



PERSONALIZED RUPTURE RISK ESTIMATION IN THORACIC AORTIC ANEURYSMS



Prof Stéphane AVRIL



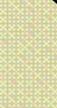
Where do I come from?

Demanget et al., Perrin et al.



MINES SAINT-ETIENNE
First Grande Ecole
outside Paris
Founded in 1816

PARIS



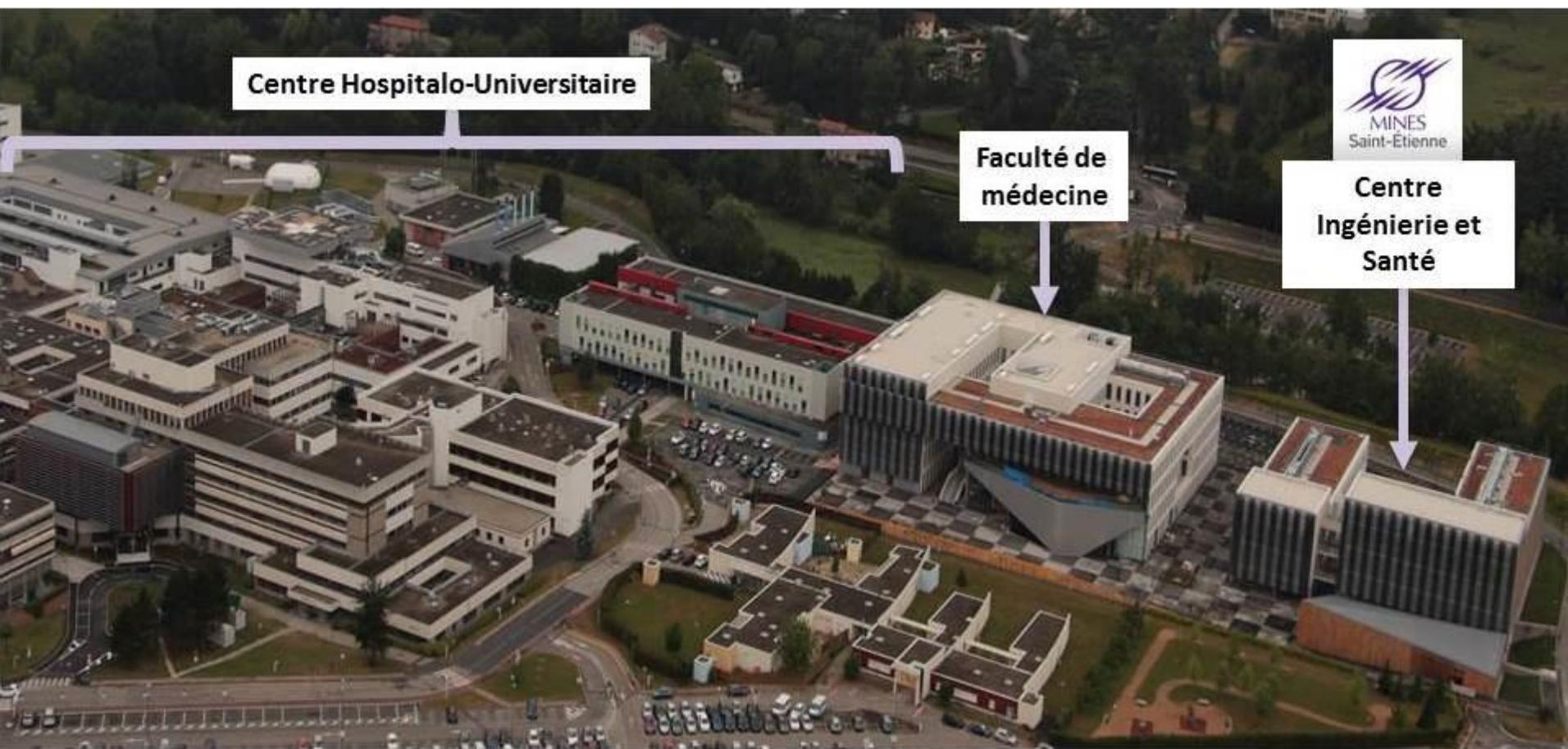
**AUVERGNE
RHONE-ALPES**



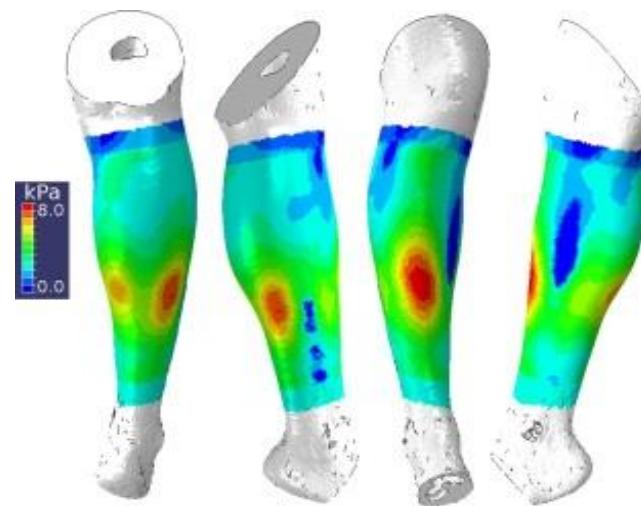
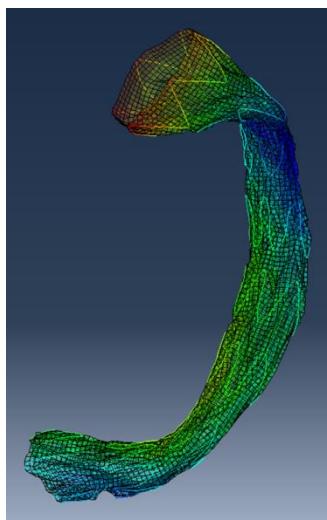
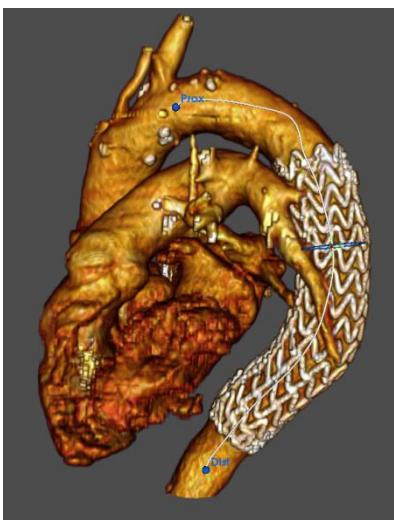
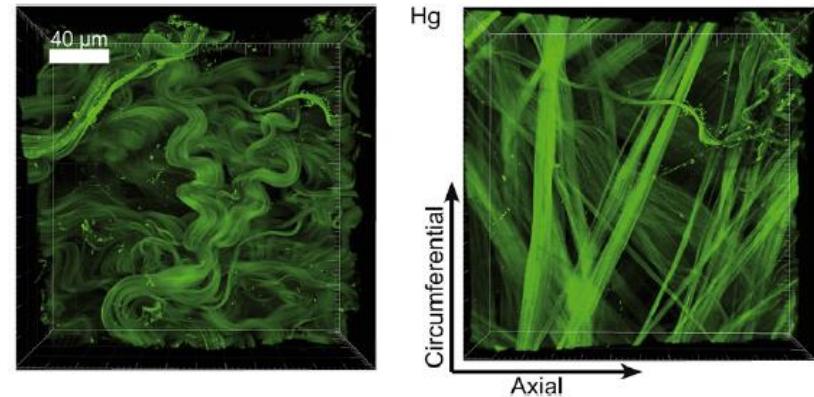
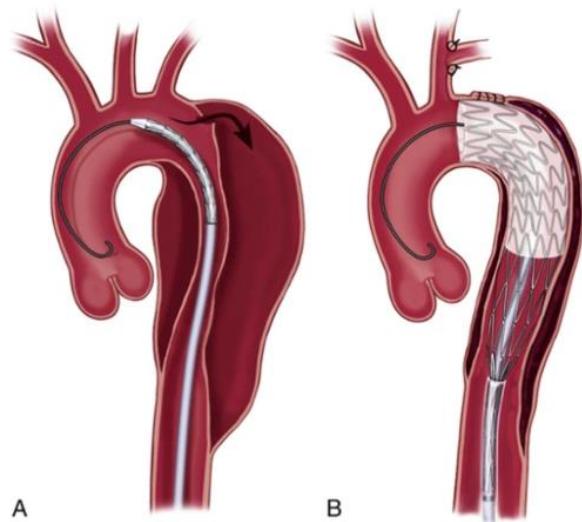
SAINBIOSE
SAnté INgénierie
BIOlogie Saint-Etienne

U1059 • INSERM • SAINT-ETIENNE

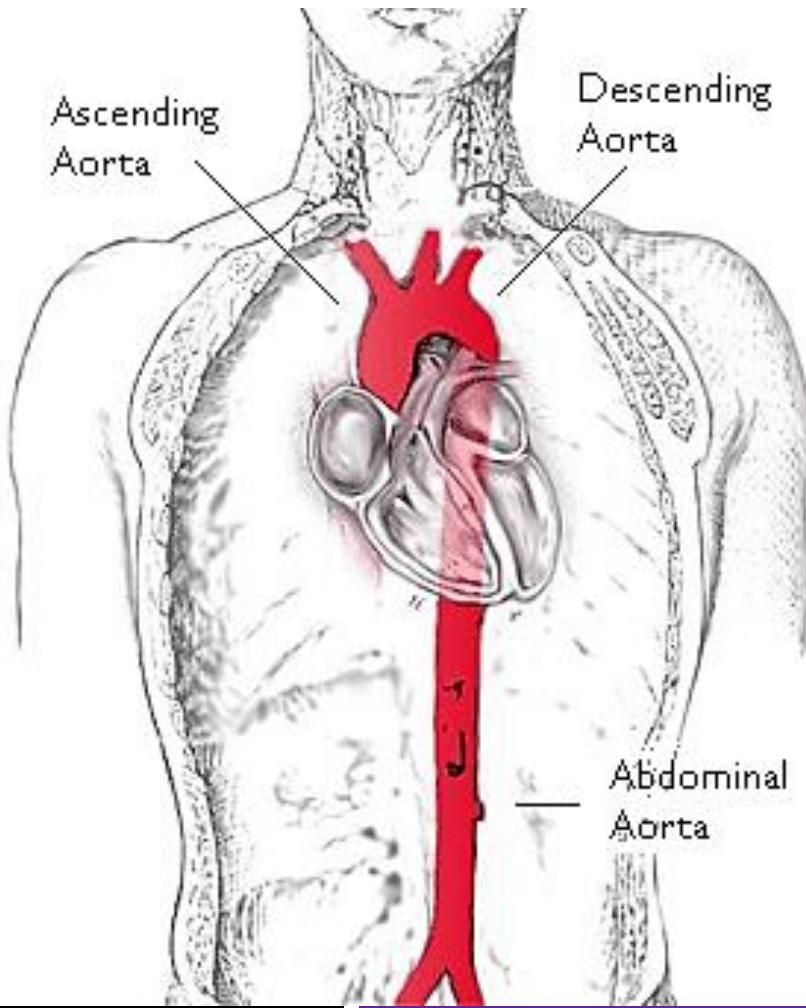
Institut national
de la santé et de la recherche médicale



