

# The Effect of Phosphodiesterase Inhibitors on BAPN-Induced Aortic Dissection

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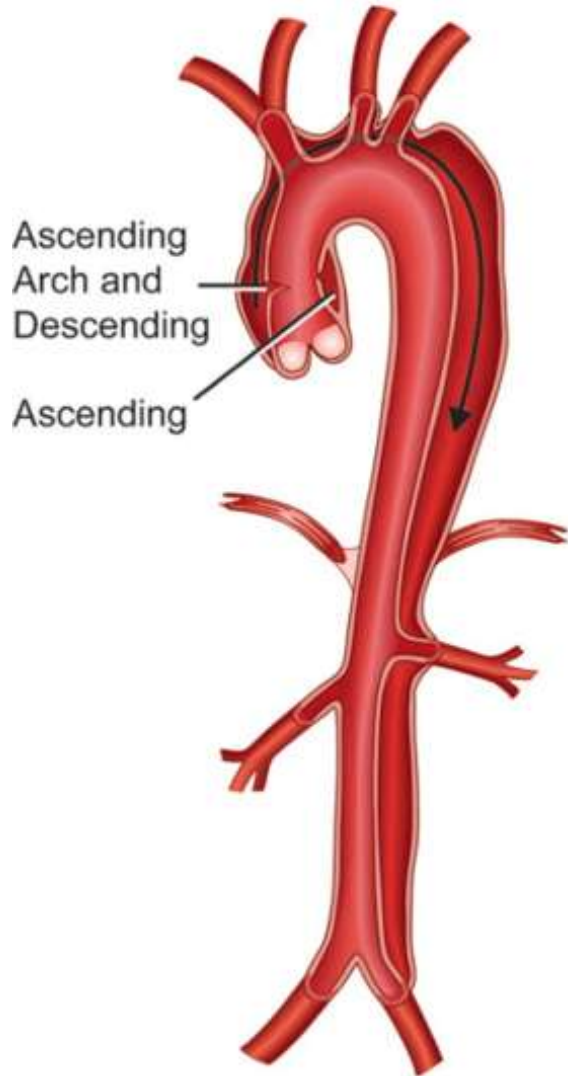
University of Kentucky



