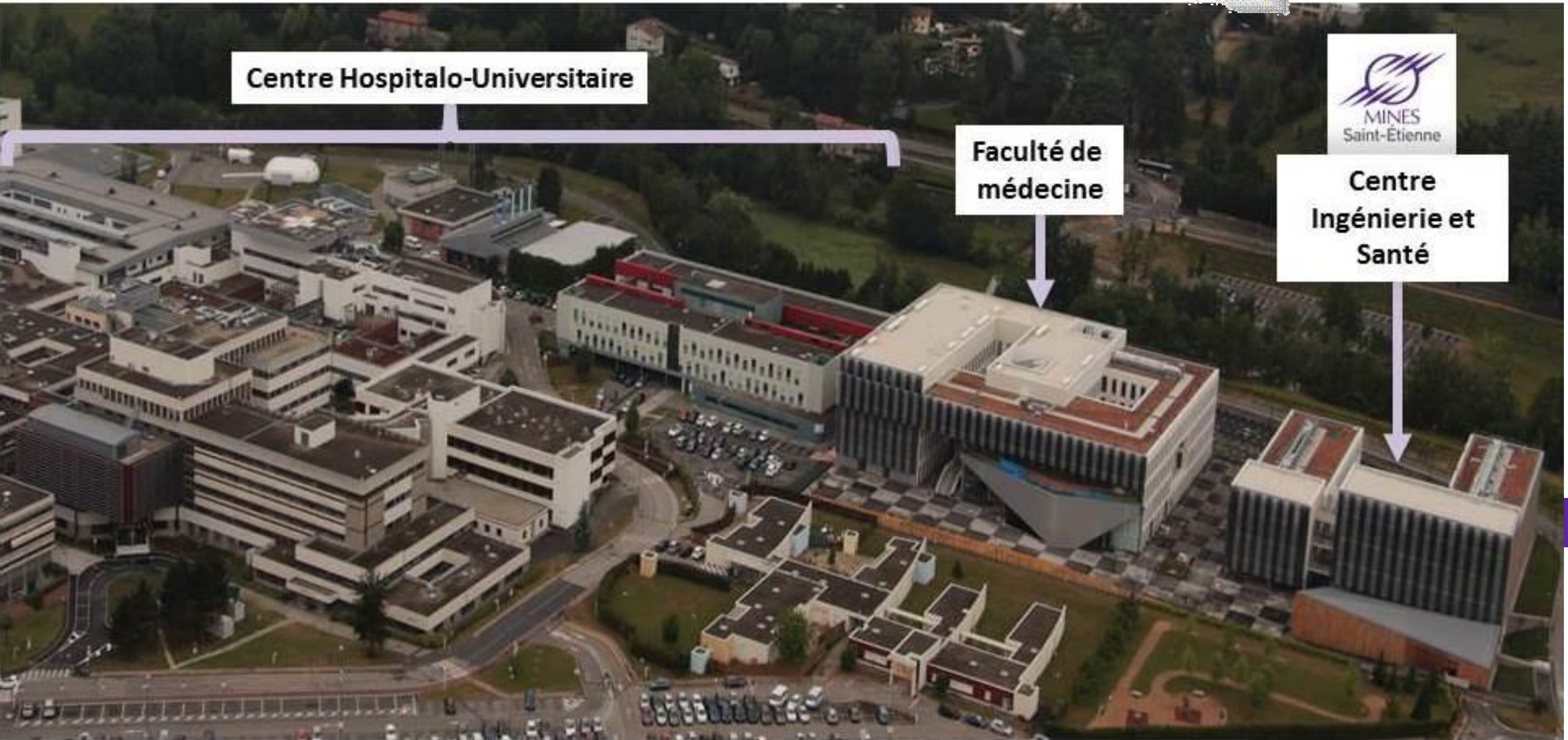
Cardiovascular continuum mechanics and medical applications

Prof. Stéphane AVRIL

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



Aortic aneurysms – state of the art in continuum mechanics

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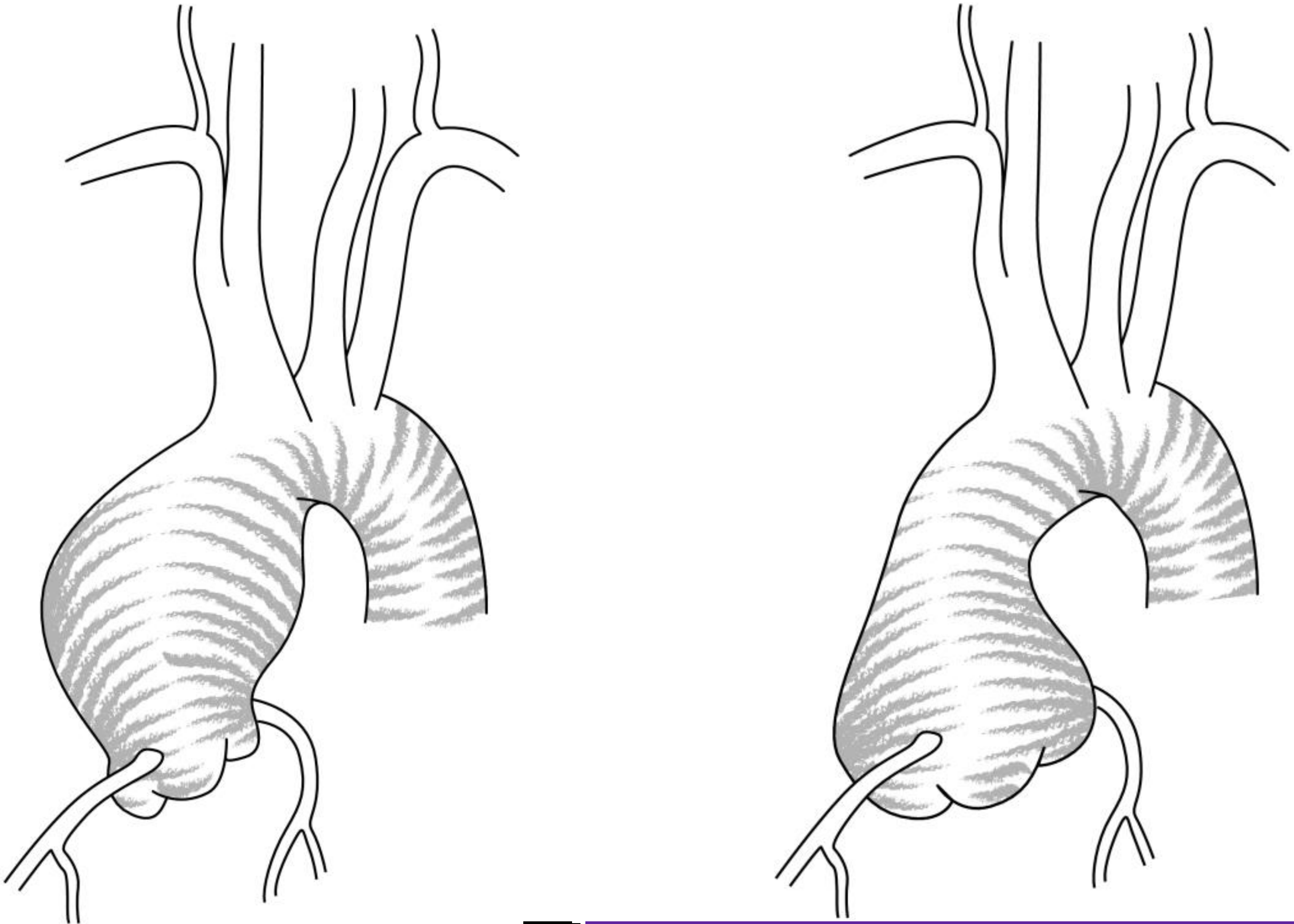
Aortic root dilatations and ascending thoracic aortic aneurysms (ATAA)



Risks: Aortic dissections

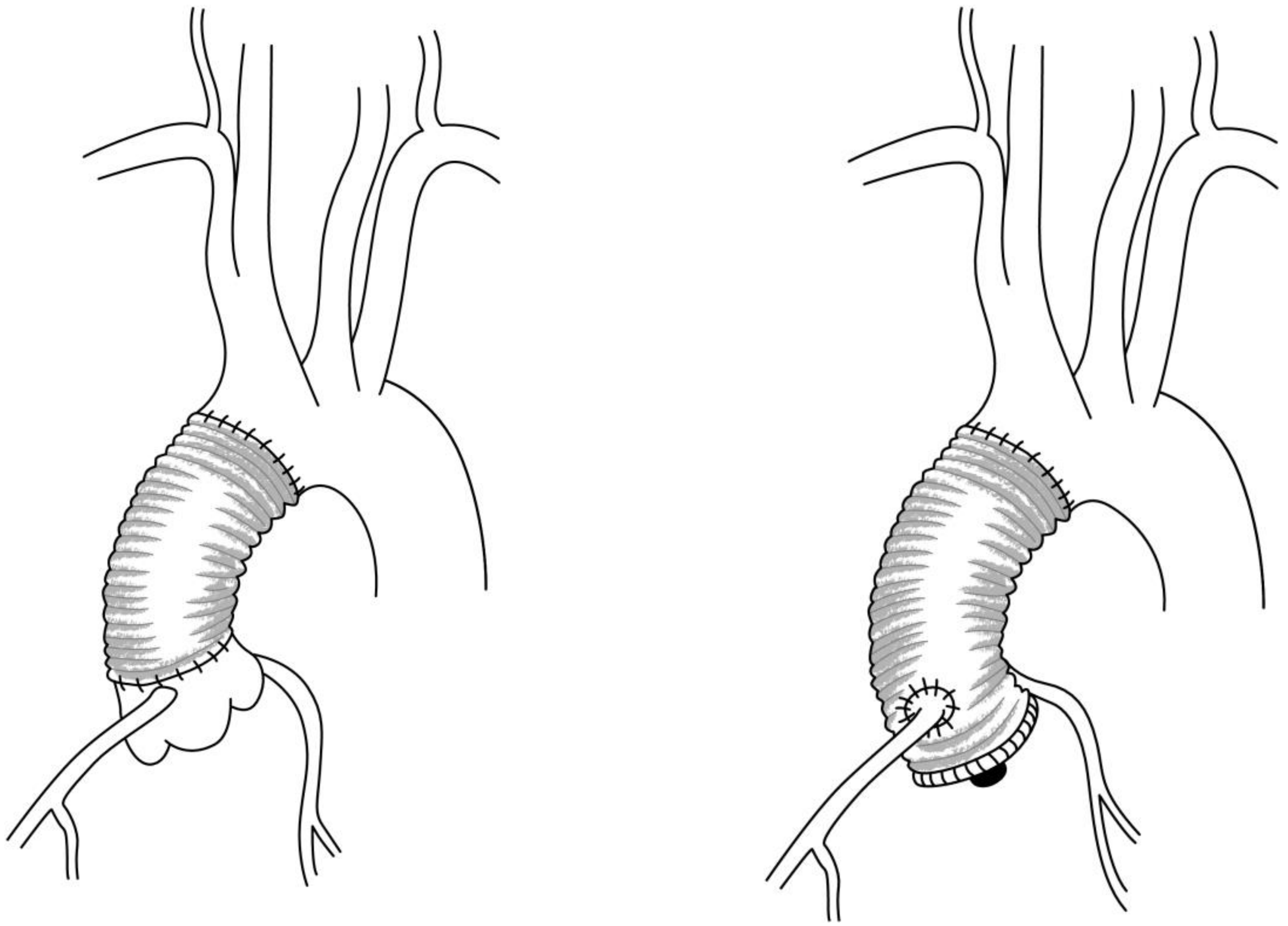
Surgical elective repair of ATAA

- Indications:
  - Aortic insufficiency requiring surgical correction
  - Size ⩾55 mm
  - Size ⩾50 mm in patients with Marfan syndrome or bicuspid valves
  - Growth rate ⩾1 cm/year

- More and more aneurysms are detected at an early stage (incidence >8% for males >65 years old).

- >90000 interventions per year in Europe and USA

Surgical techniques for ATAA repair



Context

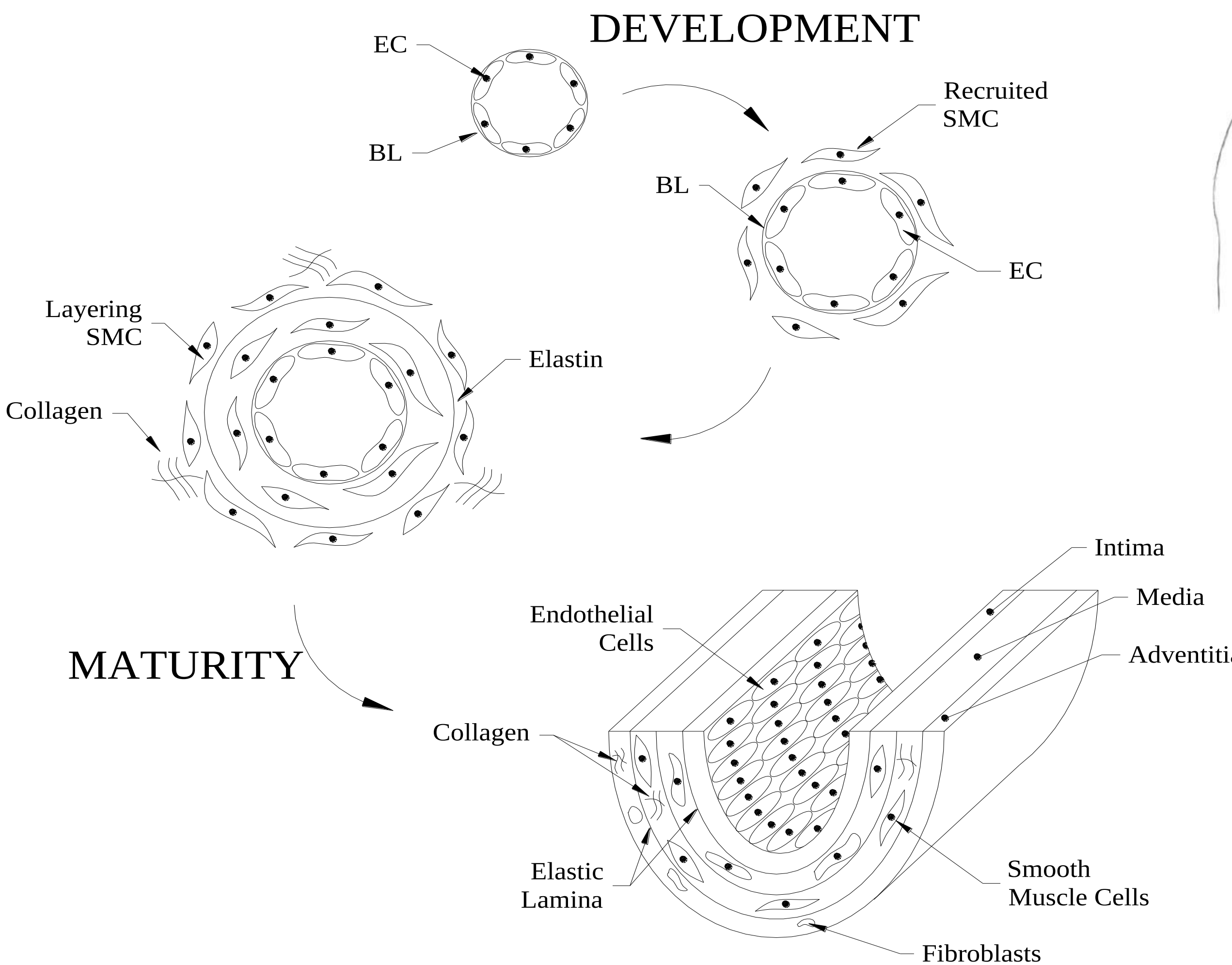
- **<u>BUT</u>:**
  - 25% ATAA < 5.5cm rupture : 15000 deaths** !
  - 60% of ATAA > 5.5 cm never experience rupture!
  - 9% mortality and morbidity after ATAA repair

