Effect of Collagen Cross-linking Therapy on Ascending Aortic Aneurysmal Tissue: An ex vivo Randomized Study

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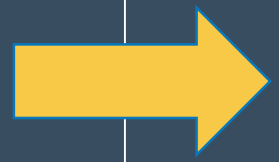
Treatment Gap:
No Prophylaxis for Ascending Aortic Aneurysm and Dissection

Proposal: ***Can we strengthen aortic tissue by enhancing Collagen Crosslinking?***

Rationale: Collagen Crosslinking

- FDA-approved application of UV-light with photosensitizer (riboflavin) to *cornea*
- 1 ex-vivo study performed on *porcine* aortas



Increases biomechanical strength

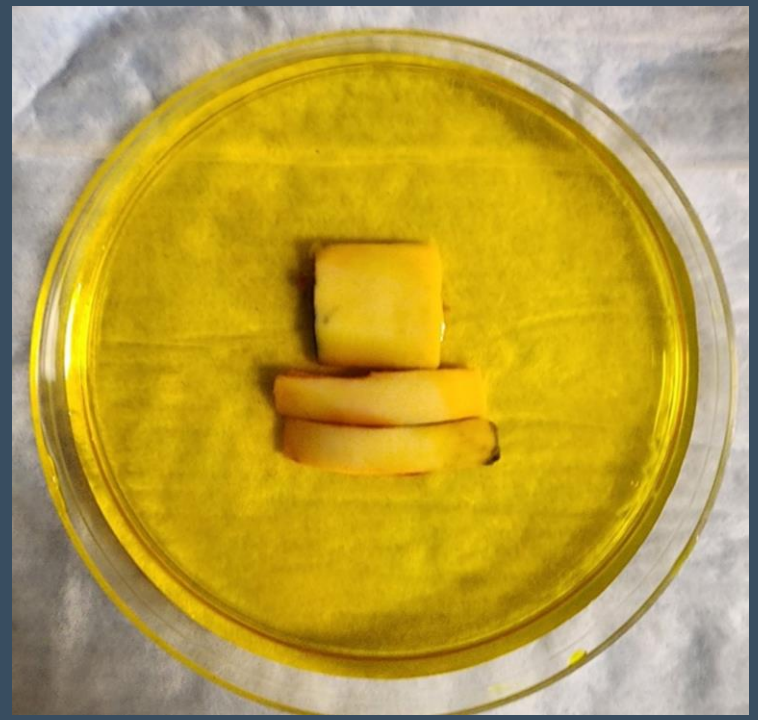
Objectives

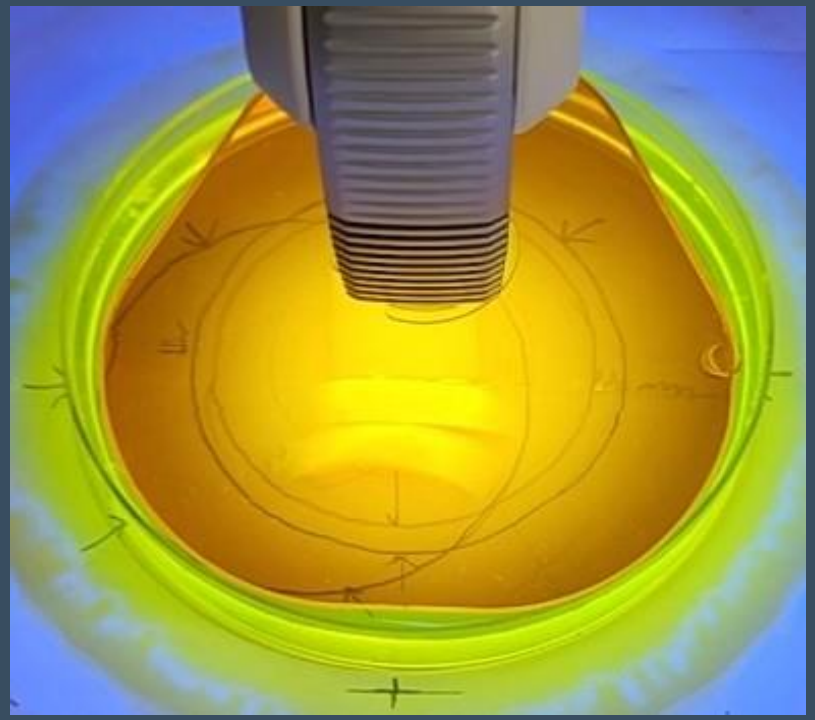
1. Assess treatment effect of UV irradiation and riboflavin on aortic tissue mechanics
2. Investigate correlation between delamination and biaxial mechanical testing