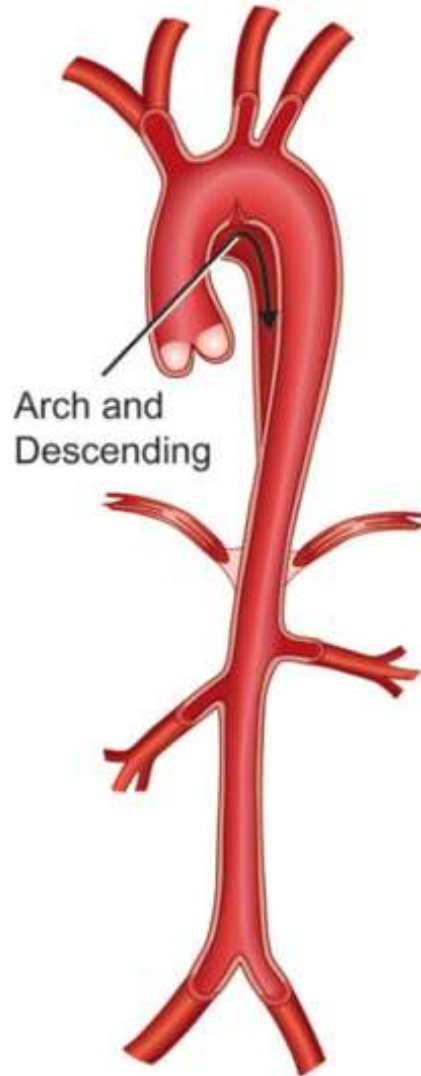
@SamTyagiMD



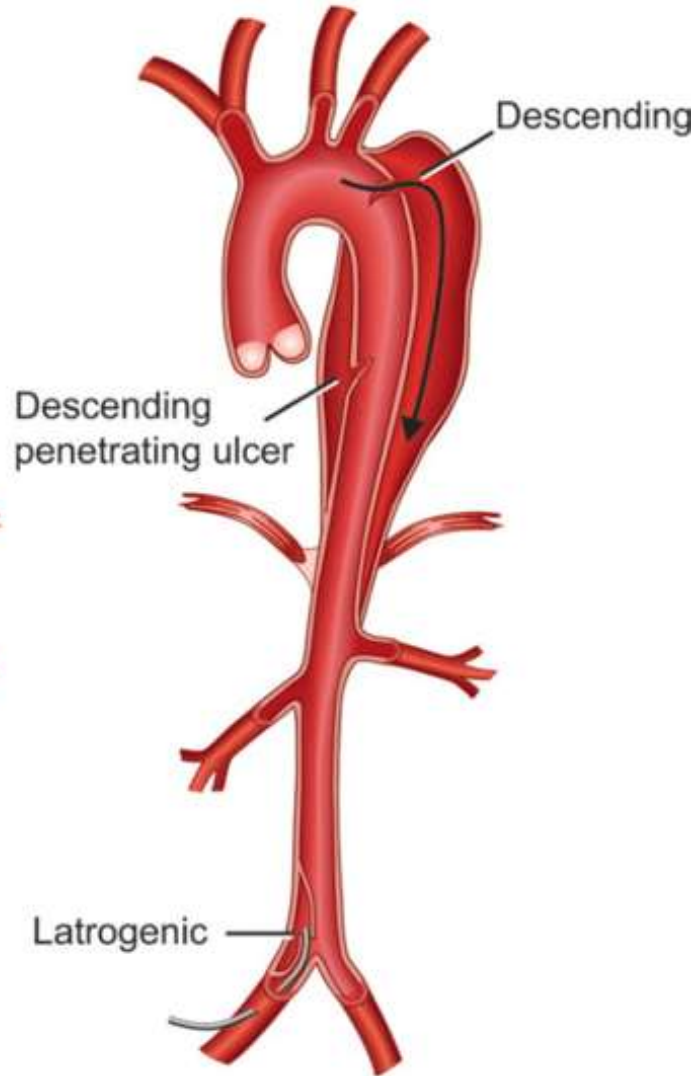
DeBakey I and II  
Stanford A

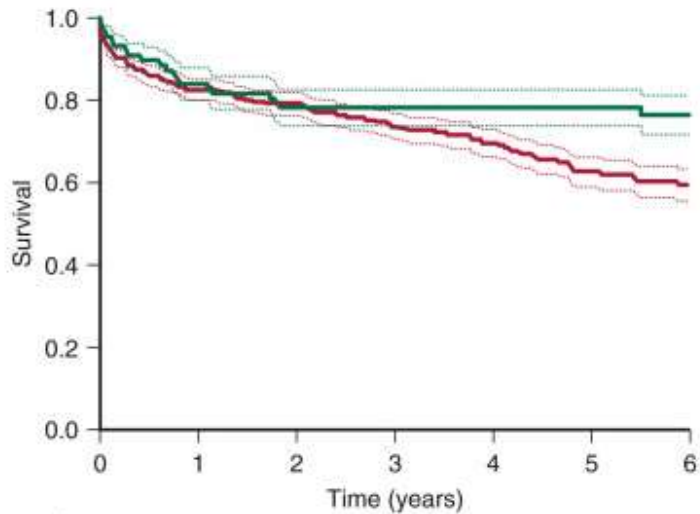


Stanford B

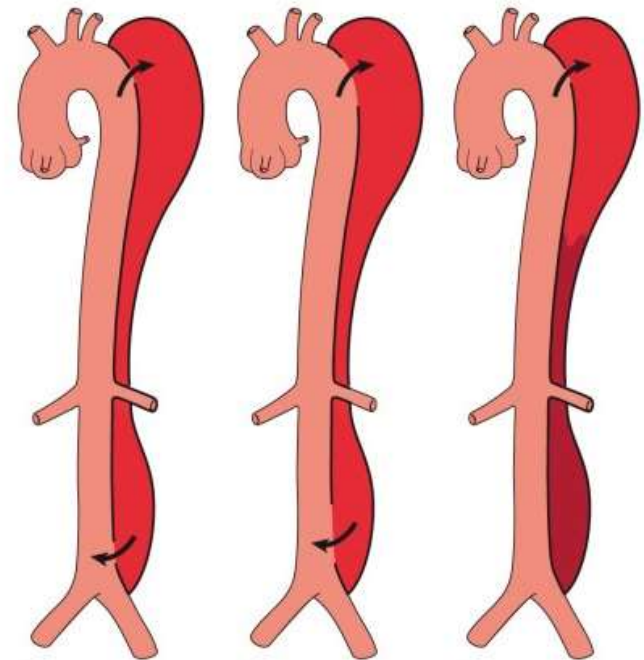


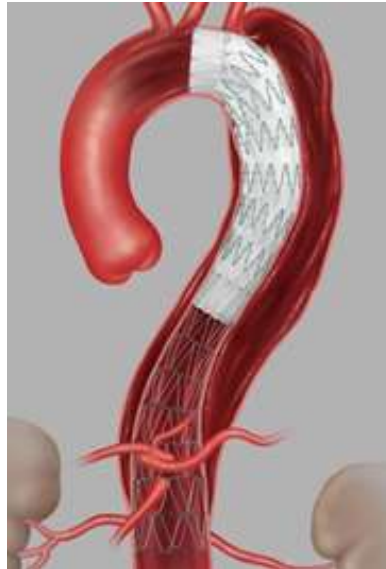
DeBakey IIIa and IIIb  
Stanford B





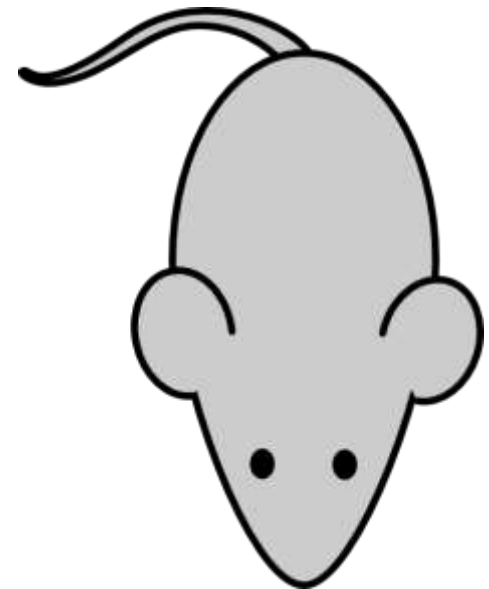
<i>Intervention:</i>							
<i>At risk:</i>	87	73	68	65	59	53	43
<i>Survival:</i>	100.0	83.9	78.2	78.2	78.2	78.2	76.4
<i>SE (+/-):</i>	0.0	3.9	4.4	4.4	4.4	4.4	4.7
<i>Medically managed:</i>							
<i>At risk:</i>	211	174	167	136	108	82	65
<i>Survival:</i>	100.0	82.5	79.2	73.6	68.9	62.6	59.3
<i>SE (+/-):</i>	0.0	2.6	2.8	3.1	3.3	3.6	3.8



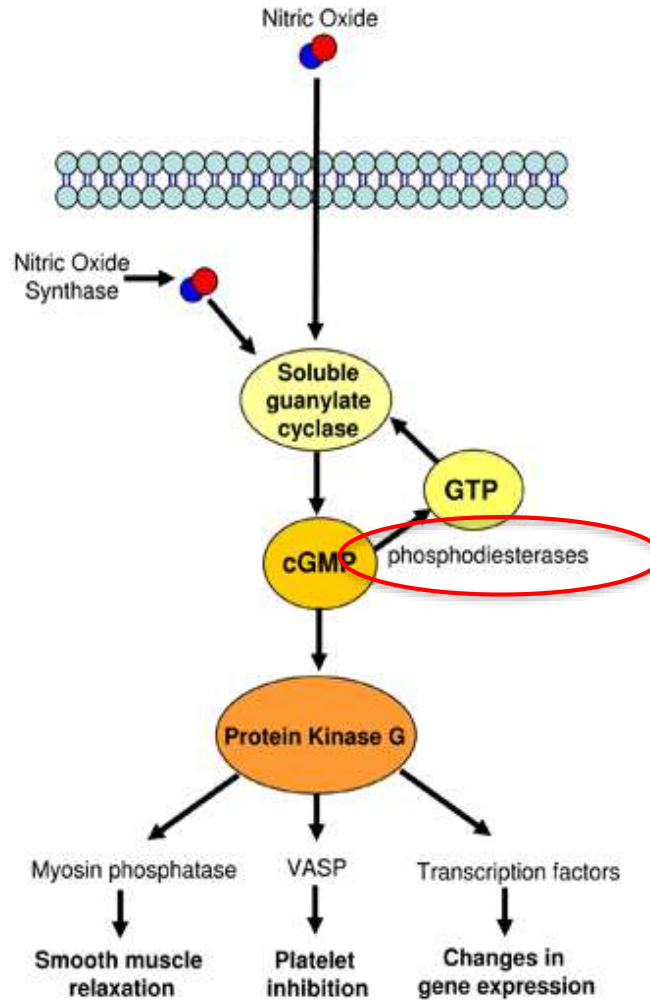


# Aortic Dissection Mouse Models

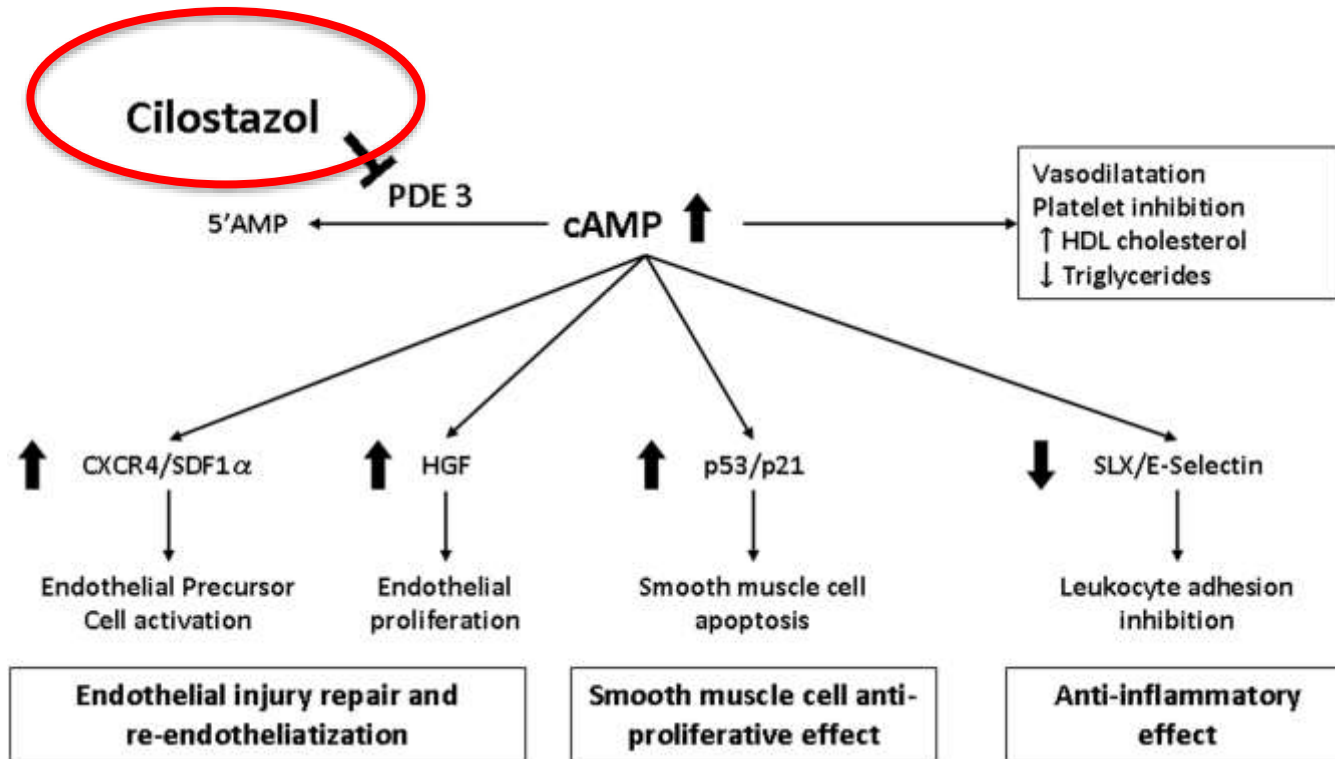
- Extracellular Matrix
  - Fibrillin-1, Fibulin-4, Lysyl oxidase, ADAMTS1, Col3a1, Col1a1, Biglycan
- SMC proteins
  - ACTA2, MyH11, TCS-1, PRKG1, LRP1
- TGF $\beta$  related proteins
  - TGF $\beta$ 2, TGF $\beta$  receptor 1, TGF $\beta$  receptor 2, Smad4, Smad3



