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UNIVERSITÉ DE LYON

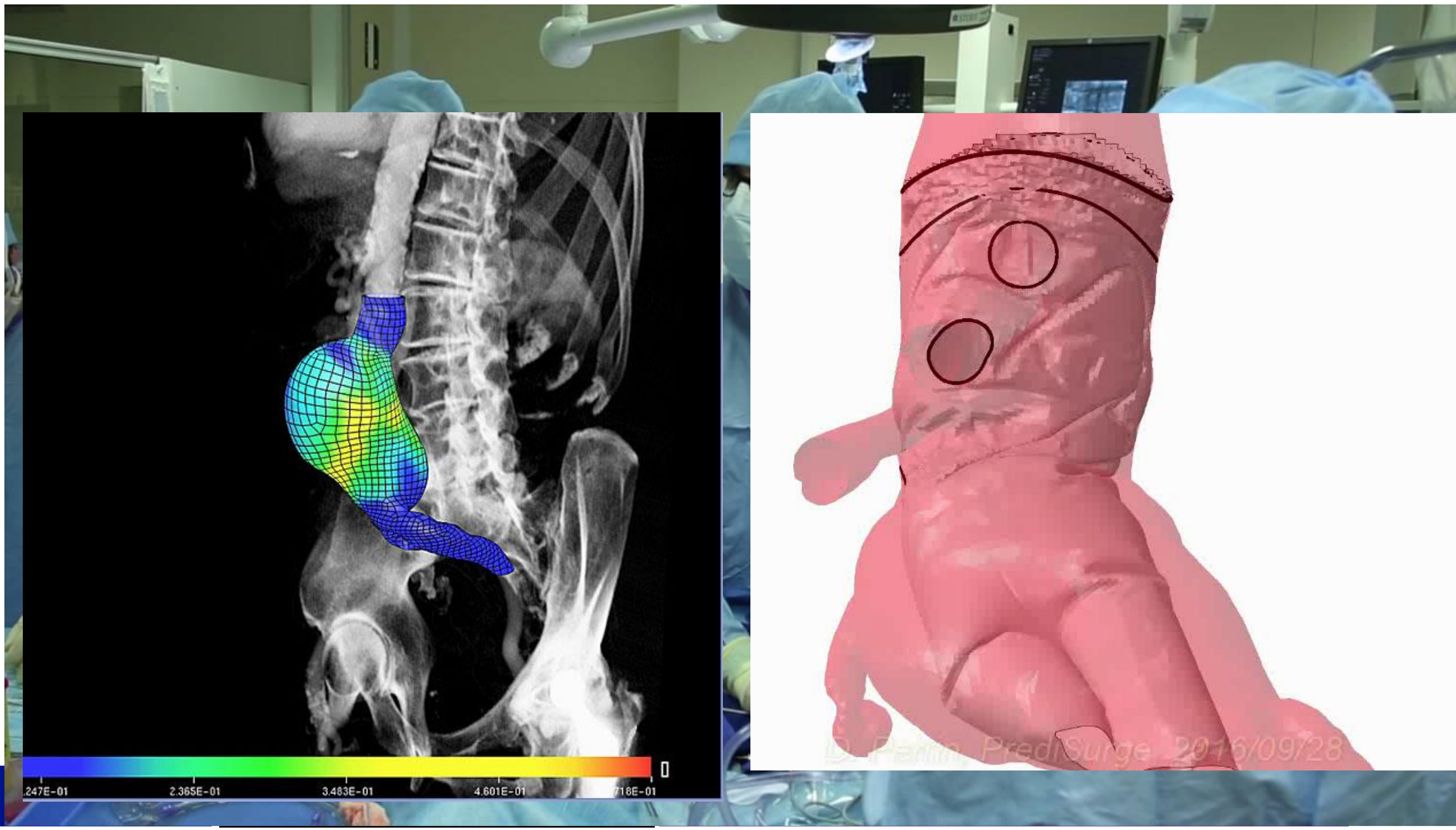
Mechanobiology of aortic aneurysms: novel approach using finite-element modeling and multimodality imaging

CHU Saint-Étienne

Prof. Stéphane AVRIL

Numerical simulation in the OR for vascular surgery?

www.predisurge.com



Basis of arterial biomechanics and mechanobiology

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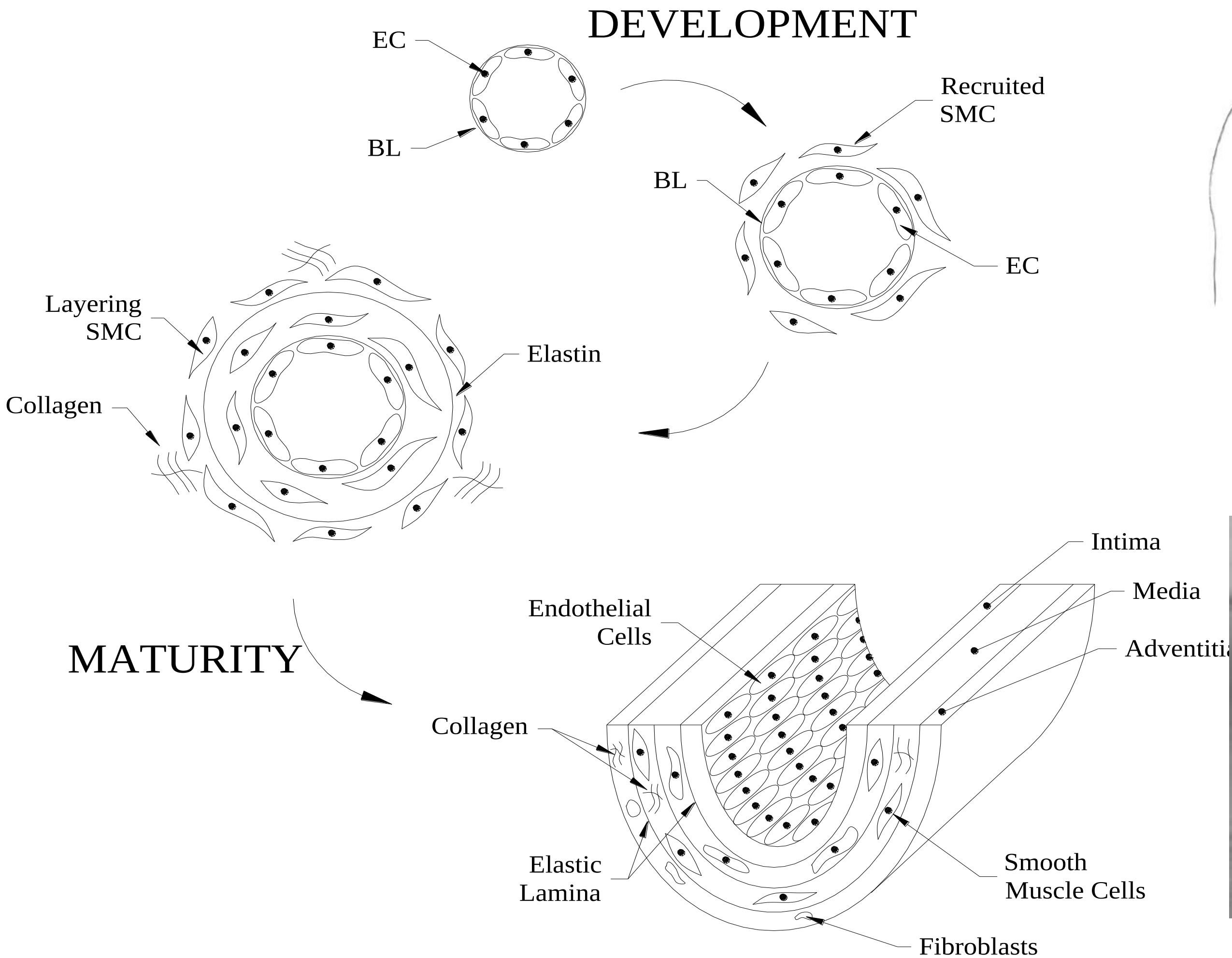
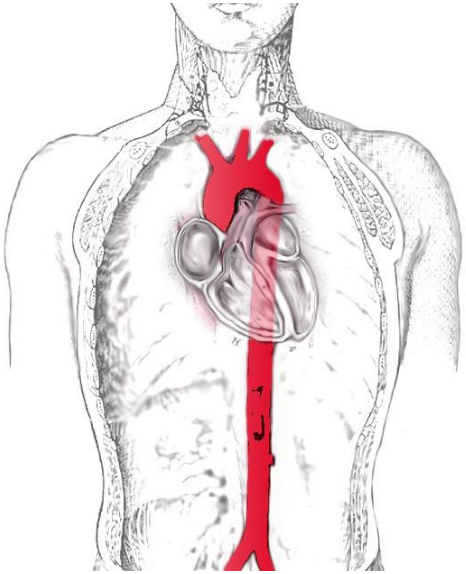
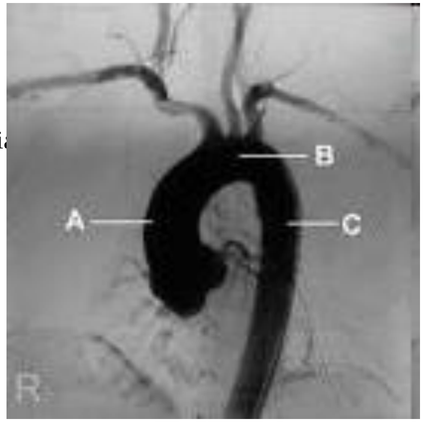
Schematic representation of aortic structure







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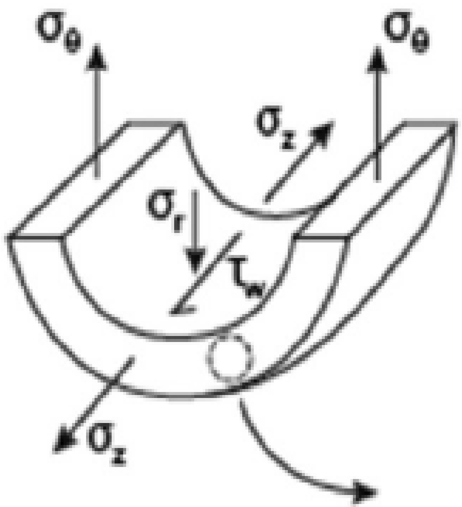
Basics of aortic mechanics

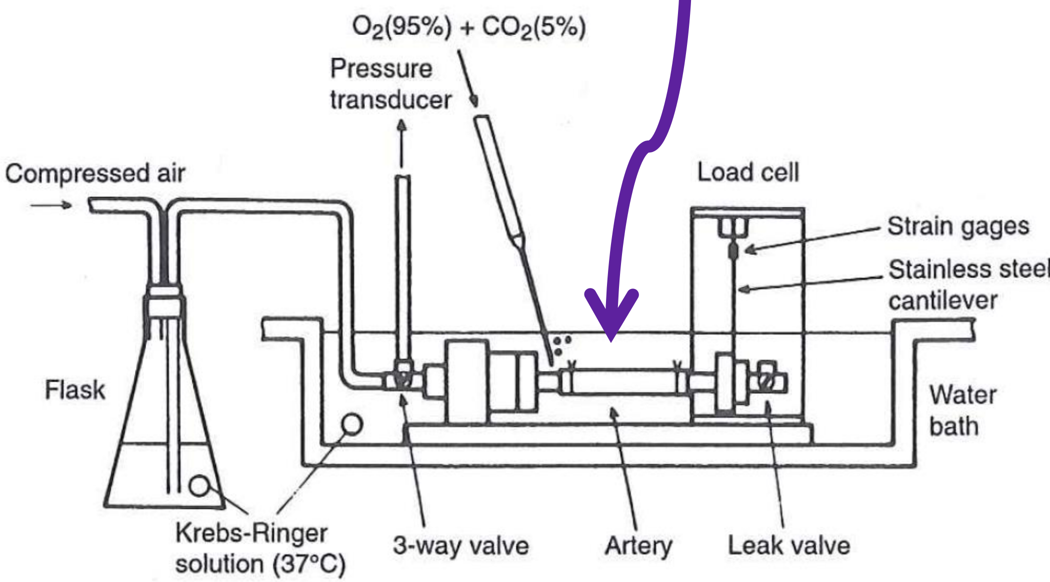


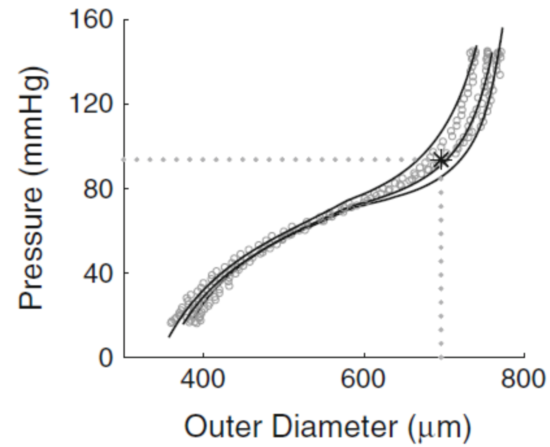
$$\tau_w = \frac{4\mu Q}{\pi a^3}, \qquad \sigma_\theta = \frac{P a}{h}$$

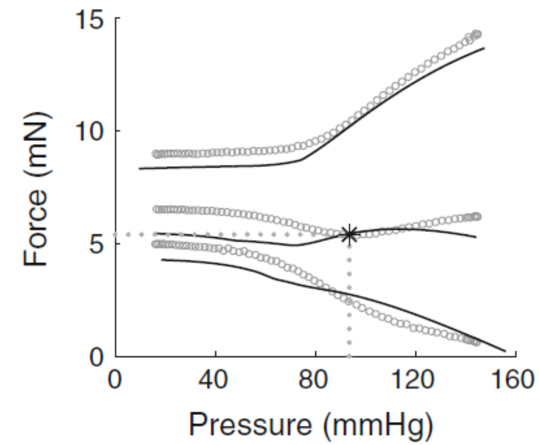
$$\sigma_z = \frac{f_z}{\pi\left(b^2 - a^2\right)} = \frac{f_z}{\pi h\left(2a - h\right)}$$

Humphrey JD (2002) *Cardiovascular Solid Mechanics: Cells, Tissues, and Organs*, Springer-Verlag, NY