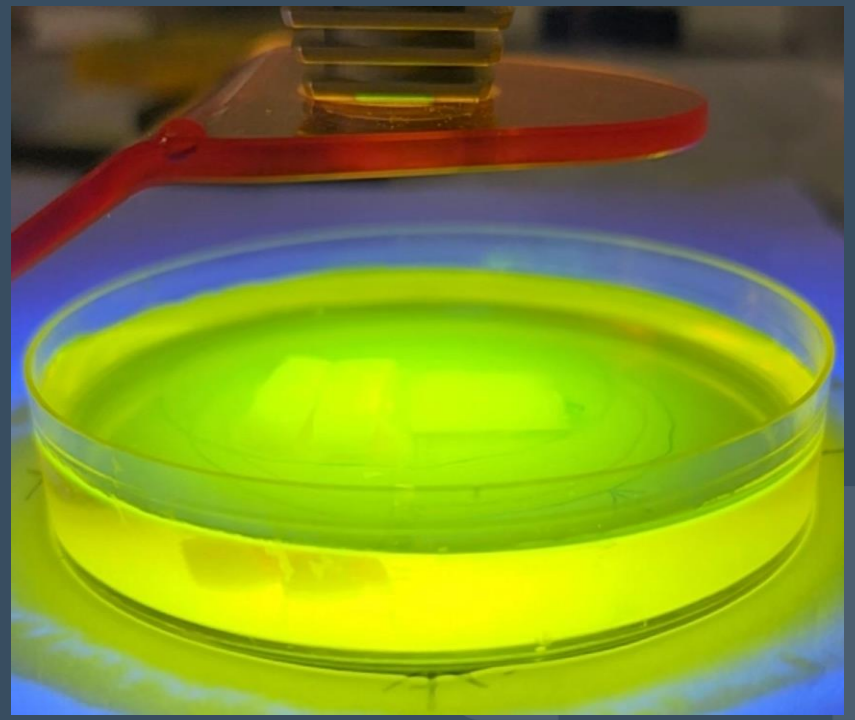
Collagen Cross-linking Therapy

0.1% Riboflavin (w/v) solution for 30 minutes