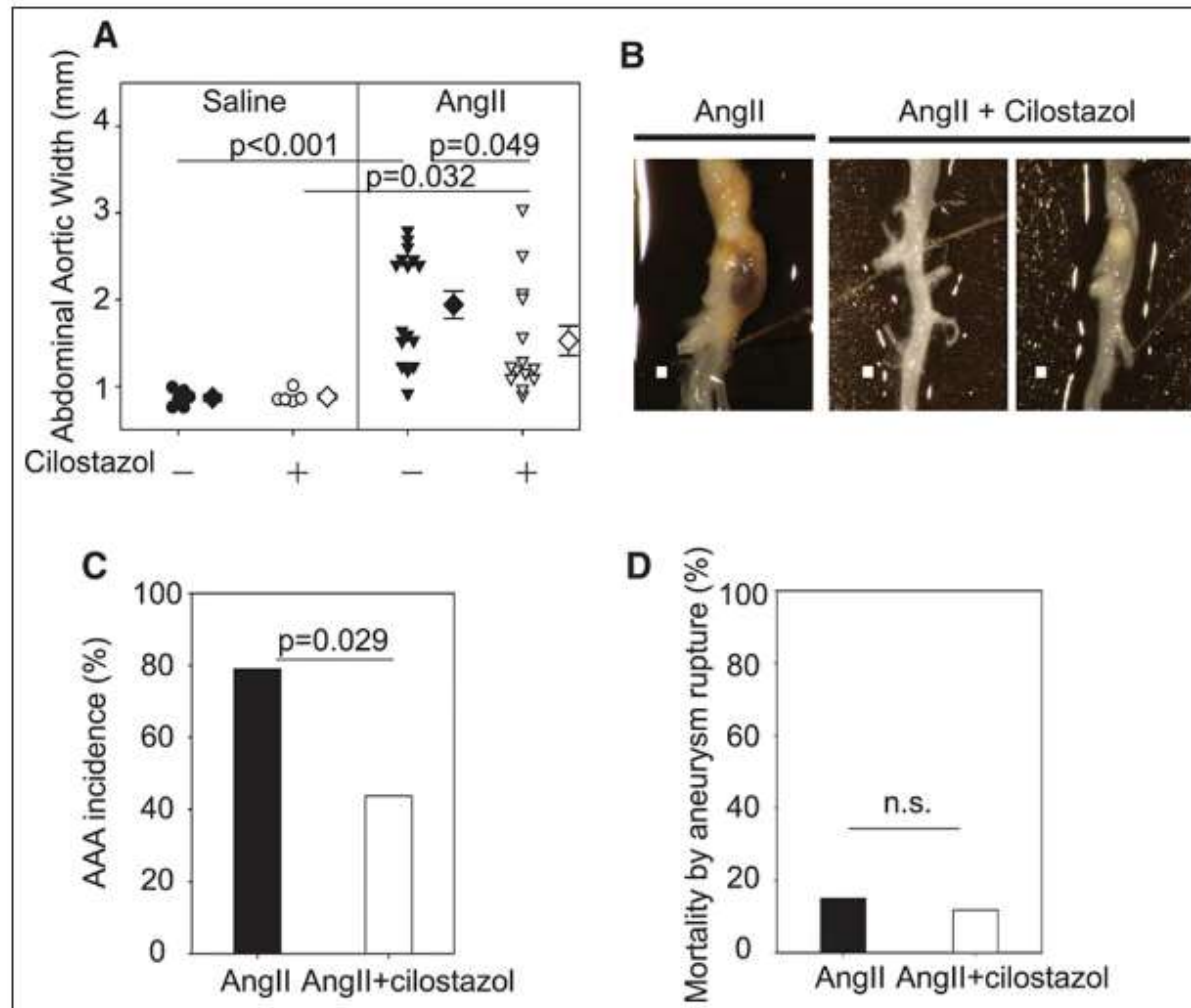
# Aortic Pathology



# Aortic Pathology

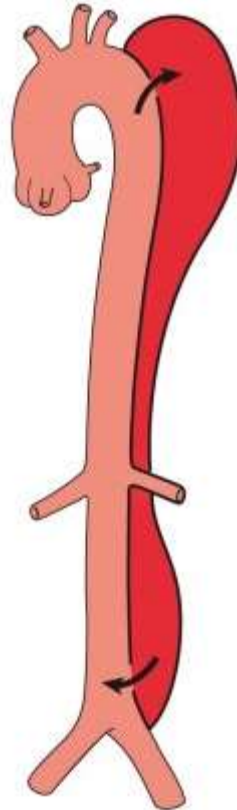


# Cilostazol Attenuates AngII AAA





?

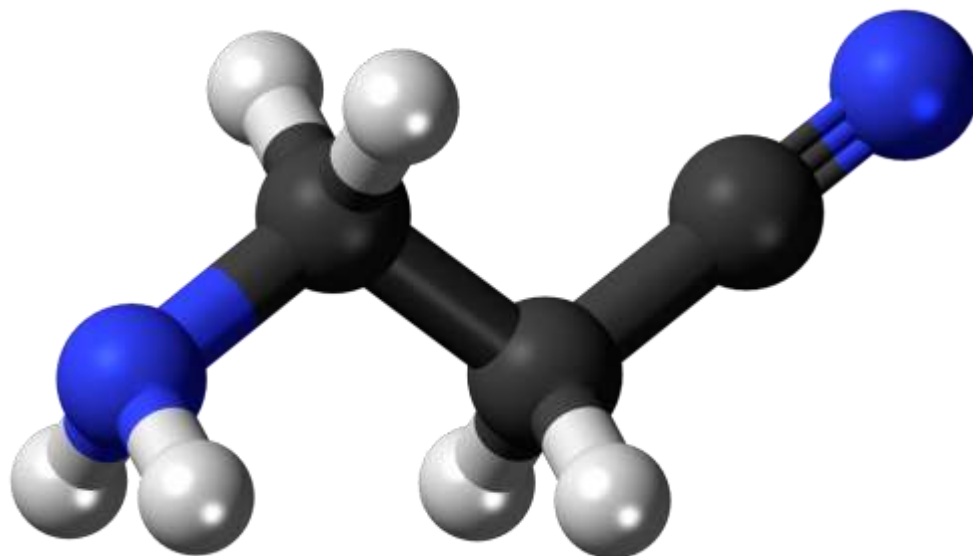


# BAPN: $\beta$ -aminopropionitrile

Irreversible inhibitor of LOX

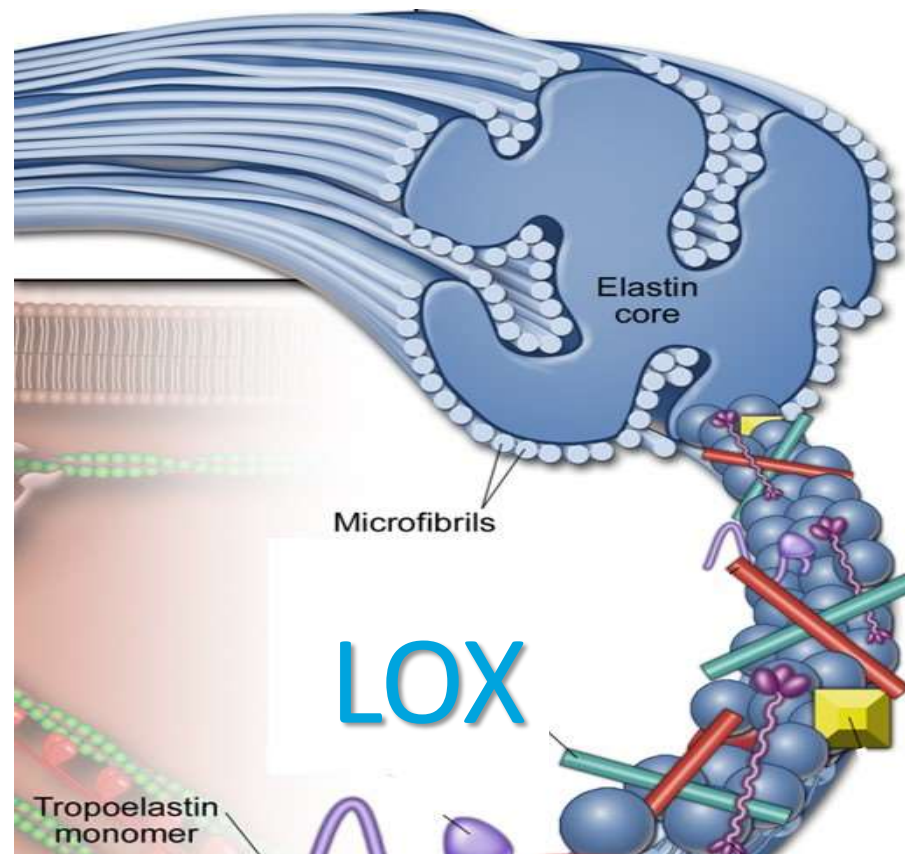


Sweet Pea



# LOX: Lysyl Oxidase Model

LOX is a copper-dependent amine oxidase that is essential for cross-linking of collagen and elastin.



# BAPN-induced Aortic Dissection in Mice



- - BAPN
- 0.5%, drinking water
- Start: 3 weeks of age

# Hypothesis: Phosphodiesterase Inhibitors Decrease the Effect of BAPN Induced Aortic Dissection



- Platelet inhibition
- Improved endothelial function and repair
- Anti-inflammatory