Functional biomechanical behavior







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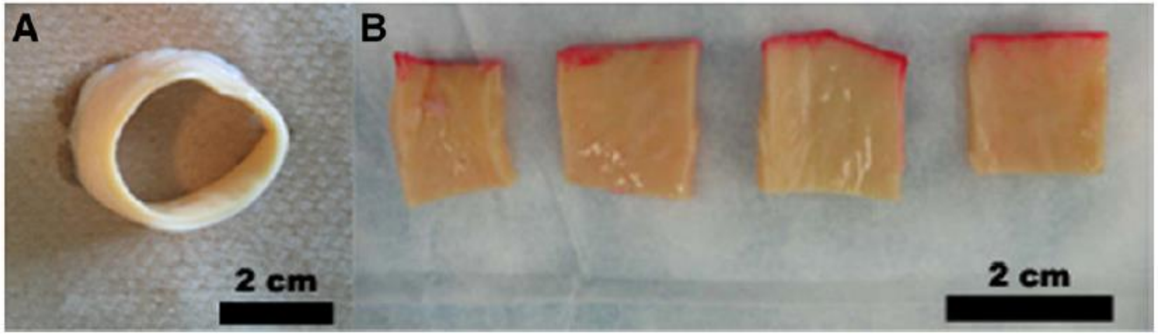
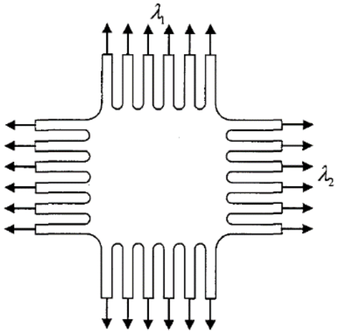
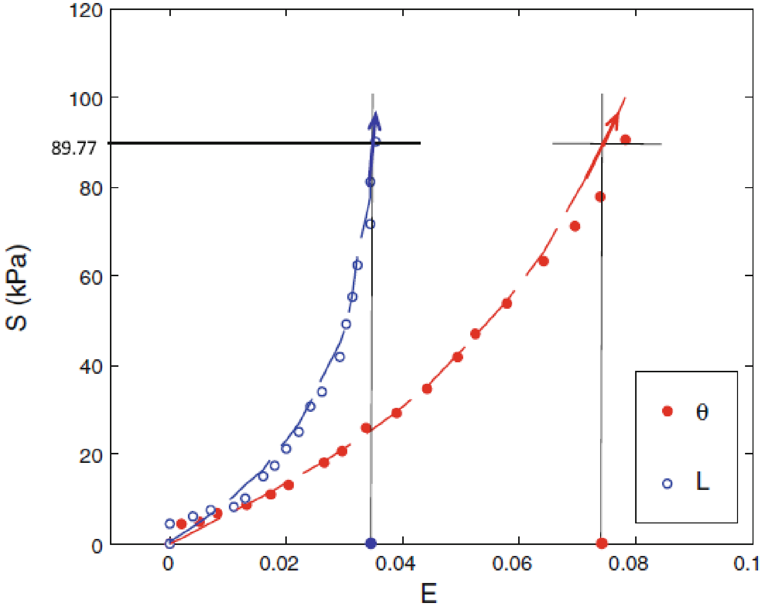
Material characterization and constitutive modeling





$$W = C_{10}\left(\bar{I}_1 - 3\right) + \frac{1}{D}\left(\frac{J^2-1}{2} - \ln J\right)$$
$$+\frac{k_1}{2k_2}\sum_{\alpha=1}^{N}\left\{\exp\left[k_2\left\langle \bar{E}_\alpha\right\rangle^2\right]-1\right\}$$



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Prediction of aneurysm rupture using biomechanics and multimodal imaging

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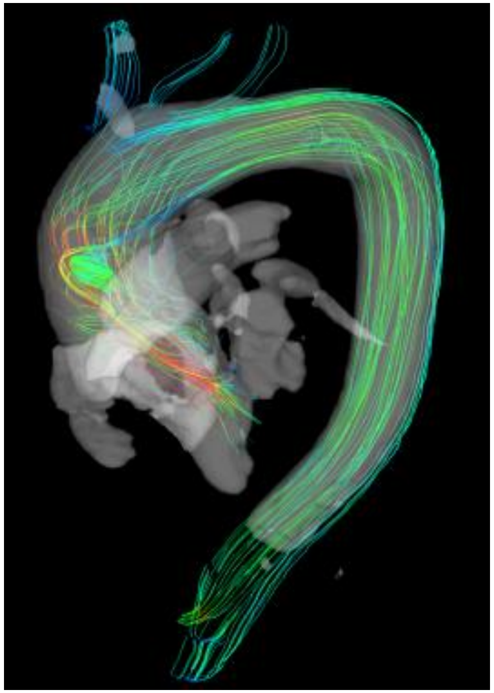
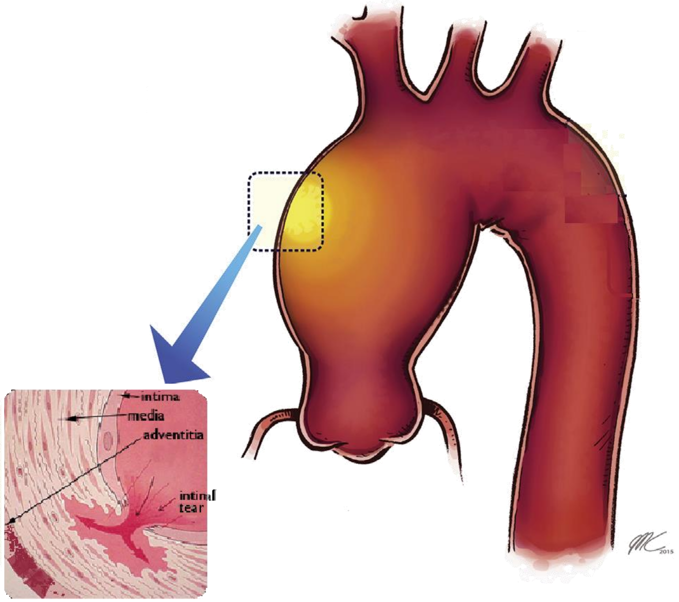
Prediction of risk of rupture and dissection





dissection

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Context

- **More and more aneurysms are detected at an early stage (incidence >8% for males >65 years old).**
- **An intervention is recommended if the aneurysm grows more >1cm/year or it is >5.5cm. This represents >90000 interventions per year in Europe and USA**
- **BUT:**
  - 25% aneurysms <5.5cm rupture : 15000 deaths**!
  - 60% of aneurysms >5.5 cm never experience rupture!
- **In summary: very high rate of inappropriate decisions and misprogramed surgical interventions!!**

** Pape et al, *Aortic Diameter ≥5.5 cm Is Not a Good Predictor of Type A Aortic Dissection Observations From the International Registry of Acute Aortic Dissection (IRAD)*, Circulation, 2007

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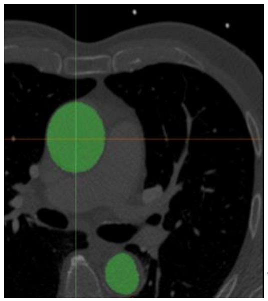
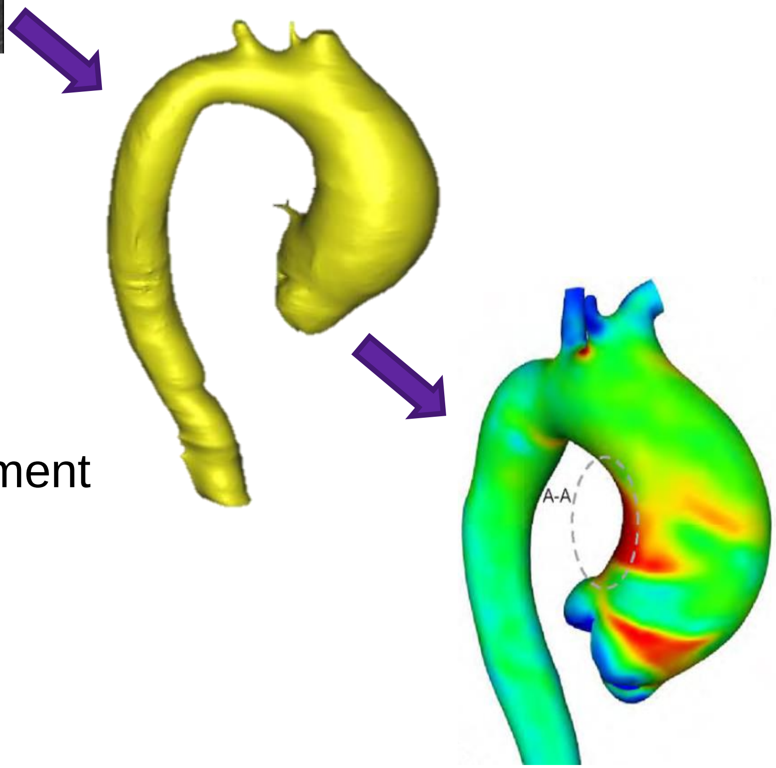
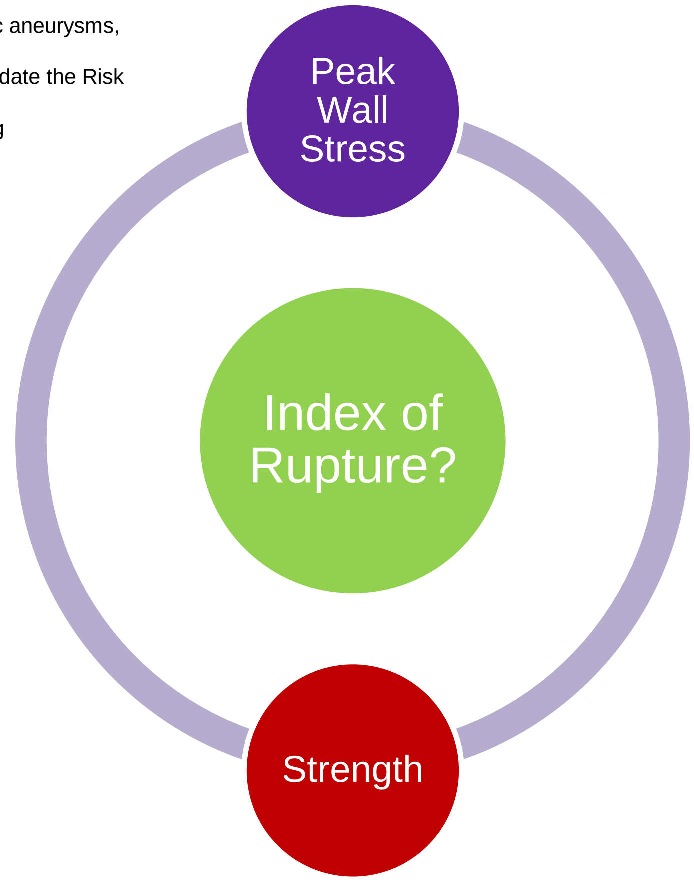
Challenges raised by rupture prediction



O. Trabelsi, et al, Patient specific stress and rupture analysis of ascending thoracic aneurysms, J. Biomech. (2015).
G. Martufi, et al, Is There a Role for Biomechanical Engineering in Helping to Elucidate the Risk Profile of the Thoracic Aorta?, Ann. Thorac. Surg. 101 (2016) 390–398.
S. Pasta et al., Constitutive modeling of ascending thoracic aortic aneurysms using microstructural parameters, Med. Eng. Phys. 38 (2016) 121–130.



Finite-element modeling



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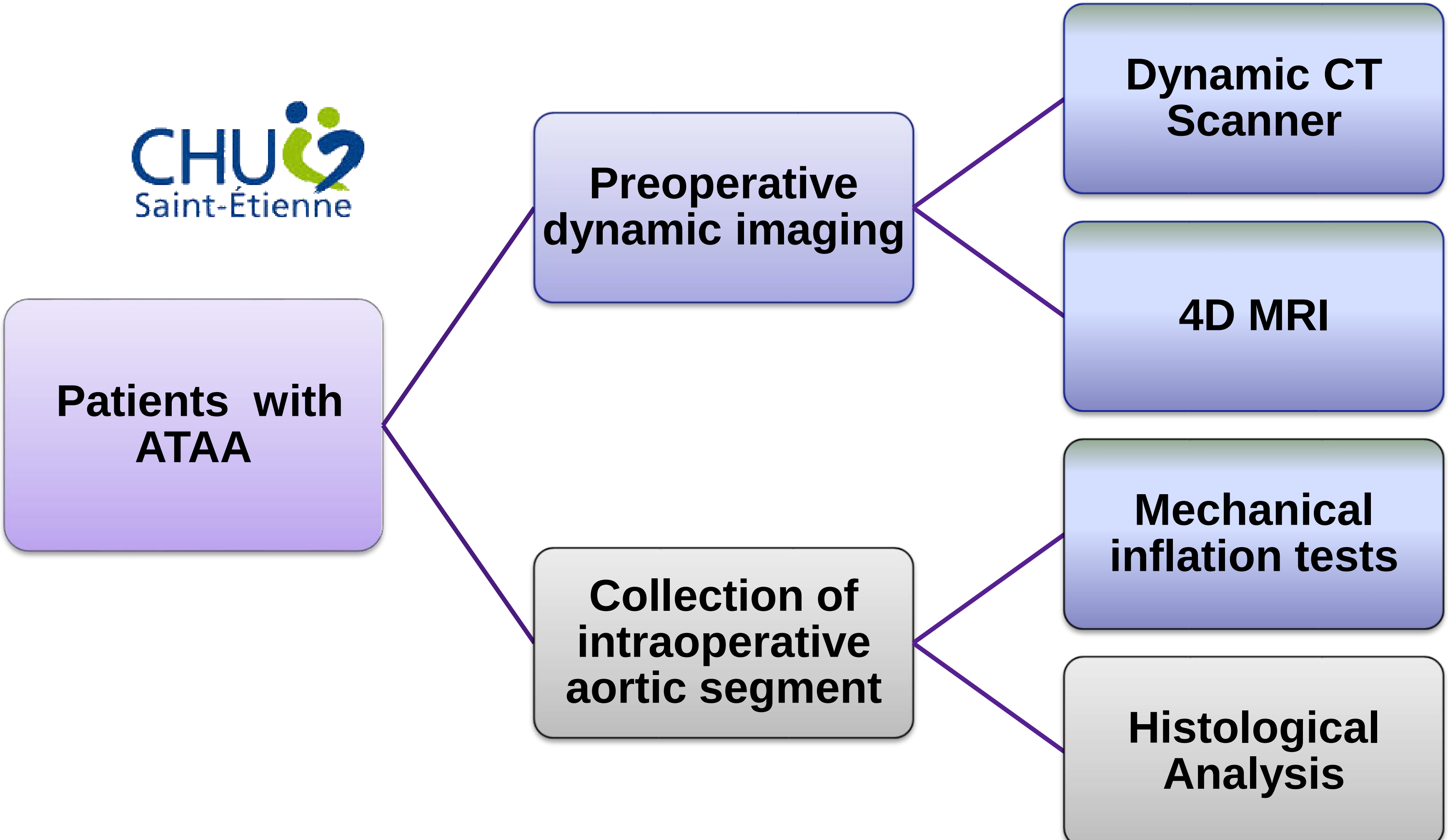
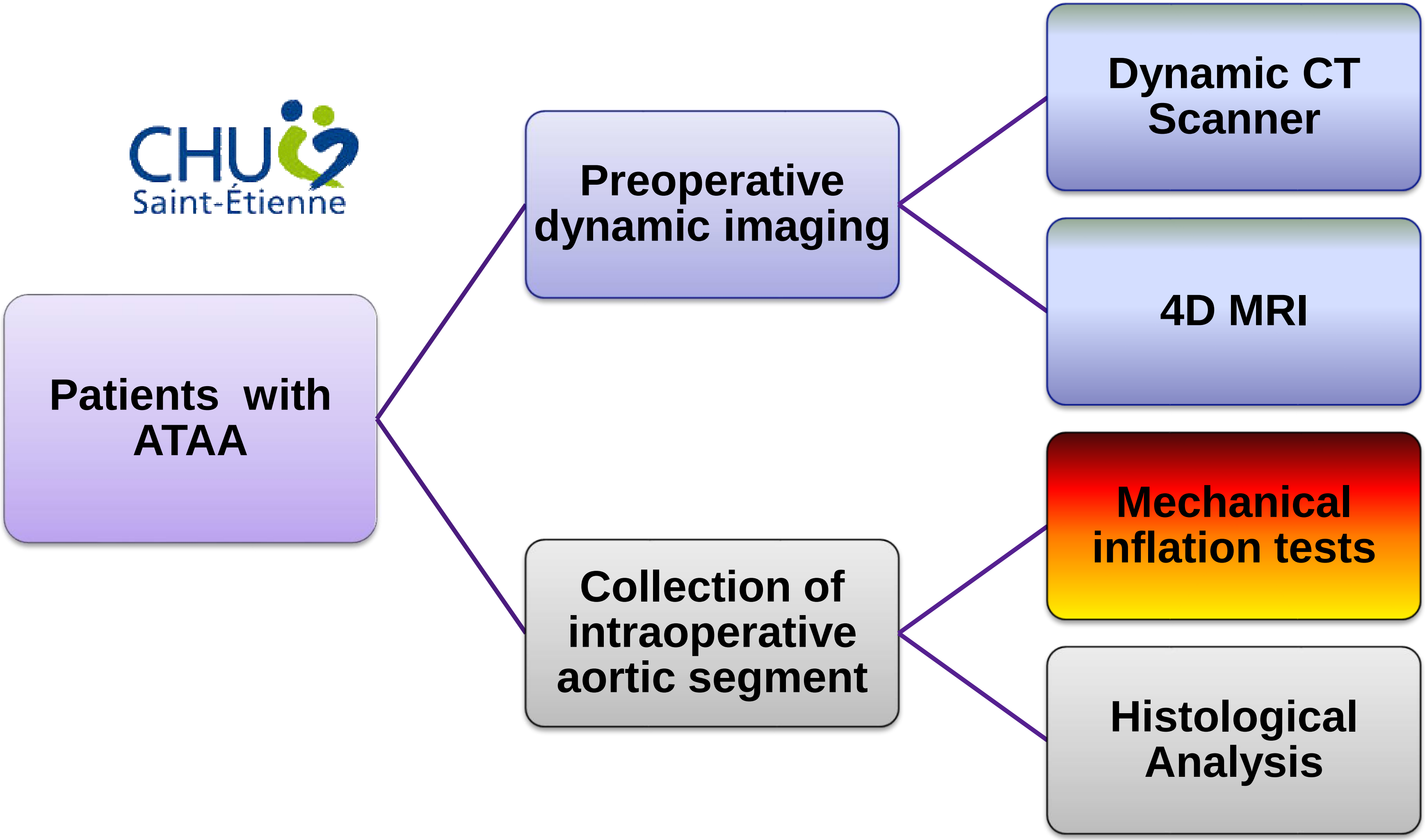
Methodology