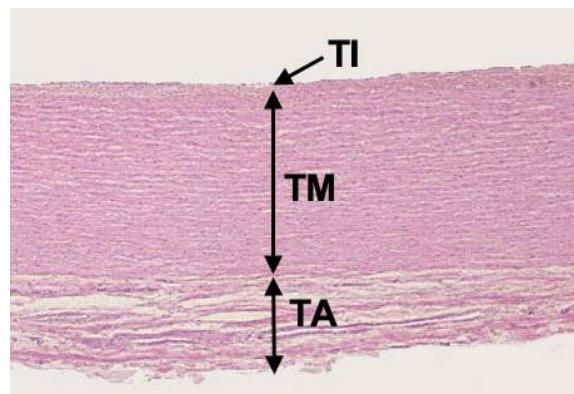
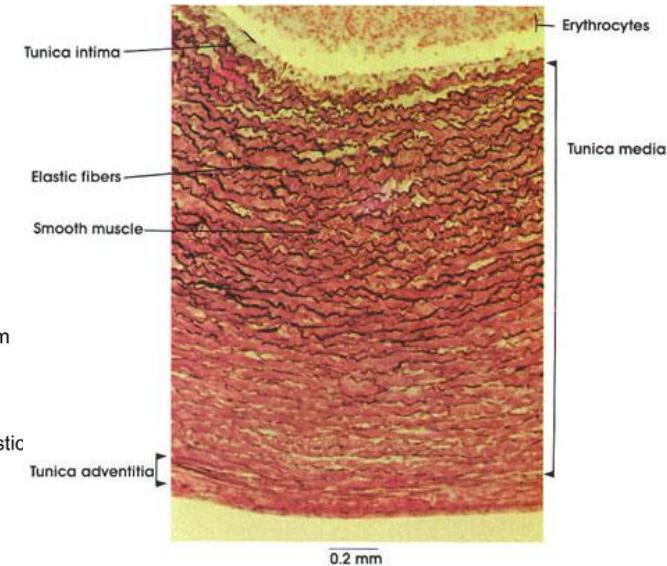
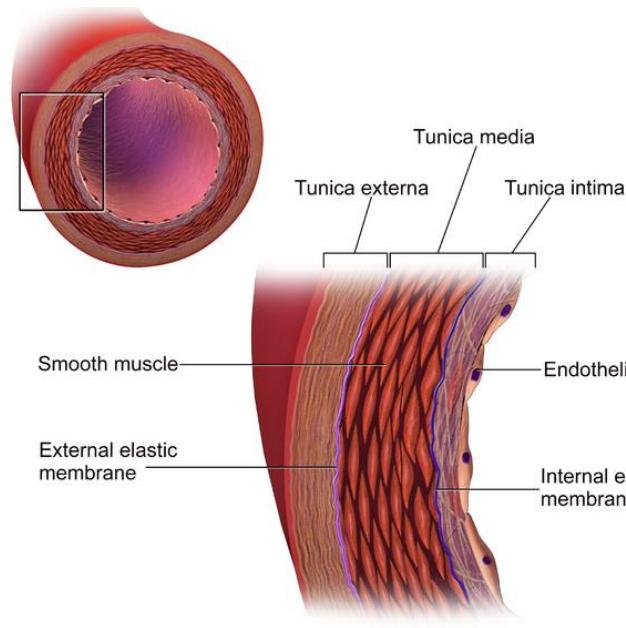
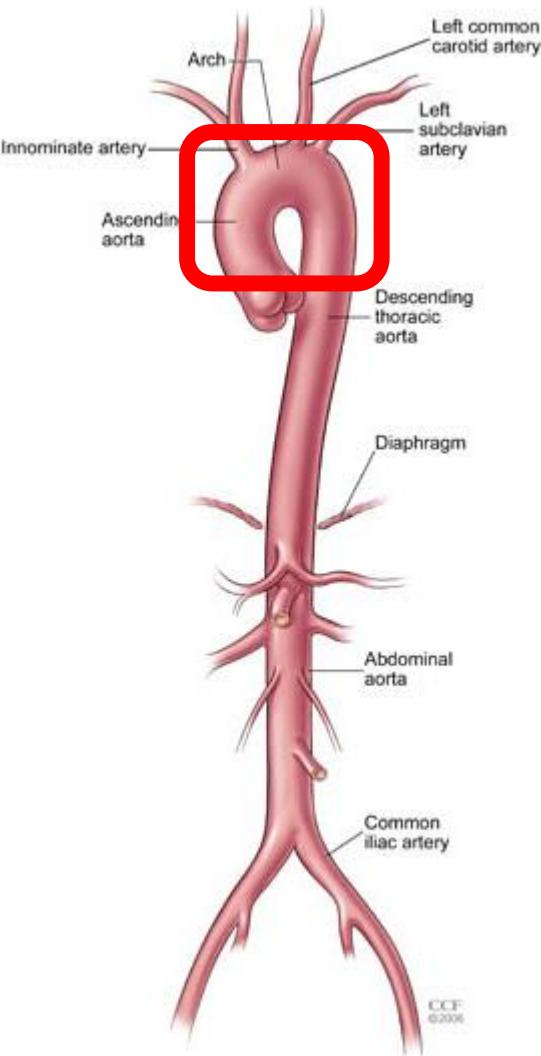
Biomechanics of soft tissues at different scales



TODAY'S TALK: THE AORTA



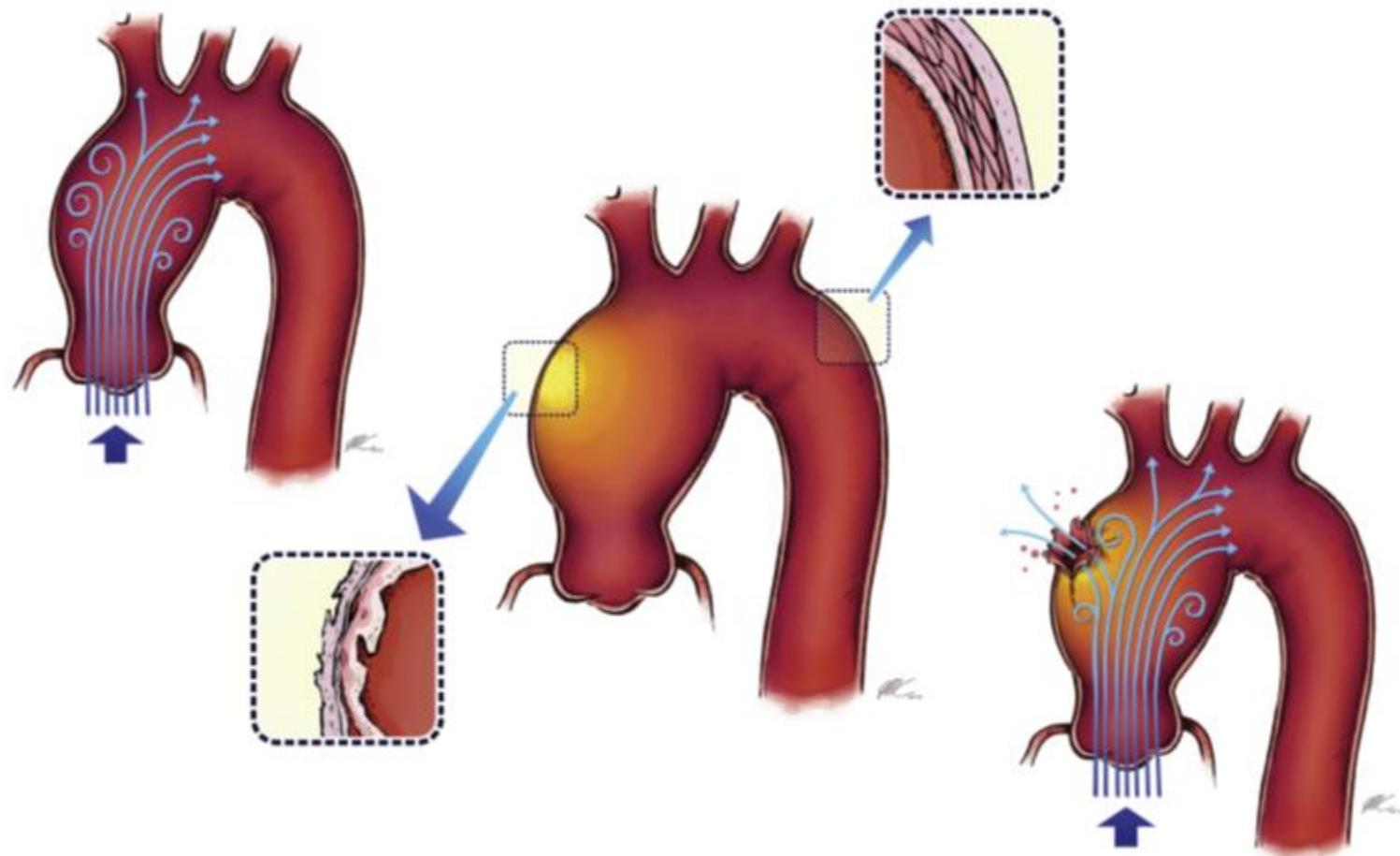
THE ASCENDING THORACIC AORTA



The size of the aorta is directly proportional to the patient's height and weight.

$\varnothing 1.2 - 3.0 \text{ cm}$

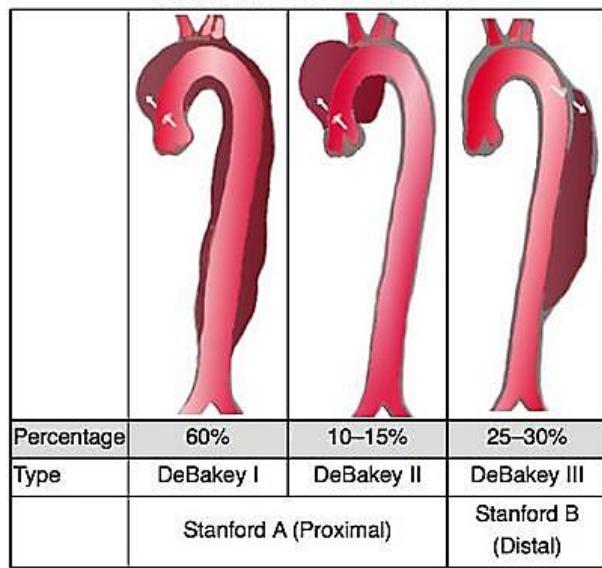
ASCENDING AORTIC THORACIC ANEURYSM



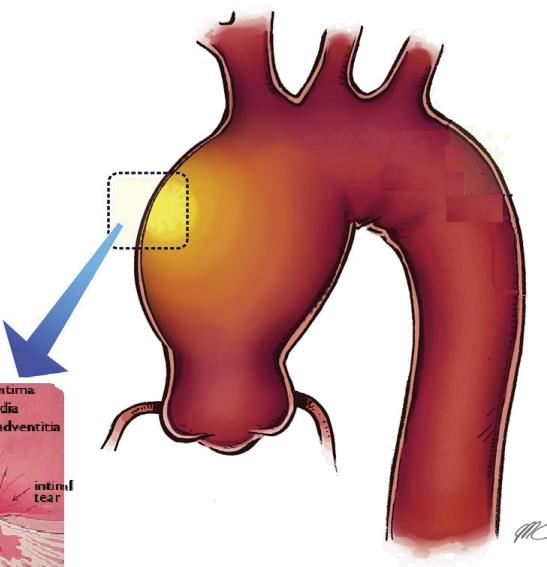
Martufi et al, Is There a Role for Biomechanical Engineering in Helping to Elucidate the Risk Profile of the Thoracic Aorta?,
Ann Thor Surg, 2016

