Tortuosity calculations, blood flow simulations, and mechanical testing of mouse aortae

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Introduction

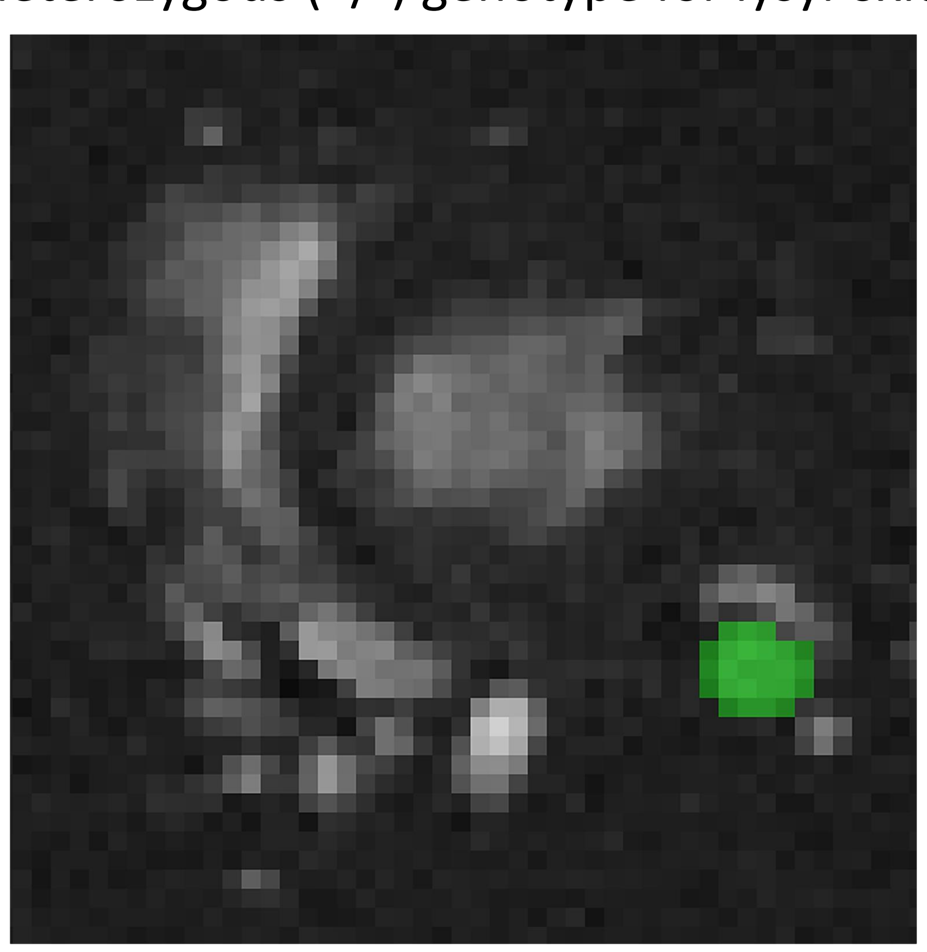
The aorta is the largest artery in the body and transports blood from the heart to distal organs. It is possible for an aneurysm (bulge) to develop in the aorta over time, which can cause the aorta to burst or dissect. Since it is such a central vessel, these events are usually fatal. Thoracic aortic aneurysms (TAA) can be operated on with high success rates; however, current diameter-based risk assessment methods only catch 40% of fatal TAA cases. Recent work suggests that **tortuosity** (see definition below) may correlate with an increased risk of aneurysm rupture or dissection. Our objective was to determine if tortuosity could supplement diameter-based risk assessments in mouse models of TAA.

Tortuosity: An accumulation of curvature, which we quantify as $T_{index} = (AL / GL - 1) \times 100$, where T is the Tortuosity Index, AL is the actual length of the vessel along the centerline, and GL is the geometric length straight from inlet to outlet.

