Understanding Cerebral Aneurysms through HPC-based Computational Modelling

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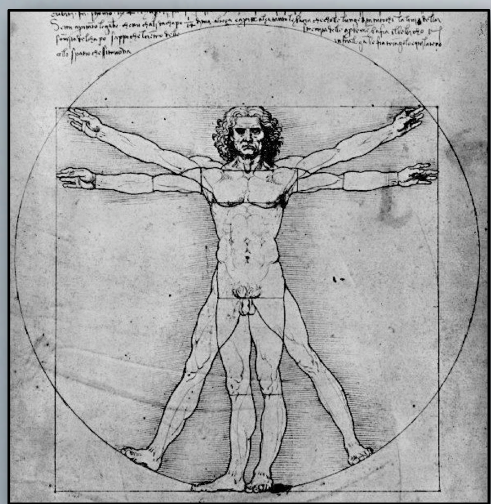
Severo Ochoa Research Seminar Series

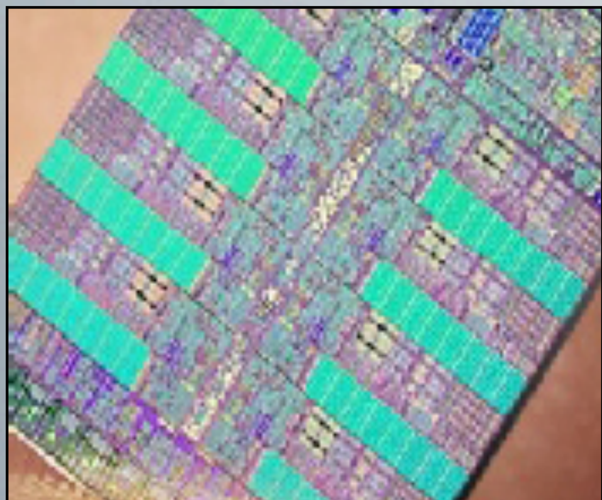
EXCELENCIA SEVERO OCHOA

Barcelona Supercomputing Center



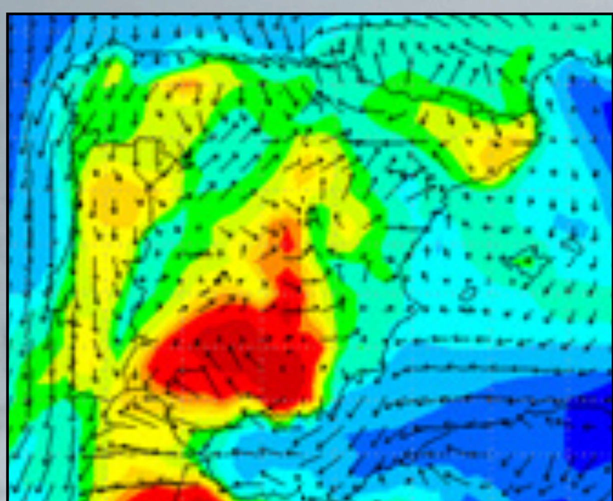
BSC & HPC in Biomedical Research

BSC-CNS Research Departments



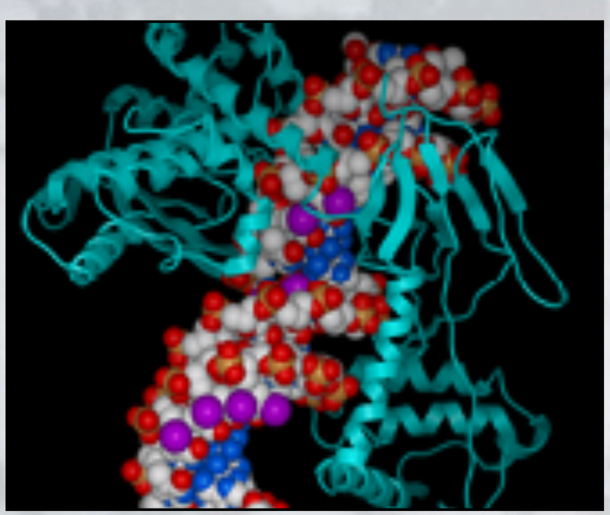
Computer Science

Performance tools
Computer architectures
Programming models



Earth Science

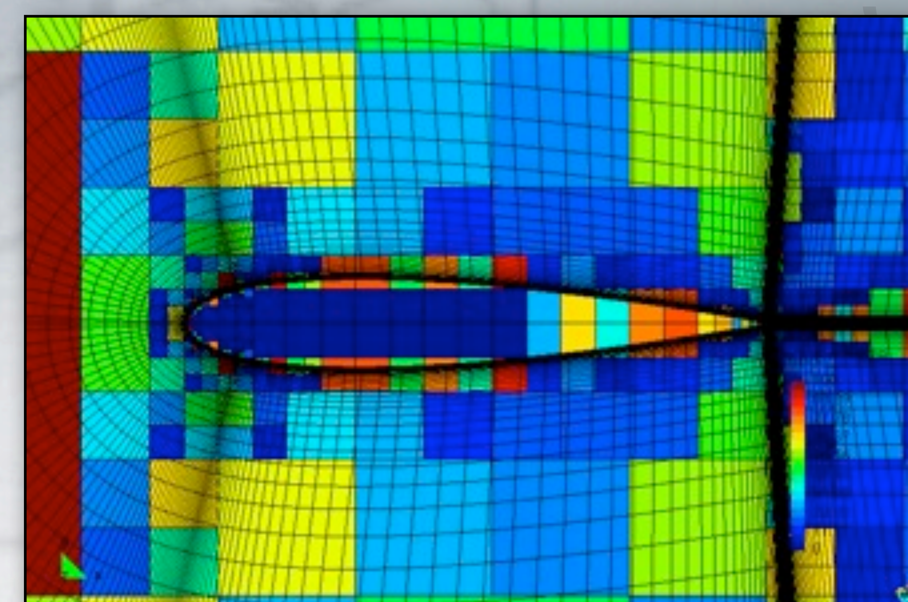
Air quality



Life Science

Genomics
Proteomics

Computer Applications in Science
and Engineering
CASE



CASE Department - Application lines

Environment

Energy

Aerospace

Trains and Automotive

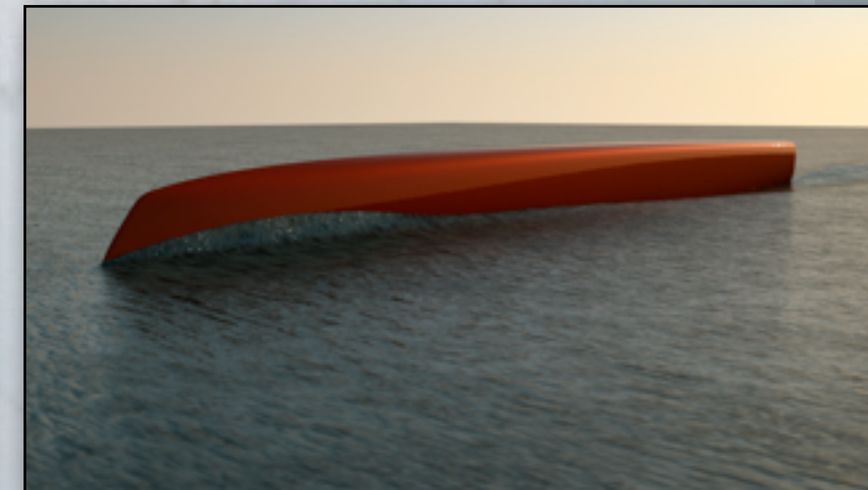
Oil and Gas

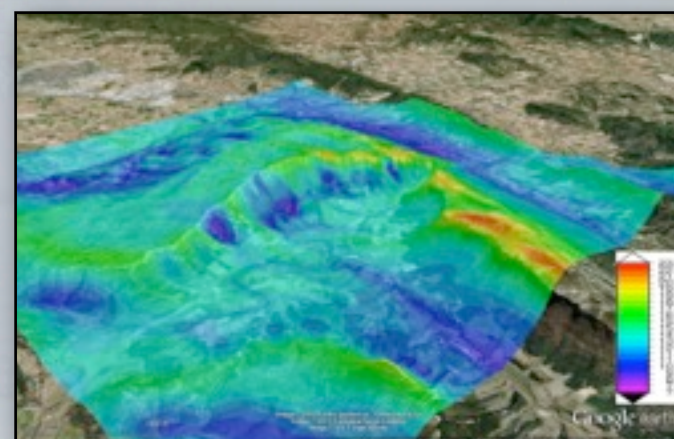
Artificial Societies

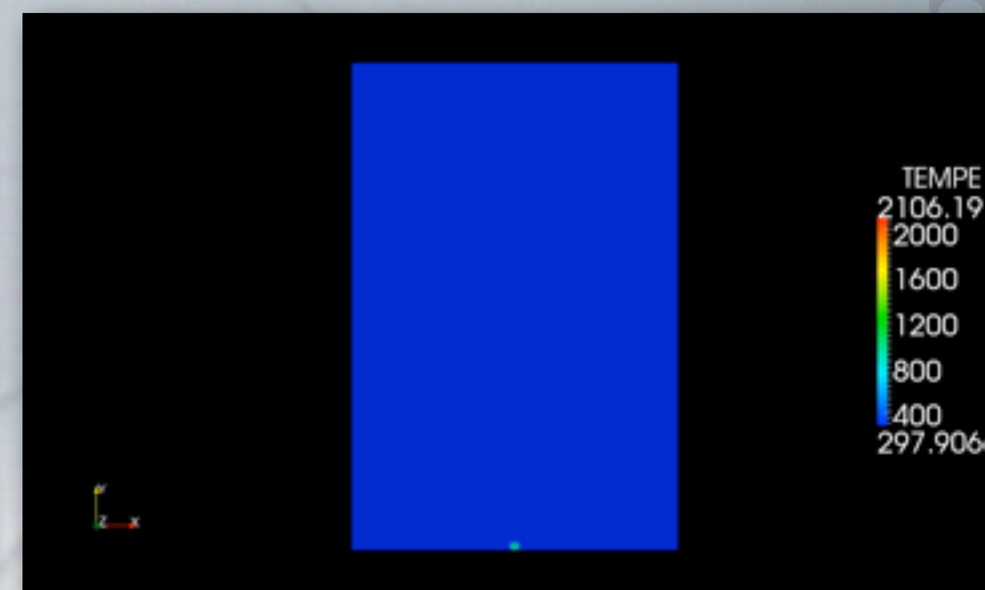
High Energy Physics

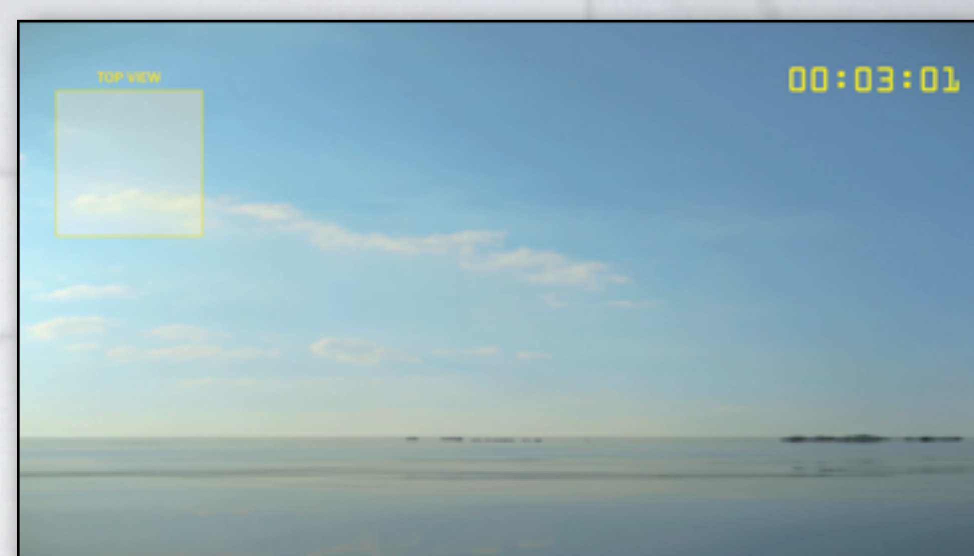
Materials Sciences

Biomechanics





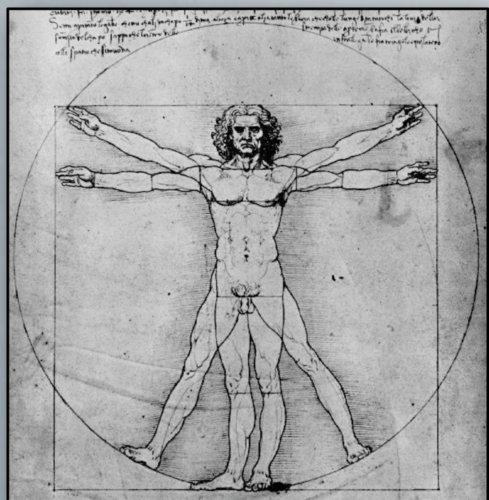




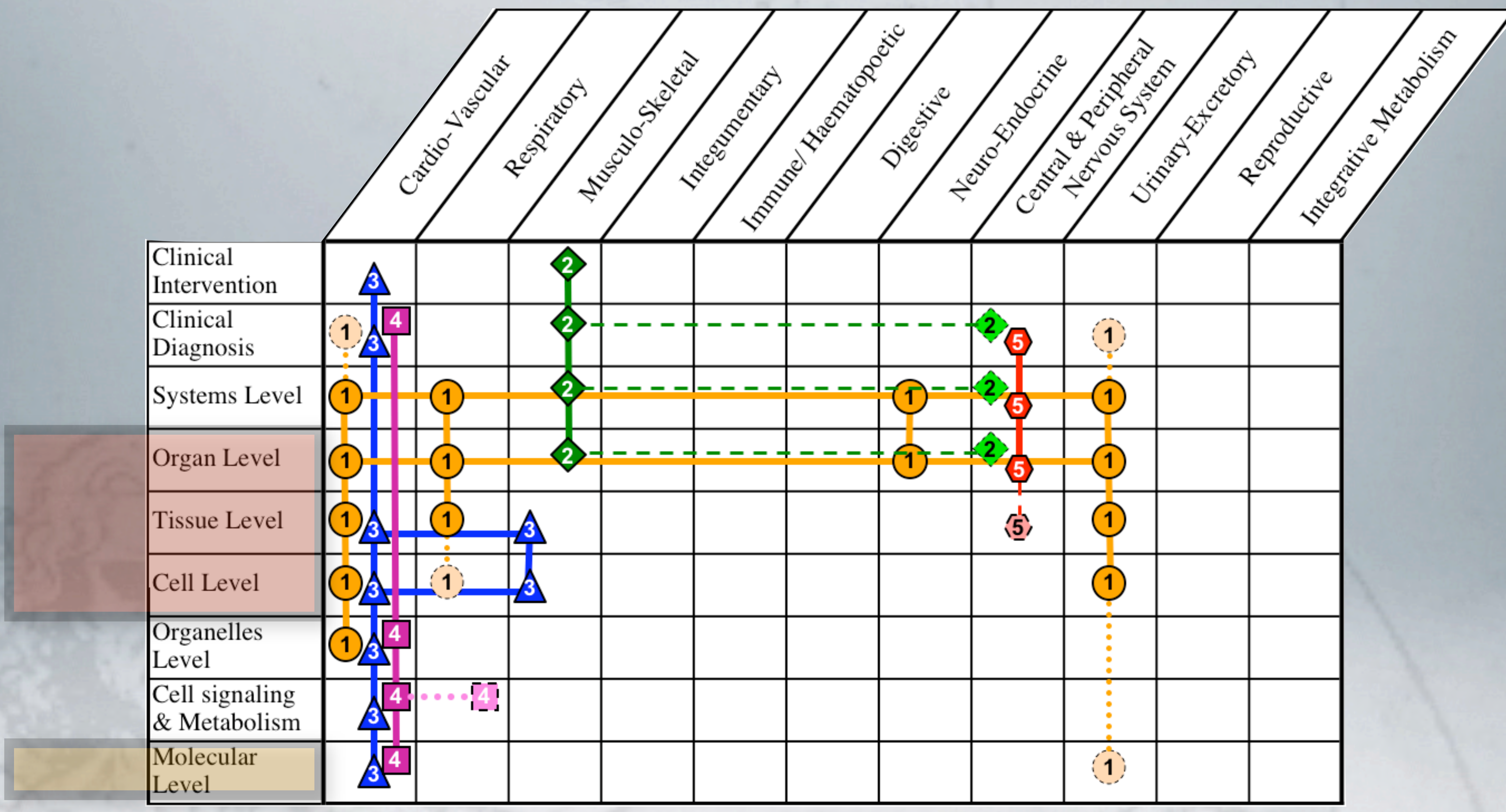
BSC-CNS is the only supercomputing center with +60 researchers devoted to HPC-based Biomedical Research:

Bioinformatics (45 Life Science Department)

Biomechanics (15 - 20 CASE Department)



Computational Biomechanics



Organ Systems vs. Levels of Organizations

Extracted from S.R. Thomas et al., VPH Exemplar Project Strategy Document. Deliverable 9, VPH NoE. 2008

Keywords

Drug action

Drug delivery

Treatment planning

Medical training

Design: prosthesis, stents, valves, bio-materials, experimental and manufacturing kits...

Study surgical procedures and treatments

...

