TOR VERGATA
UNIVERSITÀ DEGLI STUDI DI ROMA

Computational Methods for the Analysis of Ascending Aortic Aneurysms

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MEDITATE

Ansys

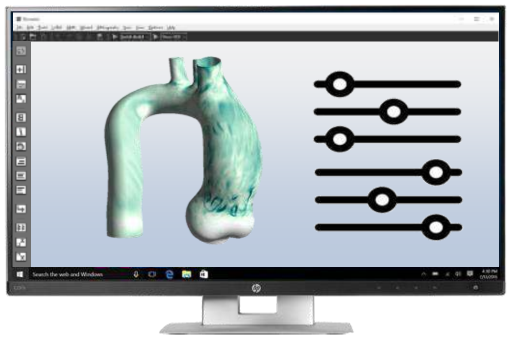
December 1st, 2023

PhD Cycle: 36
Academic Year: 2023/2024

PhD in Design, Manufacturing and Operations Engineering

Overview

Pathology

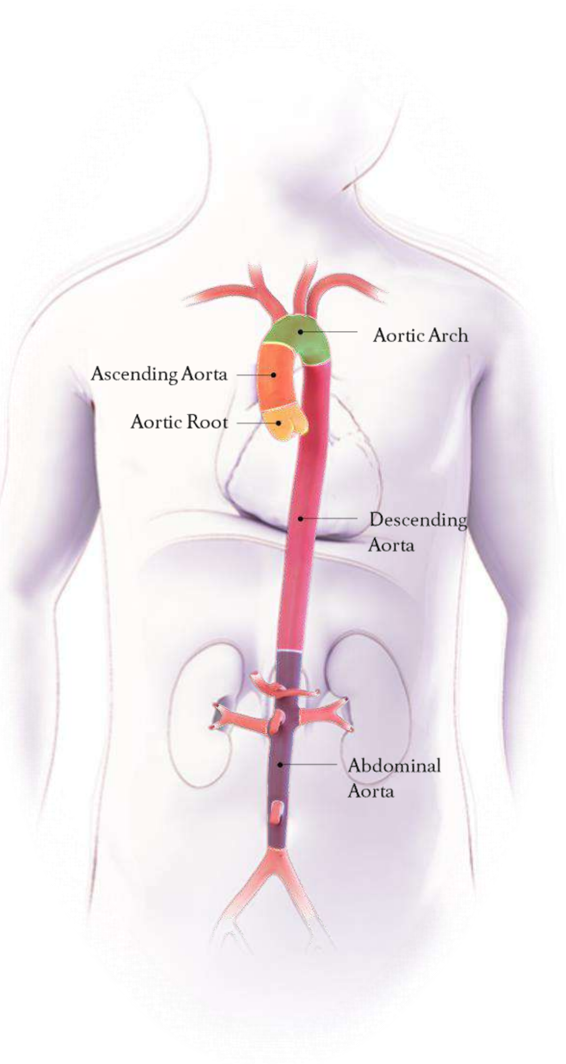


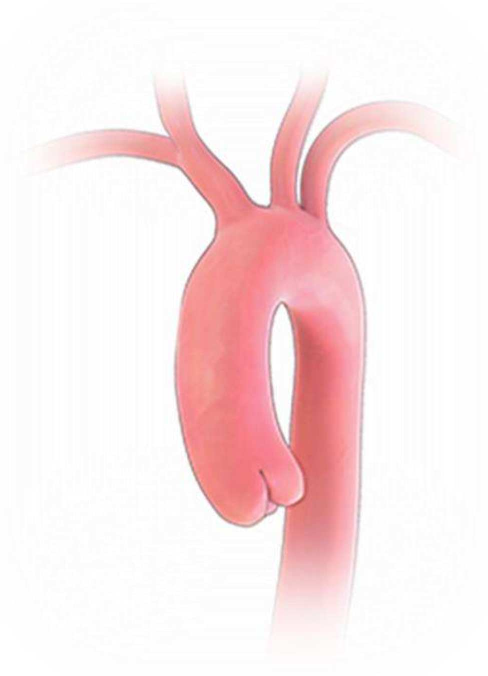
Solution

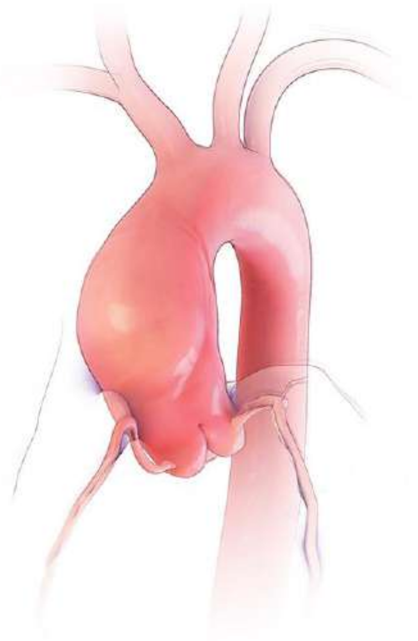
Outcome

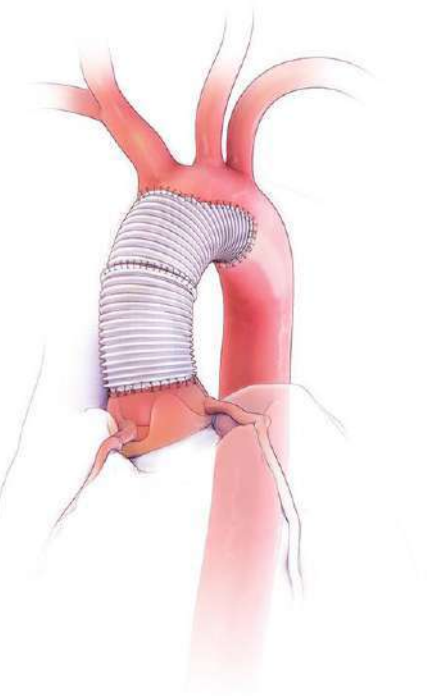
Introduction

Aortic Aneurysms




Healthy

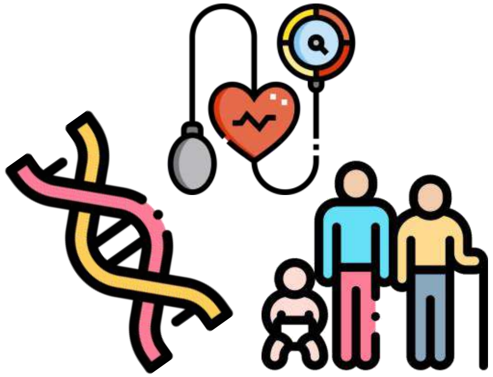

Aneurysm


Repaired

Aortic Aneurysms

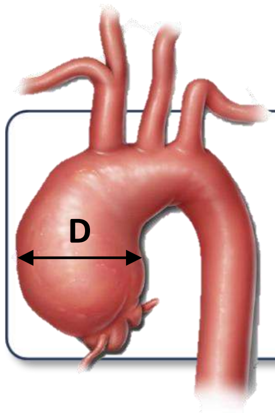
5-10 cases per 100,000 person/year

22% of patients with ruptured aneurysm die before reaching a hospital

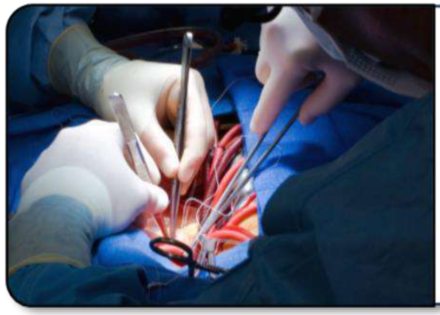


Linked to age, sex, hypertension, genetic conditions

Clinical problem



Current practice:
Surgery is determined by **diameter**.

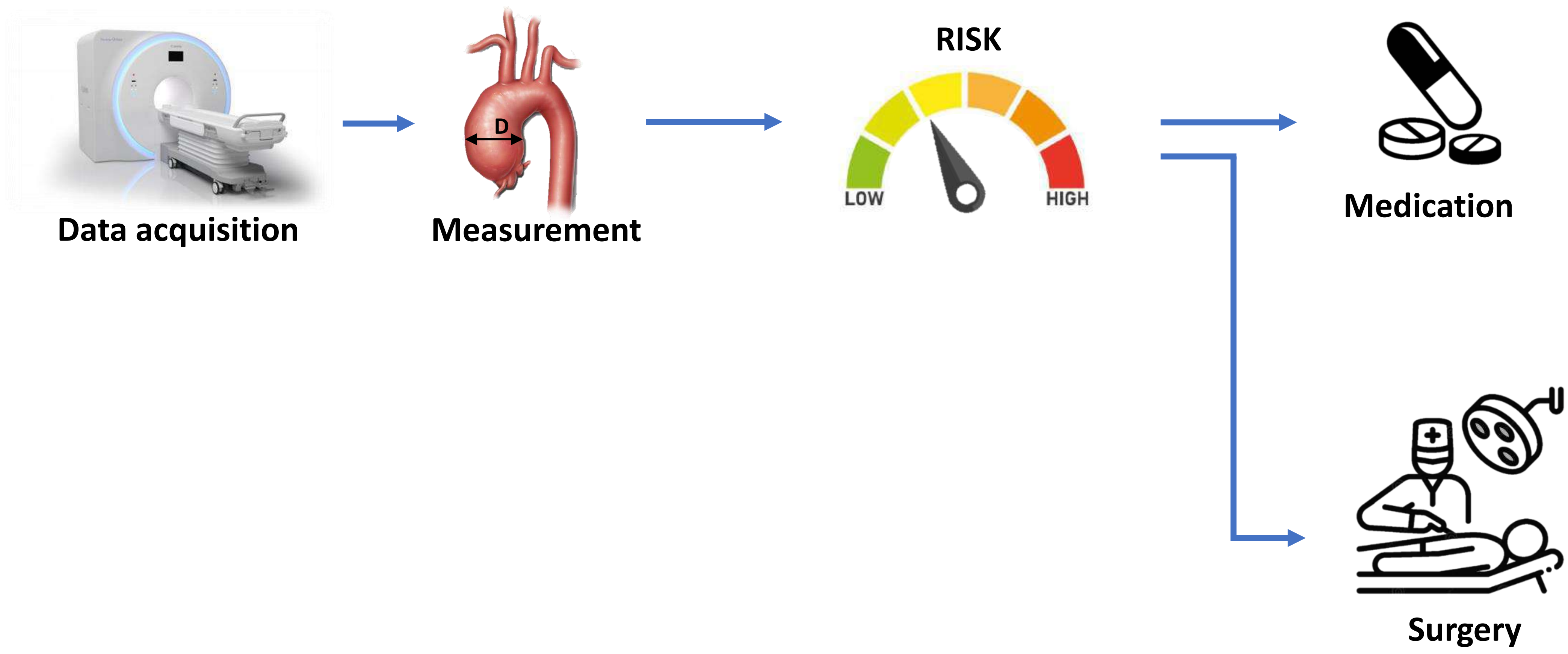


Problem:
- It's too generic
- Unpredicted aneurysm rupture
- Unnecessary intervention

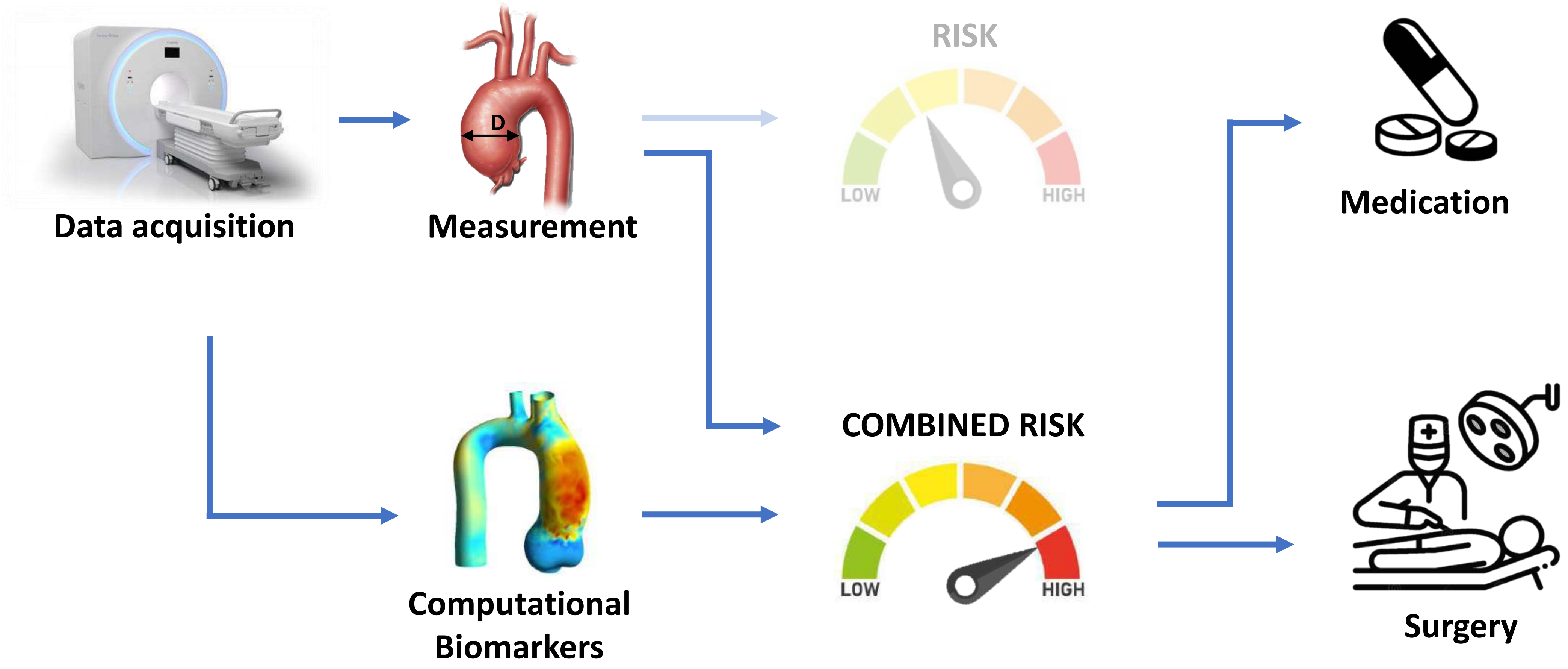
Post-operative complications:
- Hemorrhage
- Infection
- Cardiac fatigue.

Clinical need to gain insight of the patient's HEMODYNAMICS & WALL DETERIORATION for accurate personalized treatment

Surgical decision



Surgical decision

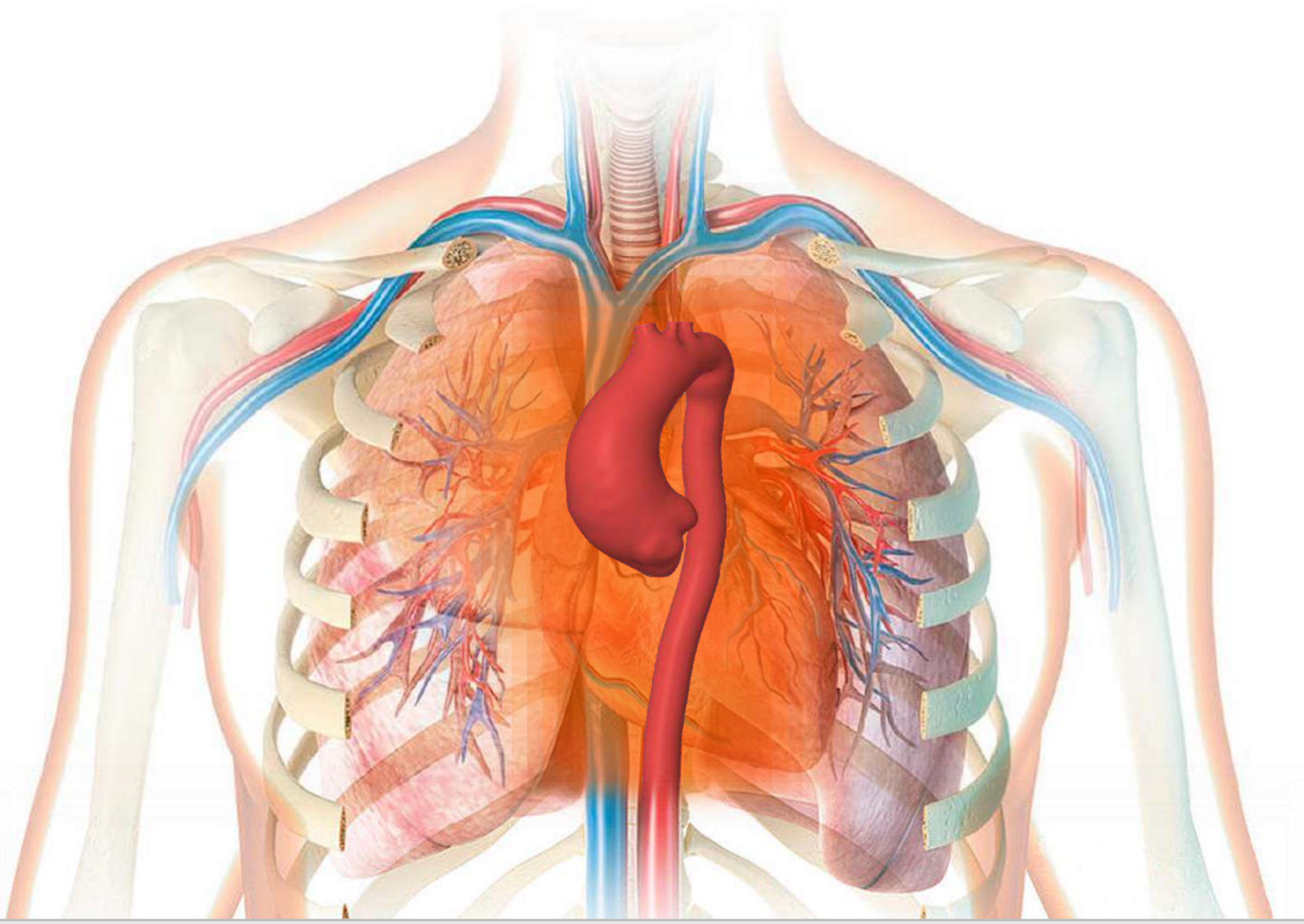


Patient specific diagnosis

Aortic Aneurysm

Patient specific:

- Aorta Shape
- Valve morphology
- Valve pathology
- Hemodynamic BCs
- Aortic wall