Irradiance of 45 mW/cm2 with 365nm UV-A light for 10 minutes

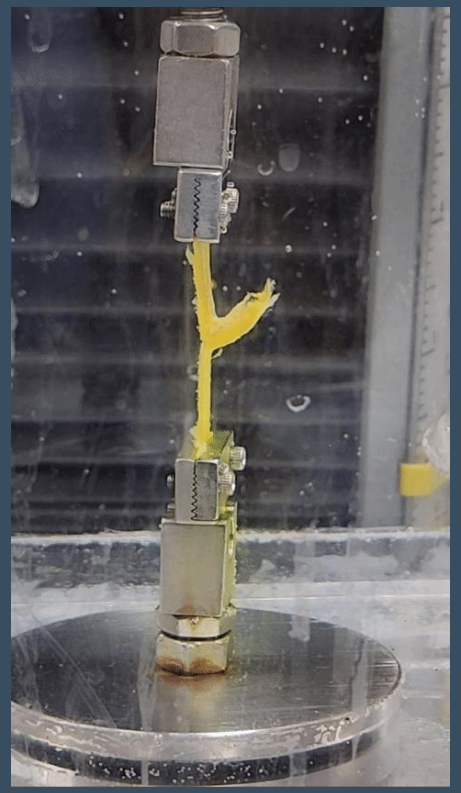




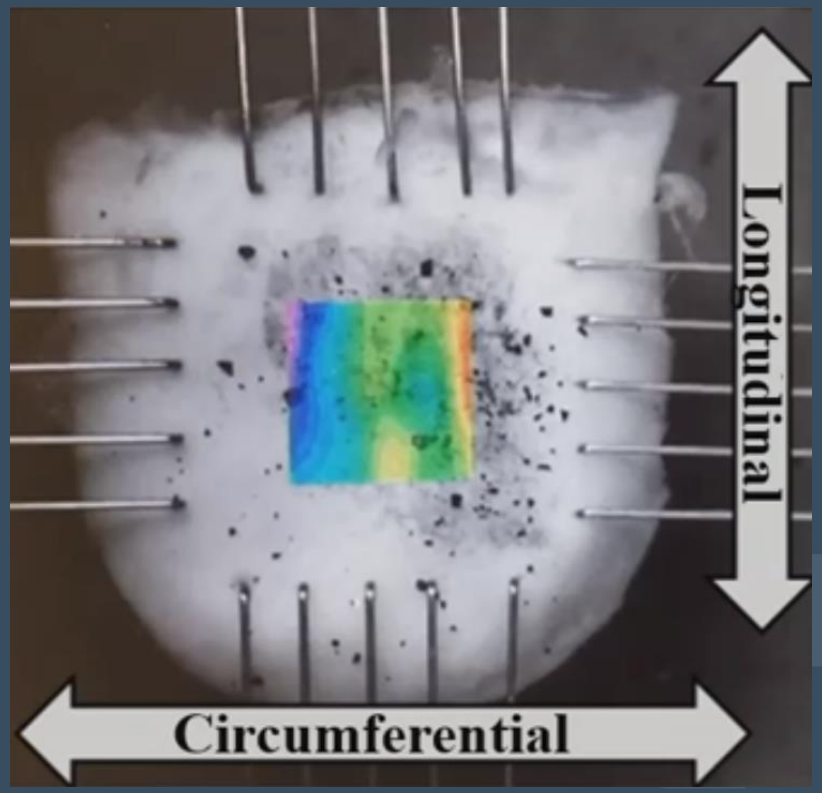