AORTIC DISSECTION

Classification of aortic dissection

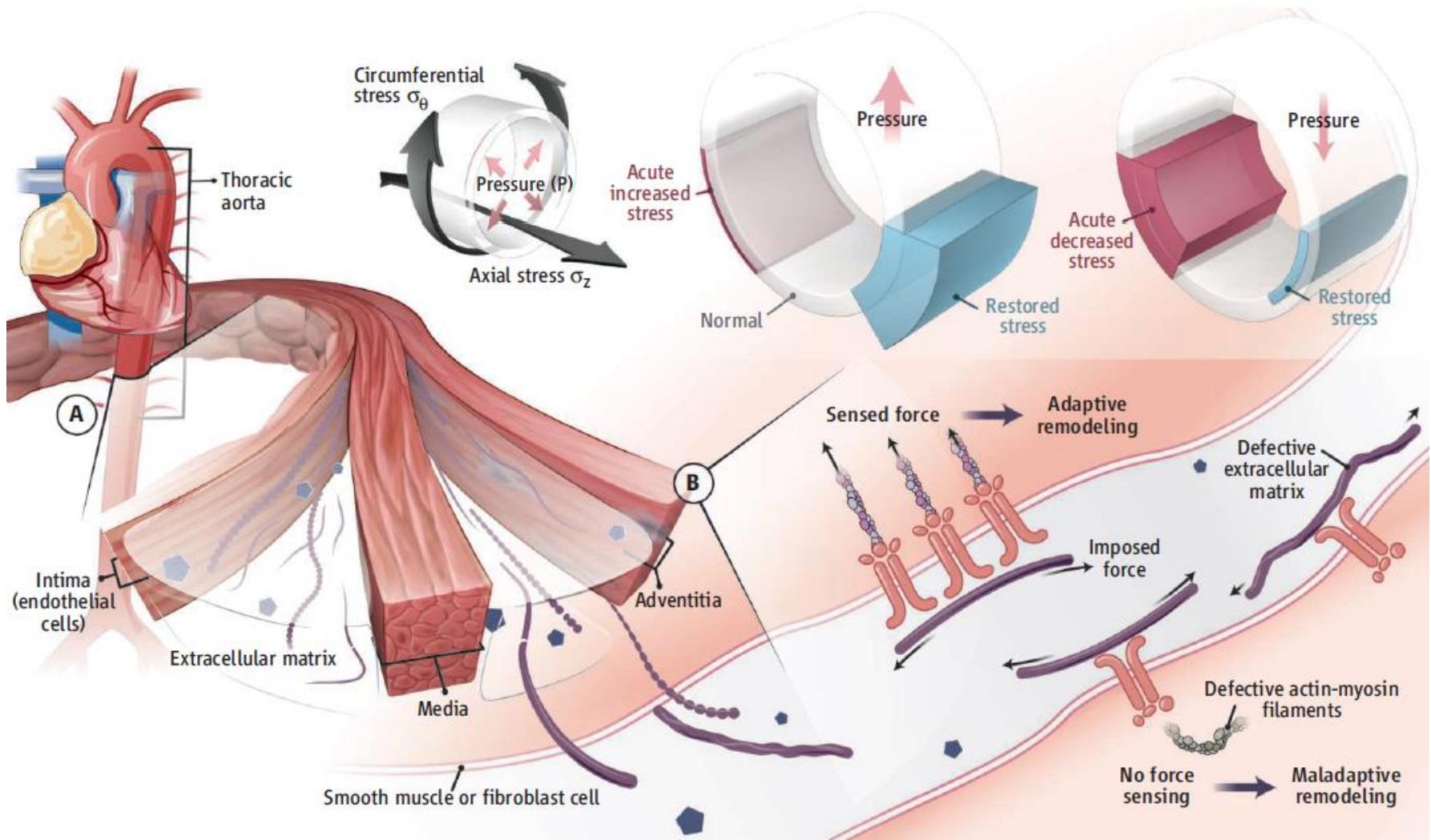


Structural aortic abnormalities: BAV, TAV..
Abnormal connective tissues: Marfan, Ehlers-danlos..



1/100 BAV \Rightarrow 50% ATAA

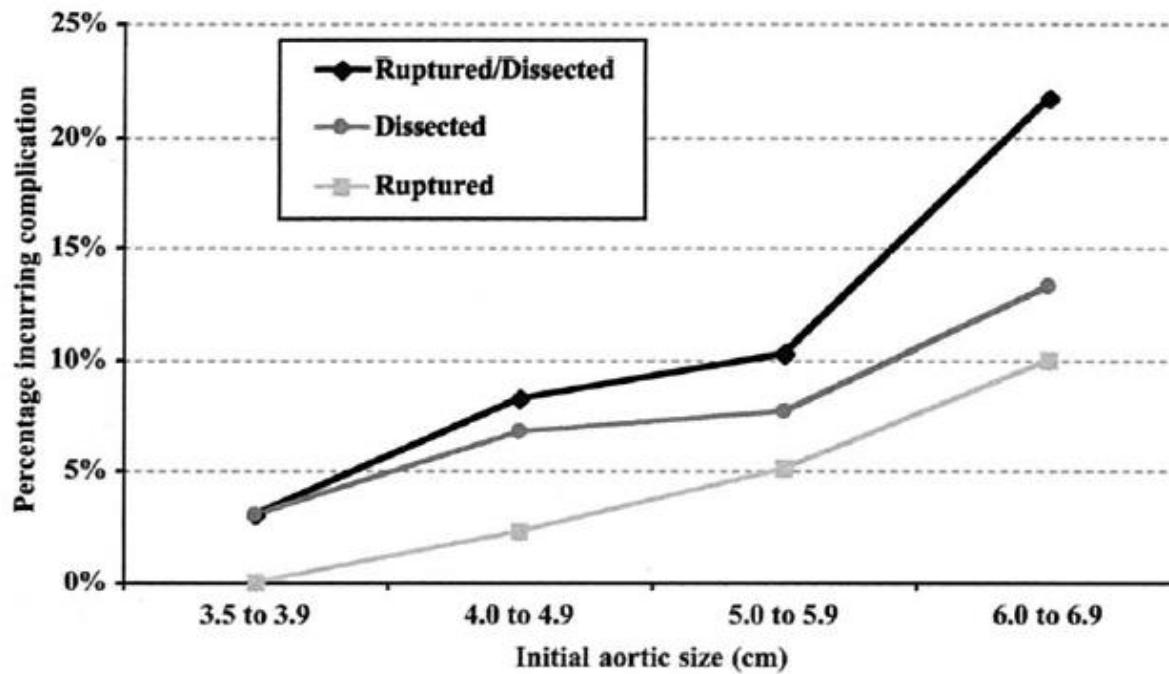
MECHANOBIOLOGICAL PROCESS



J. Humphrey et al. Dysfunctional Mechanosensing in Aneurysms. Science 344, 477 (2014)

Risk management commonly based on maximal diameter

- Davies, 2002
- Observational study in 721 patients



Davies et al, Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size, Annals of Thoracic Surg, 2002



Issue of rupture risk management

- The International Registry of Acute Aortic Dissection (IRAD): among 591 type A aortic dissection, 59% had a diameter <5.5 cm (Pape, 2007)

5.5 cm

Possible
complication

Possible
stability

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

CONTRIBUTION OF BIOMECHANICS

Fundamental knowledge

Interest for the surgeon

ATAA behaviour &
Properties

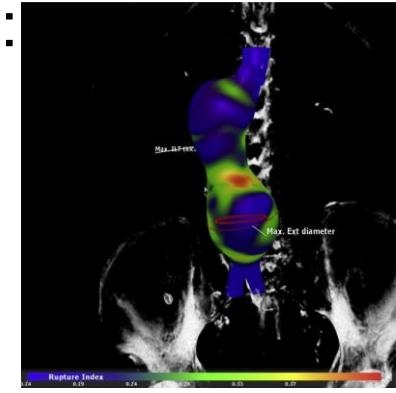
Risk assessment of
complication

- **Fillinger, 2003:** Rupture risk over time. AAA wall stress distribution was computationally determined *in vivo* with CT data, three-dimensional computer modeling, FEA, and blood pressure during observation

M. F. Fillinger, S. P. Marra, M. L. Raghavan, F. E. Kennedy. *Prediction of rupture risk in abdominal aortic aneurysm during observation: Wall stress versus diameter.* Journal of Vascular Surgery, 2003.

CONTRIBUTION OF BIOMECHANICS

- AAA (**Vascops®, Gasser, 2014**) diagnosis system:
Centerline-based maximum diameter, PWS, and
PWRI calculated using FE models (**Erhart, 2015**)
- **In vivo research on ATAA:** Biomechanics
associated with imaging is expected to constitute a
tool for risk assessment (Doyle & Norman 2015,
Martufi, 2016, Vorp 2013, Pasta 2013)
- **Trabelsi et al, 2015.**



Gasser, *A Novel Strategy to Translate the Biomechanical Rupture Risk of Abdominal Aortic Aneurysms to their Equivalent Diameter Risk: Method and Retrospective Validation*, EJVES, 2014

Erhart, *Prediction of Rupture Sites in Abdominal Aortic Aneurysms After Finite Element Analysis*, EJVES, 2015

Stone, *Prediction of Progression of Coronary Artery Disease and Clinical Outcomes Using Vascular Profiling of Endothelial Shear Stress and Arterial Plaque Characteristics The PREDICTION Study*, Circulation, 2012

Doyle and Norman, *Computational Biomechanics in Thoracic Aortic Dissection: Today's Approaches and Tomorrow's Opportunities*, Ann Biomed Engineering, 2015

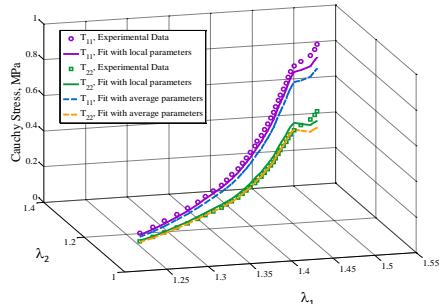
Martufi et al, *Is There a Role for Biomechanical Engineering in Helping to Elucidate the Risk Profile of the Thoracic Aorta?*, Ann Thor Surg, 2016.

O. Trabelsi, A. Duprey, J-P Favre, S. Avril. *Predictive models with patient specific material properties for the biomechanical behavior of ascending thoracic aneurysms*Annals of Biomedical Engineering. 2015.

