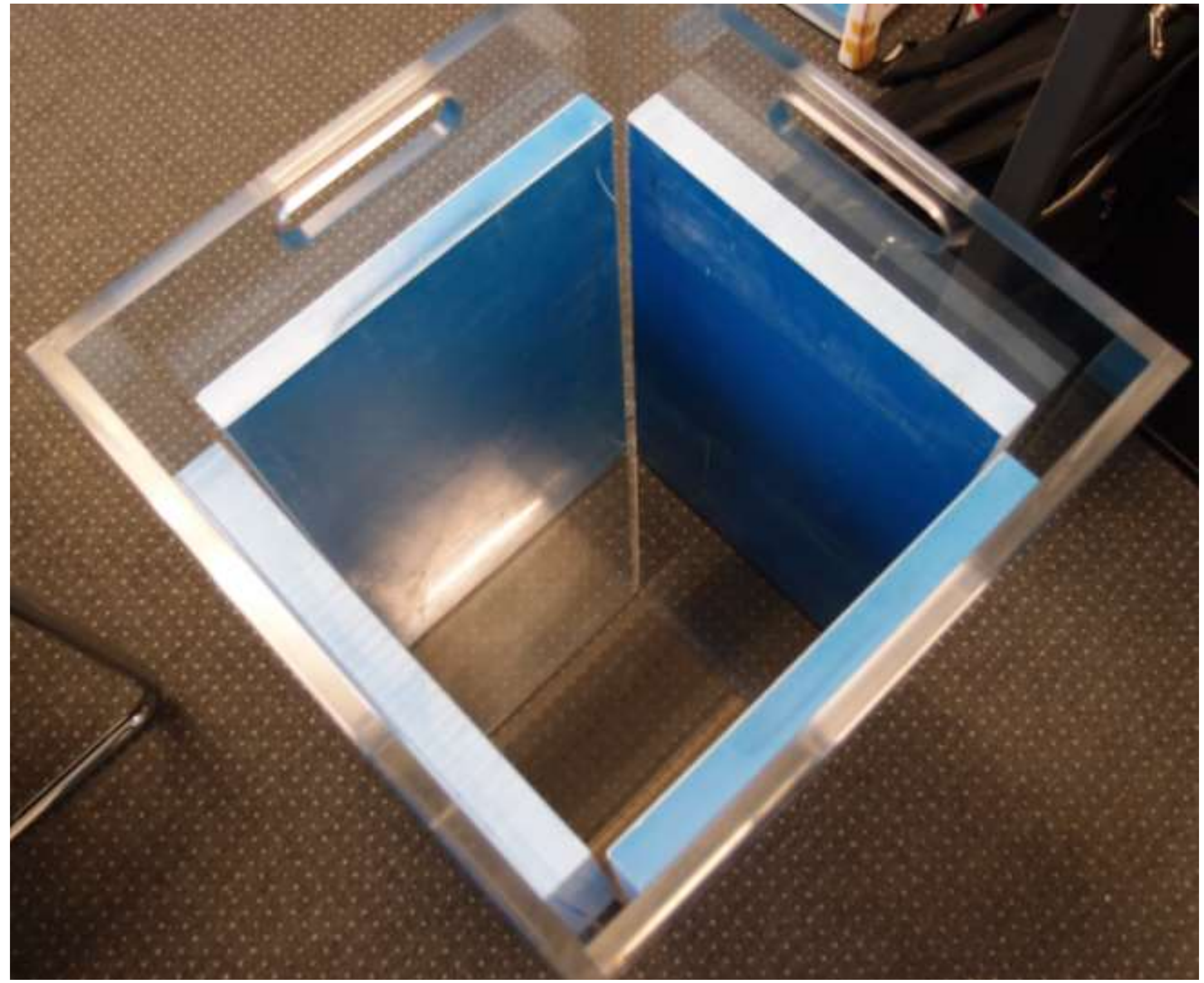
- approaches
  - analytical validation (complete): comparison against analytically calculated fields
  - validation against software (complete): comparison against FOCUS simulations with the Gamma Dose Distribution (GDD) method
  - experimental (ongoing): 3D pressure field measurements of focused US transducer distorted by predefined obstacles





Validation: Measurement Setup

- components
  - plexiglass water-tank lined with acoustic absorbers
  - removable & adjustable sample holder with mounted transducer (550kHz, 80mm diameter)
  - acoustically characterized samples of different shapes and materials (delrin, polyurethane, RTV silicone) suspended with plexiglass rods in the beam path



- measurements
  - DASY52 NEO robot arm with a needle-type hydrophone and preamplifier

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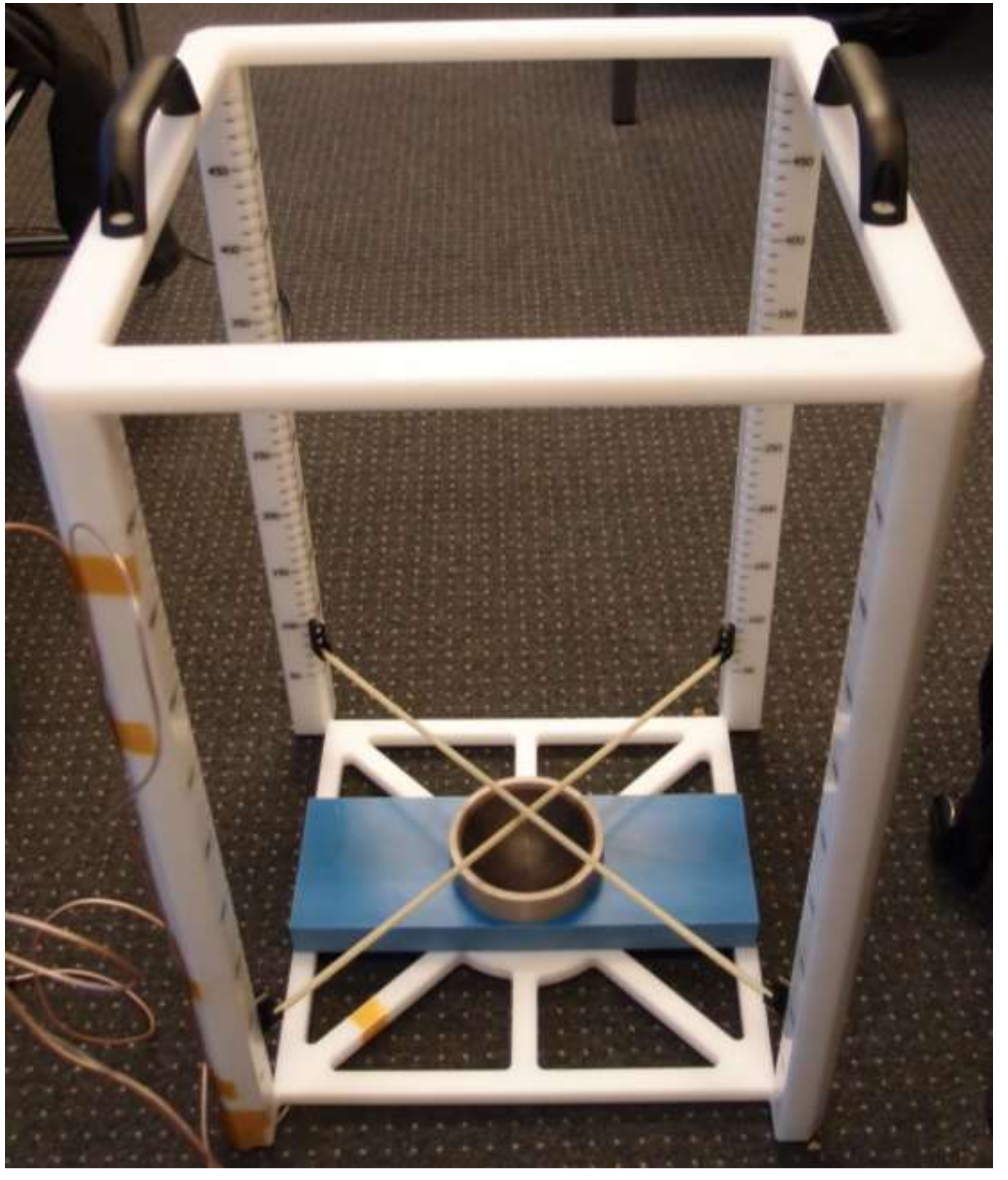

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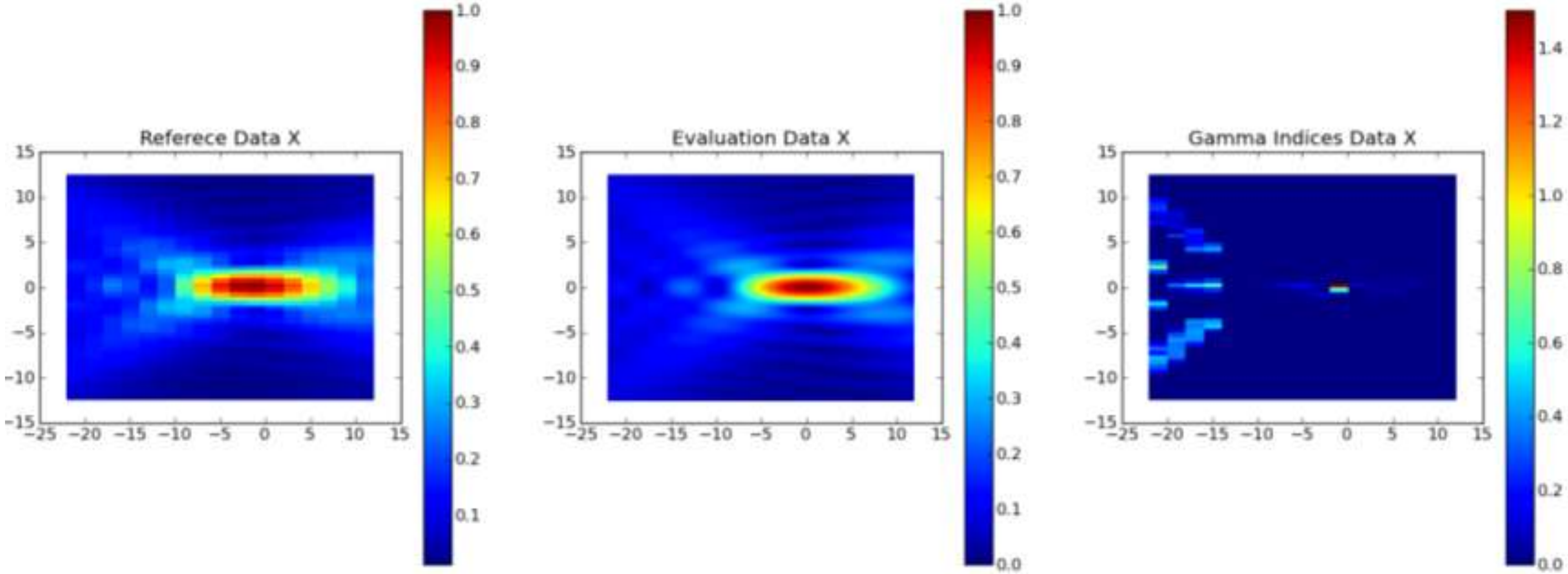
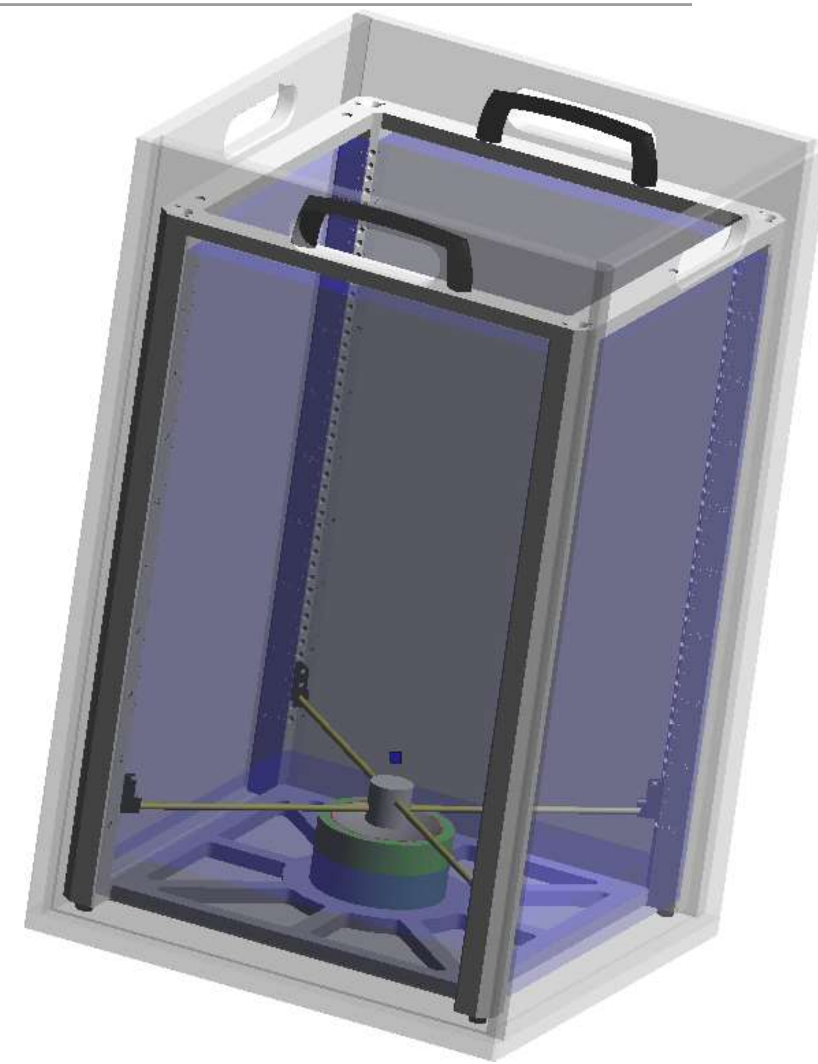
- measurements
  - DASY52 NEO robot arm with a needle-type hydrophone and preamplifier