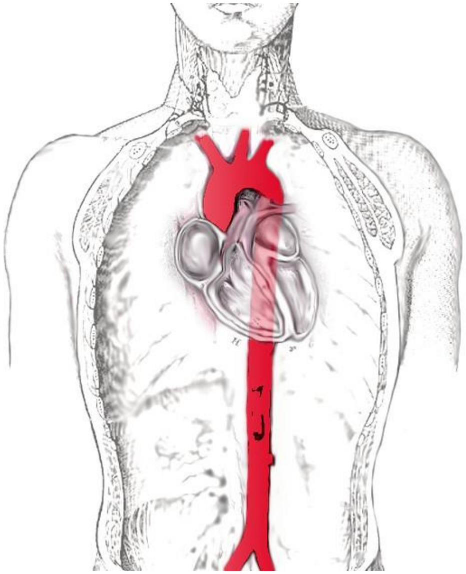
- **In summary: inappropriate decisions and misprogramed surgical interventions have major consequences!!**

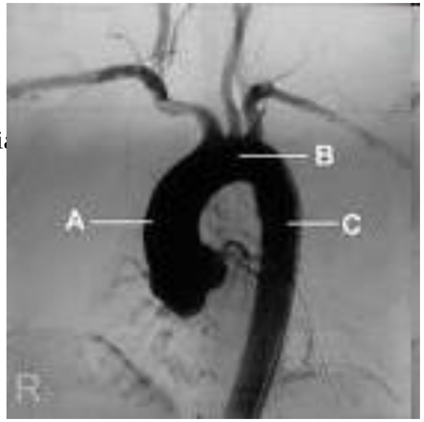
- **Need insightful assistance from biomechanics ☺☺☺**

** 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

Schematic representation of aortic structure







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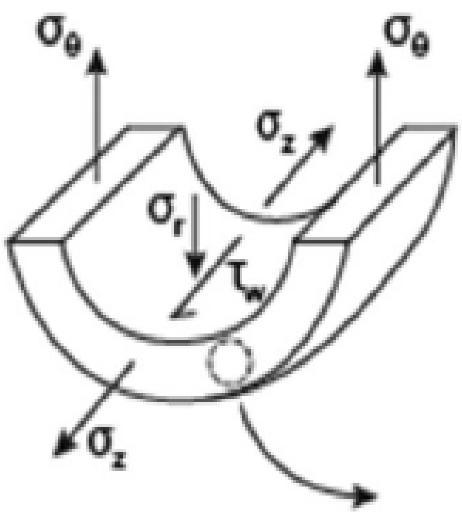
Basics of aortic mechanics

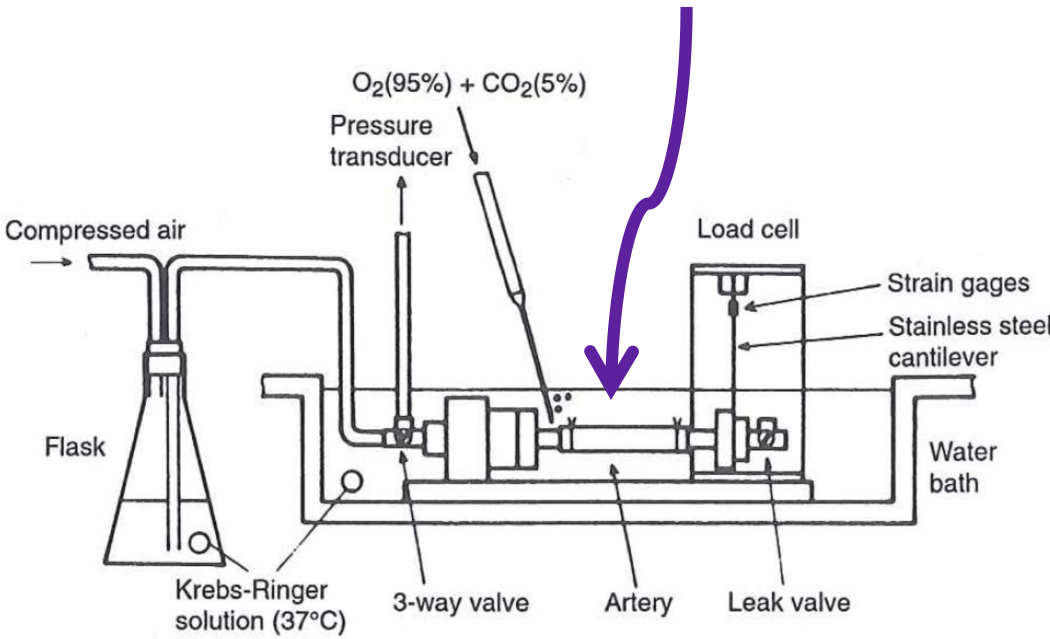


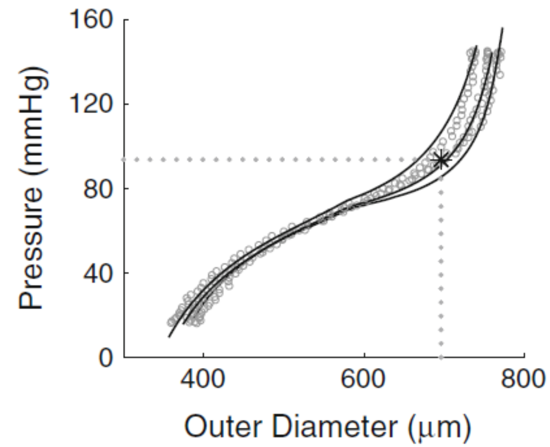
$$\tau_w = \frac{4\mu Q}{\pi a^3}, \qquad \sigma_\theta = \frac{Pa}{h}$$

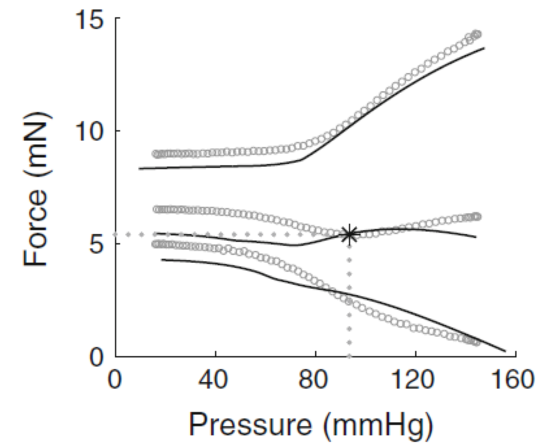
$$\sigma_z = \frac{f_z}{\pi\left(b^2 - a^2\right)} = \frac{f_z}{\pi h\left(2a - h\right)}$$

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

Functional biomechanical behavior







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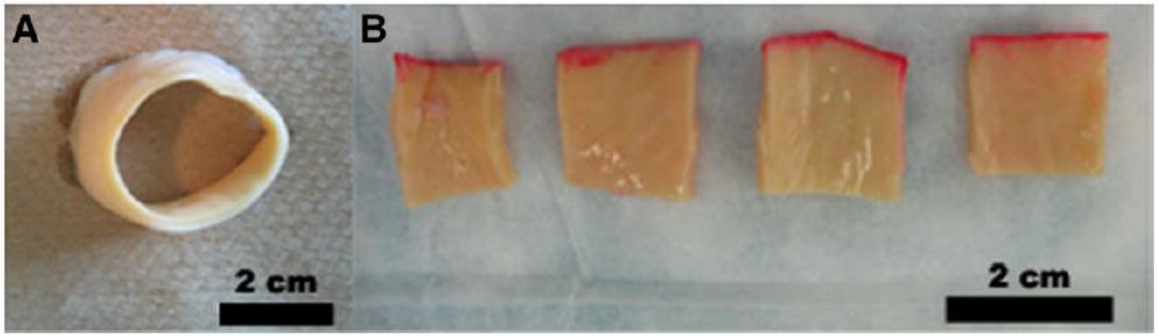
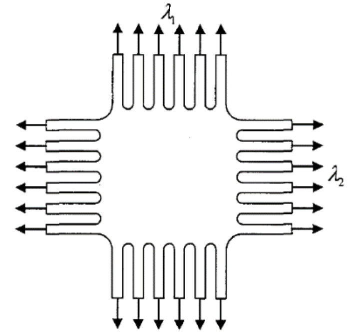
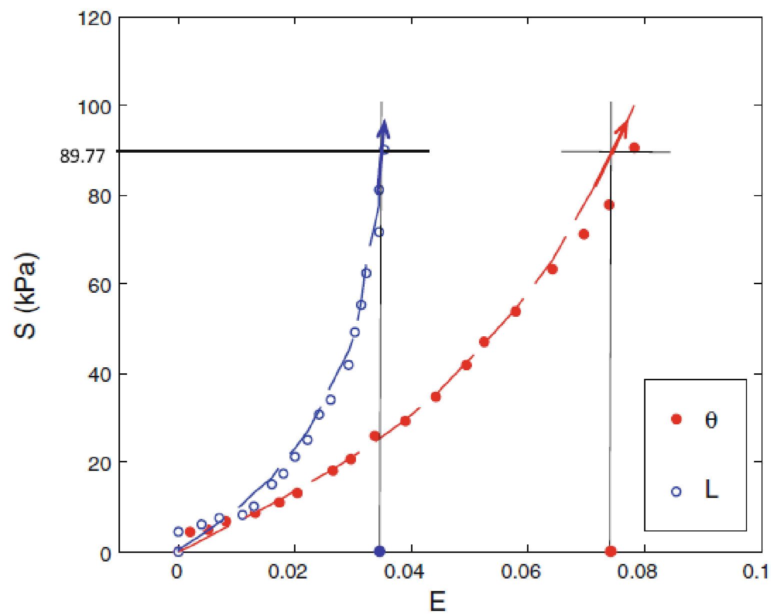
Material characterization and constitutive modeling





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



Mechanics of aortic aneurysms – Our recent contributions

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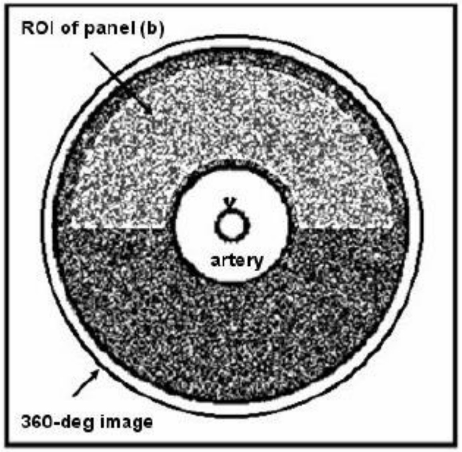
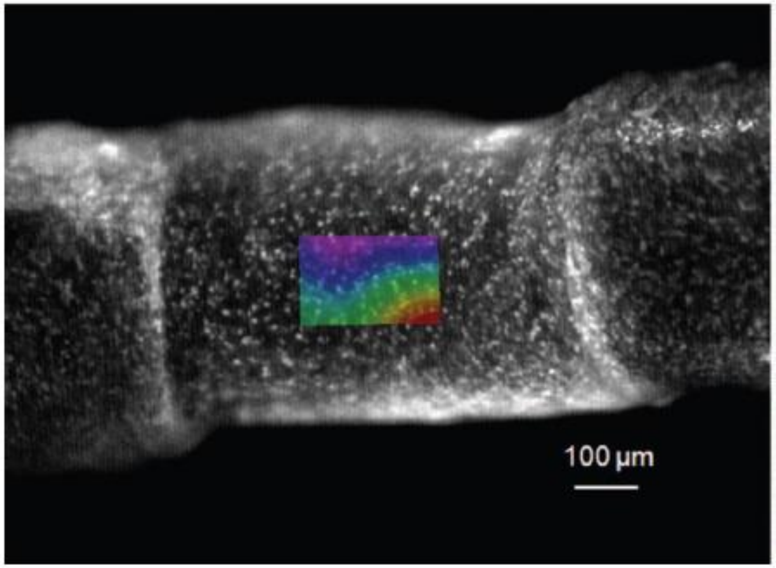
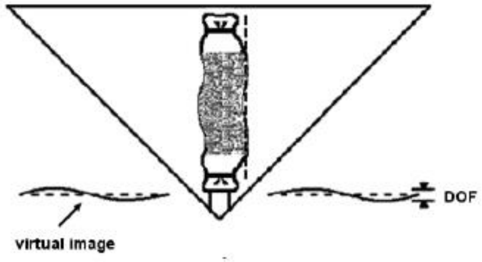
MEASUREMENT OF THE RESPONSE USING DIGITAL IMAGE CORRELATION

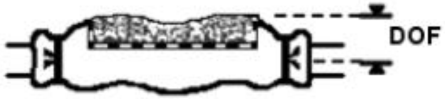
classical

panoramic





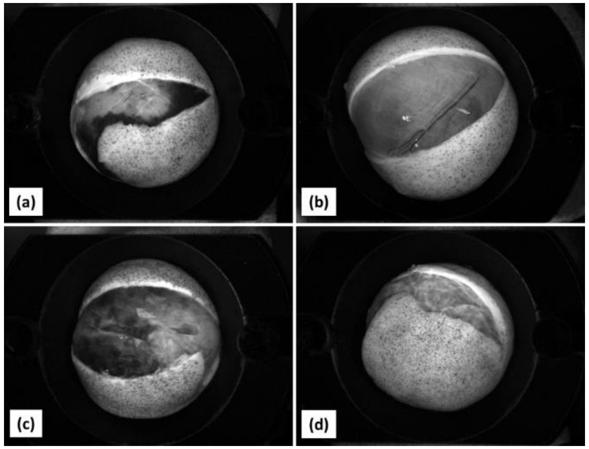




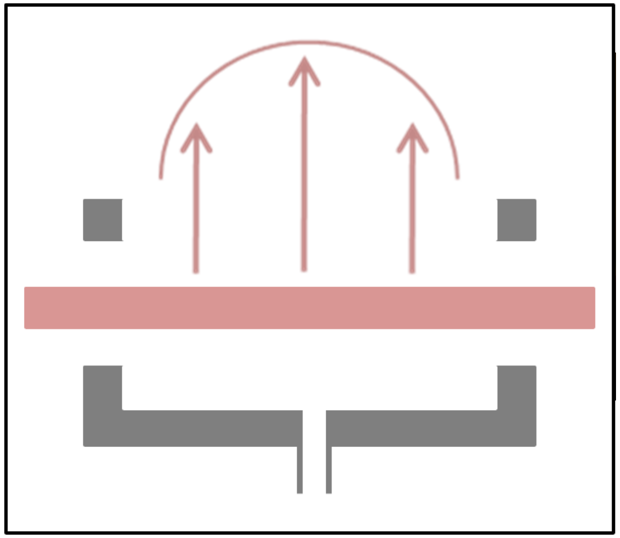
Badel et al. CMBBE, **15**, p 37-48, 2012.