Methodology



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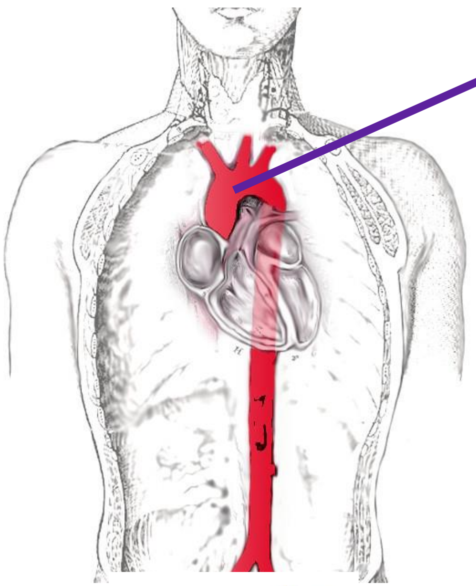
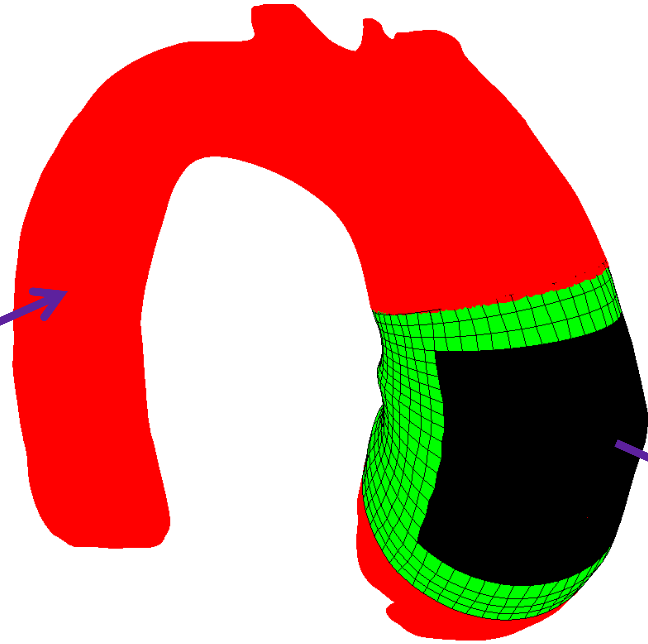
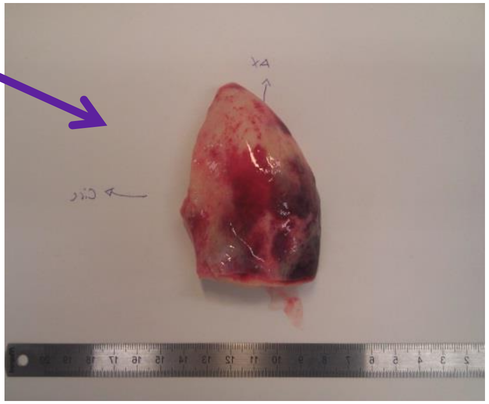
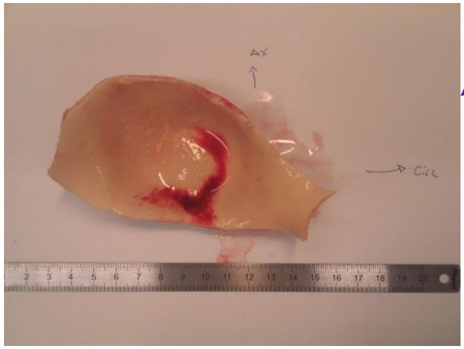
Collection of the samples









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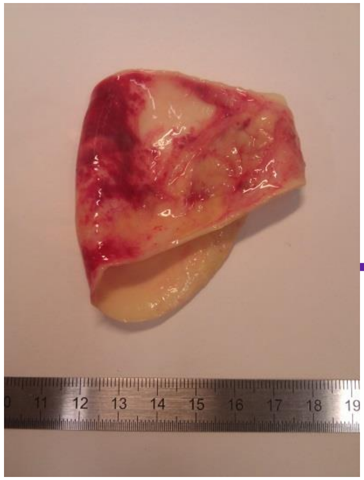
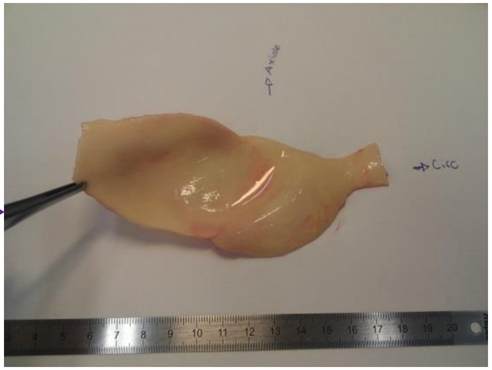
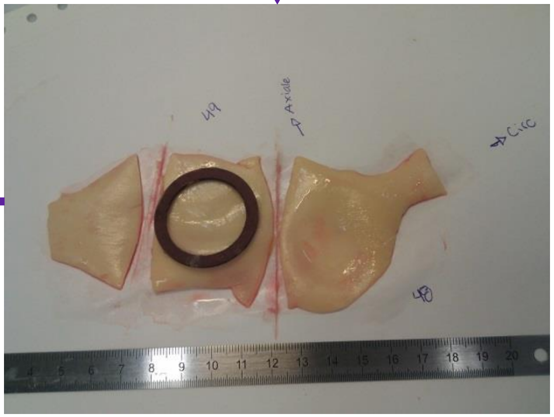
Preparation

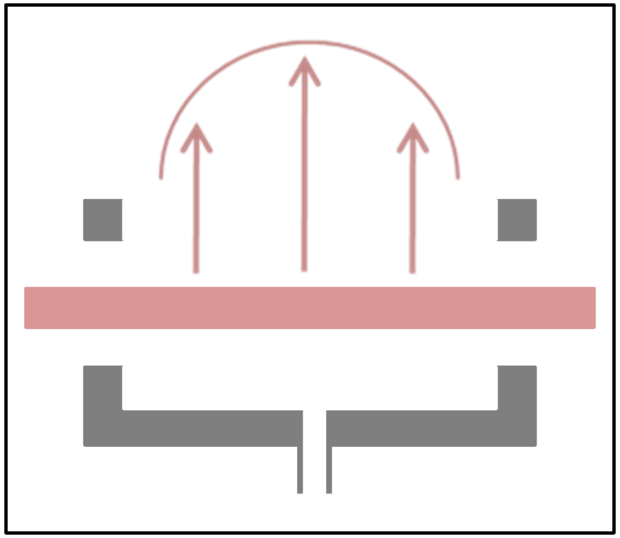


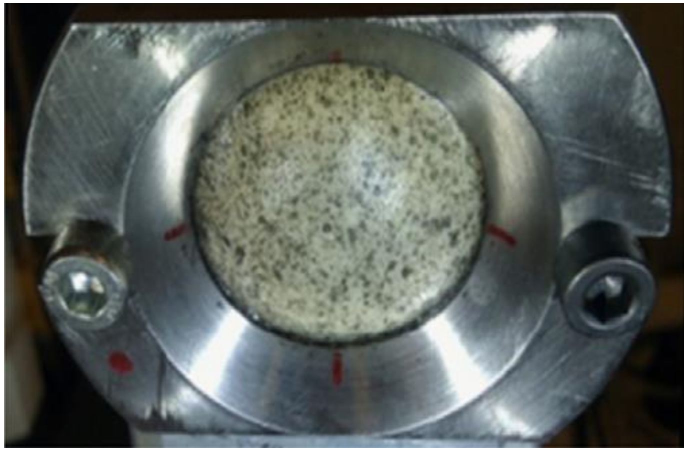




Bulge inflation test

Romo et al. Journal of Biomechanics -2014.





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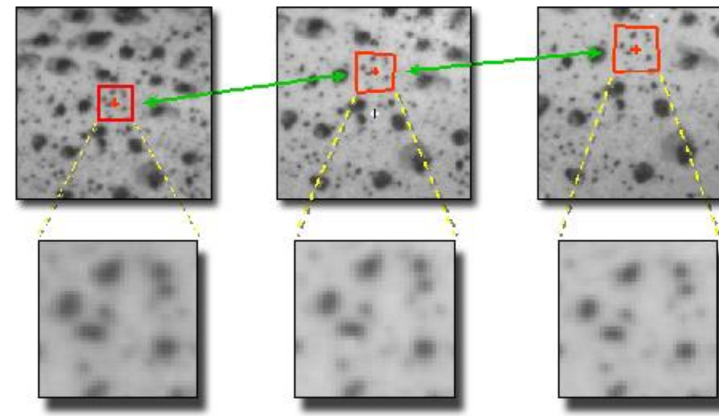
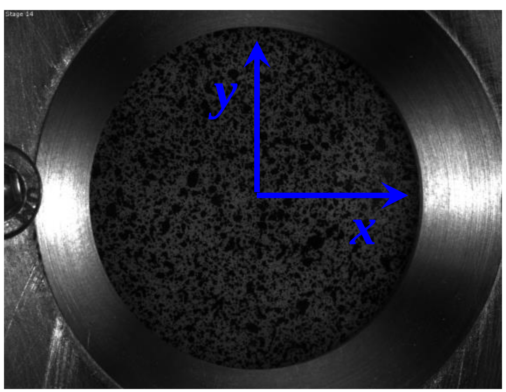
Full-field measurements using sDIC