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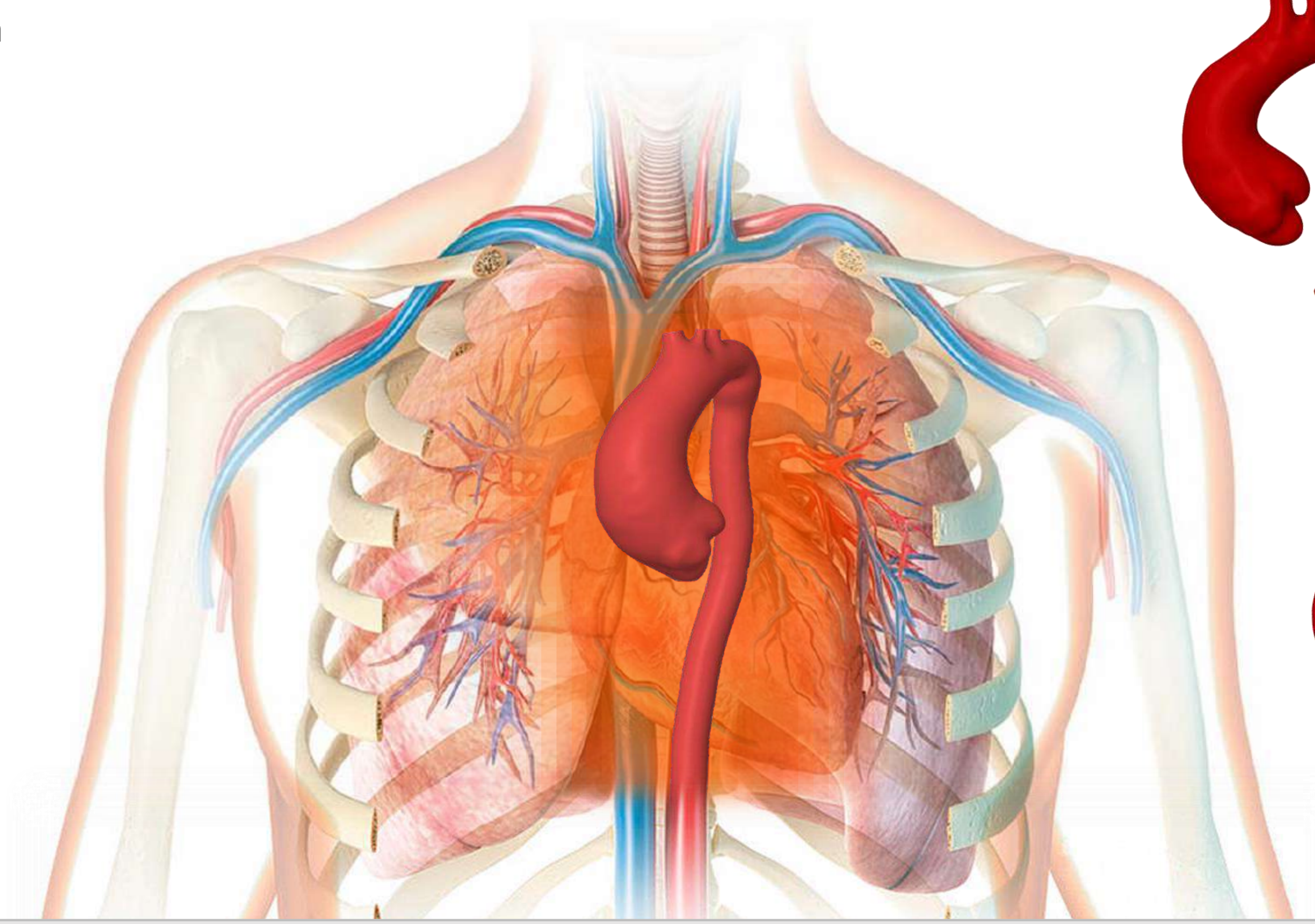

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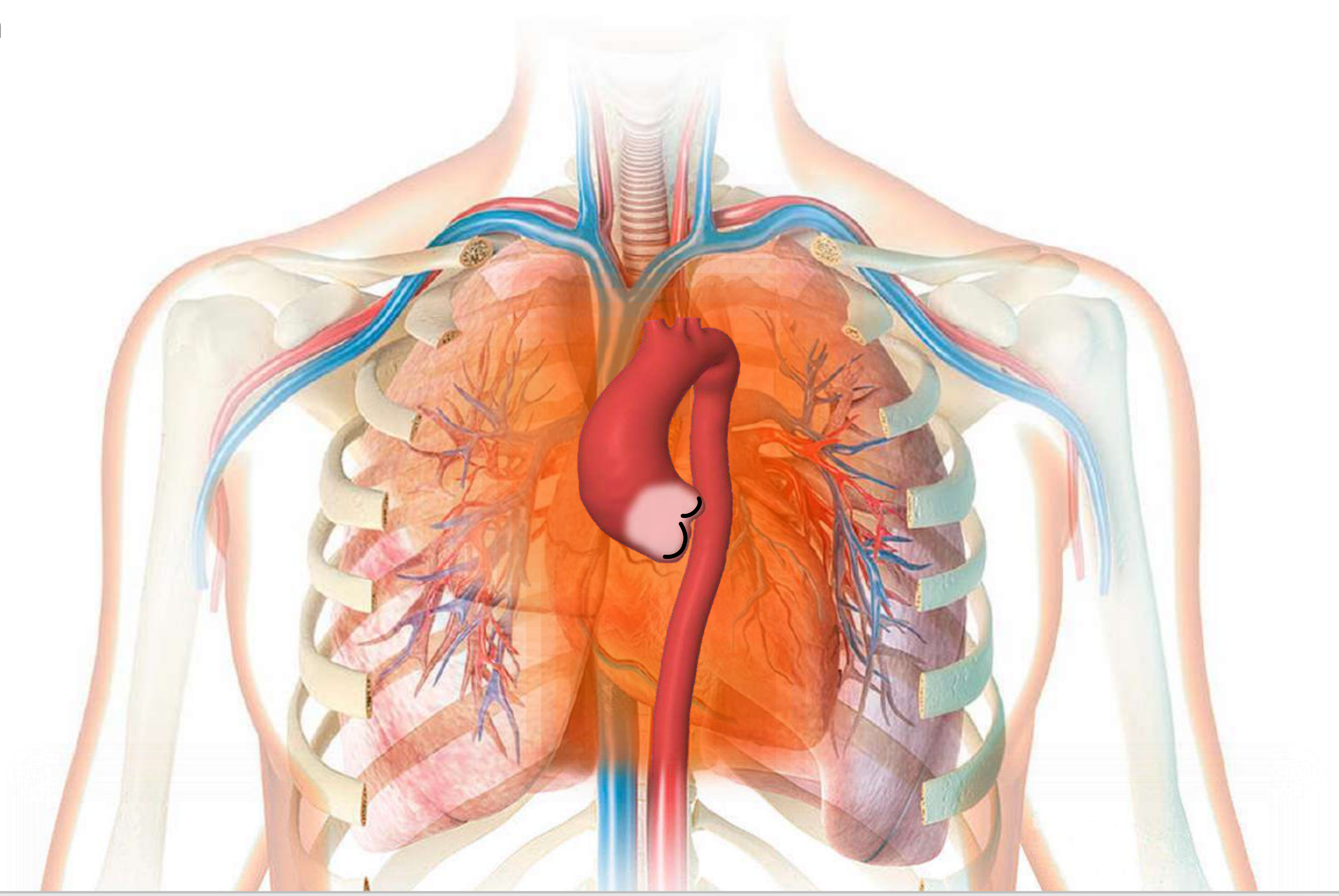

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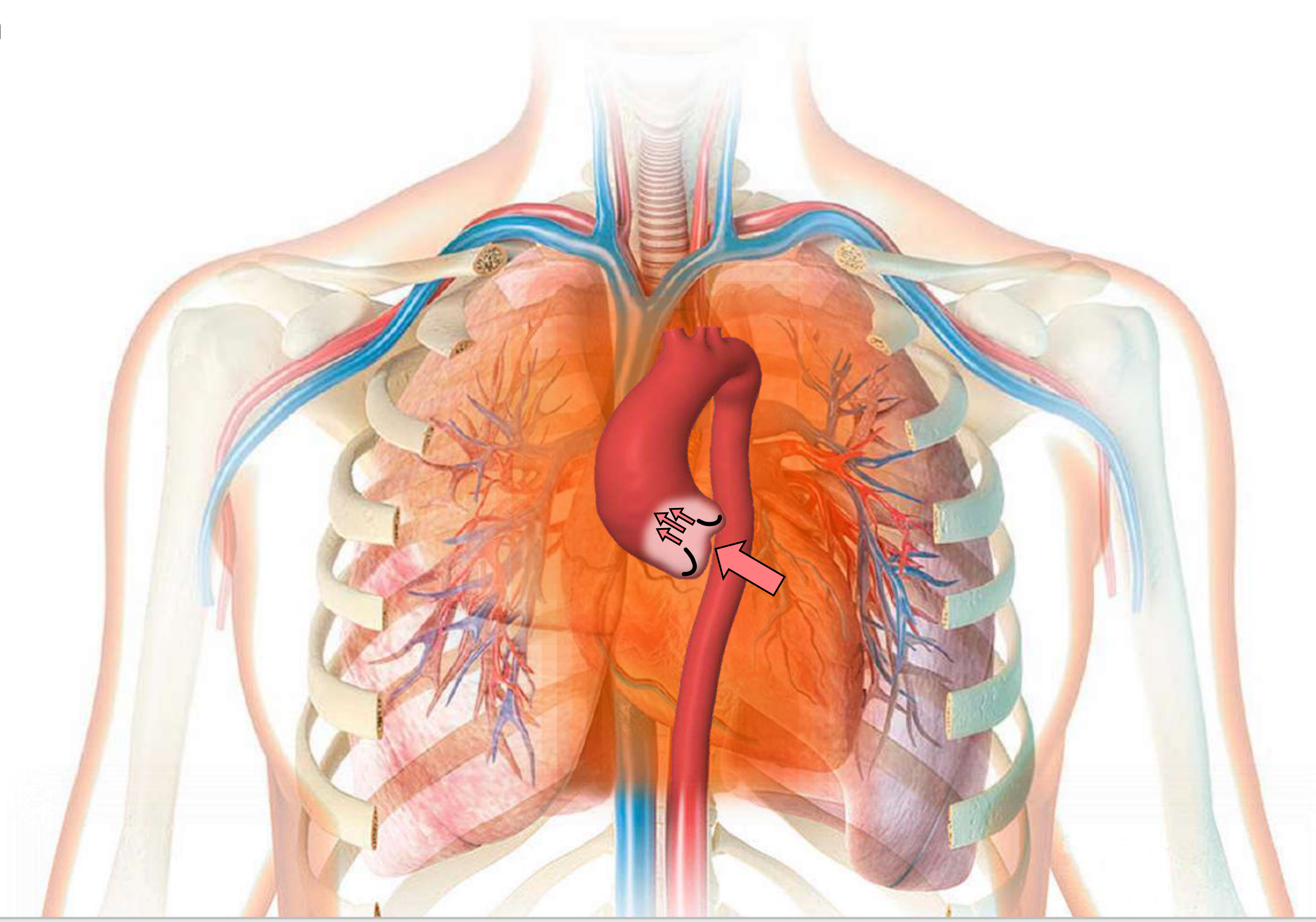
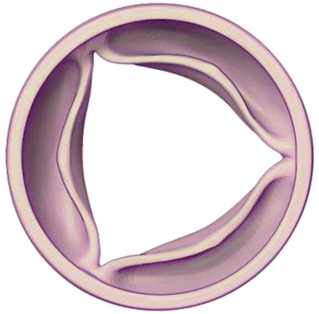
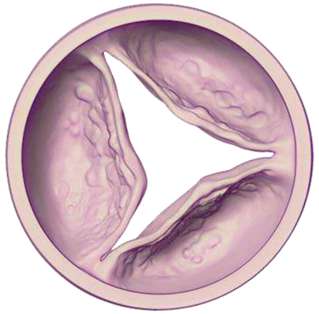




Healthy



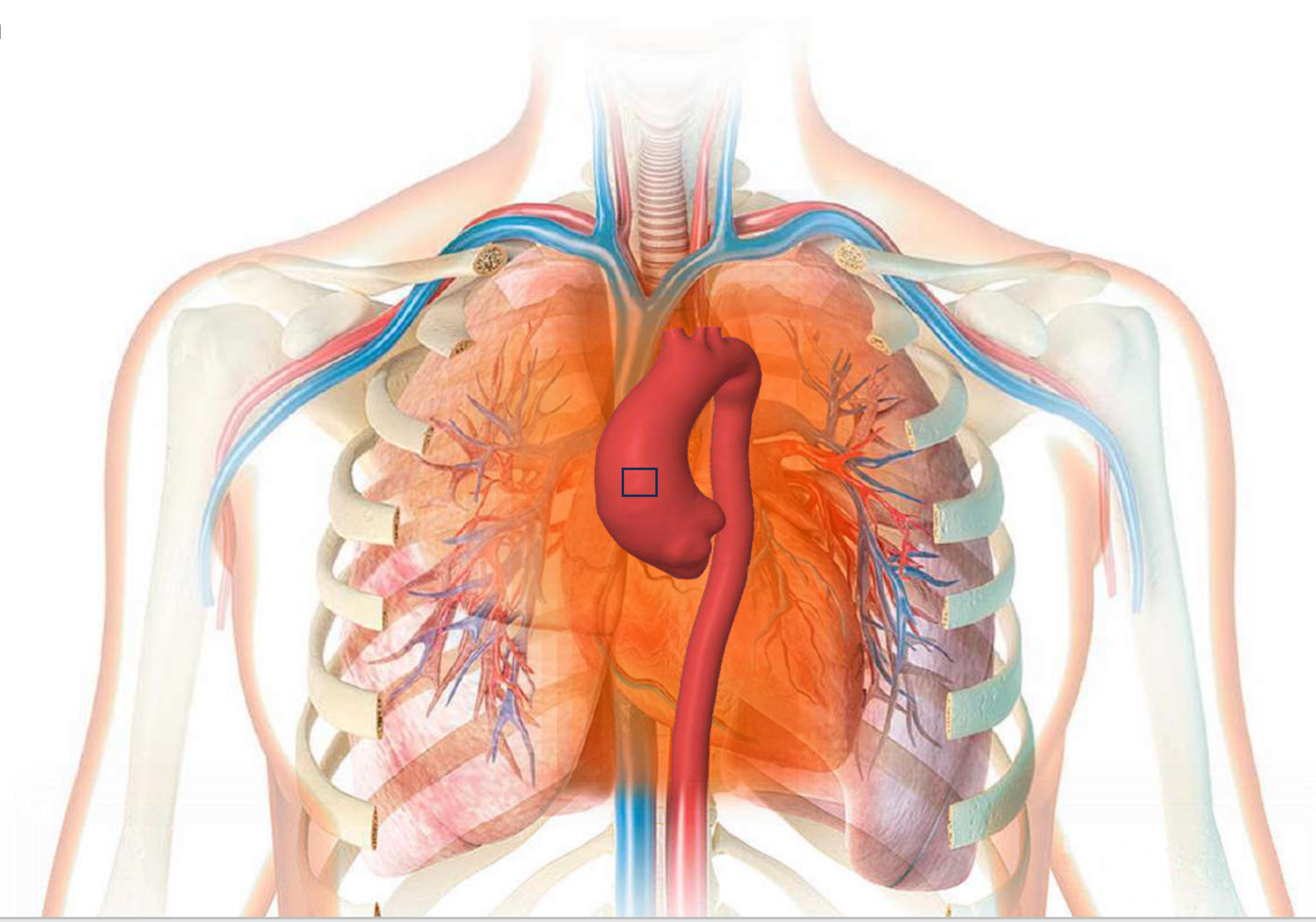
Diseased
(Stenosis)

Patient specific diagnosis

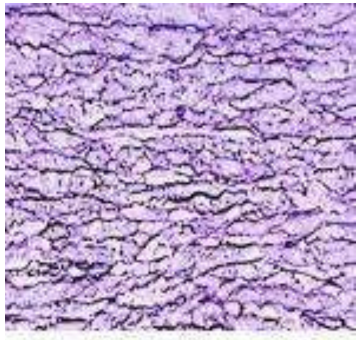
Aortic Aneurysm

Patient specific:

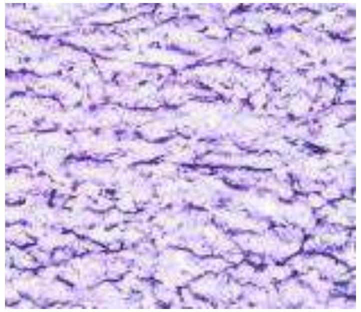
- Aorta Shape
- Valve morphology
- Valve pathology
- Hemodynamic BCs
- Aortic wall



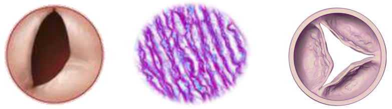
Healthy



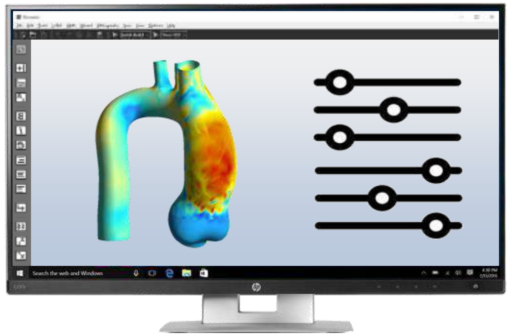
Aneurysm



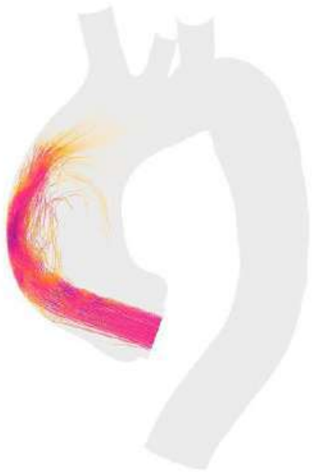
Computational tools for personalized treatment

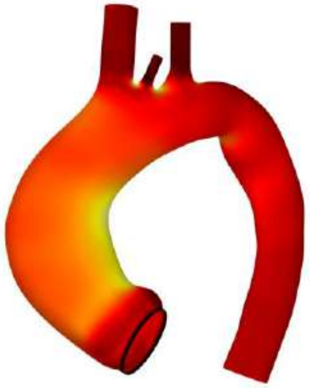

Patient specific data



Fluid biomarkers
WSS, Flow



Structural biomarkers
Stress



Section I

Computational methods for accurate turbulence and viscosity modelling

Introduction

No standardized methodology exists for the computation of cardiovascular flows

↓

CFD results are influence by the modeling set-up

↓

OBJECTIVE

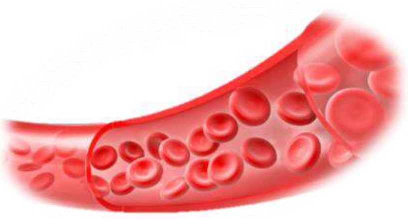
Quantify the effect of model choices CFD results

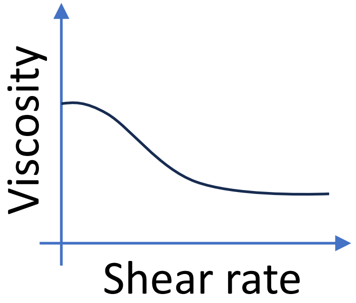
- **Viscosity**
- **Turbulence**

Introduction

Viscosity

- Blood is a mixture of plasma and red blood cells with a shear-thinning behaviour.
- Eddy development and near-wall flow is influence by this property [1].
- It is argued that, under the high shear-rates present in the aorta, the variations in viscosity are negligible and constant viscosity can be assumed.