Validation: Results I

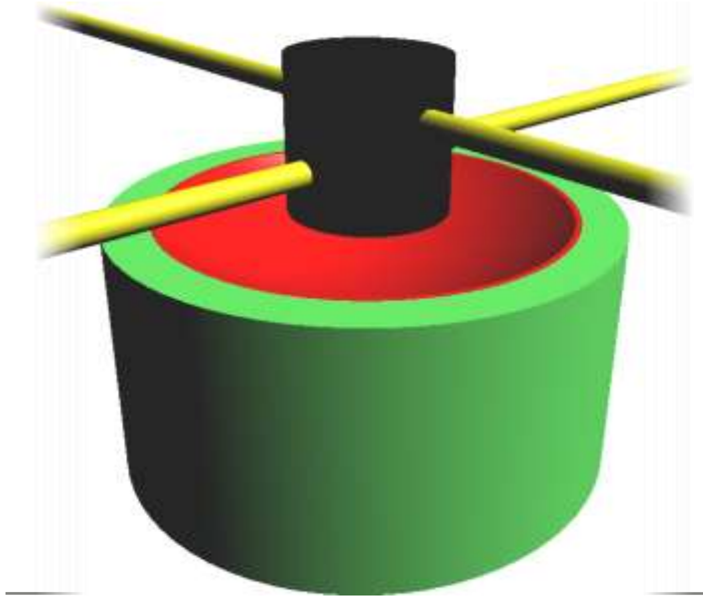
- empty water-tank (no sample) comparison
  - modified Gamma distribution comparison method
  - excellent agreement within given tolerances
  - dose criterion: 5% tolerance
  - distance criterion: $\lambda/2$

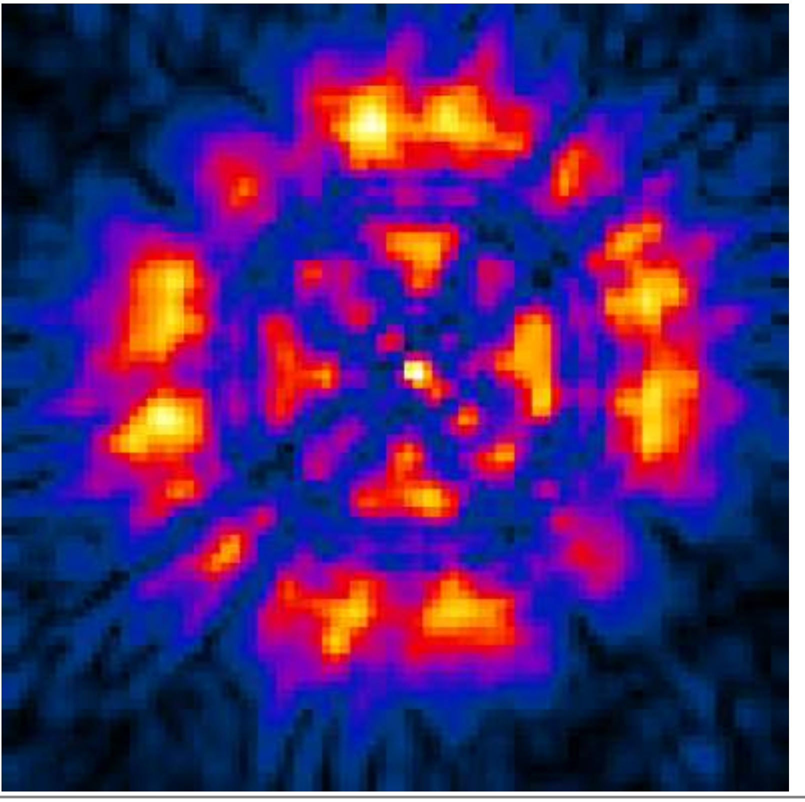


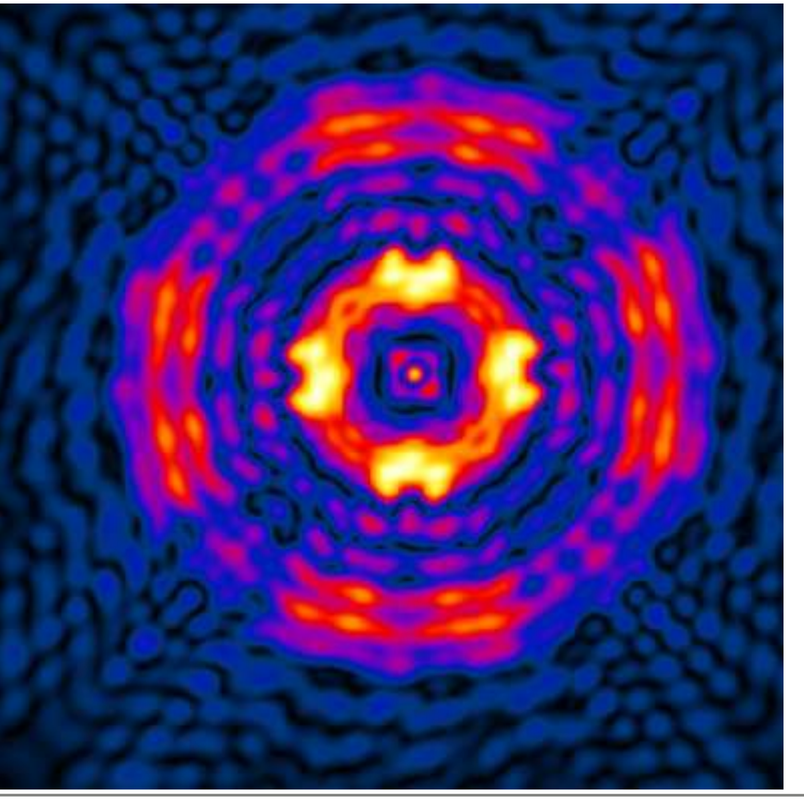


Validation: Results II

- sample comparisons
  - complex interference pattern
  - ongoing effort: need for registration/alignment, large positioning uncertainties
  - good visual agreement: reproduction of major field features, scale agreement
- polyurethane cylinder
  - speed of sound: 1700m/s
  - attenuation: 6dB/cm/MHz
  - density: 1130Kg/m^3

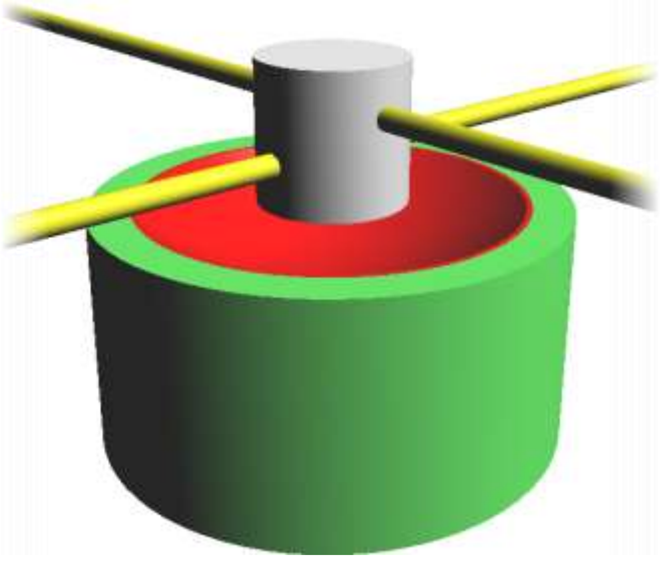


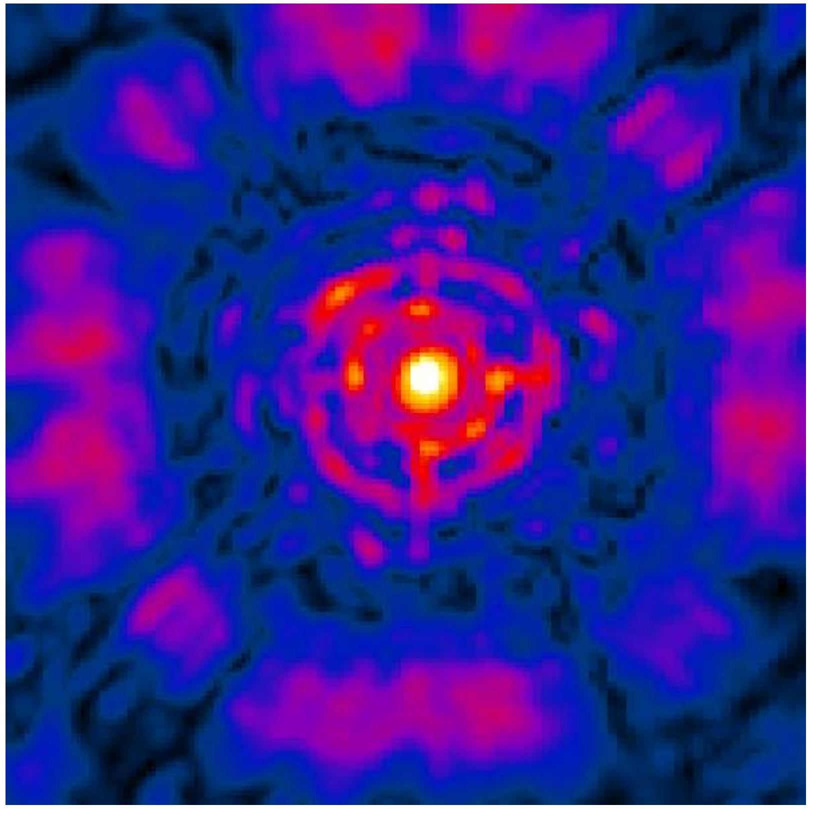


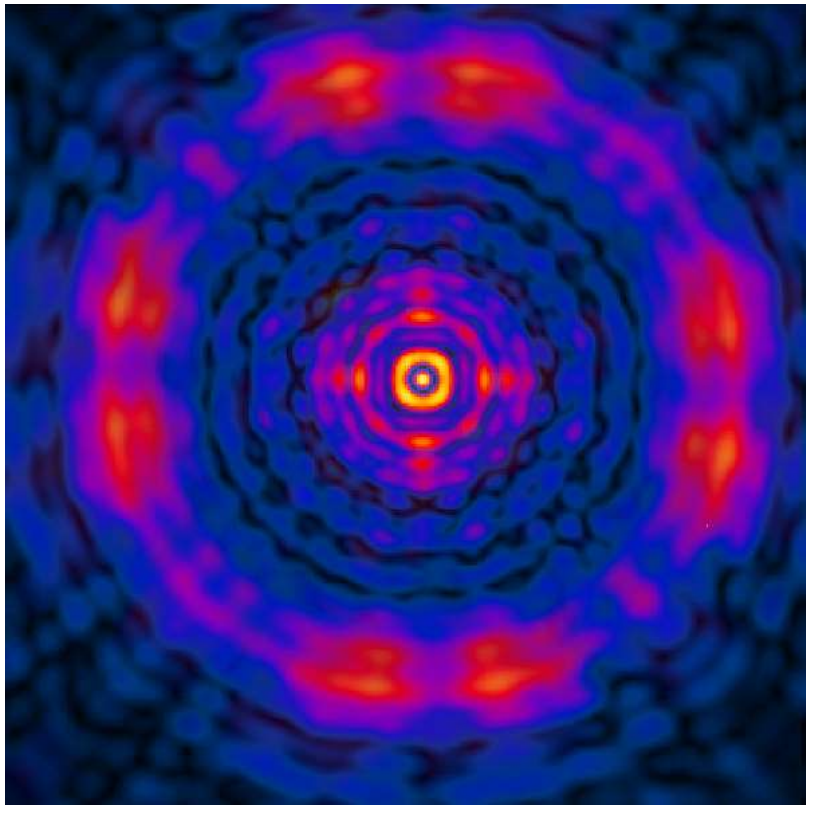


Validation: Results III

- sample comparisons
  - complex interference pattern
  - ongoing effort: need for registration/alignment, large positioning uncertainties
  - good visual agreement: reproduction of major field features, scale agreement
- delrin cylinder
  - speed of sound: 2430m/s
  - attenuation: 3dB/cm/MHz
  - density: 1430Kg/m^3