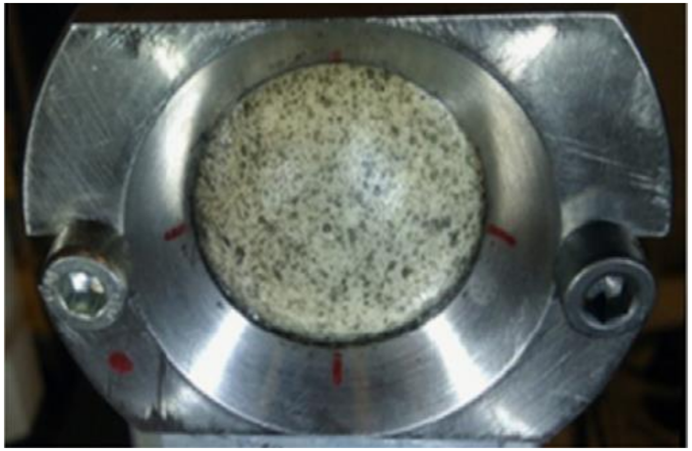
Genovese. Optics Lasers Eng, **47**, p 995-1008, 2009.

Bulge inflation test



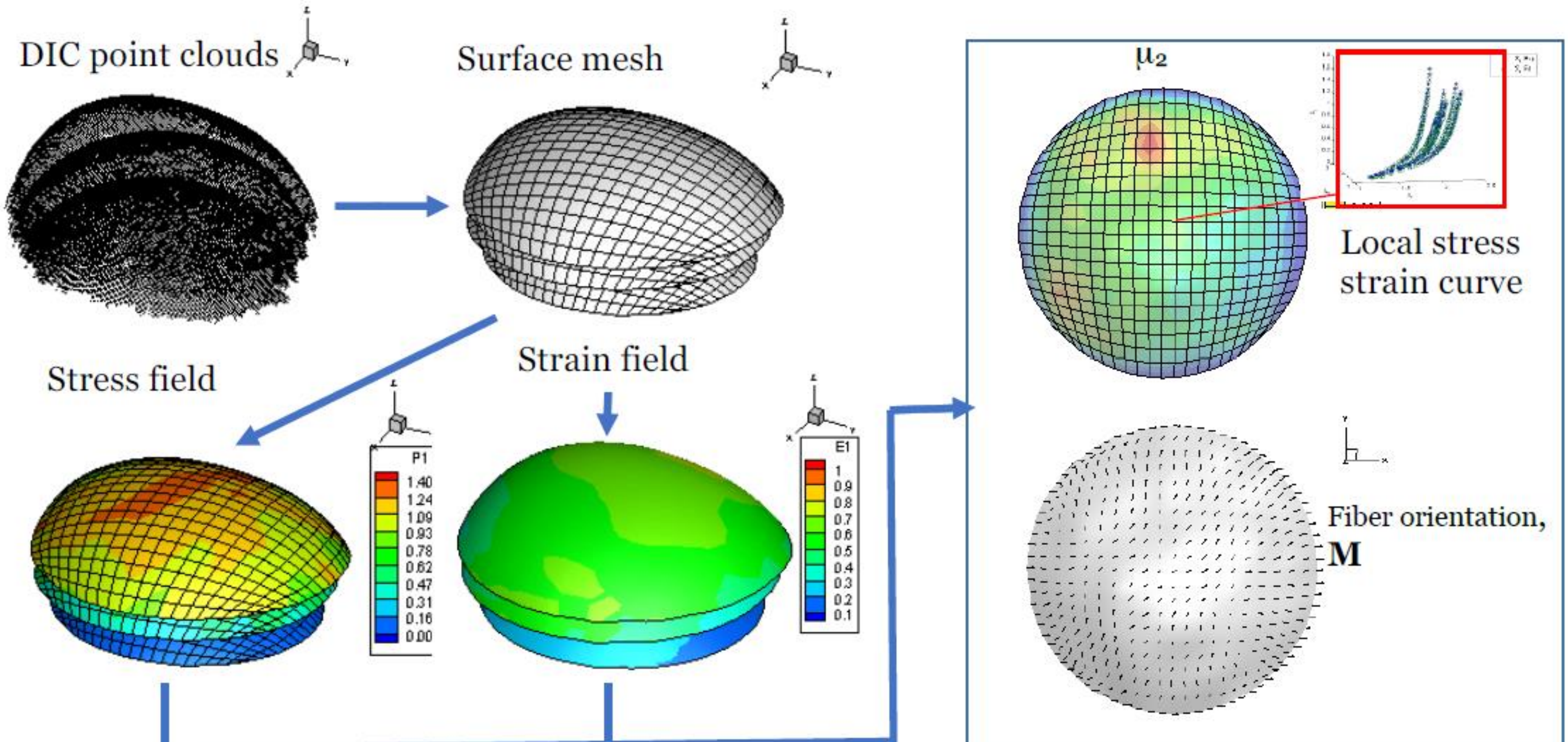
Romo et al. Journal of Biomechanics -2014



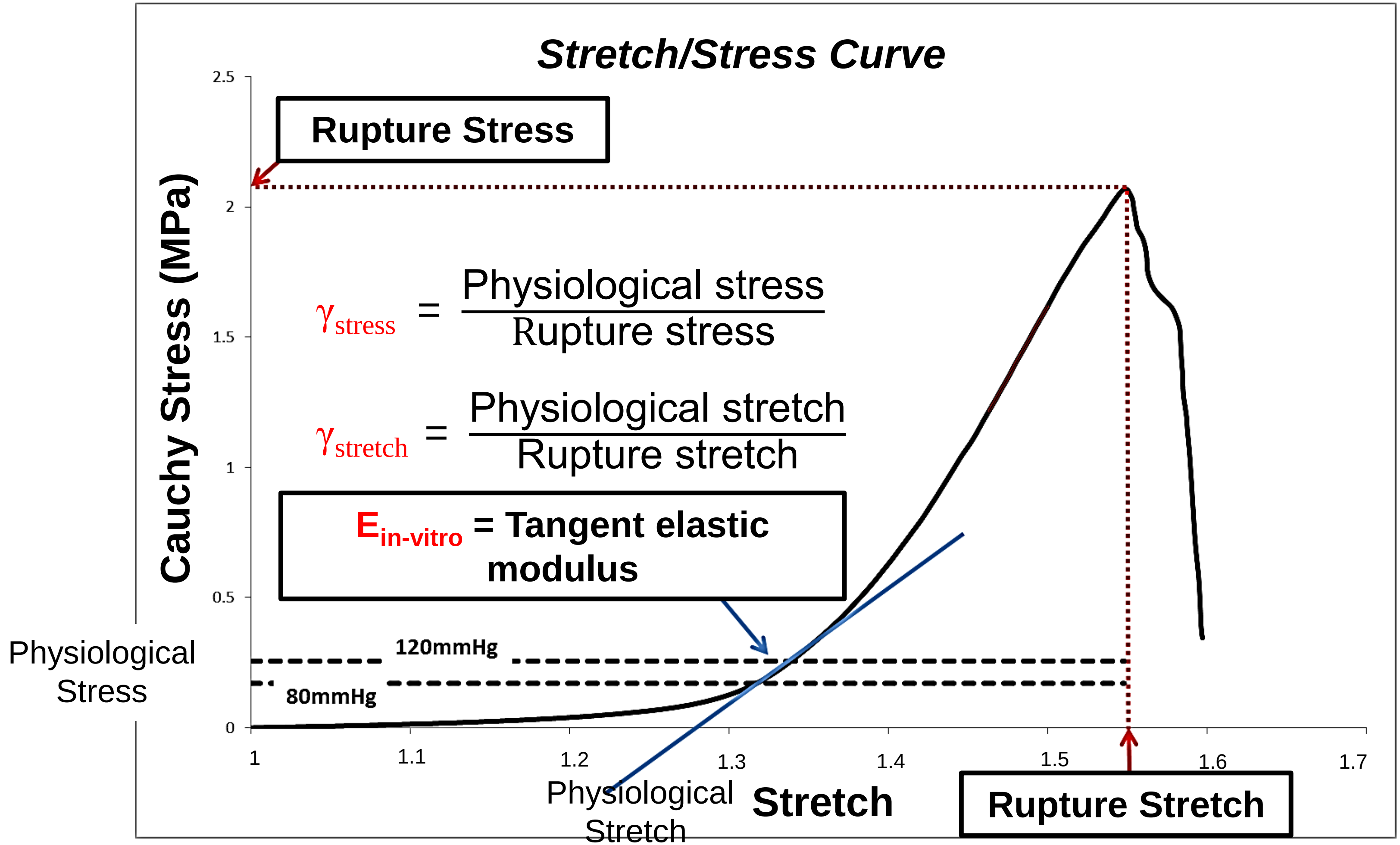


Identification of local material properties

Davis et al. BMMB – 2015.
Davis et al. JMBBM – 2016
Zhao et al. Acta Biomaterialia - 2016



Rupture risk estimation



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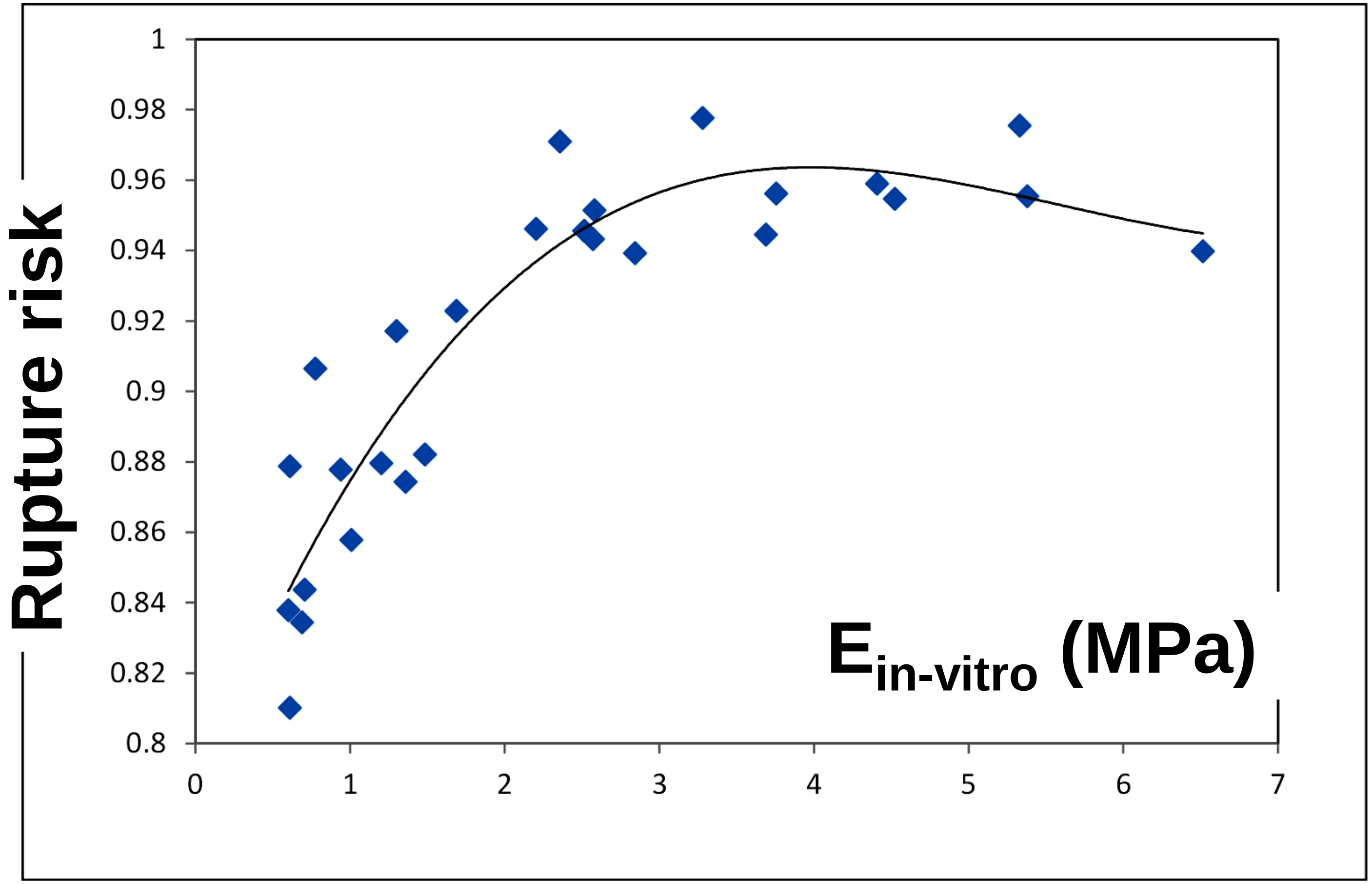
Correlation between the stretch-based rupture risk and the tangent elastic modulus



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

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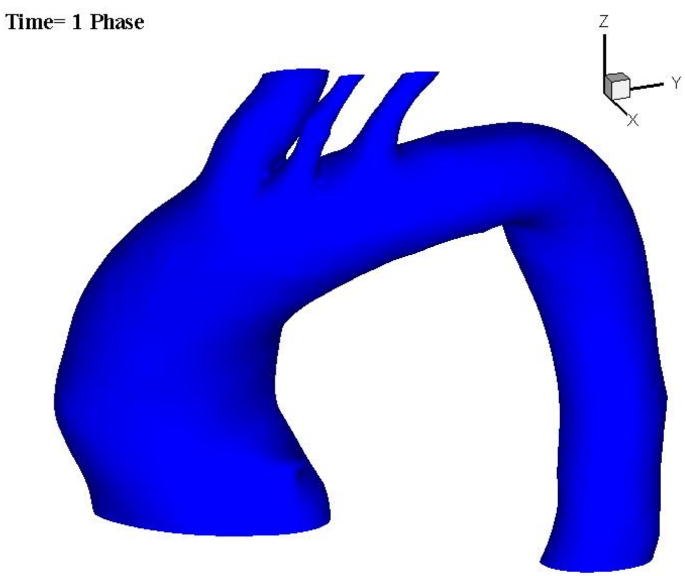
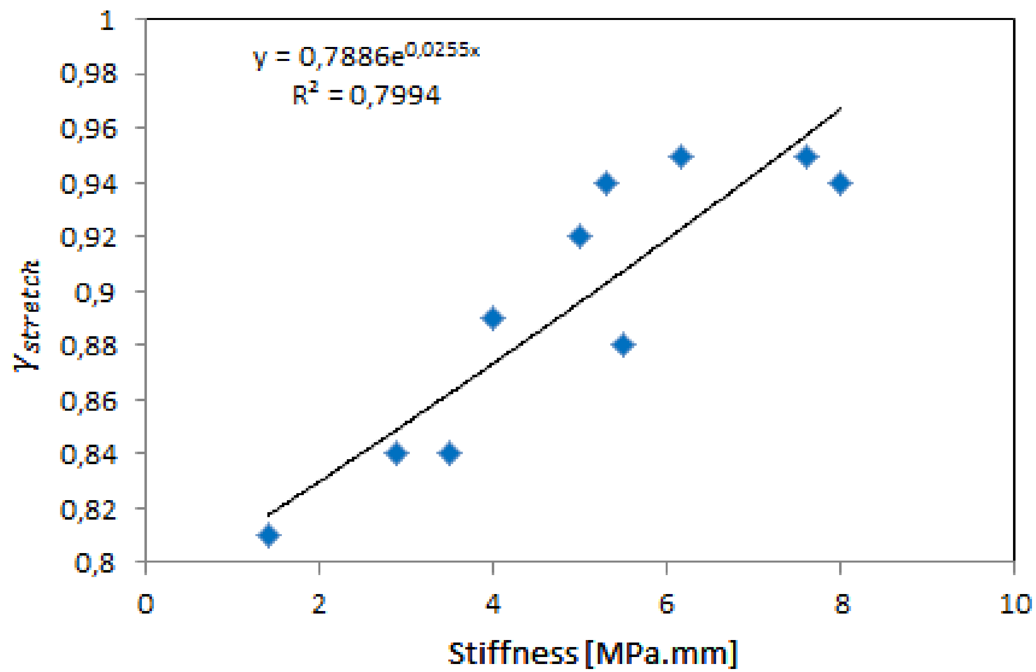
Relationship with aortic stiffness