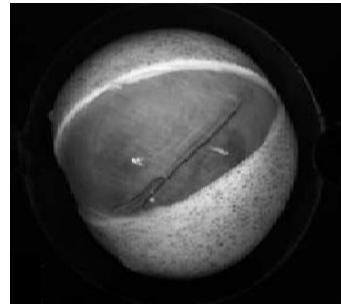
CONTRIBUTION OF BIOMECHANICS

Experimental study

Mechanical properties

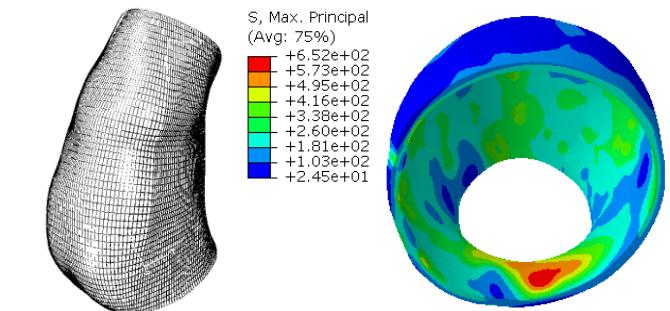


Rupture Stress

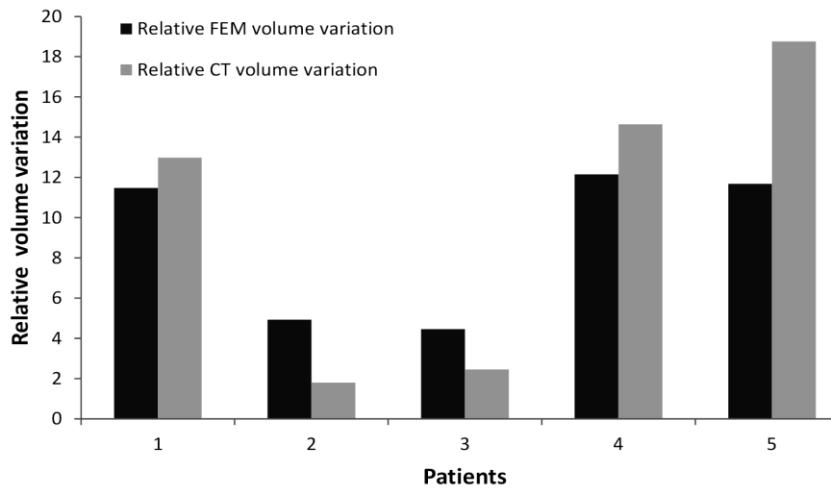


Computational study

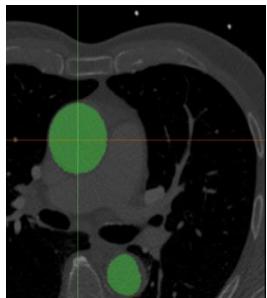
FEM Stress



Comparison between actual and predicted relative volumes variation of the aneurysm



CONTRIBUTION OF BIOMECHANICS

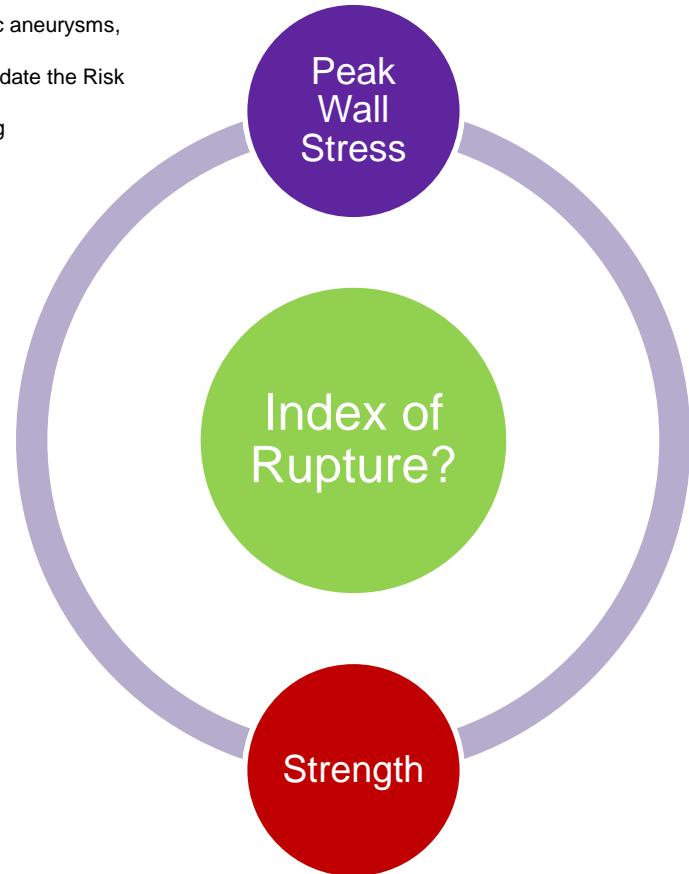
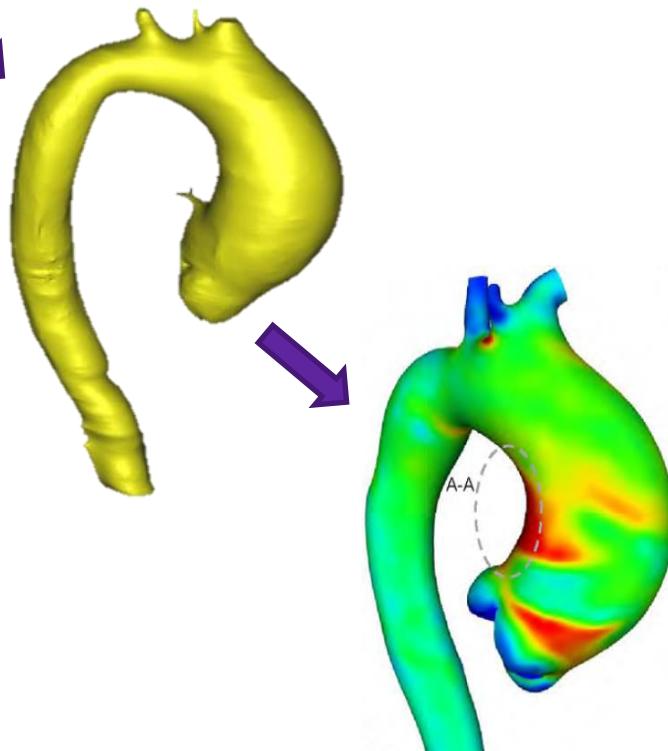


O. Trabelsi, et al, Patient specific stress and rupture analysis of ascending thoracic aneurysms, J. Biomech. (2015).

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



GENERAL PROTOCOL

2014
↑
100 Patients with ATAA
↓
2020

Preoperative dynamic imaging

Dynamic CT Scanner

4D MRI

Collection of intraoperative aortic segment

Mechanical inflation tests

Histological Analysis

GENERAL PROTOCOL

2014
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2016

31 Patients with ATAA

Preoperative dynamic imaging

Collection of intraoperative aortic segment

Dynamic CT Scanner

4D MRI

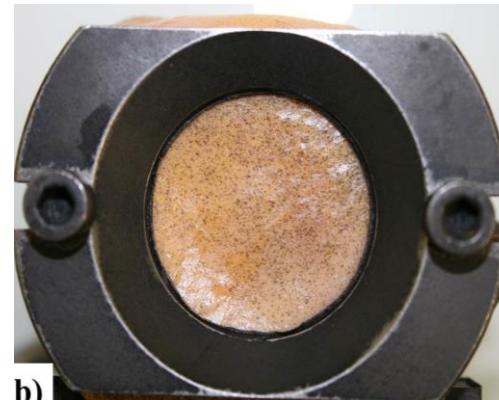
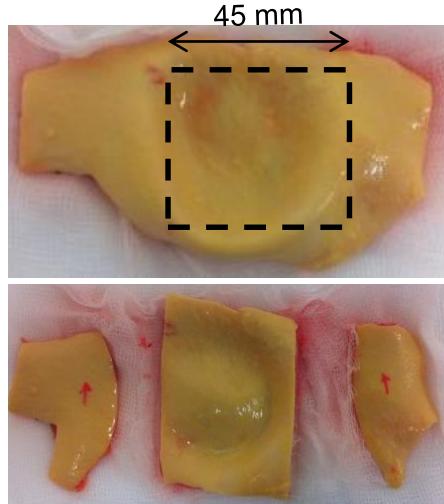
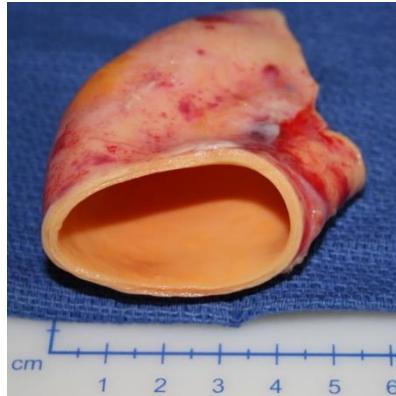
Mechanical inflation tests

Histological Analysis

EXPERIMENTAL STUDY

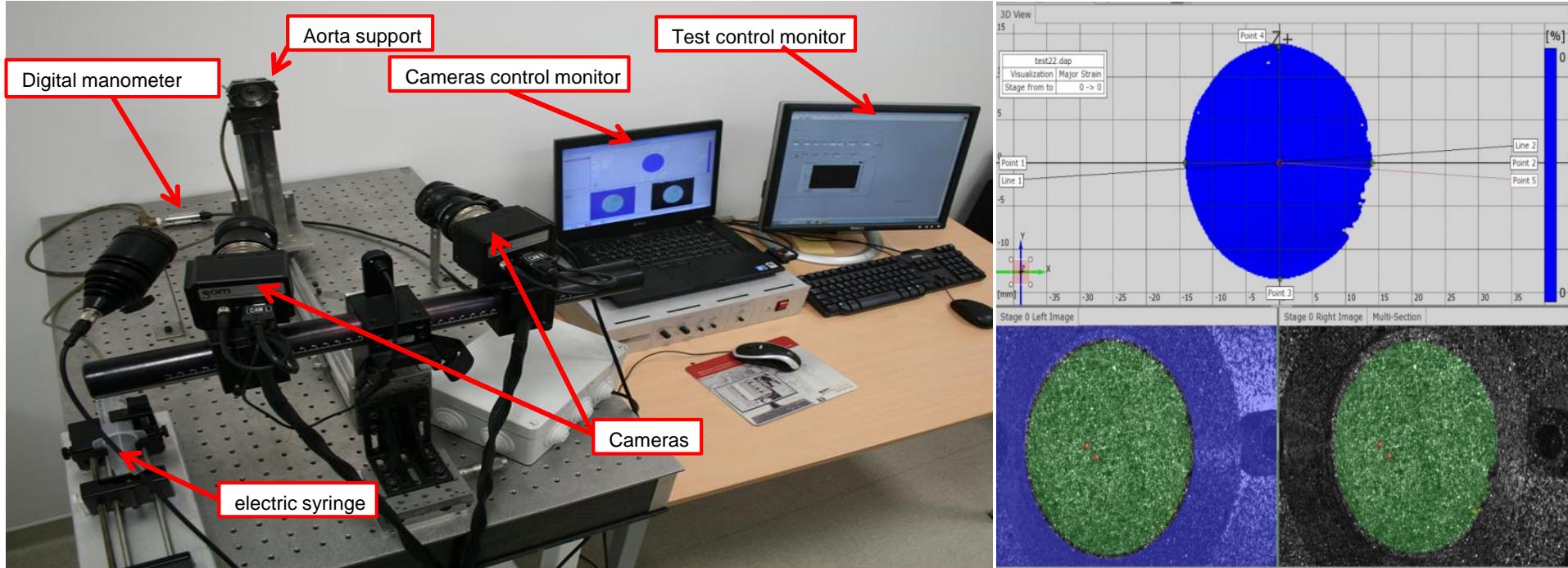
Bulge Inflation Tests: faithful physiological aortic deformation, characterize elastic and failure properties of ATAA specimens

- ✓ Mohan and Melvin, 1983: Postmortem descending thoracic aorta
- ✓ Test developed at Center of Biomedical and Healthcare Engineering (CIS), Ecole des Mines, in a collaboration with the University Hospital CHU, Saint Etienne (France)
- ✓ Patients who underwent surgical replacement of their ATAA with a synthetic graft.
- ✓ Aorta kept in physiological saline solution at 4 ° C
- ✓ Test performed within 24 hours



Aerosol particles of graphite

EXPERIMENTAL STUDY



Inverse membrane analysis + digital image correlation \Rightarrow stress & strain reconstruction.
 \Rightarrow biaxial failure properties
Rupture stress: highest value of the first principal component of the Cauchy stress reached before rupture

Trabelsi, O., Davis, F.M., Rodriguez-Matas, J.F., Duprey, A., Avril, S. Patient specific stress and rupture analysis of ascending thoracic aneurysms. Journal of Biomechanics. In press, 2015.