Part I: FUS/HIFU Multiphysics Framework

- Framework
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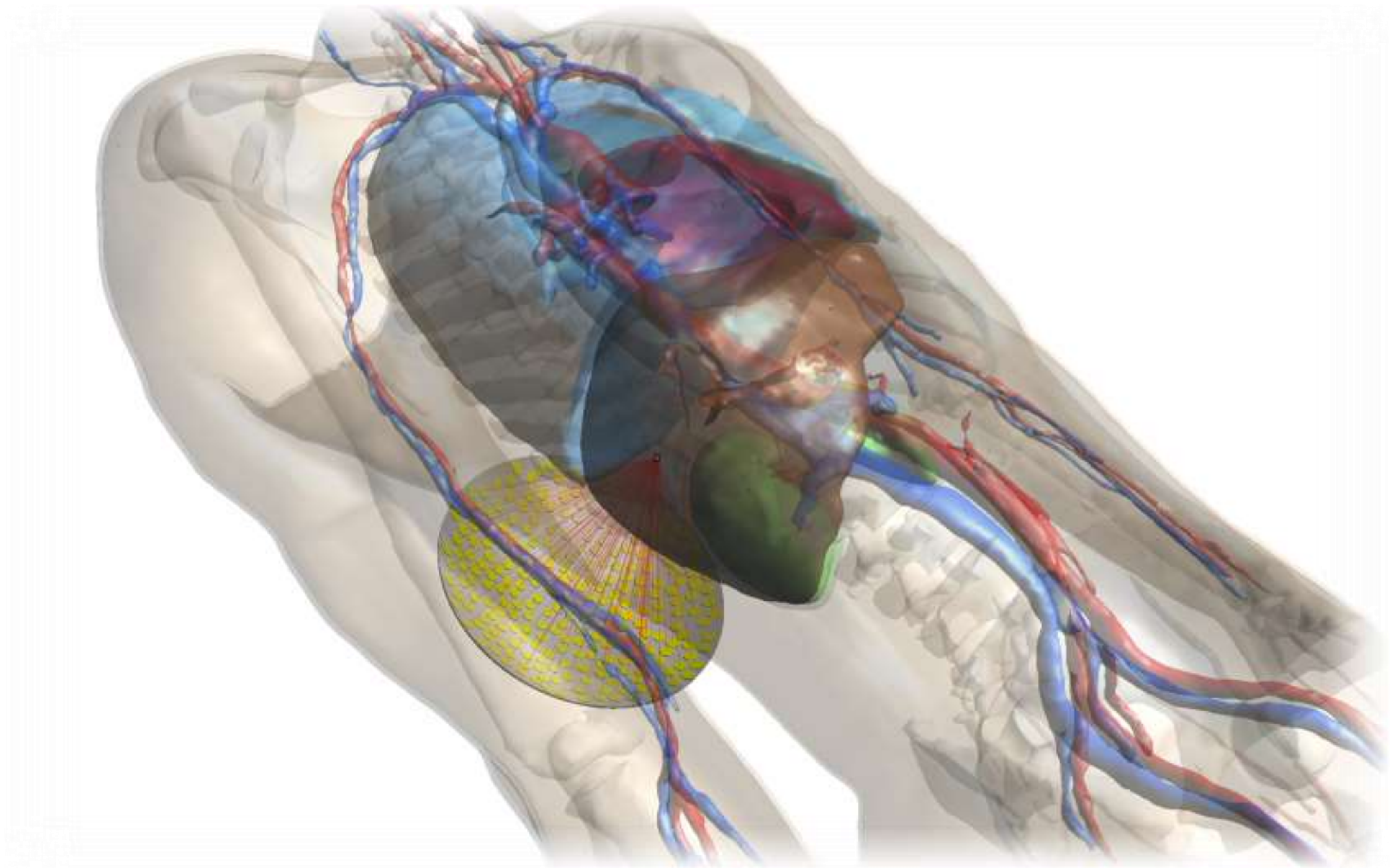
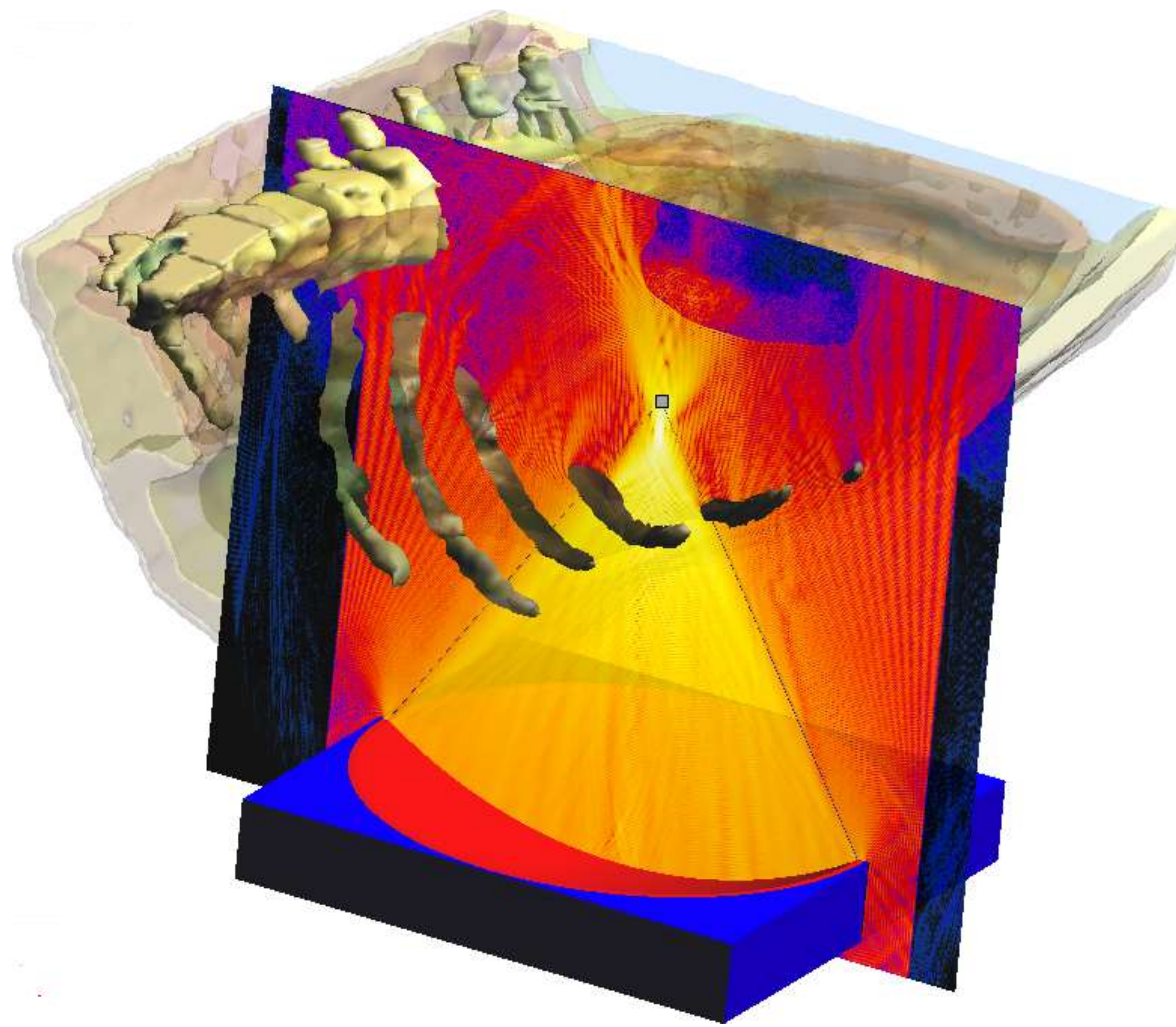


Conclusions & Future Work

- next steps
  - coupling: flow solver, microbubble solver
  - validation: complete experimental validation
- conclusions
  - a comprehensive framework that allows for full wave propagation in complex anatomical models has been developed and validated

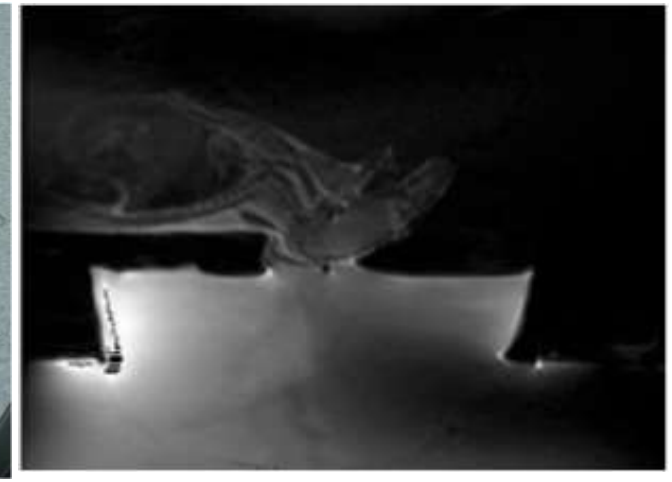
Part II: Applications

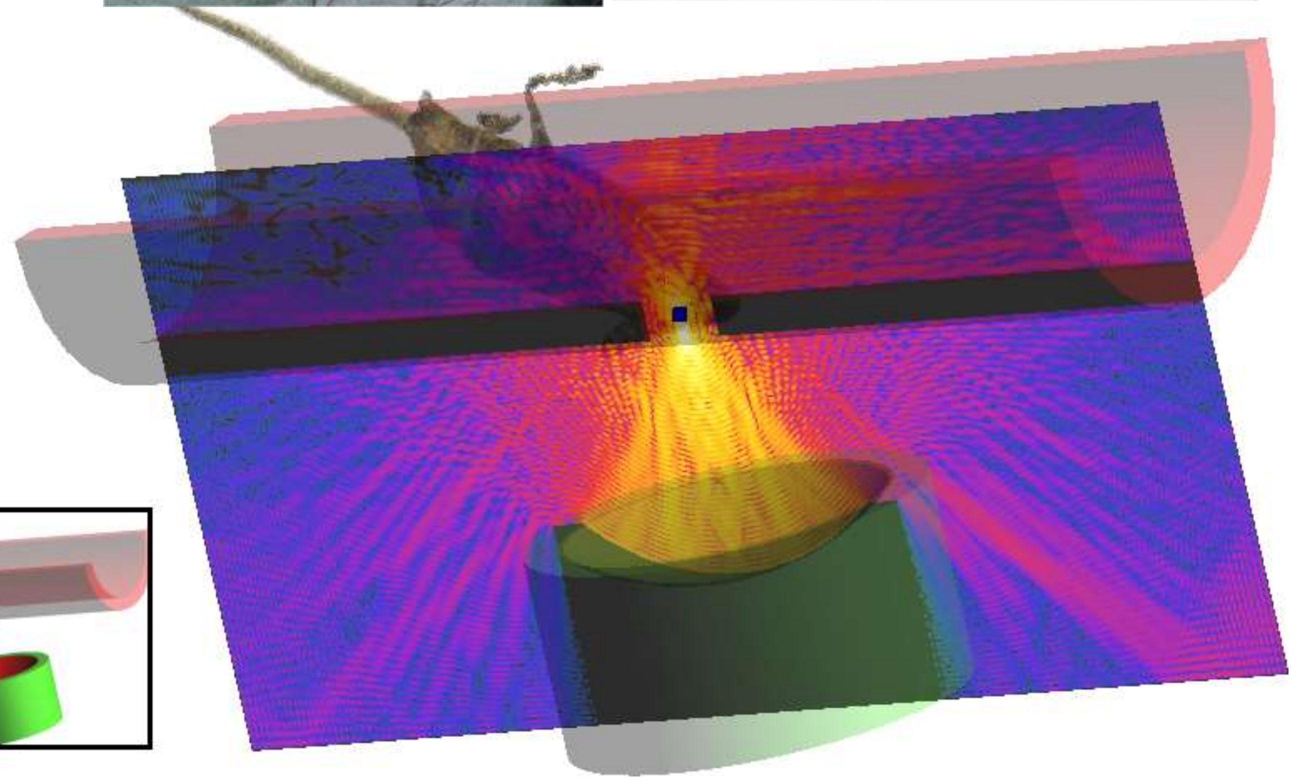
- Experimental BBB Disruption
- Neuropathic Pain Treatment
- Neck Tumor Ablation
- Renal & Hepatic Tumor Ablation