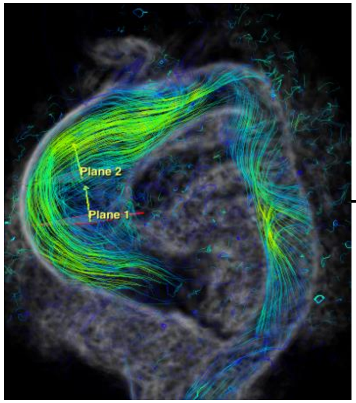
The stretch based rupture risk criterion correlates to the aortic stiffness measured by elastography techniques



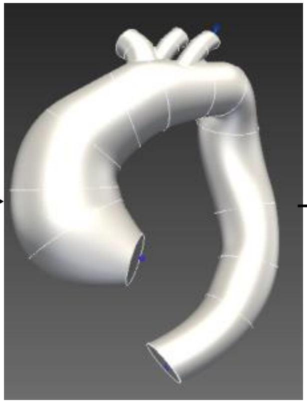


Olfa Trabelsi, Miguel A Gutierrez Cambron, Solmaz Farzaneh, Ambroise Duprey, Stéphane Avril. A non-invasive methodology for ATAA rupture risk estimation. ***Journal of Biomechanics 2017.***

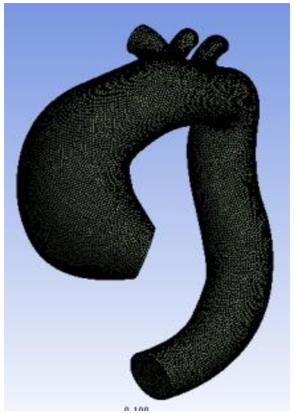
RELATIONSHIP WITH HEMODYNAMICS



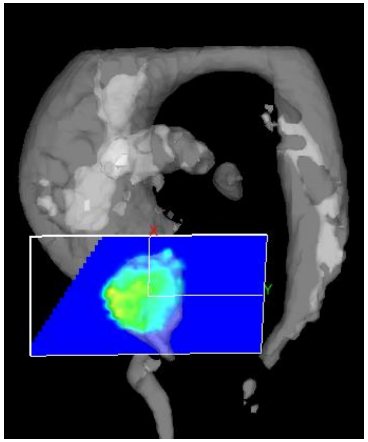
Preoperative dynamic imaging
4D MRI



CAD

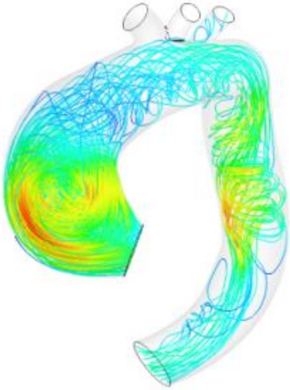


Mesh



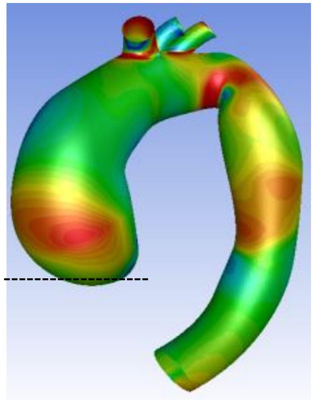
BCs

Numerical resolution



Streamlines, velocity

TAWSS



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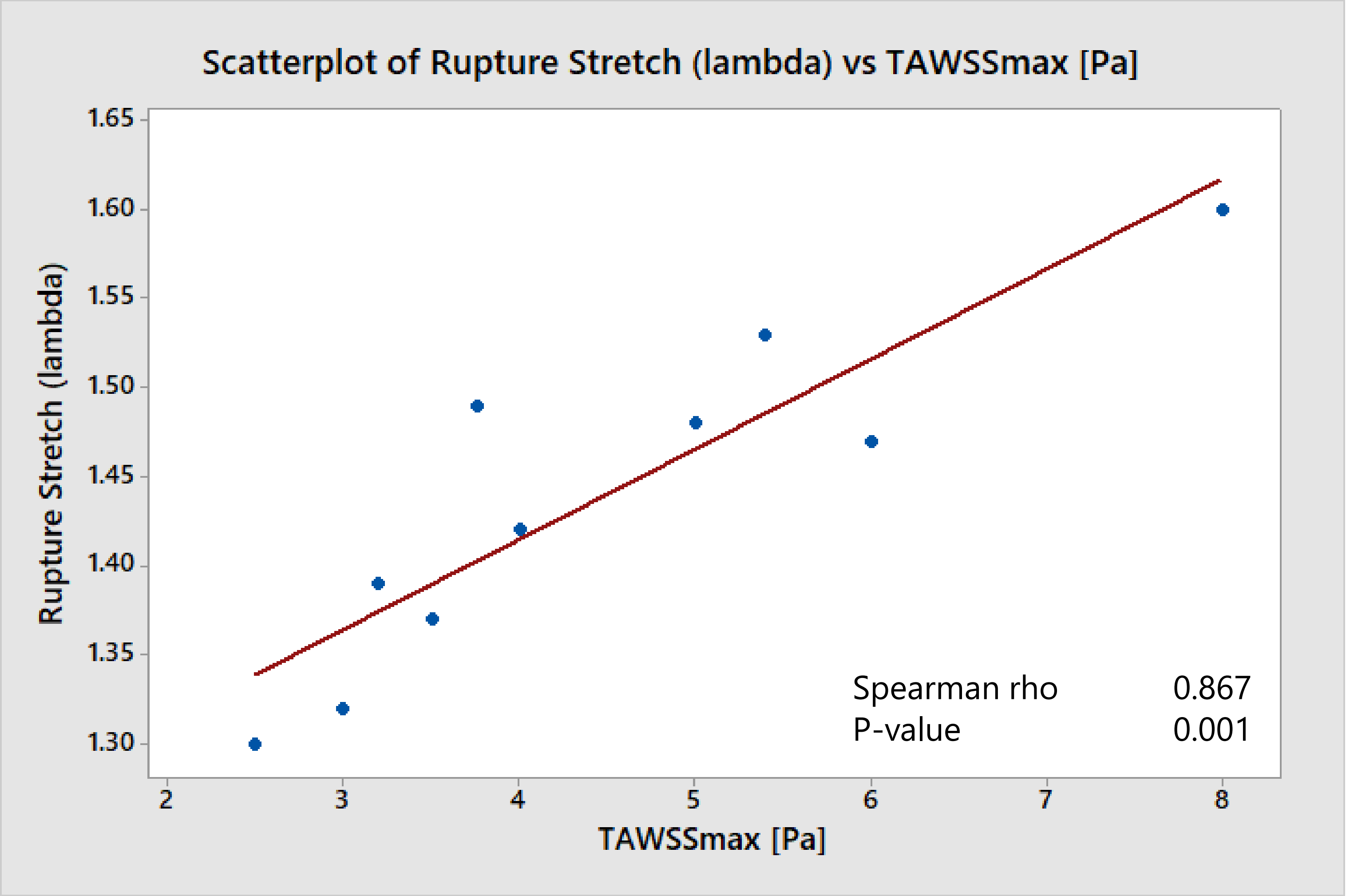
Relationship $\lambda_{rupture}$ vs. TAWSSmax [Pa]



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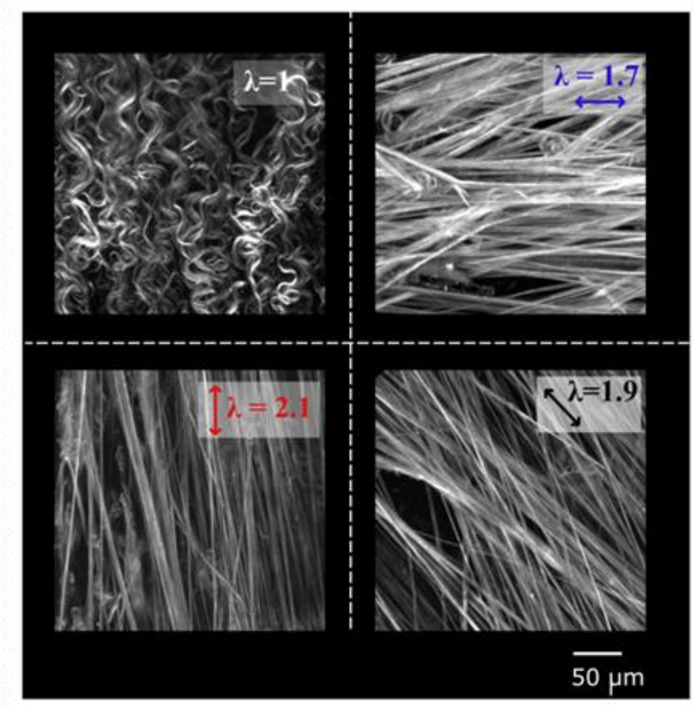
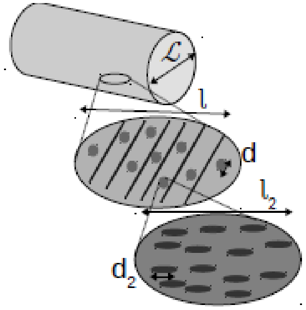
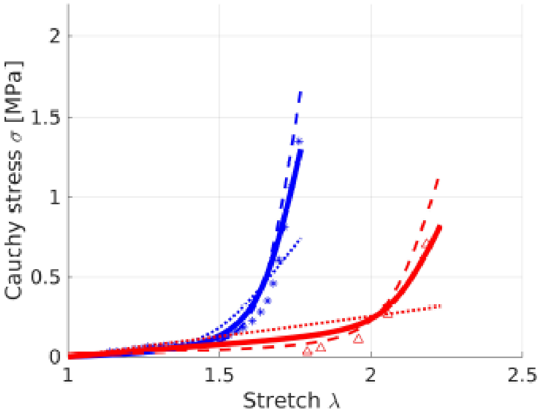
Micromechanical interpretation

- **ATAA always manifests with damaged elastic fibers, more and more collagen tends to be recruited**







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

C. Martin et al., Acta Biomater. 9 (2013) 9392–9400

Coupling mechanobiology and continuum mechanics

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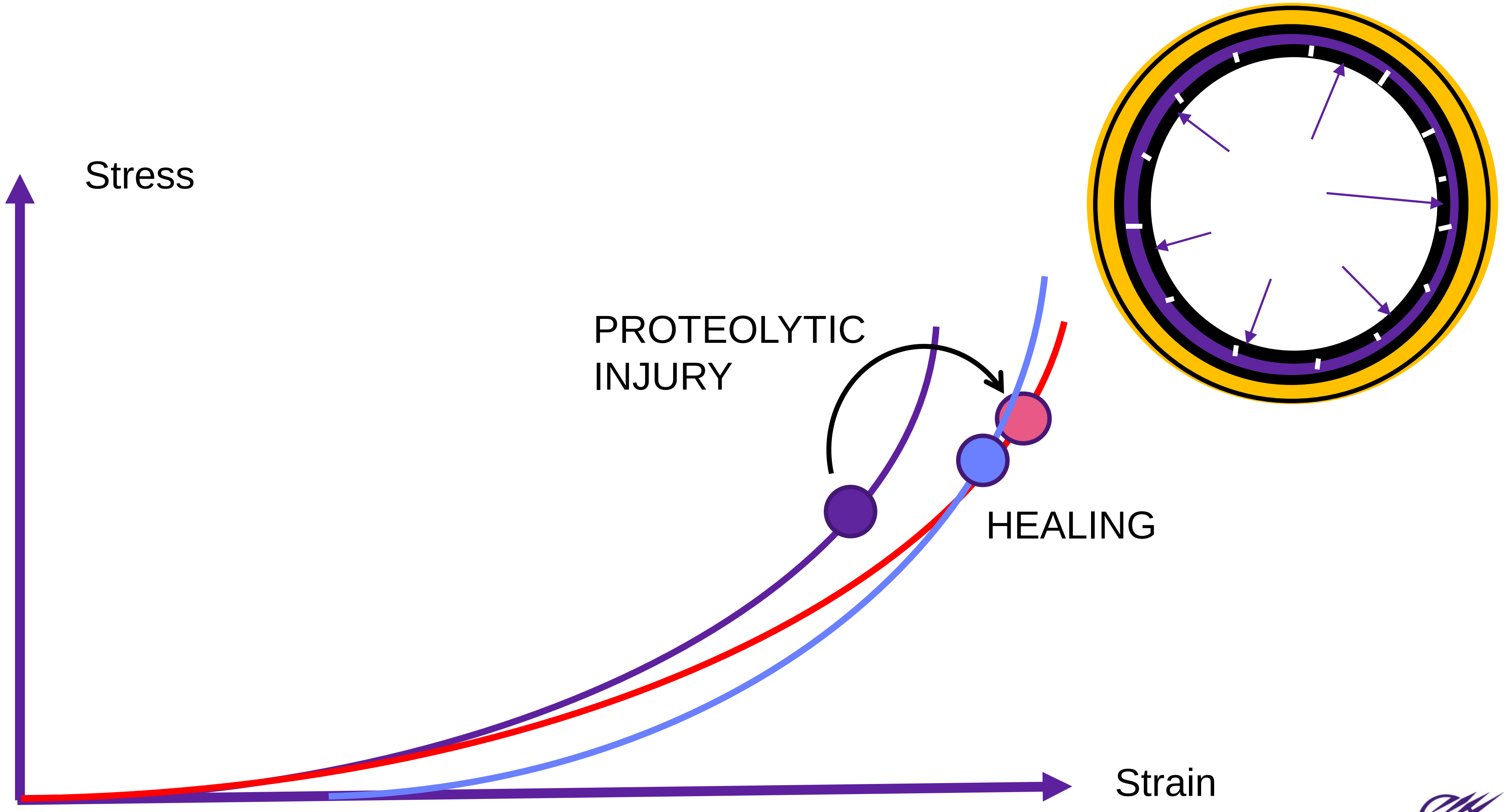
Altered mechanics induce biological responses, including gene expression, protein activation and cell phenotype