Mechanical Testing Approaches

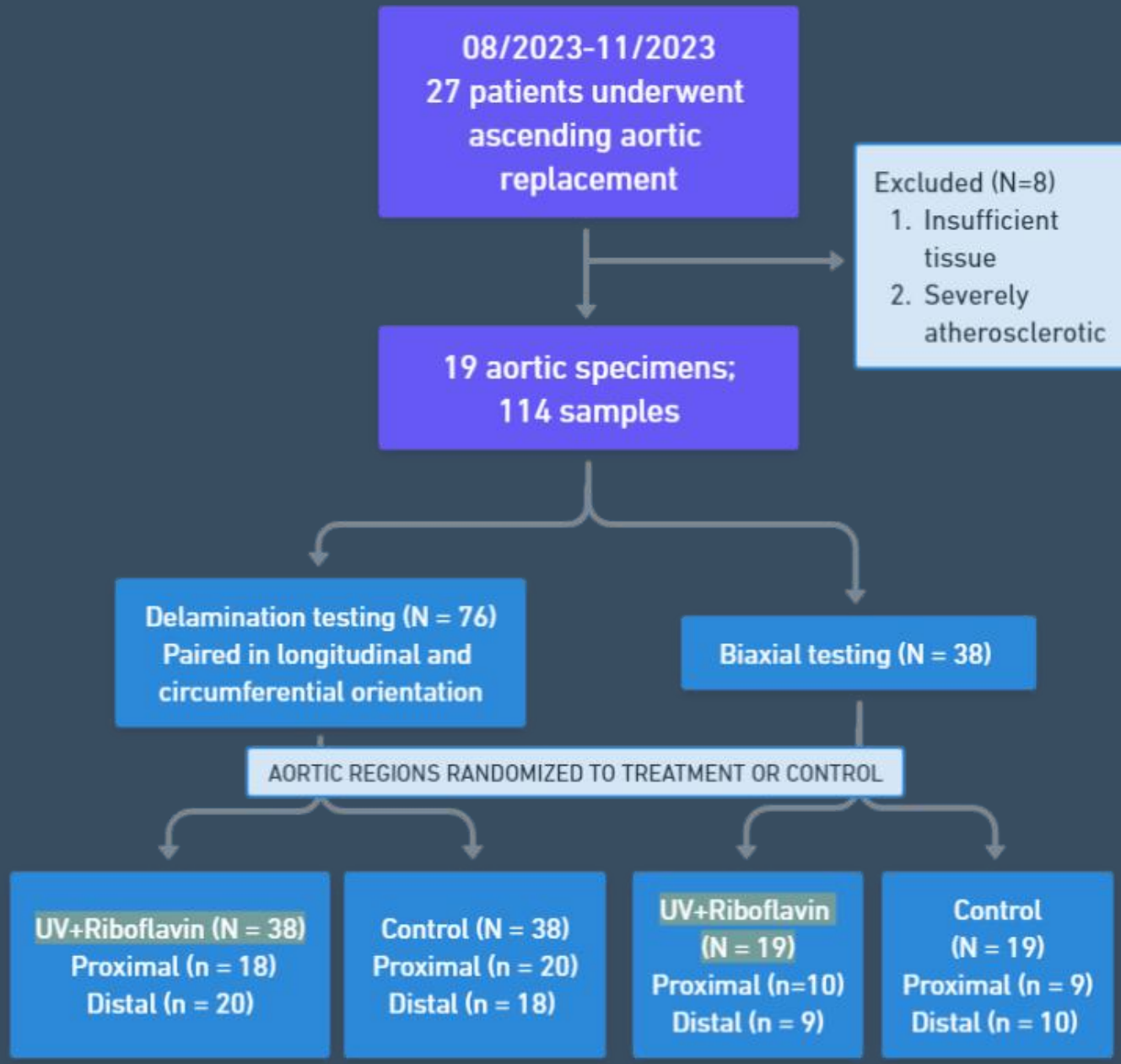
Delamination Testing = Simulate Dissection