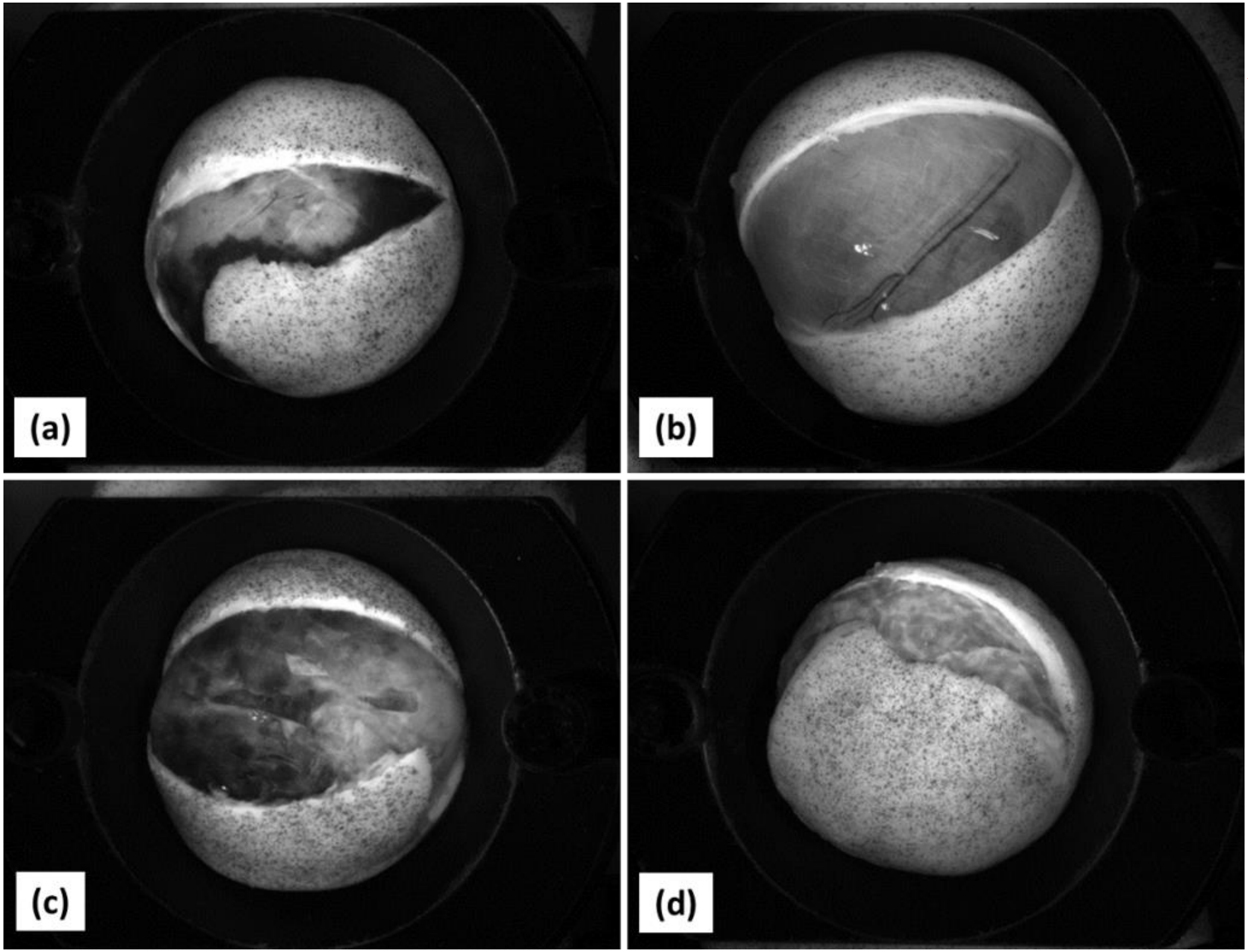


Undeformed



Deformed

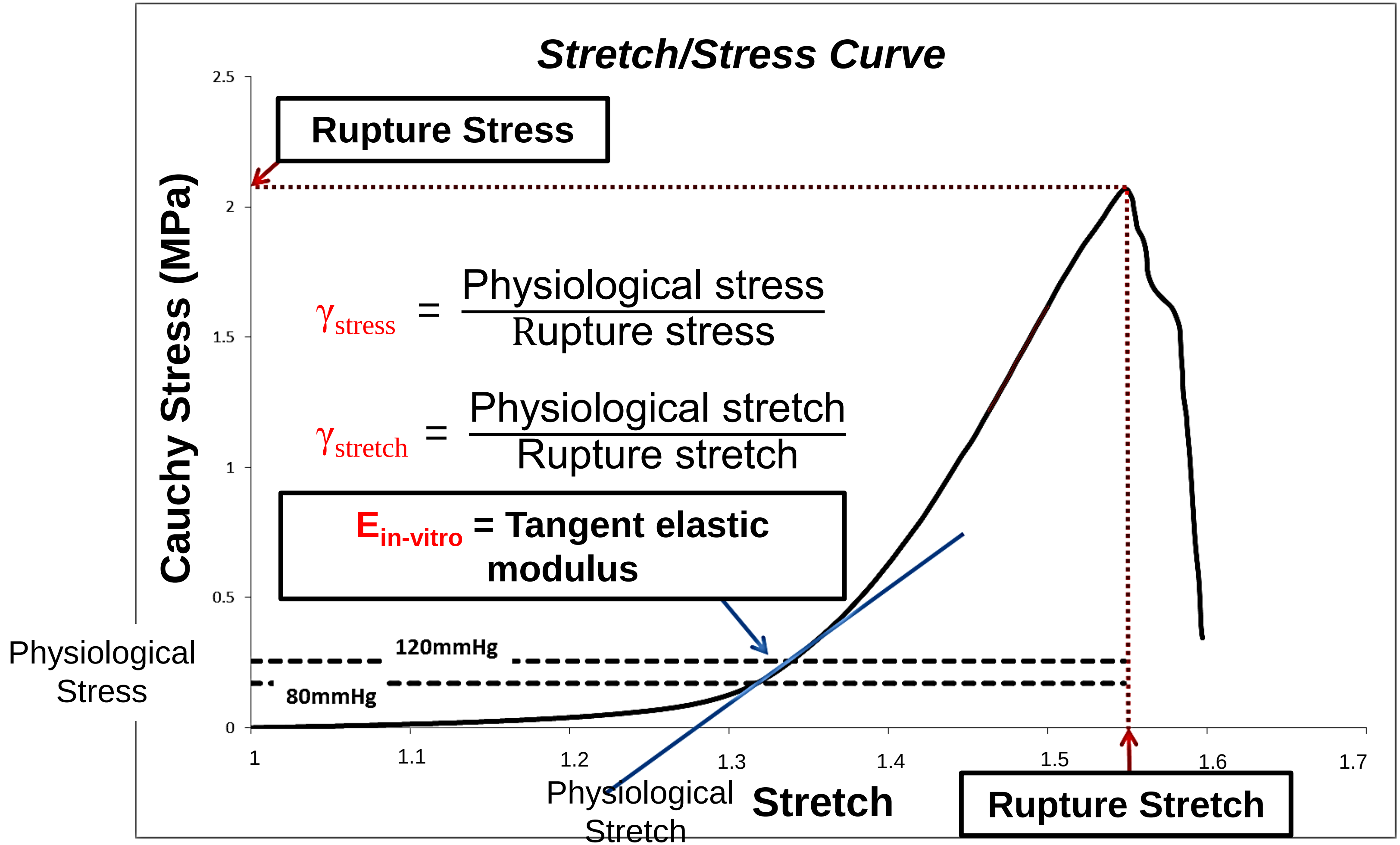
Rupture profiles



Blood flow

50% of aortas ruptured with an angle θ equal to 90 °

Rupture risk estimation



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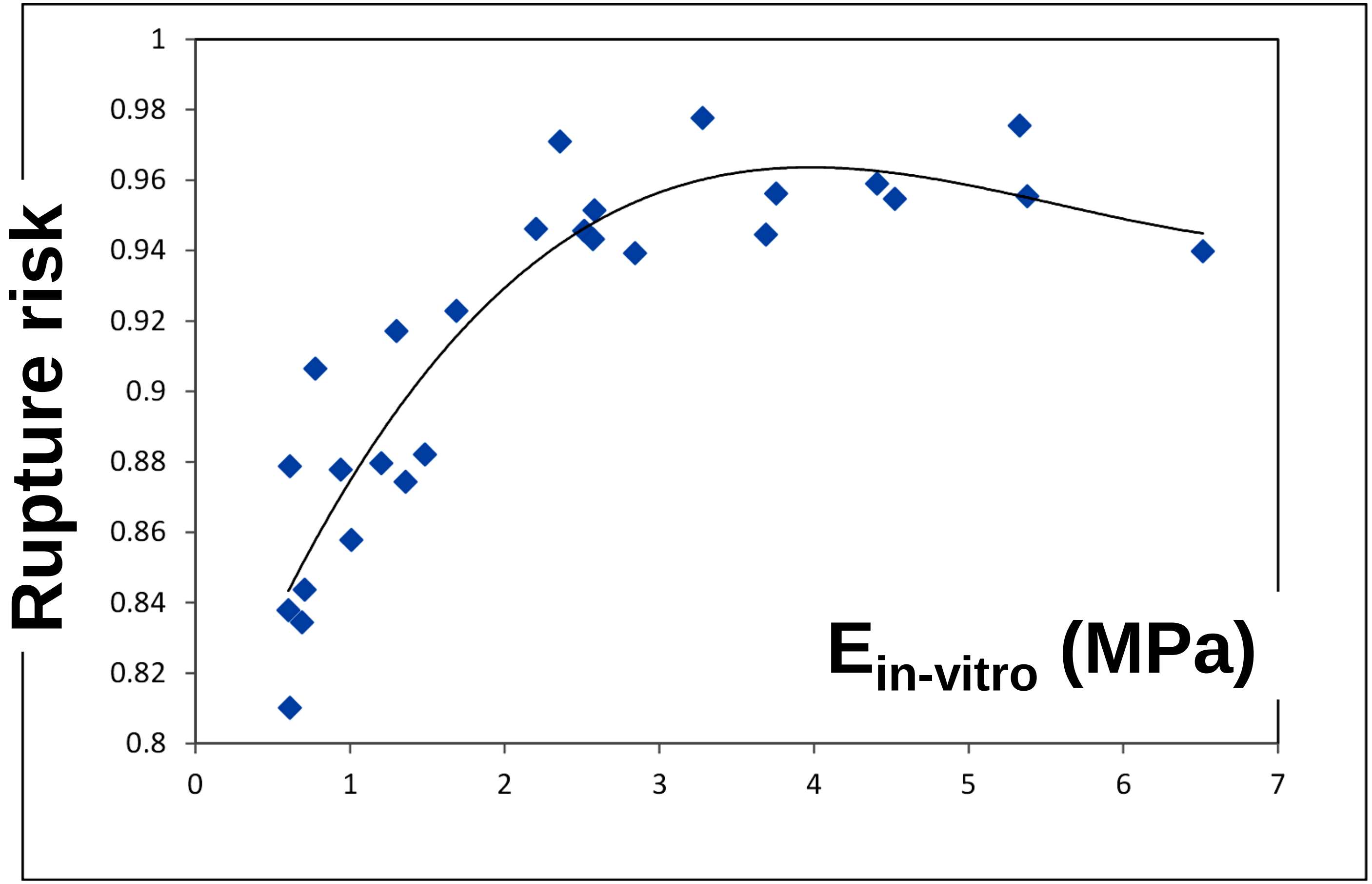
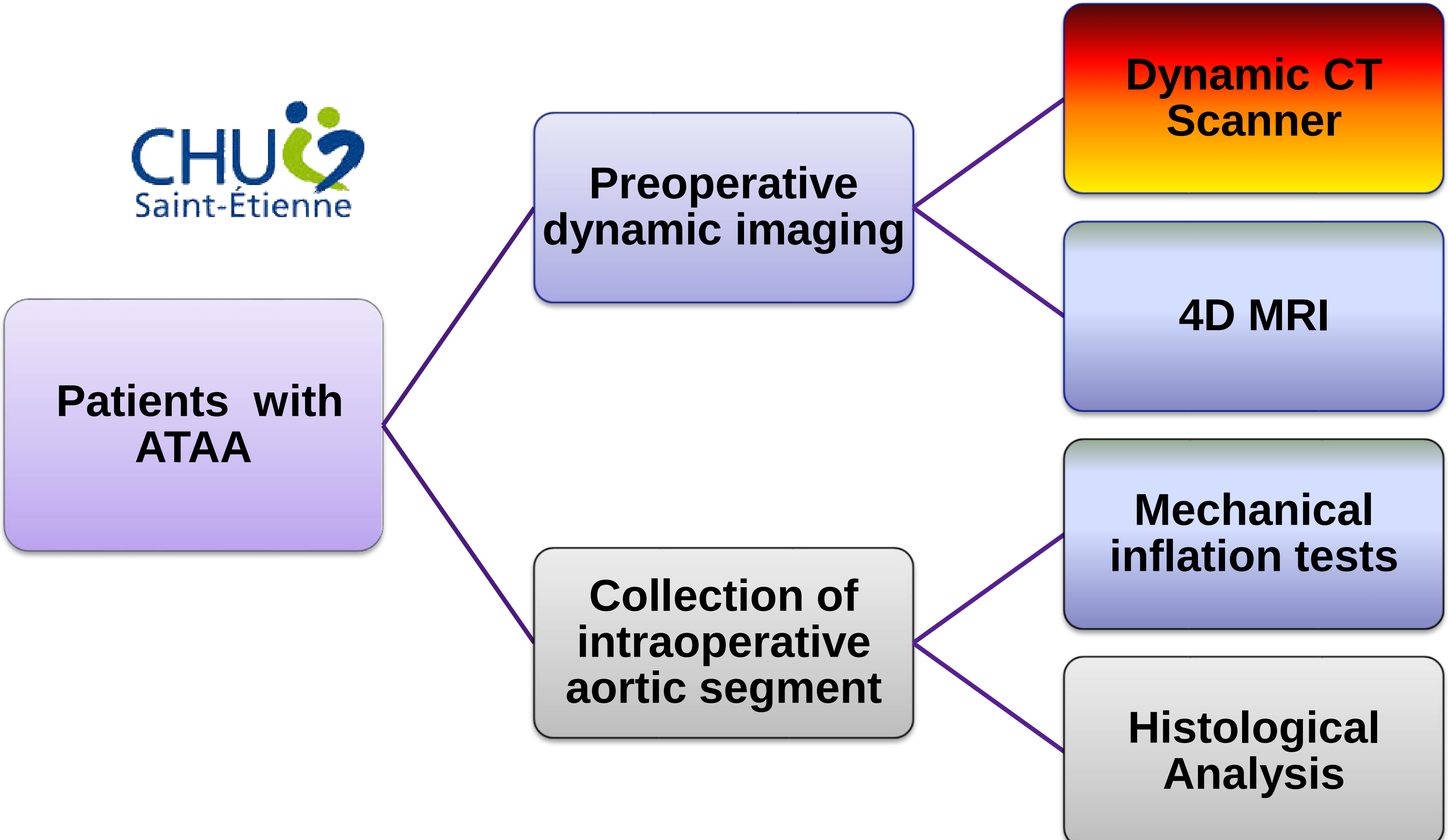
Correlation between the stretch-based rupture risk and the tangent elastic modulus



Duprey A, et al. Biaxial rupture properties of ascending thoracic aortic aneurysms. ***Acta Biomaterialia 2016.***

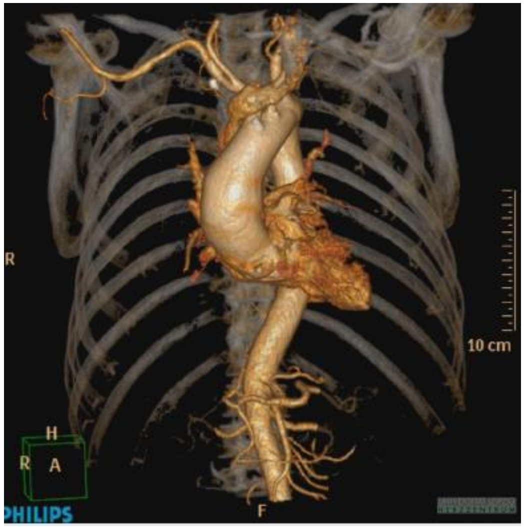
Methodology

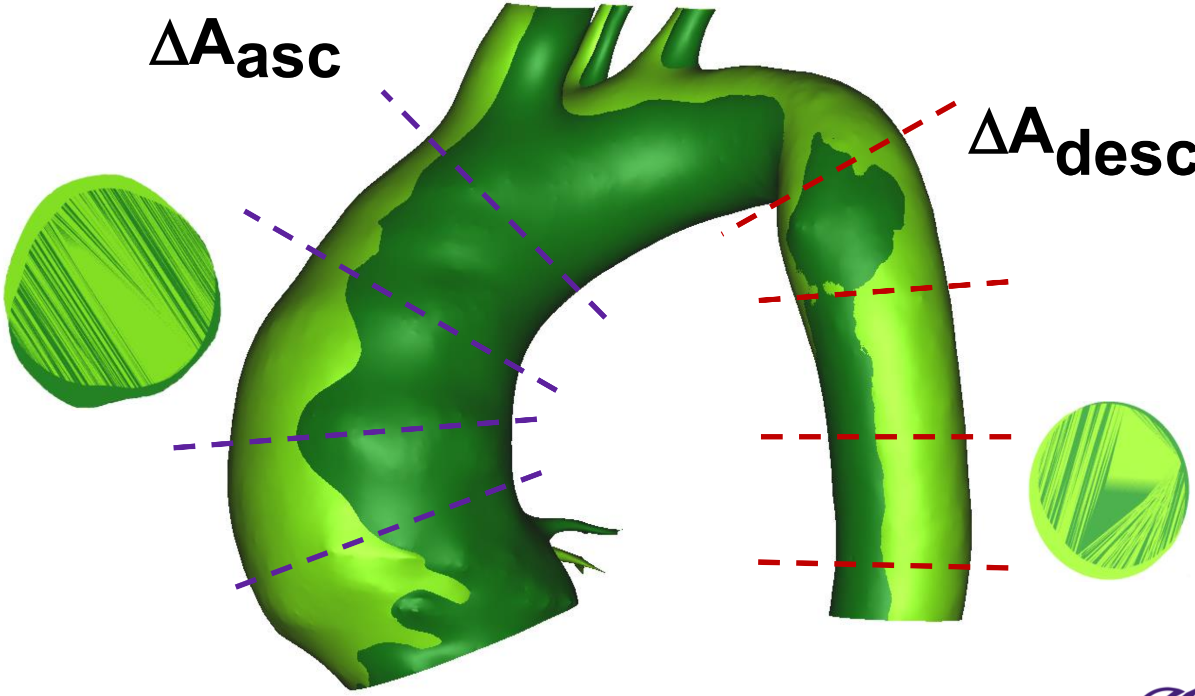


Measurement of aortic DISTENSIBILITY

- ***Aortic wall - 3D reconstruction from gated CT***

Dynamic preoperative scanners during cardiac cycle (~ 0.92 s) = 10 phases.
CT: (resolution 512x512, slice thickness of 0.5 mm)