Targets

Biomedical research: know better and deeper, improve diagnose and treatment

Pharma industry: reduce time and costs of “from-design-to-market” cycle

Medical devices manufacturers: design better devices

Medical doctors:

Healing is the final objective
Diagnose and treatment planning

Understanding biological systems
Physiological models

They provide the main motivation and insight to the problem

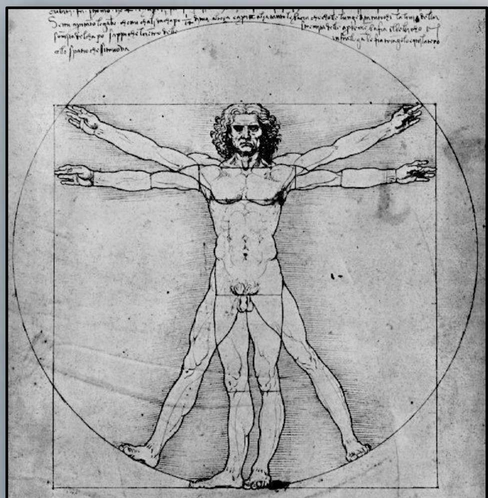
Computational scientists:

Developing computational tools to run simulations

Provide the required simulation capacity

Bio-engineers:

Develop the Physiological models
Deal with medical image processing
Design data acquisition tools



Alya Red

HPC-based Biomechanical Simulations

The Alya System

Multi-physics modular code for High Performance Computational Mechanics

Born in 2004

Designed from scratch to solve multiphysics problems with high parallel efficiency

Numerical solution of PDE's

Variational methods are preferred (FEM, FVM)

Hybrid meshes, non-conforming meshes

Explicit and Implicit formulations

Coupling between multi-physics (loose or strong)

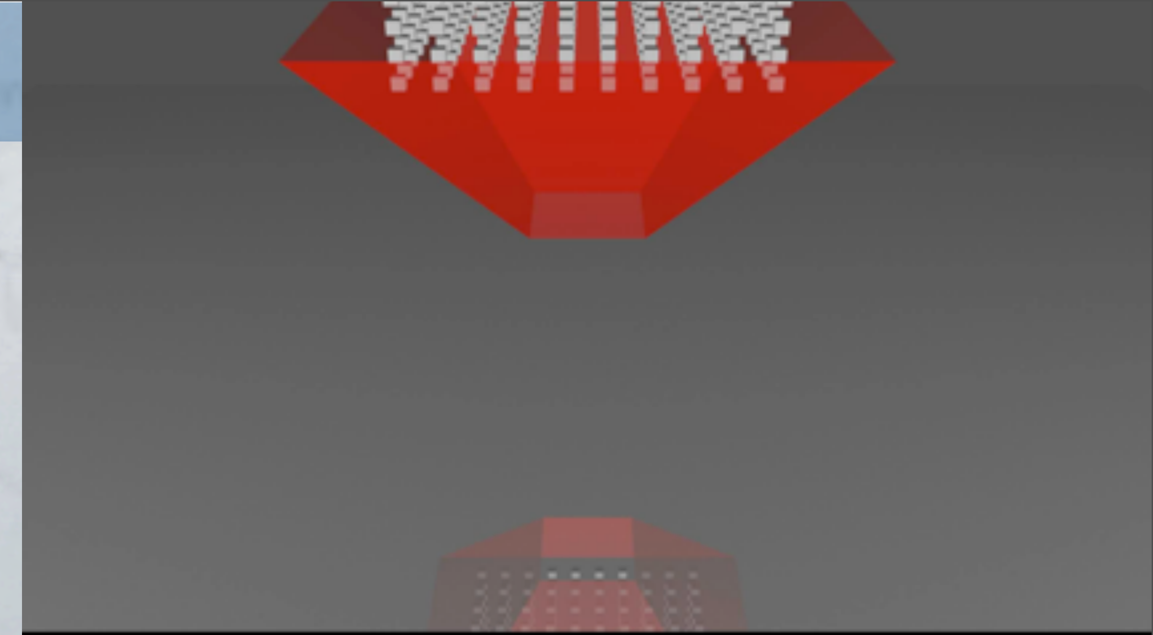
Advanced meshing issues

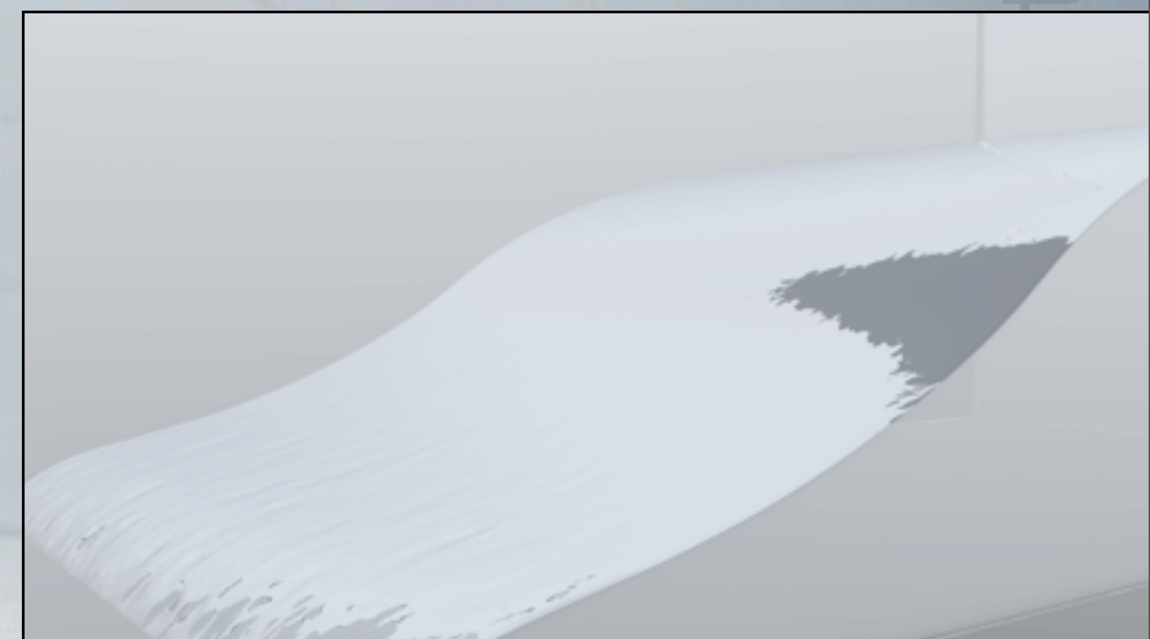
Parallelization by MPI and OpenMP

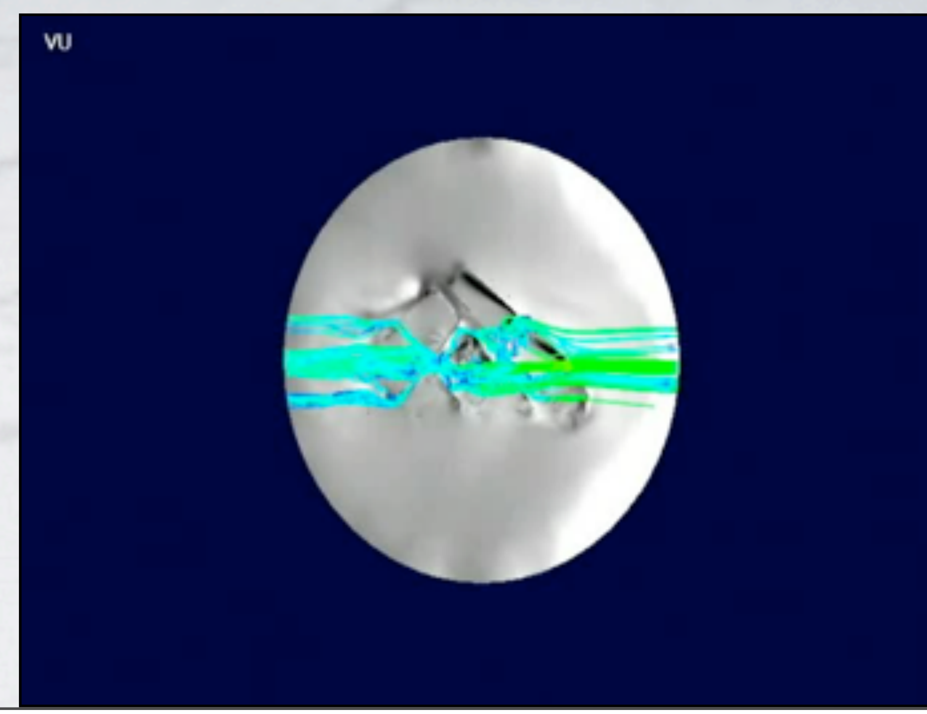
Automatic mesh partition using Metis

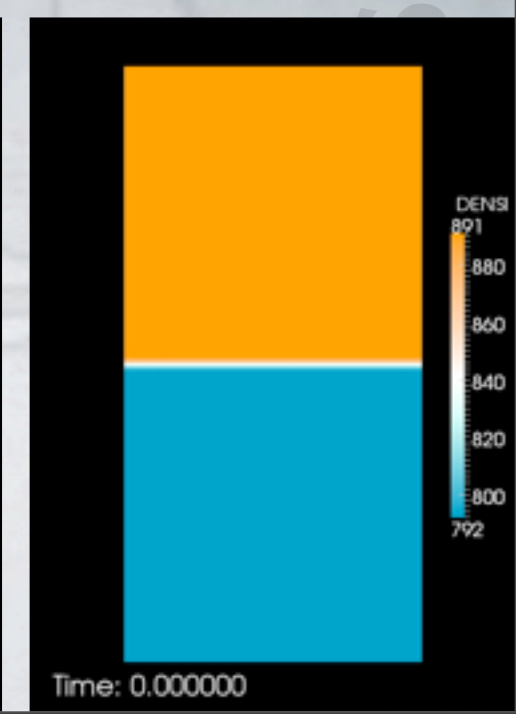
Portability is a must

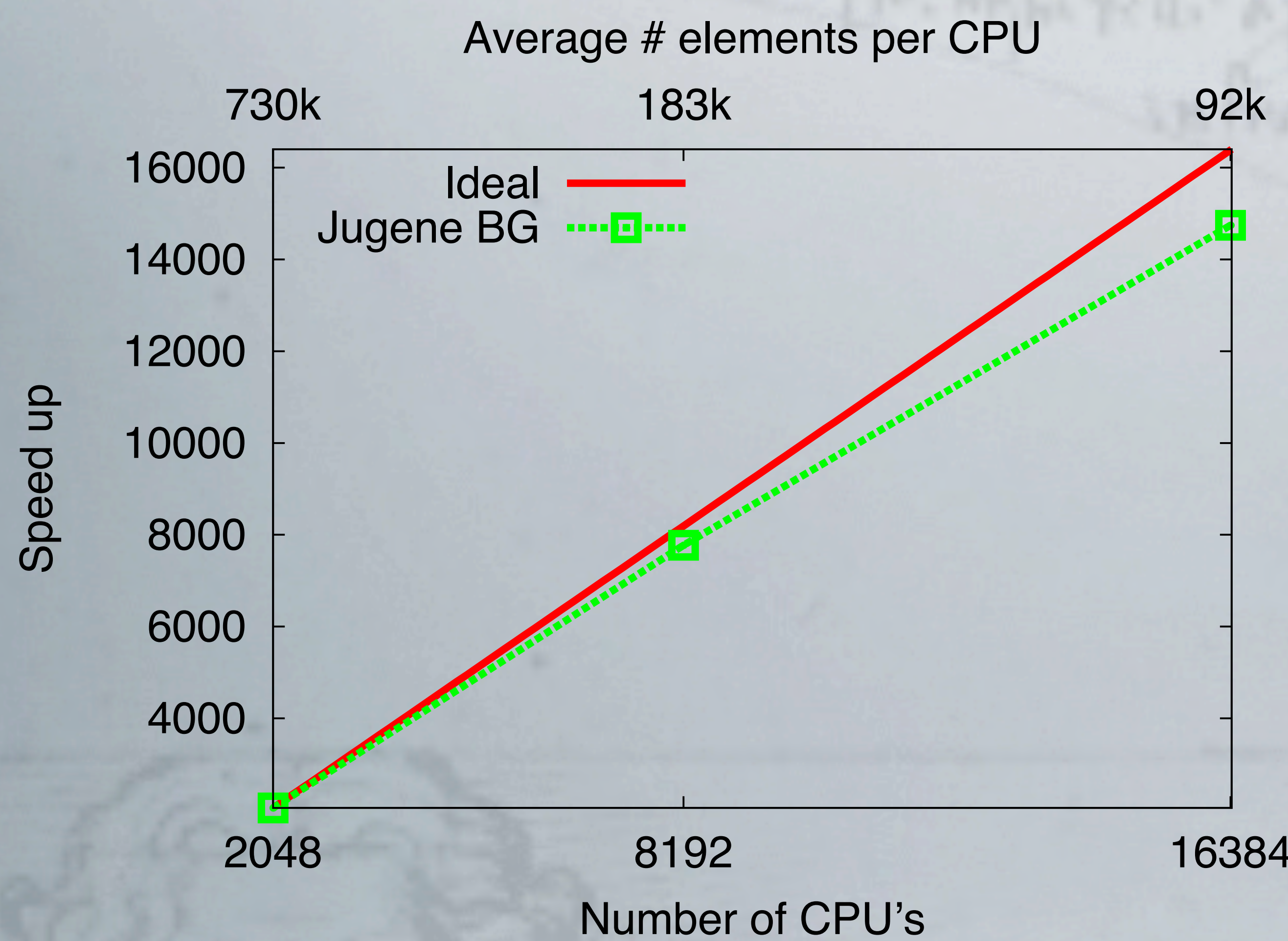
Porting to new architectures: MICs, GPUs, ...

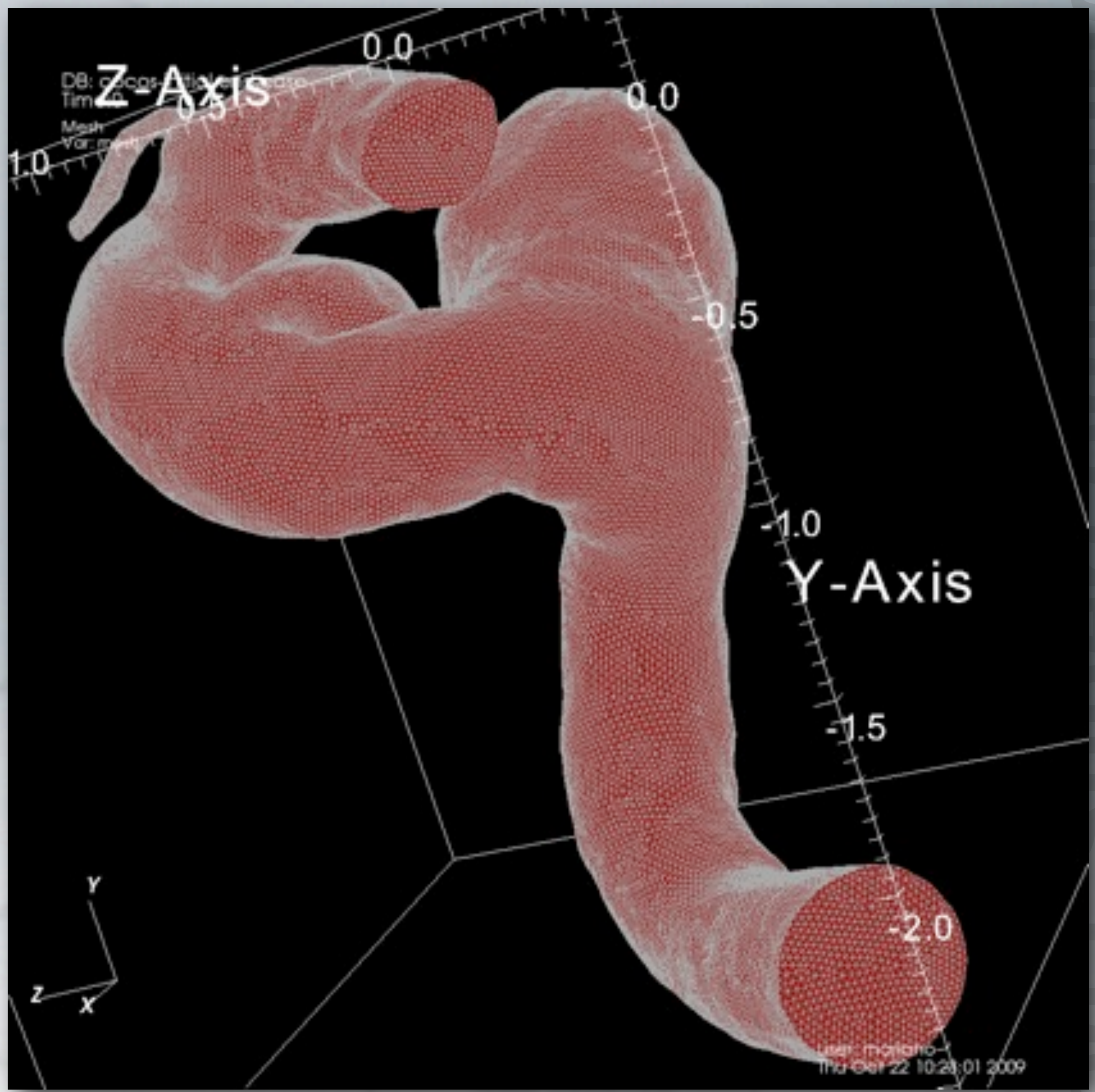












Benchmark

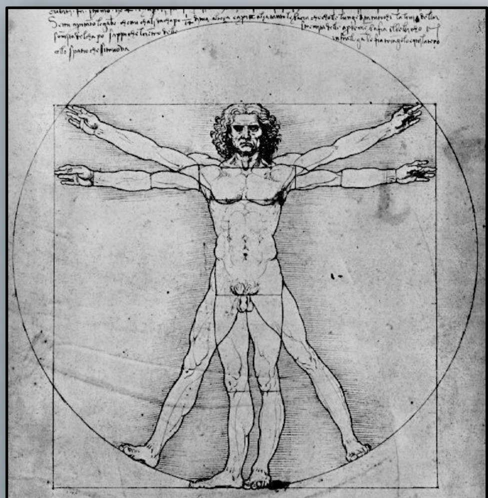
Aneurism geometry provided by R. Cebral

Uniform refinement up to 1.6B tetrahedra

Incompressible flow

Implicit formulation

Algebraic Fractional Step: BCGStab + Deflated CG



Alya Red

HPC-based Biomechanical Simulations

- Cardiac computational models
- Respiratory system
- **Cerebral aneurisms rupture risk**
- Long skeletal muscles
- Biomaterials and tissue engineering

Cerebral Aneurysms

High prevalence

Devastating consequences

Low risk if not treated...