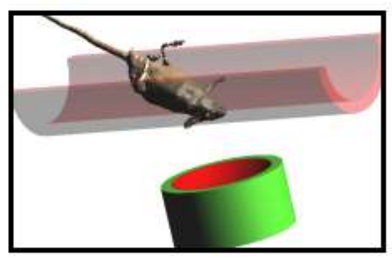


Experimental BBB Disruption

- experiment:
  - in-vivo experiments on live mice
  - combined use of FUS & UCA approach
  - assess efficacy of increasing the BBB permeability
- anatomical simulations:
  - simulation of animal stage with FUS sonication of the brain through the skull



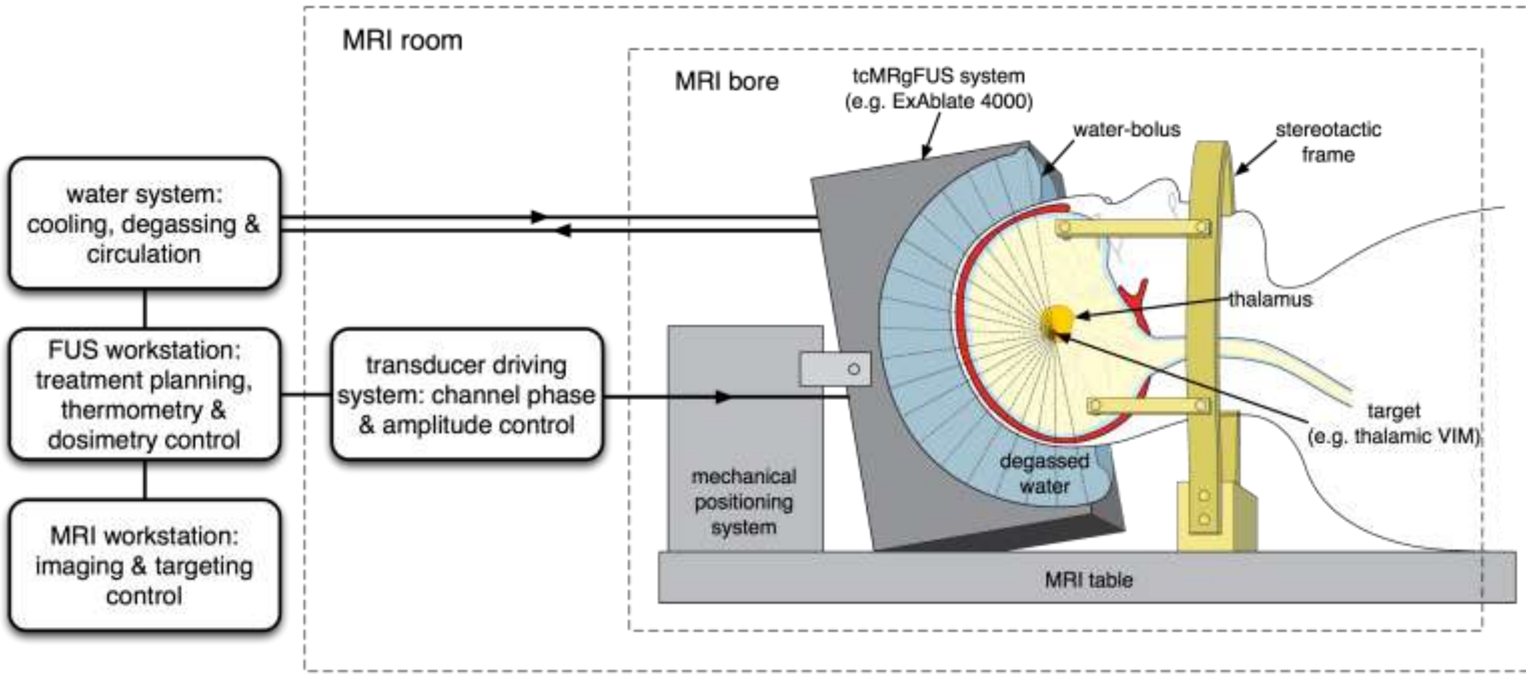




Neuropathic Pain Treatment

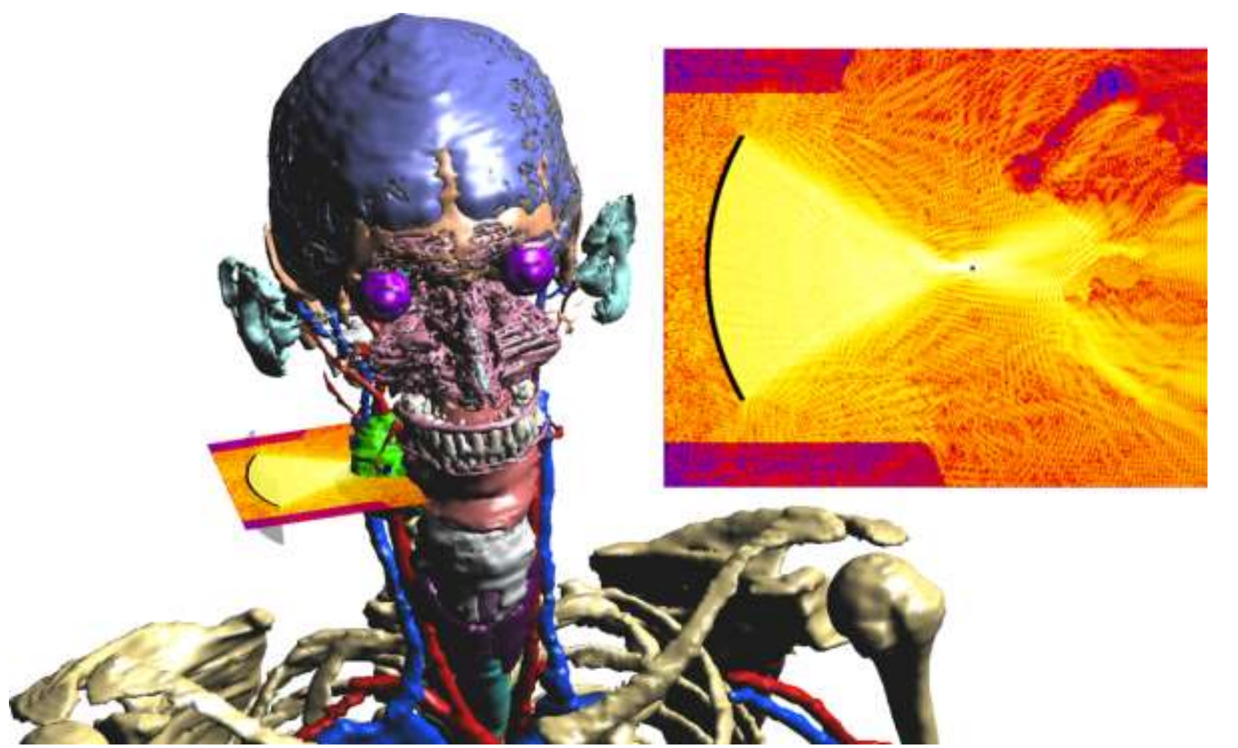
- MRgFUS in tissue ablation:
  - non-invasive and precise tissue ablation
  - minimizes the risk of bleeding and infection,
  - avoids damage to non-targeted tissue
  - does not involve ionizing radiation

- neuropathic pain treatment:
  - micro-thalamotomy on live patients to treat chronic neuropathic pain with phased-array ultrasonic transducers
  - simulations will allow for patient-specific treatment planning and parameter exploration



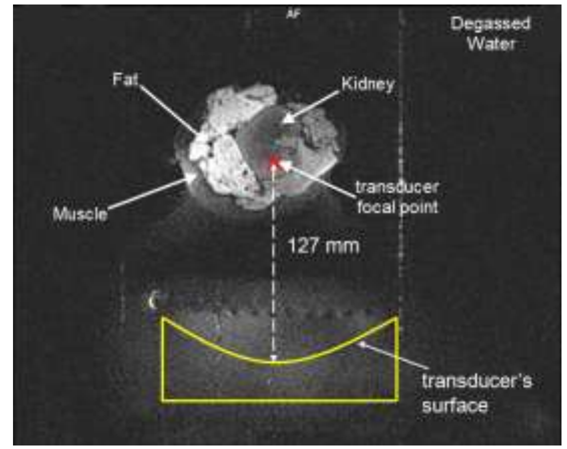
Neck Tumor Ablation

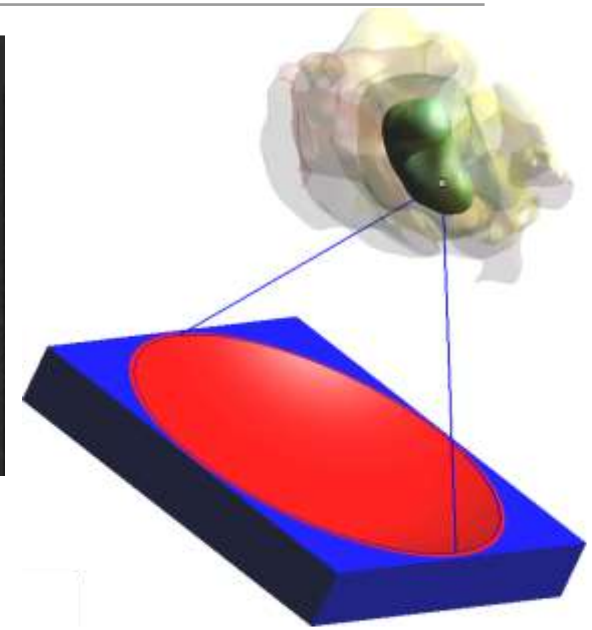
- usage of the SonoKnife applicator to ablate superficial tumors in the head and neck region (tumor volume needs to be covered by scanning)
- simulations:
  - ablation of locally-advanced head and neck squamous cell carcinomas (HNSCC)
  - anatomically detailed model segmented from MRI data (Virtual Family)
  - model tailored to take into account tissue-air and tissue-bone interfaces

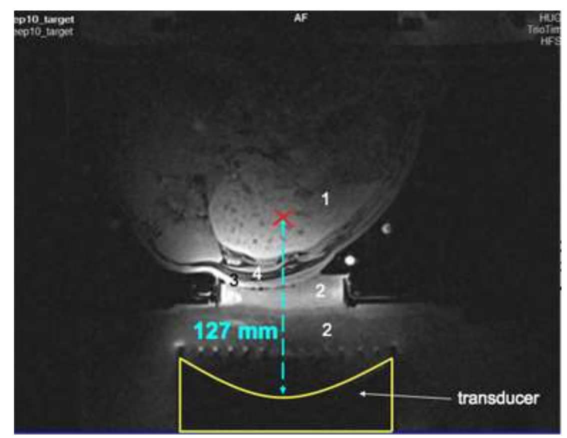


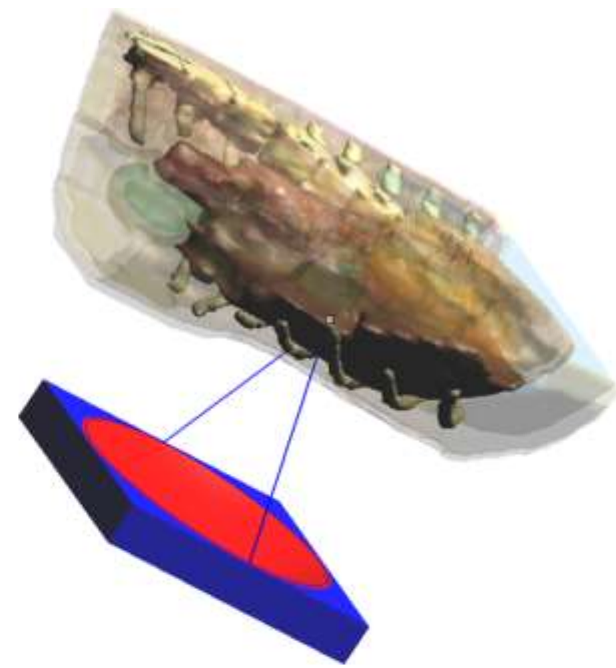
Renal & Hepatic Tumor Ablation I

- renal & hepatic tumor ablation (Salomir R, Petrusca L):
  - usage of MRgFUS to create lesions in the renal cortex and the liver is experimentally investigated on ex-vivo ovine kidneys and live sheep
- simulations:
  - segmented model of an ex-vivo kidney surrounded by fat and muscle tissue
  - segmented model of a live sheep including the ribcage and all major organs in the vicinity of the liver
  - understand unexpected focus shape