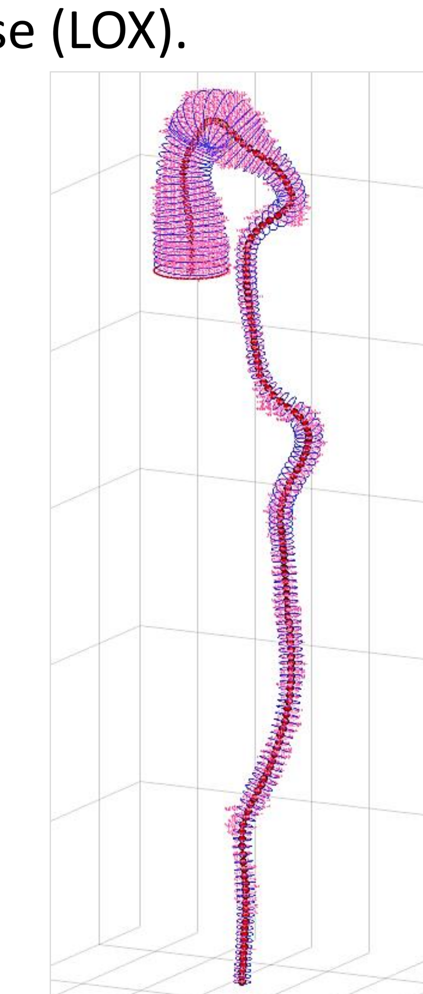
Methods

Tortuosity Calculations

Two groups of mice that were expected to develop aneurysms were monitored via MRI imaging. The first group had fibulin-4 deficiency in their smooth muscle cells, and the second had a mutation in fibulin-4 (E57K) combined with a normal (+/+) or heterozygous (+/-) genotype for lysyl oxidase (LOX).



