IMPACT OF ELASTIN BIOMECHANICS ON PROXIMAL ARTERY STIFFNESS IN PULMONARY HYPERTENSION

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Objective:

•Determine how changes in the structure and material properties of elastin, resulting from pulmonary hypertension, affects proximal pulmonary arterial stiffness.

Background:

•Chronic pulmonary hypertension leads to vascular remodeling
- Increased flow resistance in distal arteries
- Elevated stiffness of proximal arteries
- Increased hemodynamic load exacerbates cardiac remodeling and eventual right ventricular failure

•Artery Morphology
- Tunica Intima: Innermost layer consisting of endothelial cells and basement membrane
- Tunica Media: Elastic layer comprised of smooth muscle, elastic lamellae and collagen
- Tunica Adventitia: Helically oriented collagen bundles provide strength and rigidity at high strain

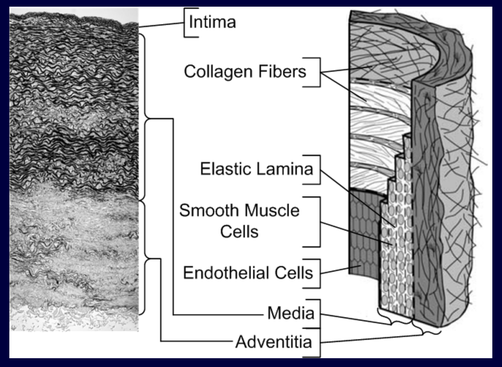

Fig. 1 Detail of artery morphology [Ref 1.]

Results:

•Morphology
- 28% average increase in tissue thickness due to hypertension
- 7% average increase in elastin content due to hypertension

• Material properties

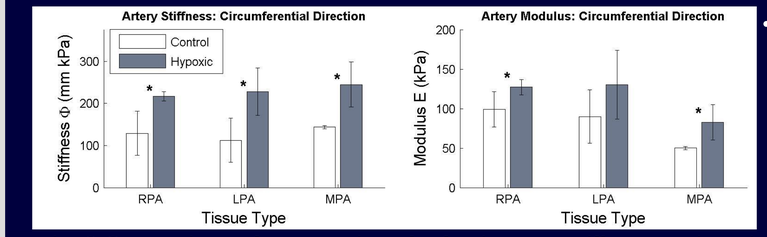

Fig. 2 Comparison of mean values for fresh artery stiffness and modulus

•Average results for arteries
- 46% increase in modulus (σ=13%, p = 0.02)
- 81% increase in stiffness (σ=23%, p << 0.05)
- Material properties calculated at 35% strain

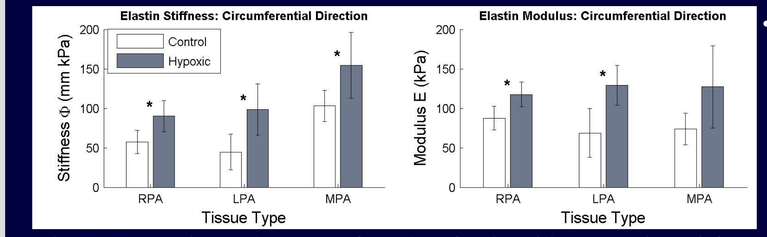

Fig. 3 Comparison of mean values for elastin stiffness and modulus

•Average results for elastin
- 85% increase in modulus (σ=45%, p << 0.05)
- 100% increase in stiffness (σ=62%, p = 0.02)
- 47% of arterial load is carried by elastin, at a minimum

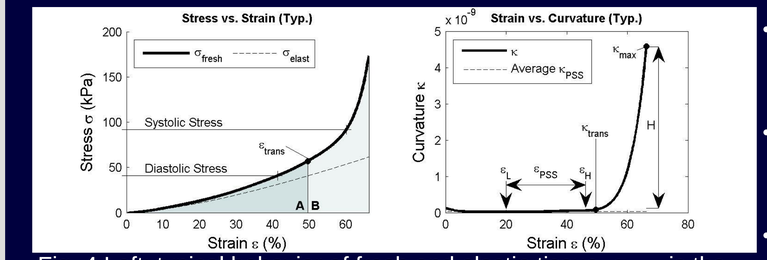

Fig. 4 Left: typical behavior of fresh and elastin tissue, σ_{trans} is the transition strain of transition from the elastin dominant (A) to collagen dominant (B) region. Right: typical curvature plot of fresh tissue

•Average diastolic strain
- 30% for control tissue
- 49% for hypertensive tissue

•Average systolic strain
- 58% for control tissue
- 69% for hypertensive tissue

•Average transition strain = 50%

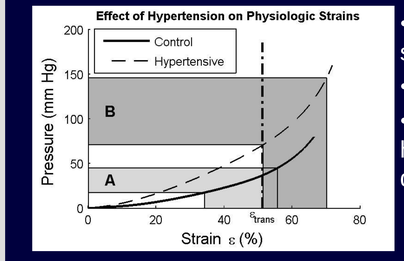

Fig. 5 Physiologic region of the stress strain curve. Control stress-strain region labeled (A), hypertensive region (B) .

- Increased pressures, due to hypertension, shifts physiologic strains to higher values
- The transition strain (ε_{trans}) is unaffected by hypertension
- Shift of the physiologic strain range to higher strains causes the hypertensive stress-strain response to operate outside the elastin dominant region
  - Increased strain stiffening leads to reduced physiologic strain range

Methods:

•Animal model
- 3-Control, 5-Hypertensive male Holstein calves (2-wks)
- Hypertension induced by hypobaric hypoxia, 2-wks, 430 mmHg

•Uni-axial stress-strain testing
- MTS, Insight 2, material testing system used to test stress-strain response of circumferential tissue sections under uni-axial load

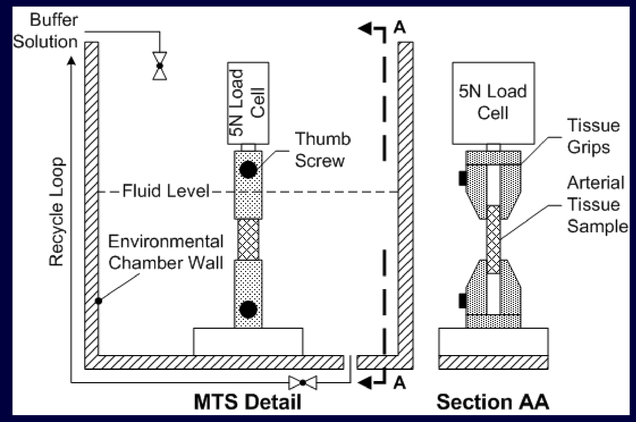

Fig. 2 Detail of material testing apparatus

•Elastin Purification
- Elastin was purified from arterial material using CNBr-formic acid digestion [Ref. 2]

•Morphology
- Artery thickness measured at with digital calipers
- Area fraction determined with image processing of VVG-elastin stained tissue sections (Matlab)

Conclusions:

•Mechanobiological adaptations of the continuum and geometric properties of elastin, in response to pulmonary hypertension, significantly elevate the circumferential stiffness of proximal pulmonary arterial tissue.

• Hypertension elevates the physiologic strain and causes the stress-strain response to operate outside the elastin-dominant stress-strain region. Although this results in increased collagen recruitment at systole, diastolic stress remains elastin-dependent.

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2.) Lu, Q., K. Ganesan, et al. (2004). "Novel porous aortic elastin and collagen scaffolds for tissue engineering." Biomaterials **25**(22): 5227-37.