Decreased Severity and Mortality of BAPN induced AoD

**Aim 1:** To determine if Cilostazol PDE3i decreases BAPN induced AoD

**Aim 2:** To determine if Sildenafil PDE5i decreases BAPN induced AoD

# Experimental Design – 85 mice - 1 month



C57BL/6J male  
~ 3 weeks old

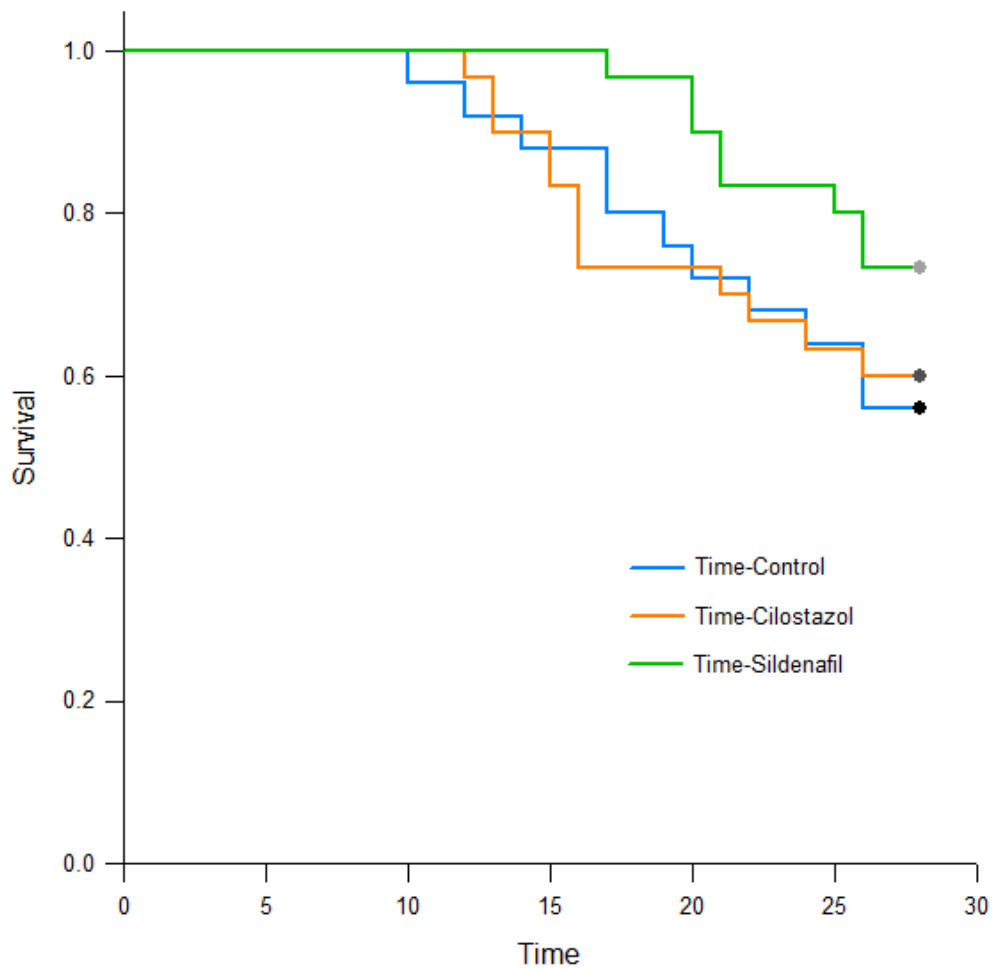
- Control Diet
- Cilostazol Diet
- Sildenafil Diet