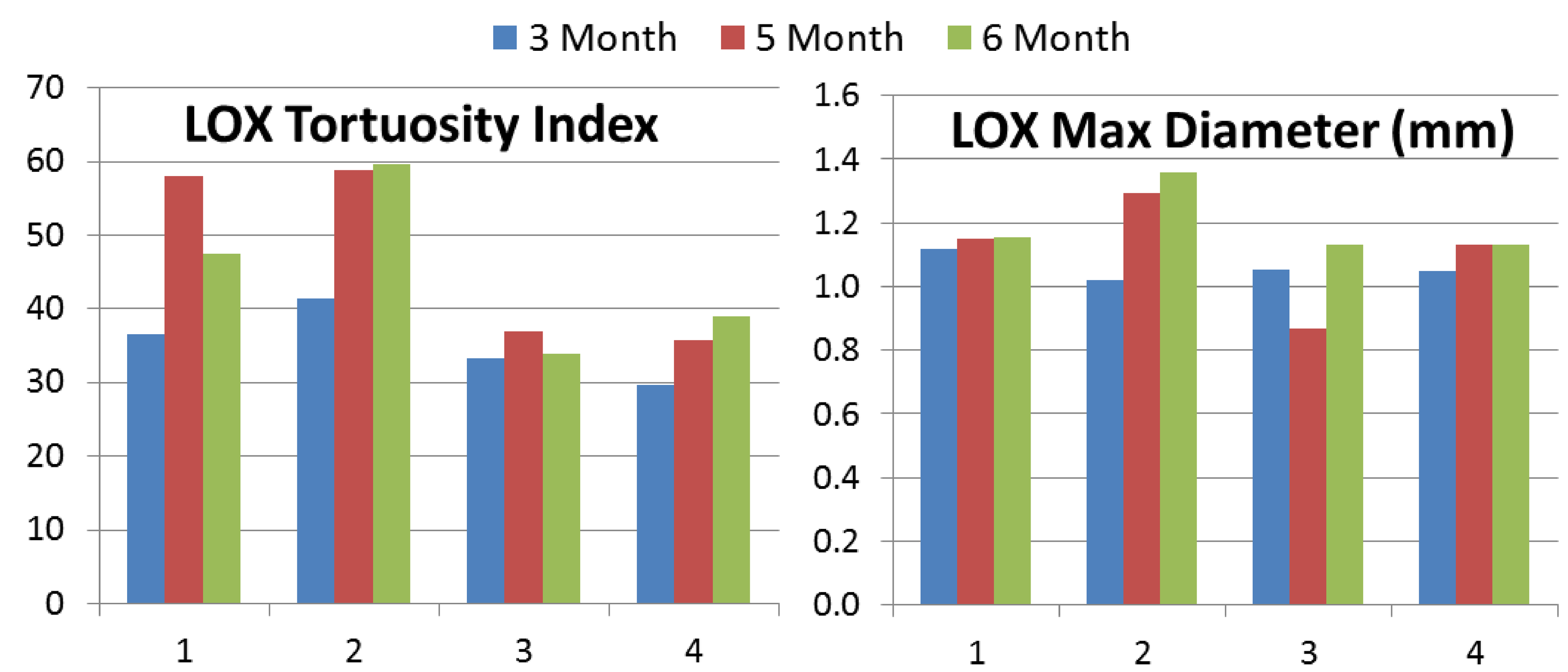
Manual MATLAB VOXA MRI image processing



MATLAB Tortuosity Geometry render

Mouse	Fibulin4	LOX
#1	E57K/E57K	+/+ (WT)
#2	E57K/E57K	+/-
#3	E57K/+	+/-
#4	E57K/+	+/-

Table 1 Genotypes of group 2



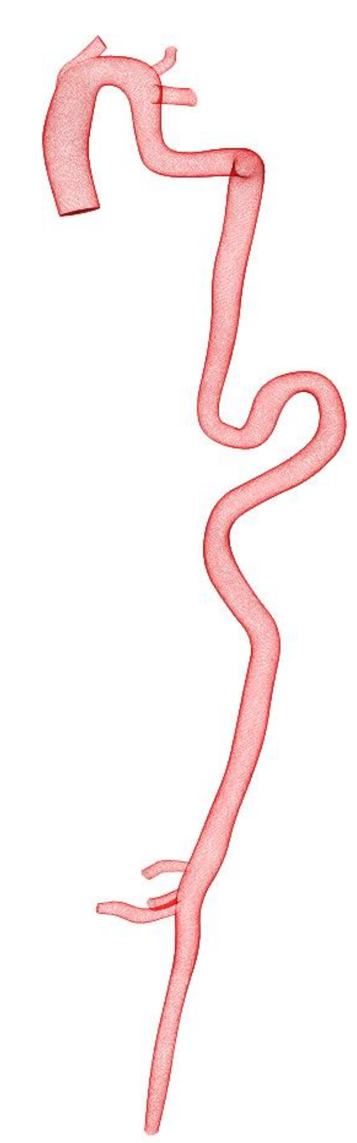
MATLAB geometry analysis results for each LOX mouse: script was written to analyze the processed versions of original MRI images. The script calculated centerlines, diameters, and curvatures along vessels input (see bottom left).

SimVascular blood flow simulations

Simulation models were created and fine-tuned with SimVascular, an open source FSI and CFD program tailored to blood vessel analysis.