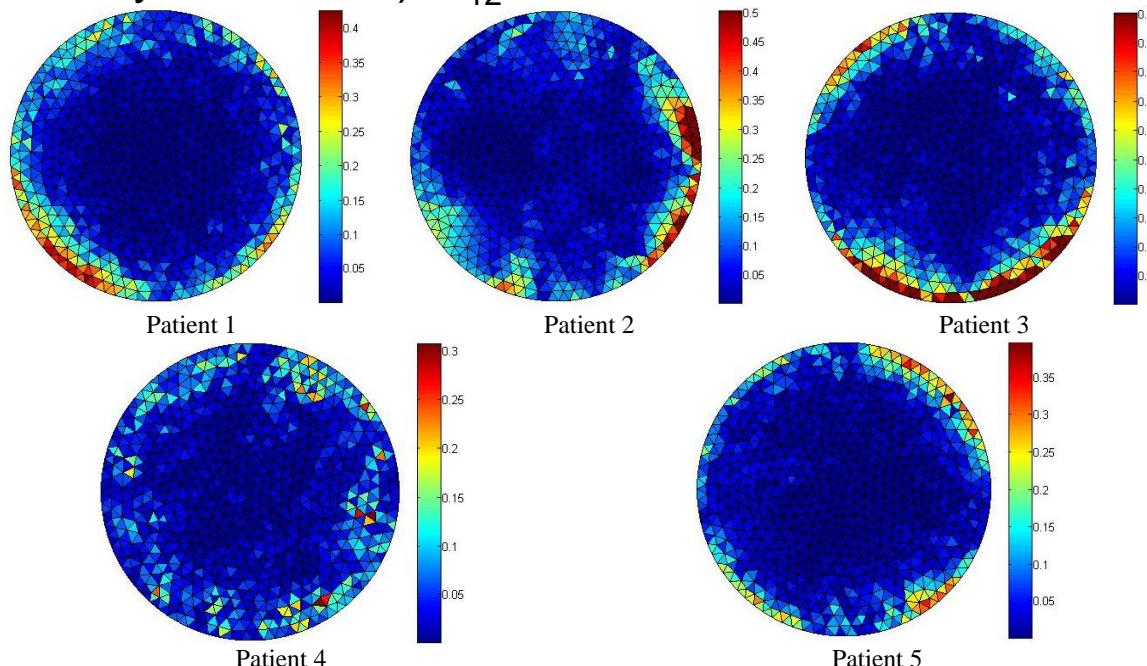


EXPERIMENTAL STUDY

Co-axiality test: stress/strain coaxiality. Isotropy indicator (Zhao et al.*)

$\mathbf{e} = \mathbf{SC} - \mathbf{CS}$, \mathbf{C} : Right Cauchy–Green deformation tensor
 \mathbf{S} : Piola-Kirchhoff stress

$e_{11}=e_{22}=0$ (symmetry of \mathbf{S} and \mathbf{C}), e_{12} near zero \Rightarrow material behavior near isotropic.



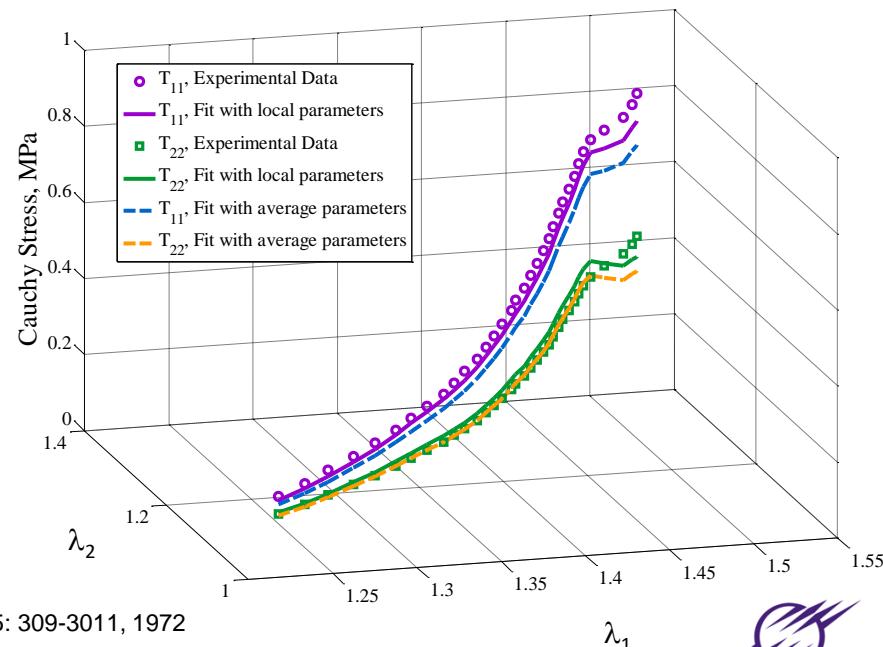
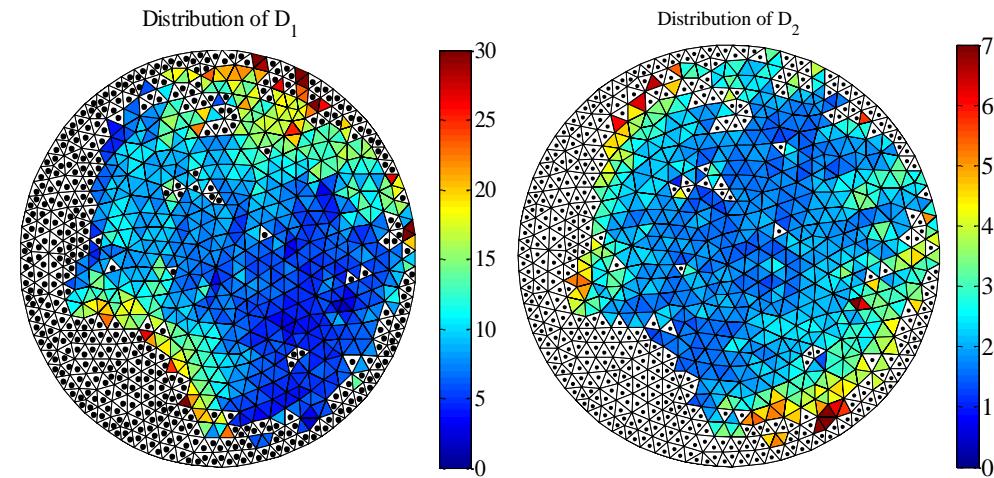
* X. Zhao, X. Chen, J. Lu. Pointwise Identification of Elastic Properties in Nonlinear Hyperelastic Membranes-PartII: Experimental Validation. Journal of Applied Mechanics. Vol 76: 061014-1/8. 2009

EXPERIMENTAL STUDY

Isotropic Model for the aneurysm: Demiray*'s model to describe the elastic response of the ATAA

$$W = \kappa(J - 1)^2 + D_1(e^{D_2(\bar{I}_1 - 3)} - 1)$$

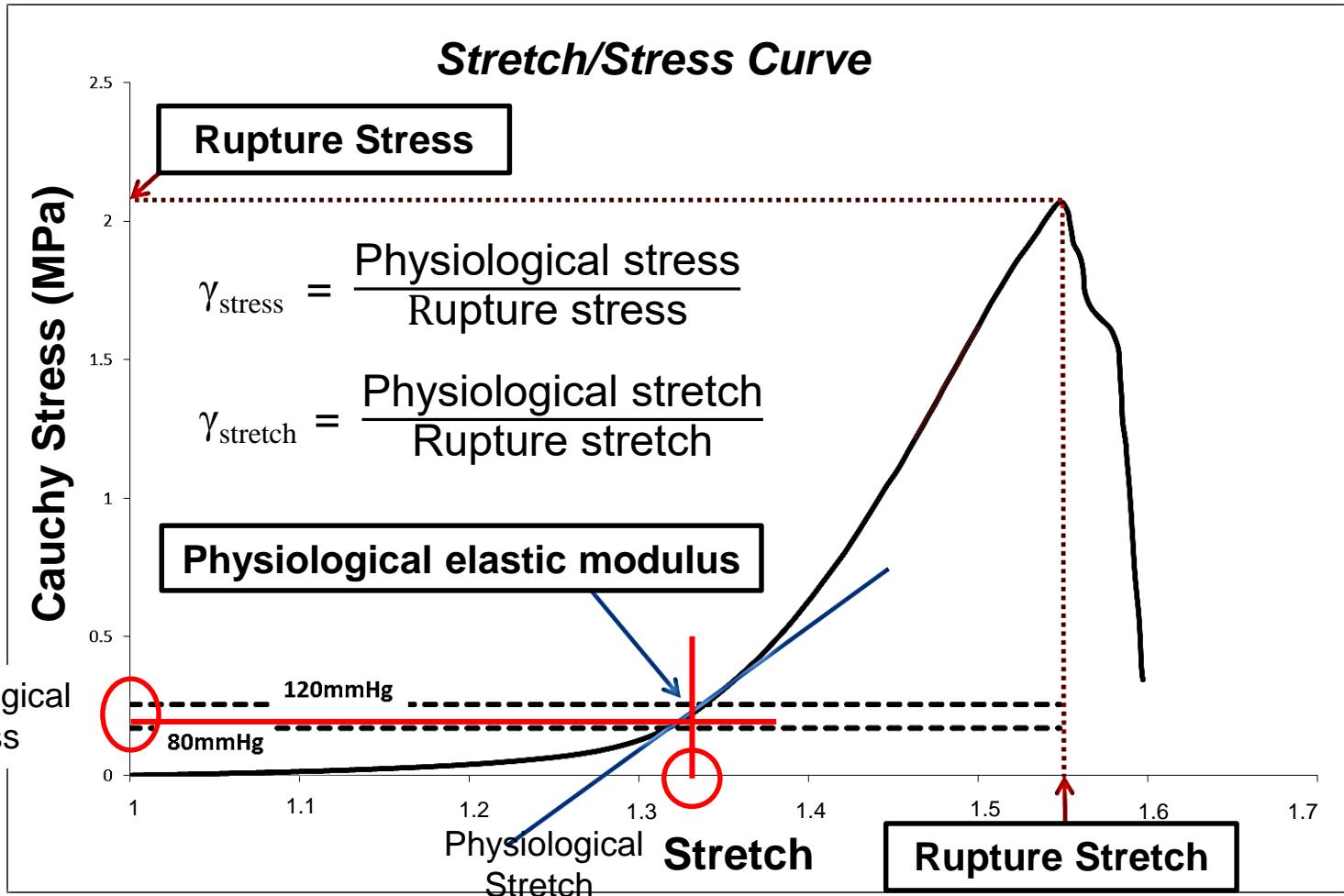
D_1, D_2 : Initial stiffness and strain stiffening response of the ATAA. κ : volumetric modulus. Incompressible response $\Rightarrow \kappa$ fixed at 1 GPa



* H. Demiray. A note on the elasticity of soft biological tissues. Journal of biomechanics. Vol 5: 309-3011, 1972