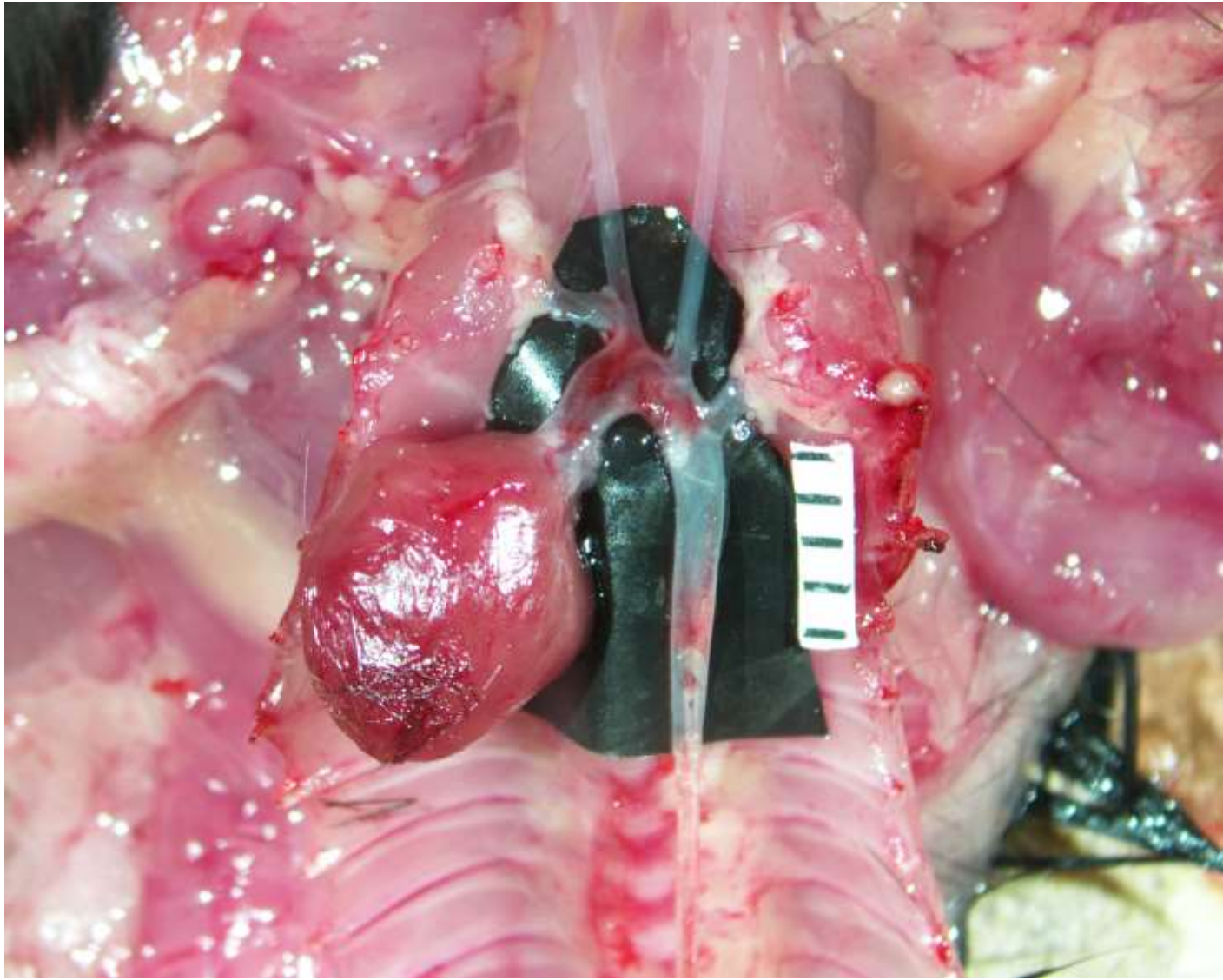


Time (Weeks)	-1	0	1	2	3	4
Body Weight	Measured weekly					
BAPN H2O						
Diet						

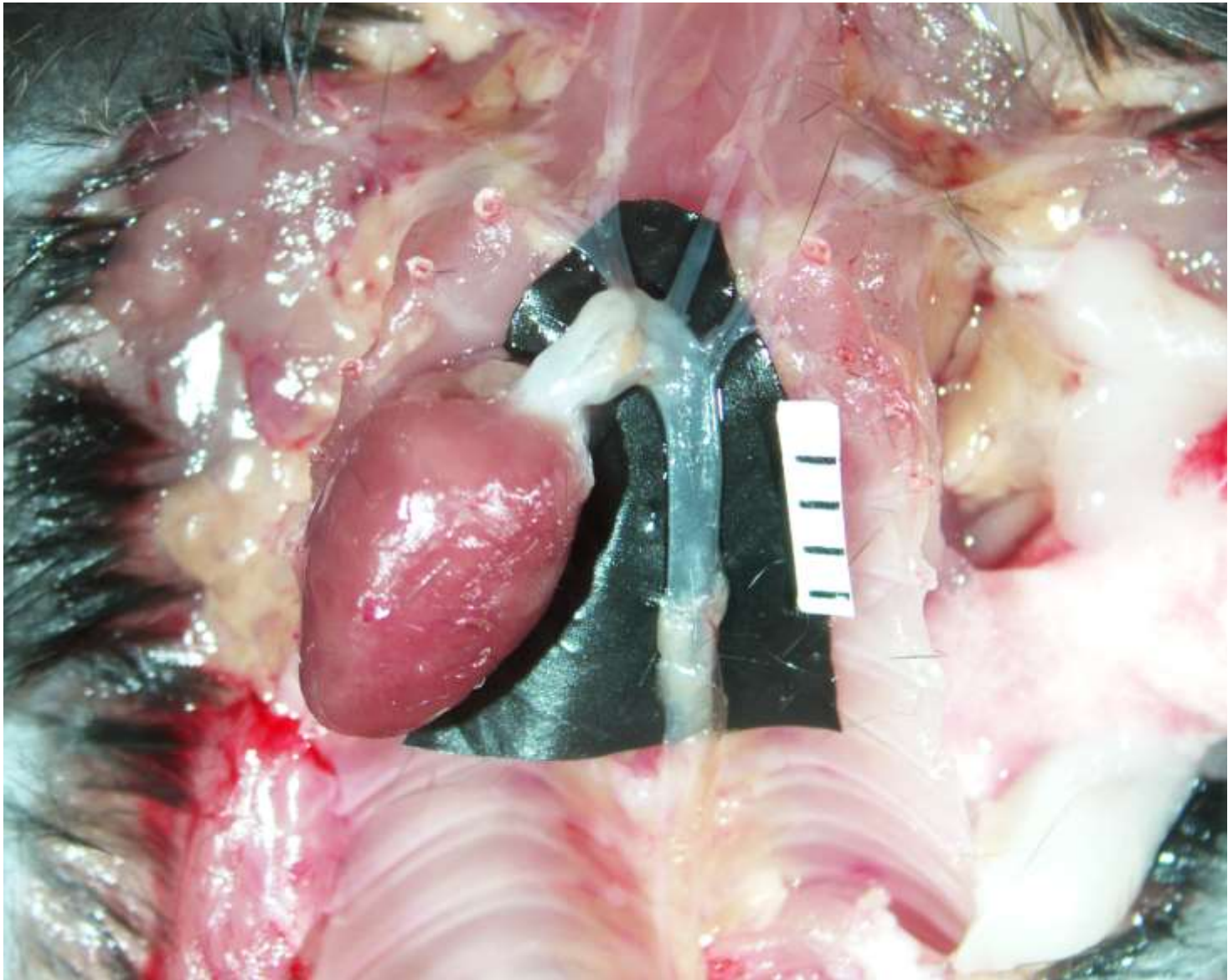
Mice sacrificed at 4 weeks

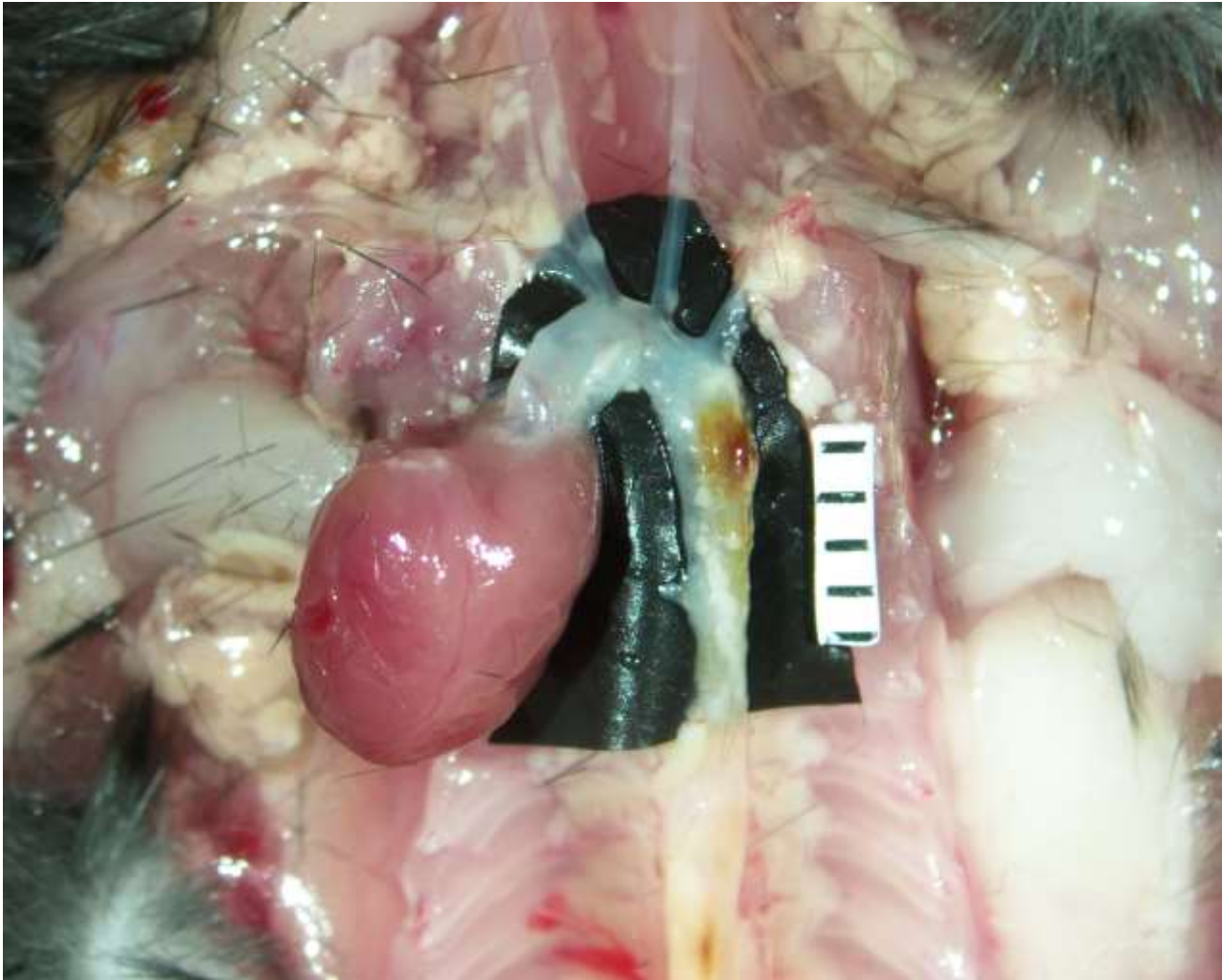
# C & S BAPN S1a + S1b Survival

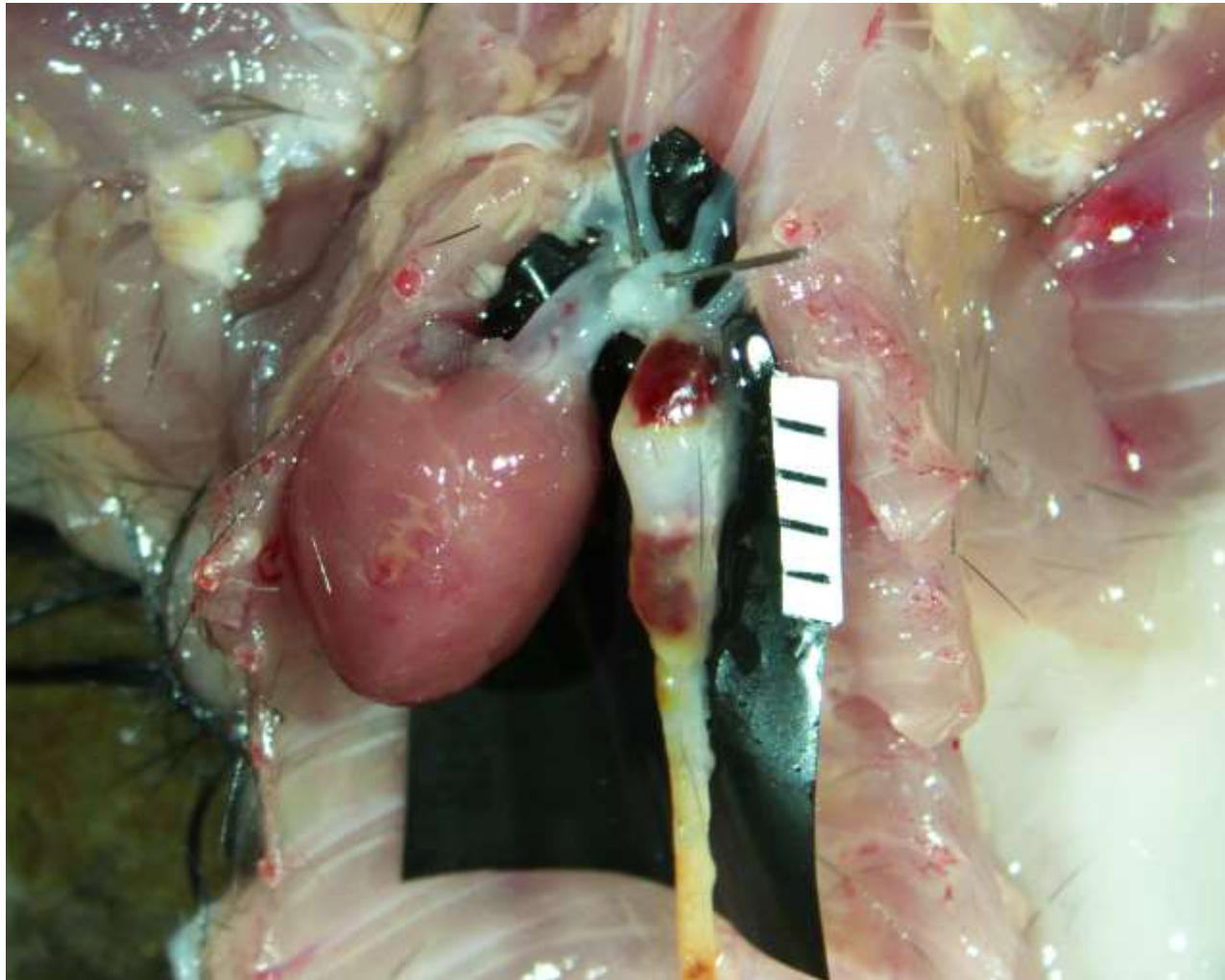


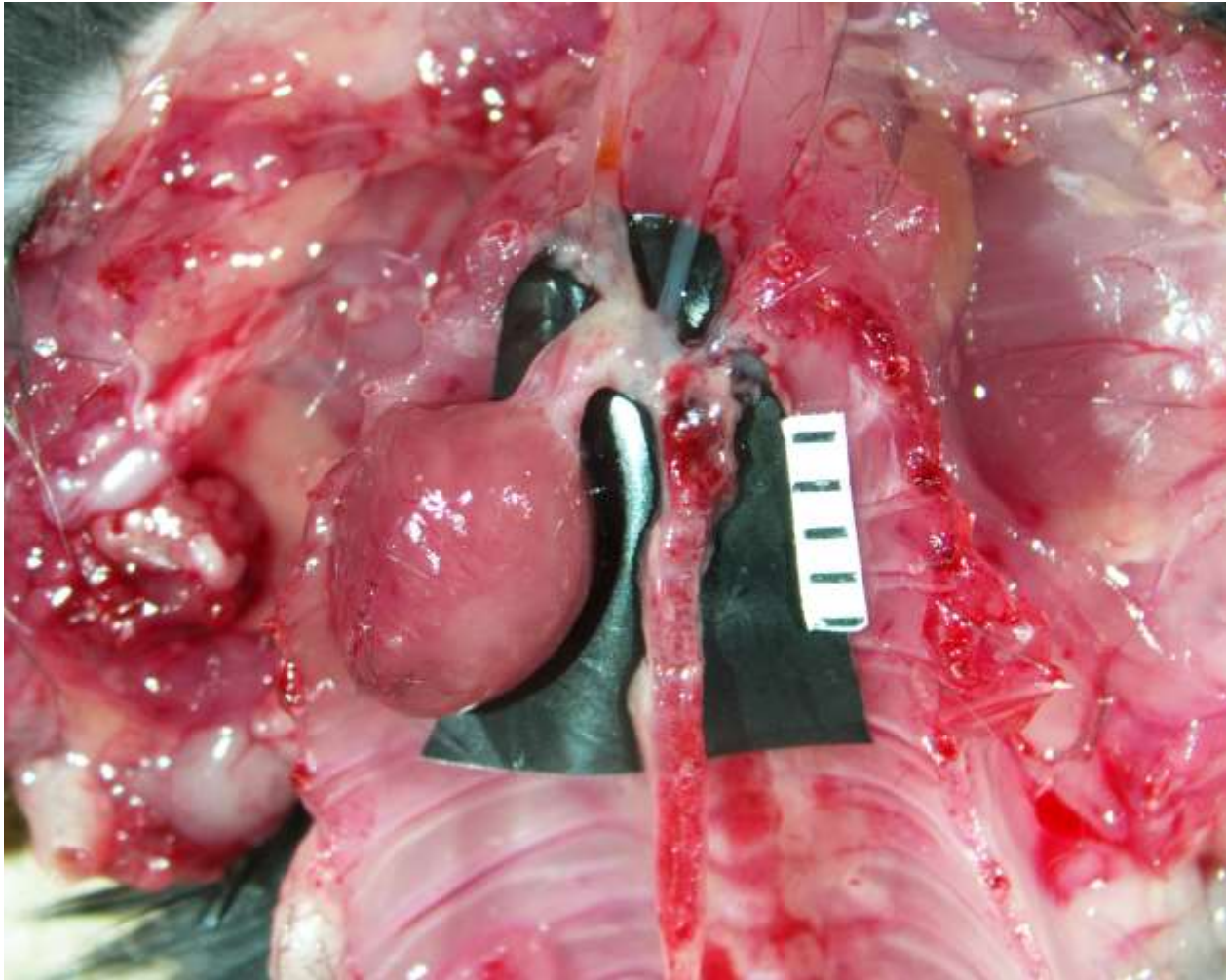