Biaxial Testing = Physiologic Deformations



Study Design and Outcomes



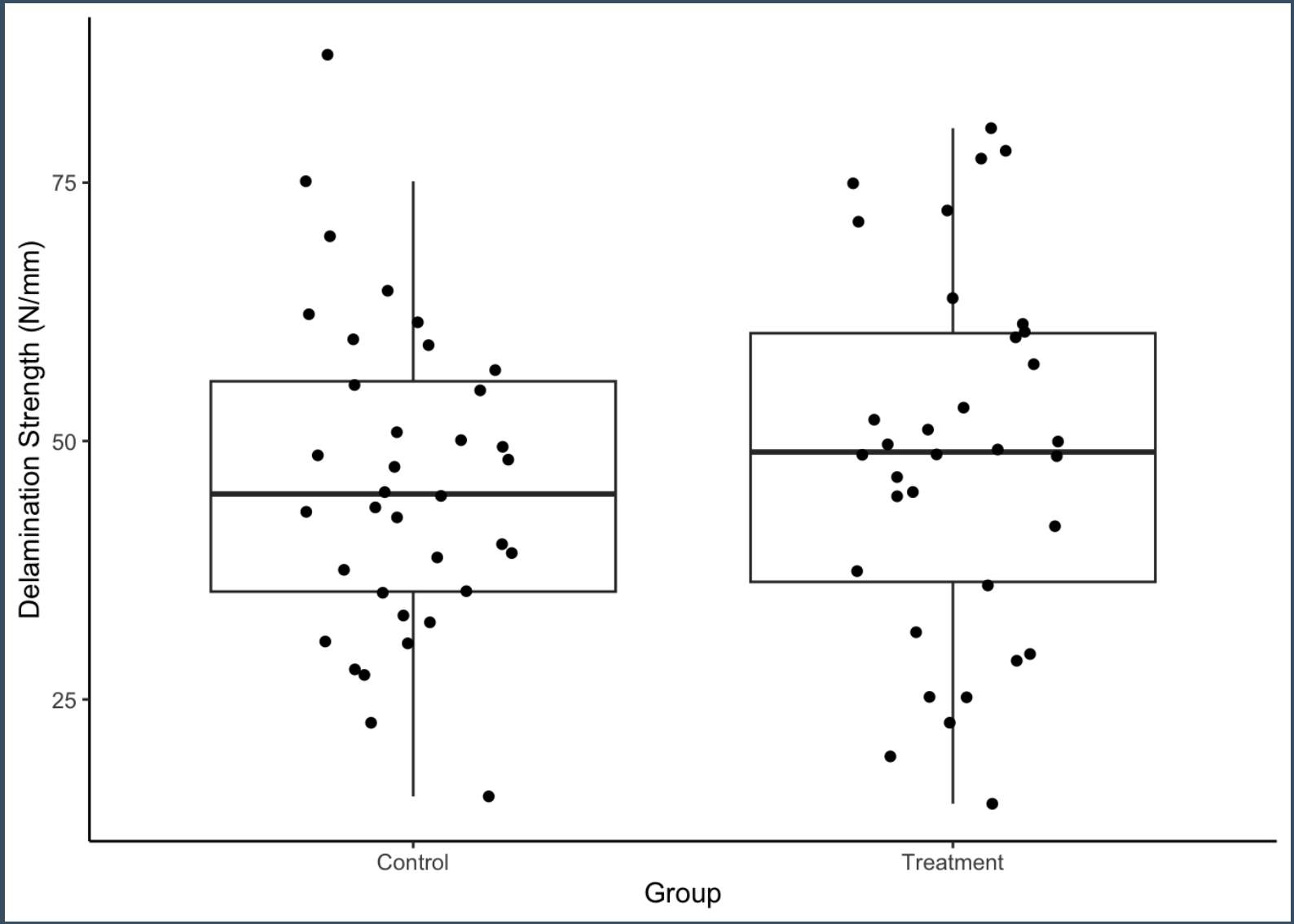
Delamination Outcome:

1. Delamination Strength (mN/mm)

Biaxial Mechanical Outcomes:

1. Stretch (mm/mm, unitless)
2. Stress (kPa)
3. Stiffness (kPa)
4. Strain-Energy Density (kPa)

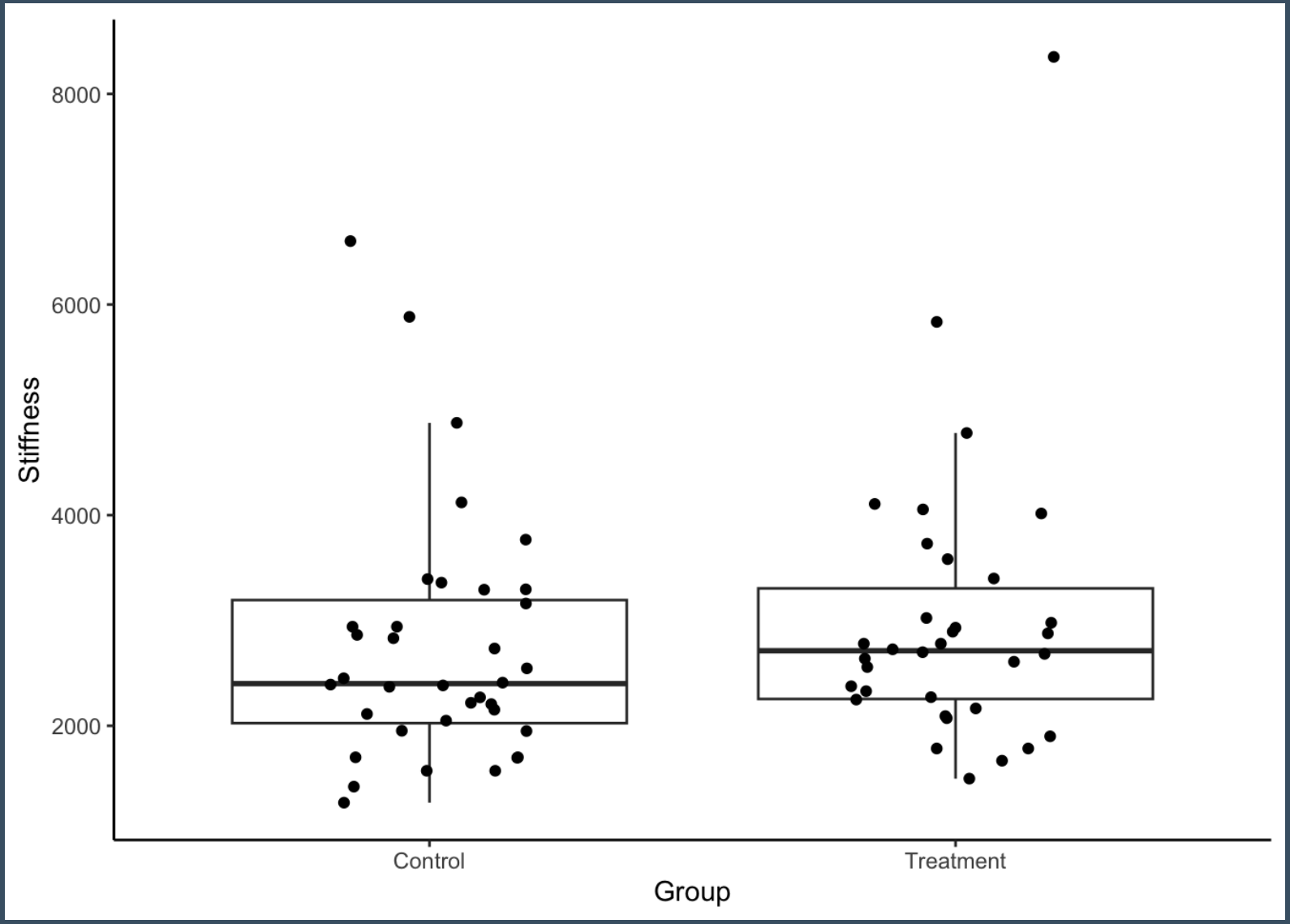
Delamination Strength (N/mm): Unadjusted



