

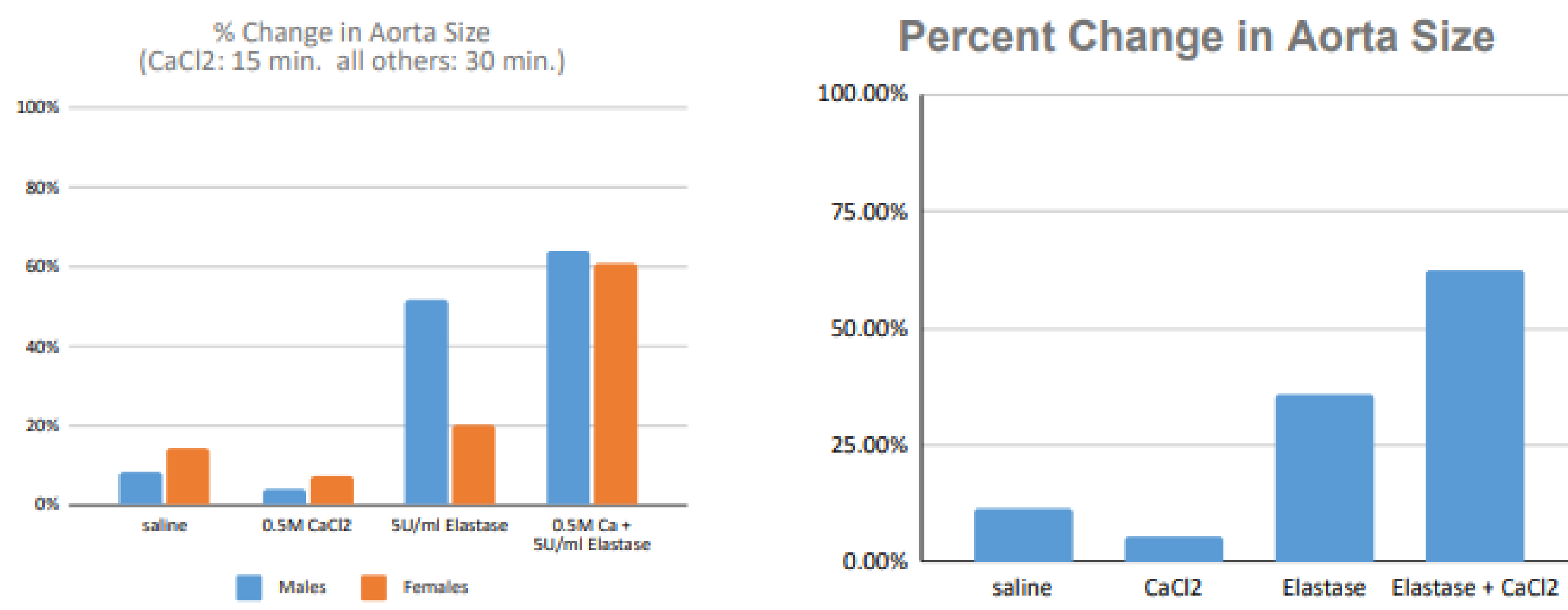
Abdominal Aortic Aneurysm Development in a Rat Model

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BACKGROUND

- Abdominal aortic aneurysm (AAA) is a progressive dilation of the abdominal aorta with eventual rupture when the aortic wall is weakened to the point that the stress on the wall exceeds the wall strength.
- The disruption and loss of the elastic matrix leading to AAA is generally considered irreversible due to the inherent inability of adult vascular smooth muscle cells (SMCs) to produce sufficient elastin
- Elastin is the key protein component of elastic fibers
- Impaired ability to organize elastin precursor molecules (tropoelastin) into mature cross-linked fibers is evident in AAAs.