... but treatment carries risk

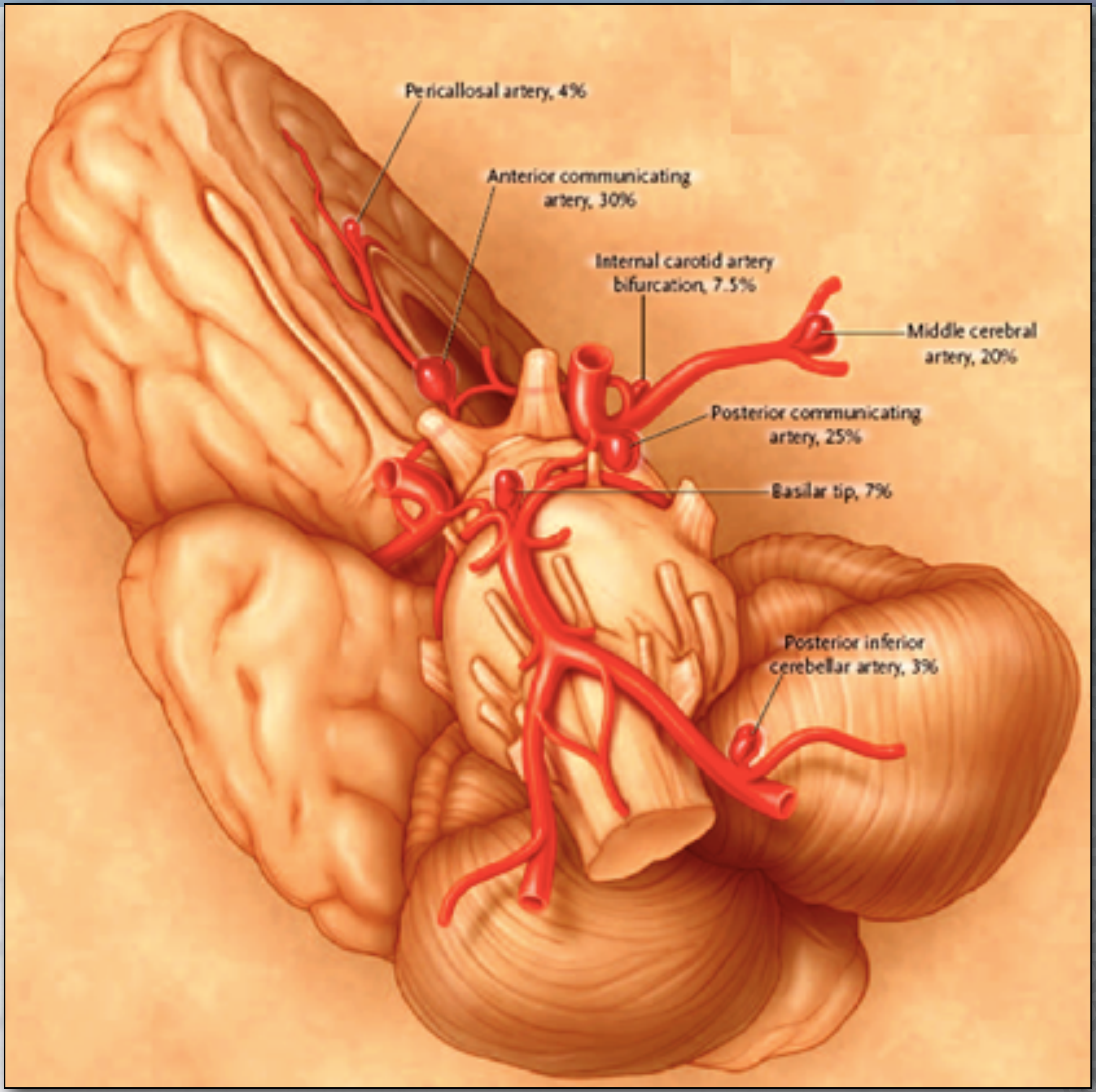
Incidentally detected

5% have aneurysms but

0.1% will broke

50% of the broken cause death

60% of survivors suffer strong impairment



High prevalence

Devastating consequences

Low risk if not treated...

... but treatment carries risk

Incidentally detected

... then, **treat or observe**?

Observe:

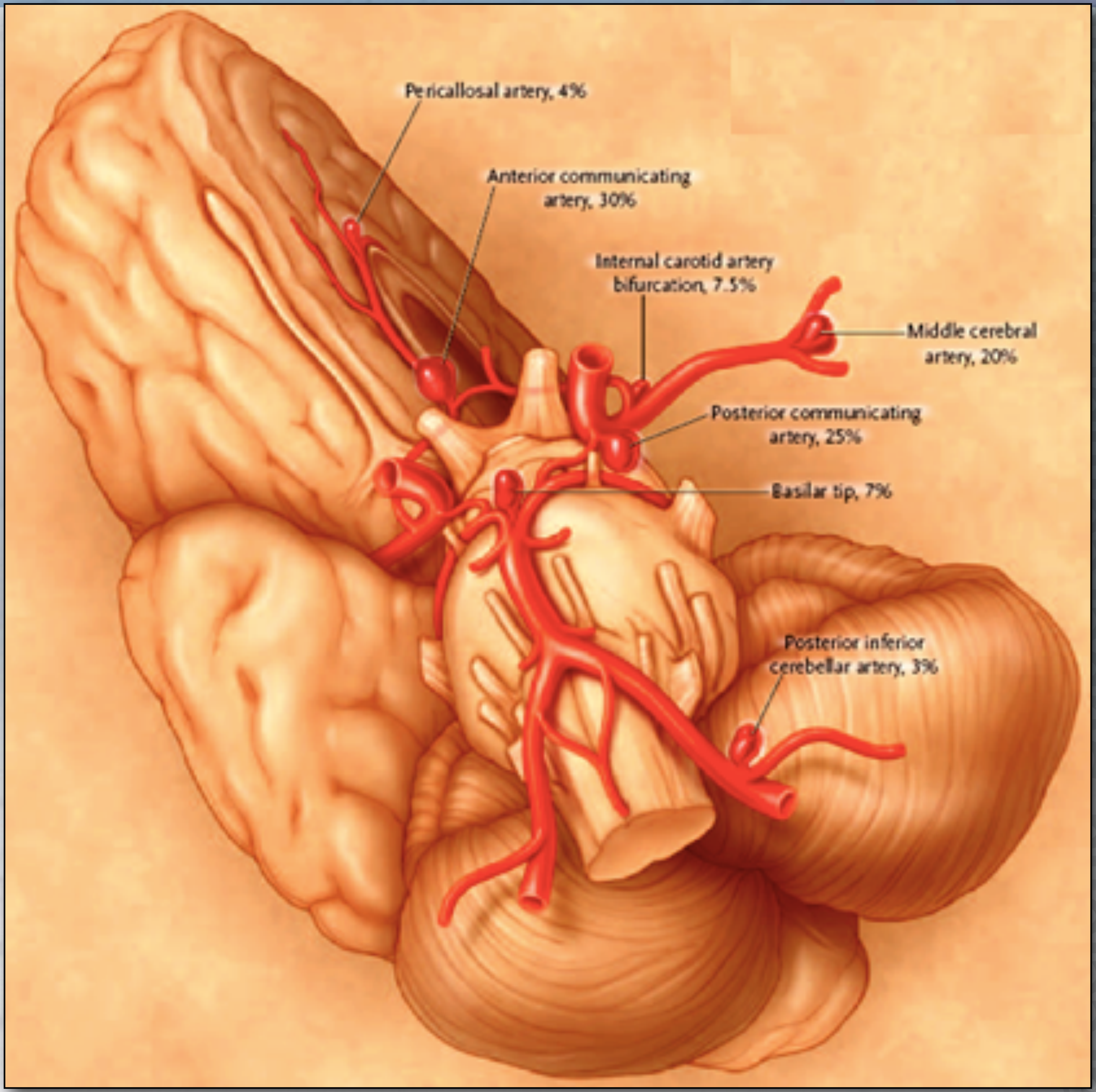
How often?

How to lower risk factors?

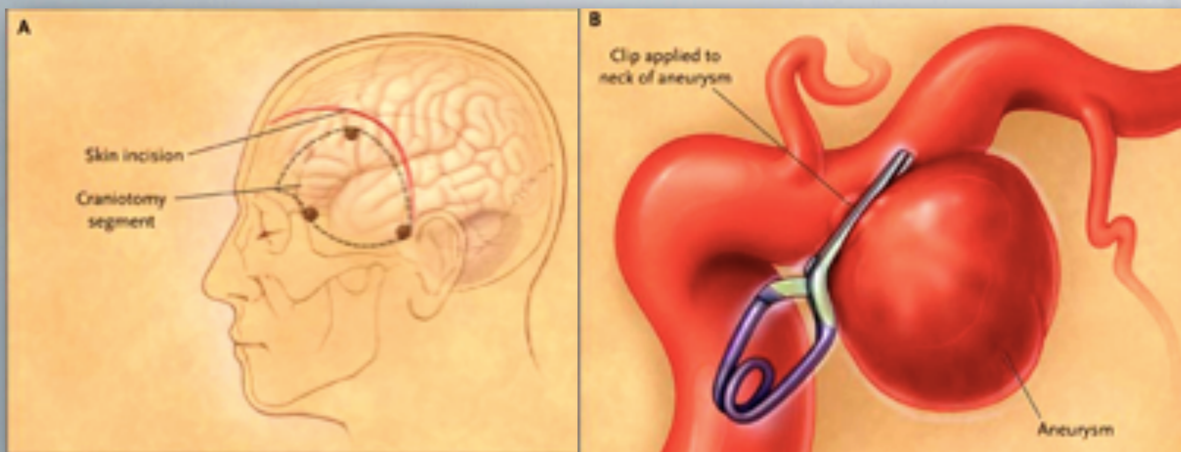
Treat:

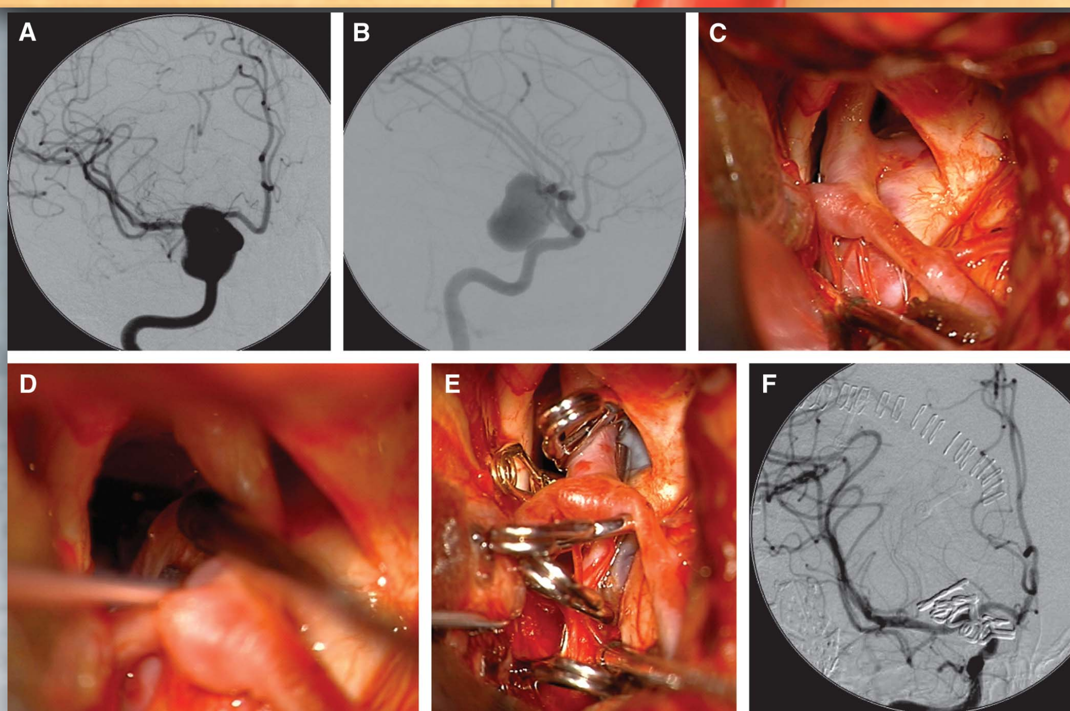
Surgically or endovascularly?

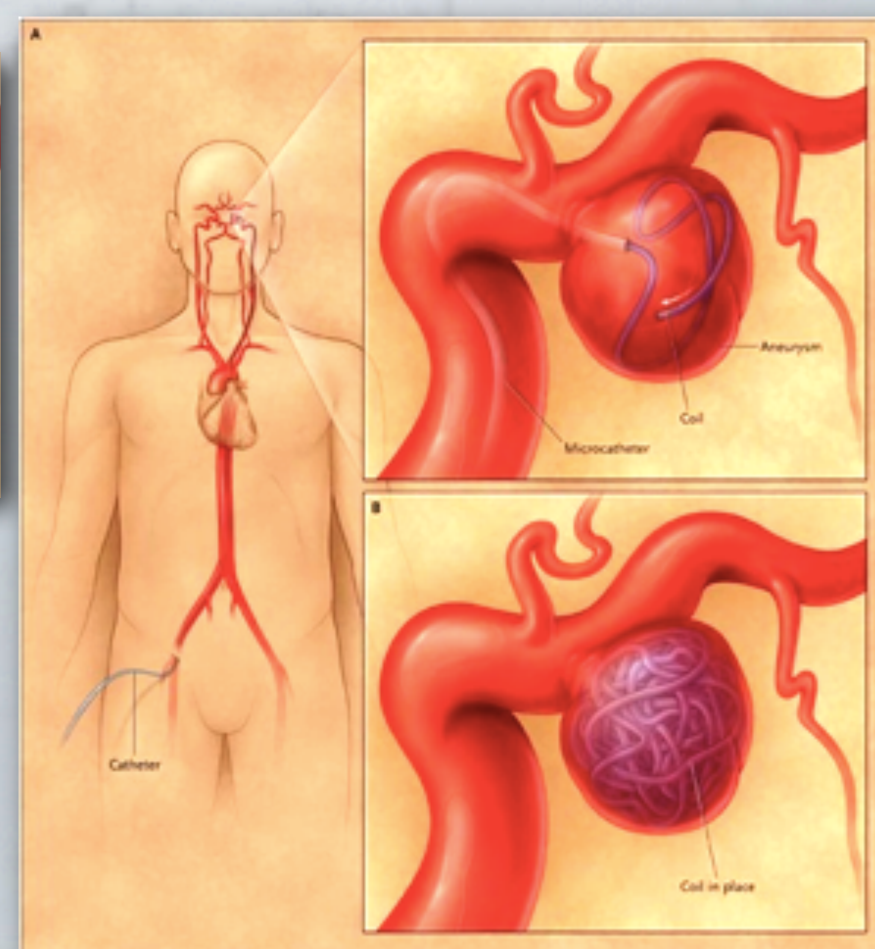
Which device?

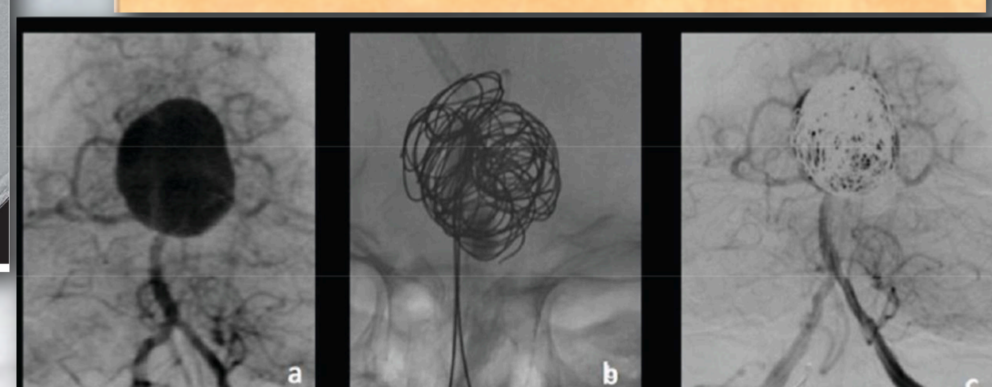


Surgical | **Endovascular**









Guide of Practice:

Treatment for all larger than 1cm

But most of the broken ones are smaller than 0.7cm!