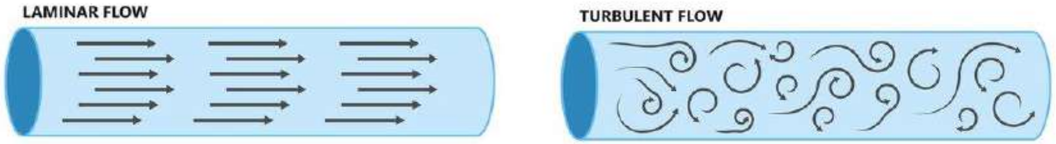




[1] Wyk et al., "Non-Newtonian perspectives on pulsatile blood-analog flows in a 180◦ curved artery model", *Physics of Fluids 27* (2015)

Turbulence

- Turbulence causes bursts of shear stress, damaging endothelial cells [2].
- Turbulence generates additional stresses on aneurysm wall leading to wall vibration and increases the rate of wall dilation [2].
- Pulsatile flow with a low averaged Reynolds number, averaged Reynolds suggests laminar flow.
- Flow deceleration during diastole favours turbulence generation.



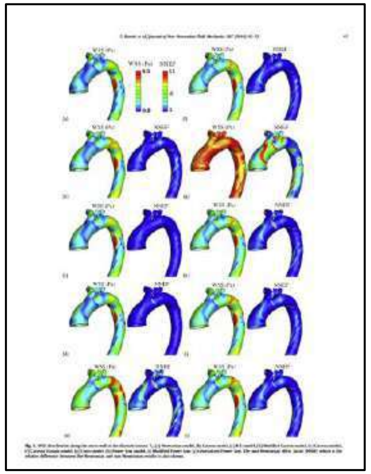
[2] Tan et al. "Analysis of flow patterns in a patient-specific thoracic aortic aneurysm model," *Computers and Structures* 87 (2009)

Previous work

Viscosity

Newtonian model causes:

- Underestimation of WSS and hemolysis
- Growth and decay of eddies
- Premature turbulent transition

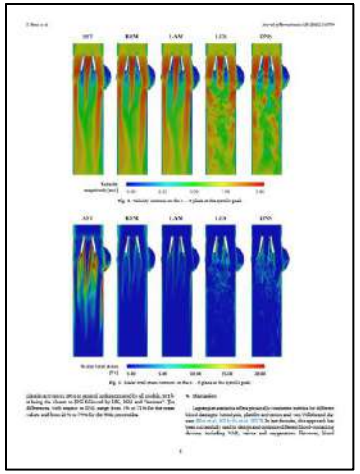


Karimi et al. *Journal of Non-Newtonian Fluid Mechanics* 207 (2014)

Turbulence

Laminar model causes:

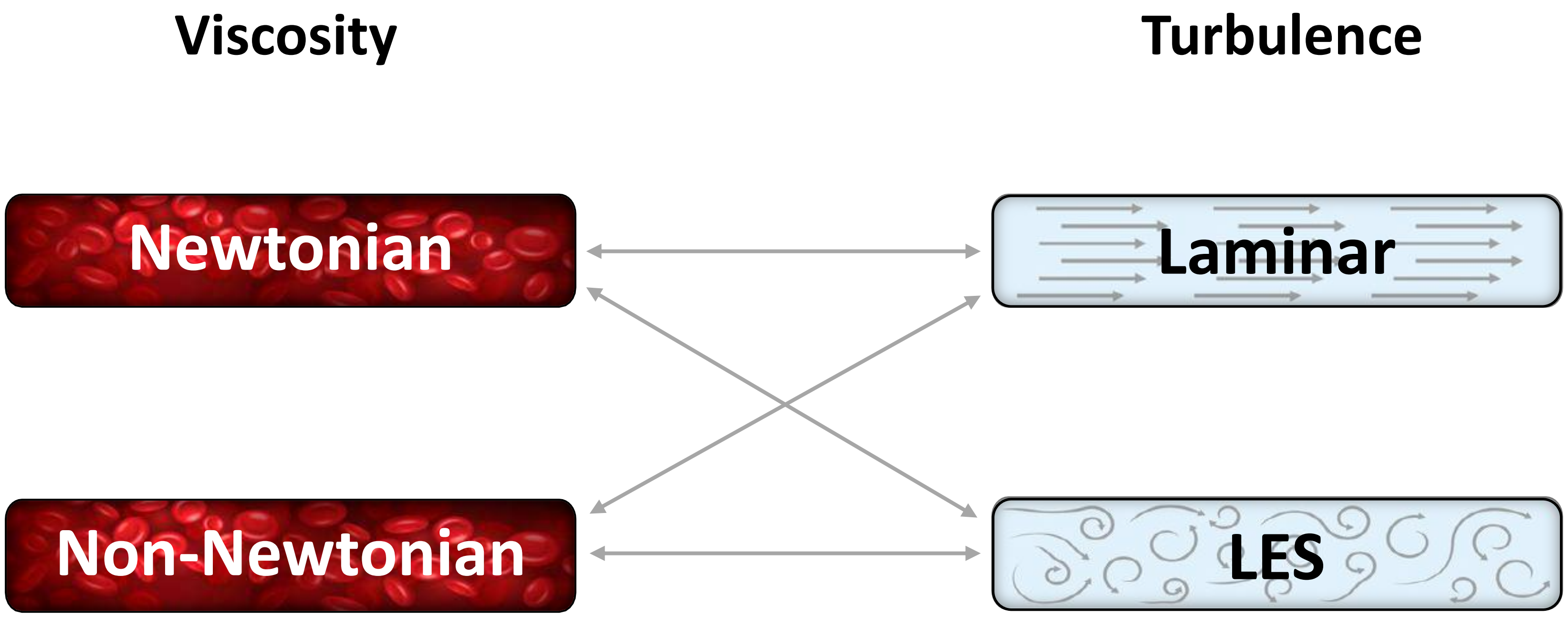
- WSS underestimated between 0-6% (depending on author)
- Platelet activation and hemolysis
- Underestimated TKE



Bozzi et al. *Journal of Biomechanics 128* (2021)

No publication exists on the combined effect of viscosity and turbulence models

Objective



Understand the interaction between models
and
the importance of the model choices

Scope

Viscosity

- **Newtonian:** $\mu(\dot{\gamma}) = \mu_\infty$
- **Non-Newtonian: Carreau viscosity (CV)**

$$\mu(\dot{\gamma}) = \mu_\infty + (\mu_0 - \mu_\infty)\left[1 + (\lambda\dot{\gamma})^2\right]^{\frac{n-1}{2}}$$

$\mu_\infty = 3.5$ mPa·s

$\mu_0 = 56$ mPa·s

$\lambda = 3.313$ s

$n = 0.3568$

Turbulence

- **No model: Laminar flow model (LFM)**
- **Turbulent: LES**

$$\frac{\partial \bar{u}_i}{\partial x_i} = 0\,,$$

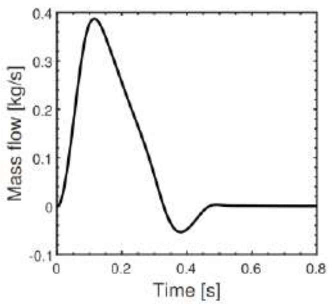
$$\frac{\partial \bar{u}_i}{\partial t} + \bar{u}_j \frac{\partial \bar{u}_i}{\partial x_j} = -\frac{1}{\rho}\frac{\partial \bar{p}}{\partial x_i} + \nu \frac{\partial}{\partial x_j}\left(\frac{\partial \bar{u}_i}{\partial x_j}\right) - \frac{\partial \tau_{ij}}{\partial x_j}$$

$$\tau_{ij} - \frac{1}{3}\tau_{kk}\delta_{ij} = -2\nu_{sgs}\bar{S}_{ij}$$

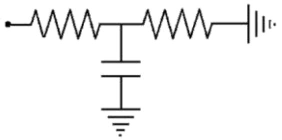
$$\nu_{sgs} = (C_S\Delta)^2|\bar{S}|$$

Dynamic Smagorinsky-Lilly (DSL) subgrid-scale turbulence model

Model setup



Mass flow inlet



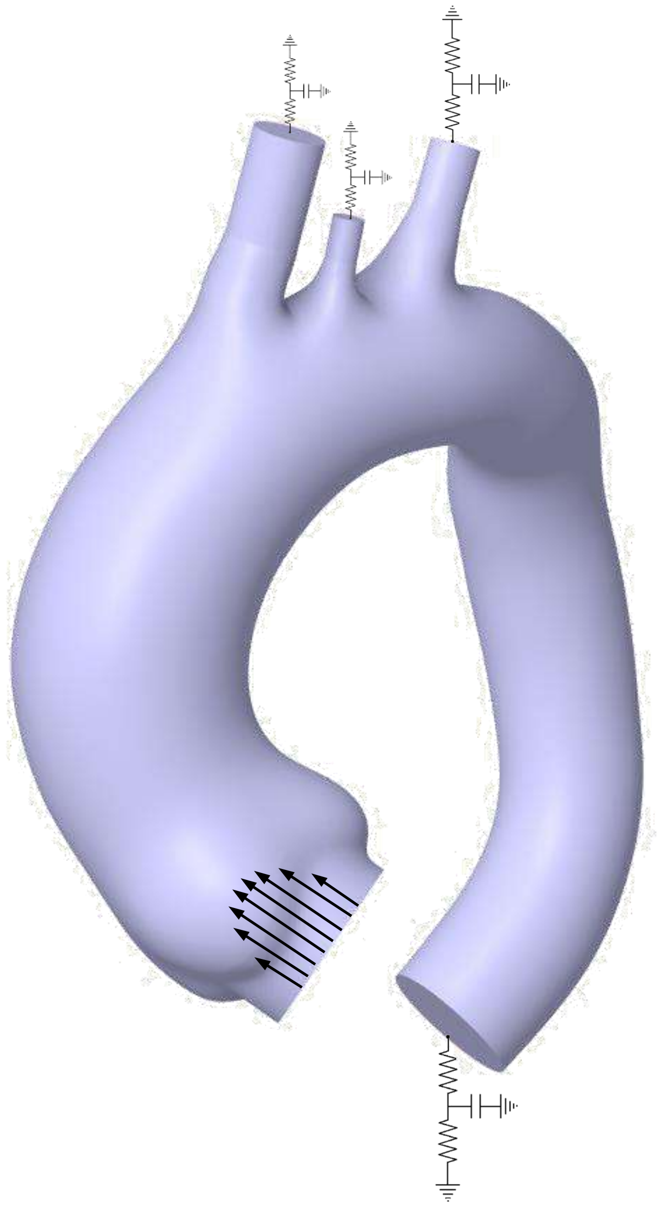
Windkessel outlets

Aortic valve

- Healthy
- Stenotic

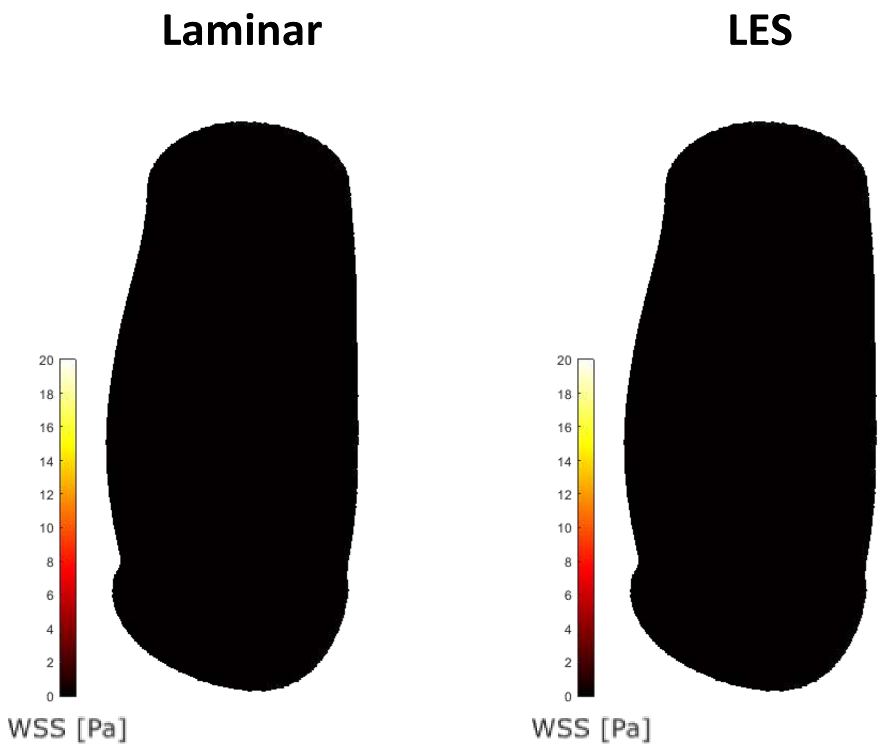
10 days per scenario

- 20 heart beats
- 32 cores



Results

- Vortex structure is influenced by the turbulence model.
- Non-Newtonian viscosity has greater impact (2.9-5.0%) on wall shear stress than Large Eddy Simulation turbulence modelling (0.1-1.4%).
- Wall shear stress is underestimated when considering Newtonian viscosity by 2.9-5.0%.
- The contribution of non-Newtonian viscosity is amplified when combined with a LES model.
- Cycle-to-cycle variability can impact the results as much as the numerical model if insufficient cycles are performed.



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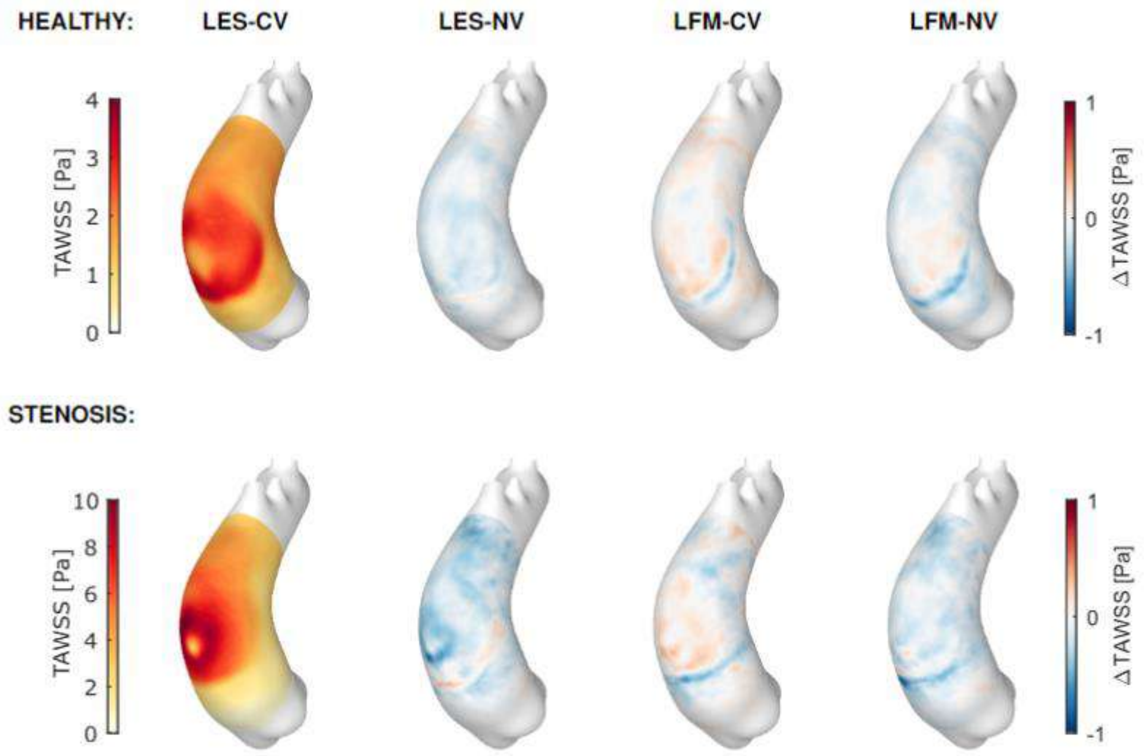

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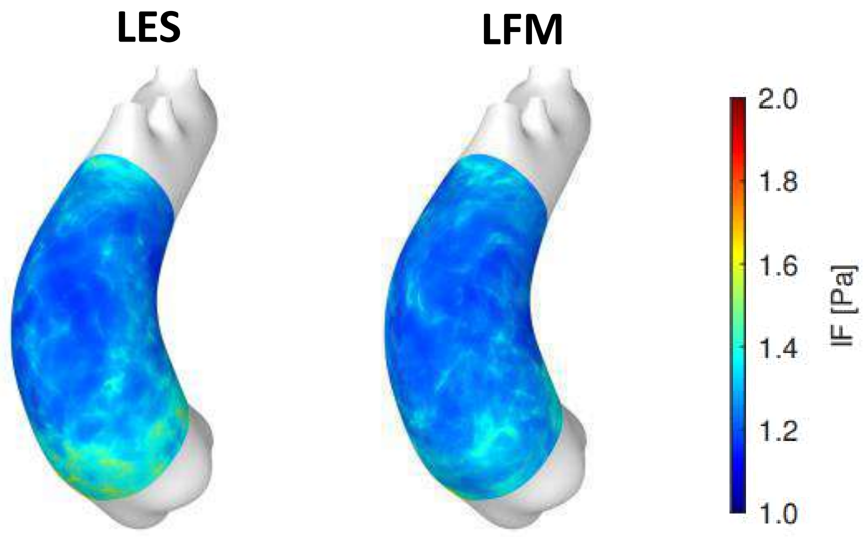

$$IF = \mu/\mu_\infty$$

Turbulence model	Healthy		Stenosis	
	Systole	TA	Systole	TA
Laminar	1.160	1.277	1.148	1.290
LES	1.165	1.286	1.166	1.297