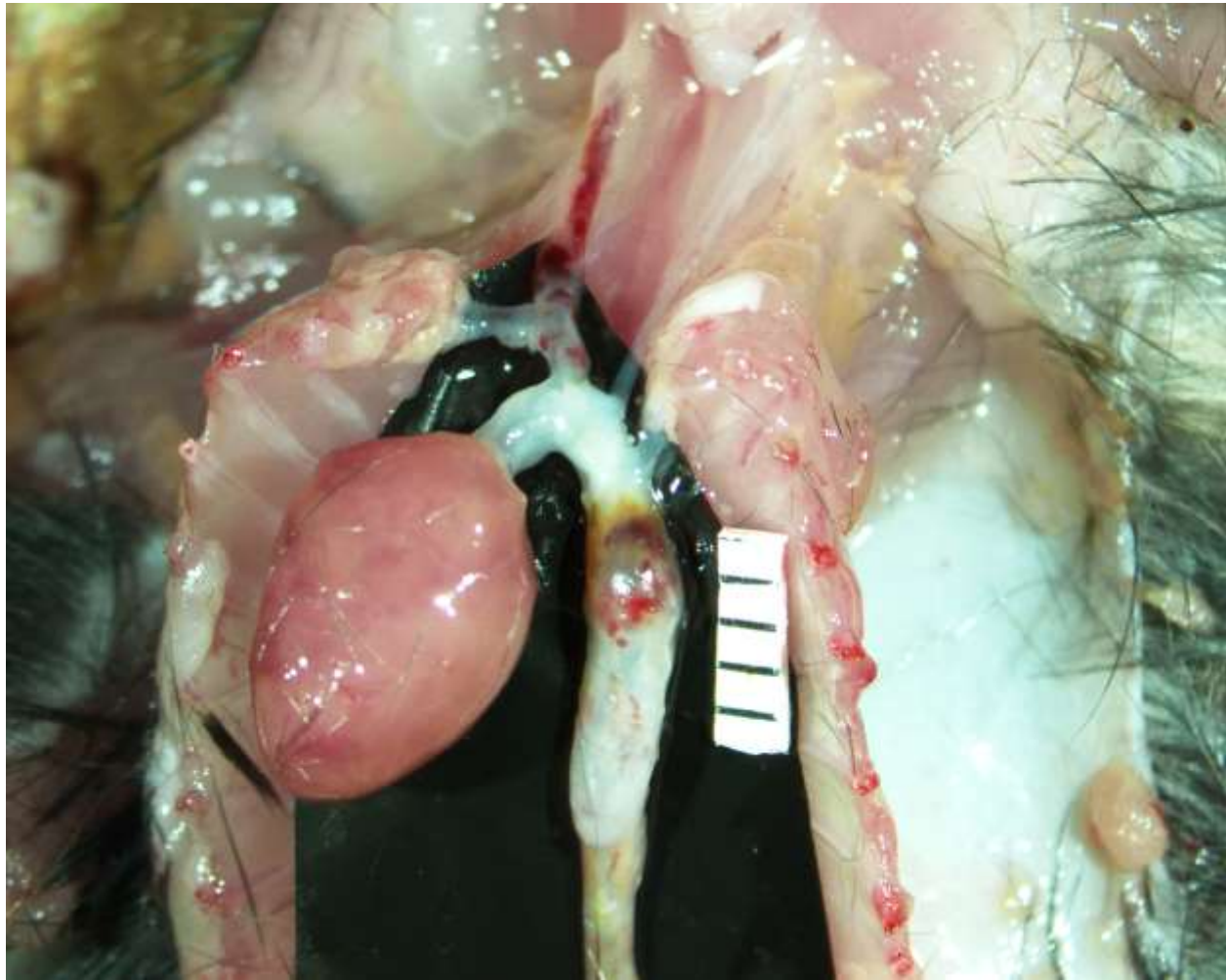




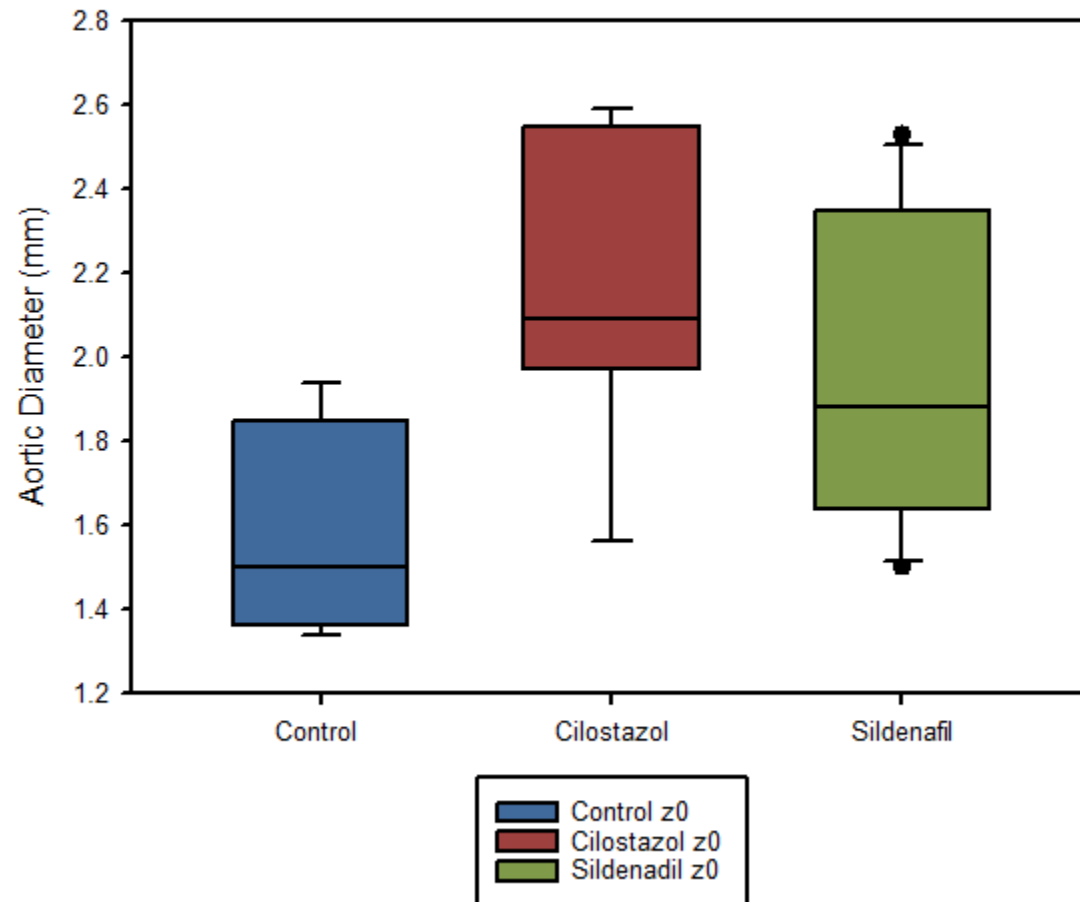




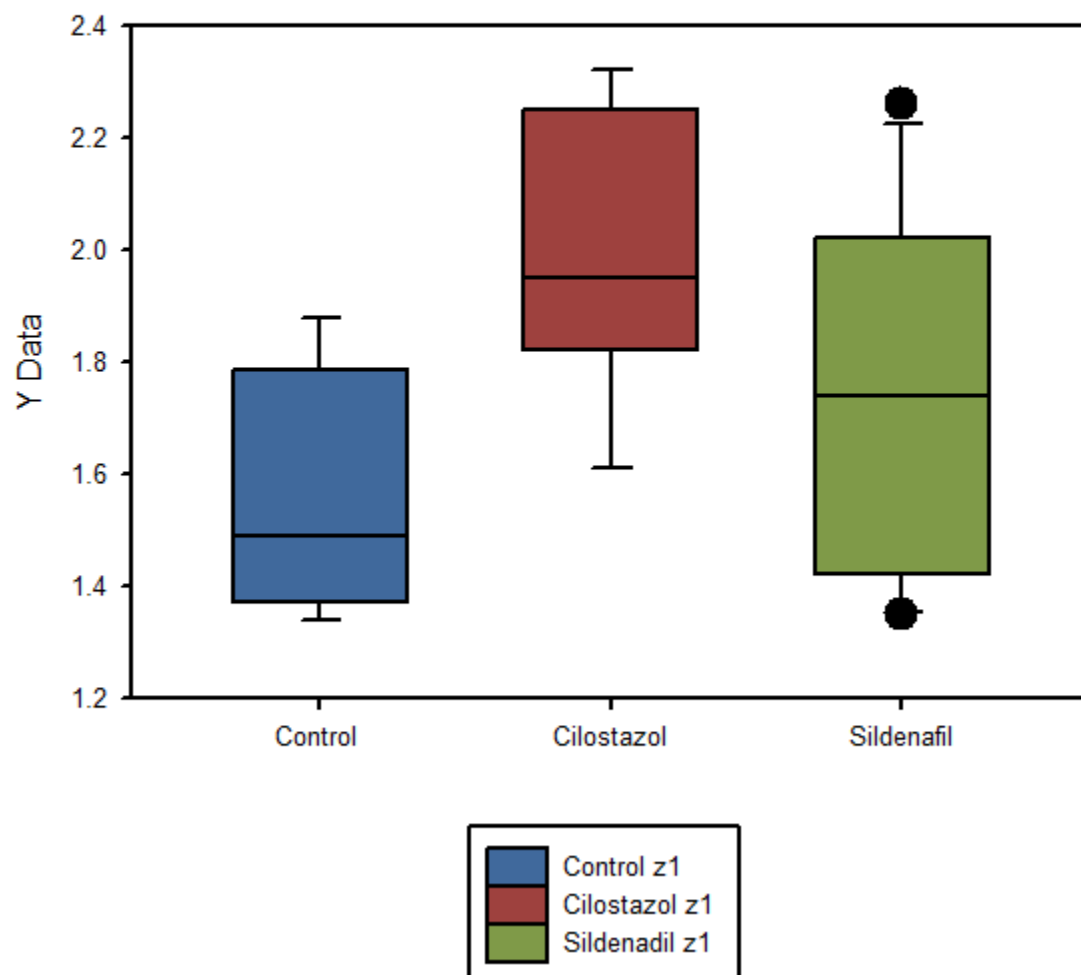




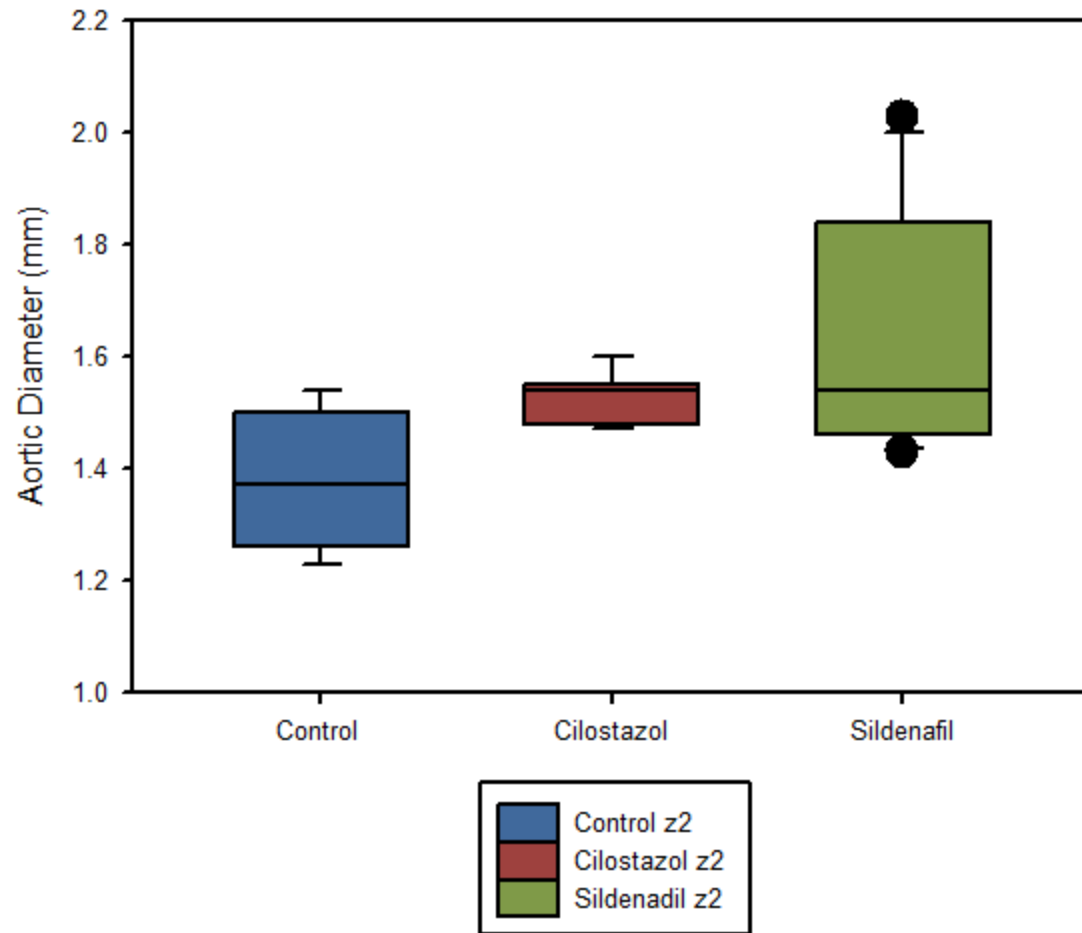
## Aortic Measurements Zone 0



## Aortic Measurements Zone 1

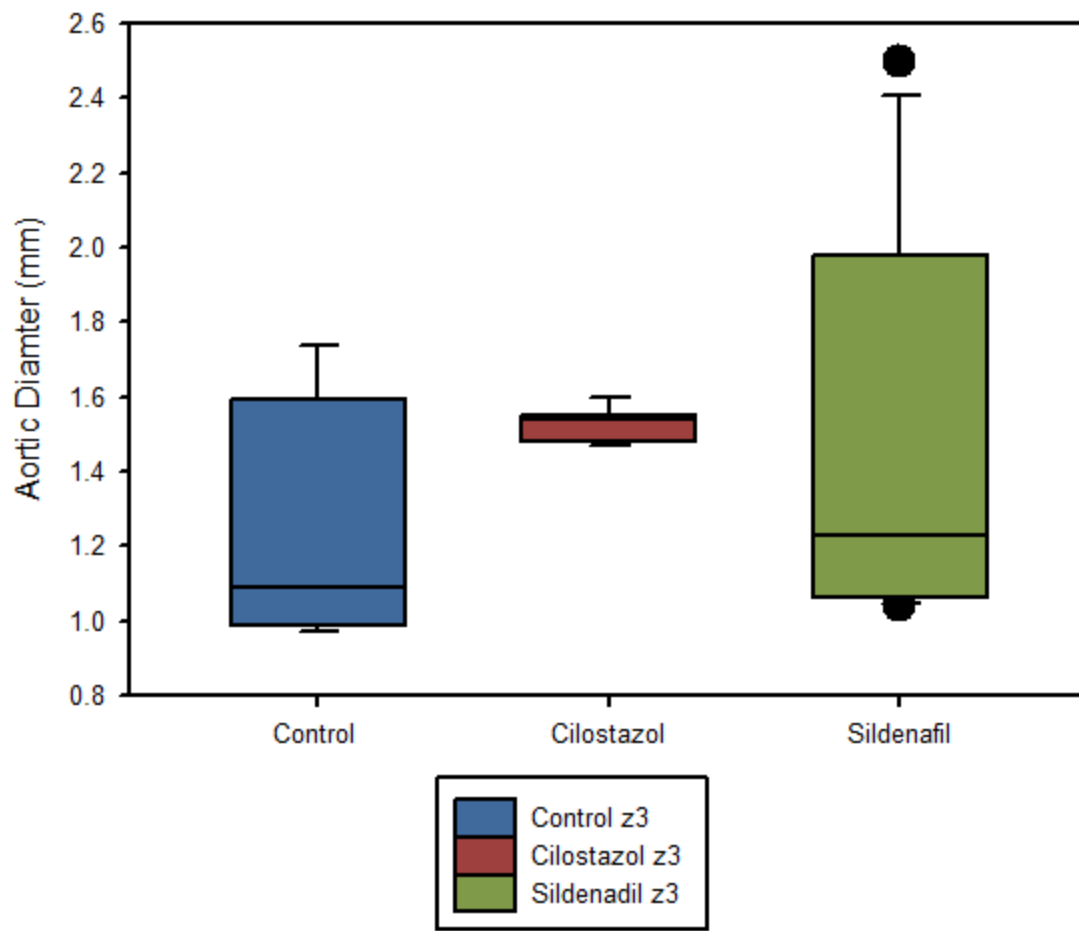


## Aortic Measurements Zone 2

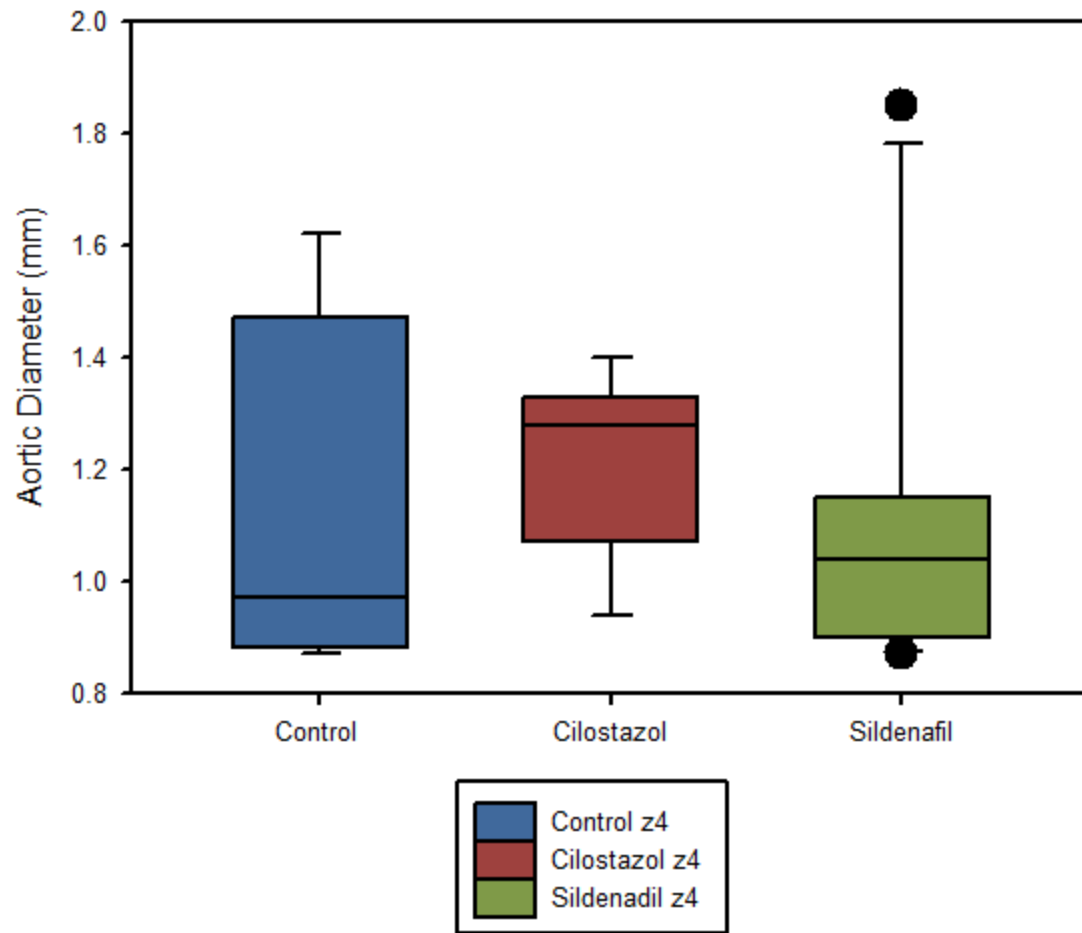




