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Tortuosity studies, blood flow simulations, and arterial wall image processing

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Abstract

Continued work was done developing fluid dynamic models of aneurysm-prone mouse aortae. Current aneurysm outcomes were compared to model data, specifically to aortic tortuosity, suggesting (with a small sample size) that tortuosity might be an important factor to consider when assessing the severity of aneurysm progressions. Moreover, image processing techniques were developed for the lab in order to better quantify changes in elastic laminae structure.

Keywords: Tortuosity, Aneurysm, Mechanics, MRI, CRIMSON, MATLAB, ImageJ, Image Processing

Introduction

"Aortic aneurysms can lead to wall rupture or dissection, which are both deadly occurrences. The risk of developing problematic aneurysms increases with age, making them a growing concern in the USA's aging population. Thoracic Aortic Aneurysm (TAA) treatment is highly effective if the TAA is diagnosed in time, however current surgical guidelines catch less than half of fatal TAA cases. Tortuosity (related to vessel length divided by the straight distance between two points of interest [as shown in Fig. 1]) has been proposed as a supplement to diameter based diagnosis of severity of TAA progression." [1]

Previous work was done tracking the evolution of fourteen mouse aortae over time by using MRI imaging. Scripts were written to calculate overall tortuosity of each aorta, as well as diameters and curvatures at various points. The goal of gathering the data was to compare tortuosity and diameter progressions and values to outcomes in the mice, to determine if higher tortuosity vessels would be more prone to developing deadly aneurysms. Moreover, 3D models were created for the purpose of simulating blood flow through the mouse aortae in question so that more information could be gathered about the stresses in the aortic walls.

Besides investigating tortuosity, the lab is interested in how changes in elastic laminae structure alter arterial wall transport dynamics. Understanding wall transport gives potential insight into drug delivery rates. This is especially

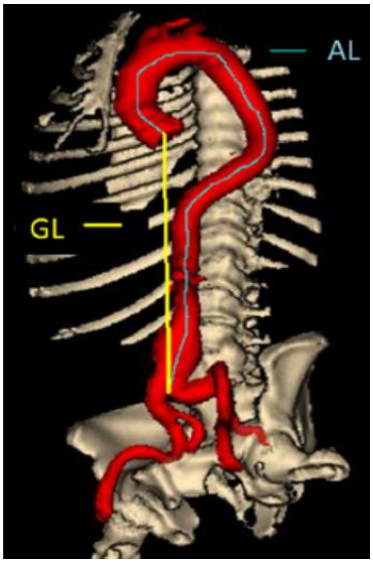

Fig. 1 Aortic tortuosity in a Marfan patient, as measured by the ratio of actual length (AL) to geometric length (GL). From Franken et al. [2]

important considering different phenotypes may have different rates depending on elastin fragmentation (which also affects the overall mechanics of the aorta).

Tortuosity

Outcomes

The data for the ten Fibulin4 Smooth Muscle Knock Out mice (SMKO) are shown in Fig. 2. So far only three mice have died the natural death needed to correlate tortuosity with aneurysm outcomes, so continued study is needed to fully understand the data. However, mice 1, 4, and 7 all experienced fatal aneurysms, which, given the preliminary outcomes is promising for the viability of tortuosity as a value that should be considered in aneurysm risk-assessement.

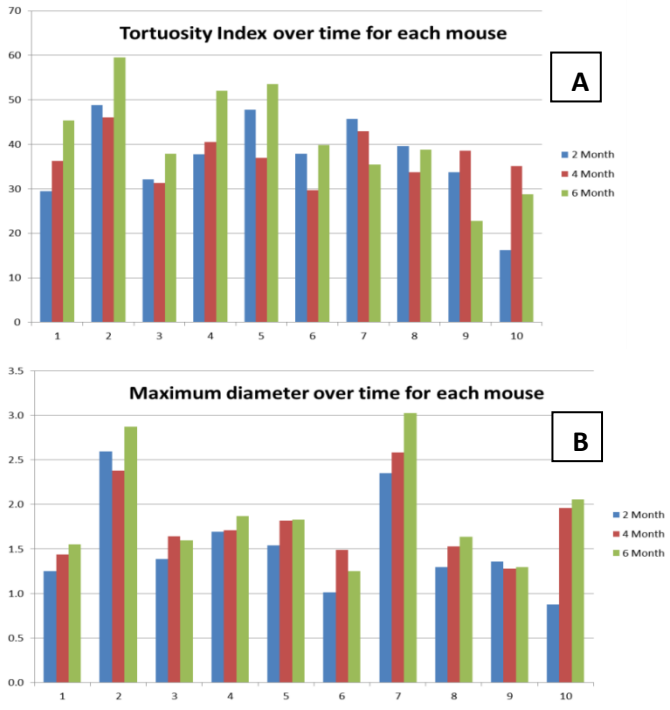

Fig. 2 SMKO Tortuosity index **(A)**, Maximum diameter **(B**

Computational modeling

Models were made of several mice in Crimson, a computational fluid dynamics and fluid-solid interaction software. These models are geometrically accurate; however mechanical properties must first be obtained from the arteries before blood flow simulation yields accurate results. Figure 3 shows an aorta model for a mouse that is not in the SMKO group. Models must still be made for the mice that have already died and had their arteries mechanically tested.