Results

P=0.8

Biaxial Stiffness (kPa): Unadjusted



Results

P=0.2

Multivariate Analysis: Significant Associations

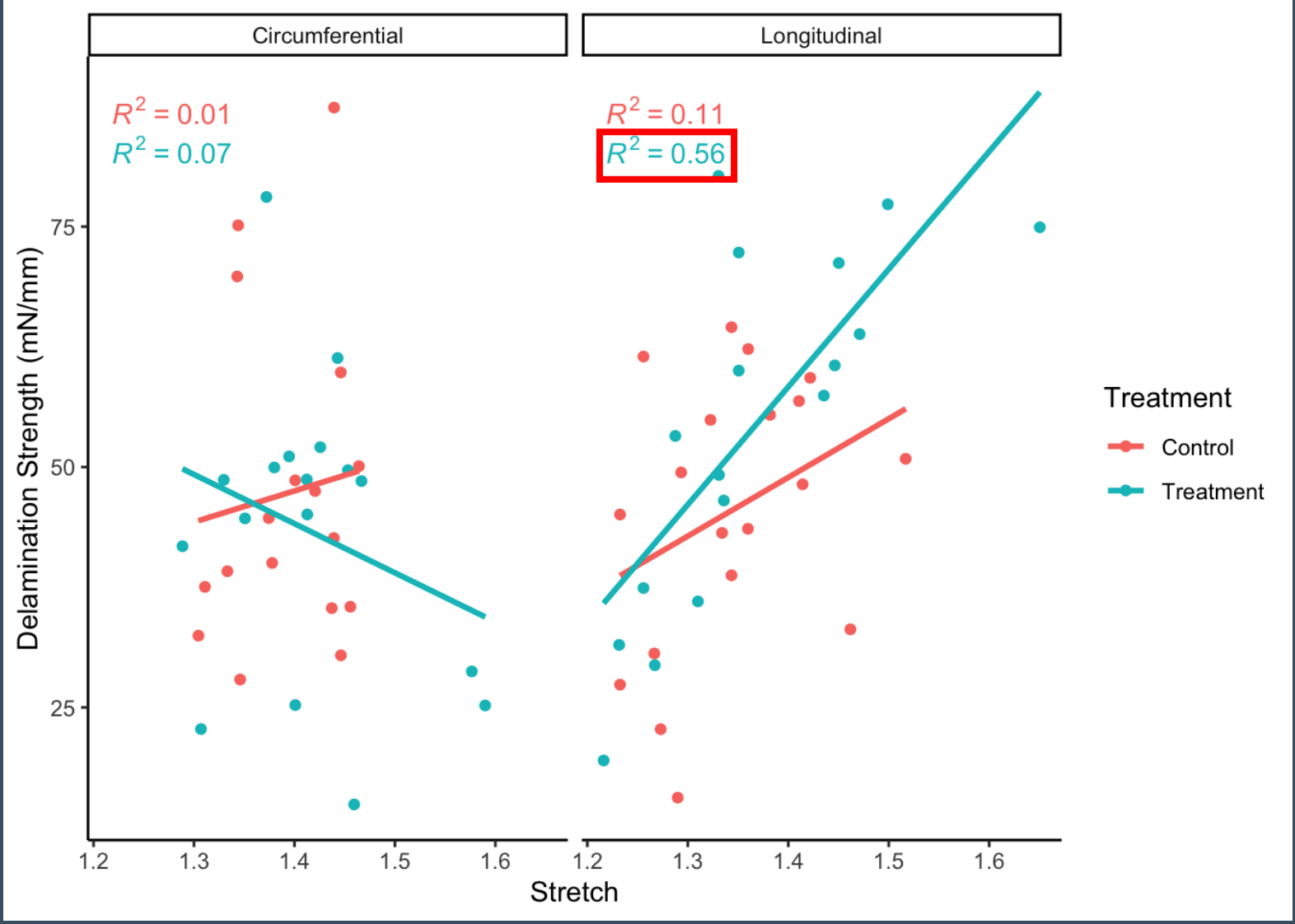
Results

Mechanical Outcome	Higher	Lower	Estimate, *P*
Delamination Strength (mN/mm)	Younger	Older	β=-0.7,P=.01
Stretch (mm/mm, unitless)	Younger	Older	β=-0.006, P<.001
	Circumferential	Longitudinal	β=-0.05, P<.001
Stiffness (kPa)	Circumferential	Longitudinal	β=-916, P<.001
	Proximal region	Distal region	β=616, P<.001
Stress (kPa)	Younger	Older	β=-3.8, P<.01
	Circumferential	Longitudinal	β=-45, P<.001
	Proximal region	Distal region	β=57, P<.001
Strain-energy density (kPa)	Younger	Older	β=-1.5, P<.001
	Proximal region	Distal region	β=7.1, P<.001

