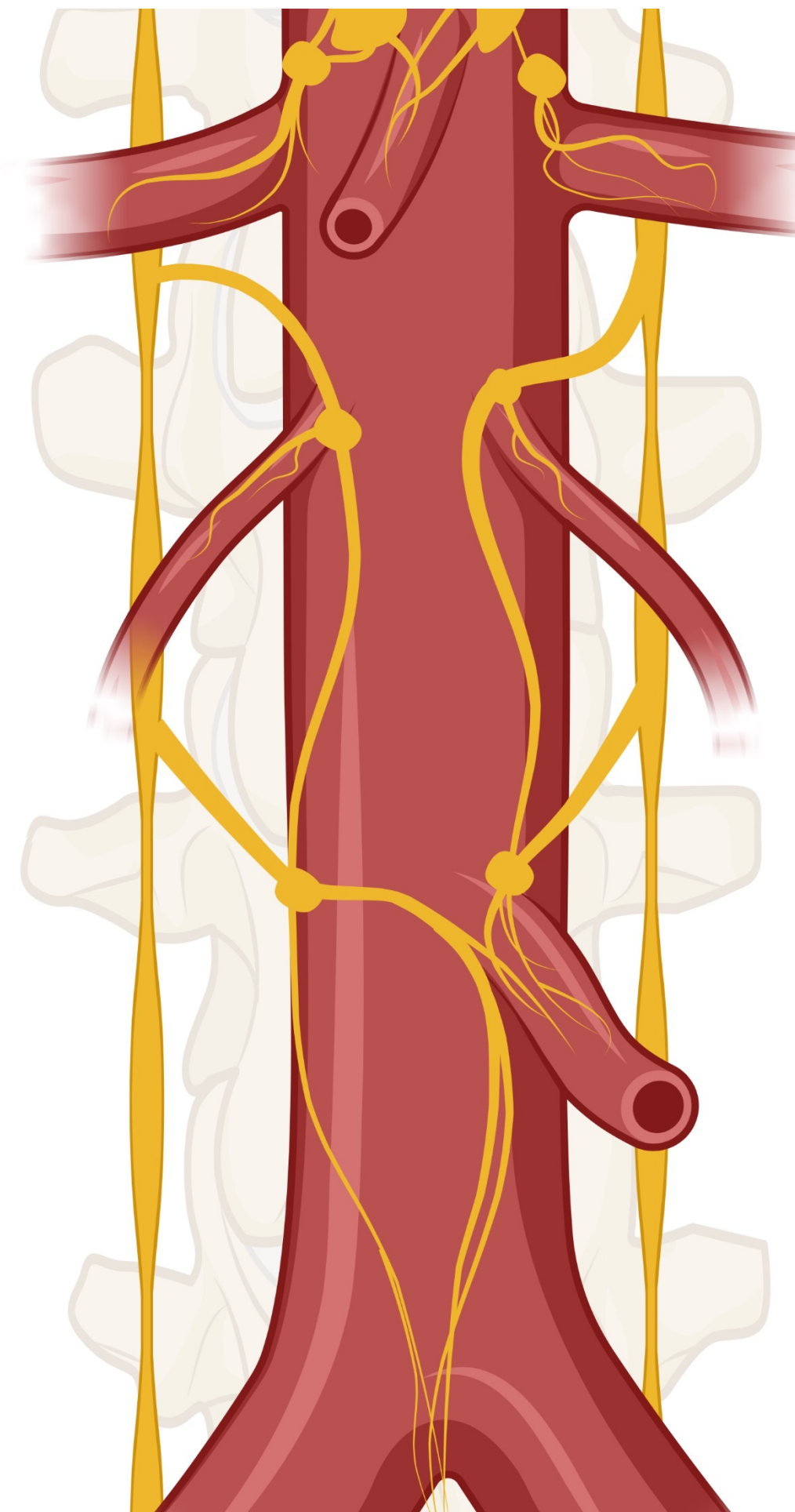


Introduction

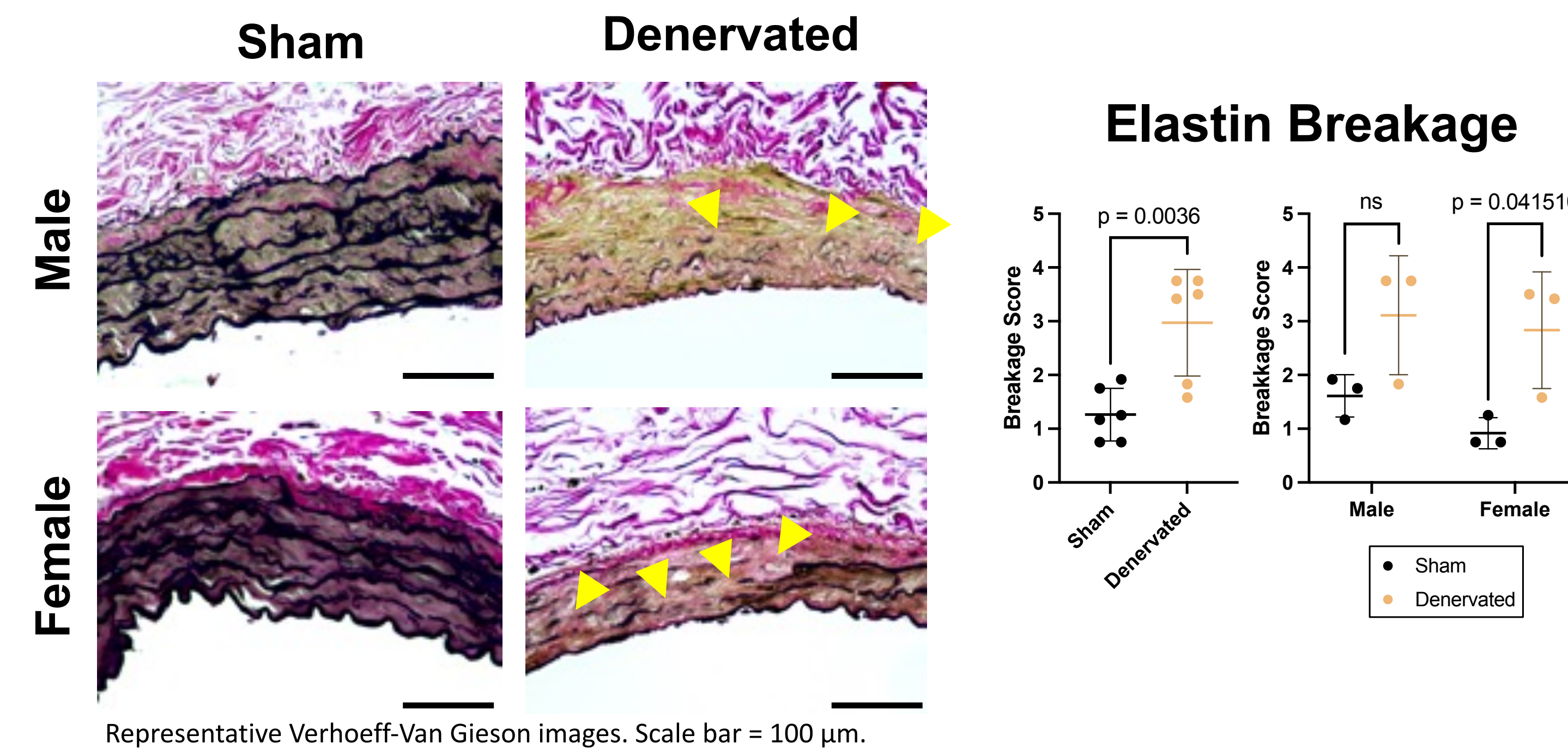
- Previous studies have identified sympathetic nervous system (SNS) signaling as a critical regulator of arterial wall homeostasis with potent effects on inflammation and vascular remodeling. [1]
- Our prior investigation of decellularized aortic conduits was marked by significant pathologic remodeling, perhaps underpinned by lack of innervation. [2] Sympathetic dysfunction may contribute to the pathogenesis of aortic diseases, including occlusive disease, aneurysms, and related vascular complications.