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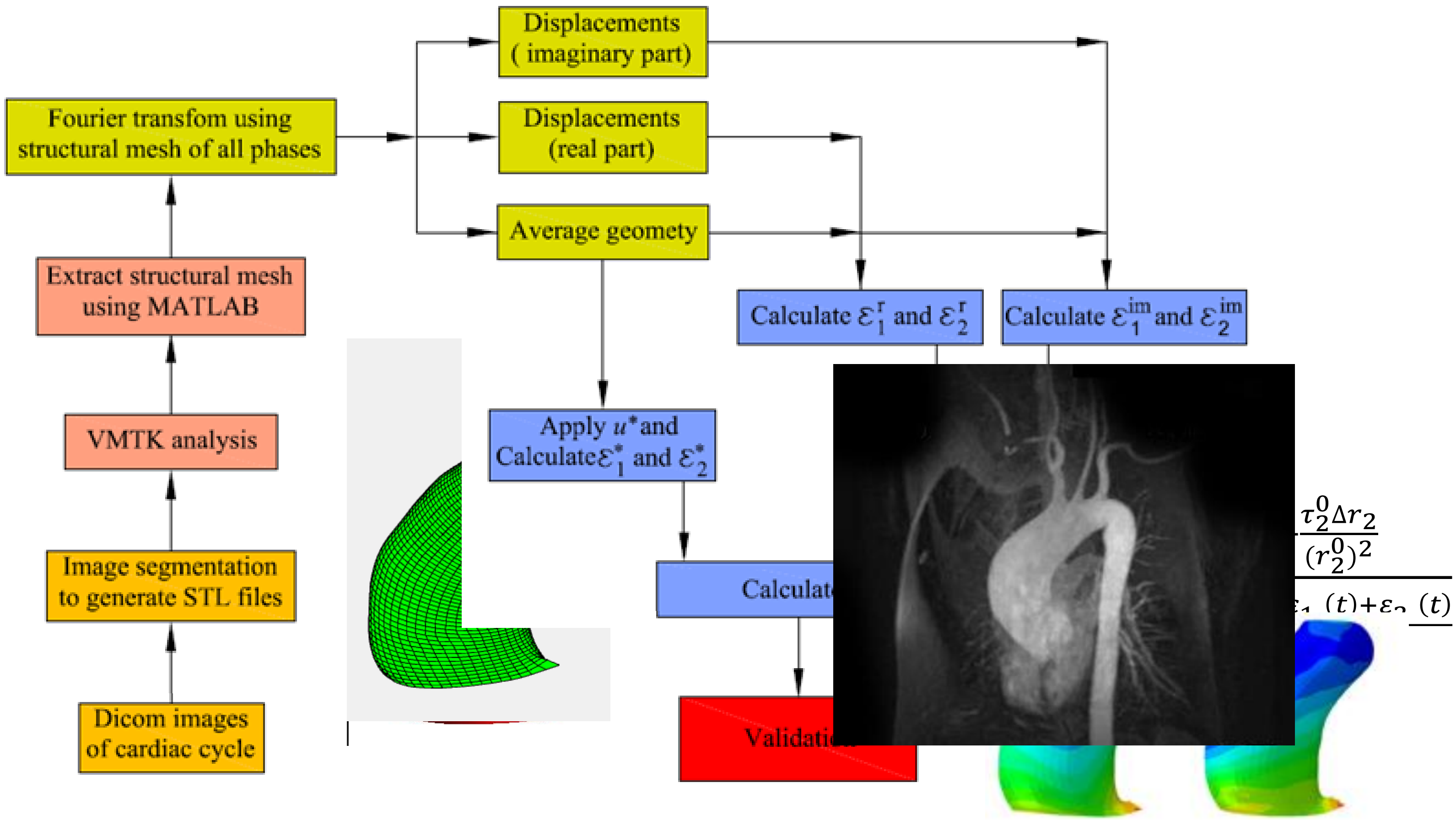
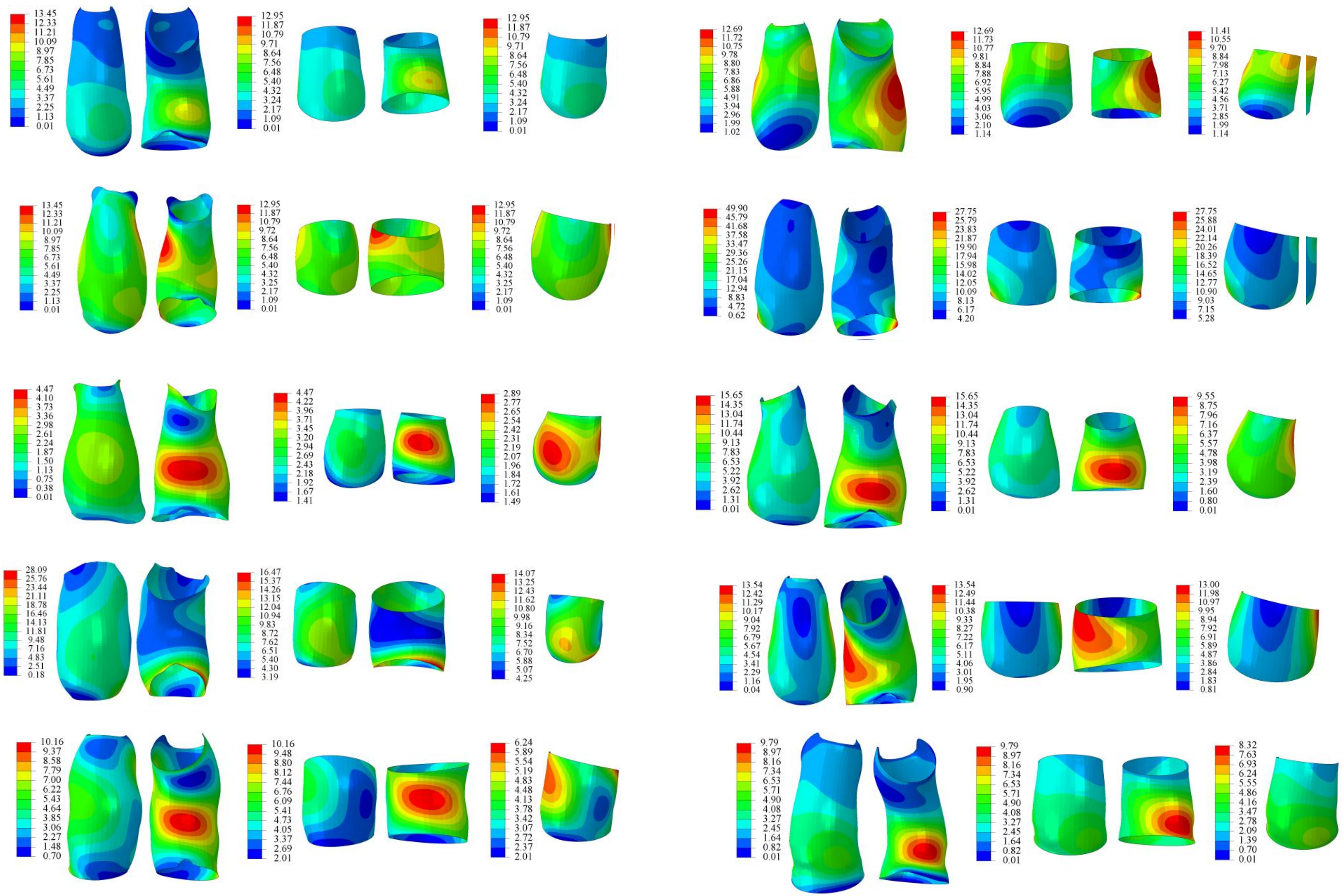
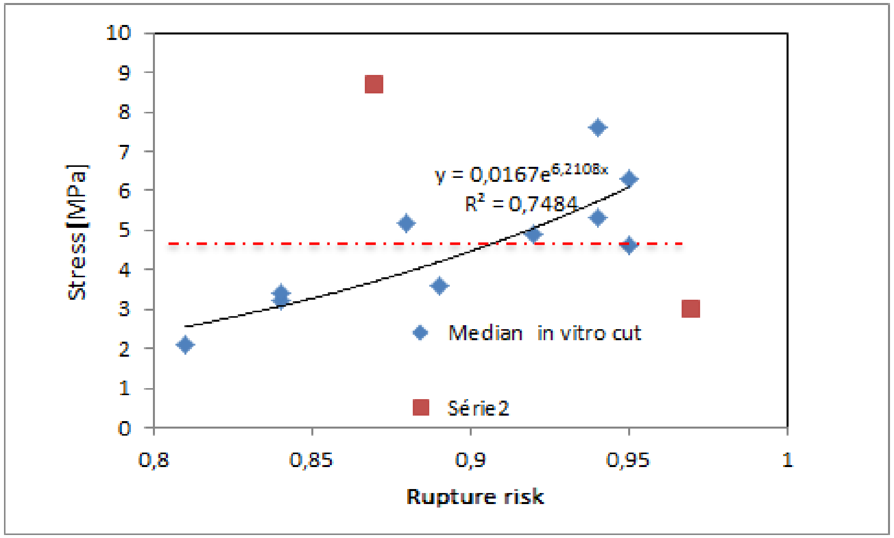
Methodology for non invasive reconstruction of in vivo stiffness distribution

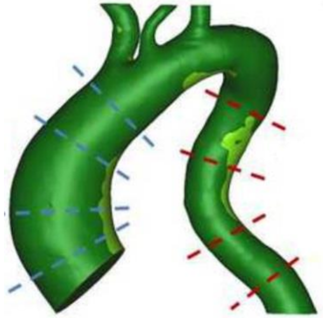


Stiffness distributions for 10 patients

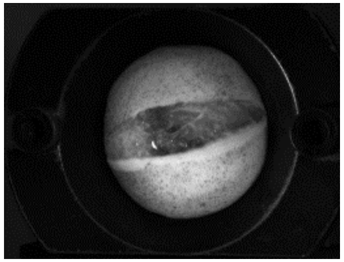


Correlation between stretch and membrane stiffness



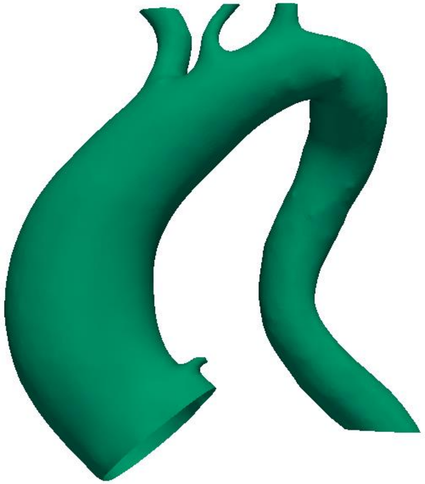


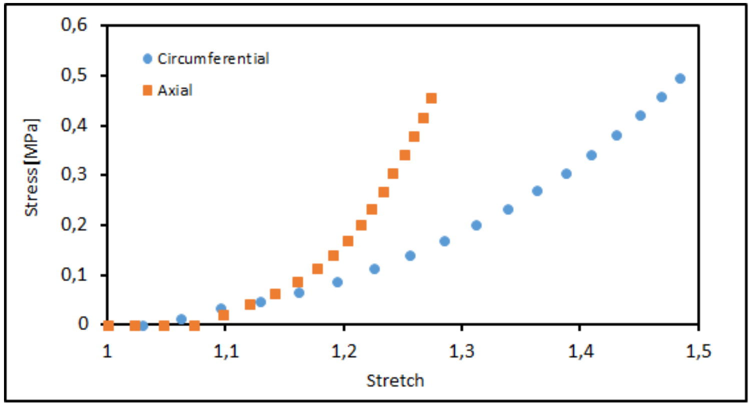
In vivo

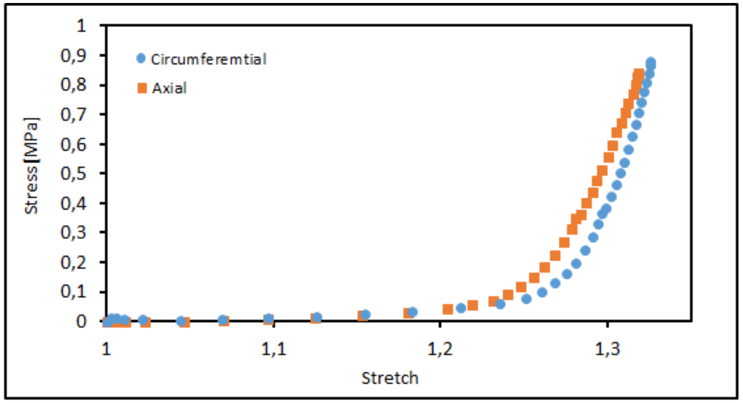


In vitro

Two examples of soft and stiff ascending aorta







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Summary

- 2 ways of defining rupture:
  - PWS – but unknown patient-specific strength
  - $\gamma_{stretch}$ correlated with in vivo circumferential stiffness

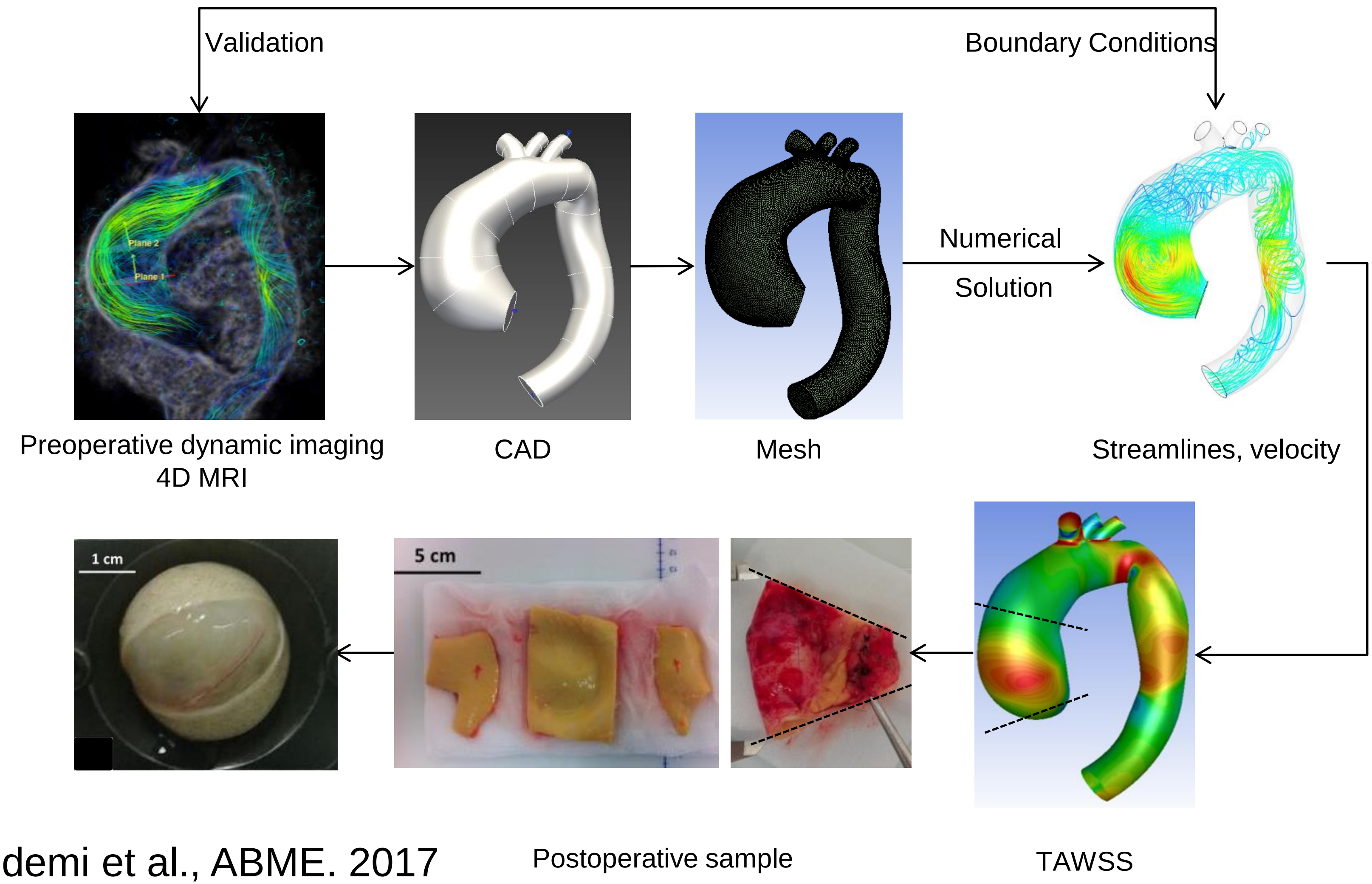
Higher distensibility $\Rightarrow$ less risk because the aneurysm can more easily withstand volume variation

Martin et al., Acta Biomater. 2013, Duprey et al., Acta Biomater. 2016.