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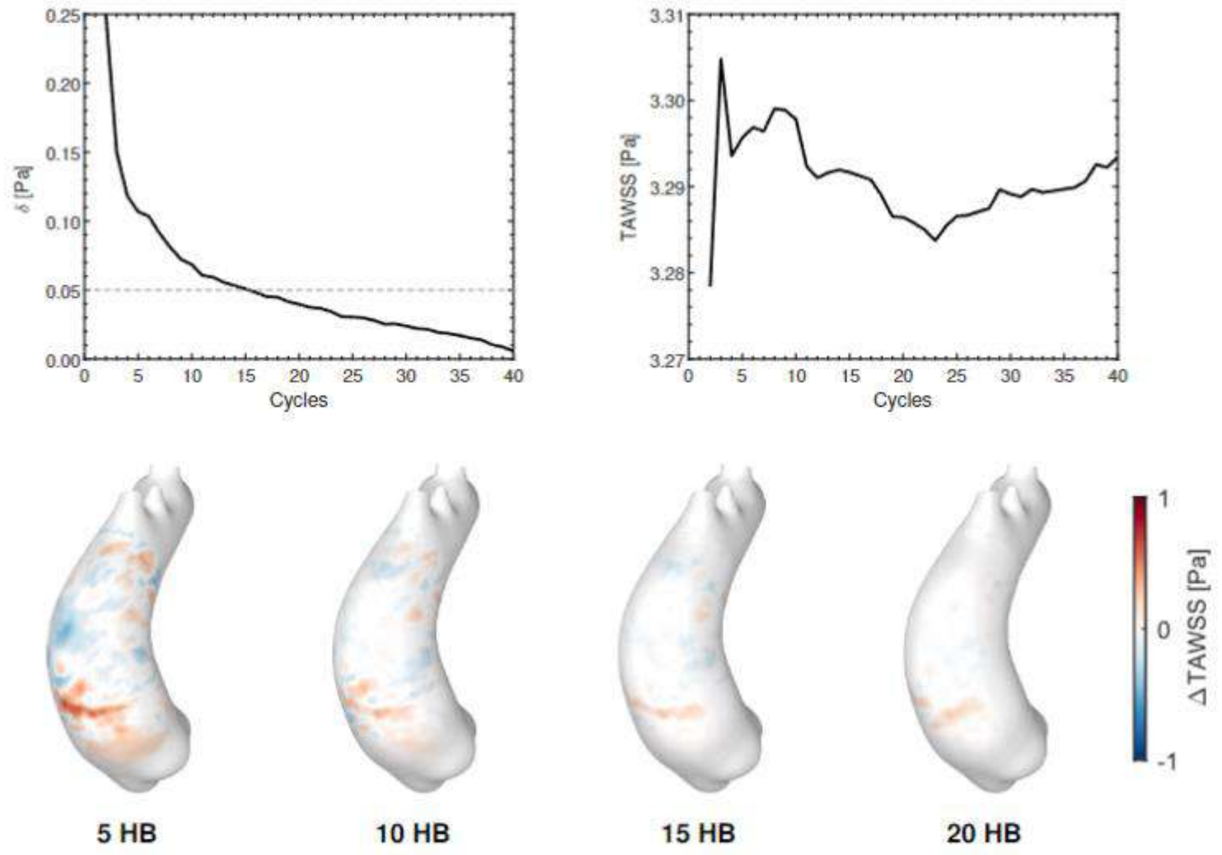


Martinez et al., "Effect of Turbulence and Viscosity Models on Wall Shear Stress Derived Biomarkers for Aorta Simulations," *Computers in Biology and Medicine,* 167 (2023)

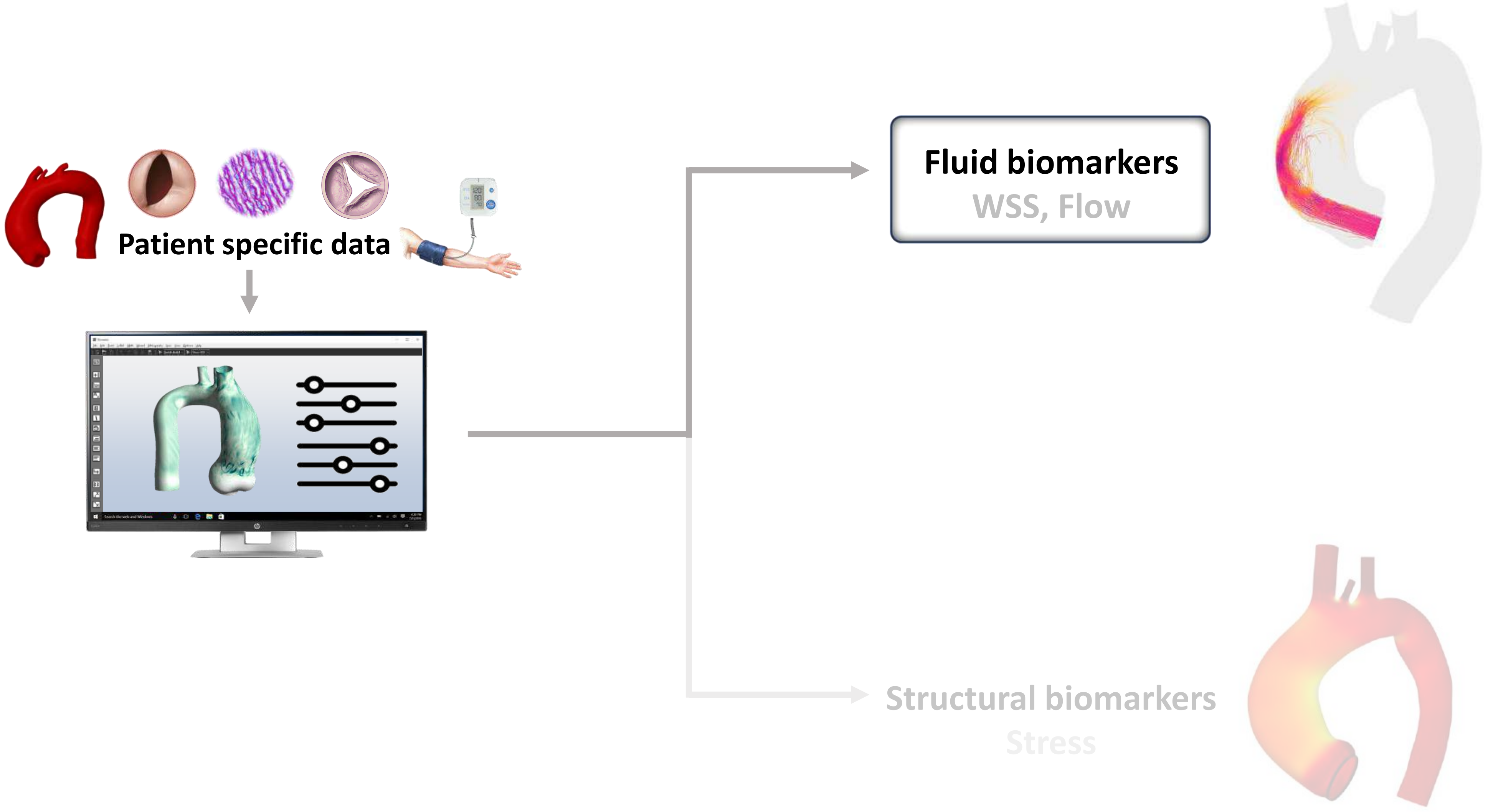
Future works

- Additional viscous models: Power law, Casson, Cross
- Realistic aortic jet shapes
- FSI effects

Section II

CFD biomarkers for aneurysm growth prediction

Computational tools for personalized treatment

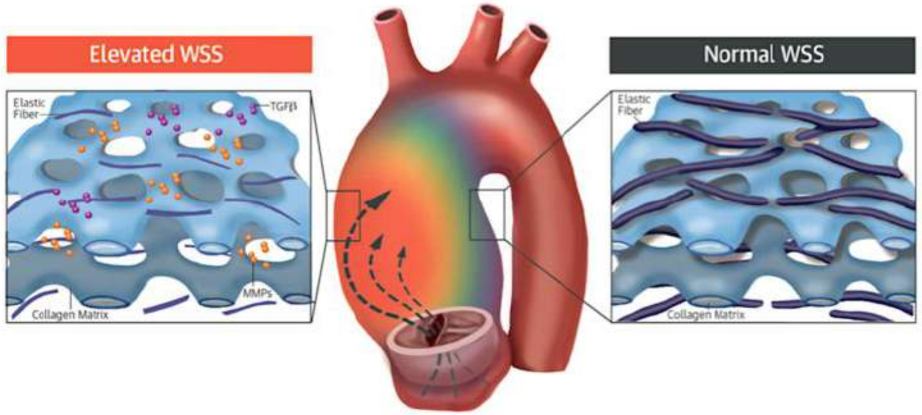


Introduction

- Hemodynamics conditions influence the biomechanical processes in the arterial wall:
  - Endothelial damage.
  - Elastin and smooth muscle cell damage.
  - Extra cellular matrix dysregulation.

- A debate exists on whether genetic conditions or hemodynamics are responsible for the development of aneurysms.

IN THIS SECTION:
The correlation between fluid biomarkers and aneurysm growth will be assessed.

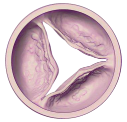


Guzzardi et al, "Valve-Related Hemodynamics Mediate Human Bicuspid Aortopathy: Insights From Wall Shear Stress Mapping,"*J. Am Coll Cardiol.* 66 (2015)

Dataset

33 patients (CHU Rennes, Dijon and Toulouse)

16 Tricuspid | 15 Bicuspid T1 | 2 Bicuspid T0



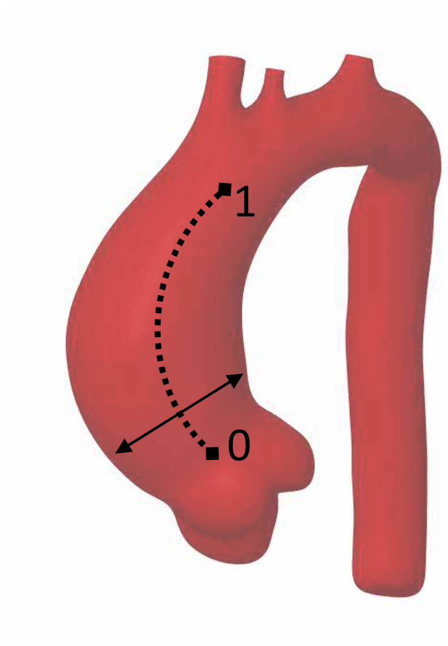
Aortic valve area and jet velocity:

- Echocardiography: 20 patients
- MRI flow: 5 patients
- No data: 8 patients

Scans with average spacing 41 months

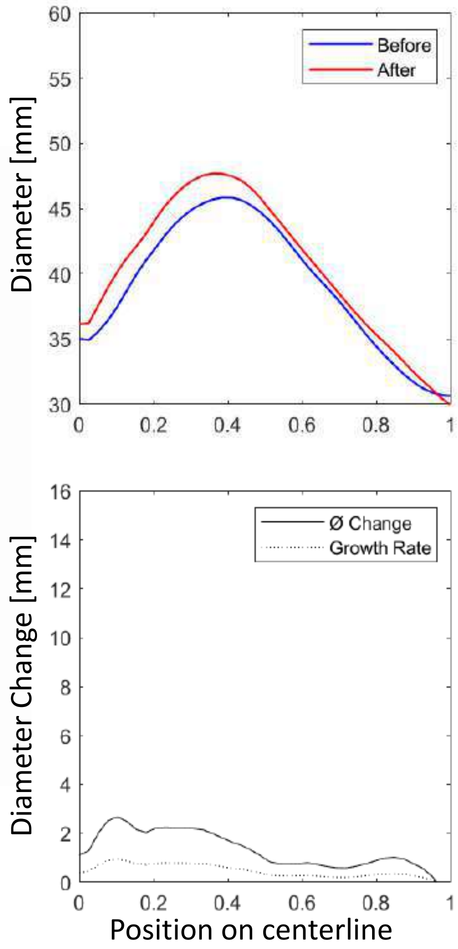
Growth analysis

Patient 1



G.R. = 0.94 mm/year

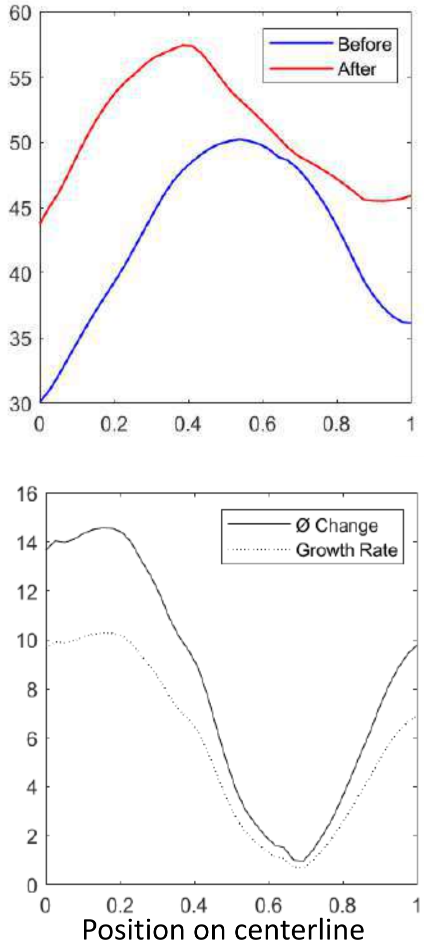
After 34 months



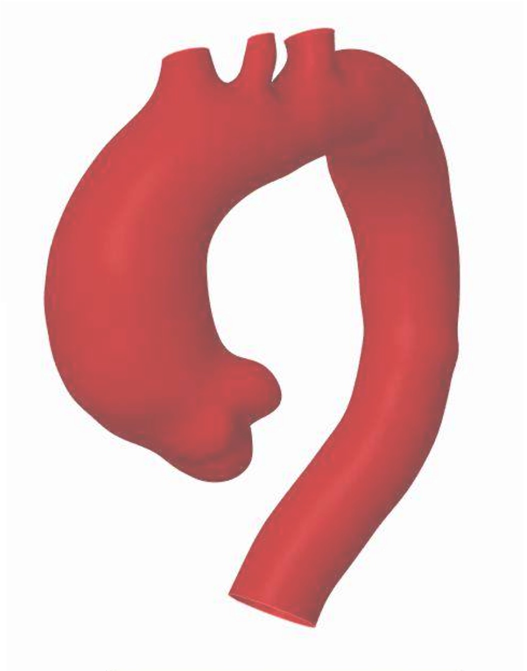
DIAMETER ALONG THE CENTERLINE

DIAMETER CHANGE AND GROWTH RATE

After 17 months



Patient 2



G.R. = 10.27 mm/year

Growth rate = Diameter change per year [mm/year]

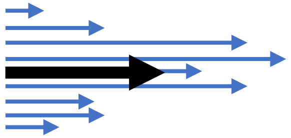
Fluid Biomarkers

WALL SHEAR ANALYSIS

FLOW ANALYSIS

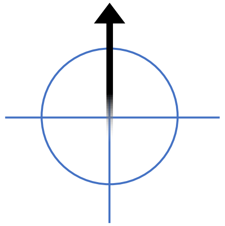
Fluid Biomarkers
Wall Shear

Time-average WSS



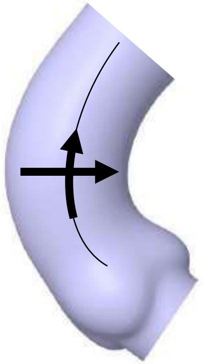
$$\mathrm{TAWSS} = \frac{1}{T}\int_0^T |\mathbf{WSS}(t)|\,dt$$

Oscilating Shear Index



$$\mathrm{OSI} = 0.5\left(1 - \frac{\left|\int_0^T \mathbf{WSS}(t)\,dt\right|}{\int_0^T |\mathbf{WSS}(t)|\,dt}\right)$$

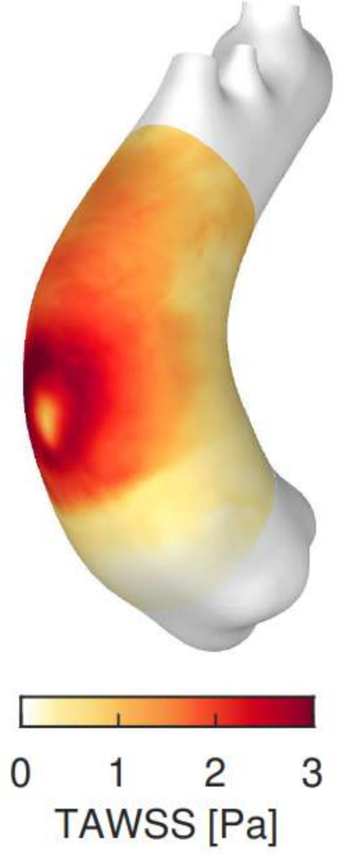
Shear Angle



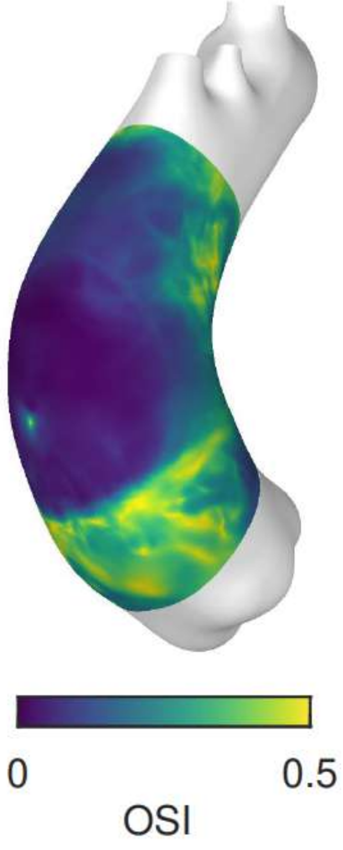
$$\mathrm{SA} = \frac{2}{\pi}\arctan\left(\frac{\mathrm{WSS}_{\mathrm{Axial}}}{\mathrm{WSS}_{\mathrm{Circ}}}\right)$$

Fluid Biomarkers
Wall Shear

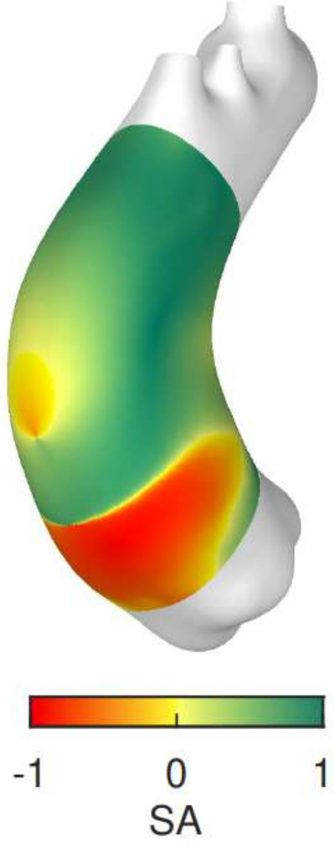
Time-average WSS



Oscilating Shear Index



Shear Angle



Fluid Biomarkers
Flow

WALL SHEAR ANALYSIS

FLOW ANALYSIS

Fluid Biomarkers
Flow

Flow Asymmetry:

Offset of flux centroid.

Normalized by mean radius.

$$FA = \frac{\|P_{Center} - P_{FMC}\|}{R_{mean}}$$

Angle: Between flow and plane

Flow Asymmetry - Bounded:

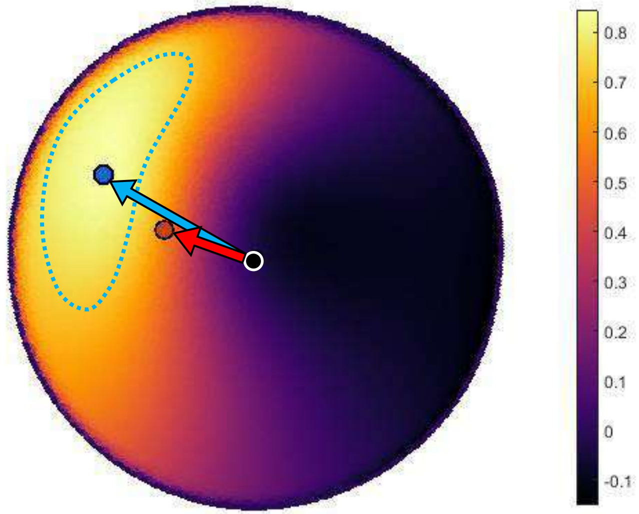
Offset of bounded fast-moving region centroid

Normalized by mean radius.