Risk Factors

Anatomical factors

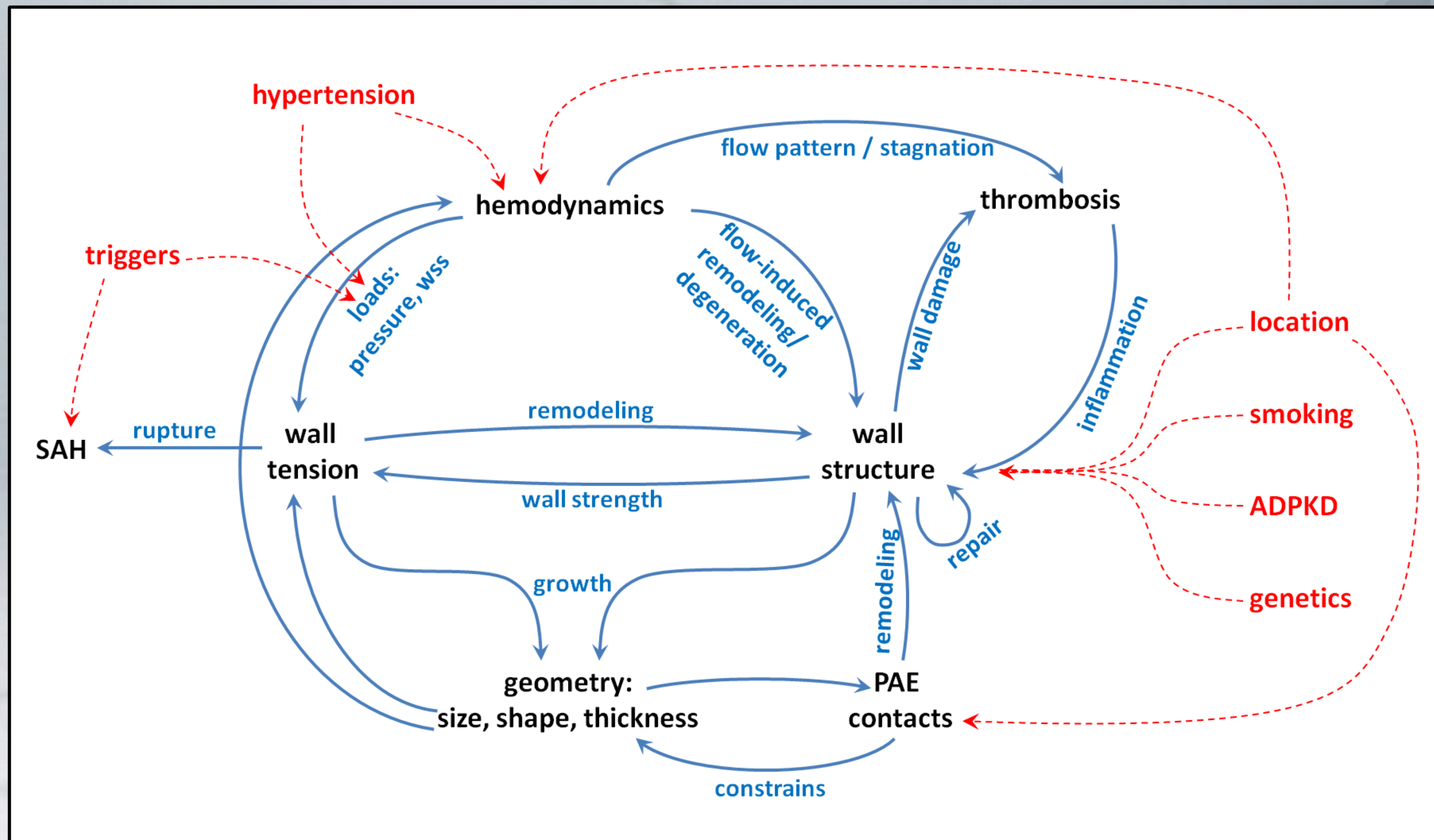
- Size
- Irregular shape
- Location:
  - Posterior circulation
  - Communicating arteries
- Circle of Willis

Clinical factors

- Previous SAH
- Smoking
- Female gender (2/3 are women)
- Hypertension
- Co-morbidities
- Age
- Activity
- Genetics

Risk Factors and Mechanisms

Cebral JR, Raschi M, “Suggested connections between risk factors of intracranial aneurysms: a review”, Annals of Biomedical Engineering, 41(7): 1366-1383, 2013

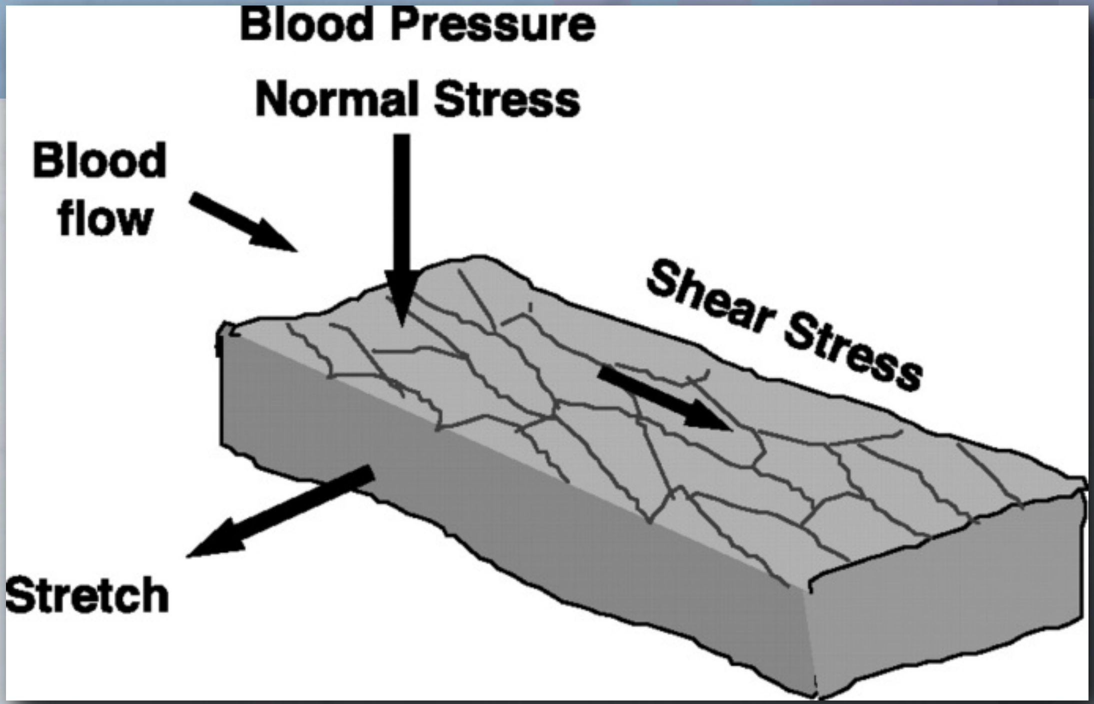


Abnormal flow => wall biology => wall deteriorates

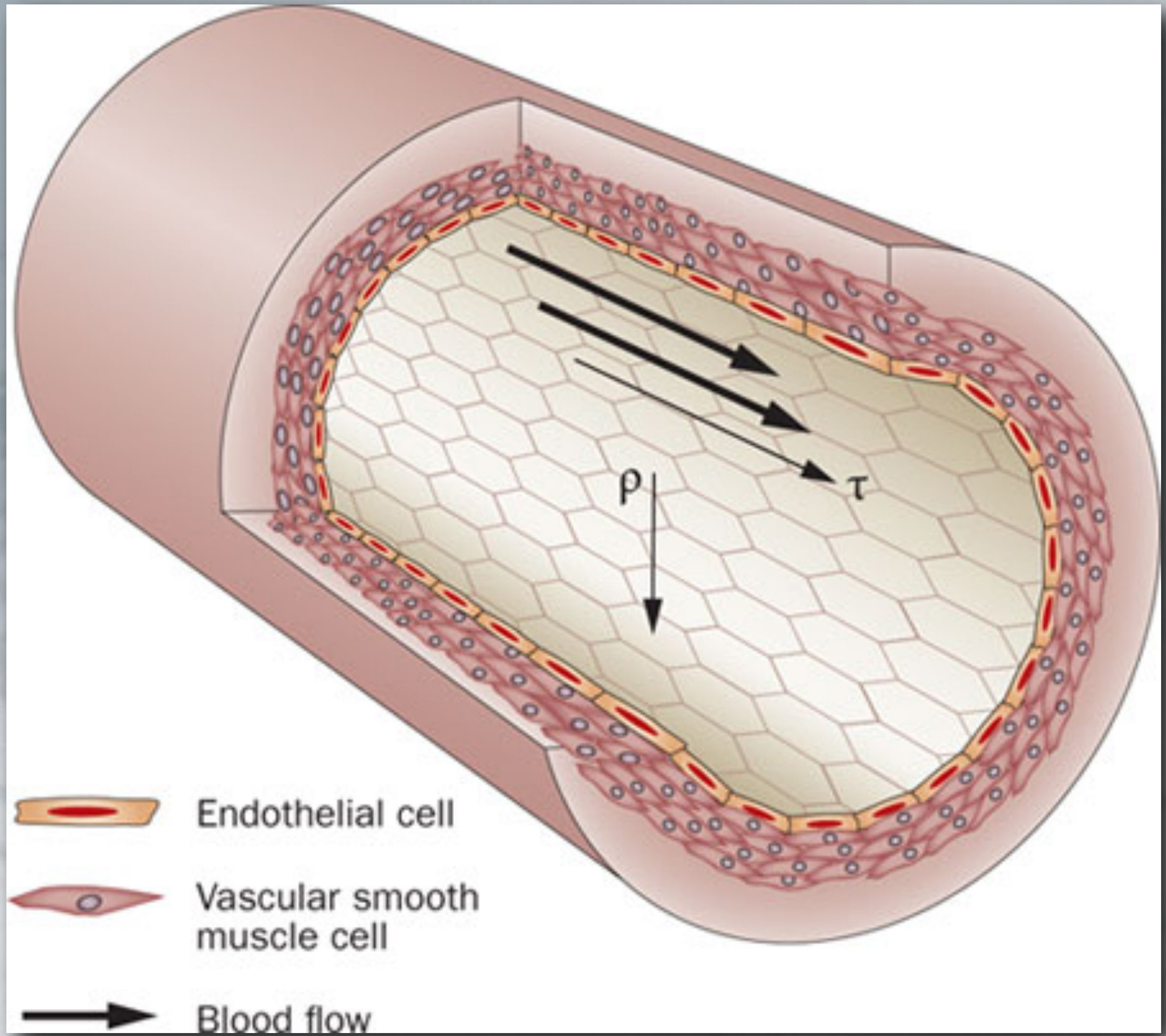
Weakening, expansion and geometry change

Mechano-biology

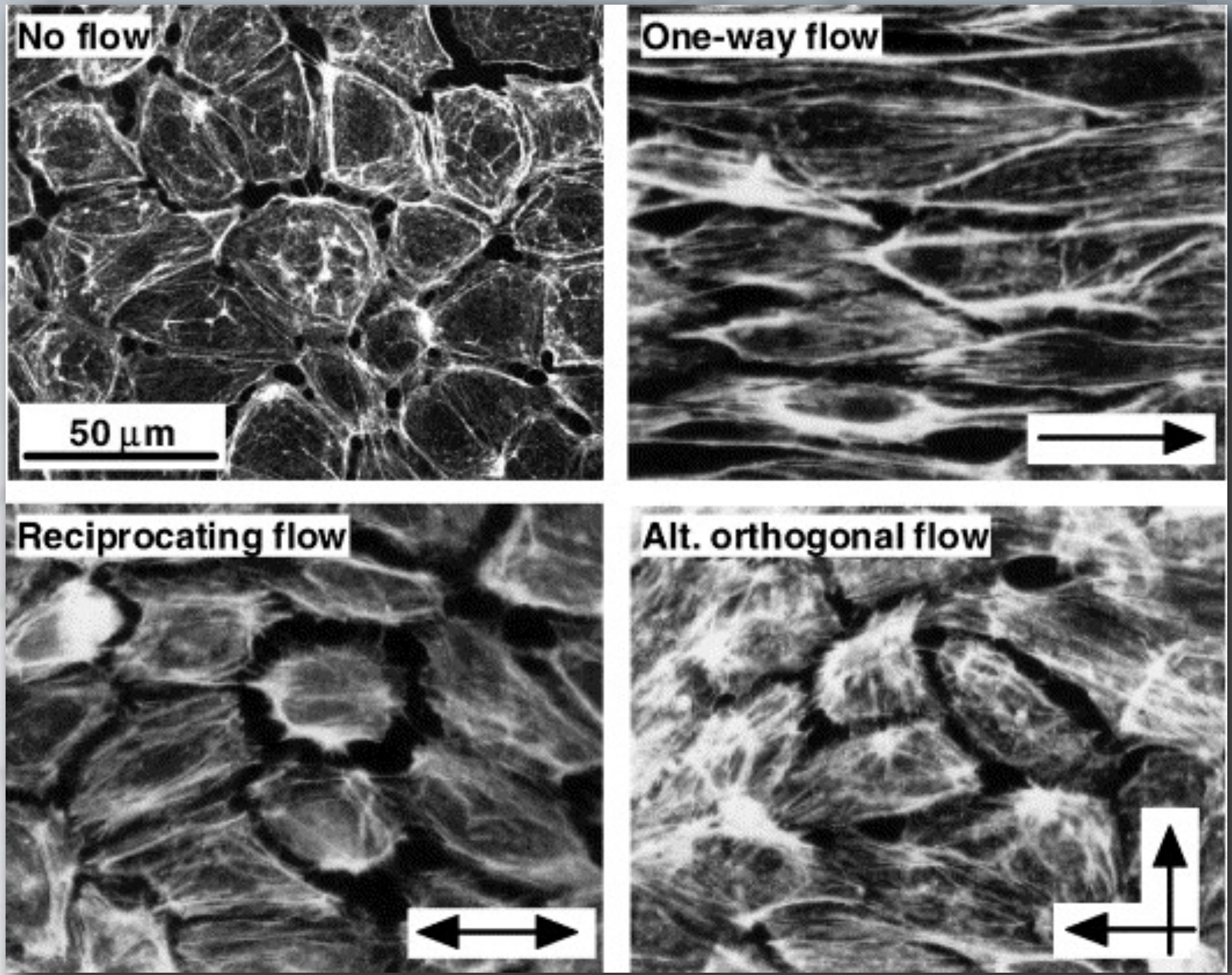
Wall shear stress (wss) determines endothelial growth



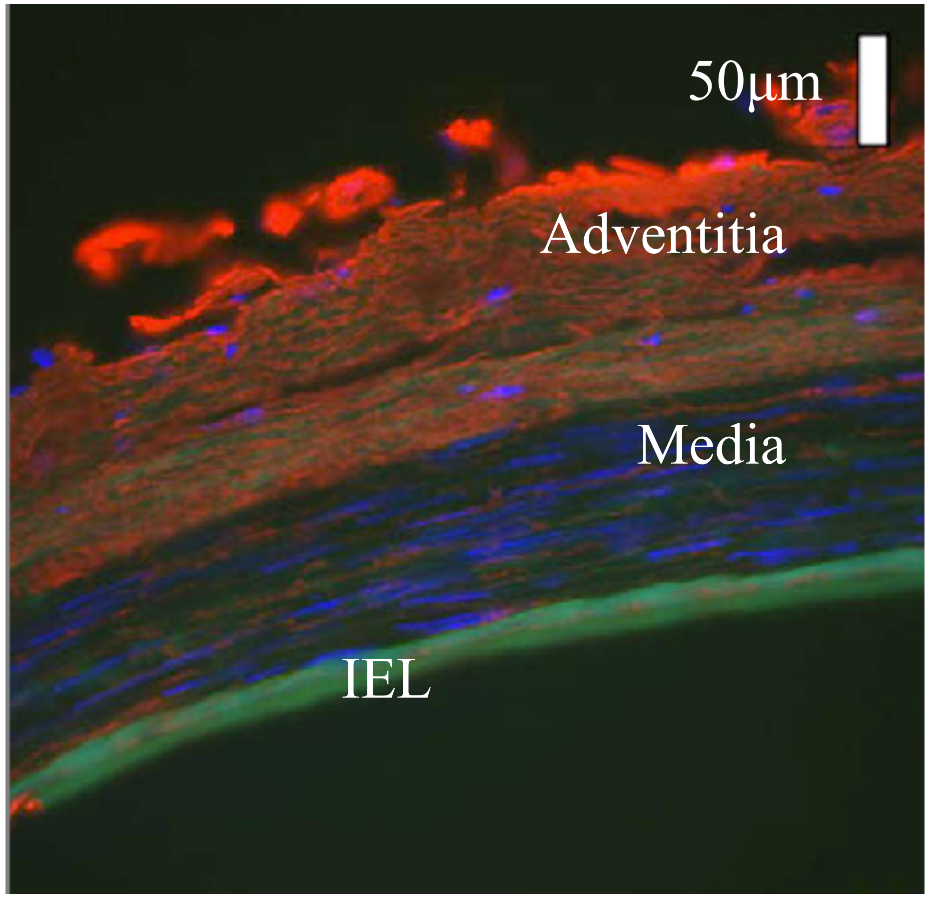
Vessel wall and blood flow

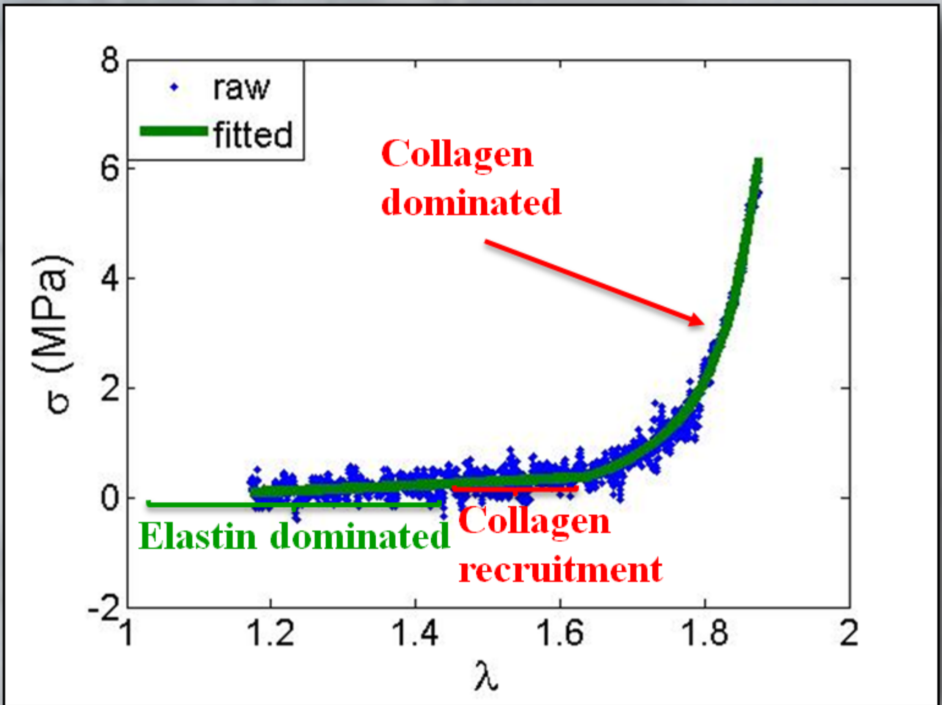


EC sensing and response to WSS



Human Cerebral Artery (basilar) (confocal microscopy)