Continuous process of proteolytic injury and tissue adaptation



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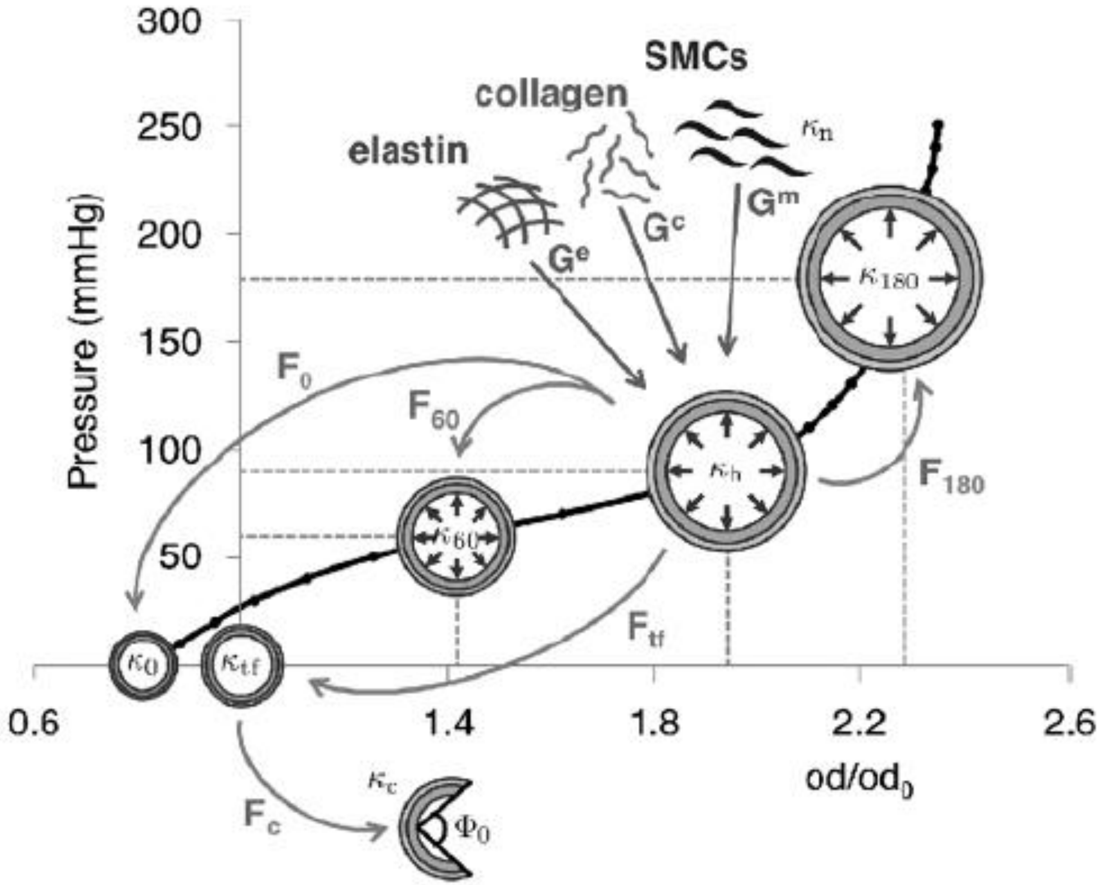
Constrained mixture theory



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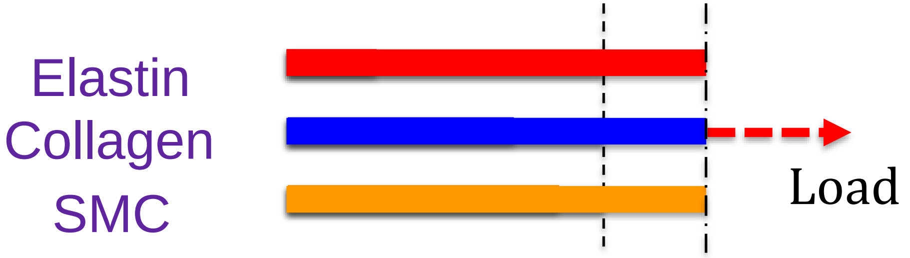
Layer-specific constitutive model

Strain-energy function based on the constrained mixture theory

$$W = (1 - D^{\mathrm{e}})\rho^{\mathrm{e}}\overline{W}^{\mathrm{e}}(\overline{I}_1^{\mathrm{e}}) + \sum_{i=1}^{n}(1 - D^{\mathrm{c}_i})\rho^{\mathrm{c}_i}W^{\mathrm{c}_i}(I_4^{\mathrm{c}_i}) + \rho^{\mathrm{m}}W^{\mathrm{m}}(I_4^{\mathrm{m}}) + U(J)$$

Deposition stretch (Λ_s^j) of each constituent

$$\mathbf{F}_{\mathrm{tot}}^{j} = \mathbf{F}\mathbf{\Lambda}_s^j$$



Humphrey and Rajagopal, Math. Models Methods Appl. Sci., 2002 ; Bellini et al, ABME, 2014

Layer-specific constitutive model

Volumetric contributions of strain-energy function

$$U(J) = \kappa(J-1)^2$$

Active contribution of smooth muscle cells

$$\Psi_{act}^{sm} = \frac{S_{actmax}}{\rho(0)}\left(\lambda_{act} + \frac{1}{3}\frac{(\lambda_m - \lambda_{act})^3}{(\lambda_m - \lambda_0)^2}\right)$$

Damage

$$D = G(\psi) = \frac{1 - \frac{\psi_0}{\psi}}{1+H} \quad \text{with} \quad H = -\frac{{\psi_0}^2}{2\omega} \quad \text{and} \quad \psi = \sqrt{2W} \qquad \omega = \frac{\Omega}{L_0}$$

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Homogenized G&R constrained mixture model

Strain-energy function based on the constrained mixture theory

$$W = (1 - D^{\mathrm{e}})\rho^{\mathrm{e}}\overline{W}^{\mathrm{e}}(\overline{I}_1^{\mathrm{e}}) + \sum_{i=1}^{n}(1 - D^{\mathrm{c}_i})\rho^{\mathrm{c}_i}W^{\mathrm{c}_i}(I_4^{\mathrm{c}_i}) + \rho^{\mathrm{m}}W^{\mathrm{m}}(I_4^{\mathrm{m}}) + U(J)$$

Elastic and inelastic decomposition of deformation gradient

$$\mathbf{F}_{\mathrm{tot}}^{j} = \mathbf{F}_{\mathrm{e}}^{j}\mathbf{F}_{\mathrm{gr}}^{j}$$

$$\mathbf{F}_{\mathrm{gr}}^{j} = \mathbf{F}_{\mathrm{r}}^{j}\mathbf{F}_{\mathrm{g}}^{j}$$

$\mathbf{F}_{\mathrm{r}}^{j}$ and $\mathbf{F}_{\mathrm{g}}^{j}$ should be calculated if the artery is not in the homeostatic state

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Homogenized G&R constrained mixture model

Collagen mass production

$$\dot{\varrho}^{j}(\mathrm{t}) = \varrho^{j}(\mathrm{t}) k_{\sigma}^{j} \frac{\sigma^{j}(t) - \sigma_{\mathrm{h}}^{j}}{\sigma_{\mathrm{h}}^{j}} + \dot{\xi}^{j}(t)$$

Inelastic deformation due to remodeling

$$\left[\frac{\dot{\varrho}^{j}(\mathrm{t})}{\varrho^{j}(\mathrm{t})} + \frac{1}{T^{j}}\right]\left[\mathbf{S}^{j} - \mathbf{S}_{\mathrm{pre}}^{j}\right] = \left[\frac{\partial \mathbf{S}^{j}}{\partial \mathbf{C}_{\mathrm{e}}^{j}} : (\mathbf{C}_{\mathrm{e}}^{j} \mathbf{L}_{\mathrm{r}}^{j})\right]$$

$$\mathbf{L}_{\mathrm{r}}^{j} = \dot{\mathbf{F}}_{\mathrm{r}}^{j} \mathbf{F}_{\mathrm{r}}^{j^{-1}}$$

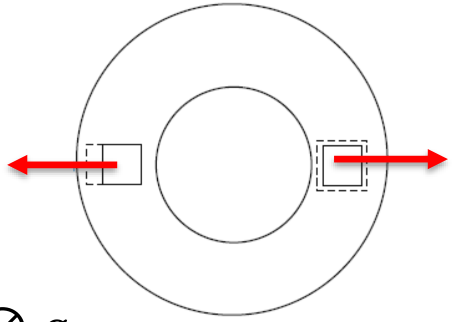
Cyron et al, Biomech Model Mechanobiol (2016) 15:1389–1403, Braeu et al, Biomech Model Mechanobiol (2017) 16(3):889-906

Homogenized G&R constrained mixture model

Inelastic deformation due to growth

$$\dot{\mathbf{F}}_g = \dot{\mathbf{F}}_g^j = \sum_{j=1}^{n} \dot{\mathbf{G}}^j$$

$$\dot{\mathbf{G}}^j = \frac{\dot{\varrho}^j(t)}{\varrho^j(t)\left[\mathbf{F}_g^{j^{-T}} : \mathbf{B}^j\right]} \mathbf{B}^j$$



$\mathbf{B}^j = a_g \otimes a_g$

Anisotropic growth

$\mathbf{B}^j = \frac{\mathbf{1}}{3}\mathbf{I}$

Isotropic growth

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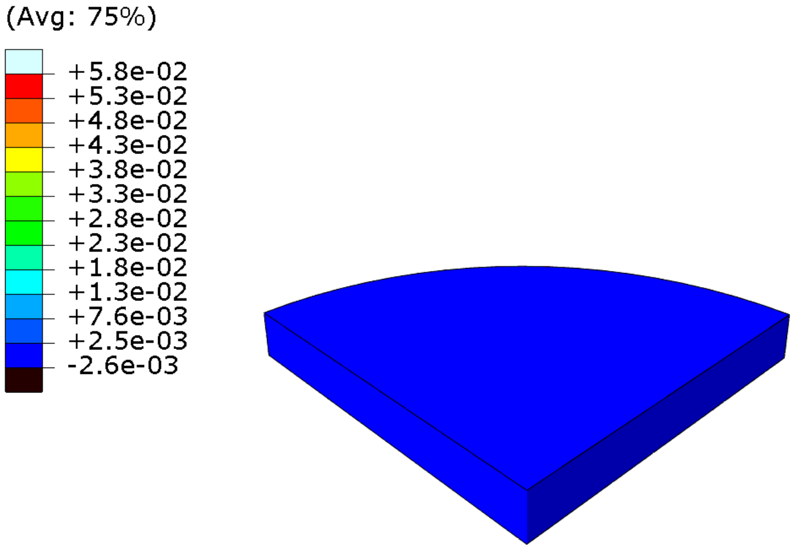
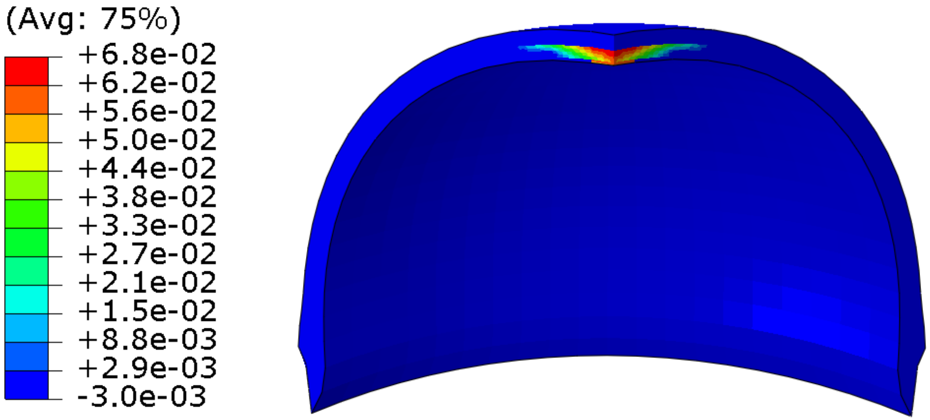
Prediction of mechanical damage in bulge inflation tests

Damage during bulge inflation test (luminal side in)





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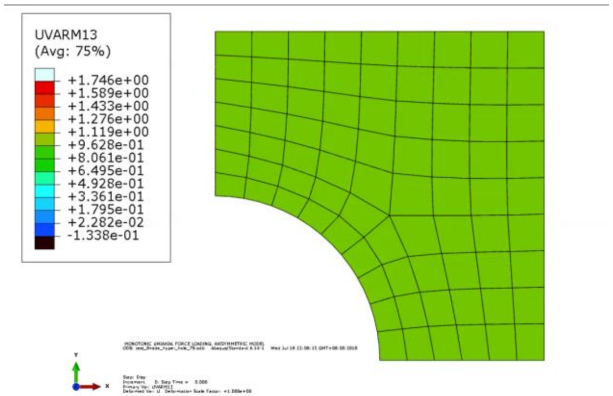
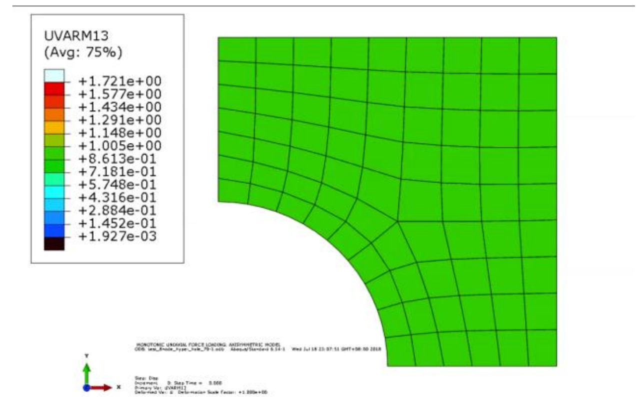
Gradient-enhanced G&R healing model

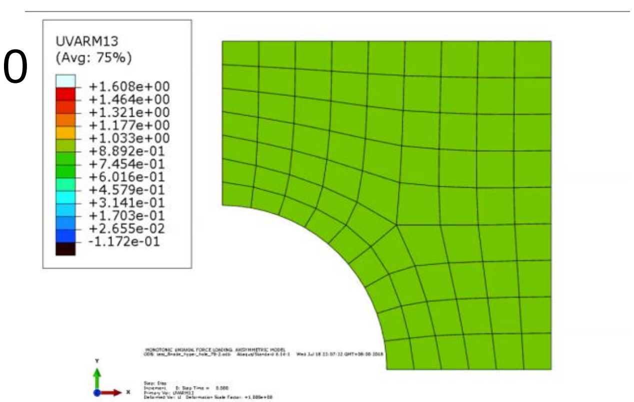
k=0



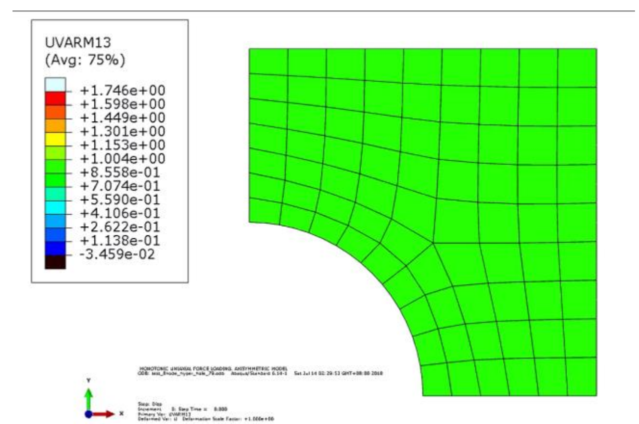
k=0.5



k=1.0



k=5.0



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Calibration of mechanobiological properties - Towards clinical applications

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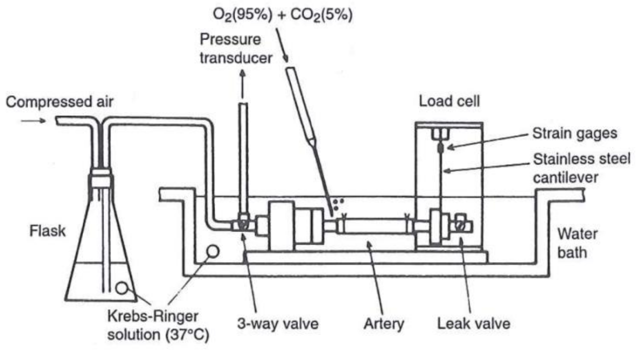
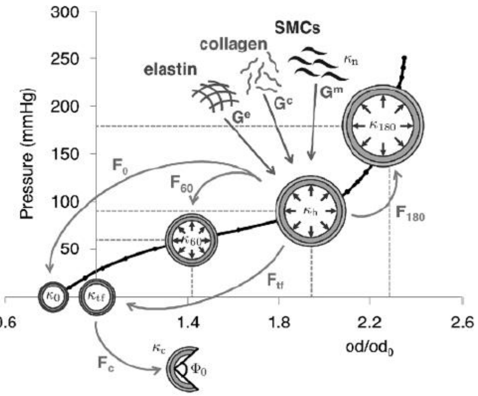
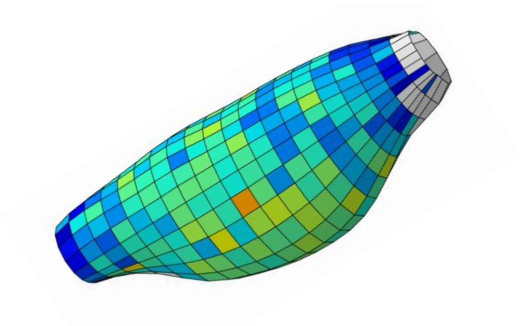
APPROACH