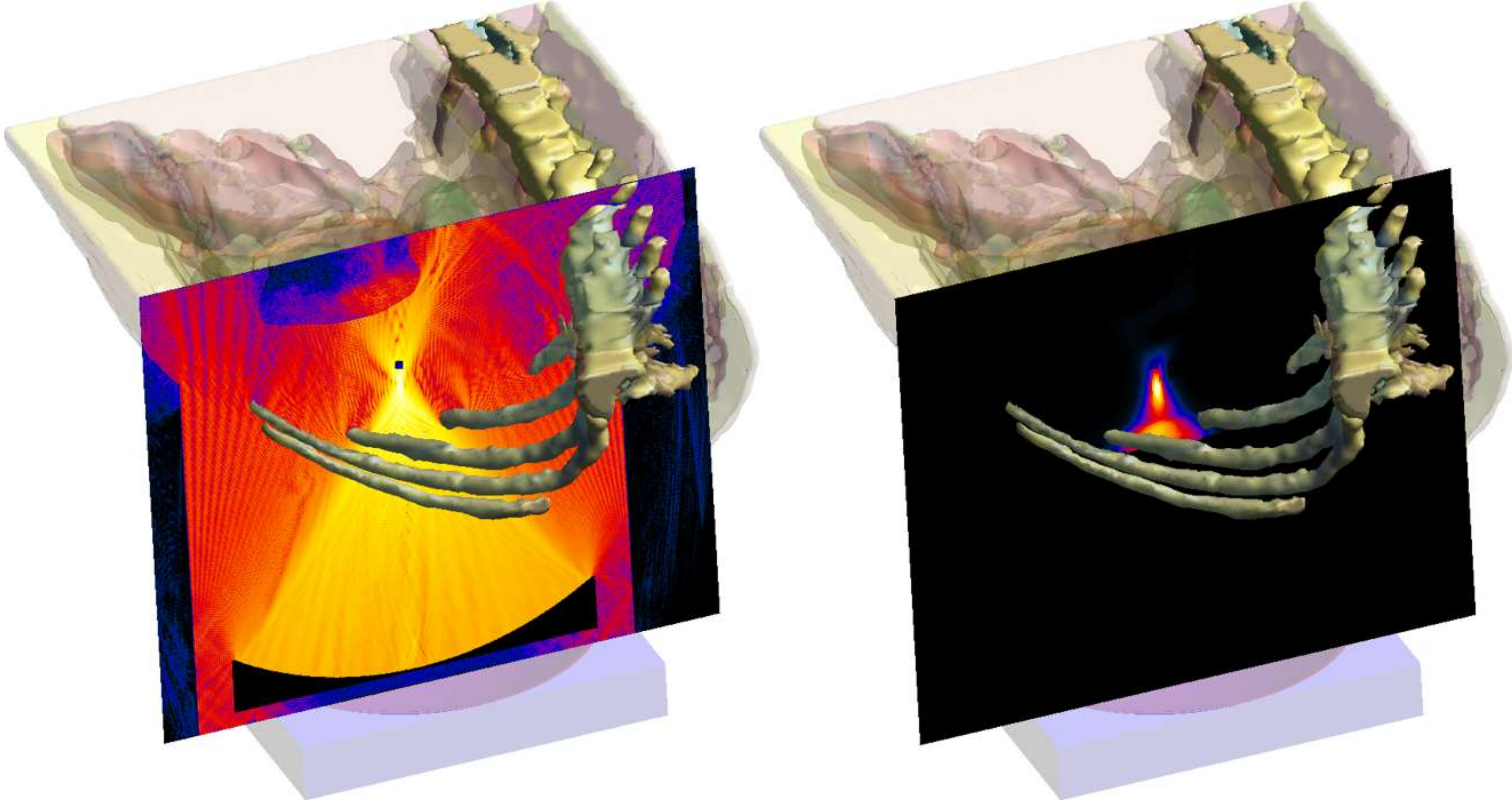








Renal & Hepatic Tumor Ablation II



Conclusions

- developed framework can be applied to investigate large range of relevant applications
  - tumor ablation
  - functional neurosurgery
  - reversible BBB opening
  - applicator development

Part III: US & Thermal Modeling of tcMRgFUS

- Introduction
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Introduction: Simulations

- why simulations?
  - treatment planning (prediction & optimization of focus size, position & intensity)
  - risk assessment & reduction (standing waves, secondary foci → hemorrhages)
  - steering range increase (safely focus in currently unreachable areas)
  - prediction/prevention of skull heating
  - parameter sensitivity studies
  - technical optimization: applicator development
- requirements:
  - patient specific
  - fast & high-resolution
  - full-wave modeling (especially for applicators without principal propagation direction, e.g. ExAblate) in inhomogeneous anatomies
  - temperature and effect prediction (e.g. lesion size)

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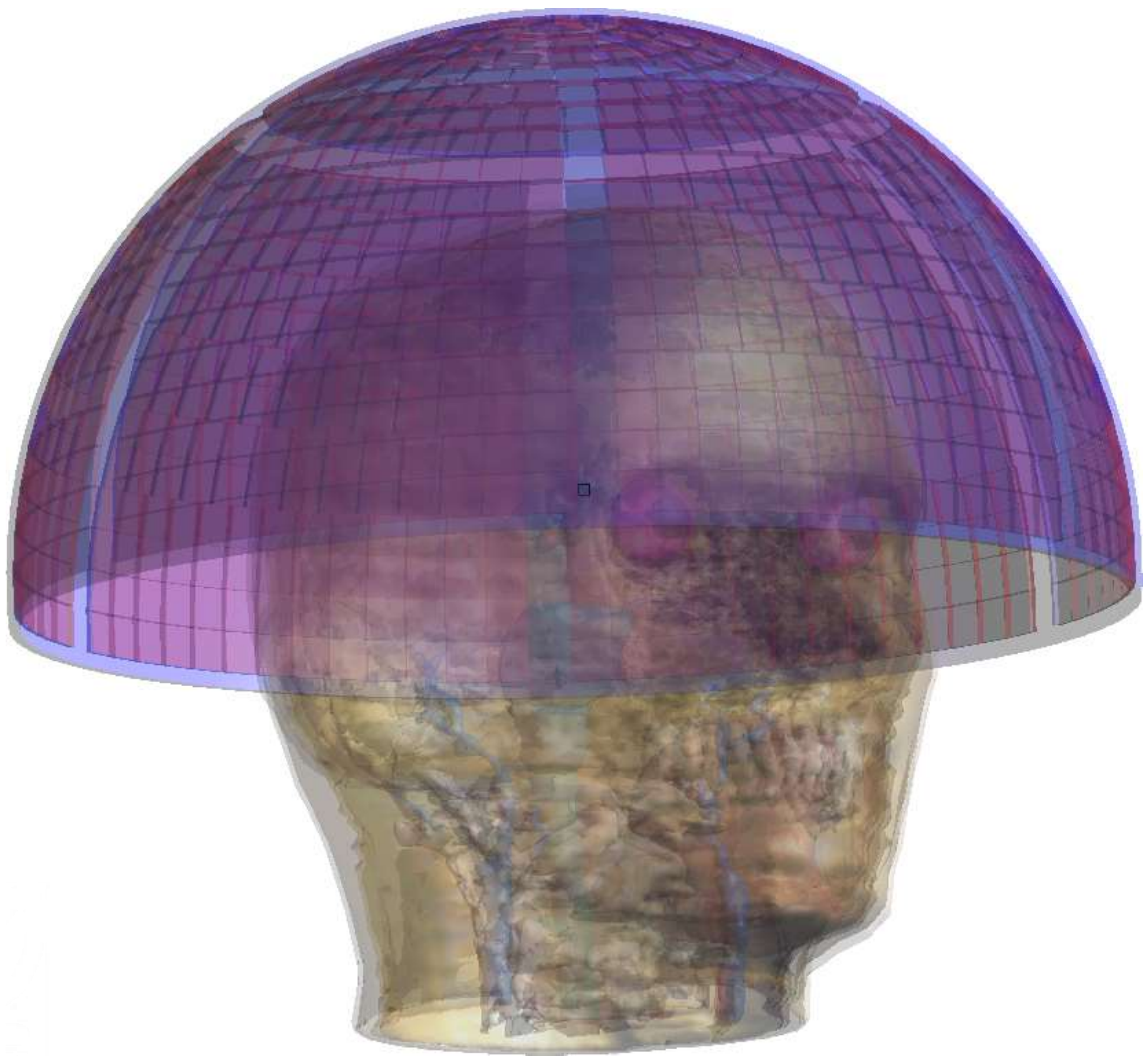
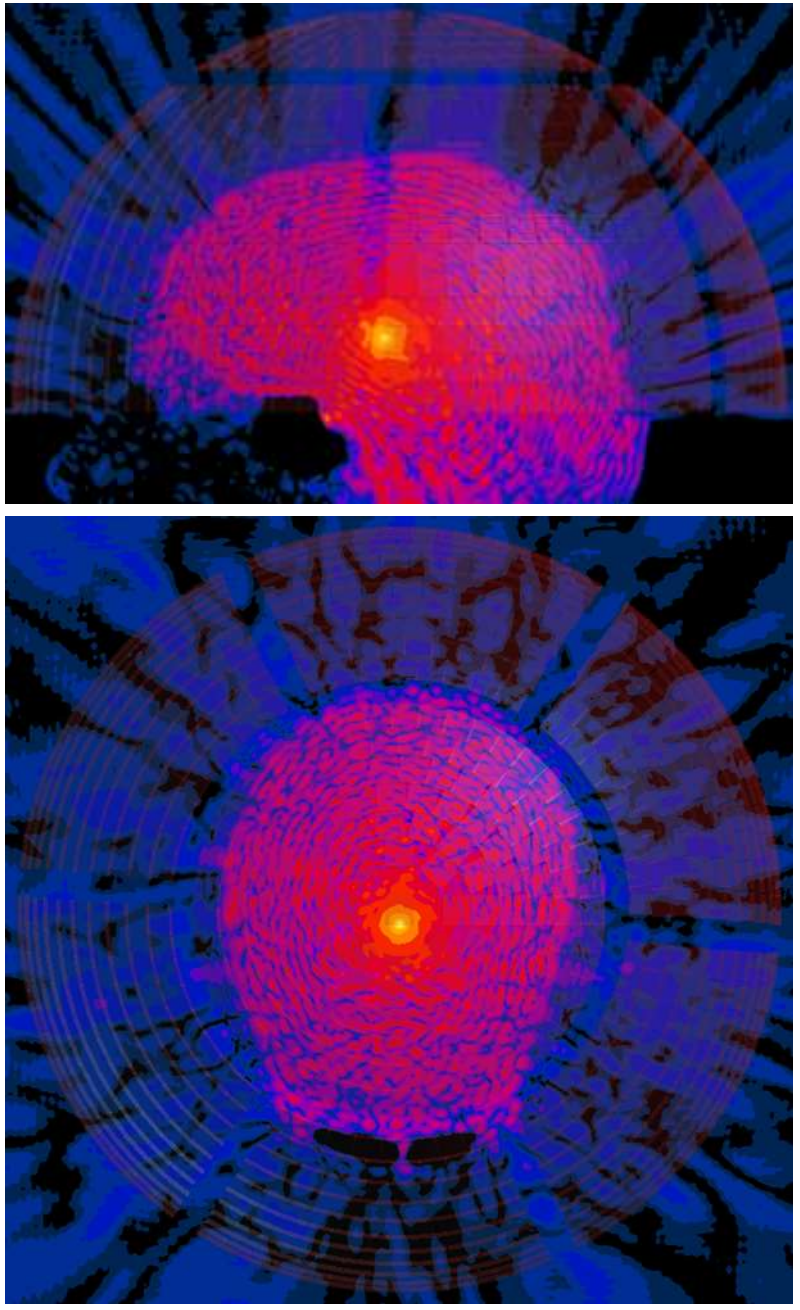
Simulations: US Setup

- applicator: ExAblate4000
  - 1024 transducer elements (area: ~1cm^2)
  - 230kHz
  - focal depth: 150mm
- head model: Duke (Virtual Population)
  - segmented from hi-res MR data of 34yr male volunteer
  - 45 tissues distinguished in the head
- simulation setup:
  - target in the thalamus: (0.0mm, -5.7mm, 22.8mm) off geometric focus



Simulations: US Simulations

- inverse propagation simulation
- element phasors:
  - distance-based / simulation-based
  - normalized to 1kW total acoustic power
- forward propagation simulation:
  - distance-based phases, fixed (120kPa) amplitudes
  - simulation-based phases, fixed (120kPa) amplitudes
  - simulation-based phases, simulation-based (norm. to 120kPa) amplitudes:
    - linear
    - non-linear: base & 1st harmonic