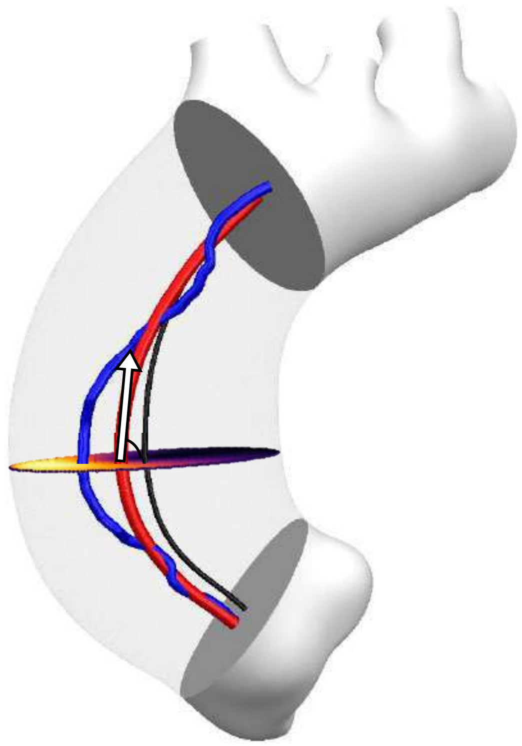
$$FA_{20\%} = \frac{\|P_{Center} - P_{FMC_{20\%}}\|}{R_{mean}}$$

Flow Dispersion:

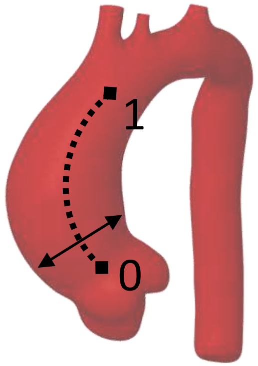
$$FD = \frac{A_{20\%}}{A_{Total}}$$

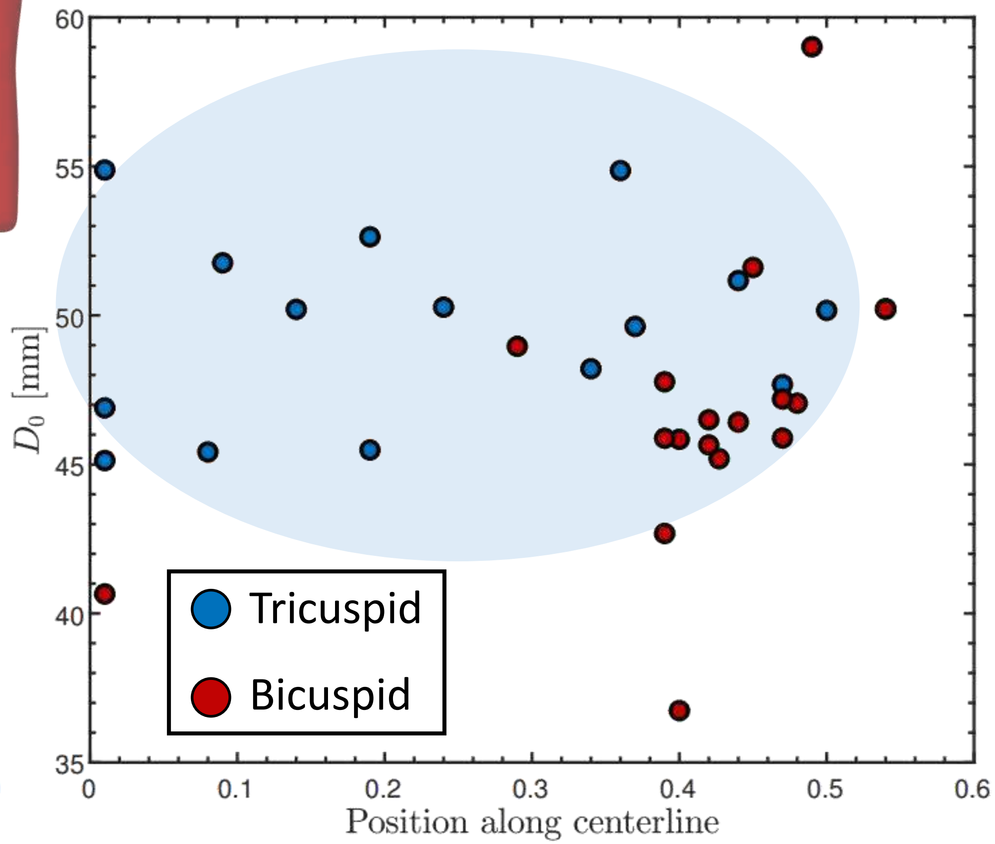


Cross-plane velocity [m/s]

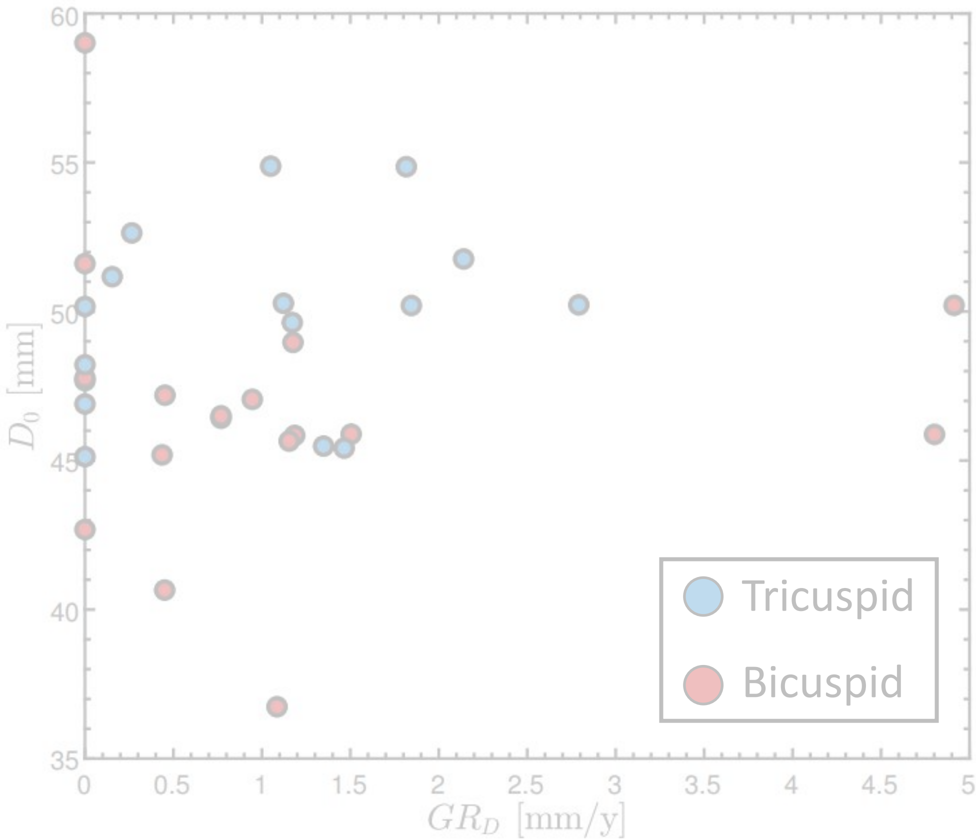


Results: Growth



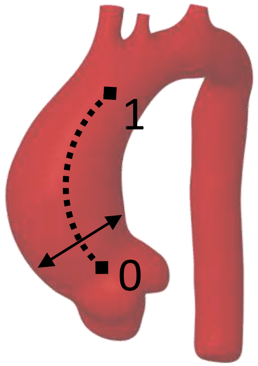


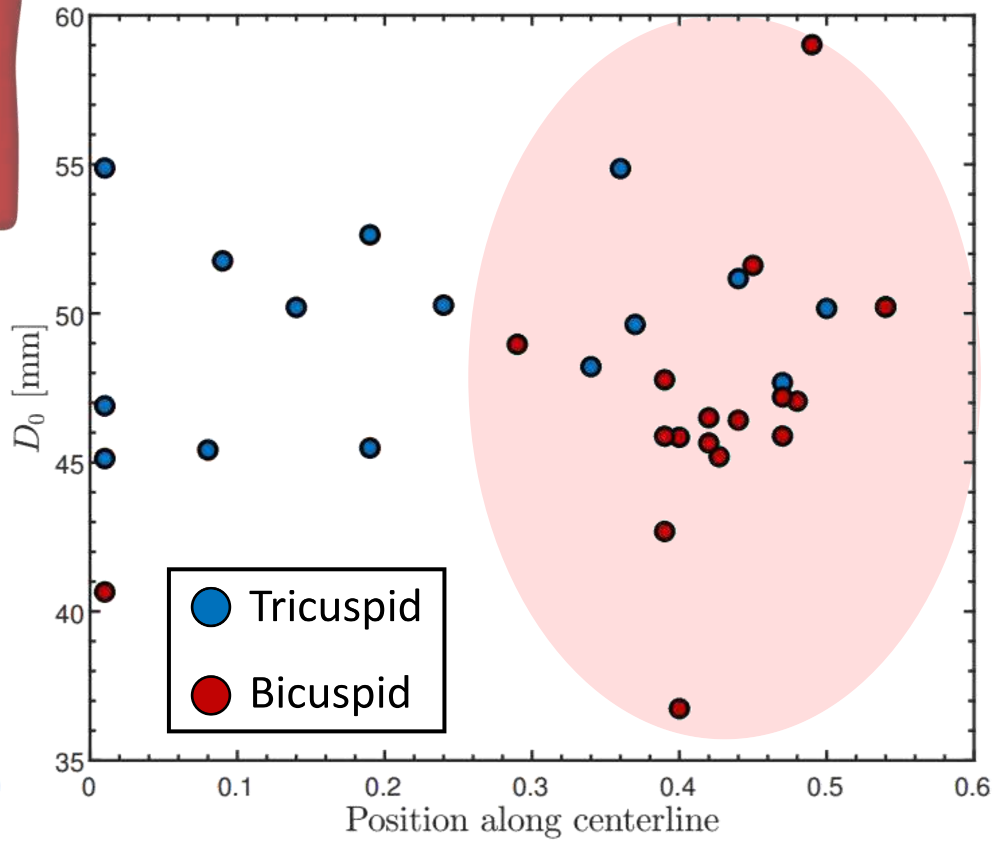
The maximum diameter was located, on average, on PC = 0.25 for TAV and on PC = 0.40 for BAV.

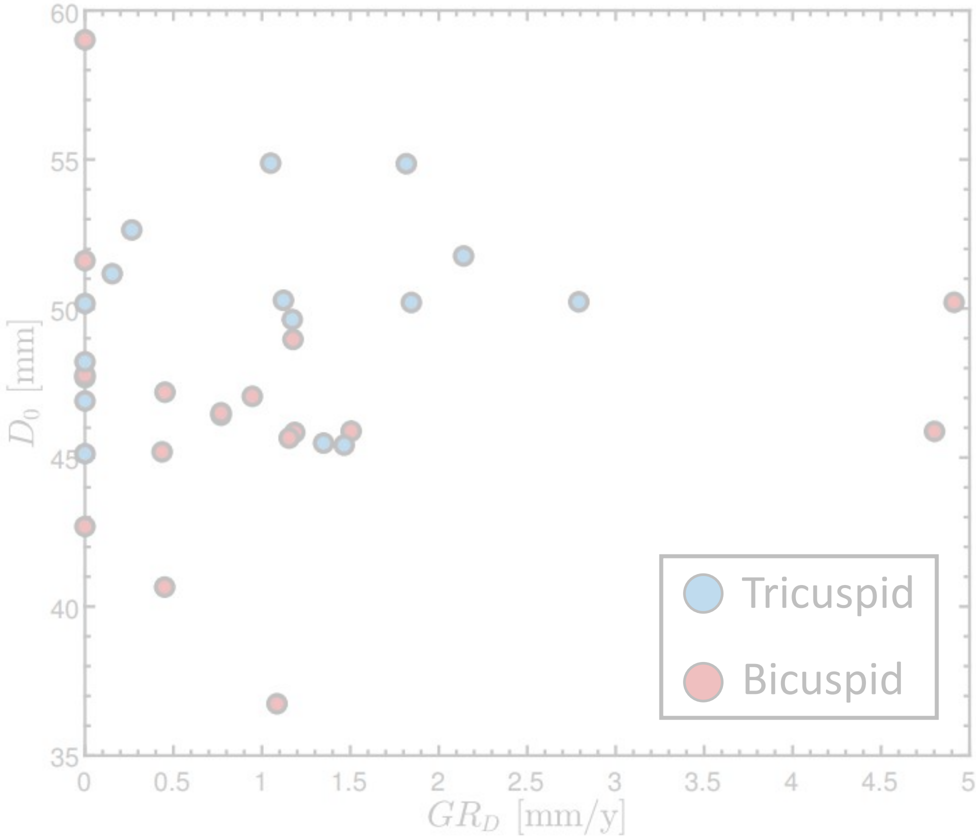


Initial diameter does not correlate with *GR* (R= 0.04)

Results: Growth



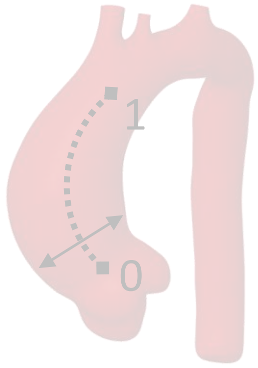


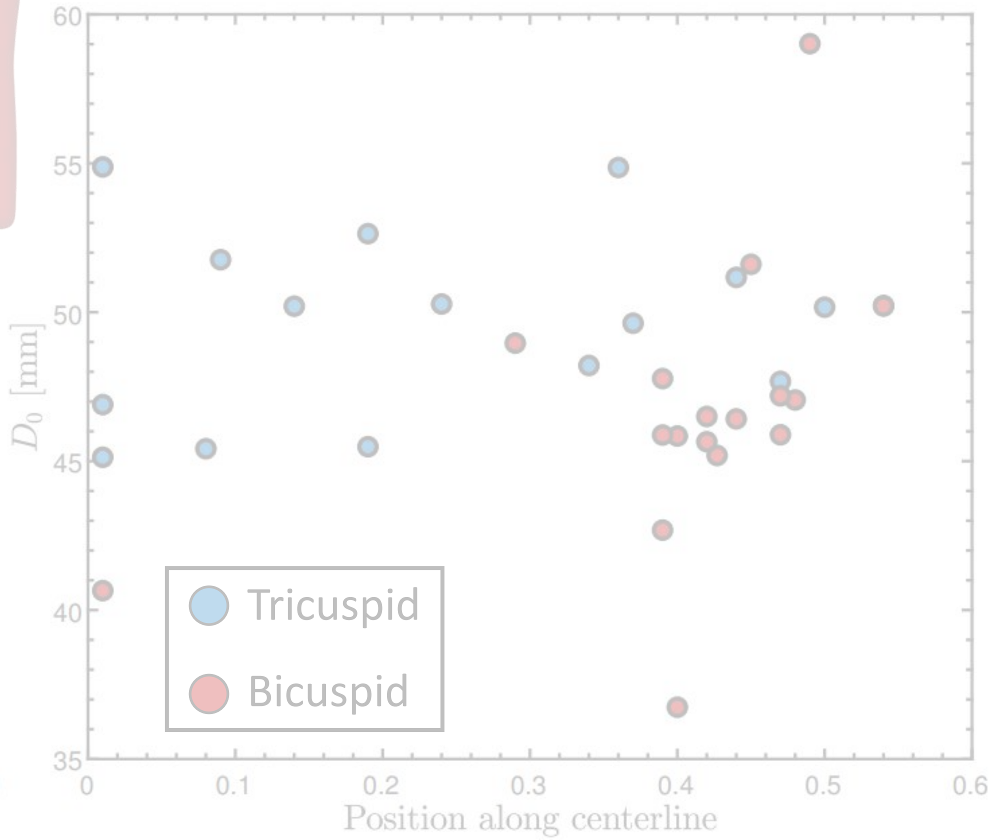


The maximum diameter was located, on average, on PC = 0.25 for TAV and on PC = 0.40 for BAV.