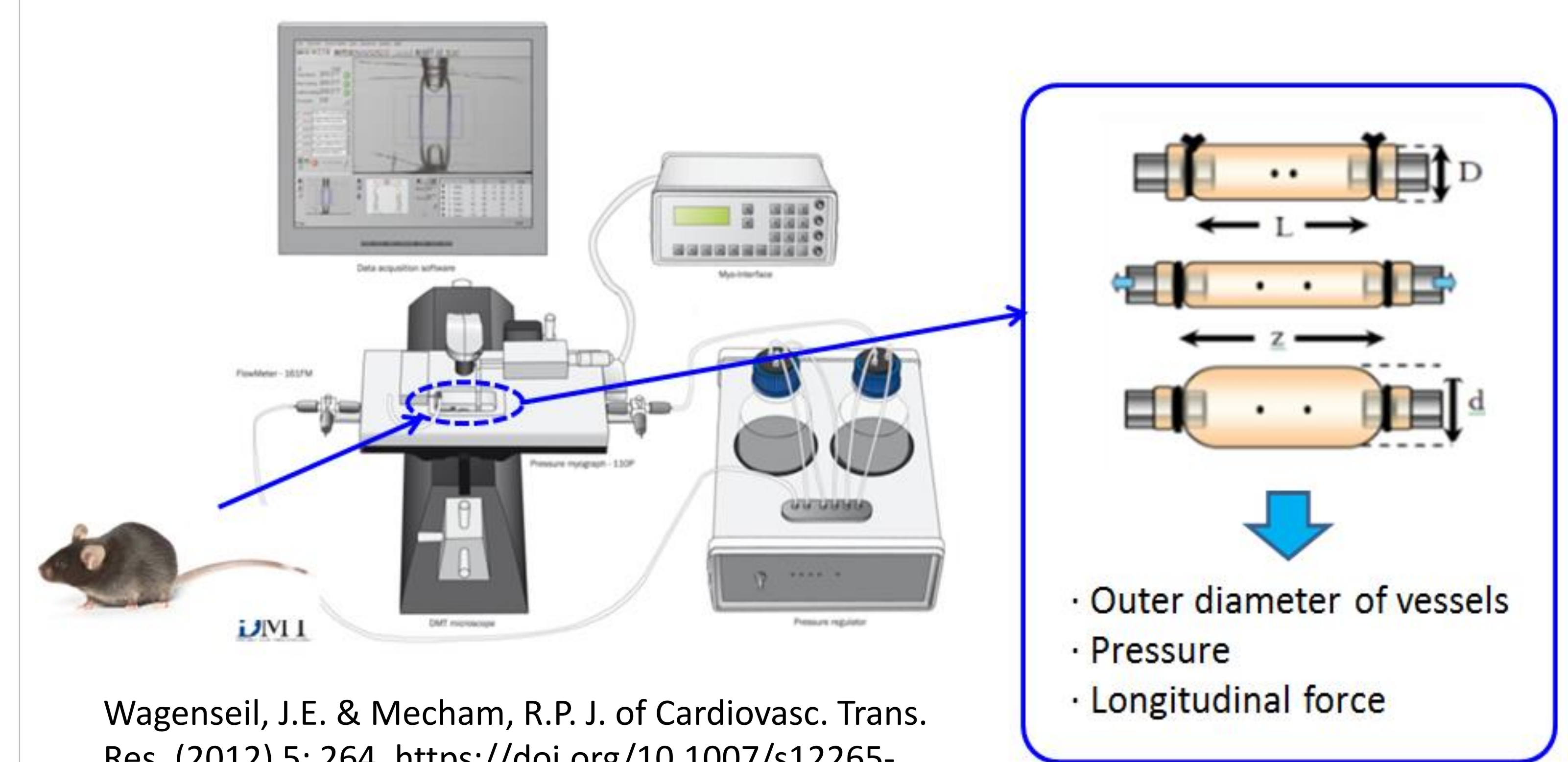
3D geometries were constructed with MRI images, and these geometries were made into meshes (grids of tiny triangles), which are used to simulate blood flow.