HYPOTHESIS:

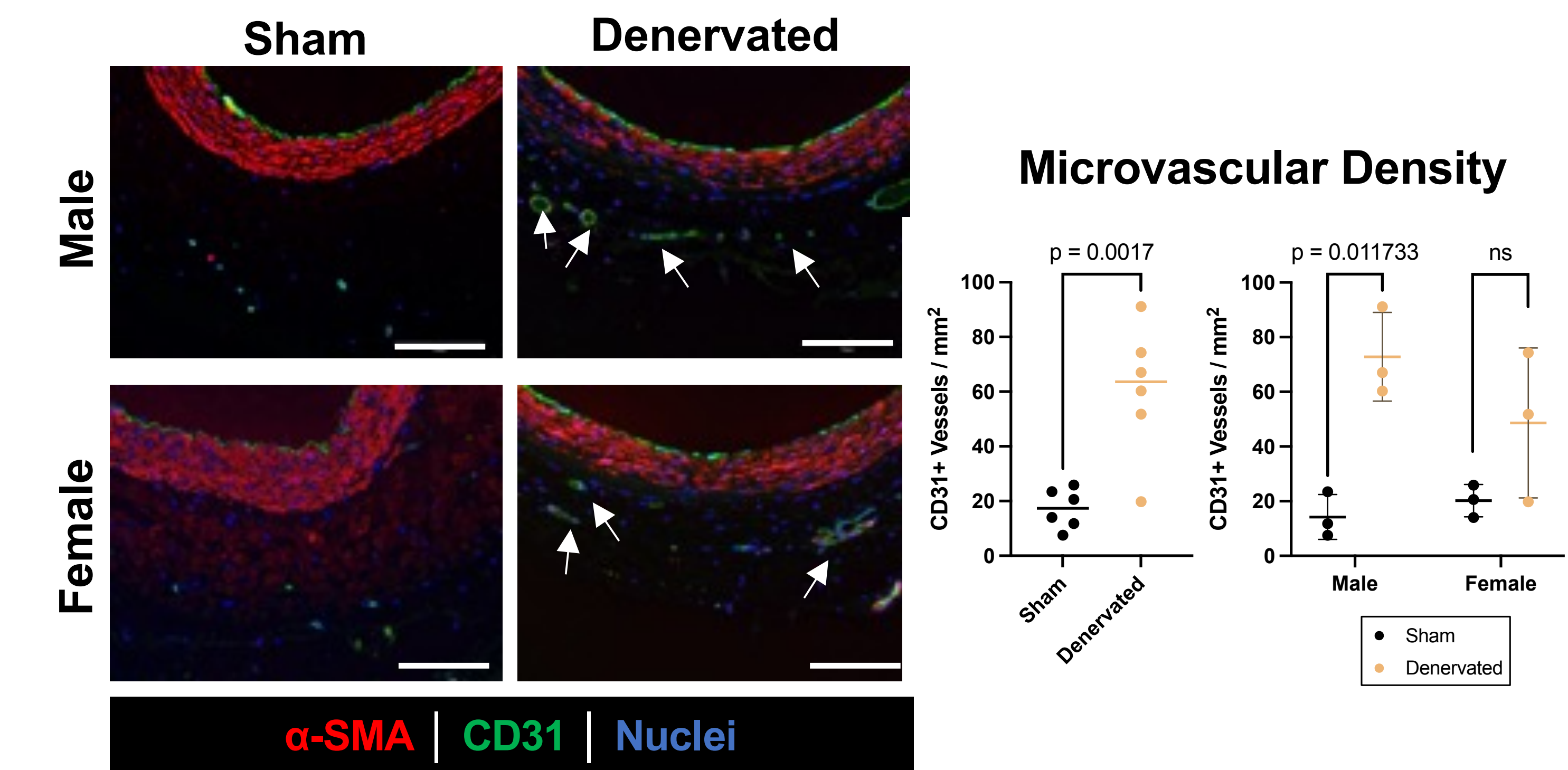
Dysfunction of aortic sympathetic innervation is a critical contributor to pathologic remodeling and aortic morphology on extended follow-up.