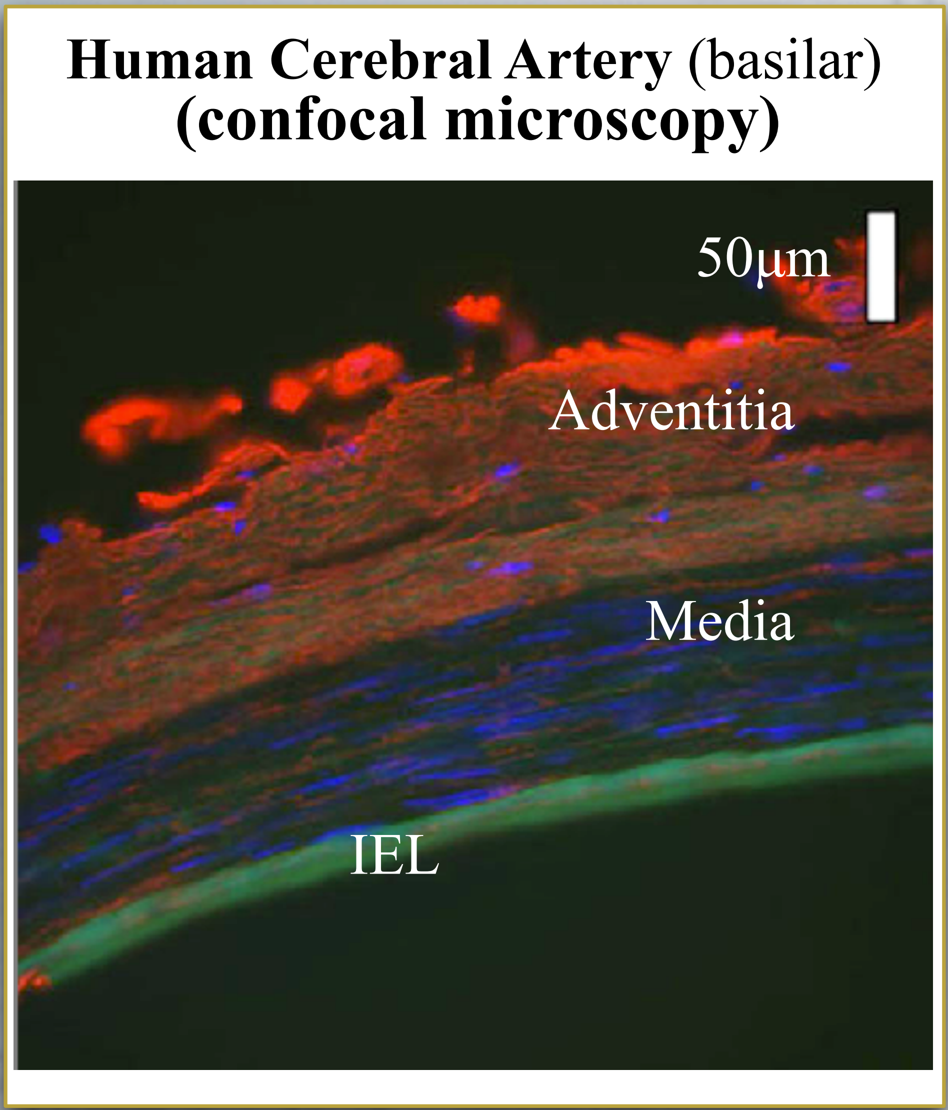


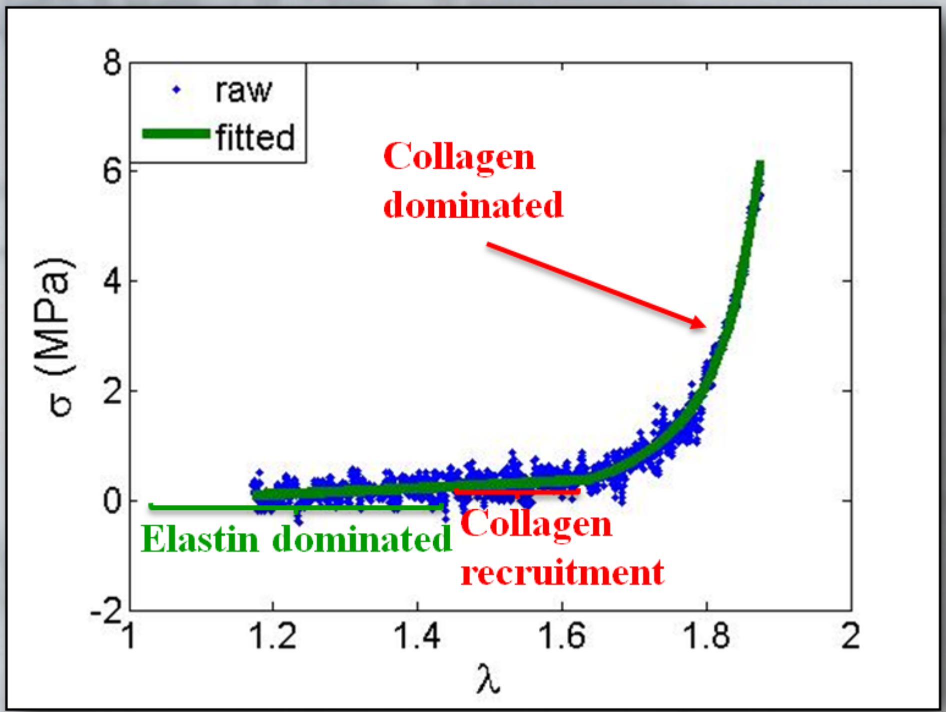
Wall Structure

Adventitia: collagen fiber bundles

Media: collagen and collagen producing cells

Internal elastic lamina IEL: elastin





Wall Structure

Adventitia: collagen fiber bundles

Media: collagen and collagen producing cells

Internal elastic lamina IEL: elastin

Adventitia: collagen fiber bundles

Media: **damaged, stop producing collagen**

Internal elastic lamina IEL: **disappears in aneurysms**

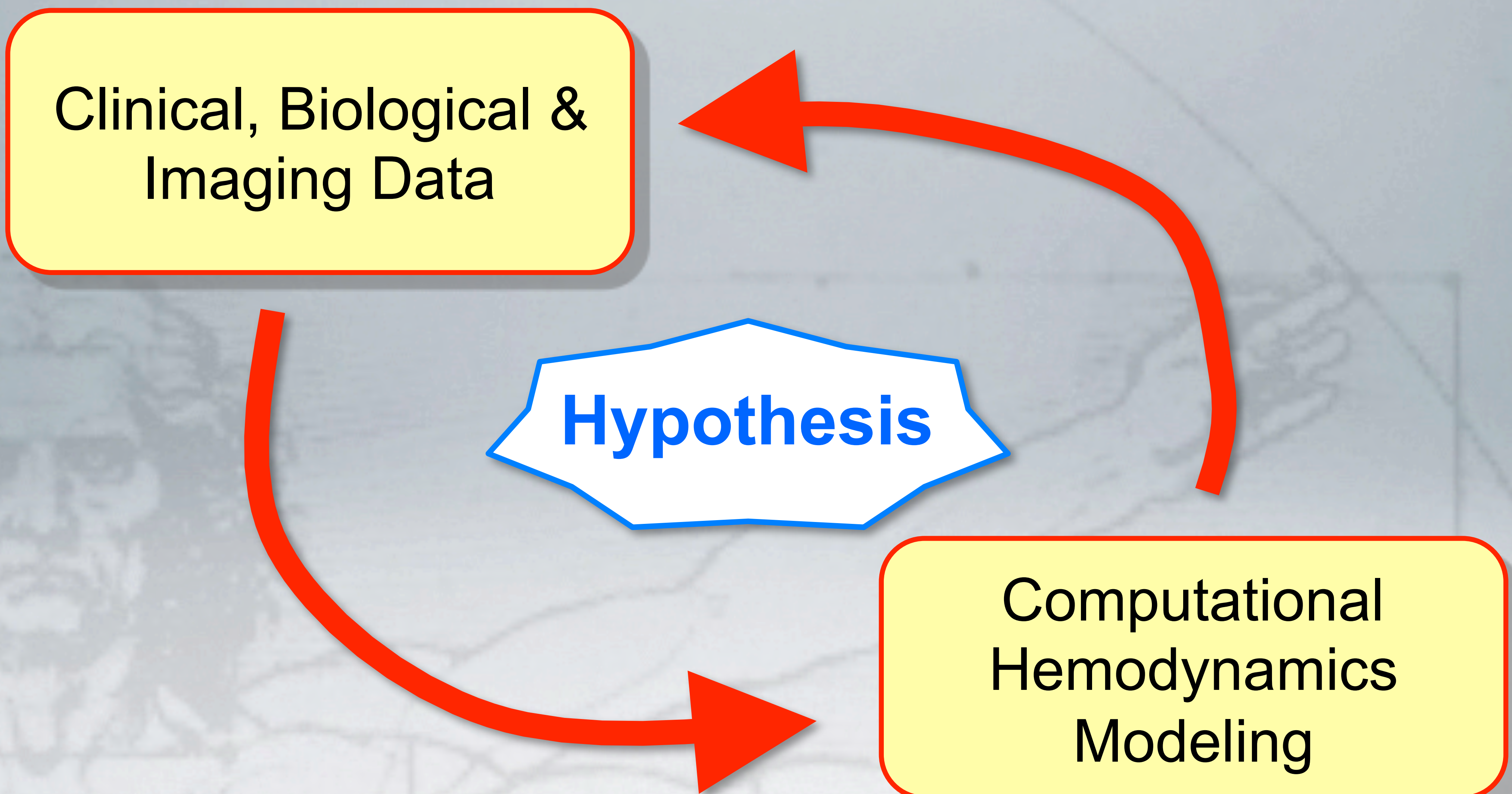
Pathobiologic responses to abnormal behavior

Two different ones:

High Wall Shear Stress	Low Wall Shear Stress
EC damage or weakening	Proinflammatory EC are “leaky”
MPP production by mural cells	Inflamatory cell infiltration
ECM degradation	MPP production by macrophages
Medial thinning	SMC proliferation and migration
Mural cell apoptosis	Thrombus formation

Which is the right one?

Cebral JR, Putman CM, “Relating Cerebral Aneurysm Hemodynamics and Clinical Events”, in Vascular Hemodynamics: Bioengineering and Clinical Perspectives. P. Yim (ed.), John Wiley & Sons, Chapter 3, pages: 346, ISBN-13: 9780470089477, 2008



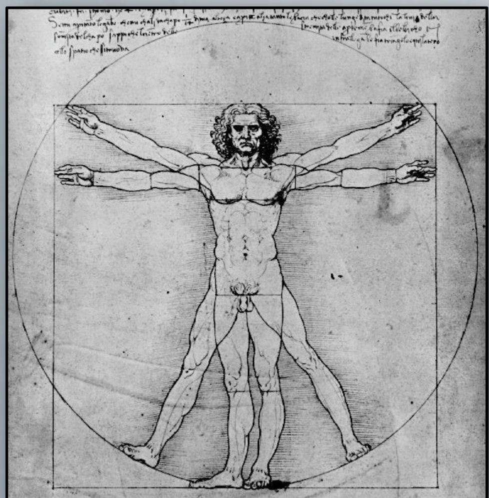
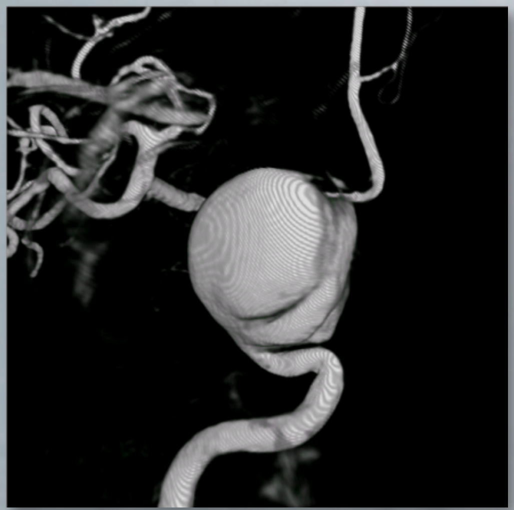