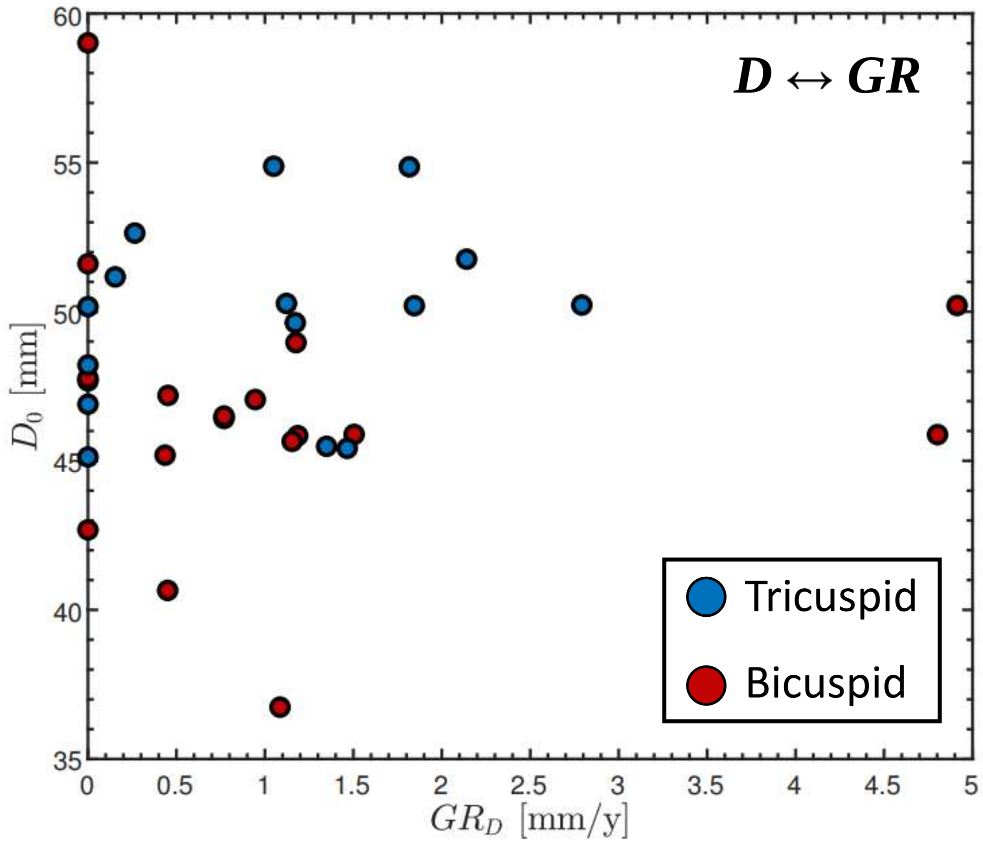
Initial diameter does not correlate with *GR* (R= 0.04)

Results: Growth





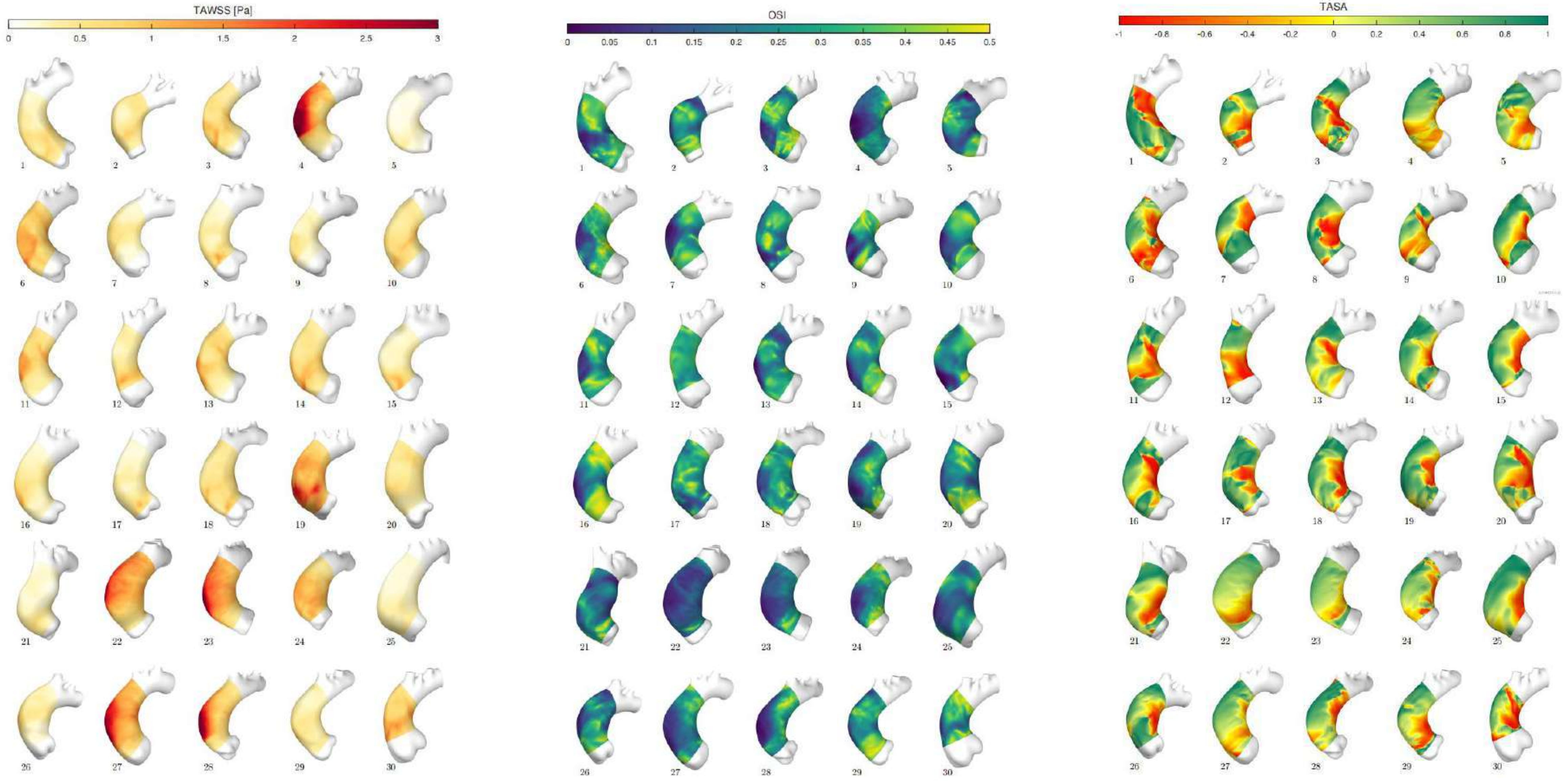
The maximum diameter was located, on average, on PC = 0.25 for TAV and on PC = 0.40 for BAV.



Initial diameter does not correlate with *GR* (R= 0.04)

Results: Fluid biomarkers

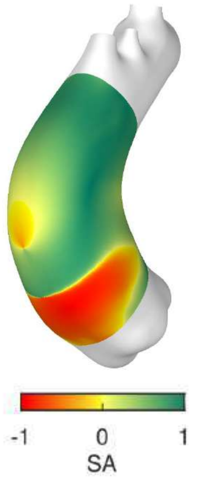
6 days per patient
- 6 heart beats
- 16 cores
- 33 patients

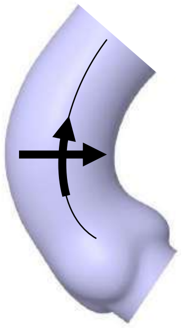


Results: Correlations

PEAK SYSTOLE SHEAR ANGLE

- External wall of BAV patients.
- Weak correlation with GR_D *and* GR_L .
- Suggest reversed and rotating flow are linked to wall degeneration.
- Agrees with previous works:
  - FSI on Marfan syndrome patients
    Pons et al., *Royal Society Open Science* 7 (2020)
  - MRI flow on BAV patients
    Minderhoud et al., *European Heart Journal – Cardiovascular Imaging* **23** (2022)





$$SA = \frac{2}{\pi}\arctan\left(\frac{WSS_{Axial}}{WSS_{Circ}}\right)$$

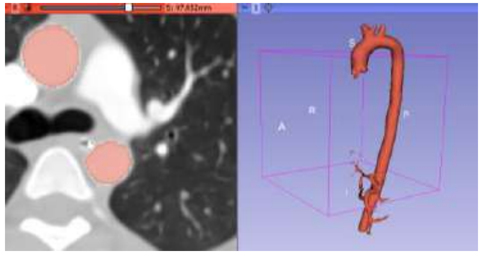
Biomarker	Measure	TAV GR_D R	TAV GR_D p	TAV GR_L R	TAV GR_L p	BAV GR_D R	BAV GR_D p	BAV GR_L R	BAV GR_L p
TAWSS	Max	-0.223	0.407	-0.274	0.304	-0.160	0.541	-0.256	0.321
	Mean	-0.054	0.843	-0.190	0.480	-0.128	0.623	-0.209	0.421
PSWSS	Max	-0.132	0.626	-0.162	0.549	-0.053	0.841	-0.148	0.570
	Mean	-0.178	0.510	-0.282	0.291	-0.095	0.717	-0.213	0.411
OSI	Mean	-0.030	0.911	0.108	0.692	-0.089	0.734	0.002	0.995
SA	TA-Mean	0.061	0.823	-0.048	0.860	0.255	0.324	0.274	0.287
	PS-Mean	0.004	0.987	-0.048	0.859	-0.482	0.050	-0.481	0.051
RFR	TA	0.034	0.899	0.073	0.787	-0.266	0.303	-0.306	0.232
	PS	0.048	0.859	0.072	0.792	0.243	0.347	0.275	0.286

- Only 17 BAV patients → Statistical relevance is debatable.
- Largest CFD study on aneurysm growth up to date.

Future Works

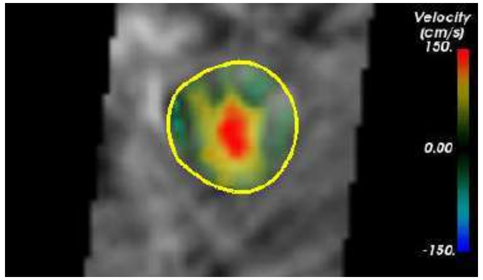
- Larger time window

  Reduce the error in the growth rate measurements.
  Follow the evolution during the initial phase.



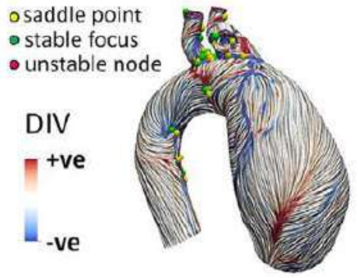
- MRI 4D calibrated aortic jet

  The spatio-temporal velocity profile of the aortic jet will severely determine the flow structure throughout the cardiac cycle, hence, the biomarkers.



- Topological WSS skeleton analysis

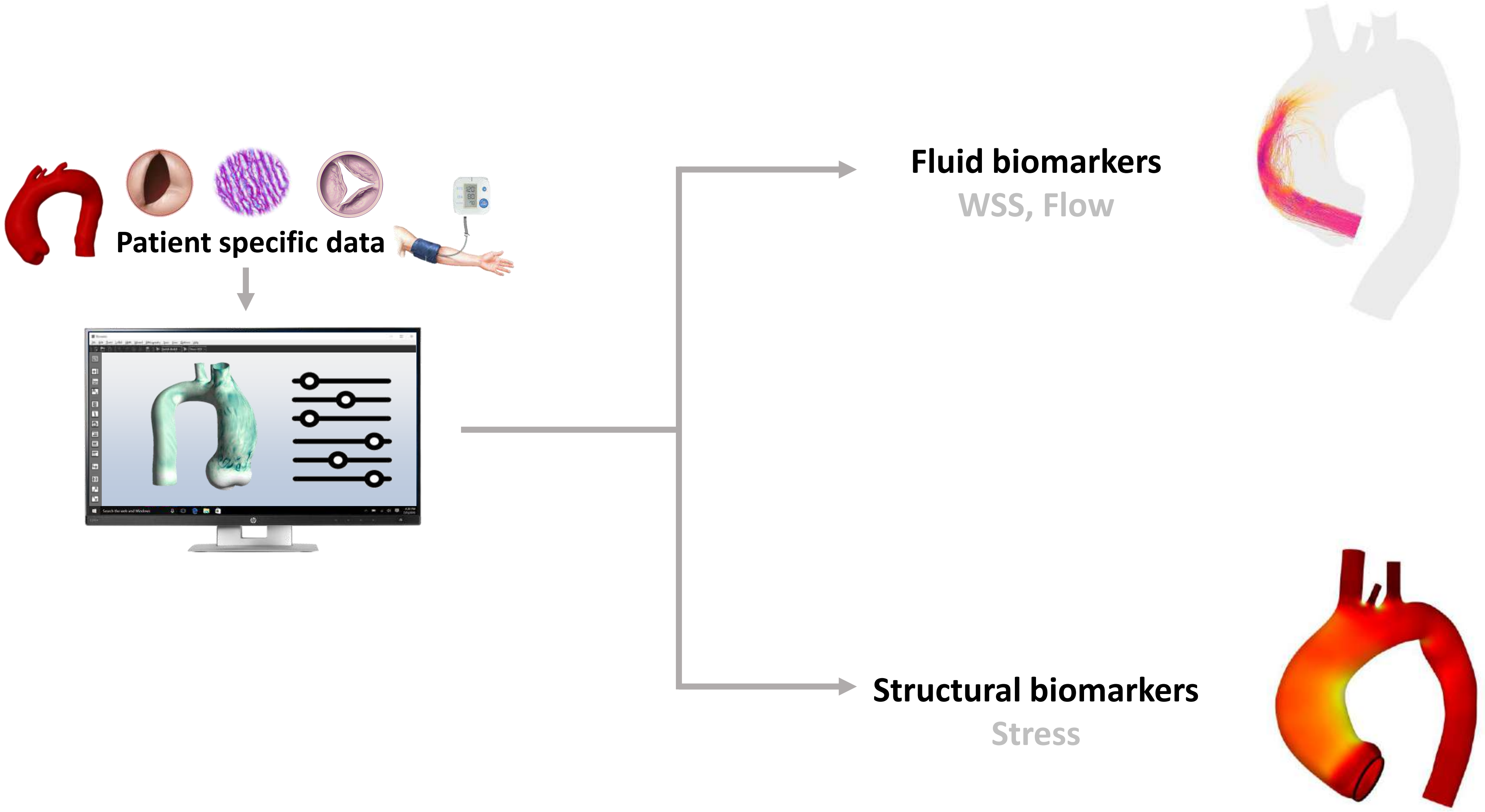
  Evaluated the topological shear variation index (TSVI) and fixed-point relative residence time (RT∇).



Section III

Patient-specific FSI models

Computational tools for personalized treatment



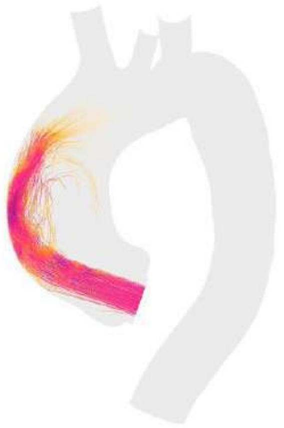
Computational tools for personalized treatment

Personalized hemodynamic conditions

- Aortic jet derived from MRI 4D flow
- Windkessel outlets calibrated with patient's data

Fluid biomarkers

WSS, Flow

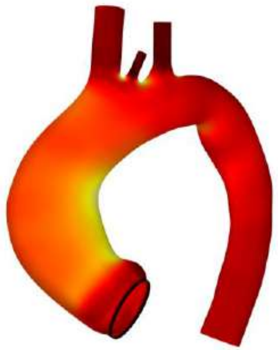


Personalized aorta wall

- Thickness
- Elasticity

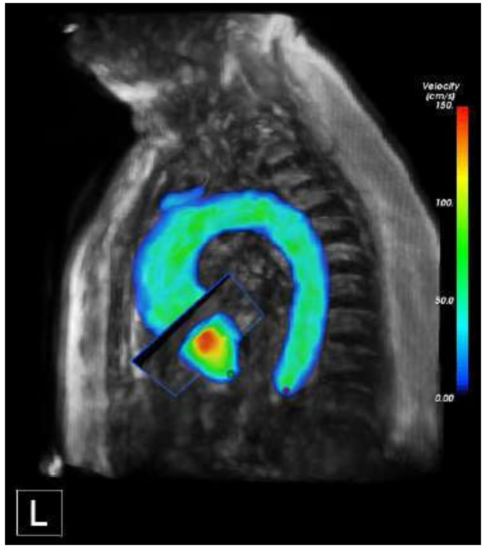
Structural biomarkers

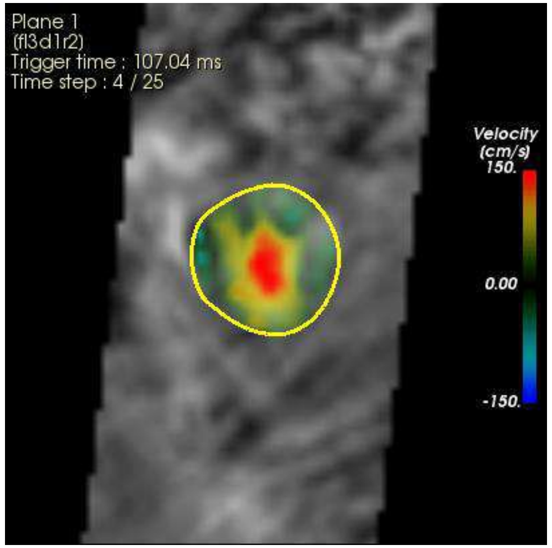
Stress

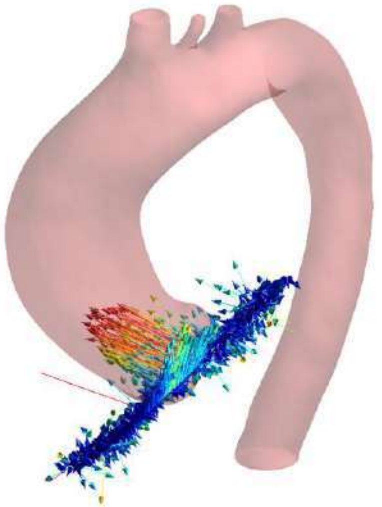


Methods: Aortic jet

MRI 4D Flow







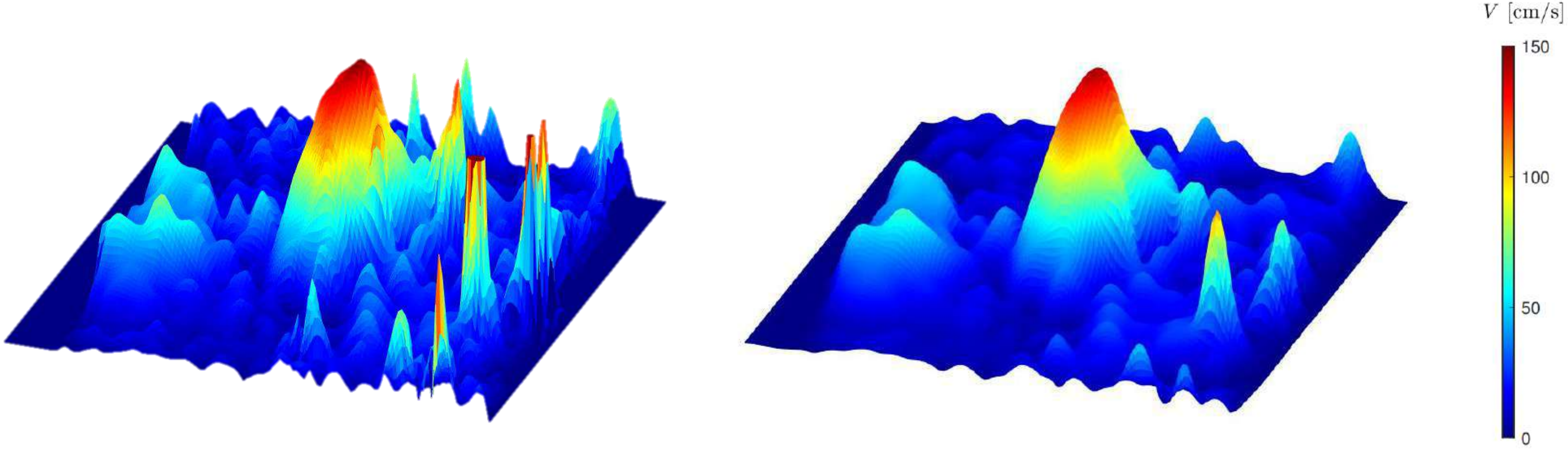
Velocity extraction on aortic valve plane