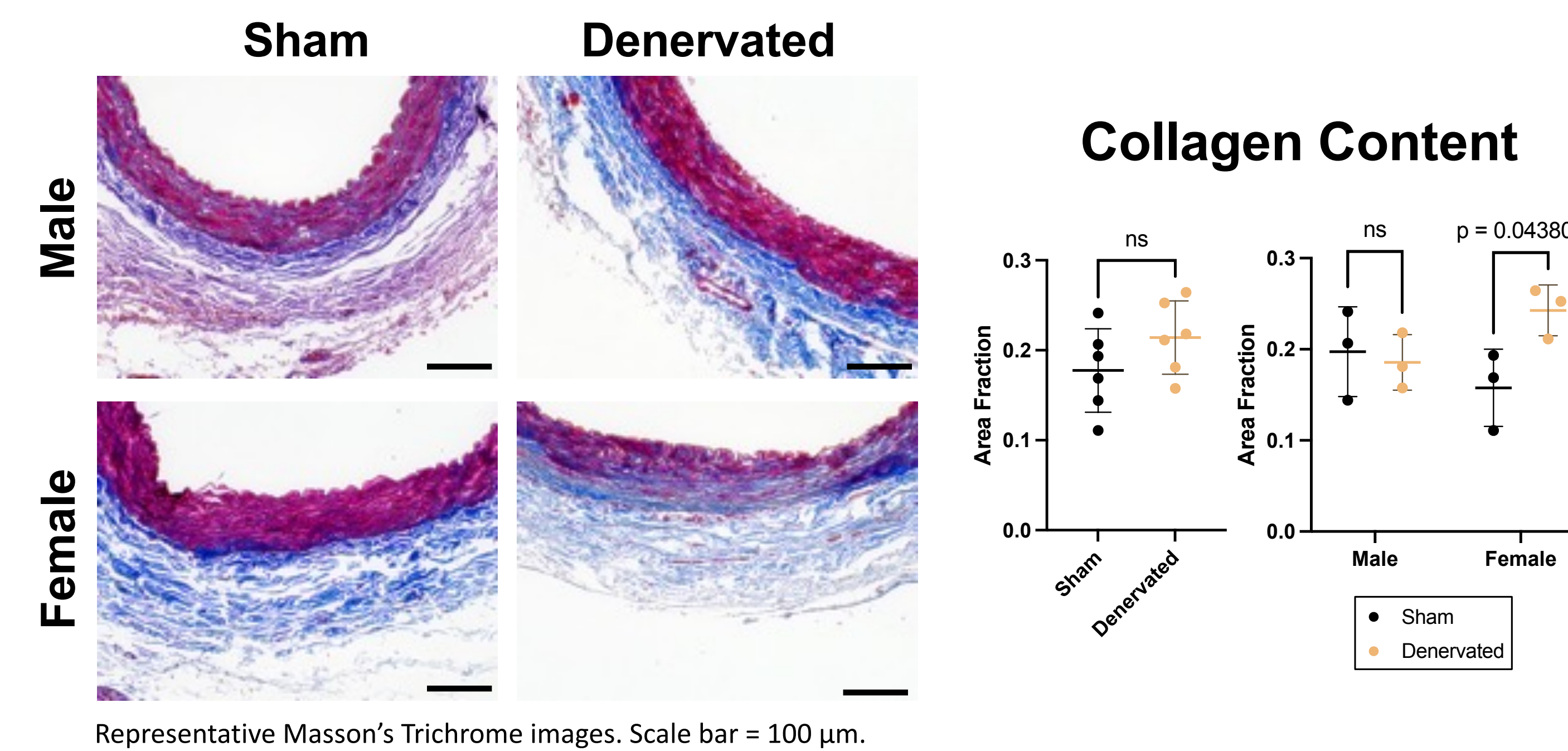
Phenol denervated aortas demonstrated significantly increased elastin breakage scores versus sham controls.