Methodology

- Patients with ATAA
  - Preoperative dynamic imaging
    - Dynamic CT Scanner
    - 4D MRI
  - Collection of intraoperative aortic segment
    - Mechanical inflation tests
    - Histological Analysis

Role of hemodynamics in rupture risk



Condemi et al., ABME. 2017

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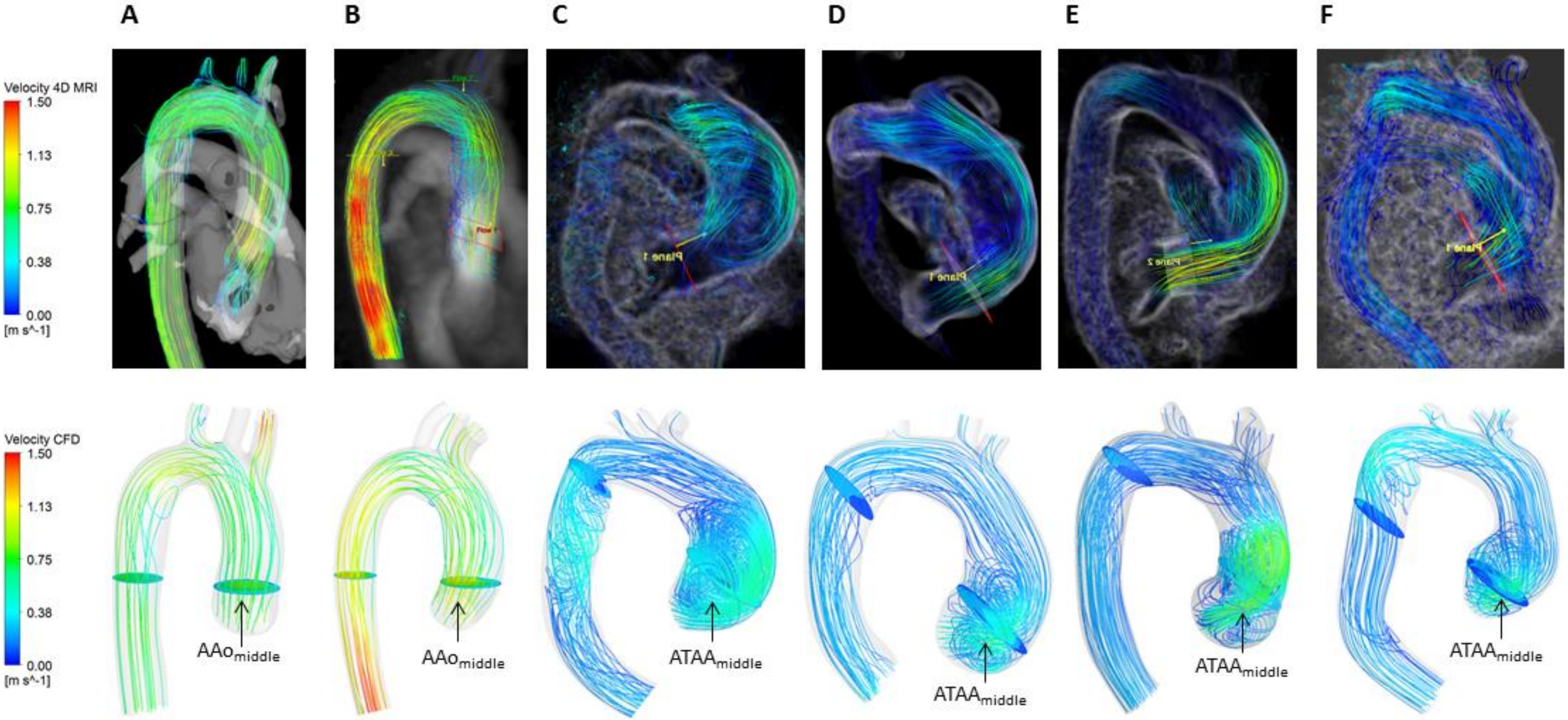
RESULTS- Flow$_{eccentricity}$ calculated from the CFD studies against the 4D MRI results



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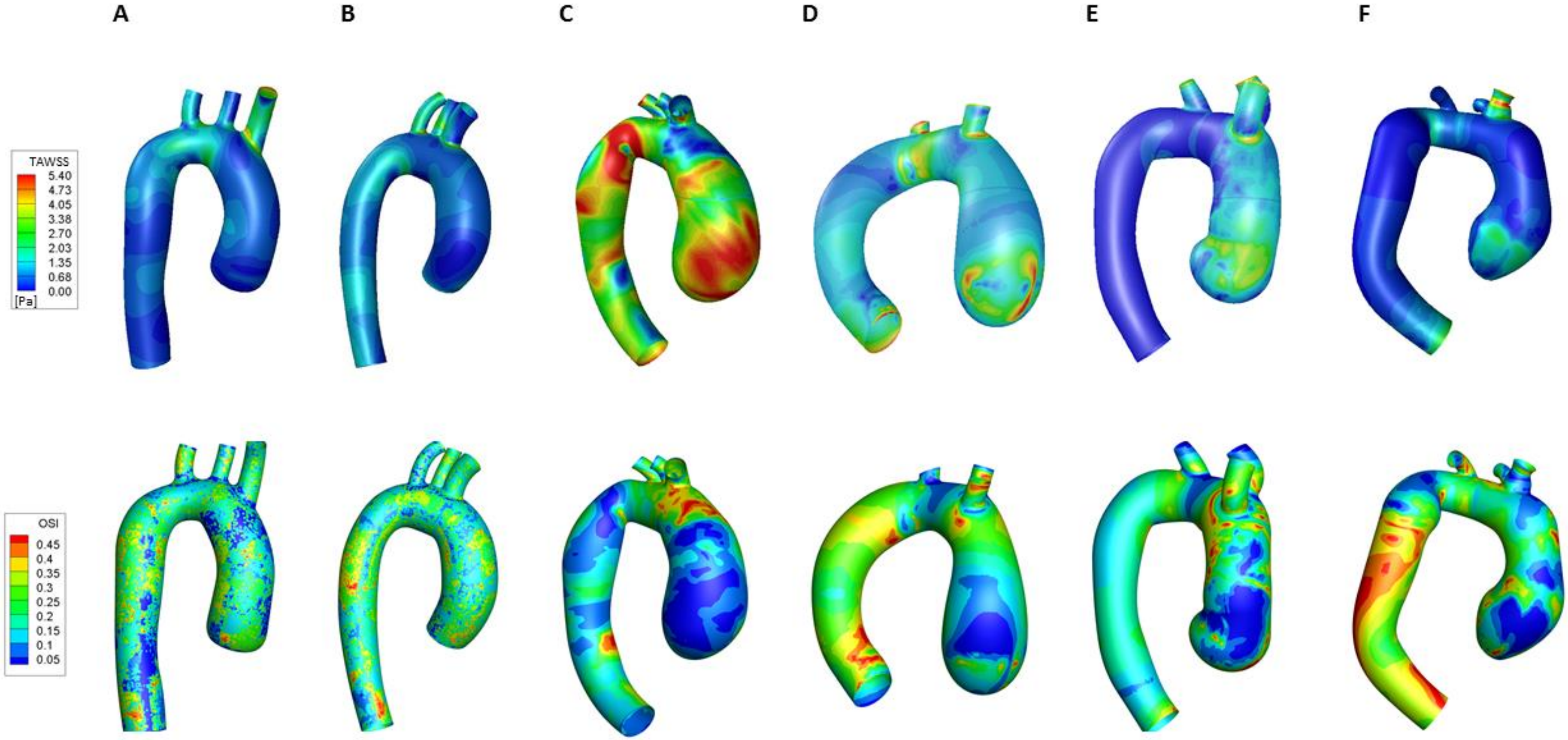
RESULTS- OSI and TAWSS



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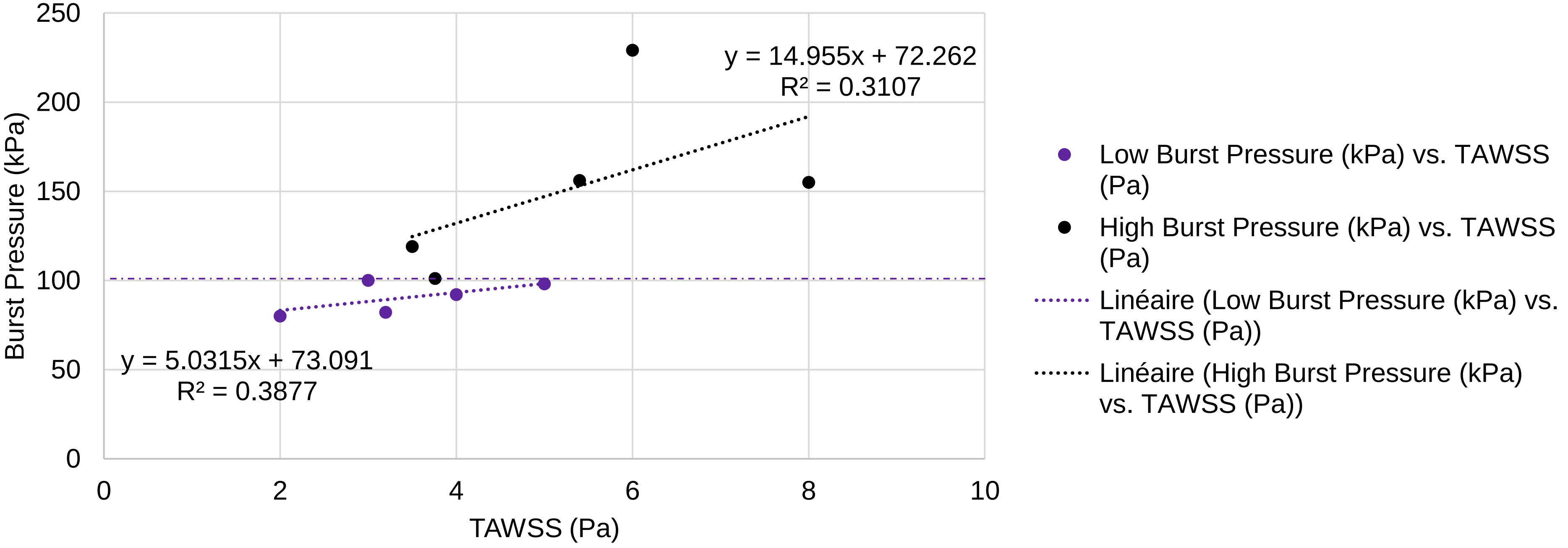
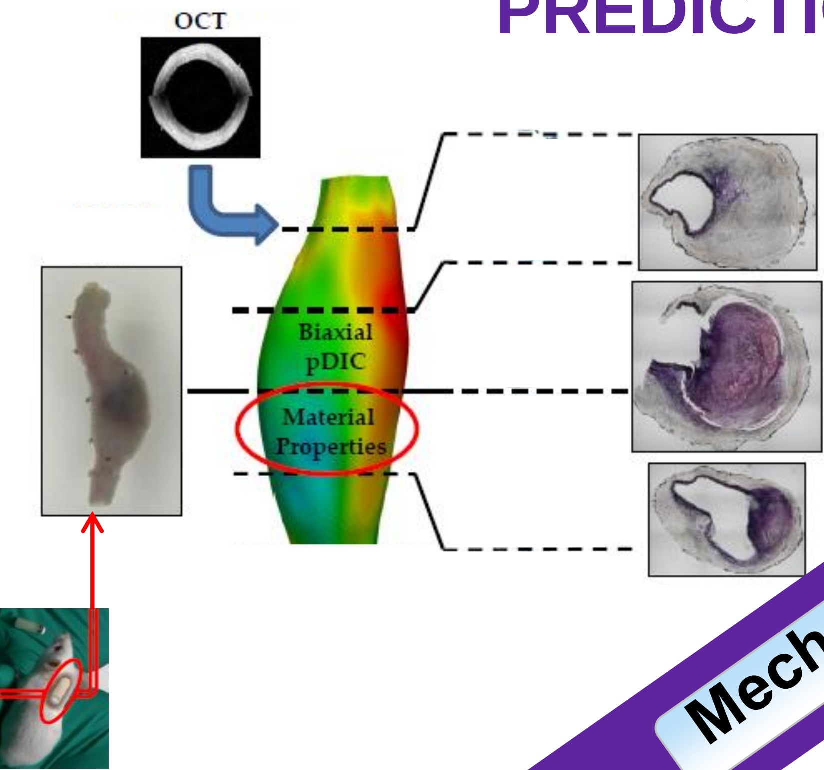
RESULTS- TAWSS versus wall properties

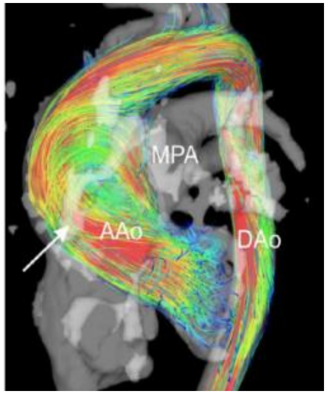


TOWARDS ATAA GROWTH PREDICTIONS



Clinical applications

Mechanobiology



European Research Council
Established by the European Commission

Development of mechanobiological models

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Understanding aneurysm growth using mechanobiology and multimodal imaging

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Altered mechanics induce biological responses, including gene expression, protein activation and cell phenotype

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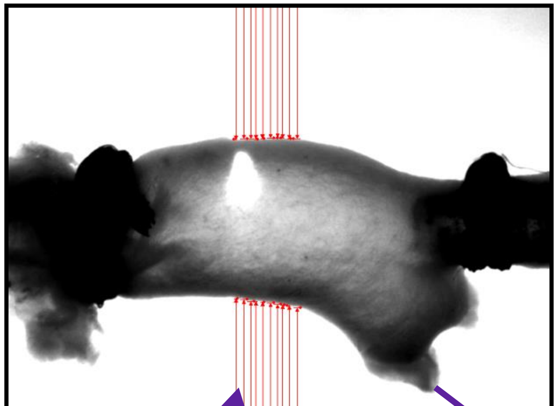
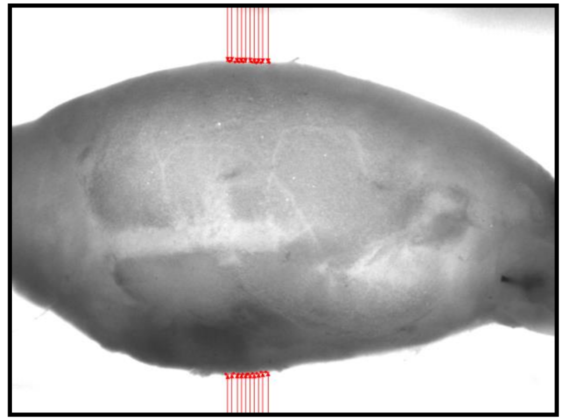
Study Design