Predictors of tissue mechanics were **age, orientation, and region**

Delamination Strength and Biaxial Stretch Correlate

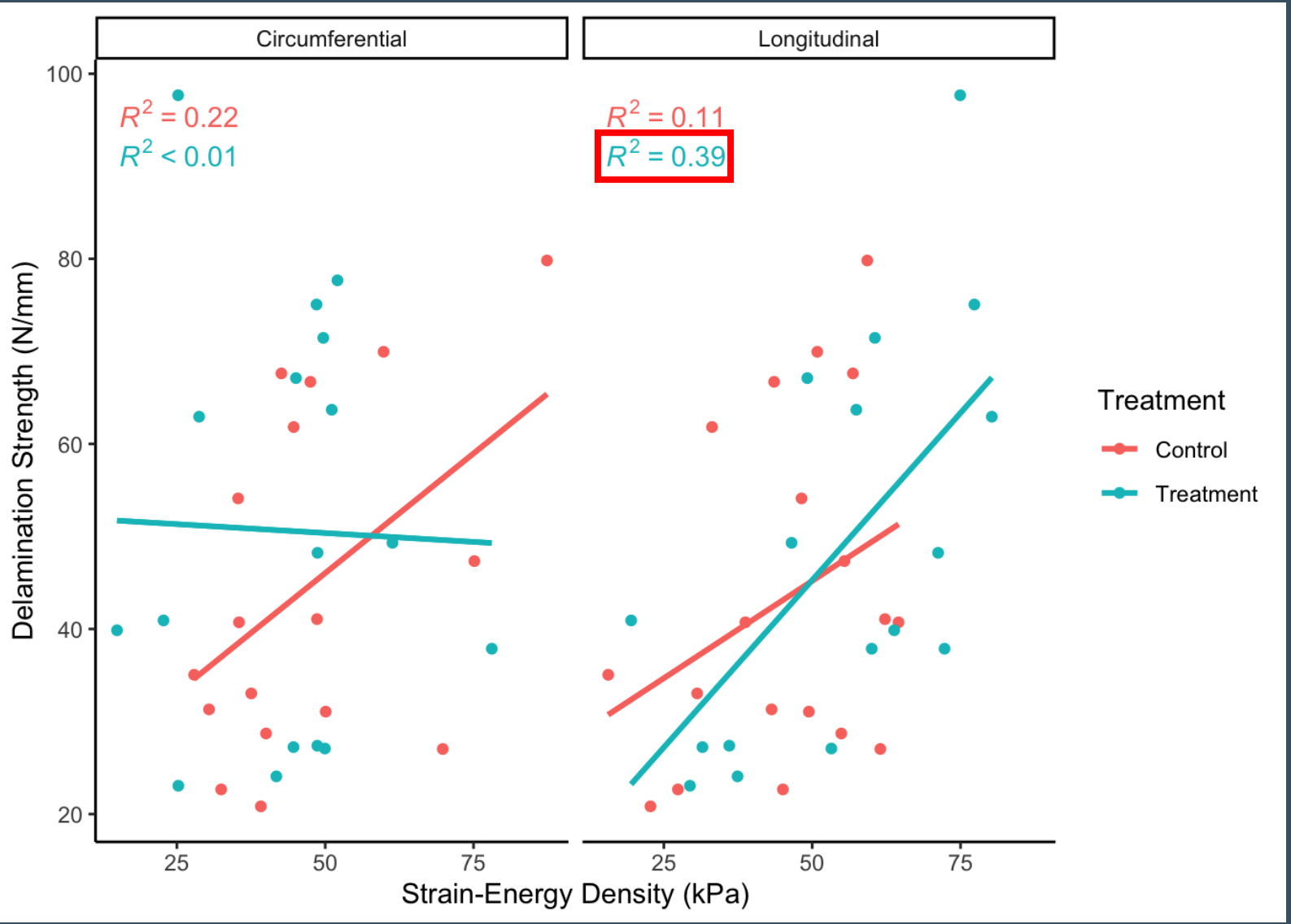
Results



Tissue with higher cross-over stretch requires more force to propagate a dissection plane

Delamination Strength and Strain-Energy Density

Results



Tissue with higher energy storage efficiency needs more force to propagate a dissection plane

Conclusions

1. No treatment effect observed on ascending aortic aneurysmal tissue with UV irradiation and riboflavin
2. Tissues with higher Strain-Energy Density require more force to delaminate. Future therapies should assess these metrics to determine treatment effectiveness.
3. Transmural treatments should be investigated to prevent aneurysmal degeneration or dissection, as topical therapies are unlikely to affect clinical aortic mechanics.