1. Experiments
2. Material model
3. Inverse method







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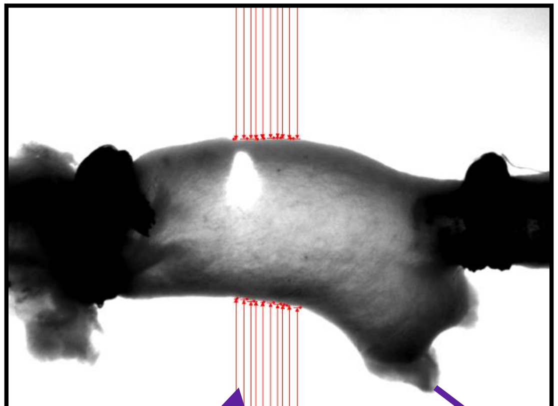
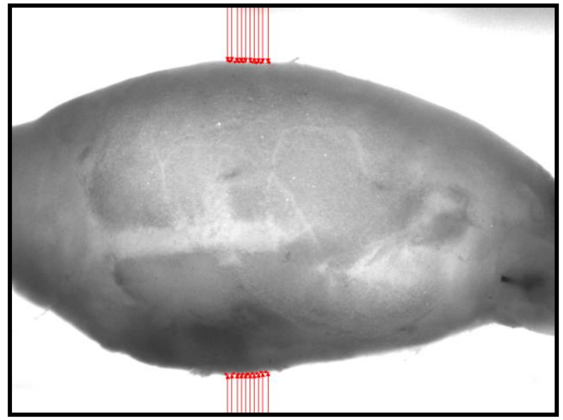
Study Design

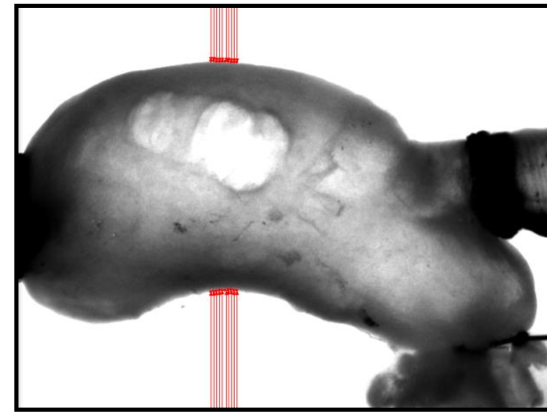
Control

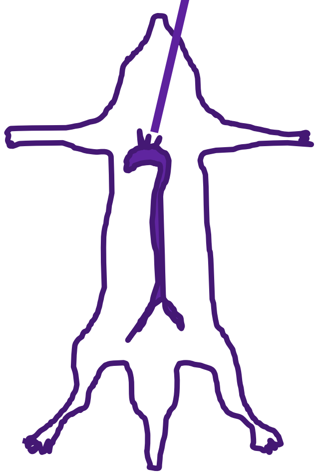


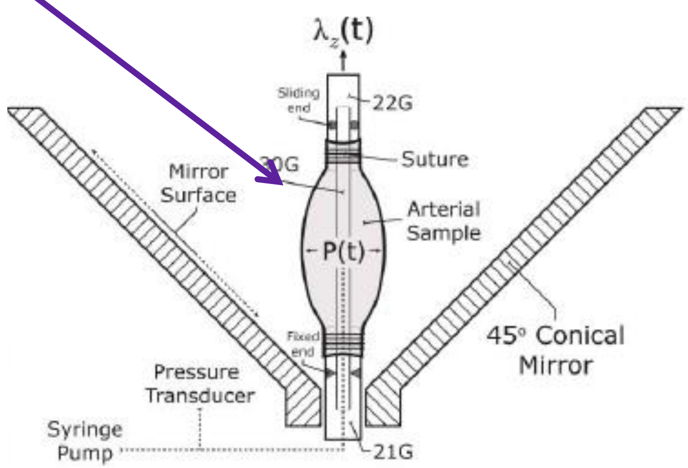
Fibulin 4 SMC KO

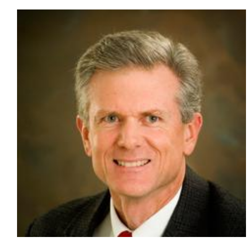


Fibrillin 1 *mgR/mgR*









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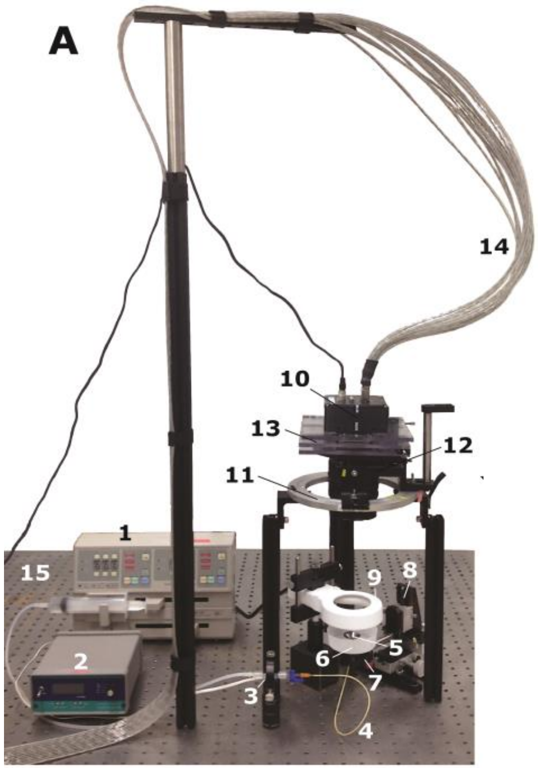
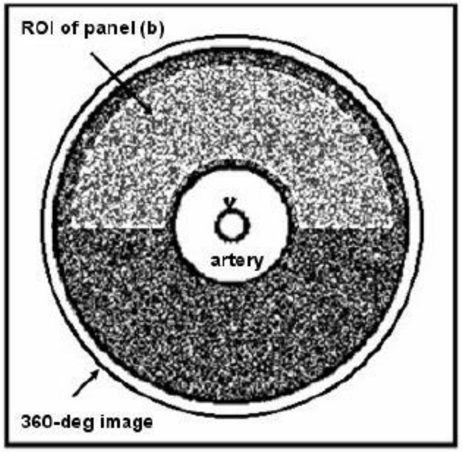
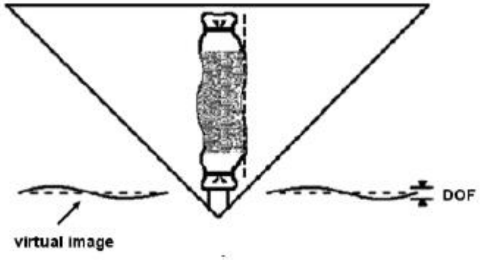
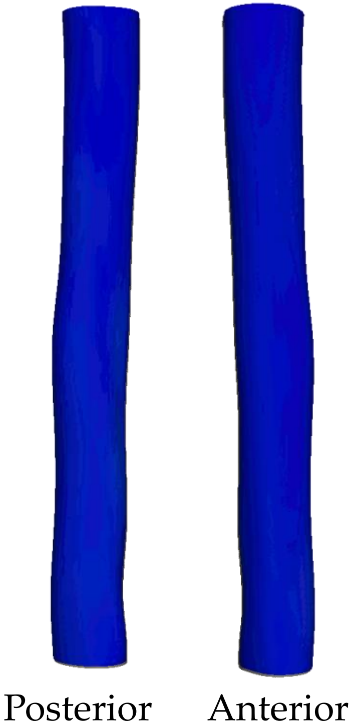
The pDIC technique









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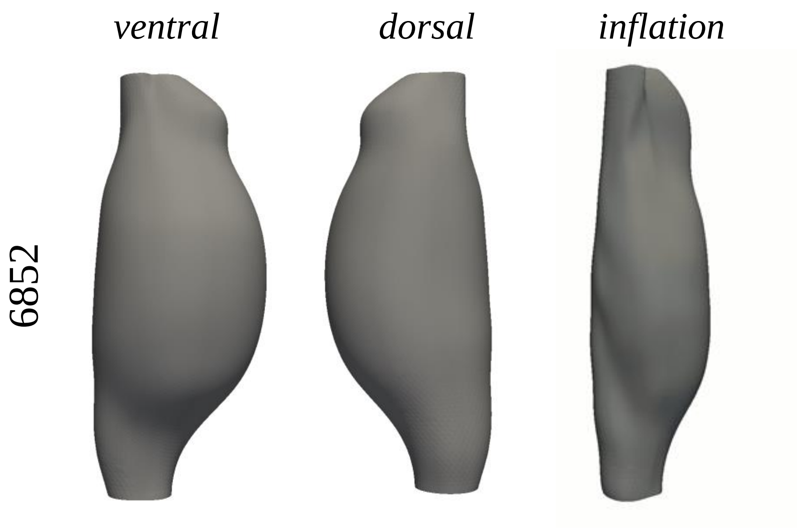
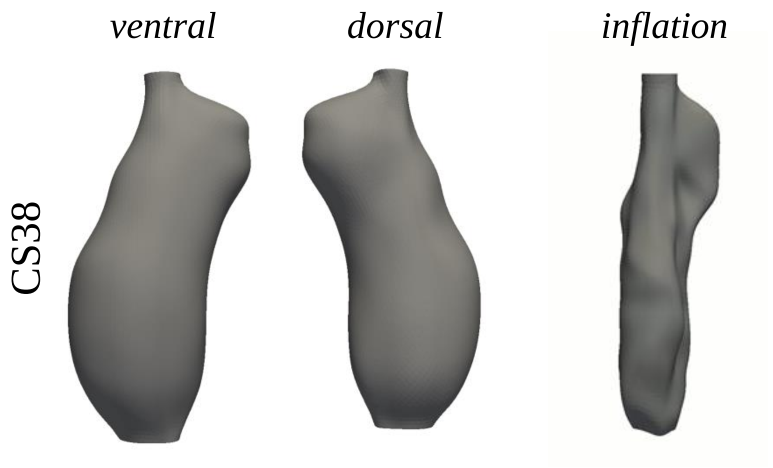
pDIC measurements

Fibulin 4 SMC KO

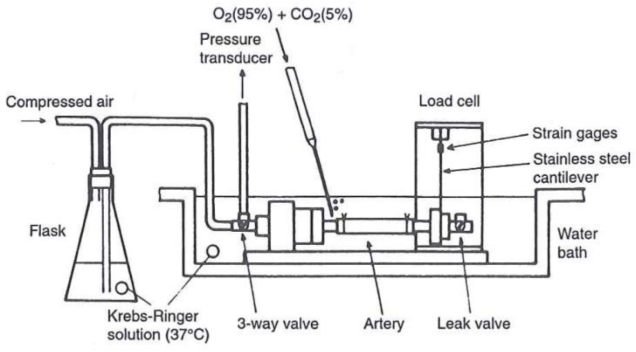


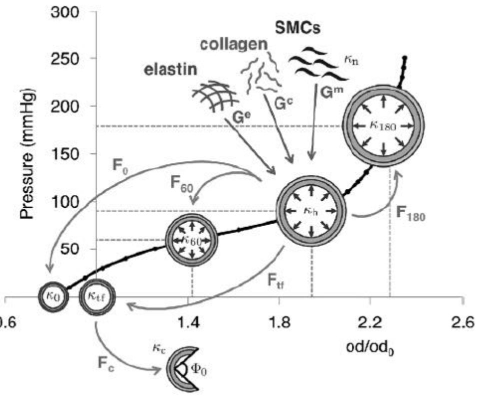
Fibrillin 1 *mgR/mgR*

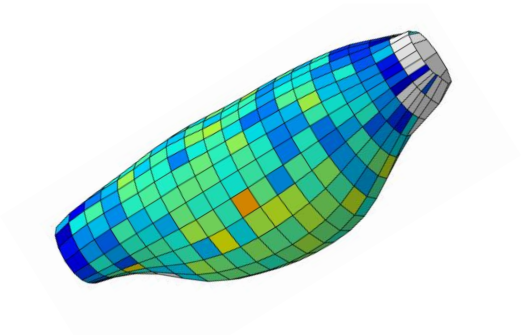


APPROACH

1. Experiments
2. Material model
3. Inverse method







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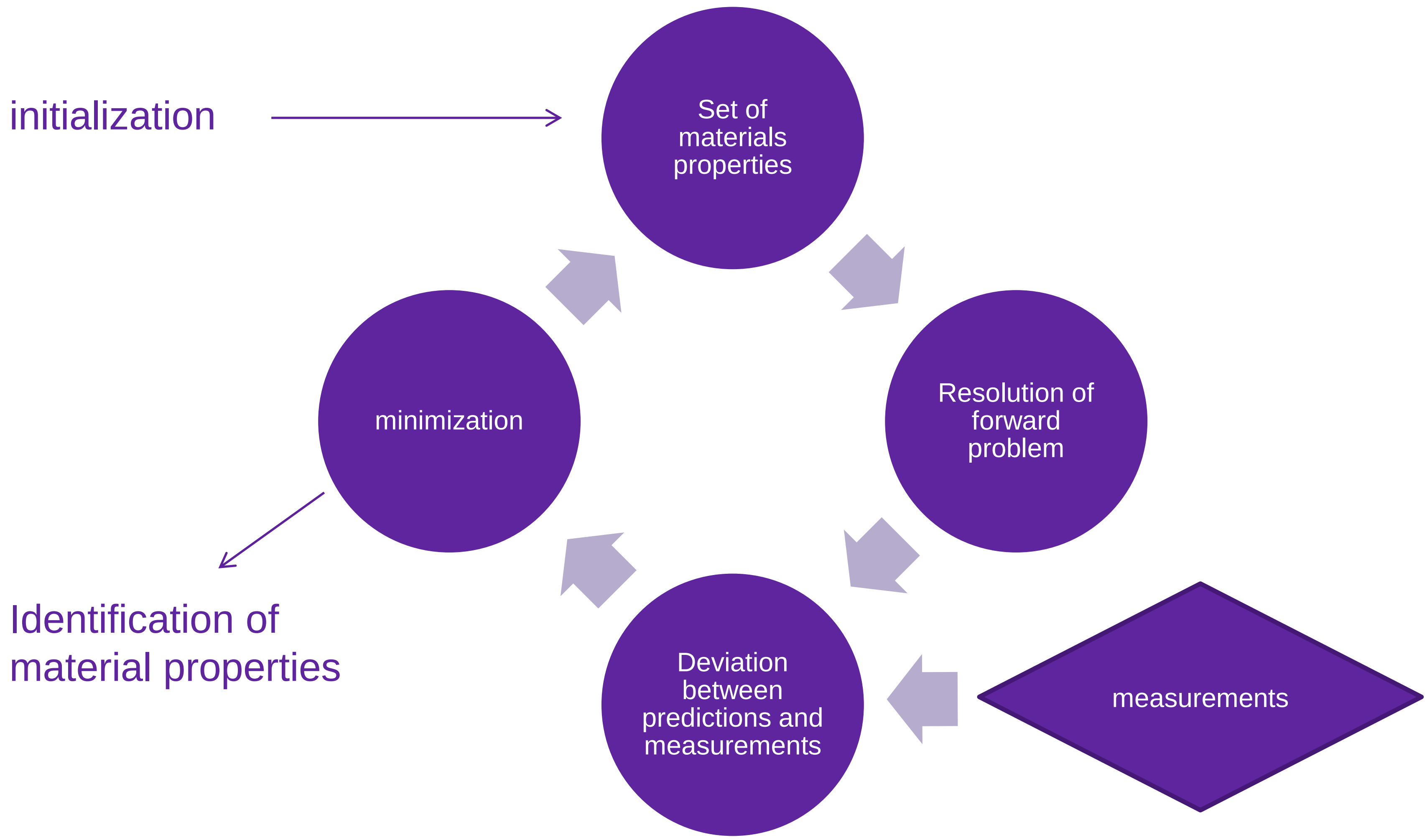
Inverse approach – traditional approach