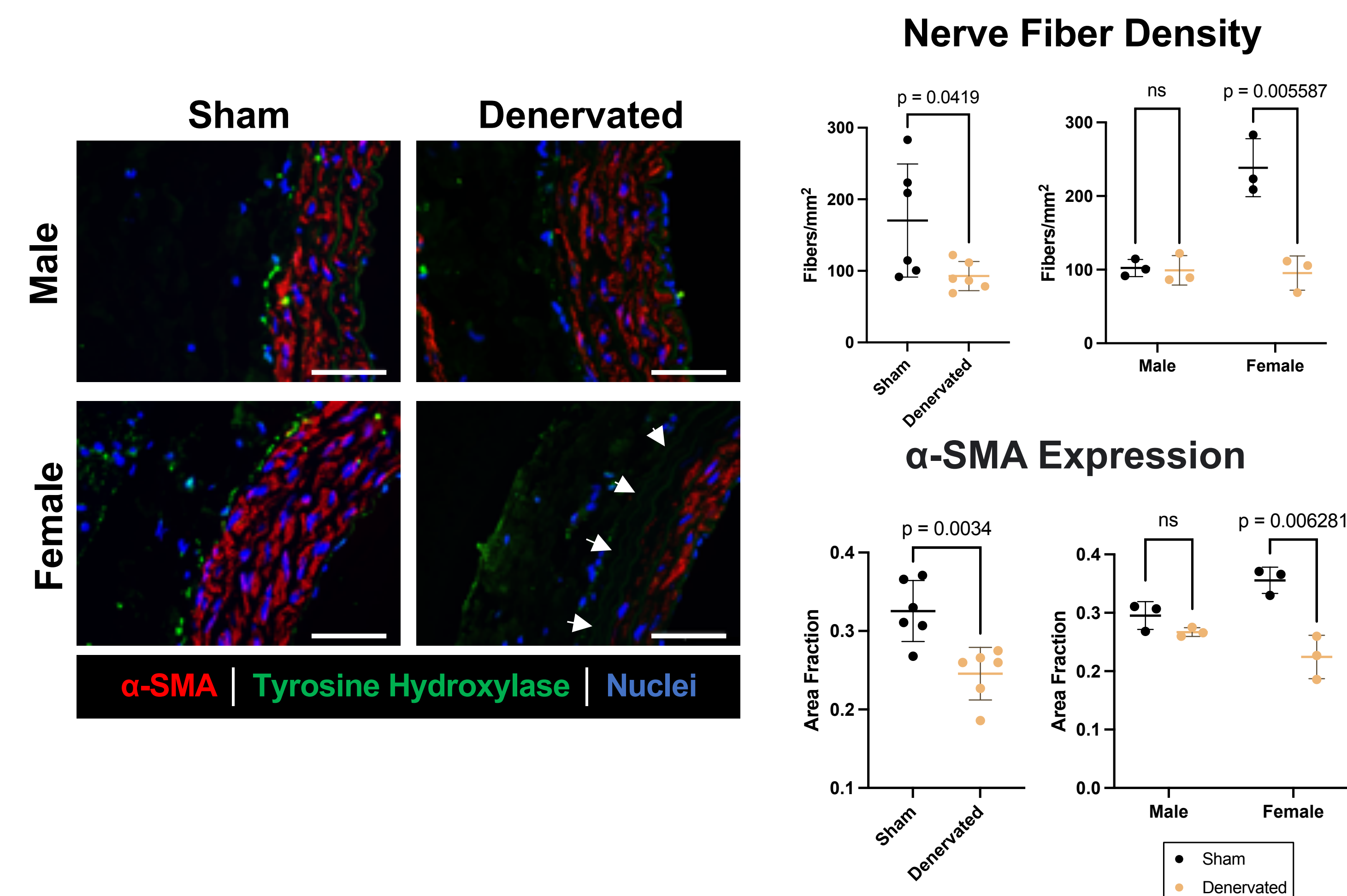
Significant aortic adventitial angiogenesis is observed after phenol denervation versus sham control.