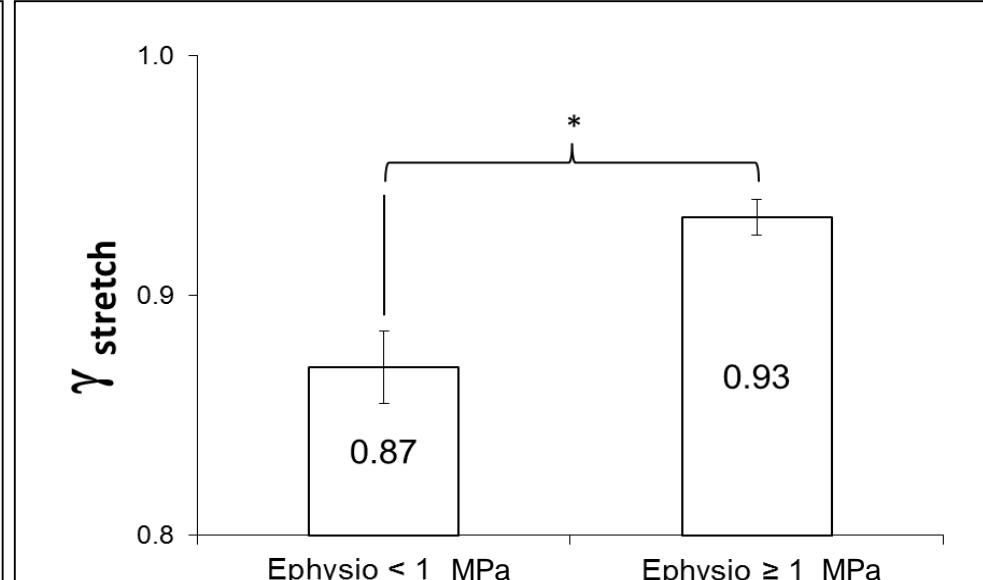
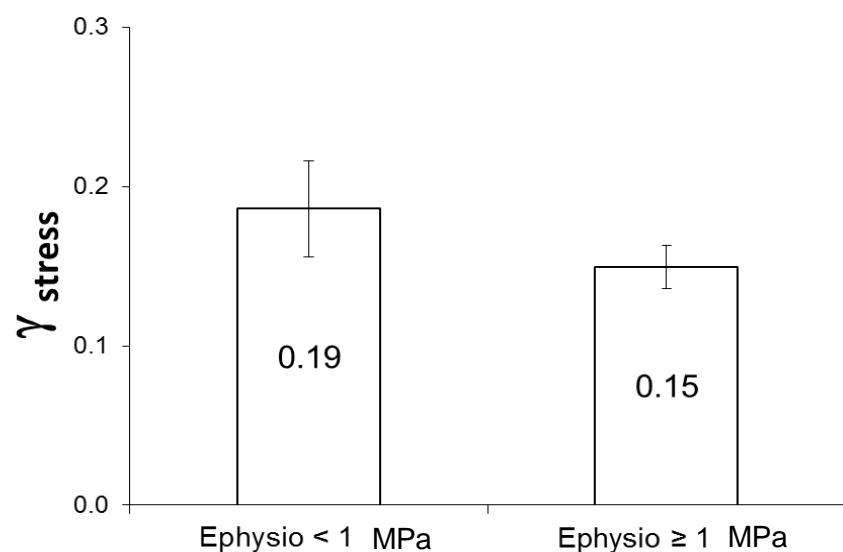
EXPERIMENTAL STUDY

Θ : Angle of rupture respect to blood flow axis, σ_{rup} : Rupture stress, λ_{rup} : Rupture stretch, E_{physio} : Physiological modulus (Laplace's law) for pressures between 80 and 120 mmHg



EXPERIMENTAL STUDY

Potential of E_{physio} to help predicting the risk of rupture

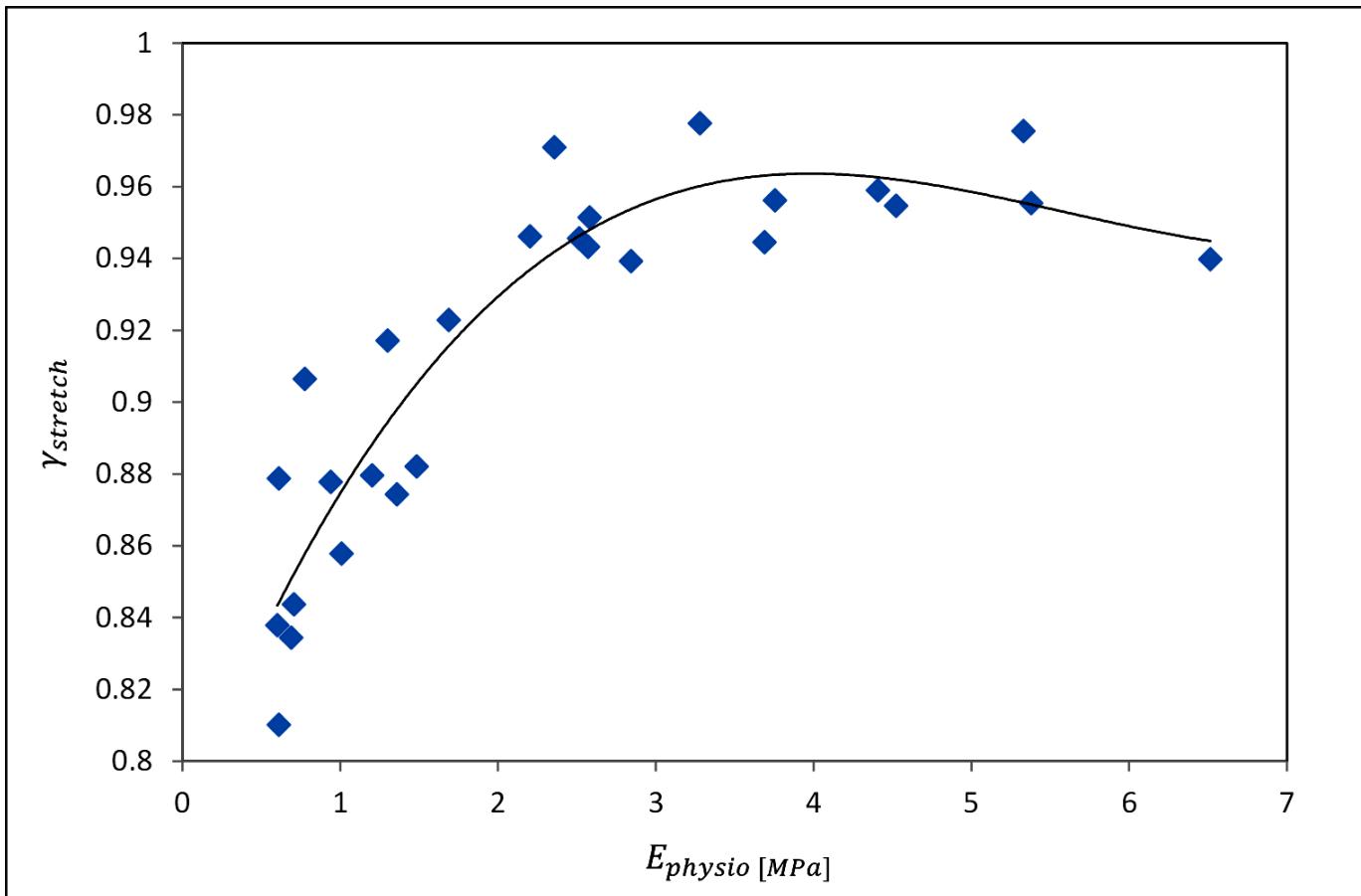


$F \uparrow$ Collagen recruitment \uparrow Tangential rigidity $E_{\text{physio}} \uparrow$

At physio. pressures: not fragmented elastin, small fraction of collagen contributes to the rigidity (relatively low $E < 1 \text{ MPa}$). Elastic fibers are highly disorganized, collagen tends to be recruited soon and will contribute significantly to the rigidity ($E > 1 \text{ MPa}$)

EXPERIMENTAL STUDY

Correlation between γ_{stretch} and E_{physio}



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



EXPERIMENTAL STUDY

- Correlation of stress and strain at rupture with age corroborated by other studies.
- Rupture: when stretching of the wall is greater than its extensibility.

2 ways to define rupture

- PWS
- γ_{stretch} correlated with E_{physio} (E_{physio} can be obtained from preoperative dynamic imaging)
 - ⇒ More the aneurysm is compliant (extensible) least risk of rupture it has because it can more easily withstand volume variation

GENERAL PROTOCOL

2014
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2016

31 Patient with ATAA

Preoperative dynamic imaging

Collection of intraoperative aortic segment

Dynamic CT Scanner

4D MRI

Mechanical inflation tests

Histological Analysis



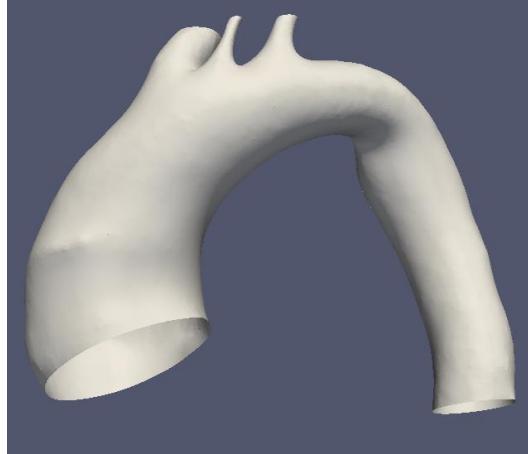
Available data for each patient

- Patient specific dynamic images (CT scans)
Segmentation of images to obtain STL files
- Patient specific blood pressure (Systole & diastole)