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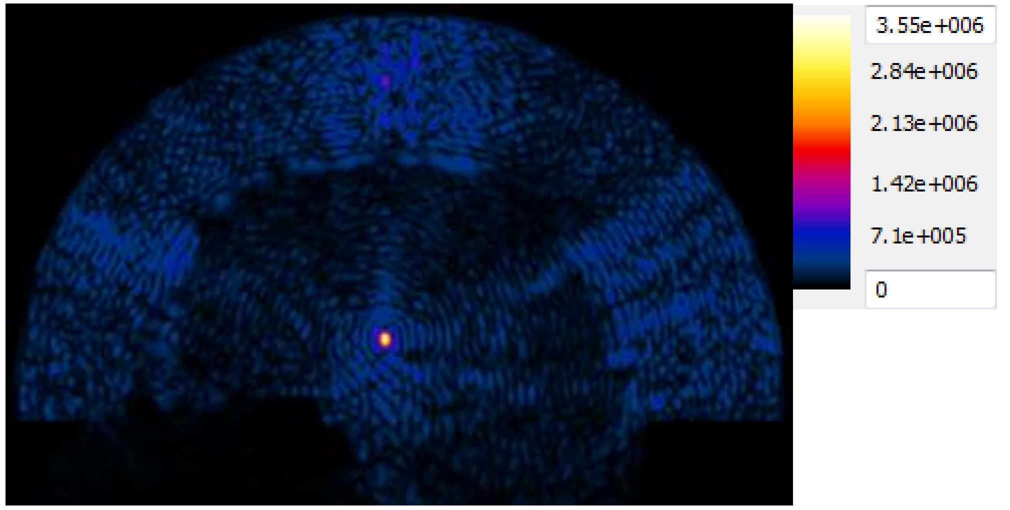

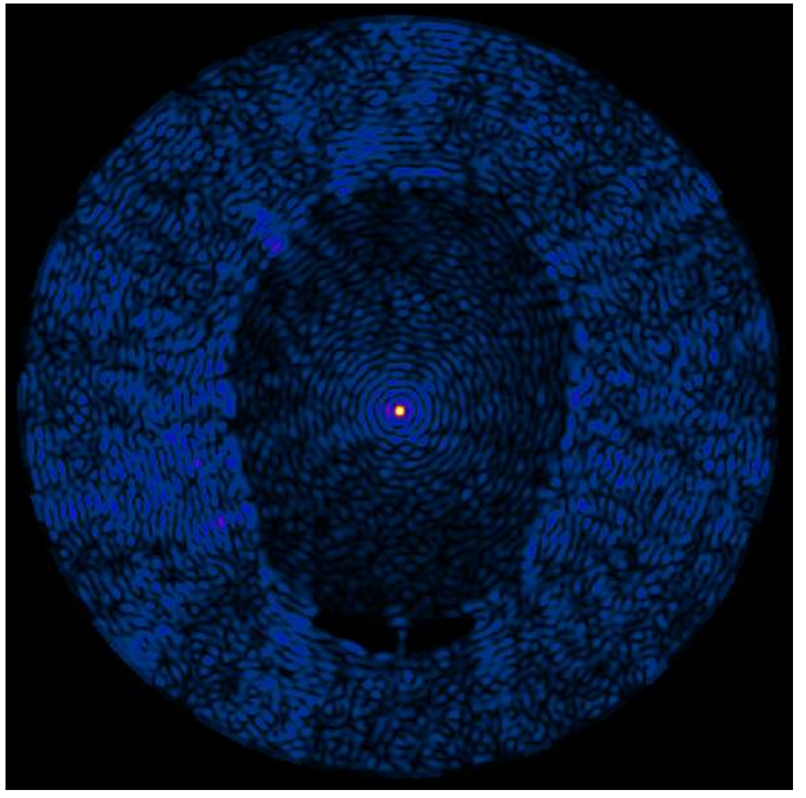

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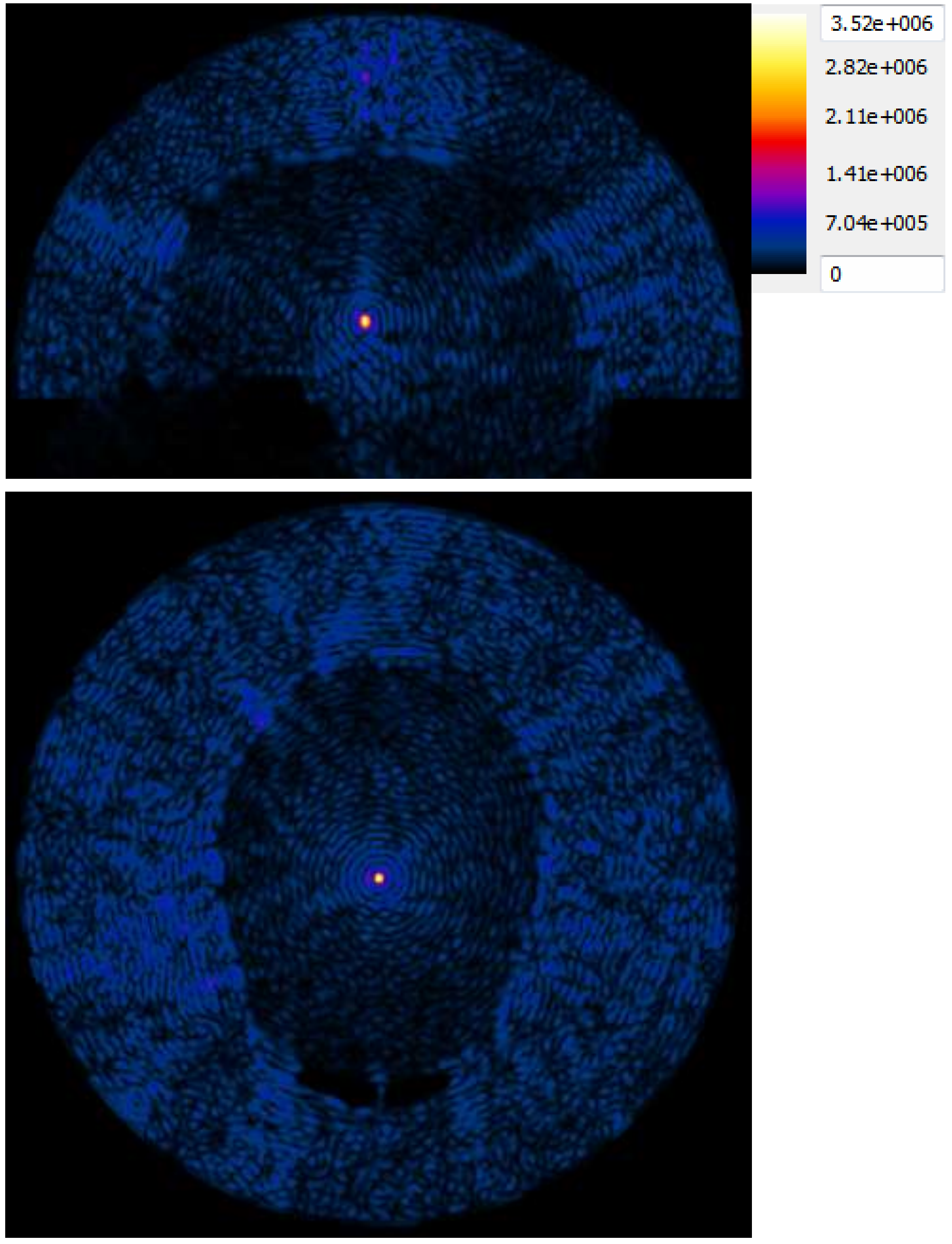
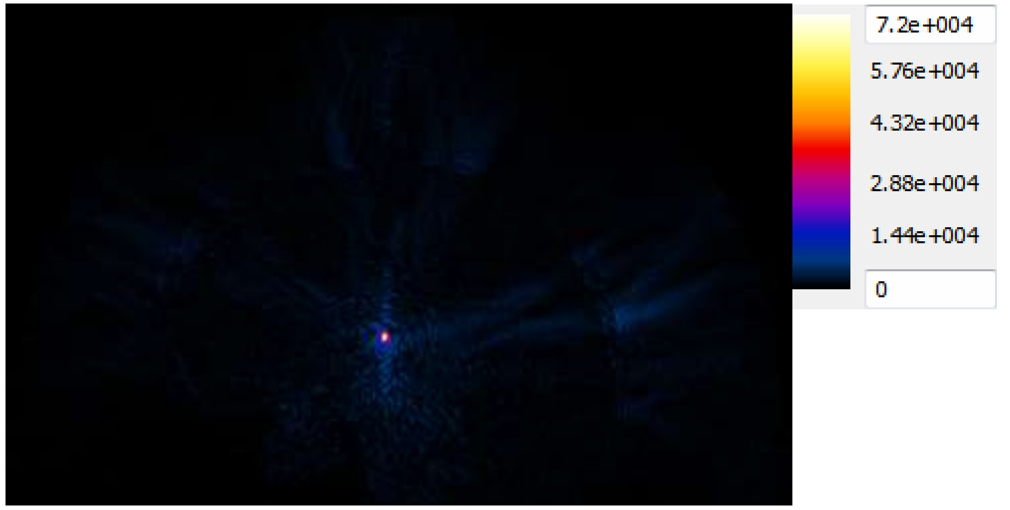
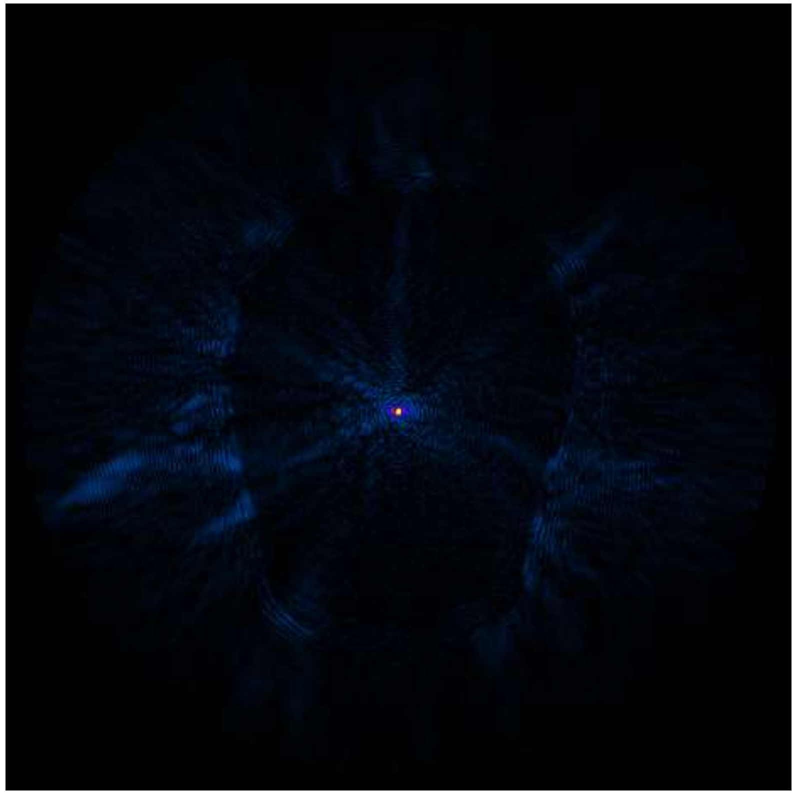
  - simulation-based phases, fixed (120kPa) amplitudes
  - simulation-based phases, simulation-based (norm. to 120kPa) amplitudes:
    - linear
    - non-linear: base & 1st harmonic



Simulations: US Simulations

- inverse propagation simulation
- element phasors:
  - distance-based / simulation-based
  - normalized to 1kW total acoustic power
- forward propagation simulation
  - distance-based phases, fixed (120kPa) amplitudes
  - simulation-based phases, fixed (120kPa) amplitudes
  - simulation-based phases, simulation-based (norm. to 120kPa) amplitudes:
    - linear
    - non-linear: base & 1st harmonic