Fbln4/LOX #4 3D mesh and velocity results



Fbln4/LOX 2 tortuous 3D mesh

Mechanical testing



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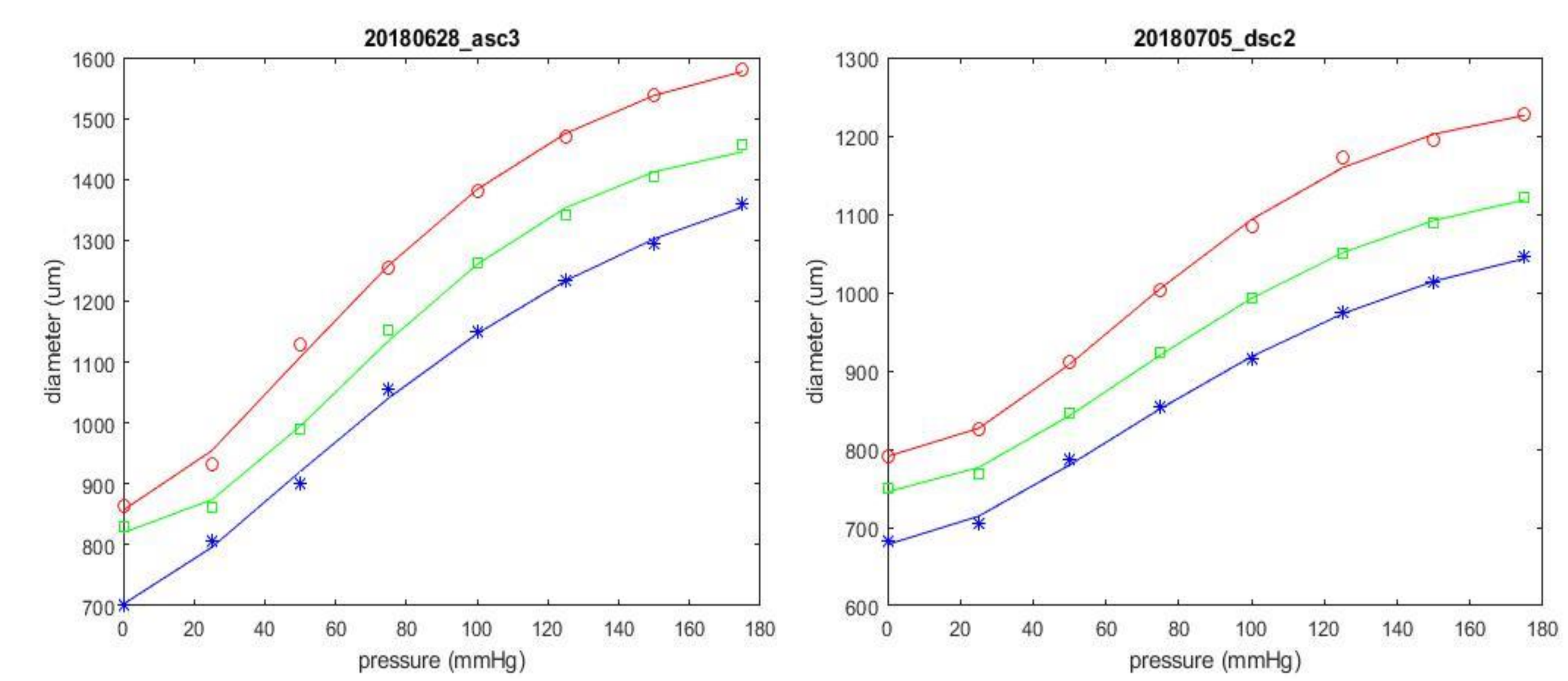
After natural death of a mouse, aortas were inspected and then mechanically tested in a pressure myograph.



Diameter vs. pressure at increasing axial stretch (red to green to blue). Ascending aorta on the left, descending on the right.

Discussion

Preliminary results show promise for the use of tortuosity and flow simulations in risk assessment of aortas. Since this study follows the same mice over their lifespan, future outcomes will be crucial for interpreting current results. We hope for some independence between diameter and tortuosity based predictions, such that both could be used simultaneously to better inform clinicians about the need to surgically intervene to prevent aortic rupture or dissection due to aneurysms.

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