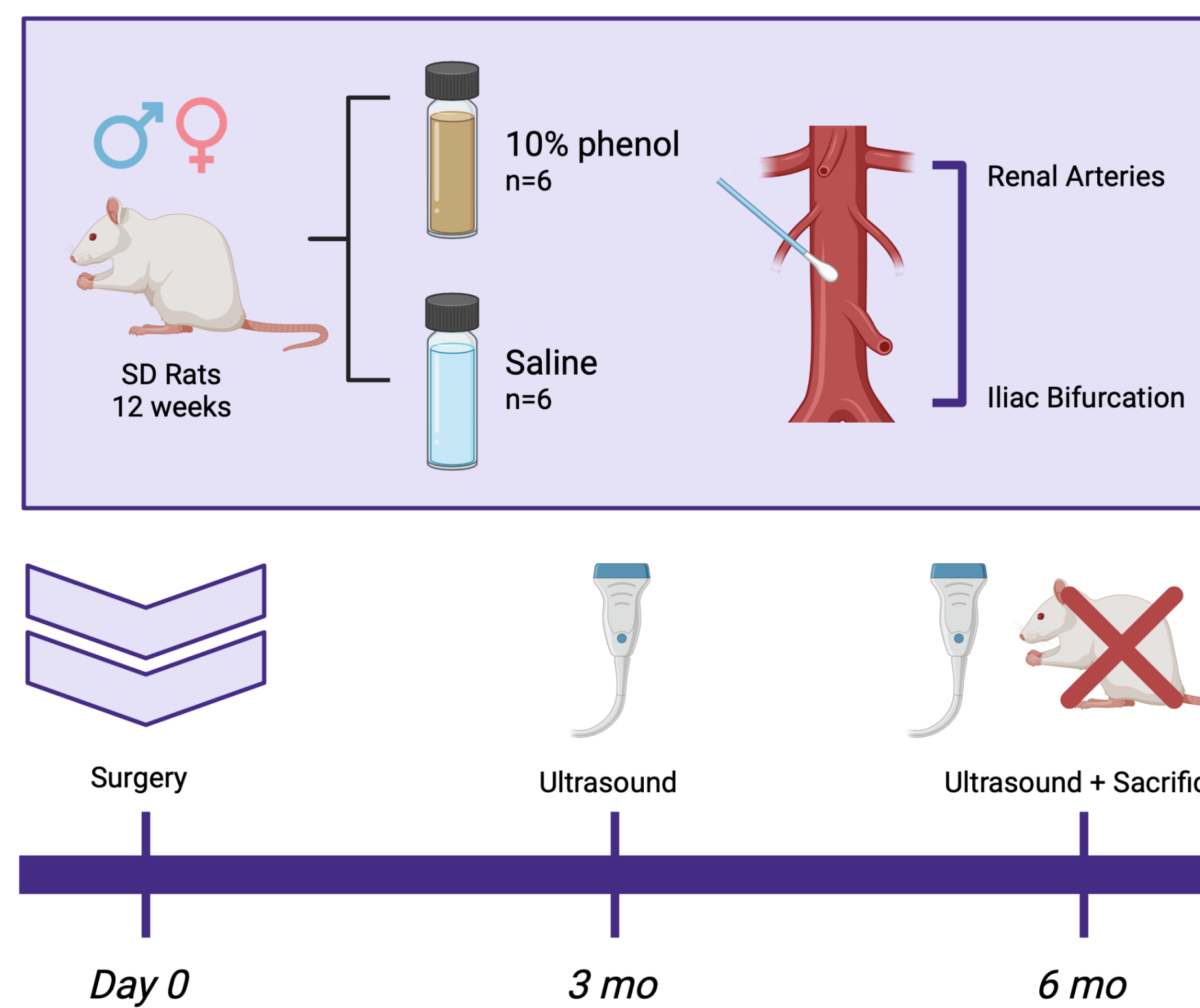
Adventitial and medial collagen content of aortas was similar between groups. Sex stratification indicated denervated females exhibited increased collagen content versus sham control.