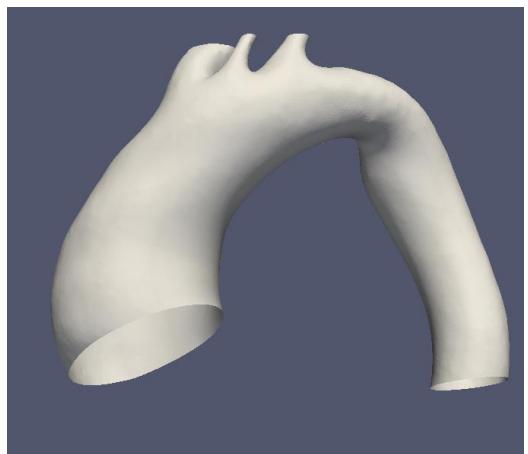




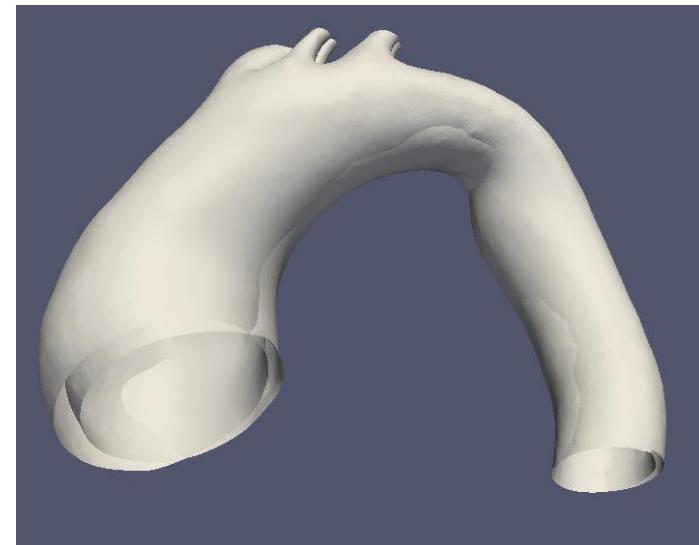
Segmentation



Diastole

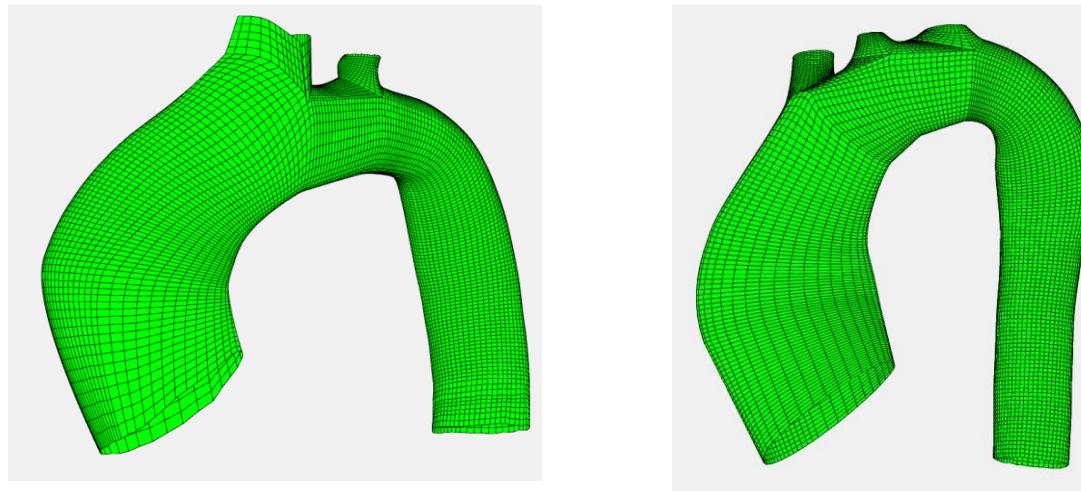
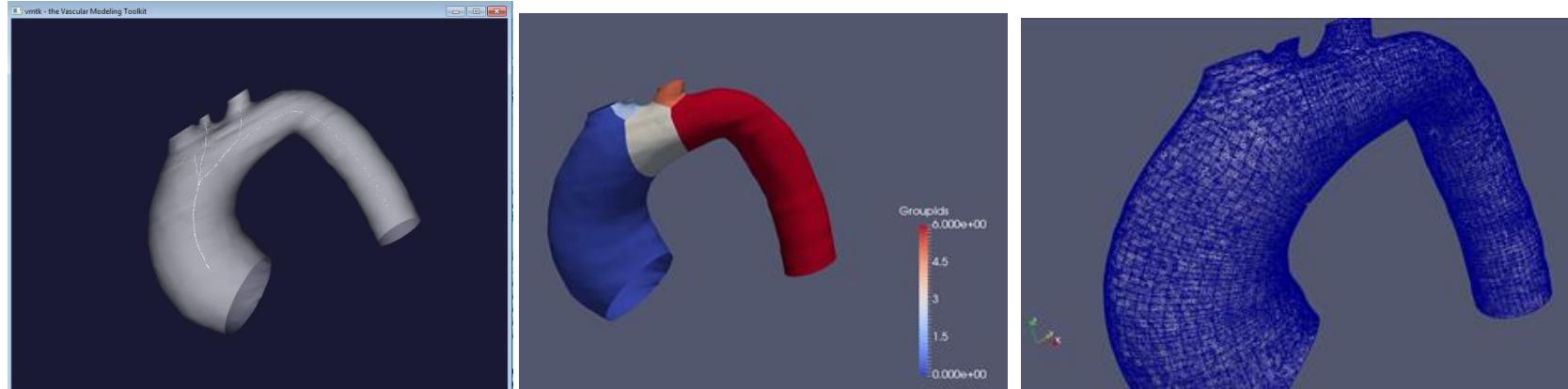


Systole

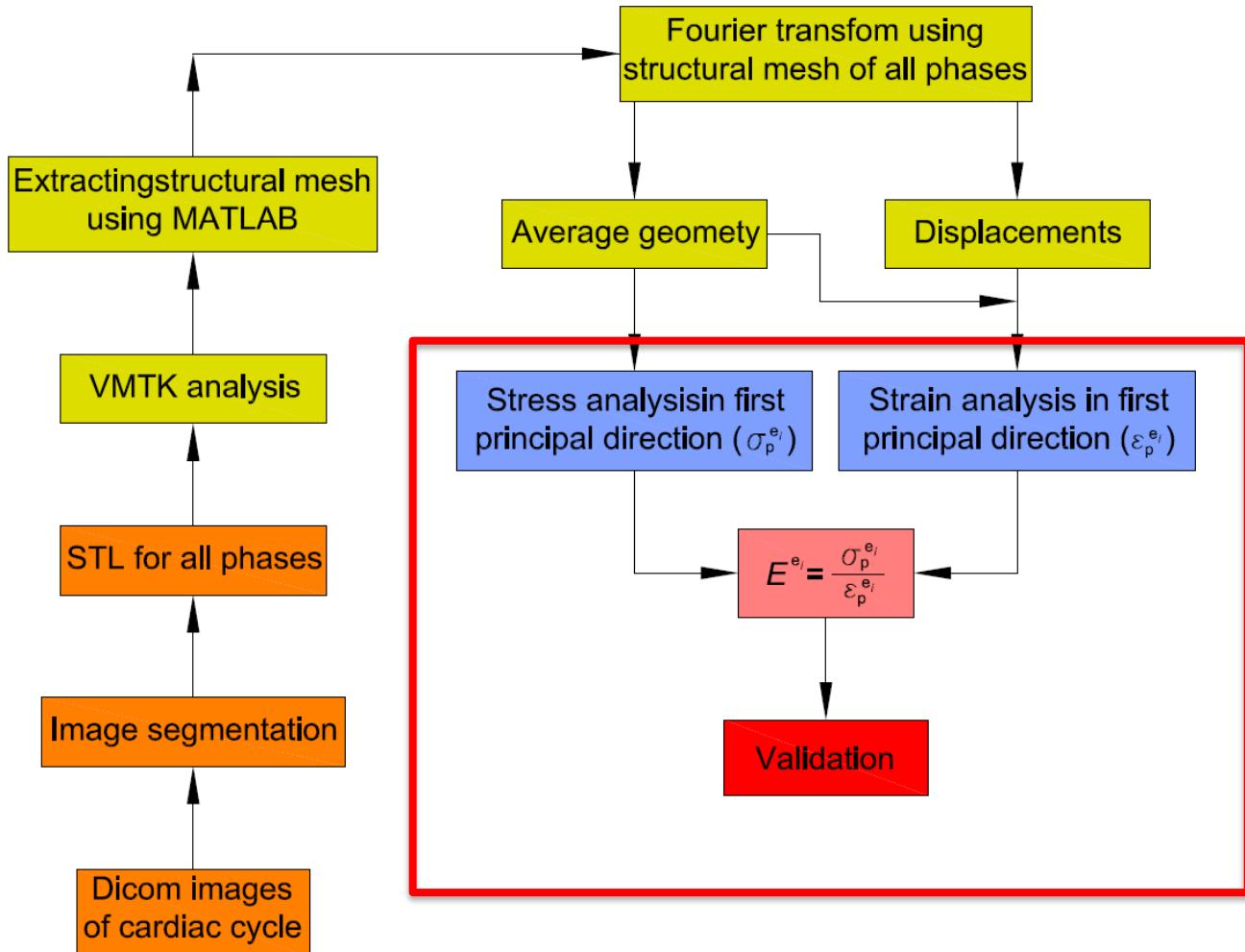




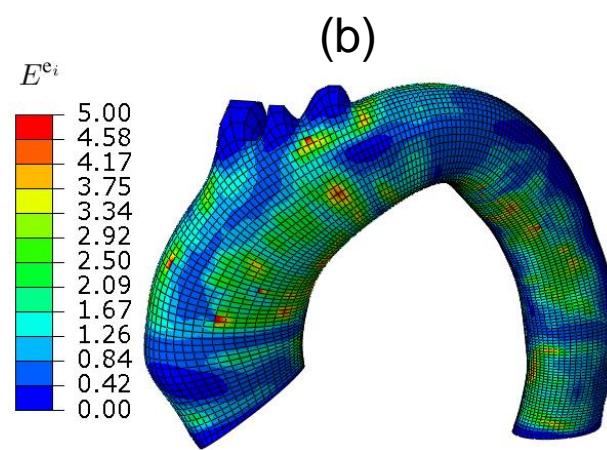
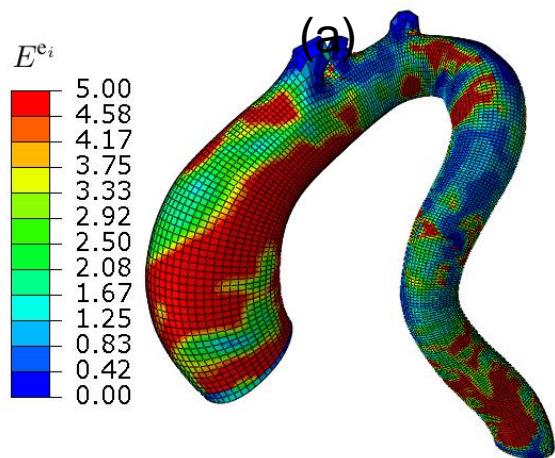
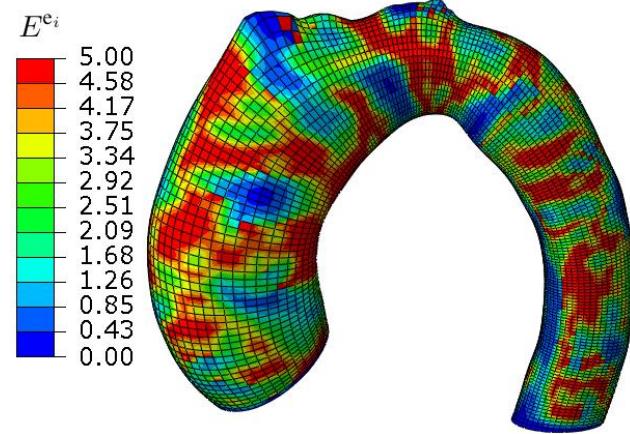
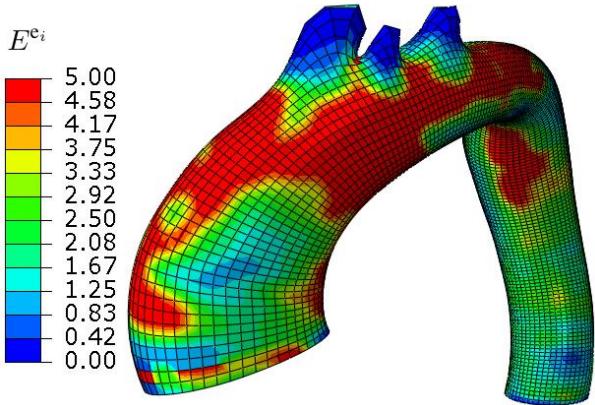
Mesh morphing