Transfer onto the fluid model

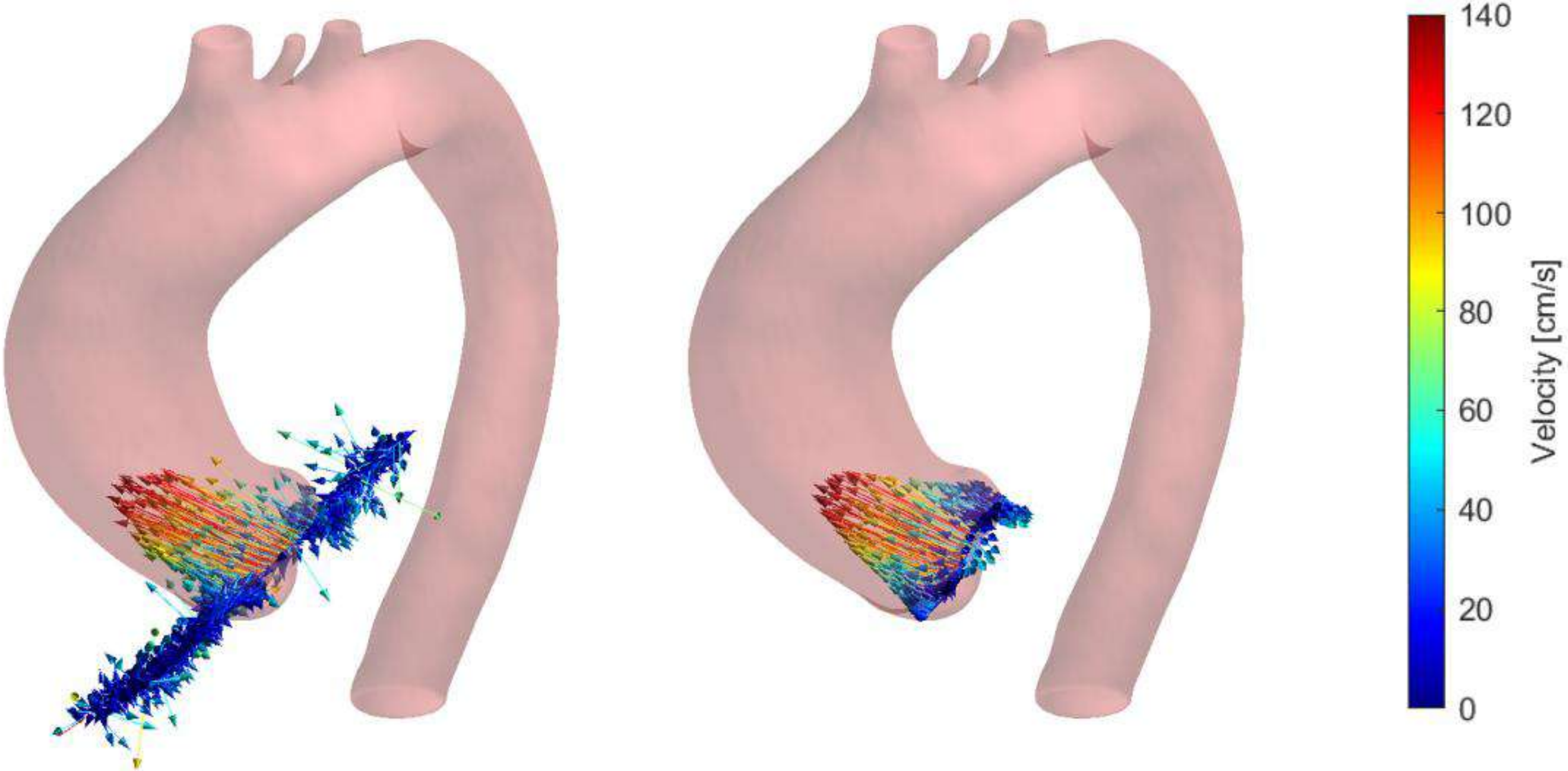
Methods: Aortic jet

Resampling and filtering:

- Finer grid (x3) using modified Akima interpolation: reduced undulations and over-flattening.
- Gaussian 2-D filter was applied to smooth each of the three velocity components. Smoothing kernel with standard deviation 2.5.



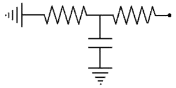
Methods: Aortic jet



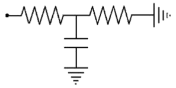
Methods: Windkessel

DATA

Measure	Value	Unit
Q_{max}	456.2	ml/s
Q_{min}	15.3	ml/s
Q_{mean}	6.89	l/min
Q_{DA}	3.48	l/min
P_{Sys}	60	mmHg
P_{Dias}	0.0	mmHg
Δt	0.1	s
A_{BT}	185.2	mm^2
A_{LCC}	20.4	mm^2
A_{LS}	67.3	mm^2



METHOD



$$R_T = \frac{P_{mean}}{Q_{mean}},$$

$$R_i = R_T / f_i\,,$$

$$C_T = \frac{Q_{max} - Q_{min}}{P_{Sys} - P_{Dias}} \Delta t\,,$$

$$C_T^* = C_T - C_{As}^{3D},$$

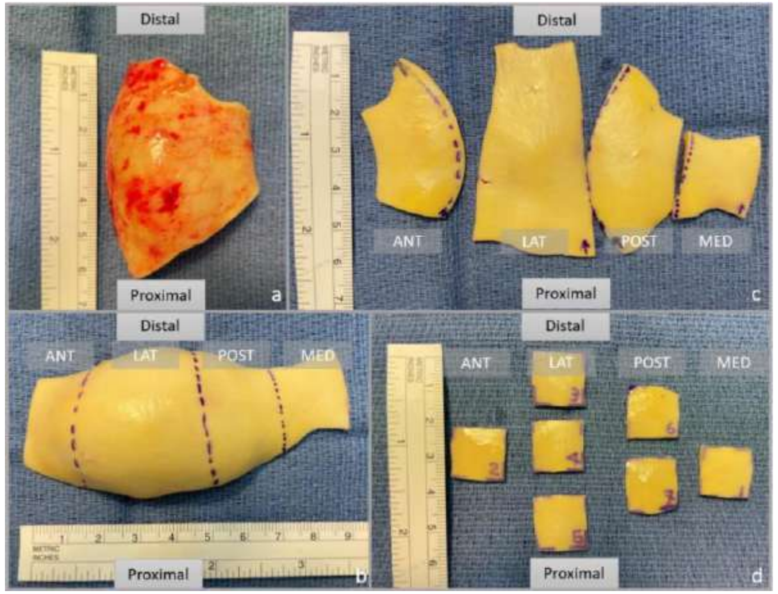
$$C_i = f_i\, C_T^* \frac{R_i}{R_{d_i}} = C_T^* \frac{R_T}{R_{d_i}}.$$

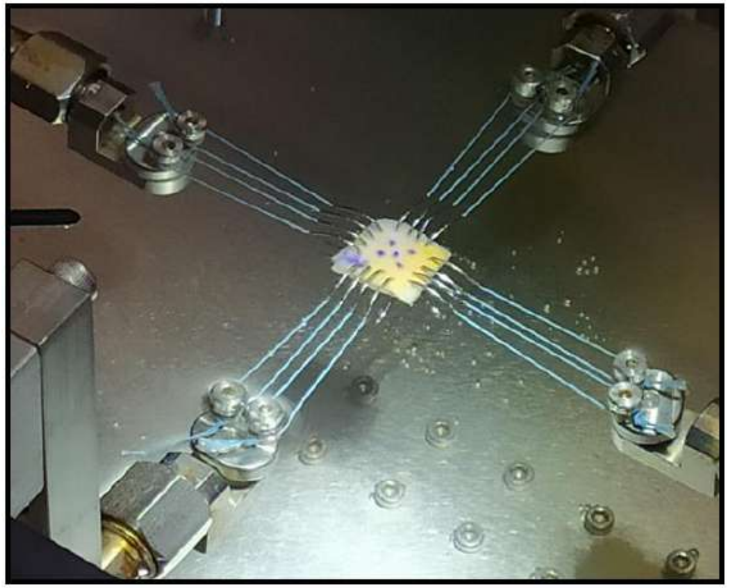
RESULTS

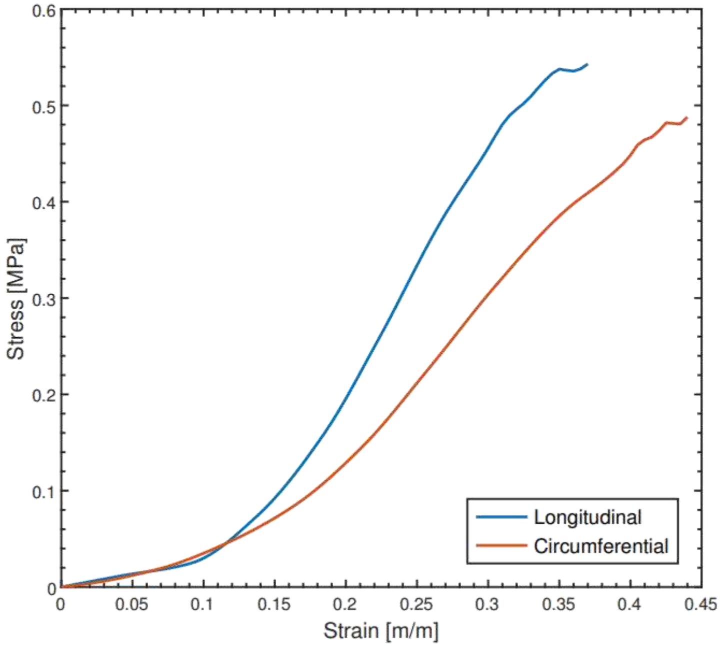
Component	Value
$R_{p_{BT}}$	3.858×10^{6}
$R_{d_{BT}}$	6.504×10^{7}
C_{BT}	1.587×10^{-9}
$R_{p_{LCC}}$	3.569×10^{7}
$R_{d_{LCC}}$	6.016×10^{8}
C_{LCC}	1.715×10^{-10}
$R_{p_{LS}}$	1.065×10^{7}
$R_{d_{LS}}$	1.796×10^{8}
C_{LS}	5.746×10^{-10}
$R_{p_{DA}}$	2.575×10^{6}
$R_{d_{DA}}$	4.340×10^{7}
C_{DA}^*	9.407×10^{-10}

Methods: Aortic wall - Clinical data

4 sections: Anterior, lateral, posterior and medial







Equi-biaxial tensile test performed in the University Hospital of Dijon.

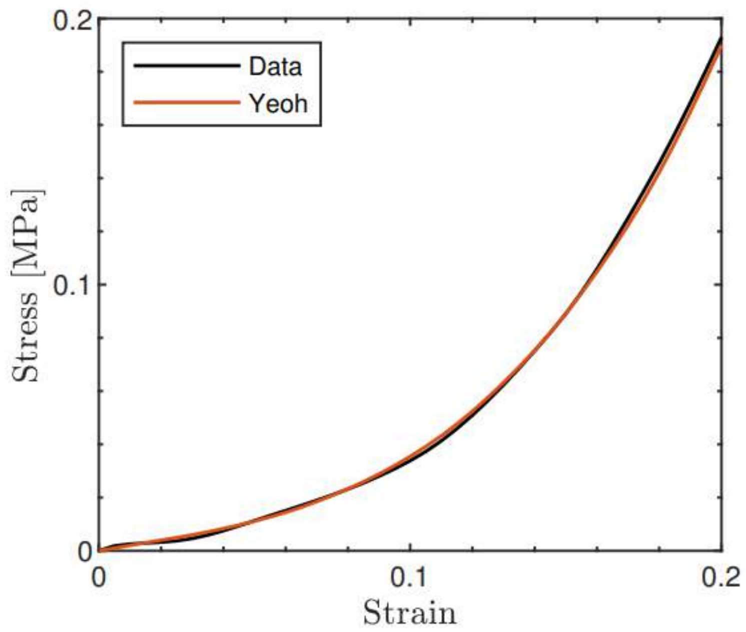
S. Lin, "Biomechanics of human ascending aorta and aneurysm rupture risk assessment", PhD Thesis, 2021.

Methods: Aortic wall - Hyperelastic material

Ascending aorta: Third order Yeoh material model.

$$W = \sum_{i=1}^{3} C_{i0}(\bar{I}_1 - 3)^i.$$

The model coefficients for each quadrant were obtained after performing a curve fitting via minimization of normalized error of the circumferential strain-stress curves.



Supra-aortic vessels and DA: Second order Yeoh material model derived from estimated pulse wave velocity (PWV).

$$\mathrm{PWV} = \frac{\alpha}{(2 \times 10^3\, r_v)^\beta} \qquad E_{\mathrm{inc}} = \frac{2 r_v \rho}{T_v} \mathrm{PWV}^2$$

Methods: Aortic wall - Model definition

Spatially varying material properties

Ascending aorta: 2 node interpolation

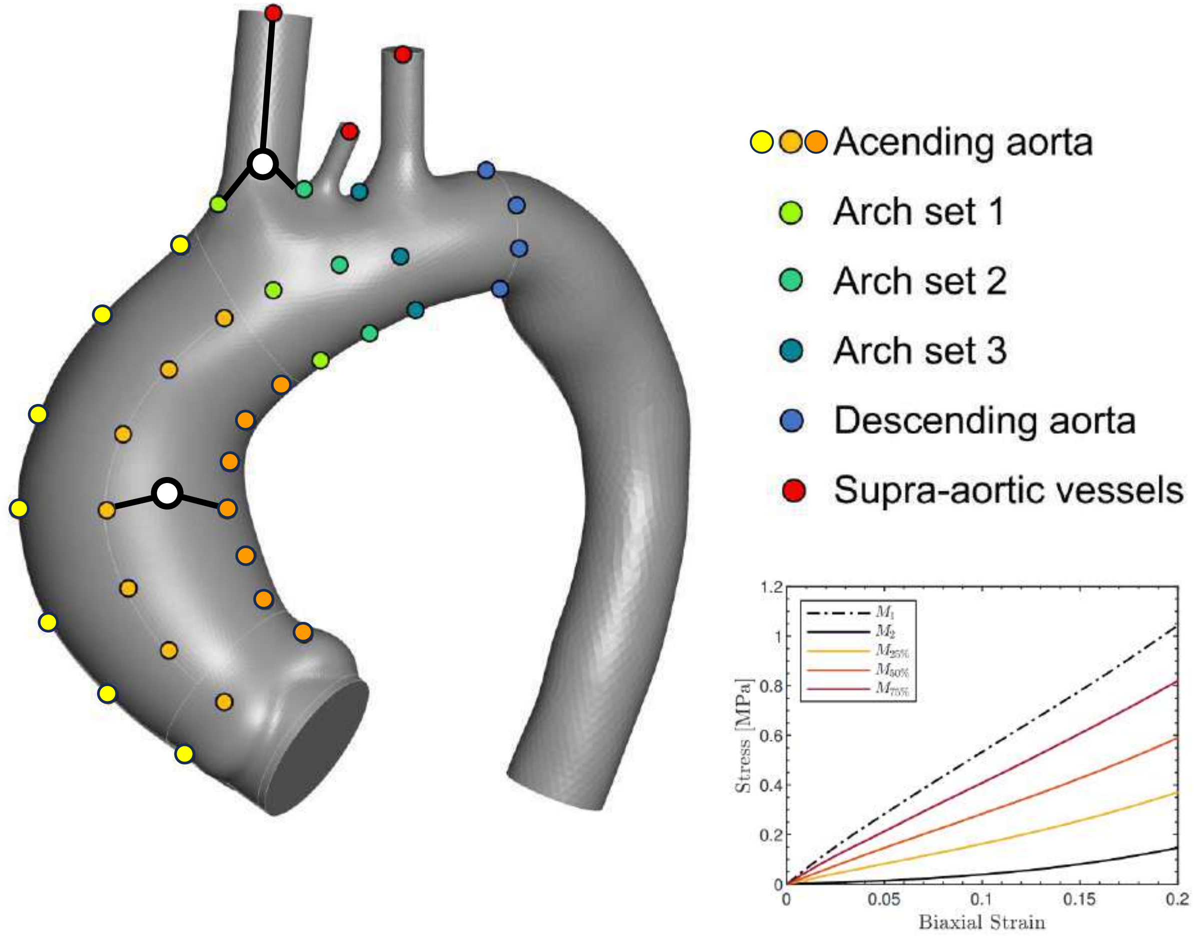
$$T_n = T_{s1}\frac{D_{n,s1}}{D_{n,s1}+D_{n,s2}} + T_{s2}\frac{D_{n,s2}}{D_{n,s1}+D_{n,s2}}$$

Aortic arch: 3 node interpolation

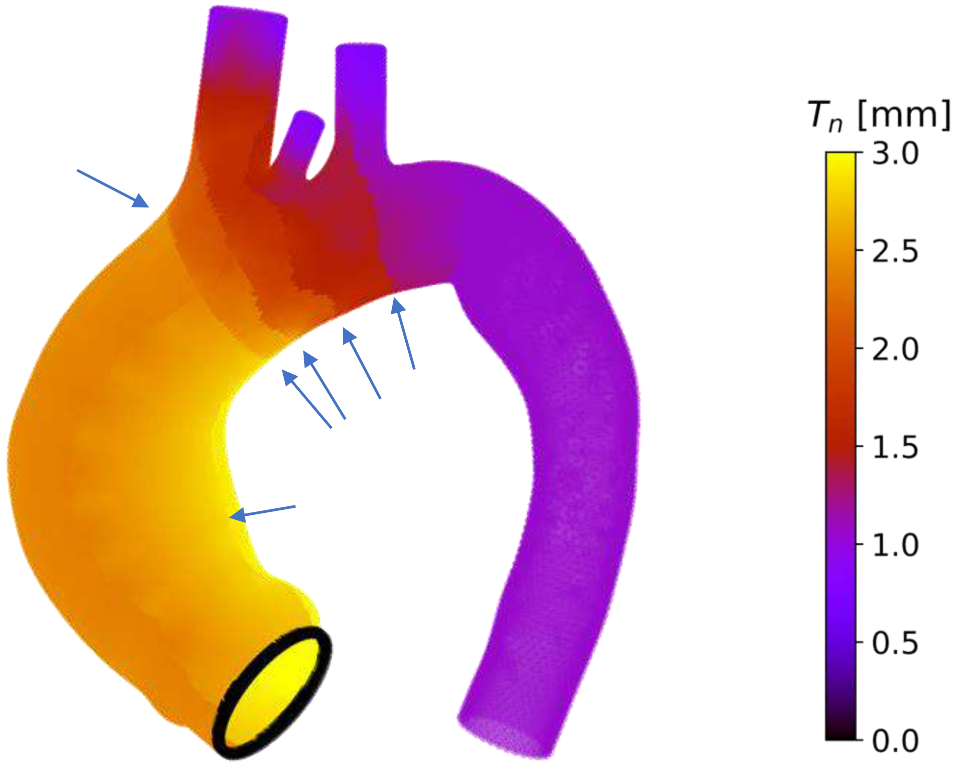
$$D_{n,v}^{\mathrm{mod}} = D_{n,v}^{*}\frac{D_{\mathrm{Lim}}}{D_{\mathrm{Lim}} - D_{n,v}^{*}},$$

$$T_n = T_n^{*}\frac{D_{n,s}^{\mathrm{Min}}}{D_{n,s}^{\mathrm{Min}} + D_{n,v}^{\mathrm{mod}}} + T_v\frac{D_{n,v}^{\mathrm{mod}}}{D_{n,s}^{\mathrm{Min}} + D_{n,v}^{\mathrm{mod}}}$$