Simulations: US Simulations

- inverse propagation simulation
- element phasors:
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  - normalized to 1kW total acoustic power
- forward propagation simulation
  - distance-based phases, fixed (120kPa) amplitudes
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  - simulation-based phases, simulation-based (norm. to 120kPa) amplitudes:
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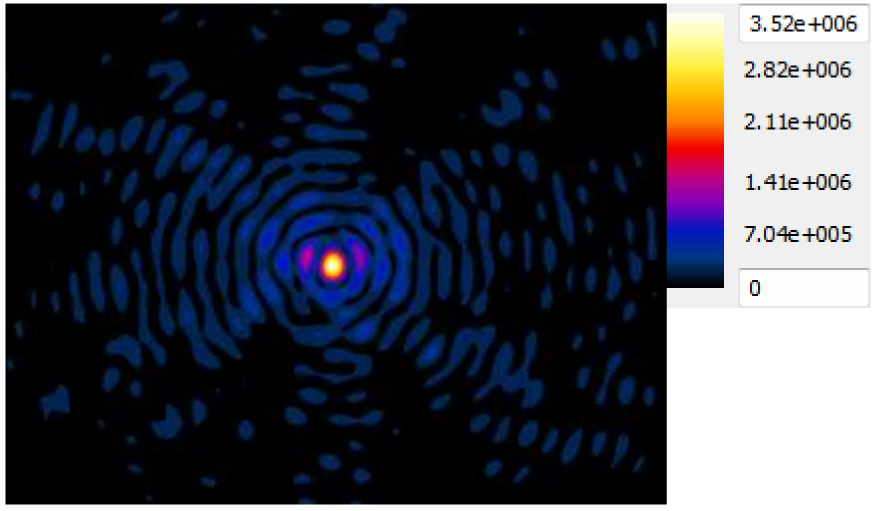
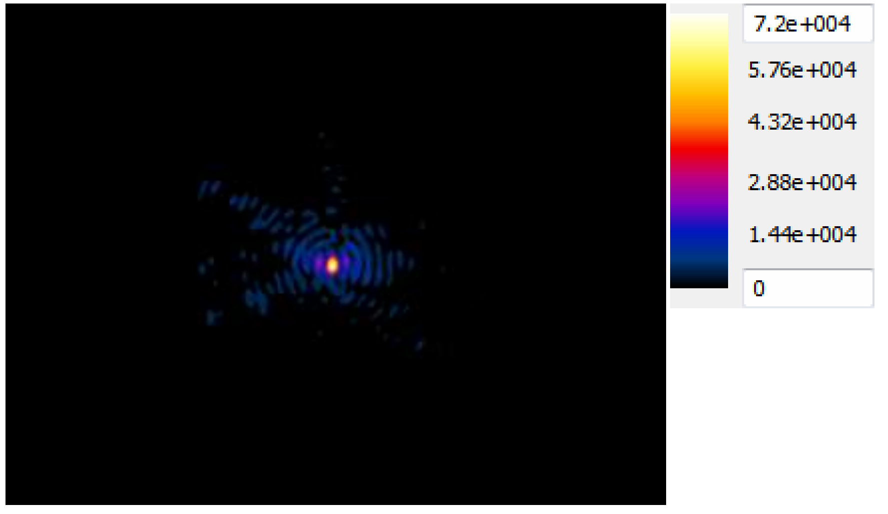
    - non-linear: base & 1st harmonic



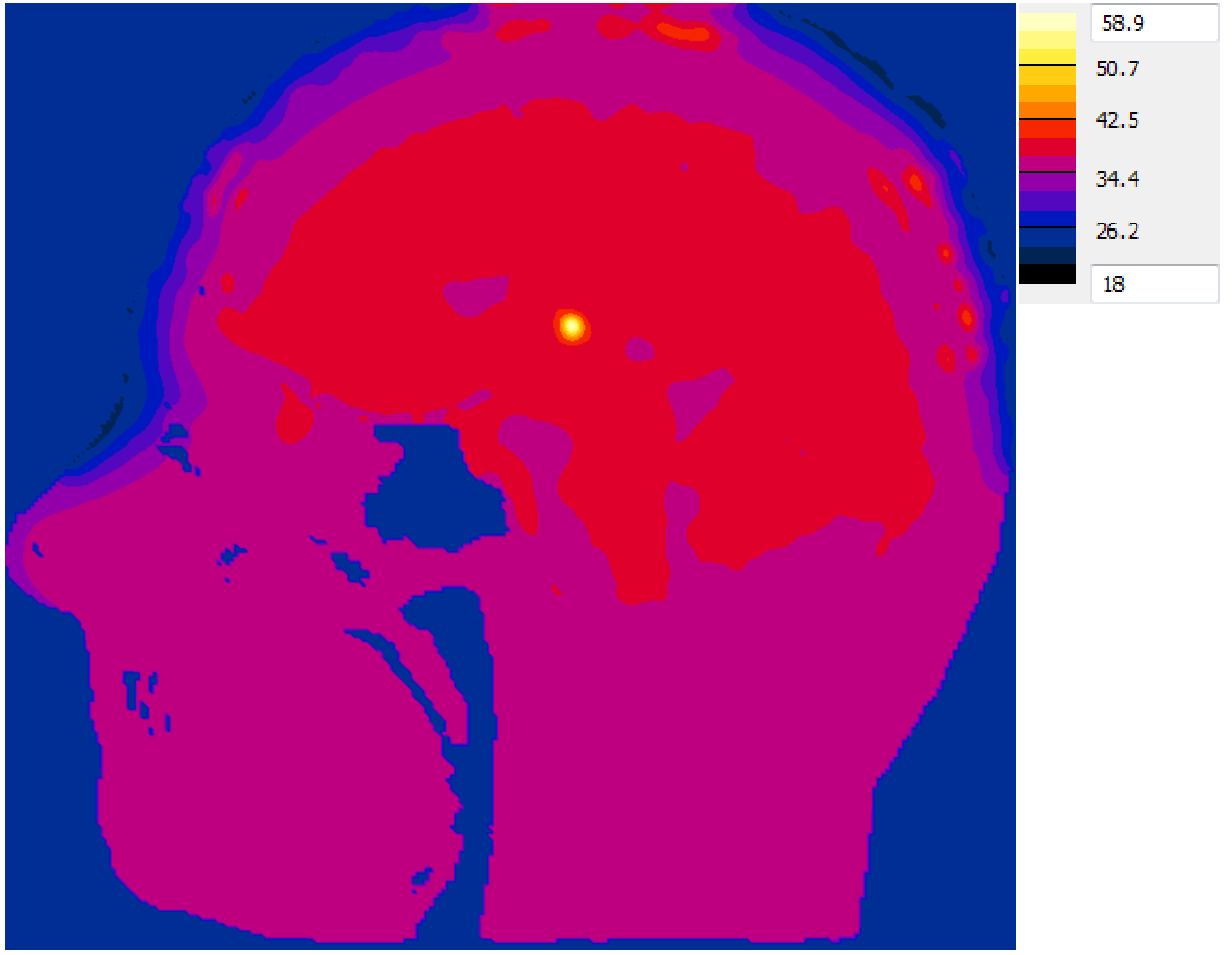


Simulations: Thermal Simulations

- heat source:

$$Q = a\frac{p^2}{\rho c}$$

- settings (all steering approaches):
  - 30’ without sonication to reach thermal equilibrium + 20” of sonication
  - convective boundary conditions for water (16ºC) and air (25ºC) cooling
  - impact of vascular shutdown on temperature increase

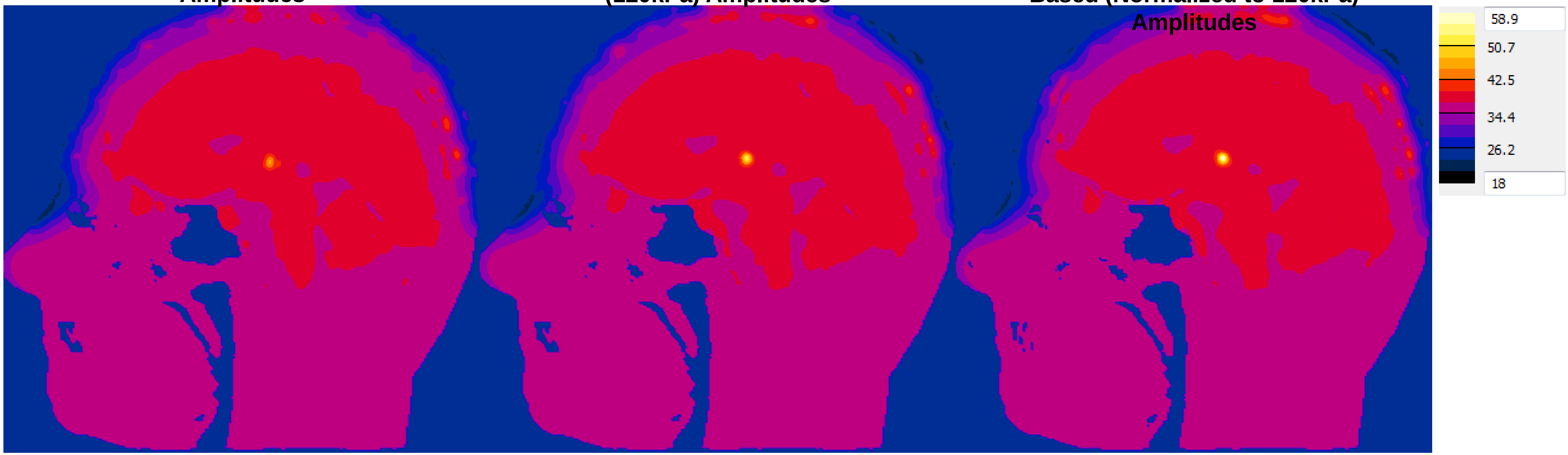


Part III: US & Thermal Modeling of tcMRgFUS

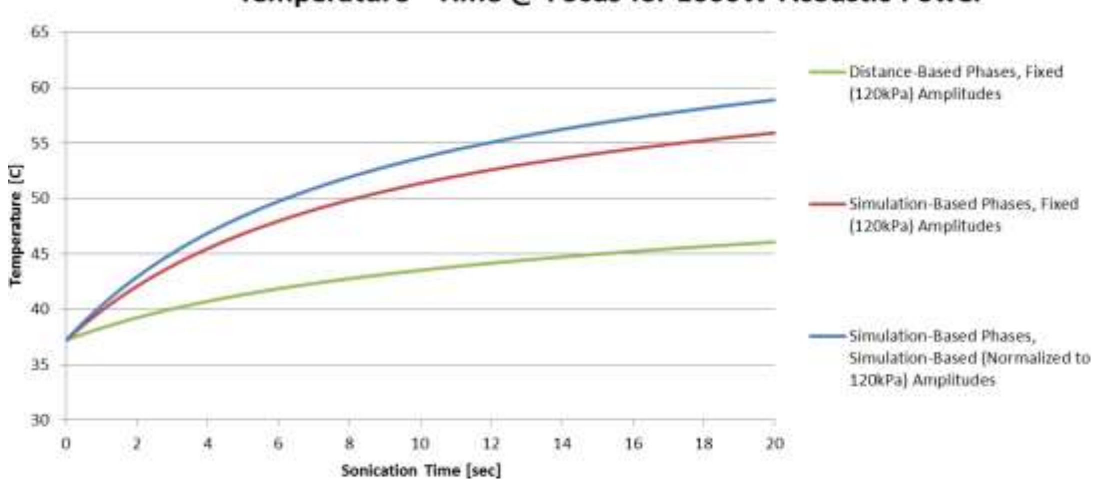
- Introduction
- US & Thermal Simulations
- Results
- Conclusions & Future Work

Results: Temperatures & Lesion Sizes

Distance-Based Phases, Fixed (120kPa) Amplitudes | **Simulation-Based Phases, Fixed (120kPa) Amplitudes** | **Simulation-Based Phases, Simulation-Based (Normalized to 120kPa) Amplitudes**



Temperature - Time @ Focus for 1000W Acoustic Power



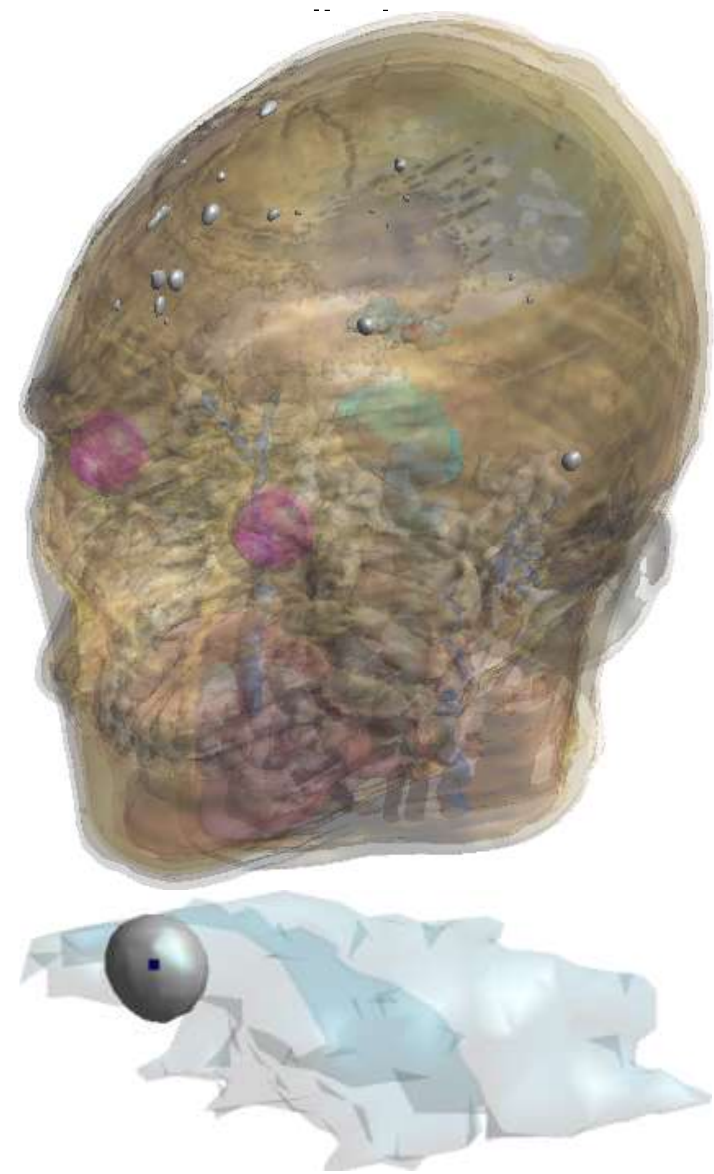
	Temperature	Focus Size [mm]											
		FWHM			45ºC			50ºC			55ºC		
	Max	dX	dY	dZ	dX	dY	dZ	dX	dY	dZ	dX	dY	dZ
Distance-Based Phases, Fixed (120kPa) Amplitudes (focus off by 1.8mm on Z axis)	48.04	3.5	3.8	4.6	2.7	2.9	4.4	N/A	N/A	N/A	N/A	N/A	N/A
Simulation-Based Phases, Fixed (120kPa) Amplitudes	55.9	4	4.1	4.6	4.7	4.7	5.2	2.9	3	3.3	0.6	0.6	0.8
Simulation-Based Phases, Simulation-Based (Normalized to 120kPa) Amplitudes	58.88	4	4.1	4.5	5.2	5.1	5.5	3.4	3.4	3.9	2	1.9	2.3