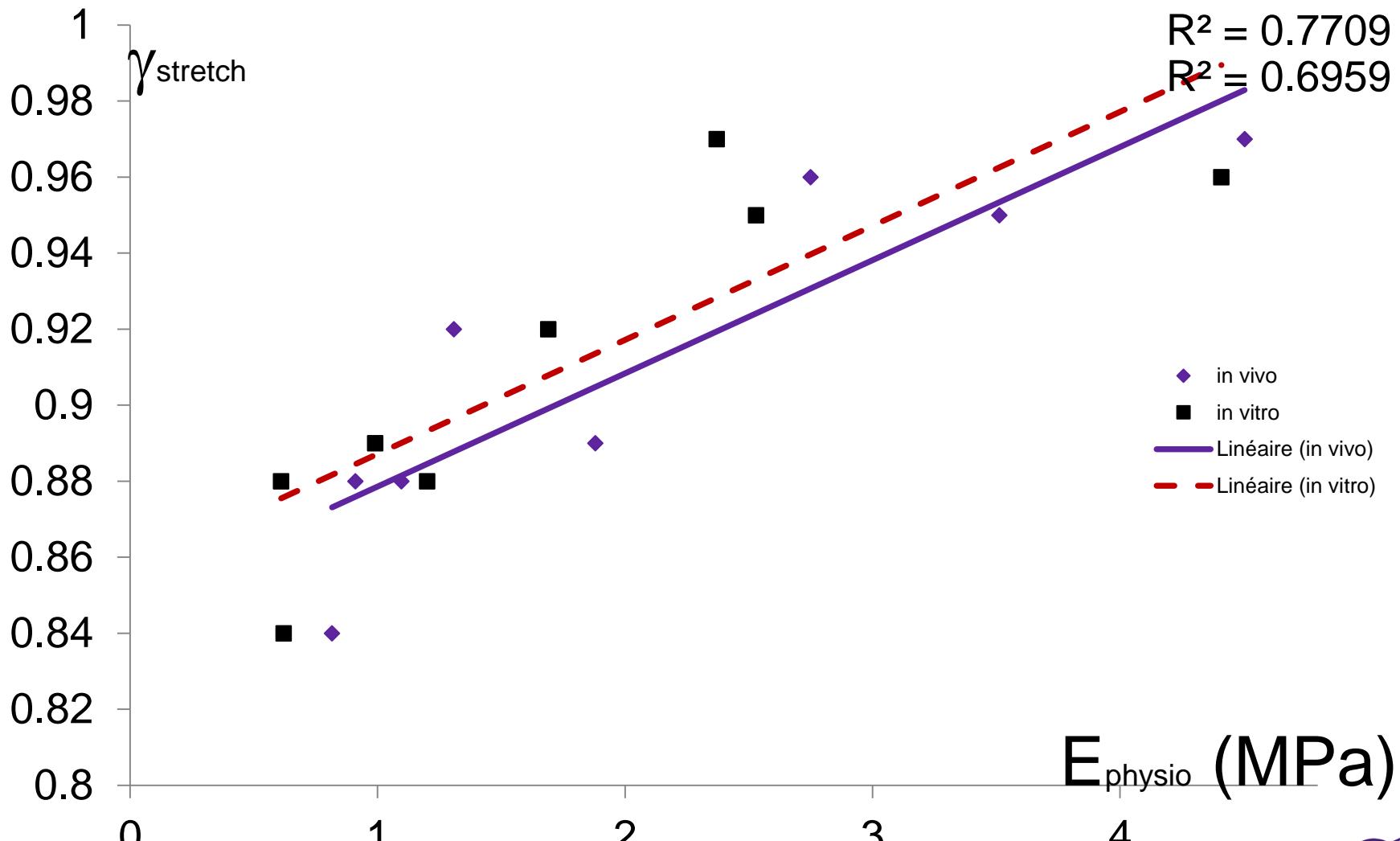
Inverse approach



Elastic modulus reconstruction



Correlation between γ_{stretch} and E_{physio}





CONCLUSION

- A rupture risk criterion based on the aortic stiffness is proposed
- A step closer to assessing preoperative risk?

GENERAL PROTOCOL

2014
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2016

31 Patient with ATAA

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Dynamic CT Scanner

4D MRI

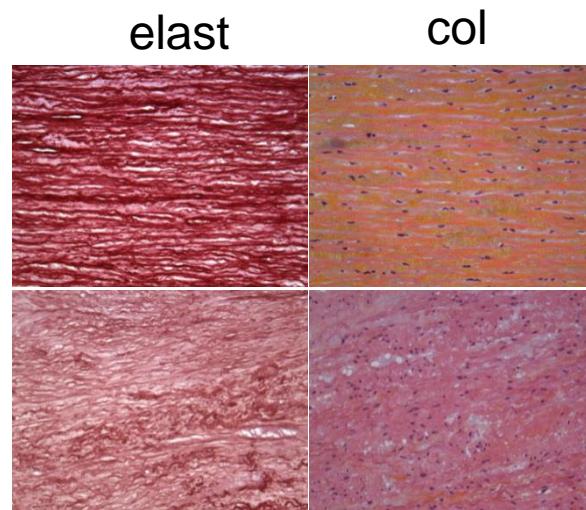
Mechanical inflation tests

Histological Analysis

Histological interpretation

- ATAA enlargement is a consequence of elastin damage
- More and more collagen tends to be recruited in the physiological range

Patient with
largest γ_{stretch}



Patient with
smallest γ_{stretch}

M.R. Hill et al., J. Biomech. 45 (2012) 762–771

GENERAL PROTOCOL

2014
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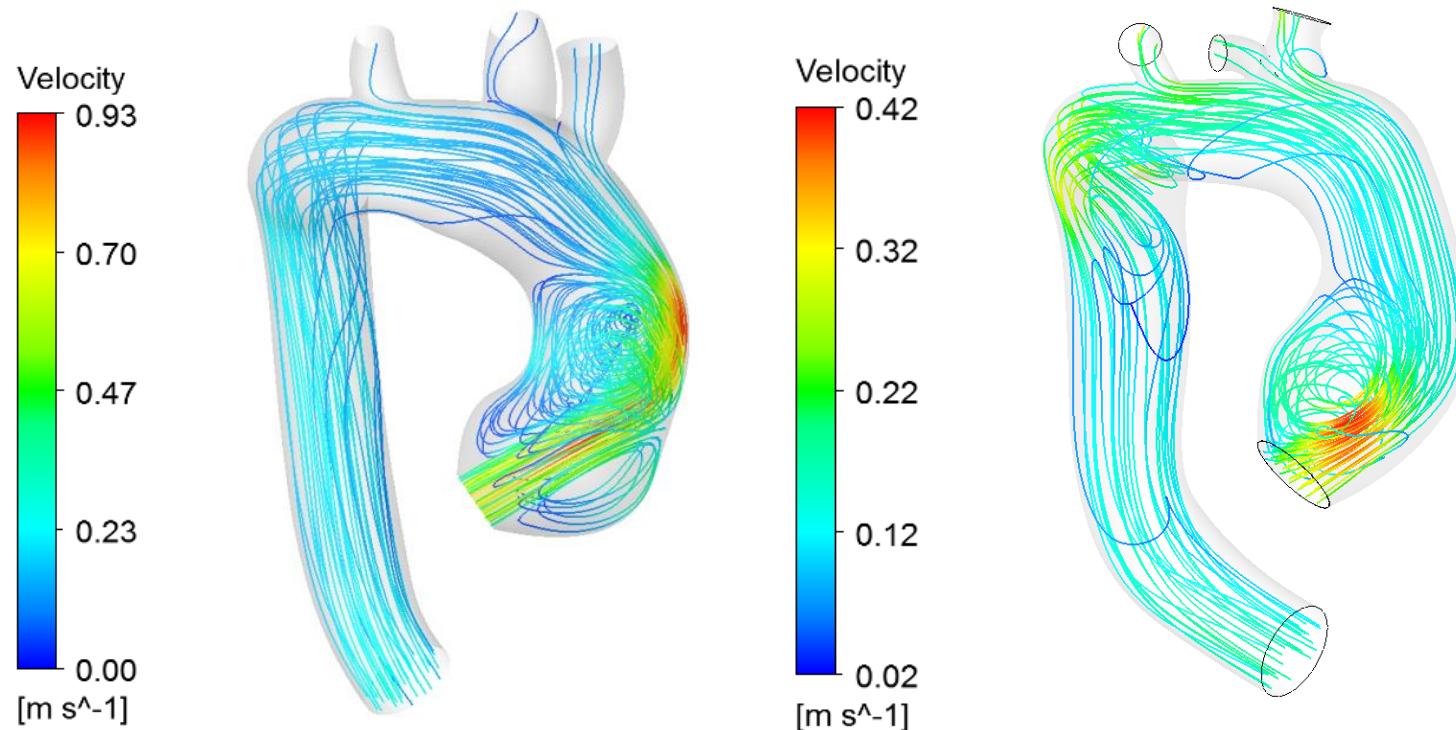
4D MRI

Mechanical inflation tests

Histological Analysis



Computer fluid dynamics





Future work

- Extend the analysis to other patients
- Define a threshold for the new risk of rupture
- Predict the long-term evolution of this criterion for small aneurysms using mechanobiological models

Acknowledgements

- Olfa Trabelsi
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ERC-2014-CoG BIOLOCHANICS



European Research Council



EXPERIMENTAL STUDY

Main studies list of uniaxial tensile tests on human ascending aorta. (CIRC: circumferential; LONG: longitudinal)

Autor	Year	Subjects Nbr	Test Nbr	Conclusions
Okamoto	2002	54 ATAA	NC	Higher resistance in young patients
Vorp	2003	26 ATAA/10 Healthy aorta post-mortem	40/14	No anisotropy / lower resistance for ATAA / No correlation between diameter and resistance
Iliopoulos	2009	12 ATAA	279	Anisotropy / LONG anterior wall most brittle / No correlation between rupture stress, ATAA diameter and age
Iliopoulos	2009	26 ATAA/15 Healthy aorta post-mortem	490/212	Decrease of elastin, no collagen/ lower rupture deformation/Higher maximal elastic modulus/ Equal rupture stress
Duprey	2010	12 ATAA	108	Maximum elastic modulus and physiological module higher in CIRC / CIRC BAV stiffer than TAV
Weisbecker	2012	14 Healthy aorta post-mortem	NC	predominant involvement of collagen fibers in tissue degradation
Garcia-Herrera	2012	23 Healthy aorta post-mortem/12ATAABAV/14ATA TAV	NC	Anisotropy for healthy aorta and BAV, not TAV / Significant reduction of rupture stress in healthy aortas depending on age
Sokolis	2012	8 ATAA TAV	192	Anisotropy / Regional variations between anterior, posterior, right and left lateral wall
Weisbecker	2013	17 Healthy aorta post-mortem	NC	Anisotropy in untreated tissue with collagenase and elastase
Pham	2013	55 ATAA	NC	Anisotropy/BAV more resistant than TAV
Martin	2013	50 ATAA	NC	Finding an Index of rupture related to diameter
Pichamuthu	2013	38 ATAA (23 BAV/15TAV)	163	Anisotropy/BAV more resistant than TAV
Forsell	2014	24 ATAA (13 BAV/11TAV)	27	BAV 2 times more resistant than TAV

EXPERIMENTAL STUDY

Main studies list of biaxial tests on human ascending aorta.

Autor	Year	Subjects Nbr	Conclusions
Peterson	1999	6 ATAA	Linear stress-strain curve for a deformation less than 20% and nonlinear beyond. No anisotropy except for one patient
Okamoto	2002	64 ATAA	Increased stress in the two directions with age
Fukui	2005	18 ATAA	Anisotropy by equibixiql constraint/ No correlation with the diameter
Choudhury	2009	5 ATAA TAV/6 ATAA BAV/5 Healthy aorta post-mortem	Lower elastic modulus at low deformation for AATA TAV than for ATAA BAV and healthy aorta / Regional variation between the front, later, large and small curvature quadrants
Matsumoto	2009	16 patients (ATAA, dissection..)/5 aorta without aneurysms	Higher initial elastic modulus for ATAA. No anisotropy
Haskett	2010	31 Healthy aorta post-mortem	Decreased compliance with age, no directional difference of the deformation / Stiffness increases with age
Azadani	2013	18 ATAA/19 Healthy aorta post-mortem	Physiological stress and stiffness significantly higher for ATAA than healthy aortas /Correlation between rigidity and ATAA diameter, but not with age / No correlation between physiological stress and ATAA diameter
Pham	2013	55 ATAA (20 TAV/20 BAV/15 bovine arches	Nonlinear and anisotropic response for TAV and bovine arches/ Linear and isotropic response for BAV / BAV stiffer in the longitudinal direction and at low voltage