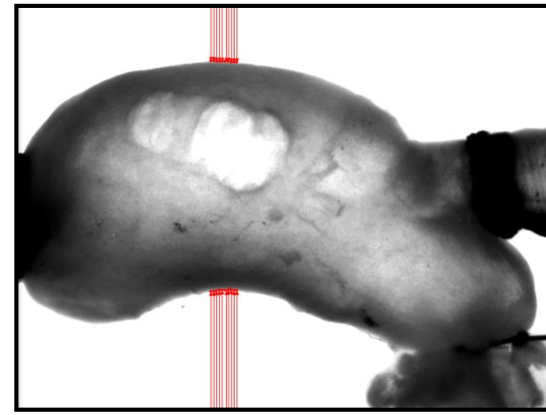
Control

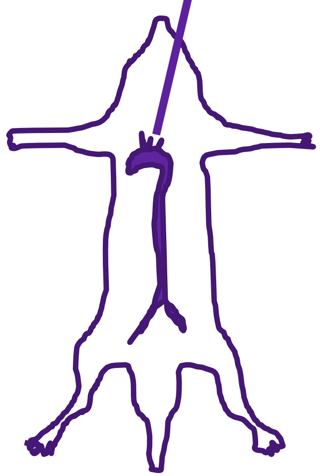


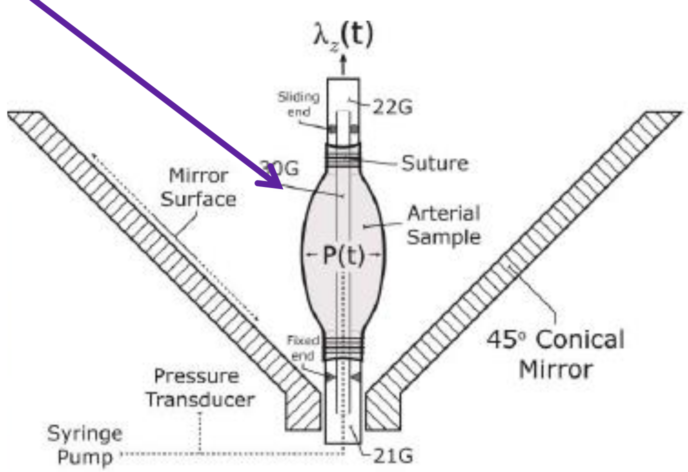
Fibulin 4 SMC KO



Fibrillin 1 *mgR/mgR*







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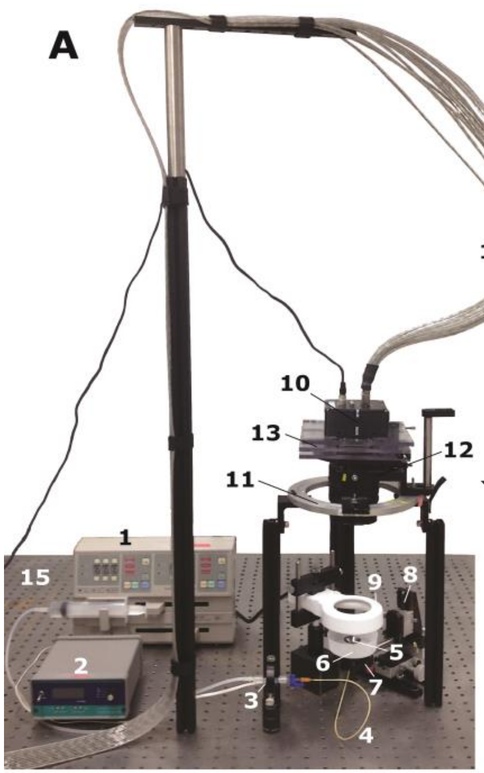
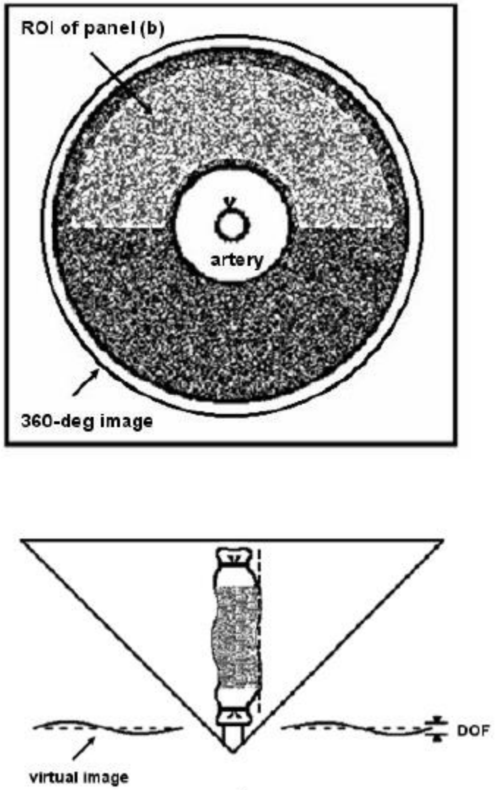
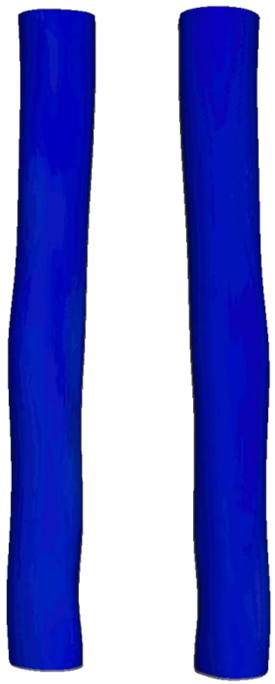
The pDIC technique







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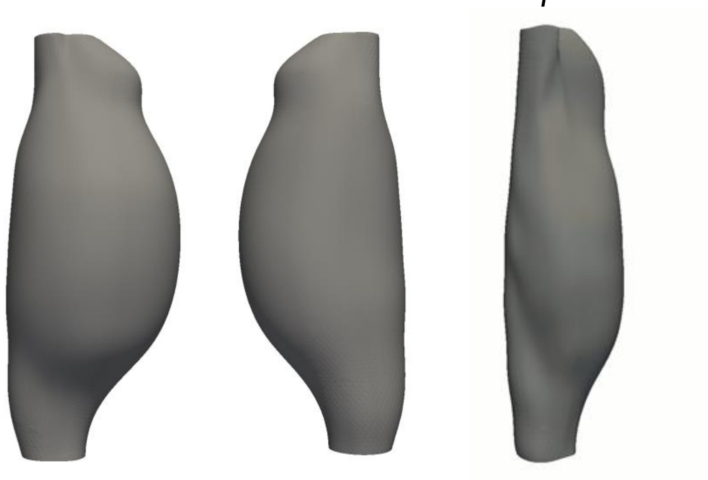
pDIC measurements

Fibulin 4 SMC KO

ventral *dorsal* *inflation*

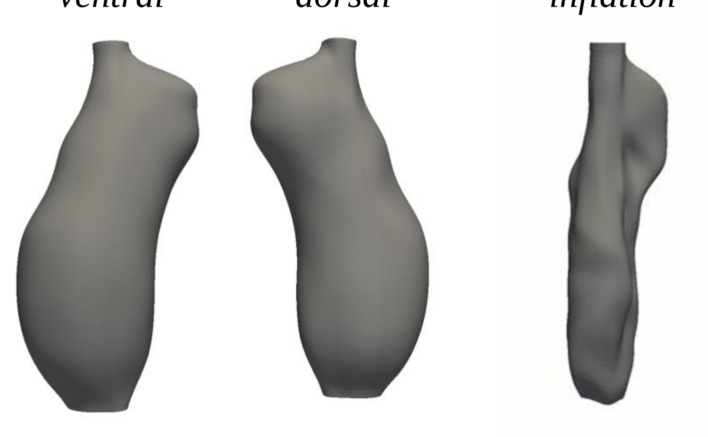
6852



Fibrillin 1 *mgR/mgR*

ventral *dorsal* *inflation*

CS38



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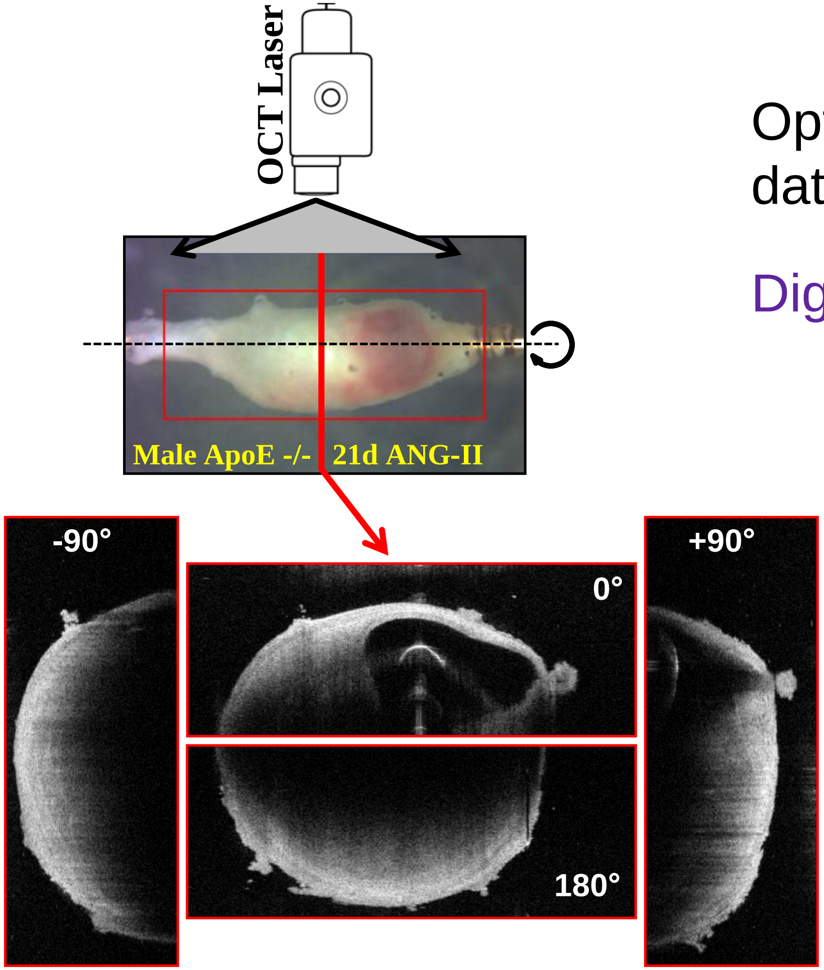
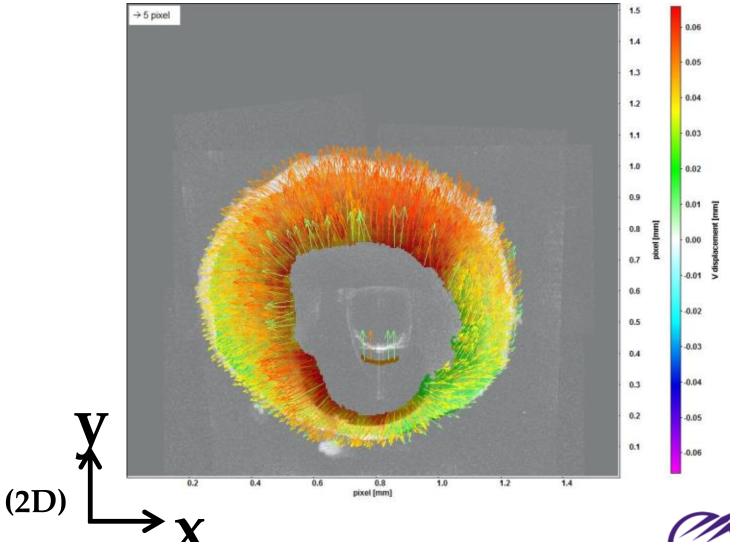
Bulk strain measurement and identification



Optical Coherence Tomography (OCT) data are available from the experiments

Digital volume correlation



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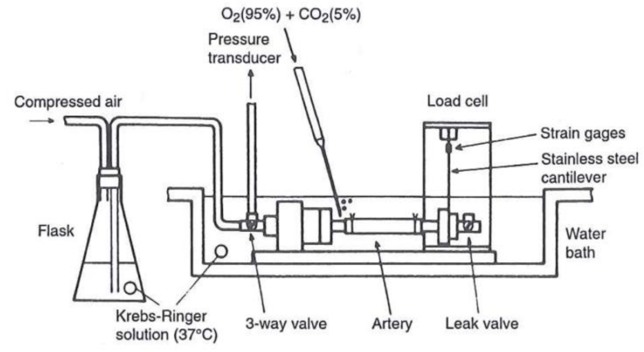
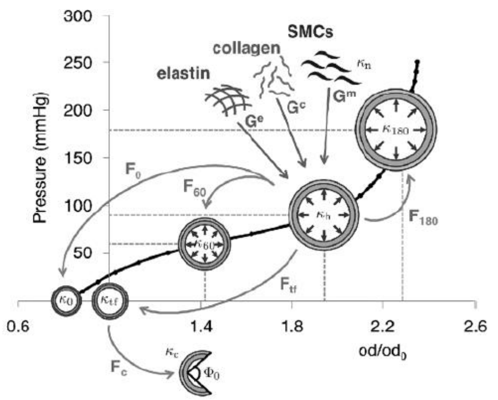
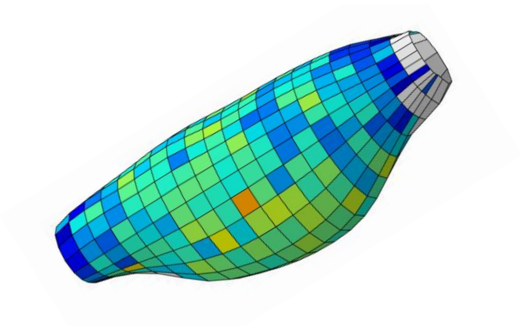
APPROACH