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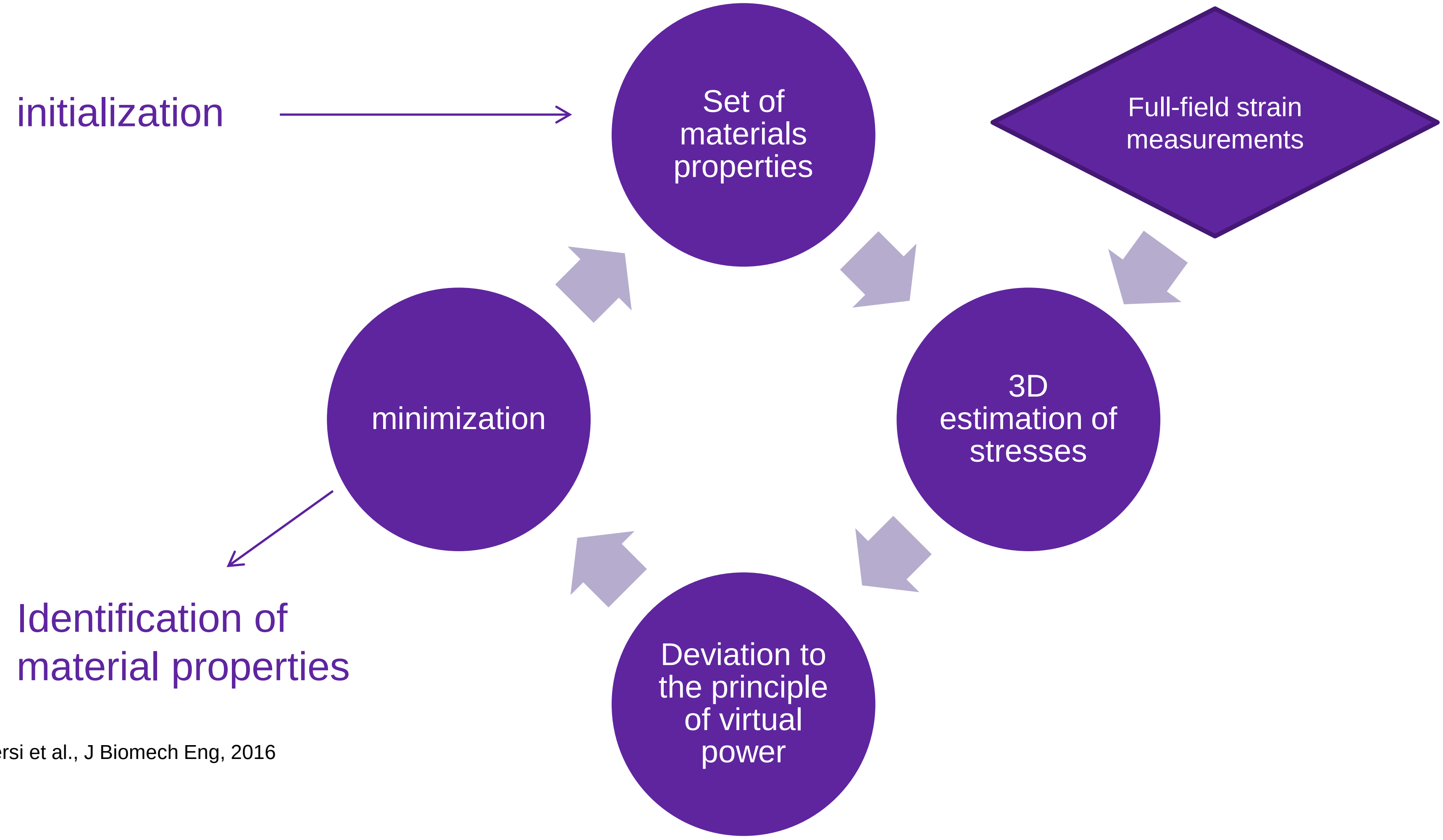
Alternative inverse approach: the virtual fields method



Bersi et al., J Biomech Eng, 2016

Minimization of the equilibrium gap using the principle of virtual power

minimization

$$J = \sum_{p} \sum_{\lambda} \left(\underbrace{- \int_{\omega(t)} \underline{\underline{\sigma}} : \left(\underline{\nabla} \otimes \underline{\xi}^{*} \right) d\omega}_{P^{*}_{int}} + \underbrace{\oint_{\partial\omega(t)} \underline{T} : \underline{\xi}^{*} \, ds}_{P^{*}_{ext}} \right)^{2}$$

Bersi et al., J Biomech Eng, 2016

Resolution:

$$\min_{c_3^1, c_3^{2,3}, c_3^4, \alpha, \beta} \left[\underbrace{\min_{c^e, c_2^1, c_2^{2,3}, c_2^4} \left[\frac{J(u)}{A} + \frac{J(v)}{B} \right]}_{\text{Linear least-squares}} \right]$$

Linear least-squares

Genetic algorithm

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Minimizing the equilibrium gap

minimization

$$J = \sum_{p} \sum_{\lambda} \left(\underbrace{- \int_{\omega(t)} \underline{\underline{\sigma}} : \left(\underline{\nabla} \otimes \underline{\xi}^{*} \right) d\omega}_{P^{*}_{int}} + \underbrace{\oint_{\partial\omega(t)} \underline{T} : \underline{\xi}^{*} \, ds}_{P^{*}_{ext}} \right)^{2}$$

Bersi et al., J Biomech Eng, 2016

Resolution:

$$\min_{c_3^1, c_3^{2,3}, c_3^4, \alpha, \beta} \left[\min_{c^e, c_2^1, c_2^{2,3}, c_2^4} \left[\frac{J(u)}{A} + \frac{J(v)}{B} \right] \right]$$

Linear least-squares

Genetic algorithm

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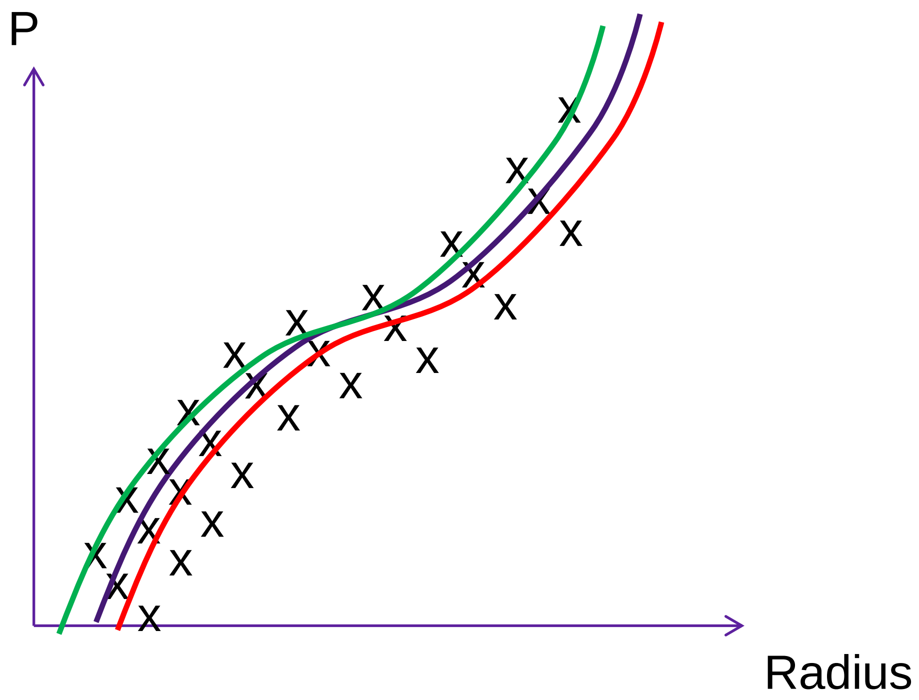
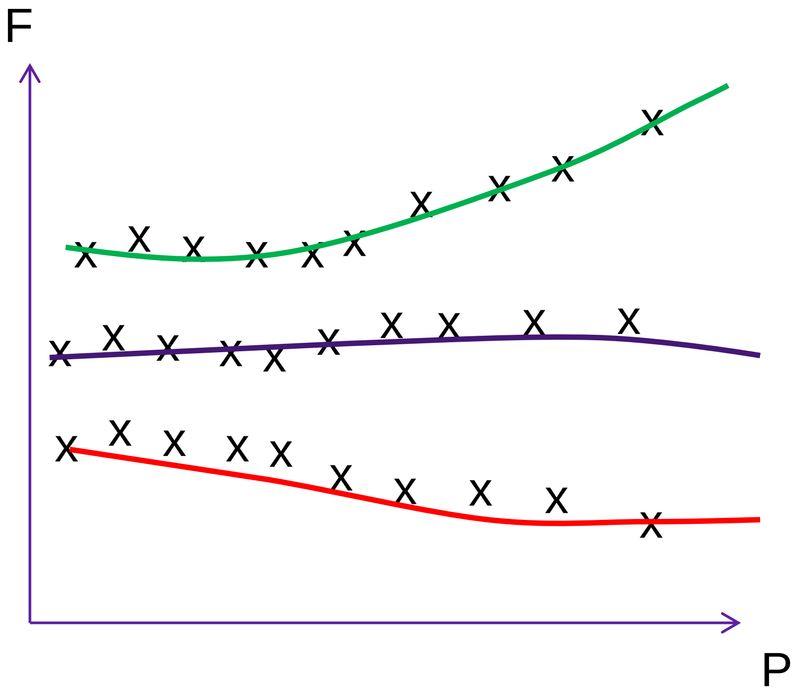
Similar to material fitting at every position





Crosses represent external virtual work for every pressure and axial stretch
Solid lines represent internal virtual work
The goodness of fit is evaluated with the R^2 value

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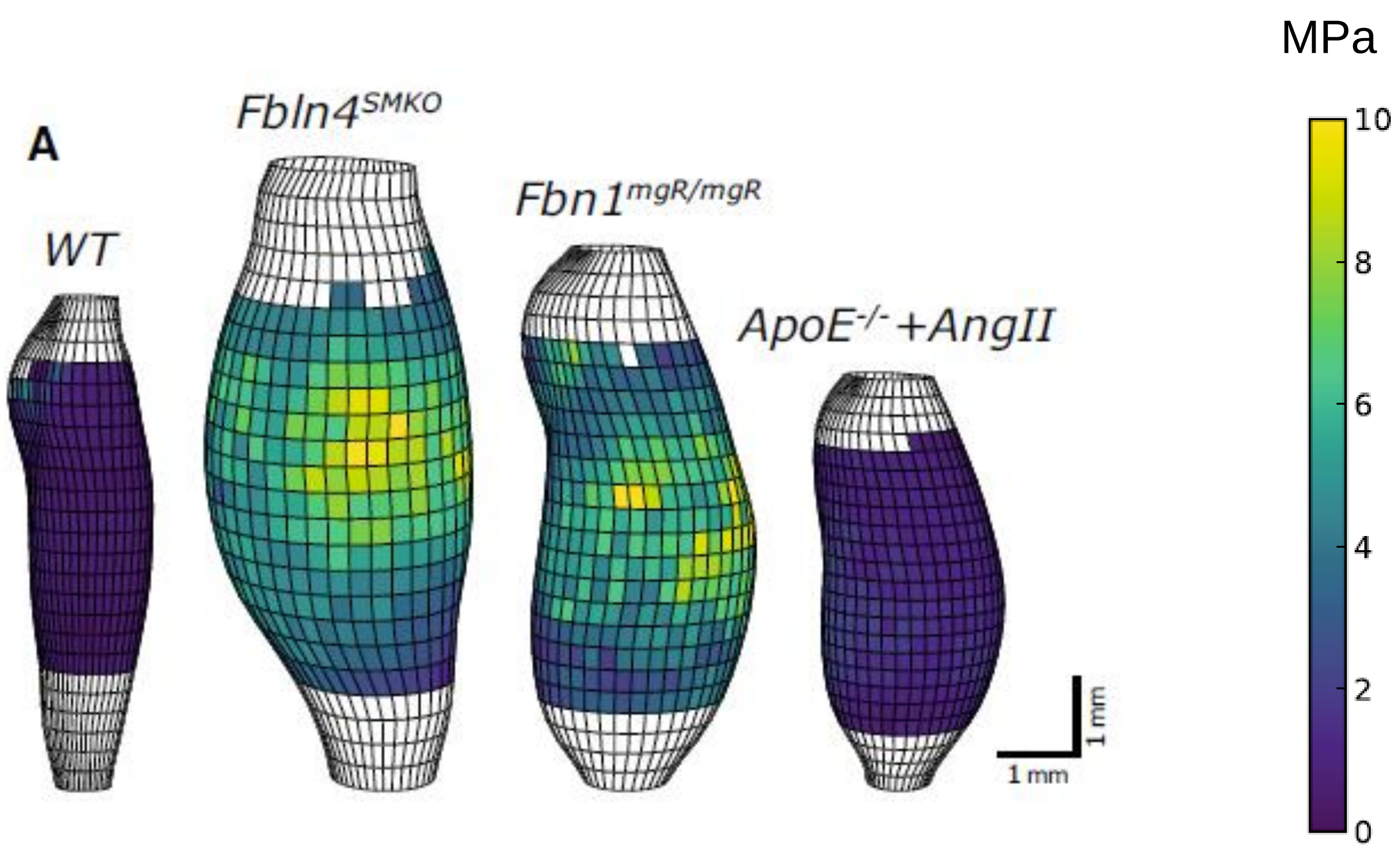
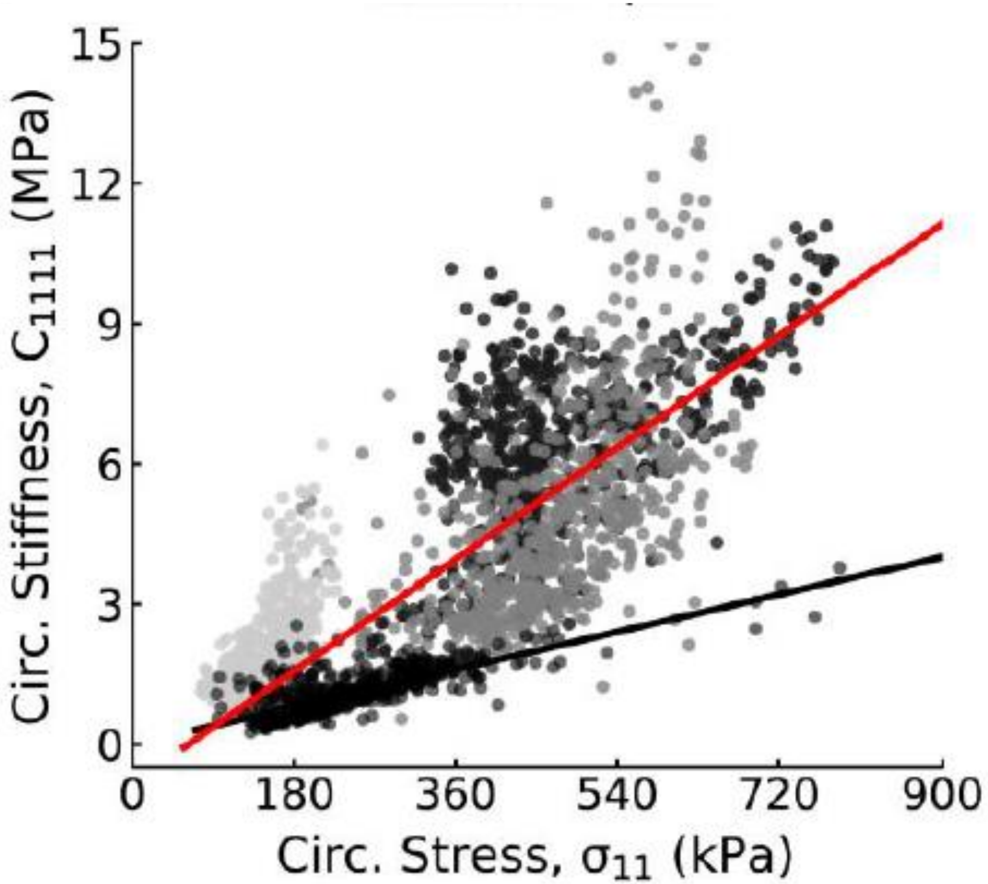
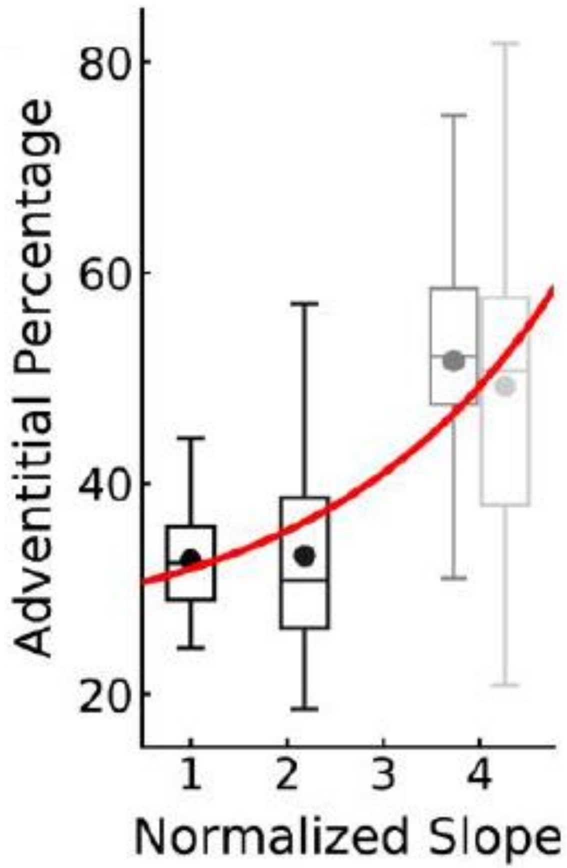
Full-Field Material Parameter Estimation vs stiffness distribution