DESIGN

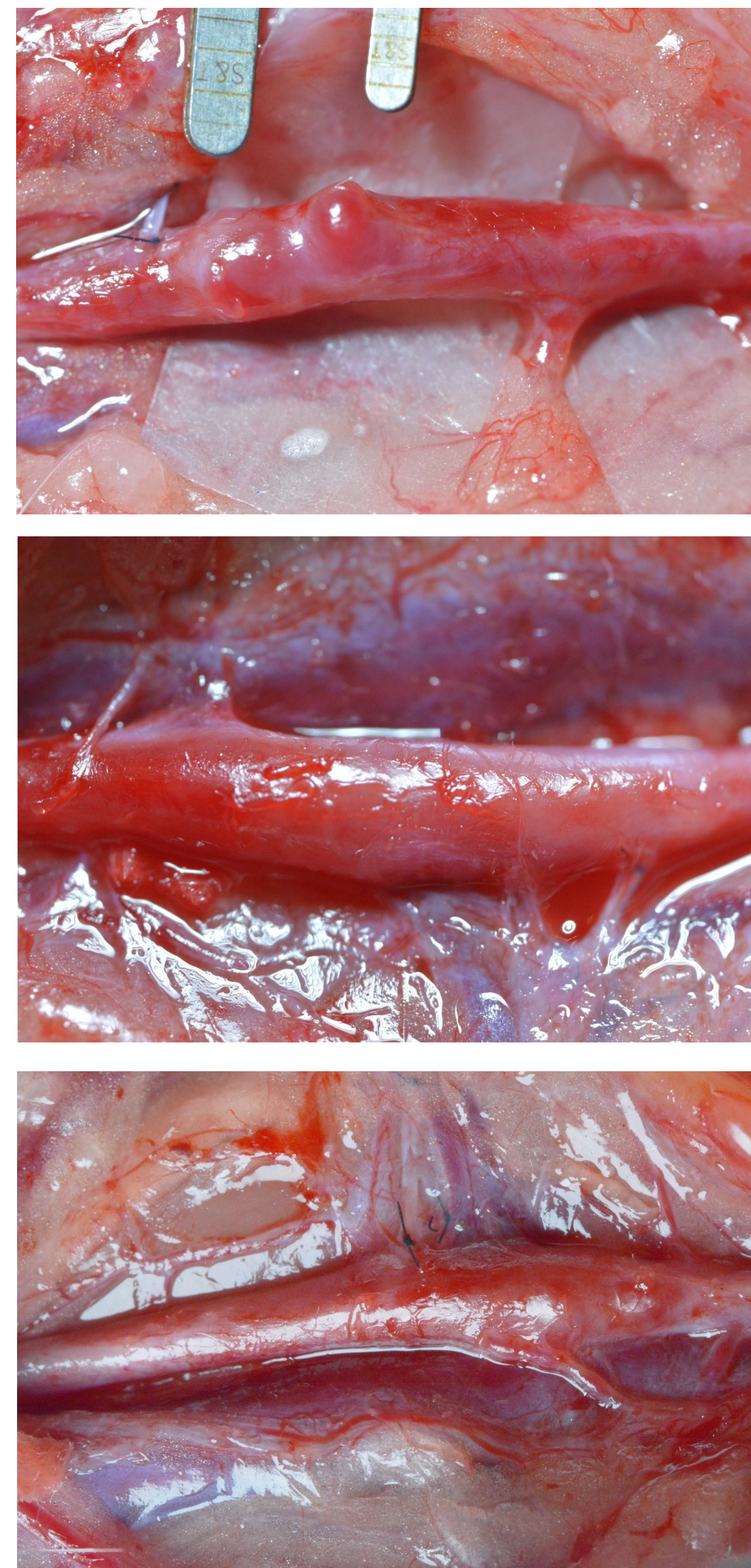


- Short term (1 and 3 month) treatment protocols employed
- Experiments analyzed by gross observation at sacrifice with histological examination of the aneurysmal aortic tissue
- Determination was made for optimal treatment protocols which generate >50% increase in vessel diameter

INTERVENTION AND IMPACT

- No effective medical treatment exists so far for AAA.
- To date, surgical intervention is the only viable options to treat large, rupture-prone aortas.
- However, it has recently become technically feasible to deliver chemical or genetic payloads to the vascular walls, either by perfusion of the afflicted area or by direct delivery by contact with a balloon or stent carrying the payload in the form of viral vectors or nano-particles

Rat AAAs Following Treatment Protocol



RESULTS

- AAA successfully created using enzymatic treatments designed to weaken vessel wall
- Most successful protocol has employed exposing the aorta to 0.5M CaCl₂ and 5 U/ml elastase for 30 minutes when compared to saline controls
- Using the optimized approach, we have achieved increases in vessel diameter of greater than 60%

CONCLUSION

- Having a method to create AAA will allow us to study genetic interventions to prevent or reverse this condition
- The next phase of the study we will analyze gene expression in the aneurysm to determine whether it mimics a genuine aneurysm
- This will be followed by delivery of nano-particles or viral vectors with genes known to stimulate SMCs
- The results of these interventions will be followed by histologic and genetic analysis of the affected areas at various times after treatment.

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