DA: Constant properties

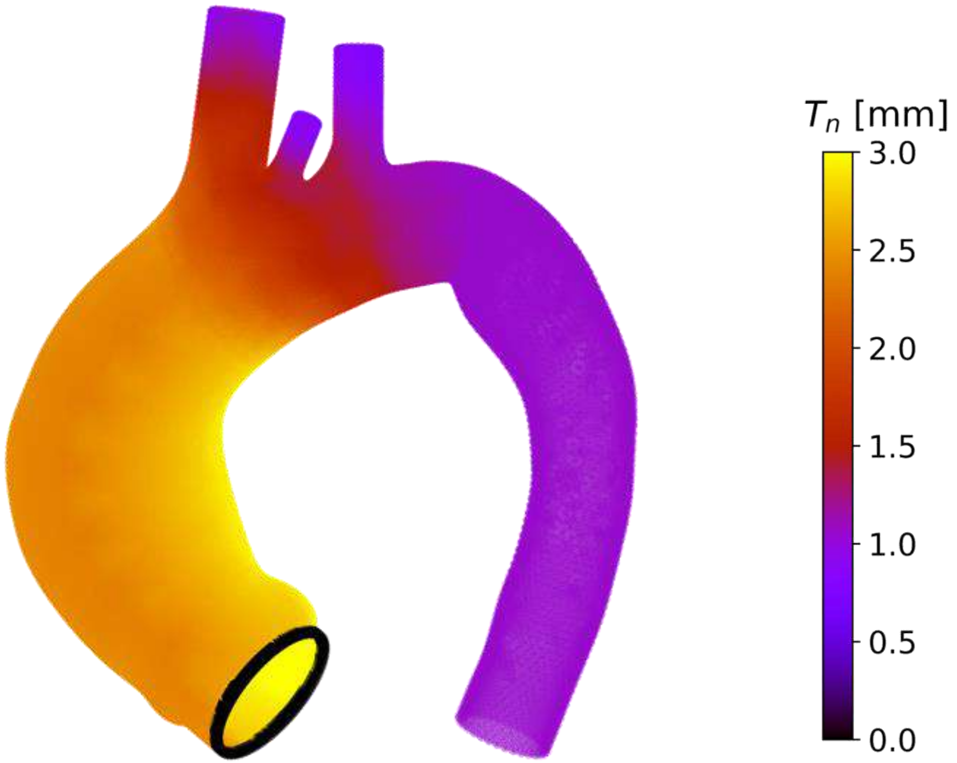


Methods: Aortic wall - Model definition



Initial

Methods: Aortic wall - Model definition



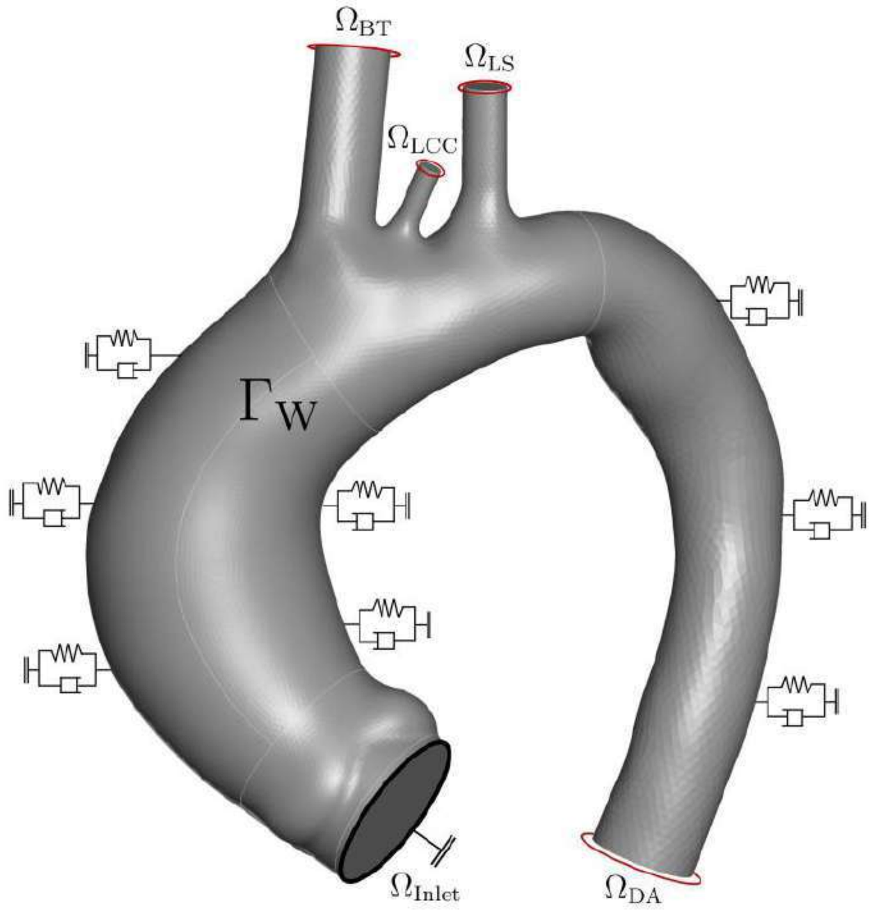
Smooth

Methods: Aortic wall - Boundary conditions

- **Radial displacement on outlets**
- **Viscoelastic support on wall**

$$K_{n_j} = (K_{\text{Soft}} + W_d W_j K_{\text{Spine}})\, A_n\, e_{n_j},$$

Coefficient	Value
K_{Soft}	1.5×10^4 Pa/m
K_{Spine}	10^6 Pa/m
W_d	0.53
W_x	0.60
W_y	0.02
W_z	0.04

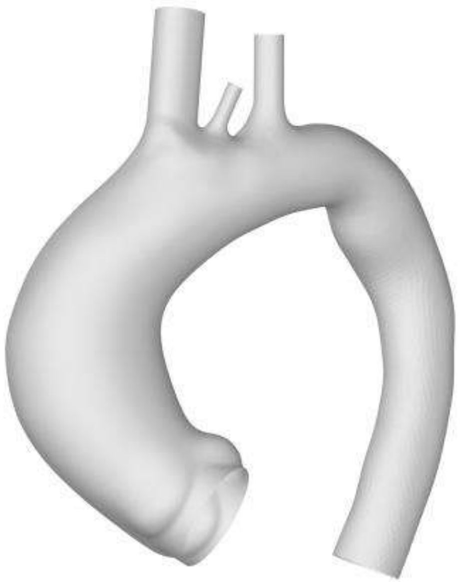


Geronzi et al., "Calibration of the Mechanical Boundary Conditions for a Patient-Specific Thoracic Aorta Model Including the Heart Motion Effect," *IEEE Trans Biomed Eng*. 70-11 (2023)

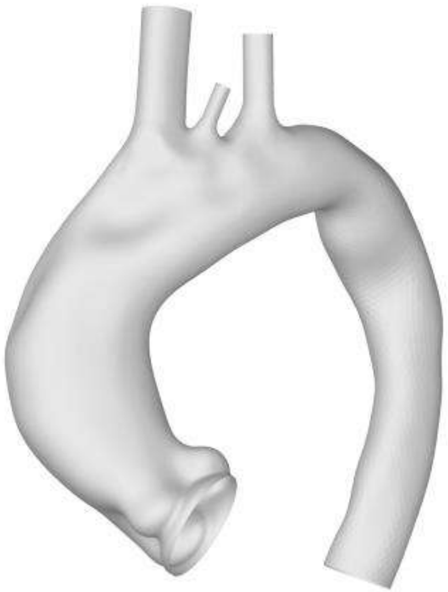
Methods: Aortic wall - Zero pressure

Augmented Sellier’s Inverse Method

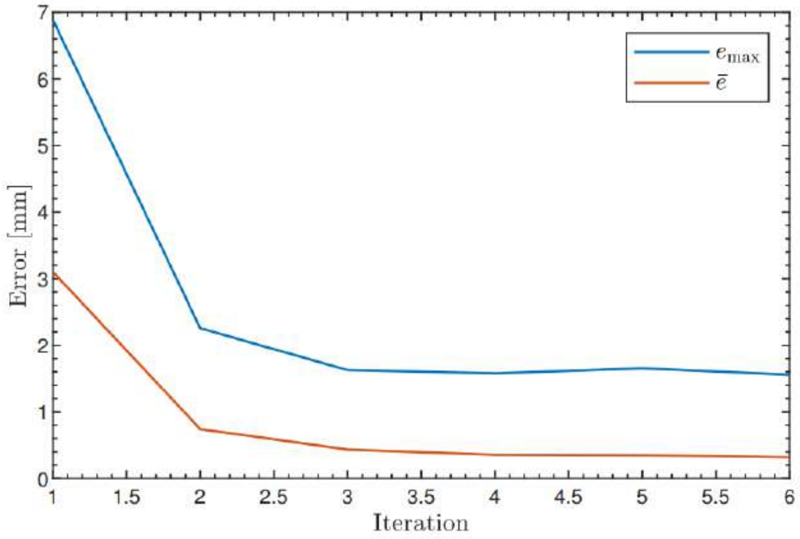
- Inverse problem: loads and final deformation are known, initial geometry is to be computed.
- The zero-stress state will be approximated by the zero pressure state.



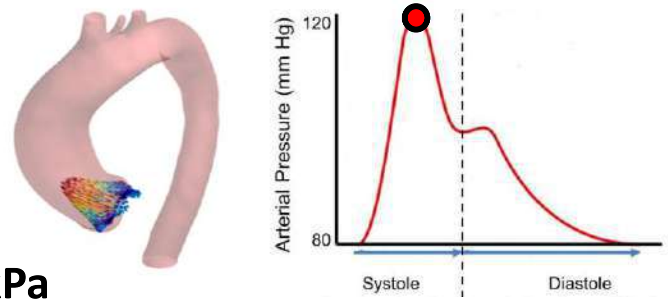
Reference

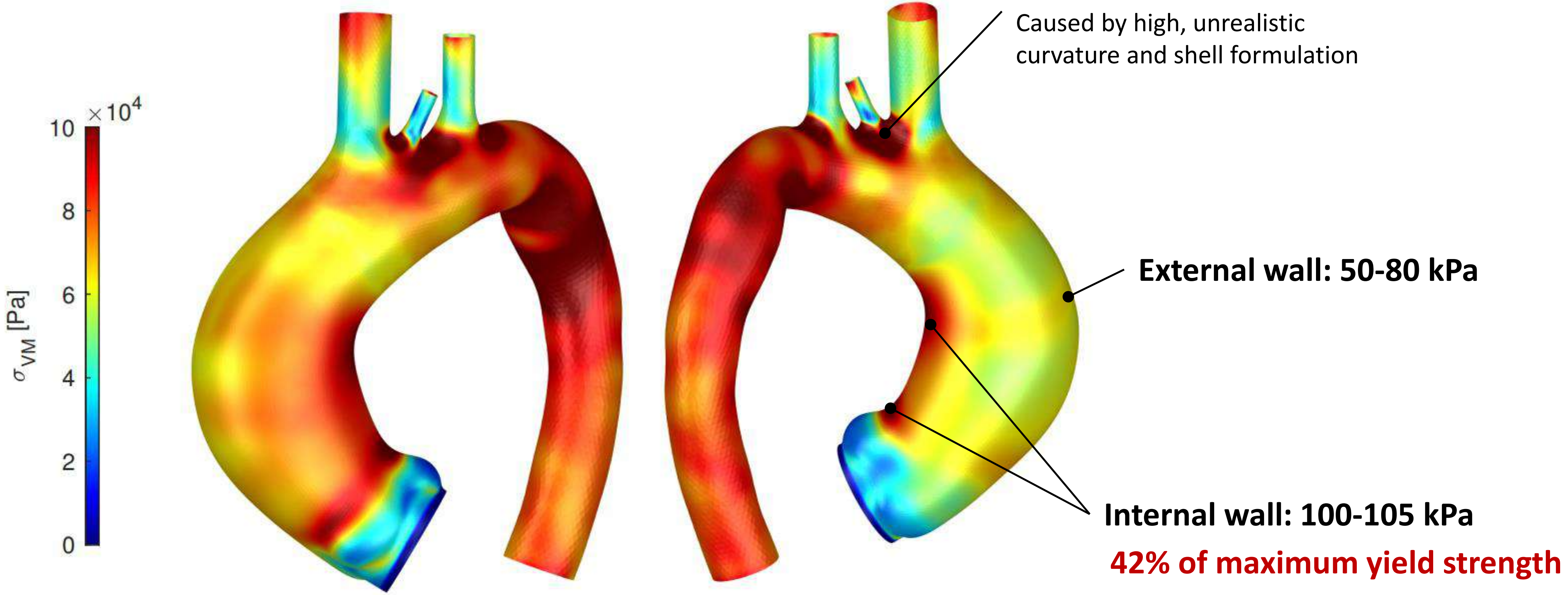


Zero pressure



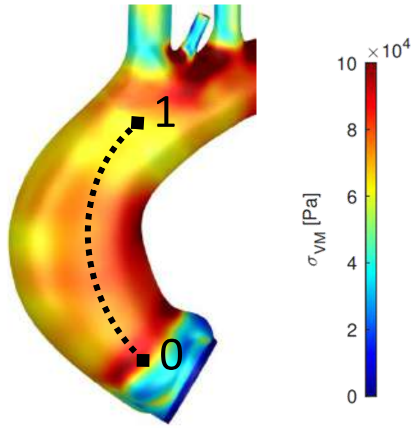
Results: Stress



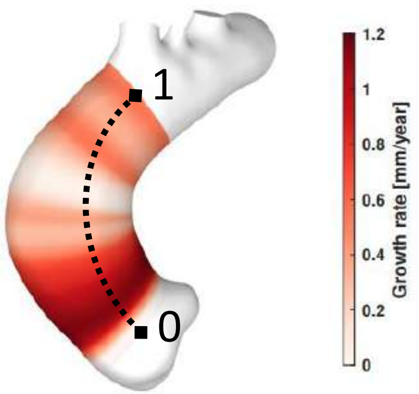


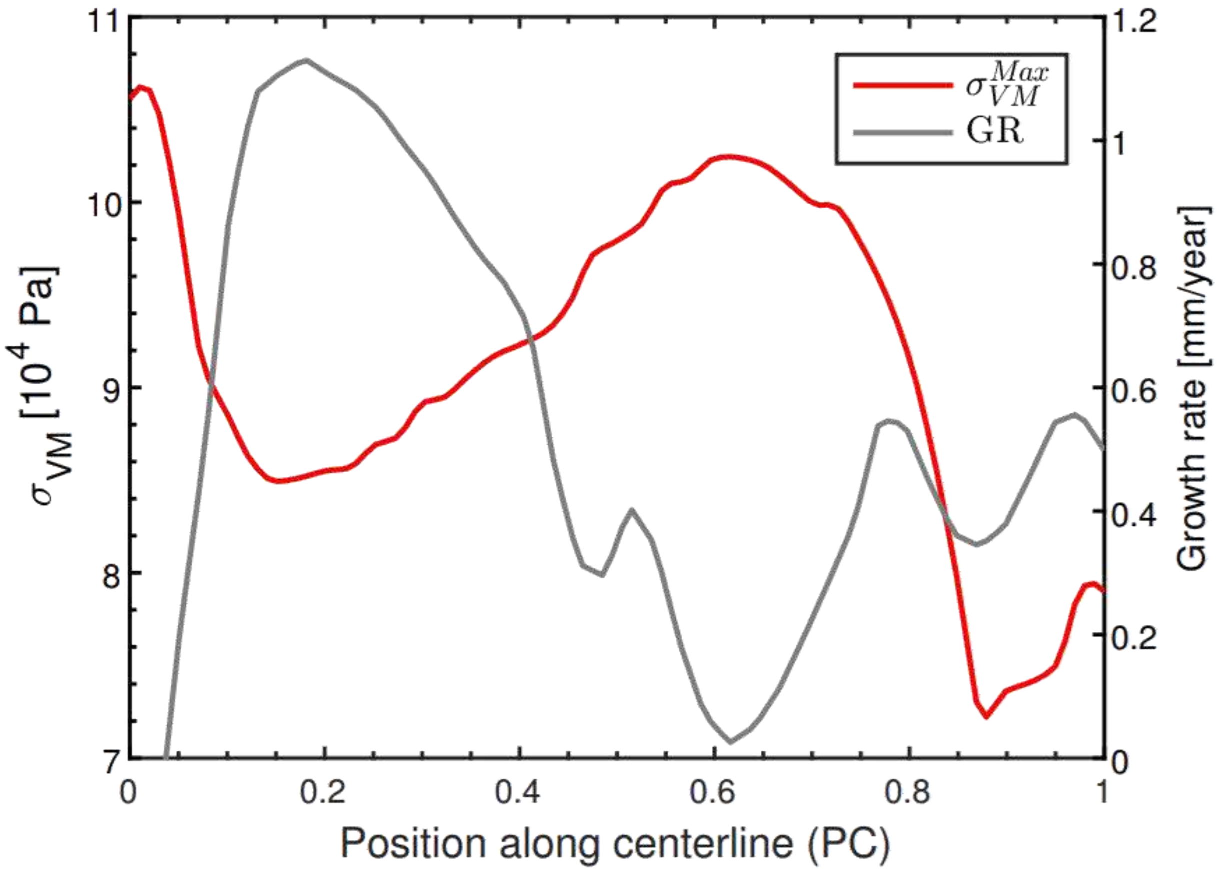
Results: Stress - Growth

Stress



Growth rate





- No evidence of a correlation between stress and aneurysm growth.
- Locations with highest stress concentration show null growth.

Conclusions

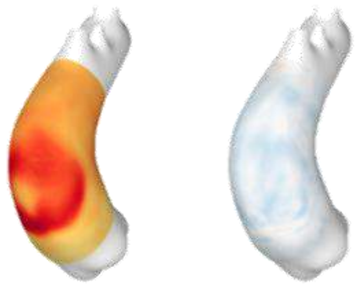
Clinical outcomes: one patient only, it is not possible to hypothesise on the relationship between growth and stress.

A large cohort should be analysed, considering both healthy, stable and dilating aneurysms.

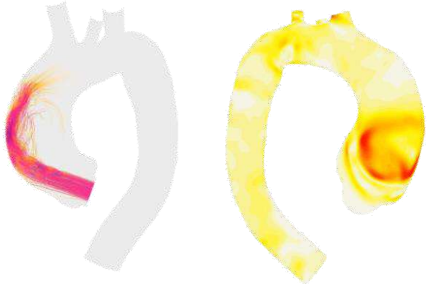
A model combining patient specific hemodynamics and aorta wall has been presented. Further improvements will enable an accurate estimation of risk of rupture.

Final conclusions

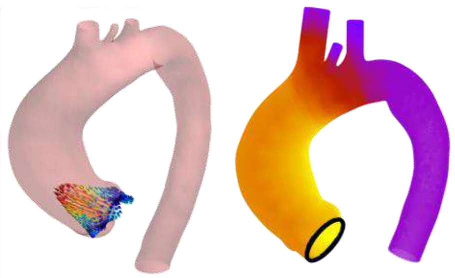
Final Conclusions



- Non-Newtonian viscosity is necessary.
- LES is optional, but computational requirement is negligible.



- Aneurysm growth could be related to:
  - BAV: Peak systole shear angle.
- Larger cohort with MRI flow data is needed.



- Hemodynamic personalization requires MRI 4D flow data.
- Aorta wall definition requires spatially varying thickness and elastic properties.
- Accurate risk of rupture estimation requires high fidelity models.

The work has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 859836, MeDiTATe: "The Medical Digital Twin for Aneurysm Prevention and Treatment".