1. Experiments
2. Material model
3. Inverse method







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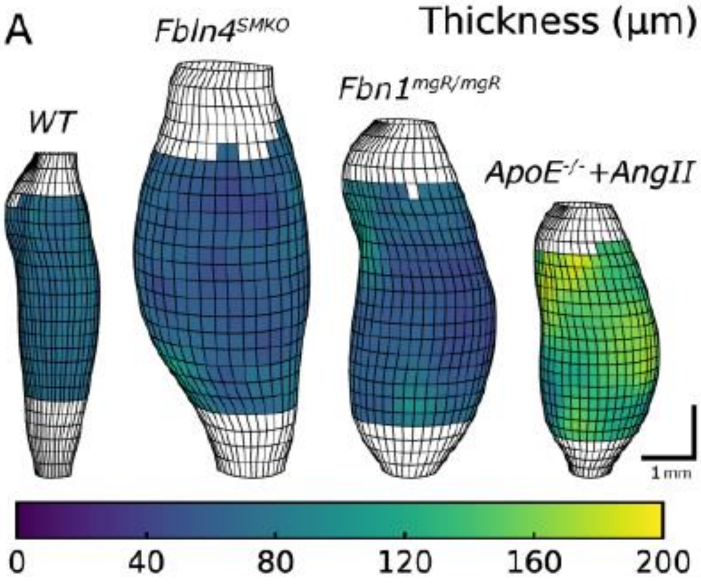
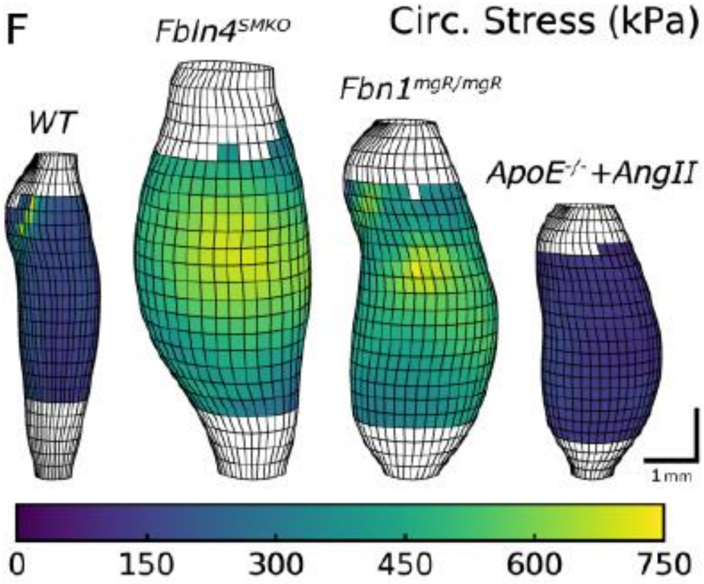
Full-Field Material Parameter Estimation vs thickness distribution





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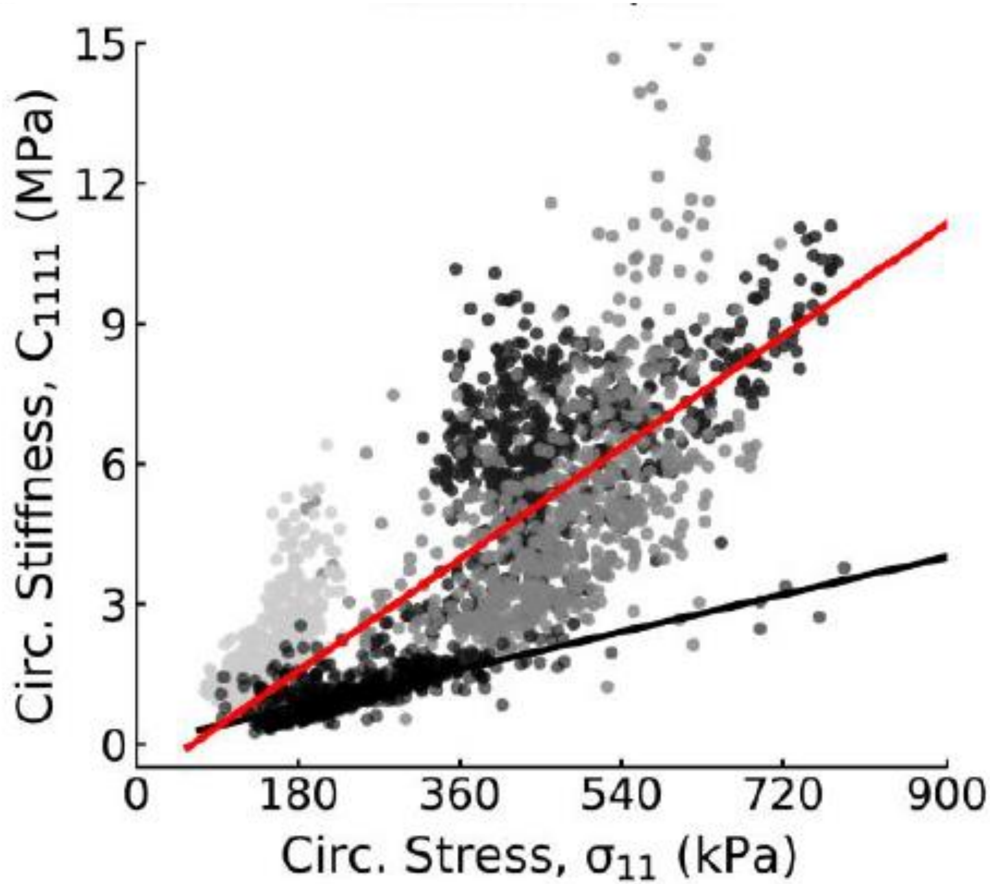
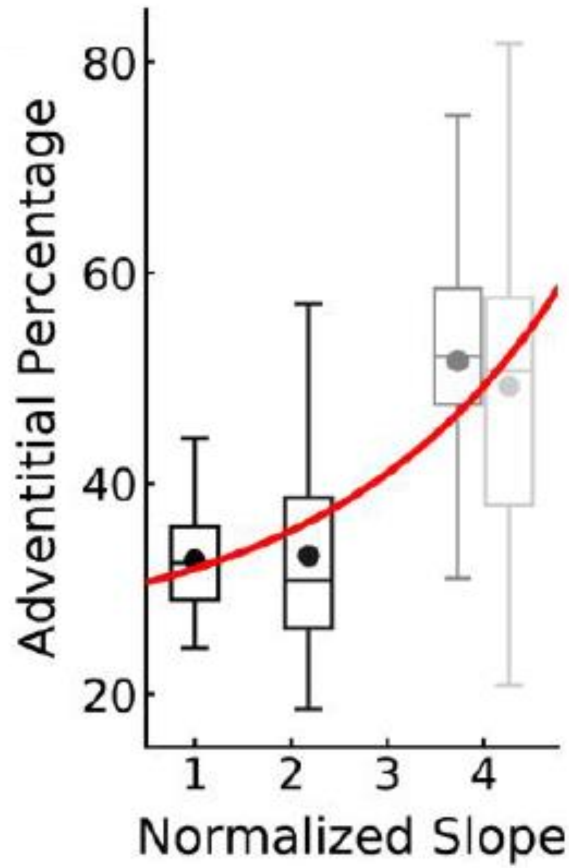
Full-Field Material Parameter Estimation vs local stress





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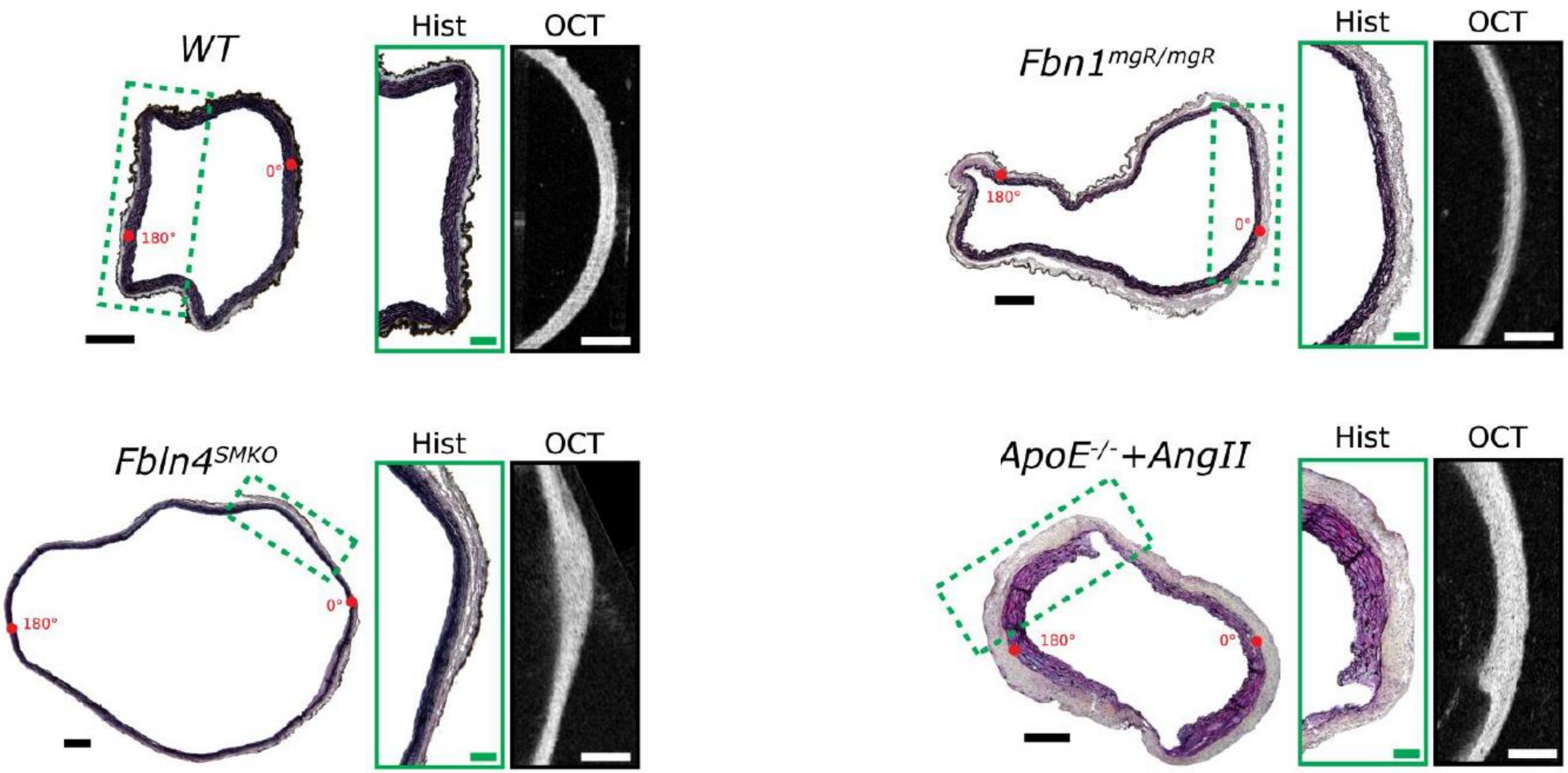
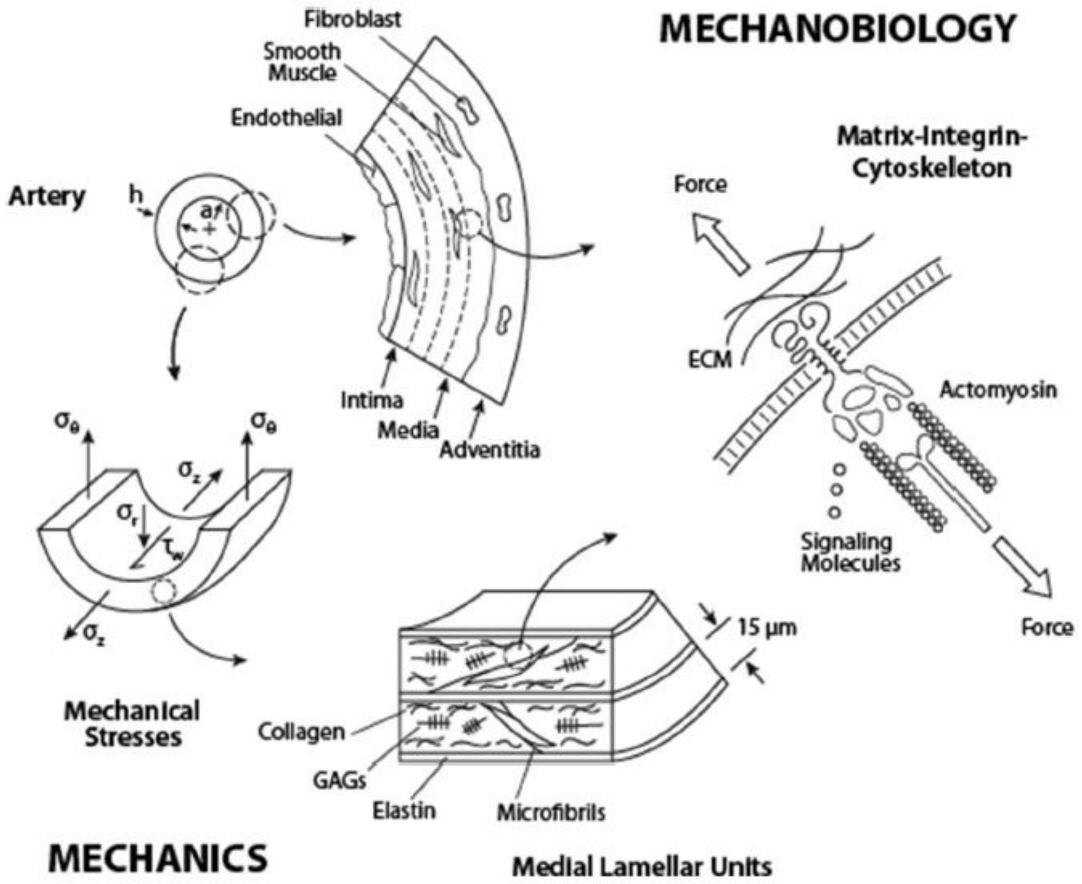
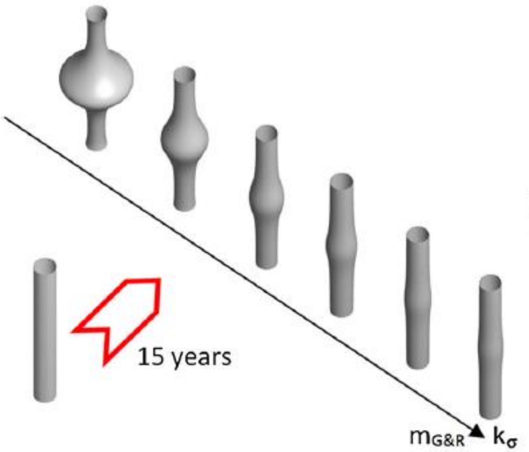
Correlation with tissue µstructure

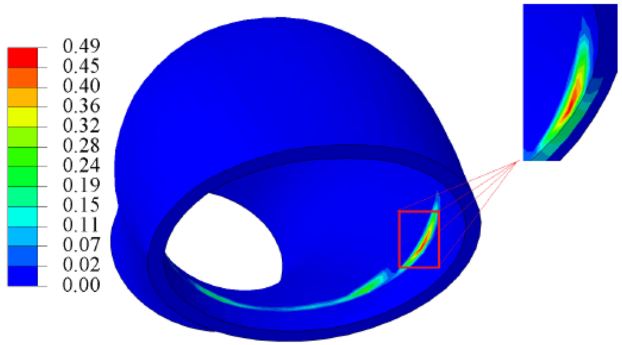


Predictions of vascular adaptation and disease development





Cyron et al, BMMB, 2016, Mousavi et al, IJNMBE, 2018



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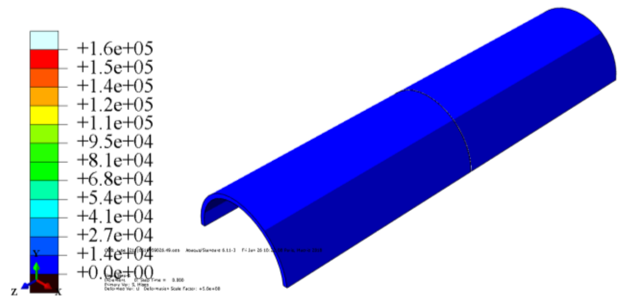
Vision

- Our vision is that the evolution of the strength and of the wall stress of the aorta during the growth of an aneurysm can be predicted on a patient-specific basis by a **computational model**.
- On the basis of an MRI examination, our computational model, accessible by surgeons as an interactive intuitive user interface, would permit to predict when an aortic aneurysm is going to reach a critical size or a critical rupture risk.



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