Results: Temperature Iso-Surfaces: 45^{o}C

Distance-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Simulation-Based (Normalized to 120kPa)

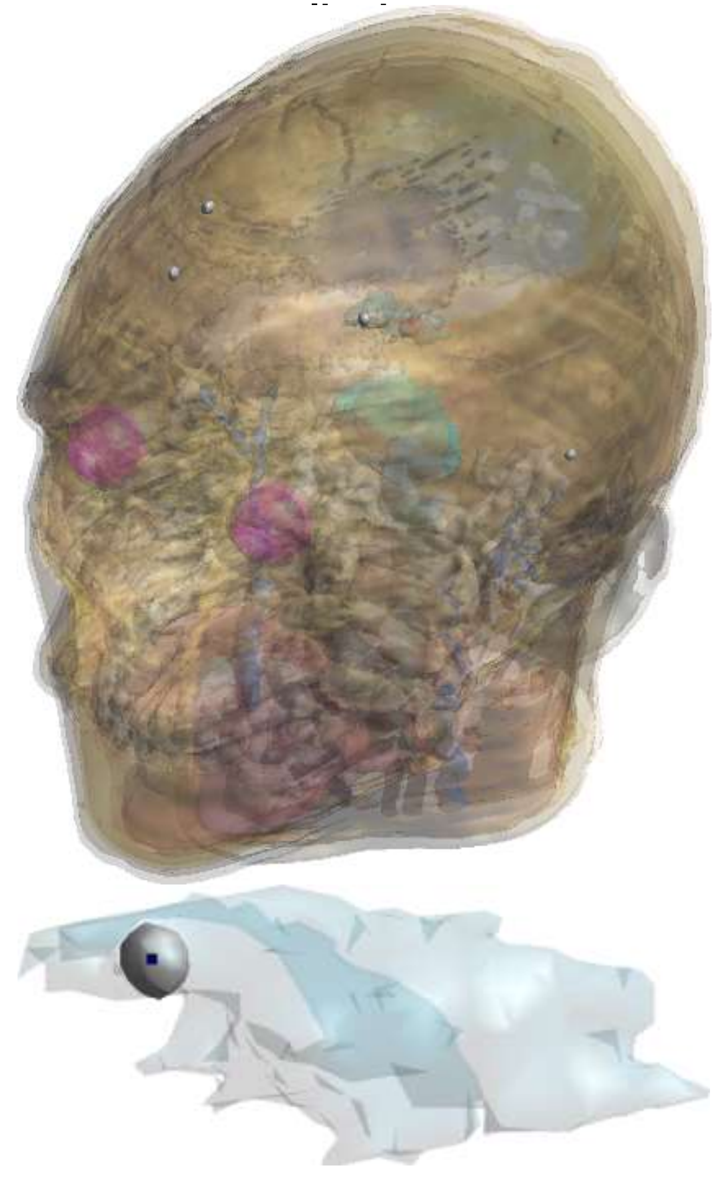


Results: Temperature Iso-Surfaces: 50ºC

Distance-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Fixed (120kPa) Amplitudes

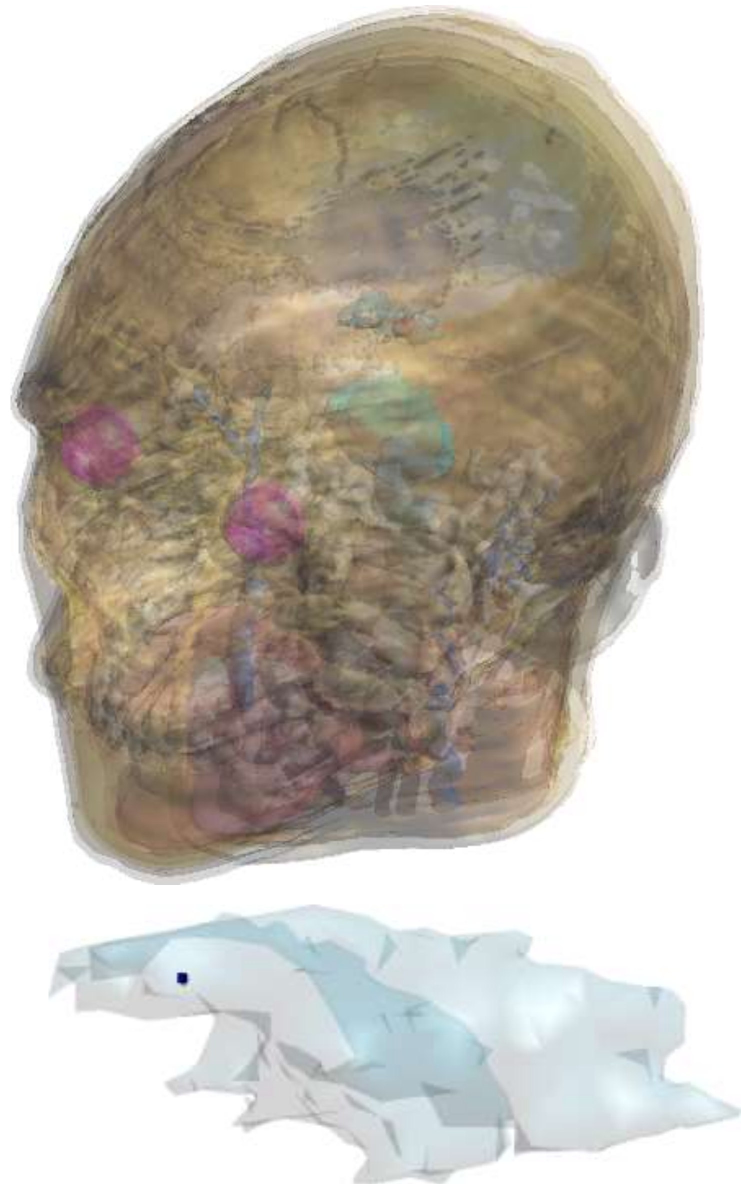
Simulation-Based Phases, Simulation-Based (Normalized to 120kPa)



Results: Temperature Iso-Surfaces: 55ºC

Distance-Based Phases, Fixed (120kPa) Amplitudes

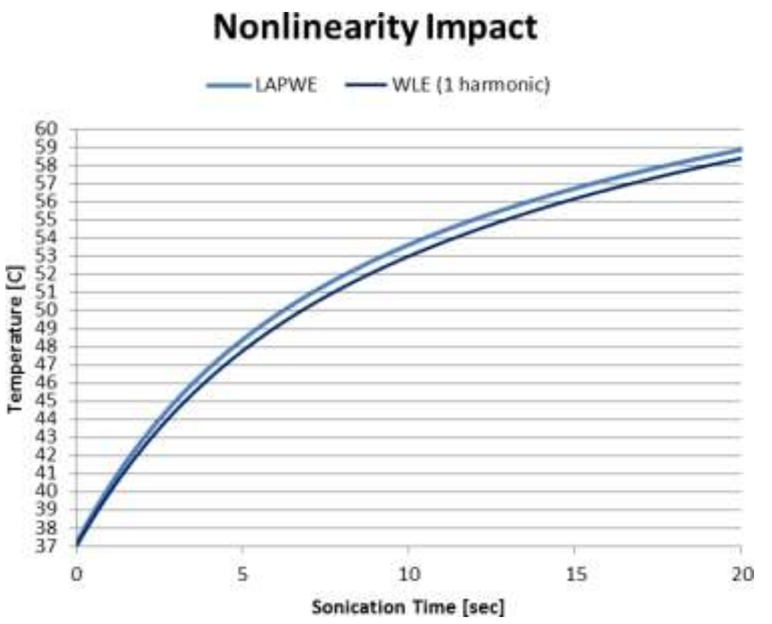
Simulation-Based Phases, Fixed (120kPa) Amplitudes

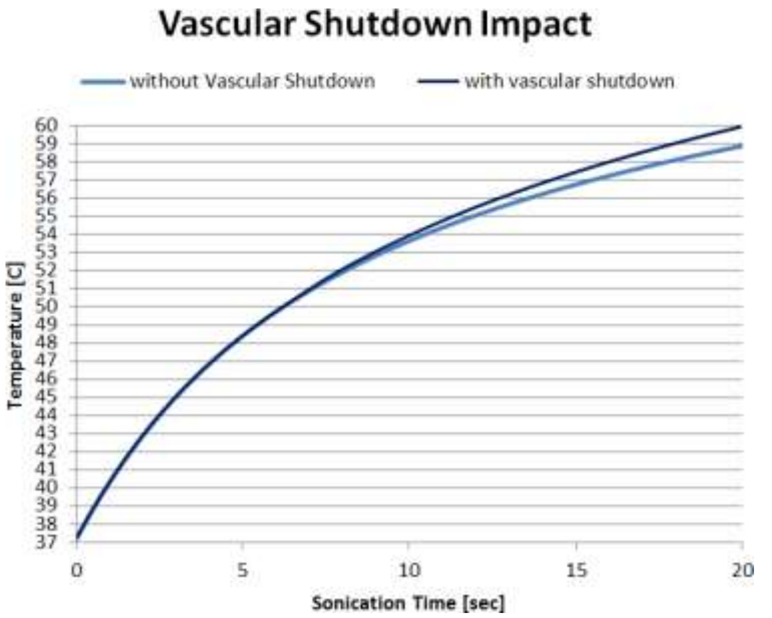


Simulation-Based Phases, Simulation-Based (Normalized to 120kPa)

Results: Non-linearity & Vascular Shutdown

- non-linear US propagation
  - performed for 3rd steering approach
  - negligible impact on pressure & temperature results
  - pressure amplitude & frequency not high enough to induce strong harmonics/energy deposition
- vascular shutdown
  - complete shutdown assumed between 50°C and 51°C
  - +1°C temperature in focus area





Part III: US & Thermal Modeling of tcMRgFUS

- Introduction
- US & Thermal Simulations
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Conclusions

- application to tissue ablation in the brain with ExAblate (quantitative)
  - full-wave, HPC enabled (~5’ for linear) US simulations with high anatomical and physical complexity
  - could help improve efficiency, increase attainable focus locations, reduce treatment time and risk
- examined
  - impact of focusing strategy & focus shifting
  - temperature increase
  - lesion shape & size
  - impact of non-linear US propagation
  - Impact of vascular shutdown

Future Work

- apply this approach to the 650KHz system
- extended validation
  - ultimate goal: ex-vivo/in-vivo MR thermometry validation
- optimization
  - alternative steering approaches
  - hot-spot reduction
  - time-modulated steering
  - goal weighting

Outline

- Introduction
- Part I: FUS/HIFU Multiphysics Framework
- Part II: Applications
- Part III: US & Thermal Modeling of tcMRgFUS
- Conclusions & Future Work
- Acknowledgements & Funding

Conclusions

- comprehensive framework for modeling of FUS and induced effects has been developed
  - full-wave acoustic solver ideally suited for complex wave propagation in inhomogeneous anatomical models
  - cavitation modeling
  - induced heating and tissue damage
  - integrated into multi-physics framework (flow, EM, CRD, mechanics…)
  - HPC enabled, high resolution
- realism in simulations
  - detailed anatomical models & segmentation platform for model creation
  - comprehensive tissue parameter databases, towards personalized tissue properties and dynamic tissue models
  - sophisticated thermal models (perfusion/thermoregulation tissue damage, dose)
- framework has been applied to wide range of relevant applications

Conclusions

- can be used for quantitative assessments and investigation of mechanisms / parameter studies (example: tcFUS)
- goal: patient specific treatment optimization

future work:

- importance of validation of software and models; ongoing
- optimization of steering

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