Image based hemodynamics modeling

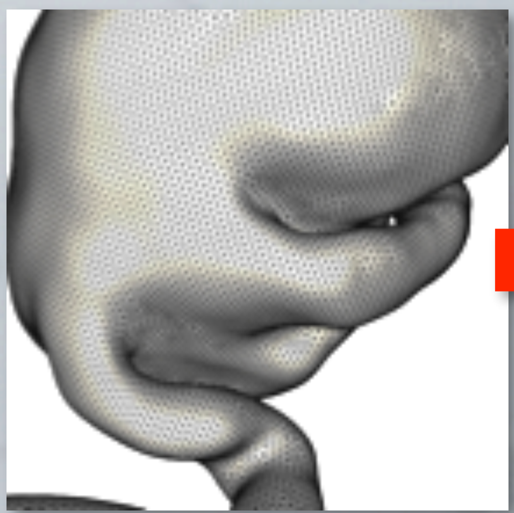
Image based hemodynamics modeling

imaging

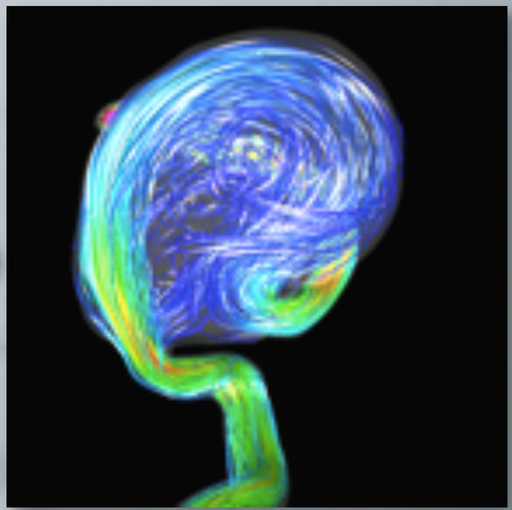


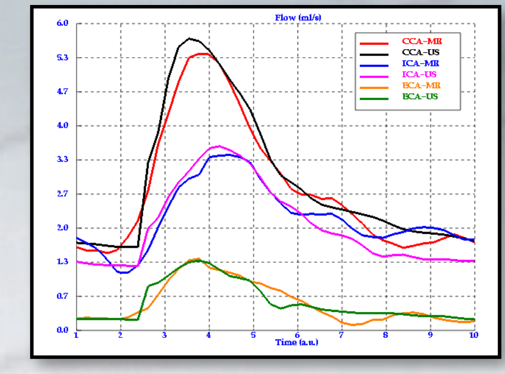
geometry modeling

meshing



flow visualization

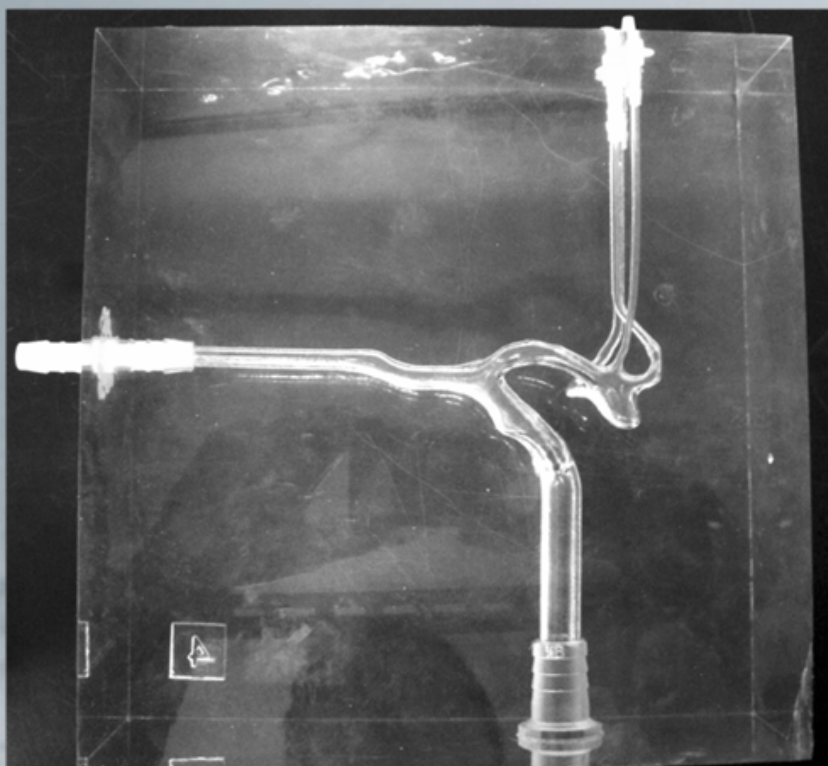


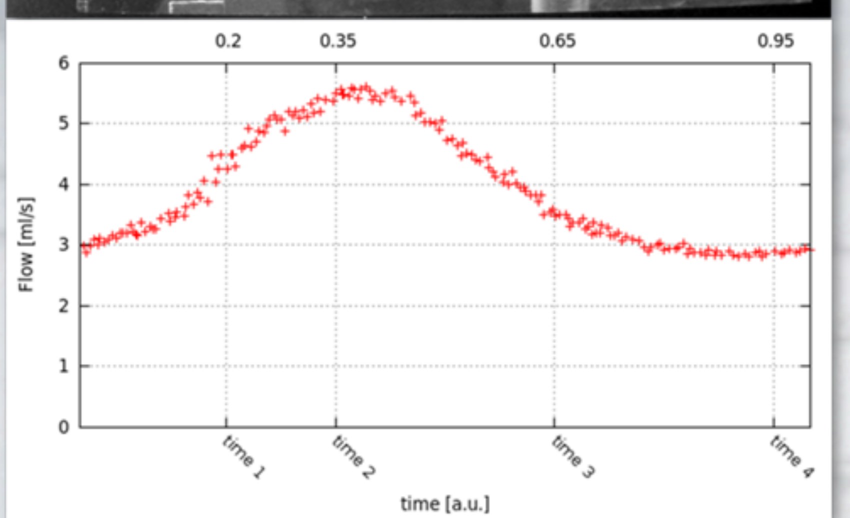


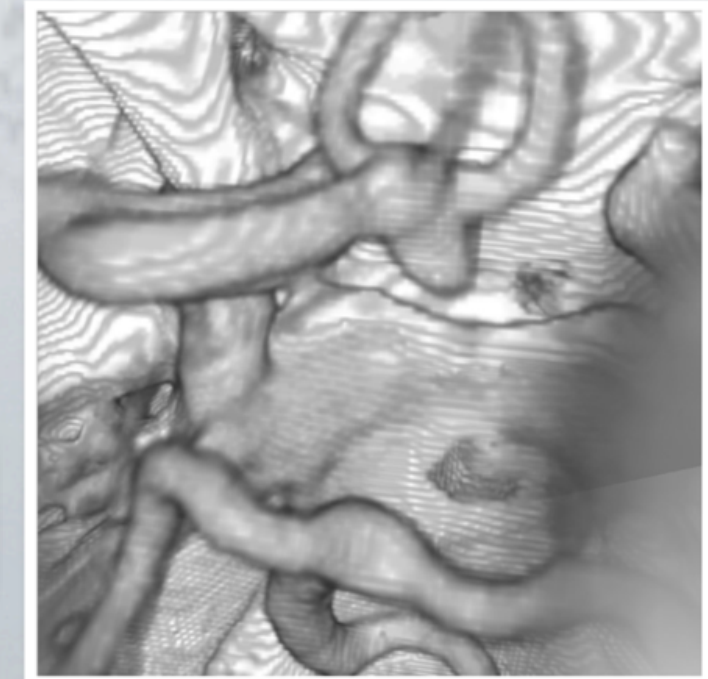
flow conditions

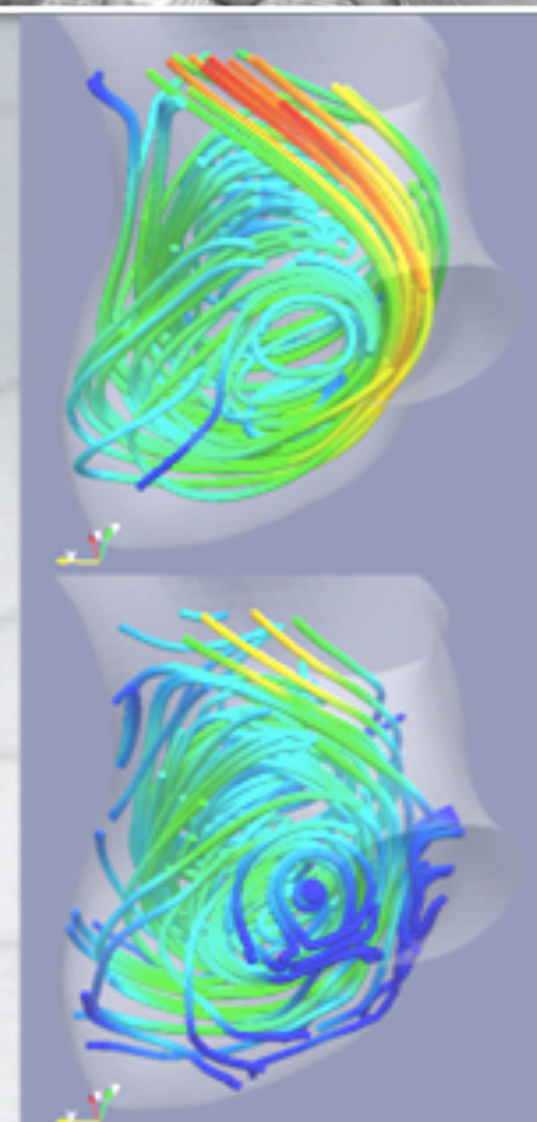
numerical solution

Validation: CFD vs. PIV



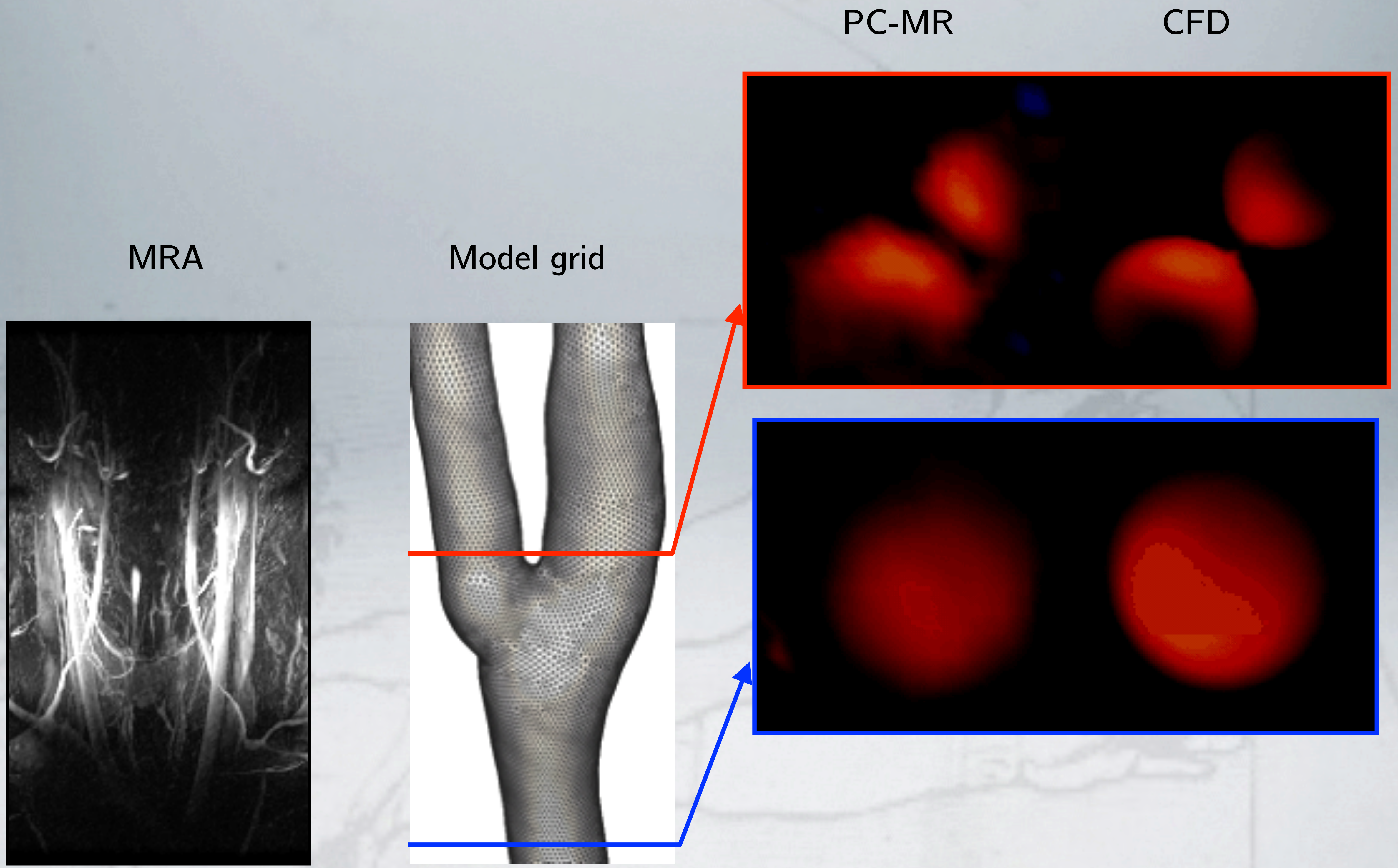






Consistent flow pattern

Validation: CFD vs. PIV



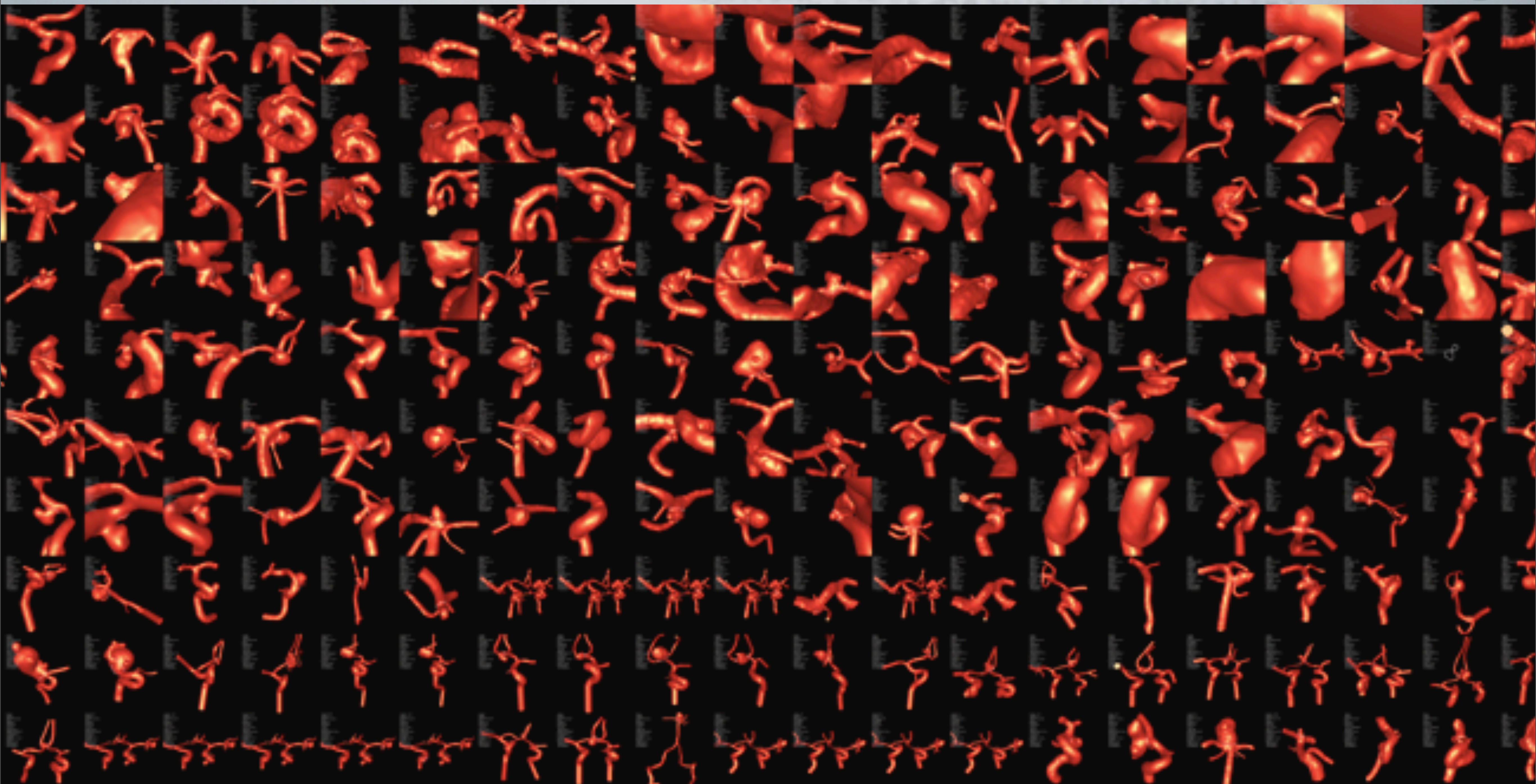
Observations

CFD models can be made patient-specific

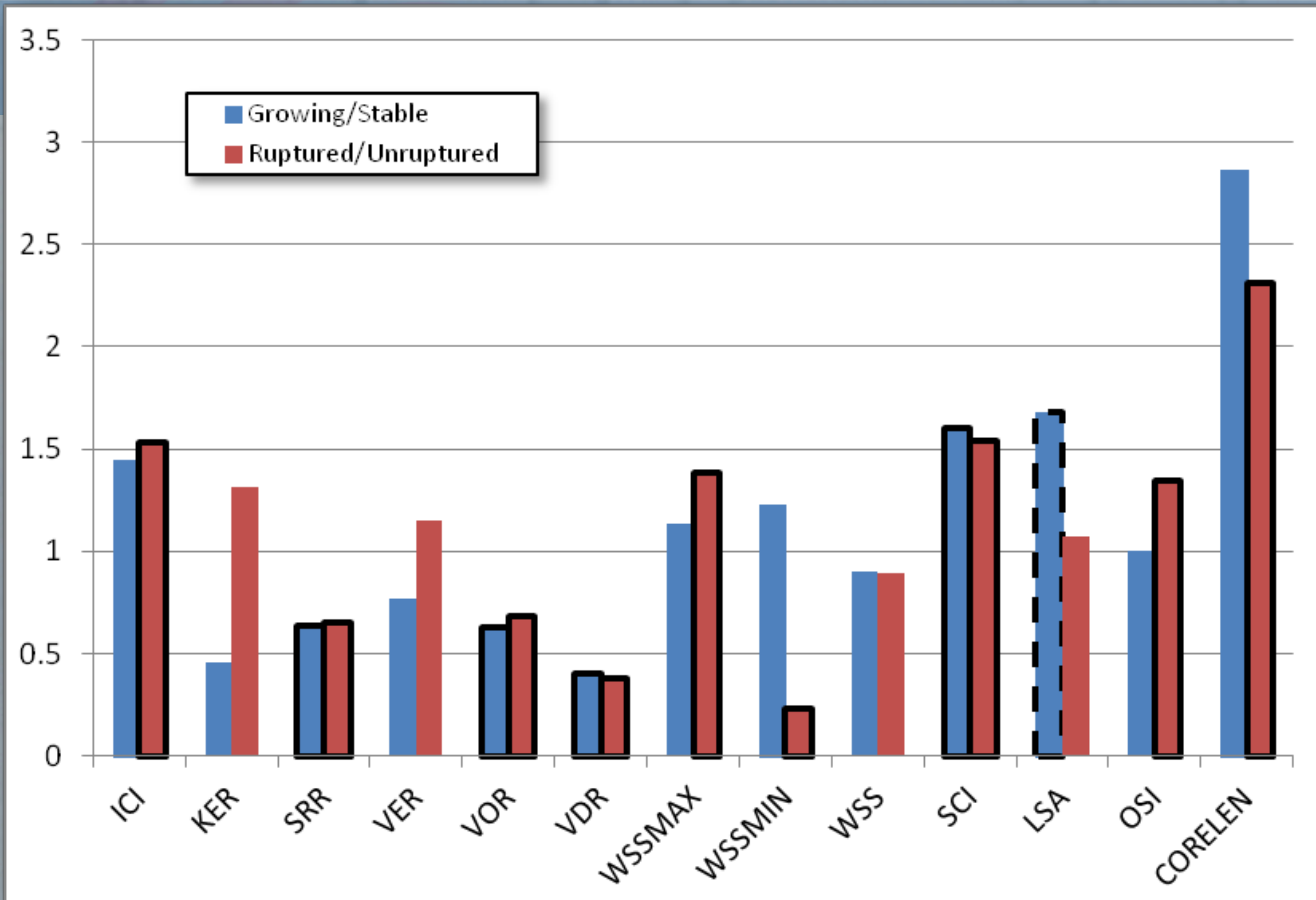
CFD models can provide quantitative hemodynamics information

Image-based CFD models are able to realistically represent the in vivo flow conditions

Cerebral Aneurysms



Cebral JR, Mut F, Weir J, Putman CM, "Association of hemodynamic characteristics and cerebral aneurysm rupture", AJNR, 32(2): 264-270, 2011



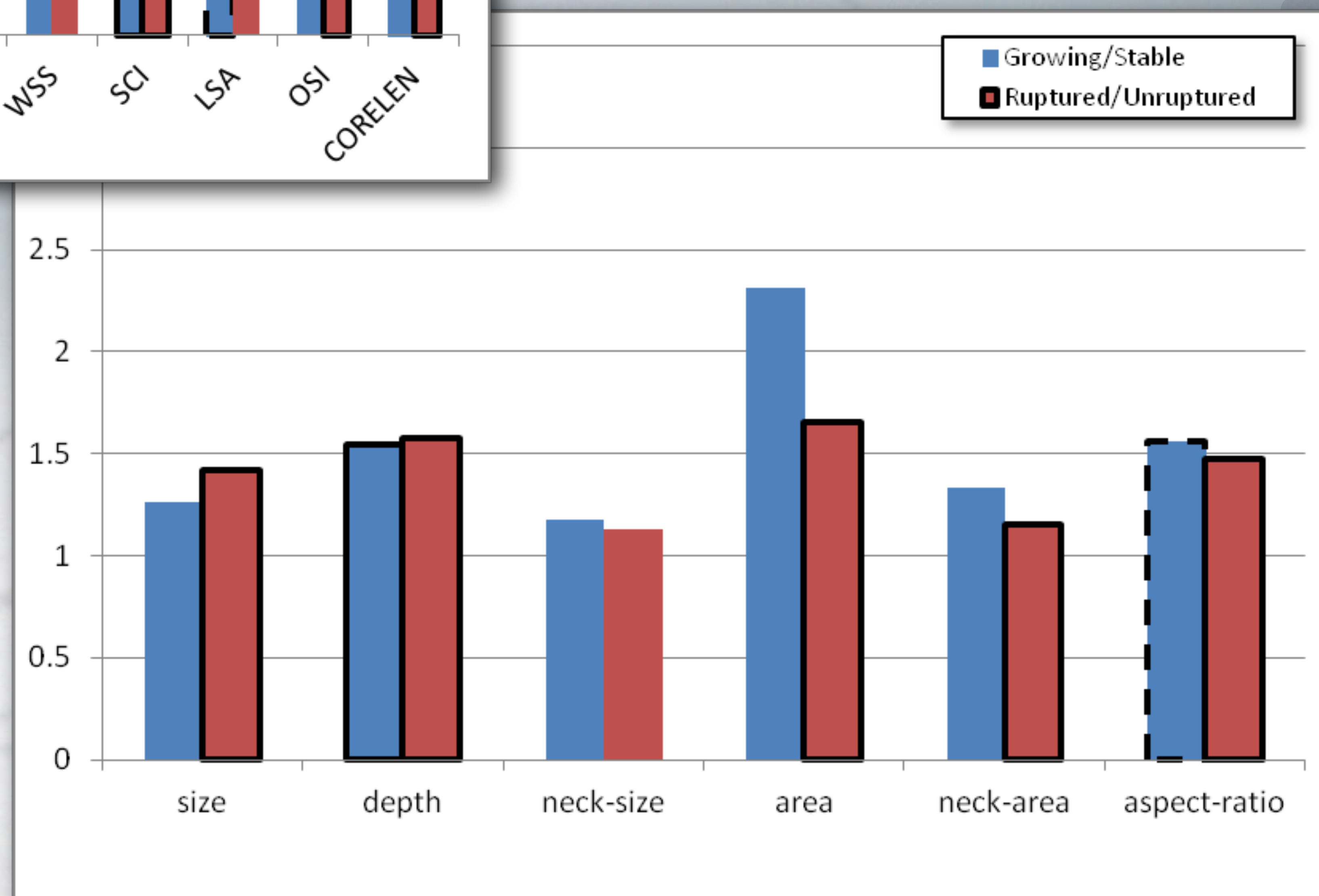
Global aneurysm characteristics

Longitudinal data:

Growing vs. Stable

Cross sectional data:

Ruptured vs. Unruptured



Cerebral Aneurysms

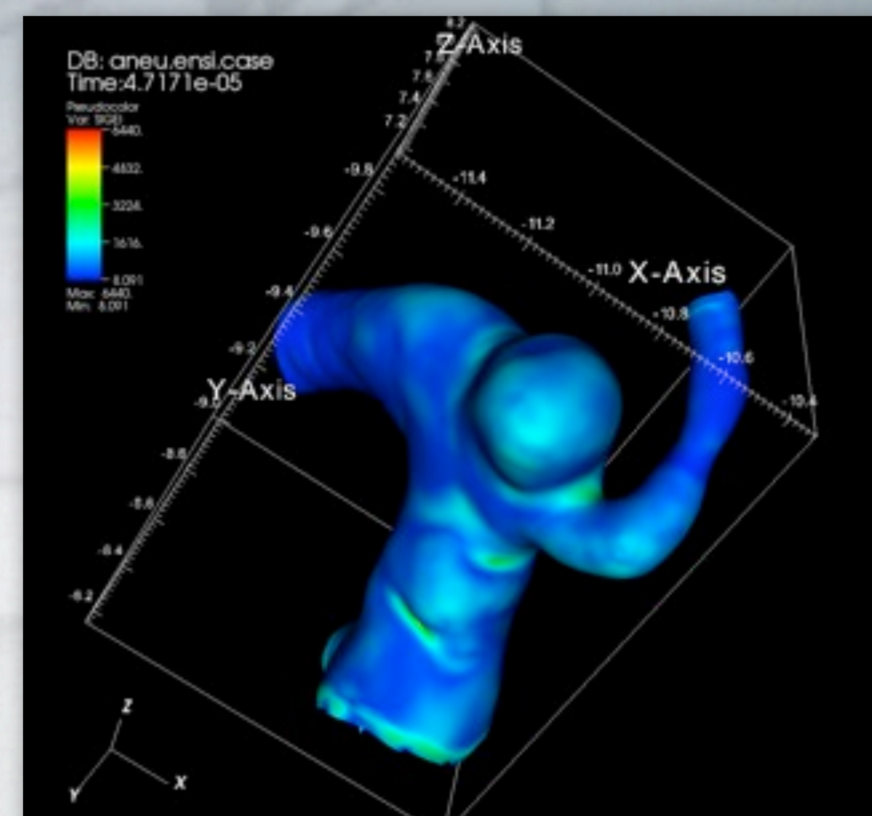
Observations

Growing aneurysms tend to have concentrated inflows that induce complex flows and concentrated wall shear stress distributions with large areas of low WSS

Aneurysms typically grow towards the dome, but also at the body or neck

Contacts with peri-aneurysmal environment structures can affect the hemodynamics and aneurysm growth

Local conditions that cause focalized aneurysm growth still under investigation

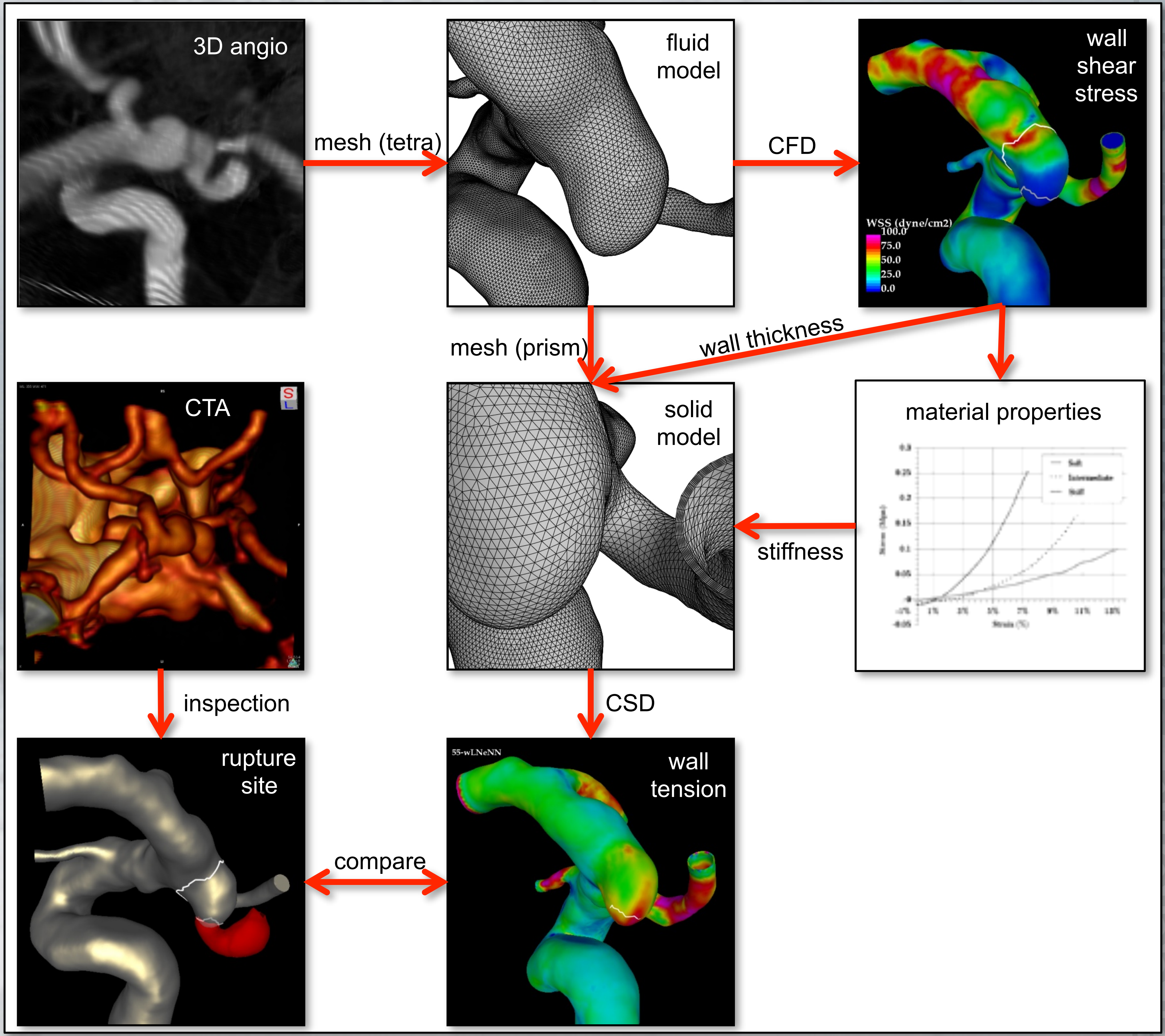


Study design:

Compare rupture site

with

wall tension



CFD + CSM

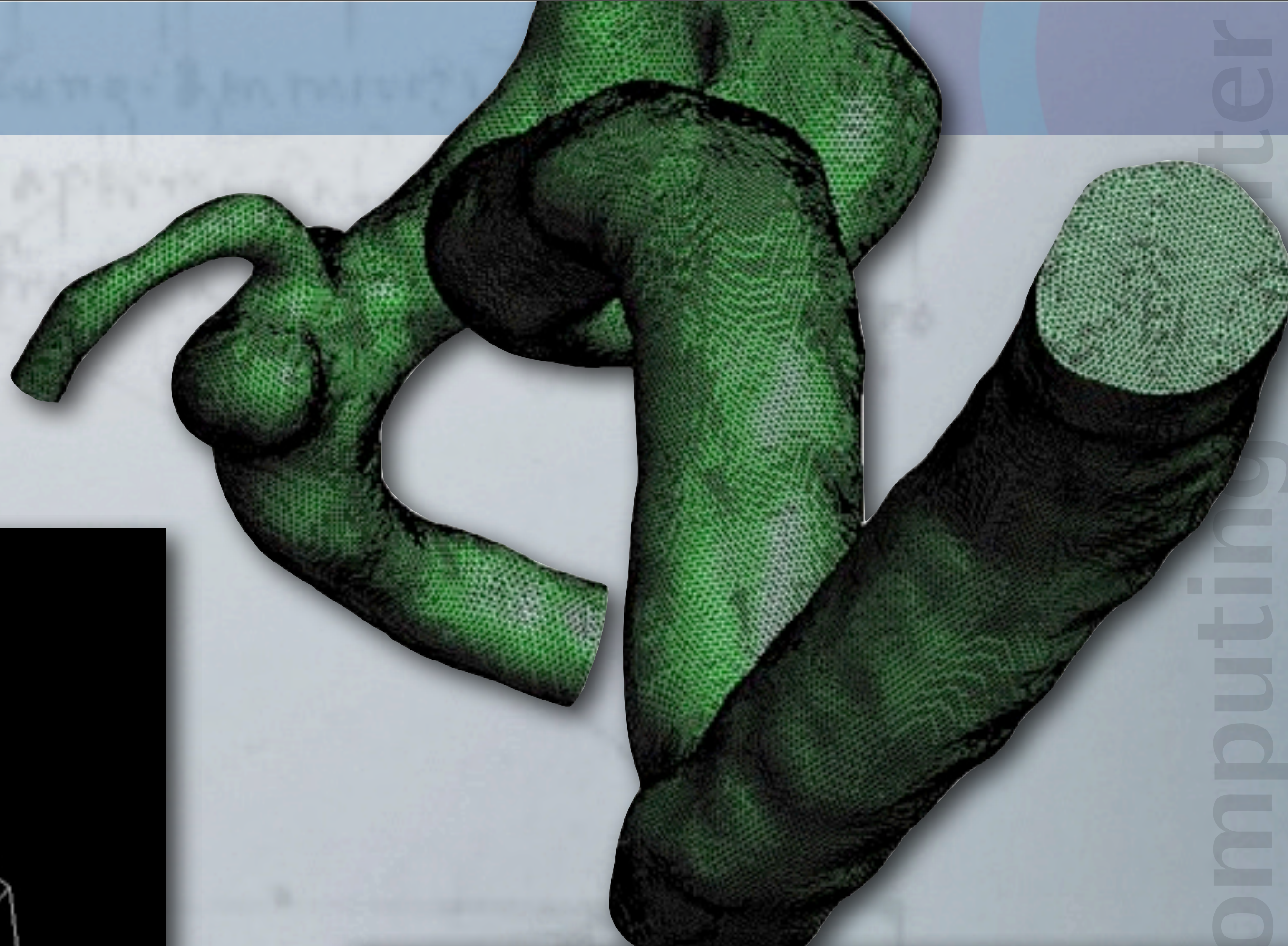
CFD provides the WSS (peak, mean, max) and the surface mesh

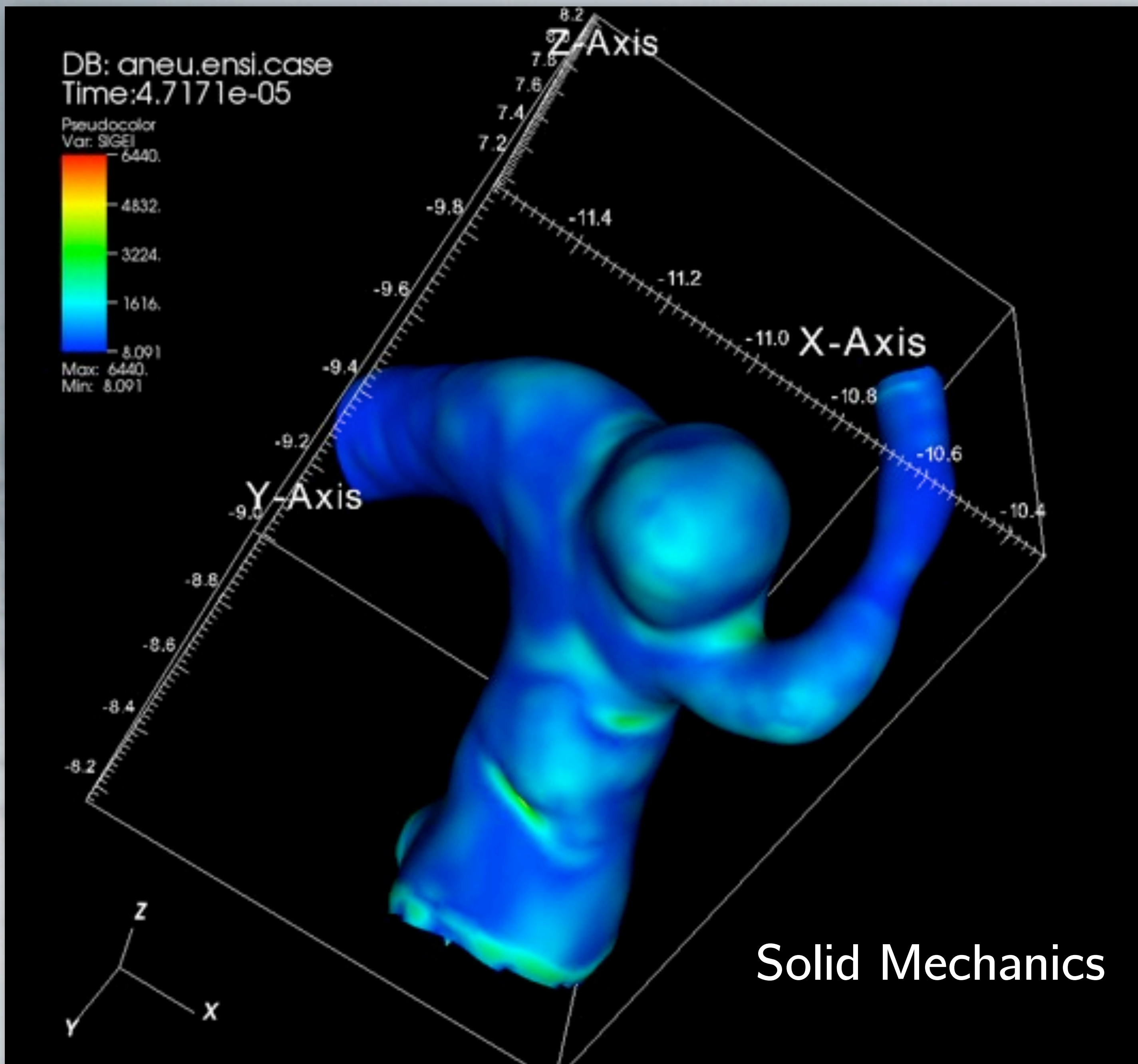
A 3D solid mesh is created by extrusion, 200 - 500 K prisms

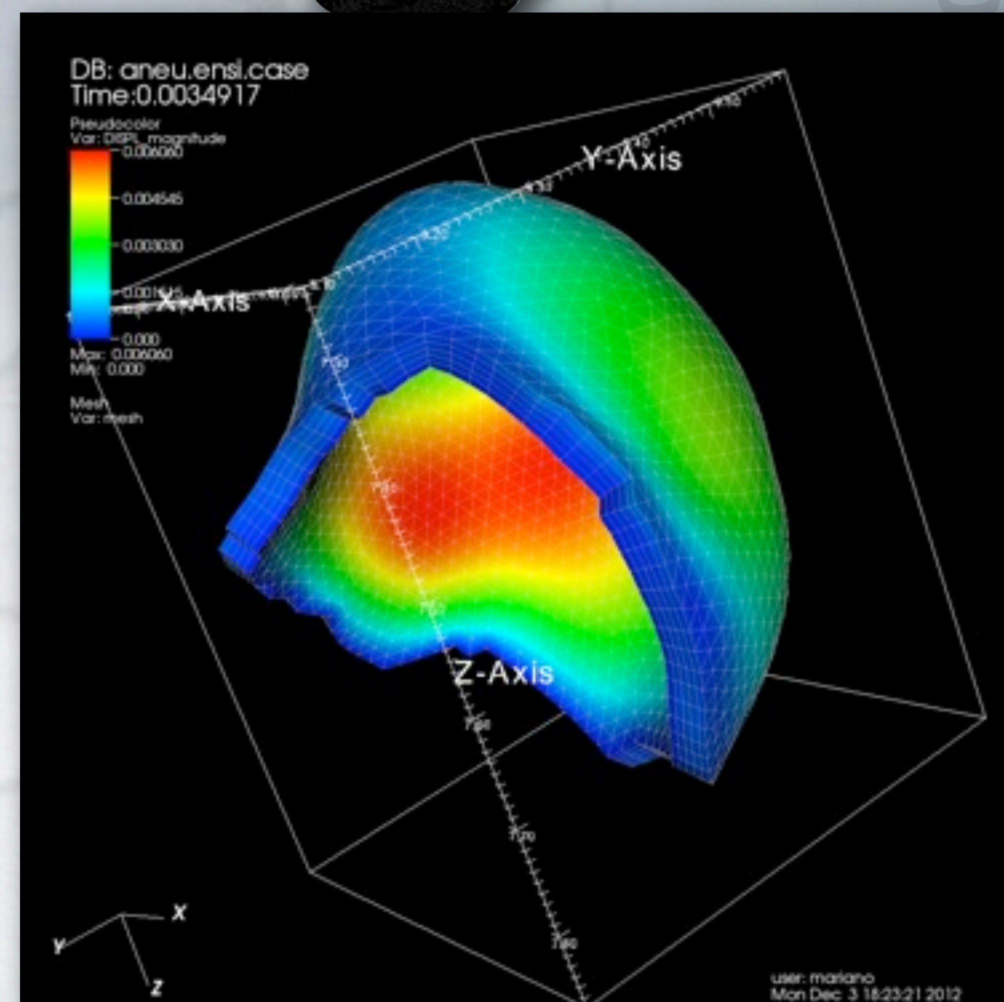
Hyperelastic material, large deformations