Bersi et al, BMMB, 2018

Full-Field Material Parameter Estimation vs local stress





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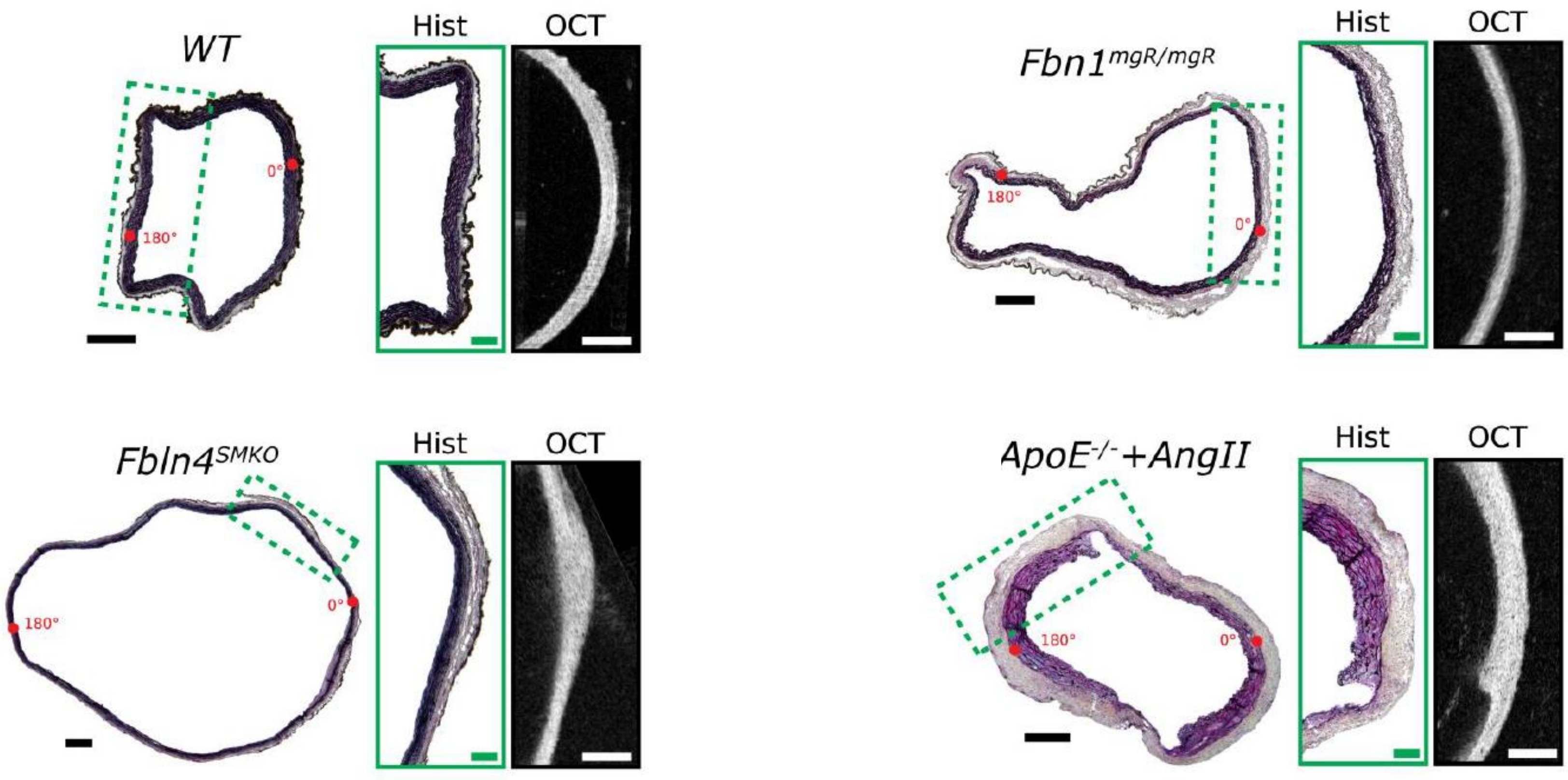
Correlation with tissue µstructure



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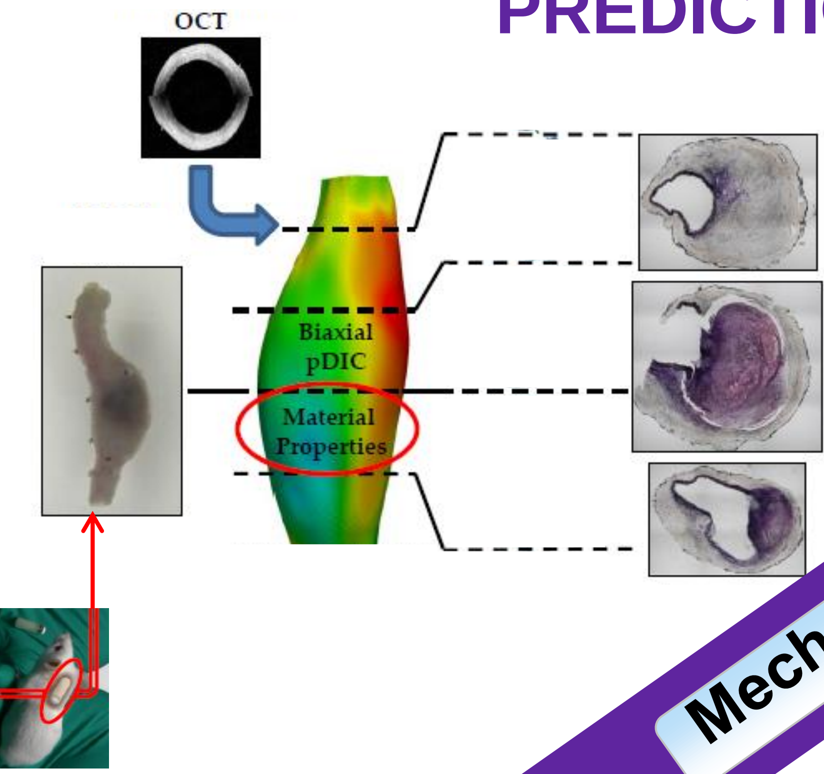
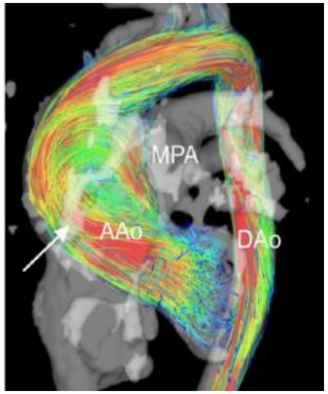
TOWARDS ATAA GROWTH PREDICTIONS



Clinical applications

Mechanobiology



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Development of mechanobiological models

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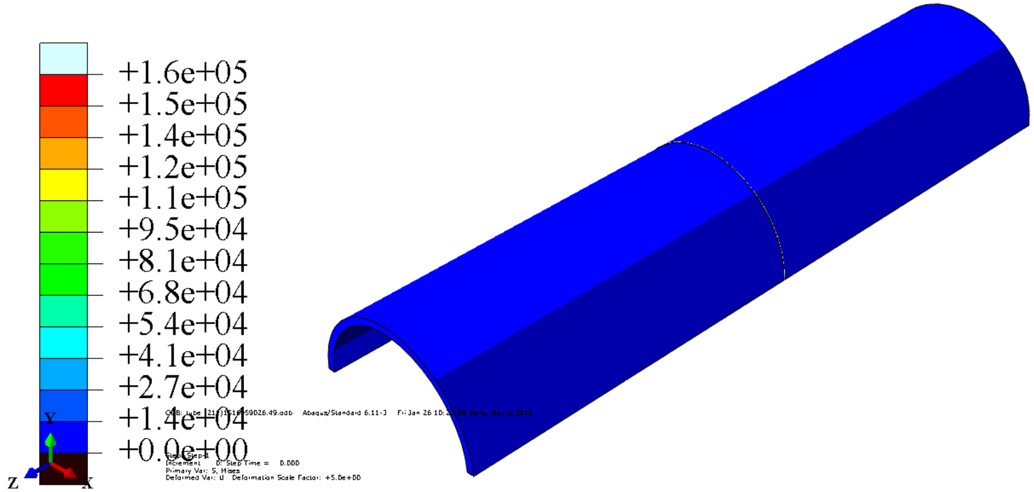
Vision

- **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.**



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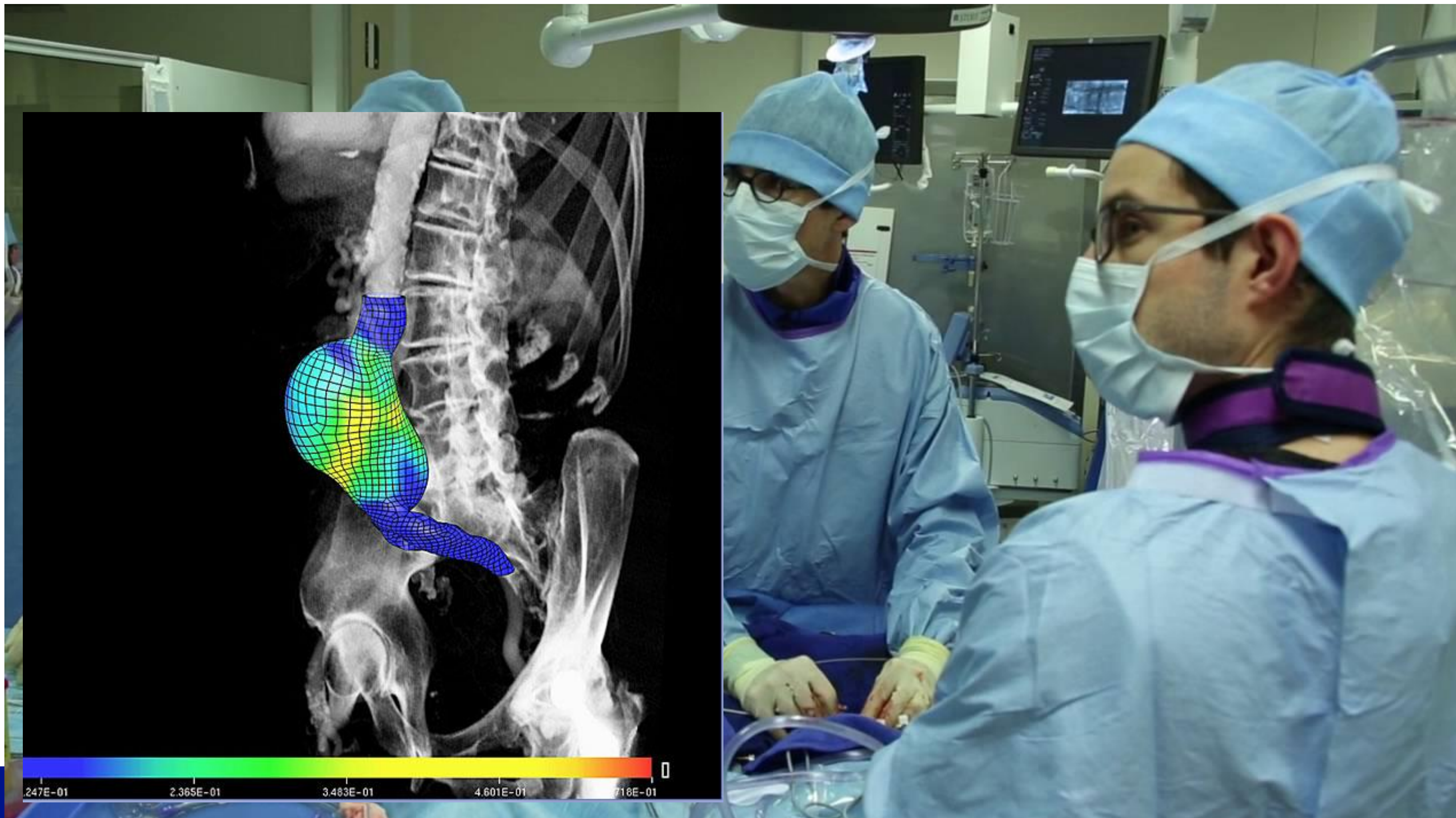
Computational mechanics in the OR for vascular surgery?

www.predisurge.com



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