### Aortic Measurements Zone 3



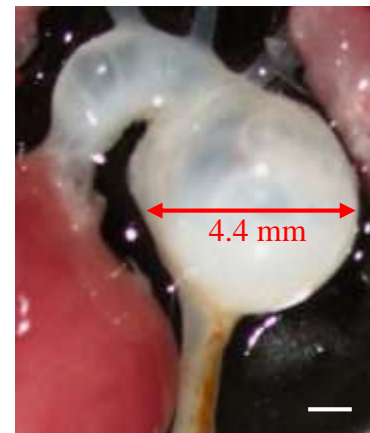
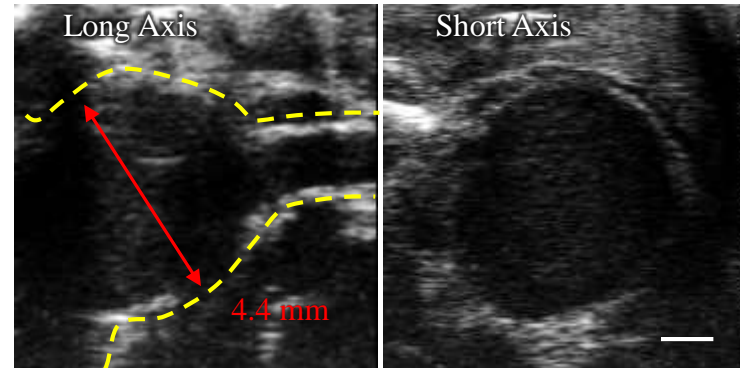
## Aortic Measurements Zone 4



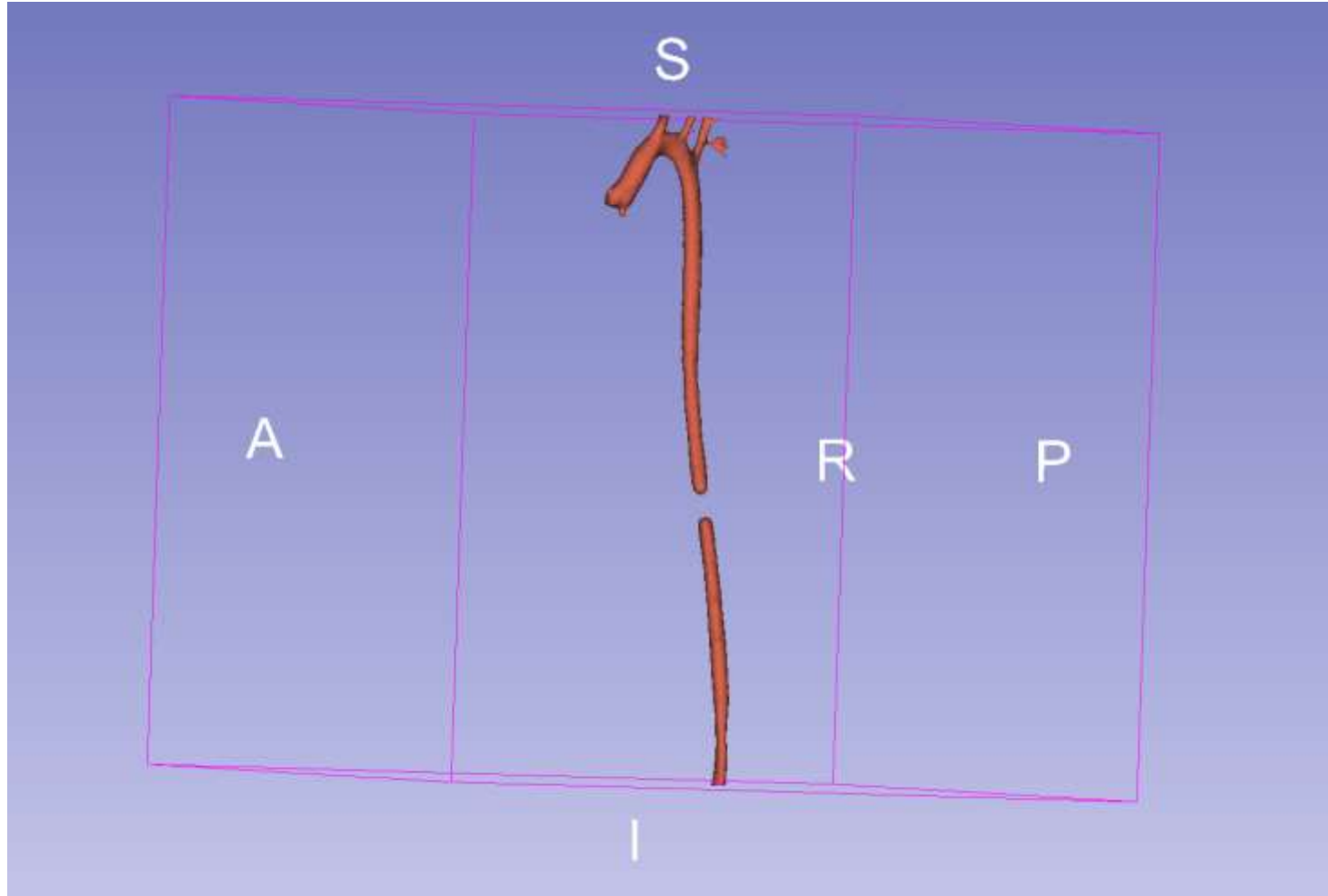
# Future Plans

- Verify drug delivery with ELISA aortic tissue
- Severity Score
- 3-month study – survival
- Ultrasound measurements of progression of Aortic disease in vivo
- Characterize Aortic Tissues by Histology

# High Frequency Ultrasound in Mice



# Micro CT – 20 $\mu\text{m}$ resolution



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University of Kentucky



Early Faculty Career Development Award  
Vascular and Endovascular Surgery Society



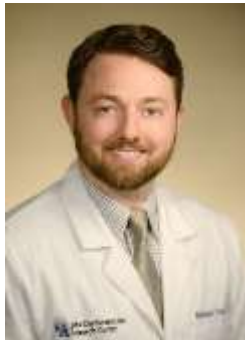
## The Lab

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