Each run takes a few minutes in Marenostrum

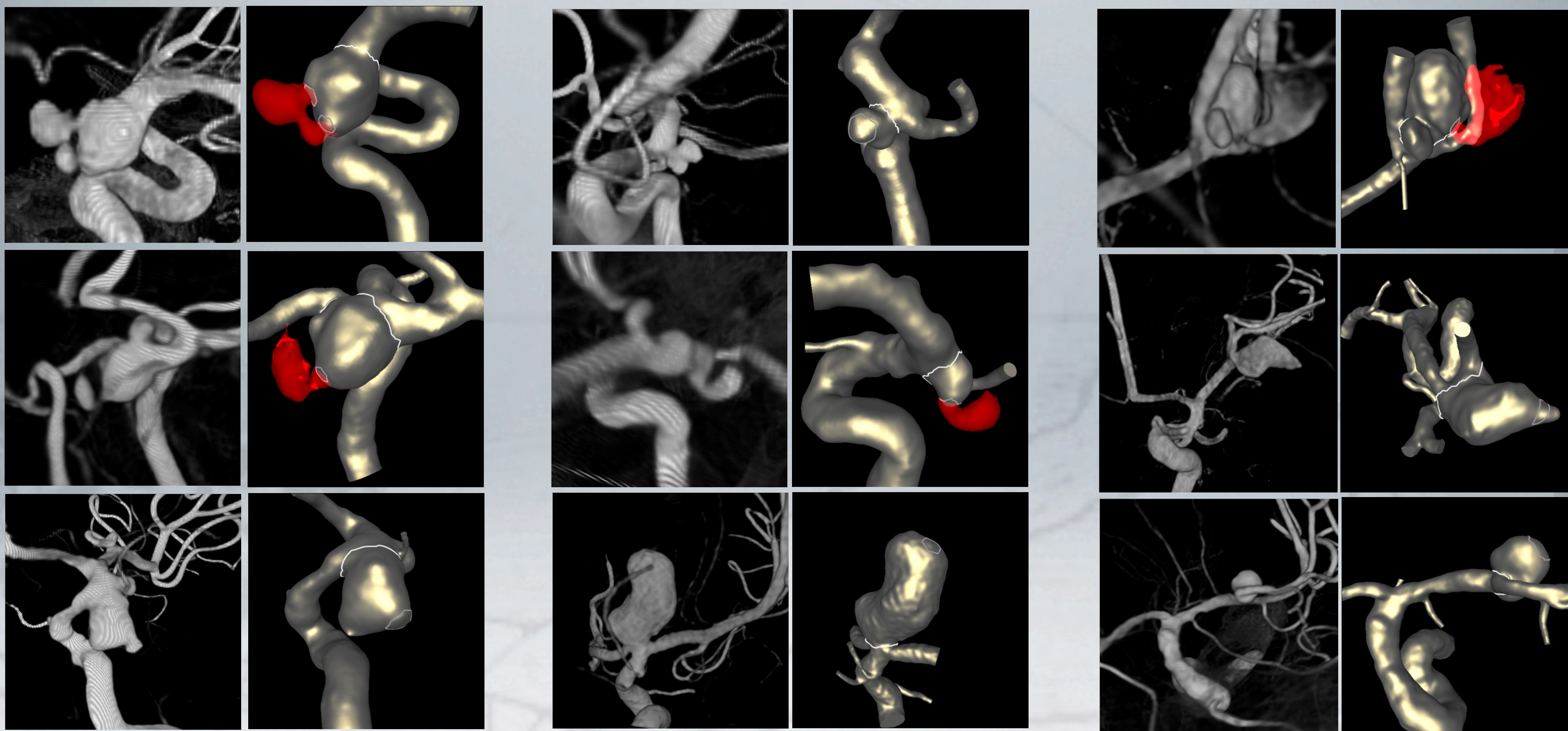
Cerebral Aneurysms







Nine patients



Strategy

Module material properties from Wall Shear Stress coming from CFD

Hypothesis:

High WSS weakens the wall => make it thinner

Low WSS weakens the wall => make it thinner

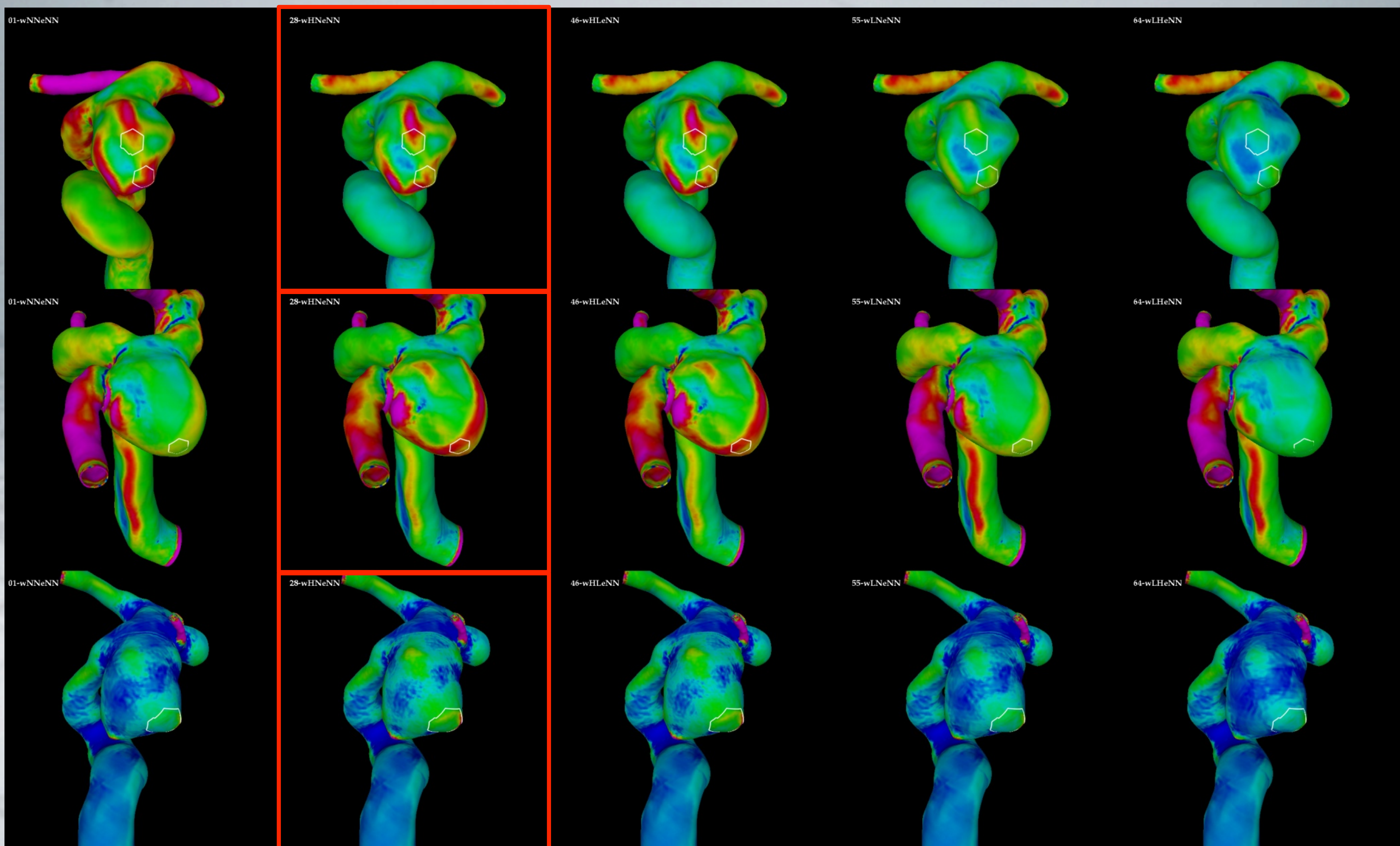
Analyze Rankine damage criteria

See wether its maxima coincides with the rupture sites

Show Movie

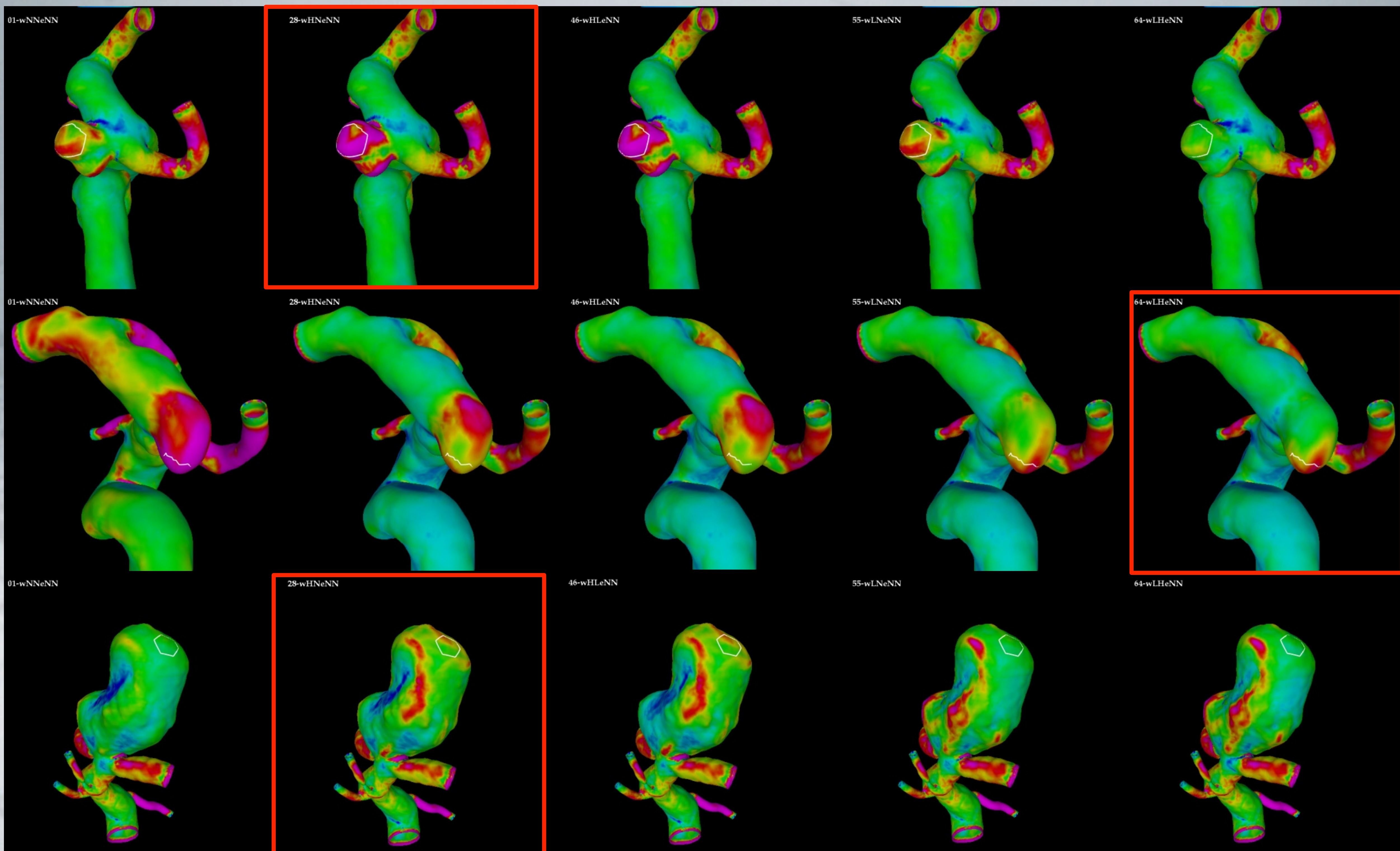
Cerebral Aneurysms

uniform	thin => high	thin => high	thin => low	thin => low
		thick => low		thick => high



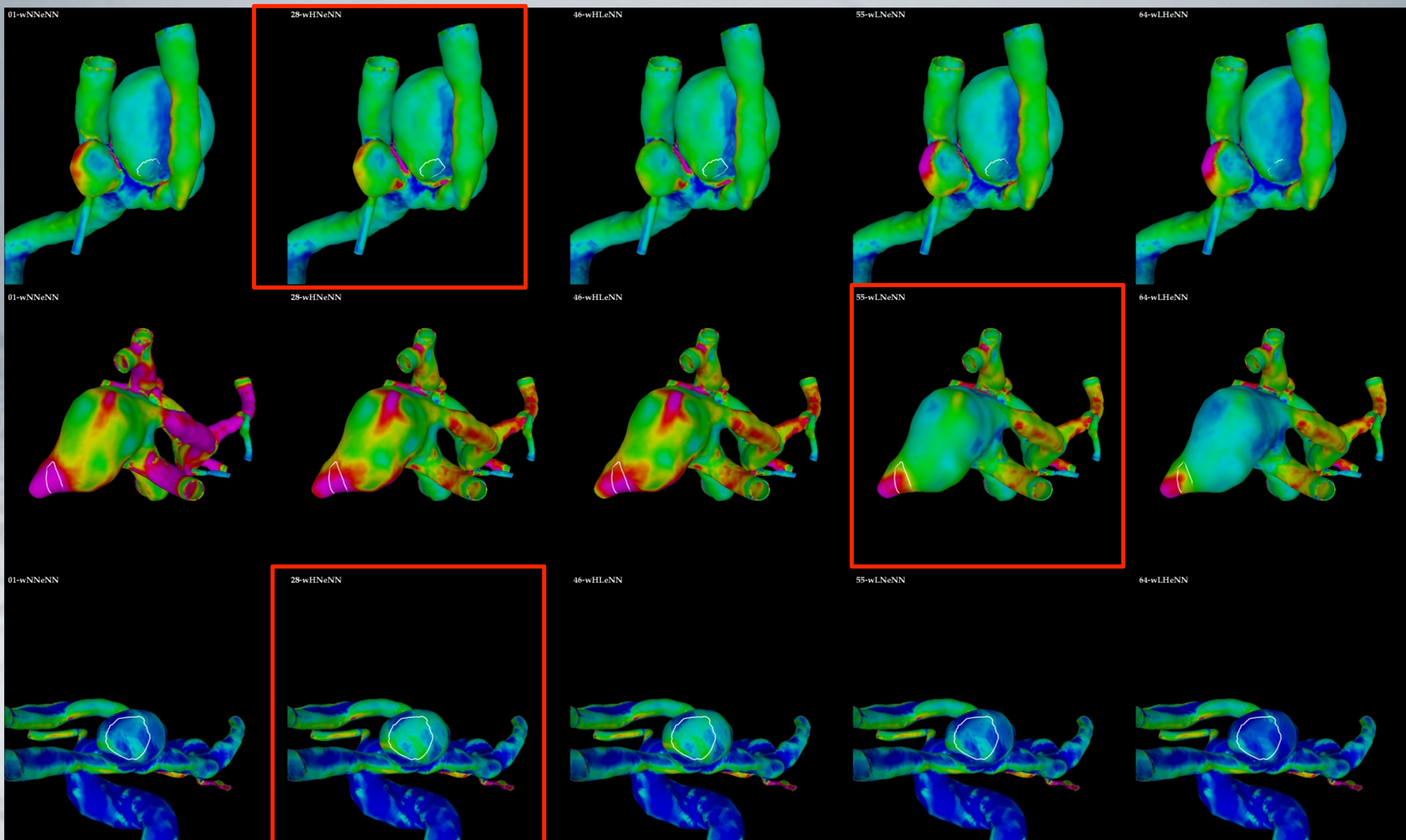
Cerebral Aneurysms

uniform	thin => high	thin => high thick => low	thin => low	thin => low thick => high



Cerebral Aneurysms

uniform	thin => high	thin => high thick => low	thin => low	thin => low thick => high



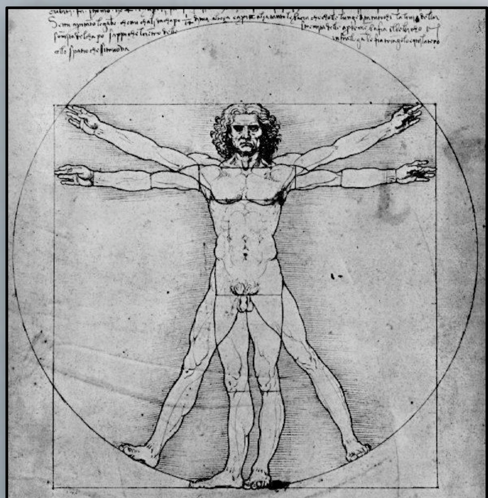
Observations

Thinner walls in regions of **high WSS** best explains
7-8 / 9 sites of aneurysm rupture

Thinner walls in regions of **low WSS** best explains
1-2 / 9 sites of aneurysm rupture

Two possible pathways to rupture?

Other factors?



Conclusions

Conclusions

Computer models are a powerful tool for:

Basic Science: propose and test hypotheses about mechanisms of aneurysm formation, growth and rupture

Risk Assessment: identify conditions that predispose aneurysms for rupture

Device Evaluation: test devices on “virtual patients”

Treatment Planning: identify conditions that promote fast and stable aneurysm occlusion after treatment

Improve material models, including material layers

George Mason

Juan R Cebral, PhD

Rainald Löhner, PhD

Fernando Mut, PhD

Daniel Sforza, PhD

BongJae Chung, PhD

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