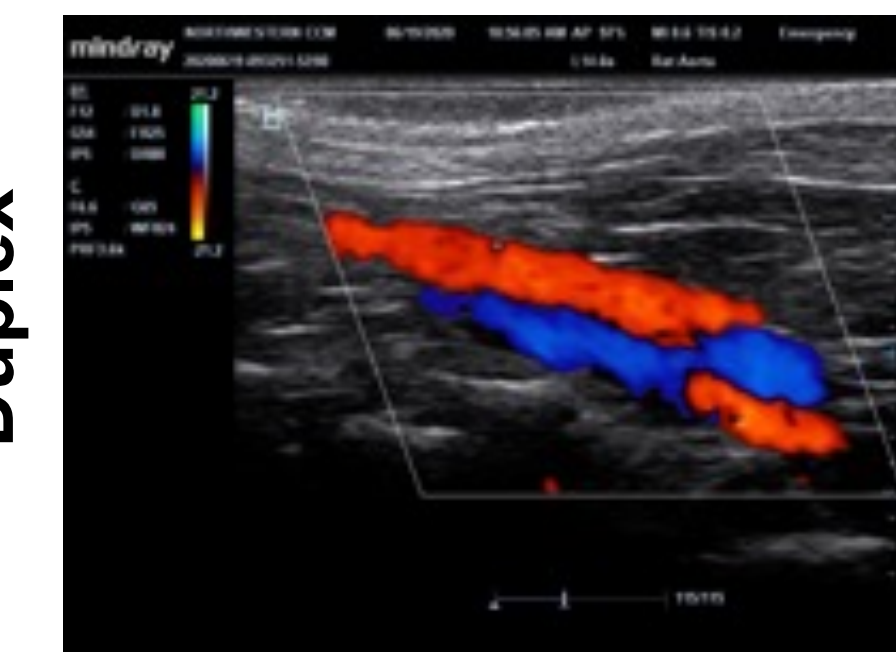
Denervated aortas revealed a significant decrease in nerve fiber density and medial alpha smooth muscle actin (α -SMA).



Methods



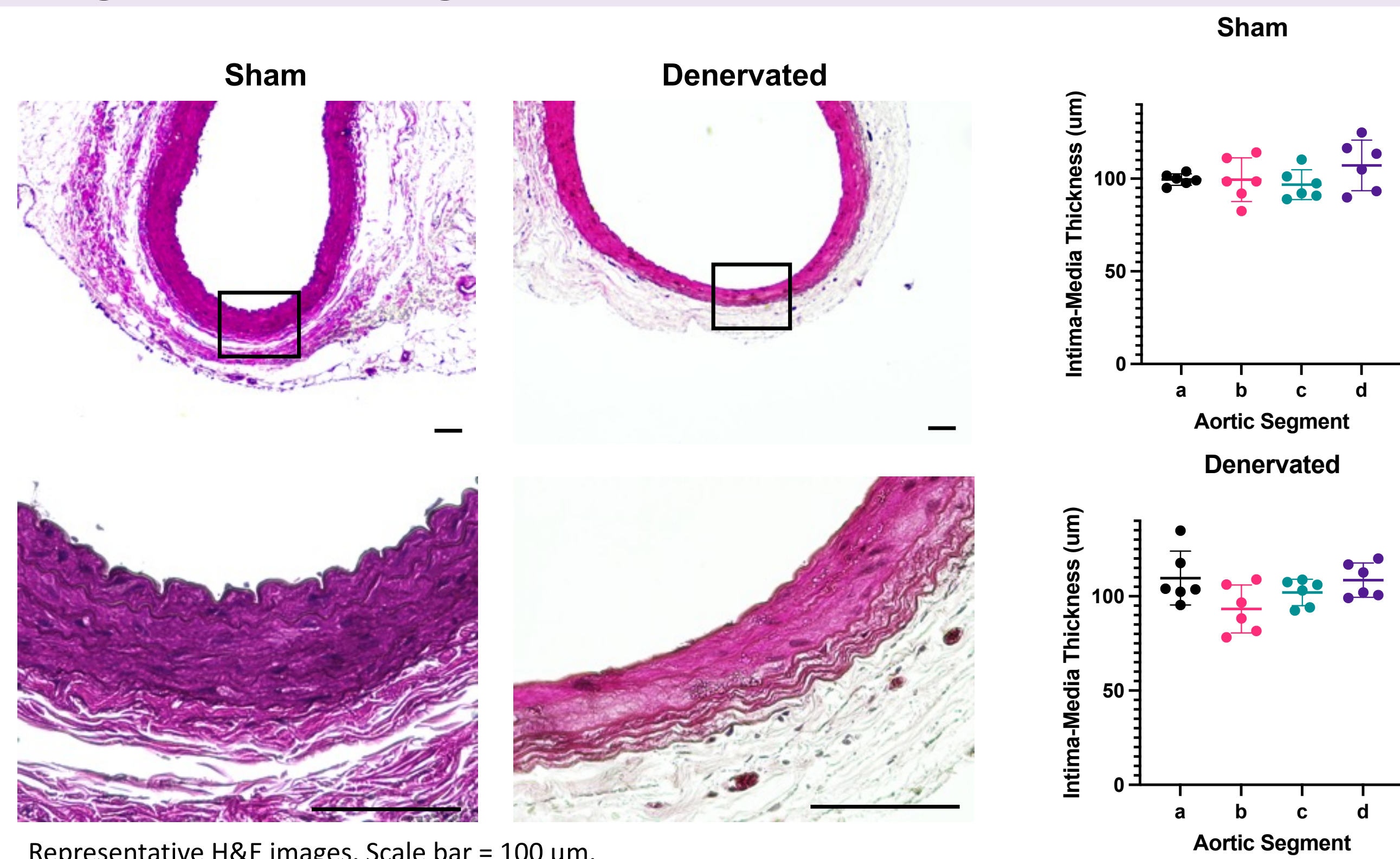
Duplex



- Aortas were divided into four segments from lowest renal artery to iliac bifurcation (a-d).
- Tissue analysis conducted encompassing morphology, histology, & immunohistochemistry.

Results

Denervated aortas exhibited variations in intima-media thickness with b-segment exhibiting the lowest intima-media thickness.



Conclusions

- 1. Extracellular Matrix Remodeling:** Topical phenol-based denervation results in loss of elastin morphology with increased elastin breakage scores
- 2. Nerve Fiber Density:** Denervated aortas demonstrate significant loss of sympathetic nerve fiber density on extended follow-up
- 3. Loss of Vascular Smooth Muscle Cells:** Significant loss of α -SMA and medial cellular density are observed after phenol denervation
- 4. Adventitial Angiogenesis:** Marked angiogenesis is observed within the adventitia after phenol-based denervation
- 5. Sexual Dimorphism:** Dimorphic response to phenol-based denervation include collagen content, baseline nerve fiber density, and medial vascular smooth muscle cell loss

IMPACT:

Our investigation revealed sympathetic denervation induced morphologic and histologic features partially shared with aortic pathologies. These findings underscore the importance of integrating sympathetic innervation in vascular disease states with additional consideration of the SNS as a therapeutic target for cardiovascular disease broadly.

Future Directions

- Investigate the role of the SNS in pathologic animal models
- Explore strategies to modulate aortic innervation as a therapy
- Expand investigation to other aortic pathologies, such as type B aortic dissection

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- [1] Cañes L, Alonso J, Ballester-Servera C, Varona S, Escudero JR, Andrés V, et al. Targeting Tyrosine Hydroxylase for Abdominal Aortic Aneurysm: Impact on Inflammation, Oxidative Stress, and Vascular Remodeling. *Hypertension*. 2021;78(3):681-92.
- [2] Jiang B, Suen R, Wang JJ, Zhang ZJ, Wertheim JA, Ameer GA. Vascular scaffolds with enhanced antioxidant activity inhibit graft calcification. *Biomaterials*. 2017;144:166-75.