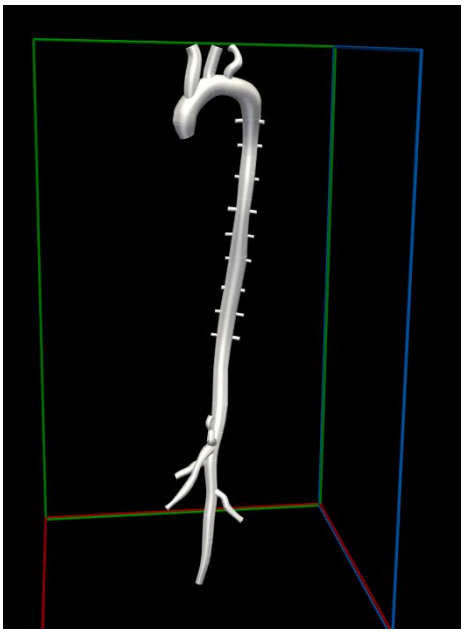

Fig. 3 Crimson model of mouse aorta, with manually added intercostals.

Mechanical testing

After mice die of ruptured aneurysm, their arteries are mechanically tested with a myograph. The results of these tests yield pressure-diameter curves which can in turn give mechanical constants for the section of the aorta being tested. Figure 4 shows the ascending and descending aorta results for mouse #1. Notice there are three curves on each graph; from red to blue these curves represent pressure-diameter values at increasing axial stretch ratios.

Image Processing

The problem of clarity

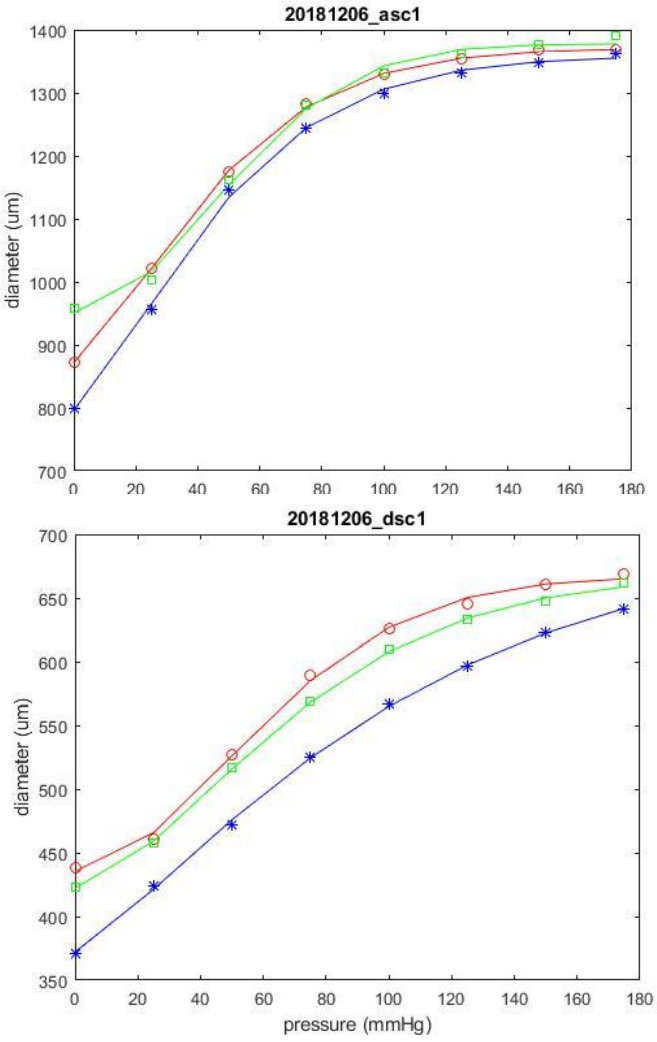

Fig. 4 Pressure diameter curves for SMKO #1 aorta. Ascending aorta on top, and descending aorta on the bottom.

Stacks of images were obtained of mouse arterial walls in order to quantify changes in elastic laminae structure and determine how it affects wall transport. As Fig. 5 shows, these images can be difficult to use, for instance in order to quantify the number of holes in each elastin layer. There are at least three elastin layers present within these image stacks, and since the layers are wavy, one cannot simply separate the layers by excluding some images in the stack. As a result, a protocol and script were written in order to isolate the luminal elastin layer from the rest.

Image processing protocol overview

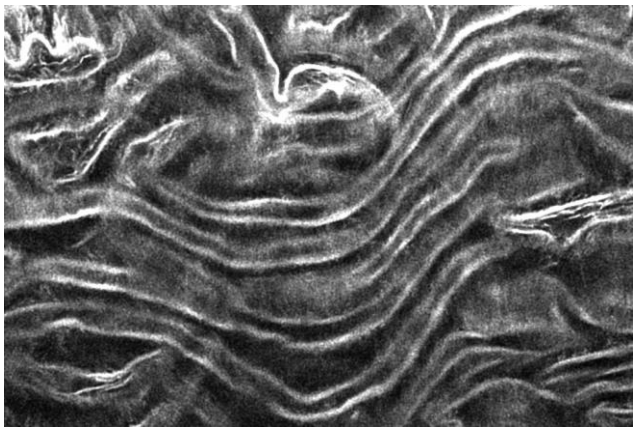

Fig. 5 Original image (z-projection of whole stack) of elastin in the arterial wall.

In order to isolate the luminal elastin layer, the image stack was processed in ImageJ. First, the stack was "resliced", in order to get a side view of the wall. This side image was processed using Automatic Local Thresholding functions that turn the images into binary white and black pictures; where the resulting value of a pixel is determined in contrast with the intensity of its neighboring pixels.

Once binary pictures were obtained, script (that was developed this semester) went through each image in the stack and suppressed every pixel beyond the first elastin layer, working from the lumen outward. The resulting mask was then multiplied by the initially resliced image, which was in turn resliced into the original stack view and projected into a single image. The above process is shown in Fig. 6, and the final image in Fig.7.

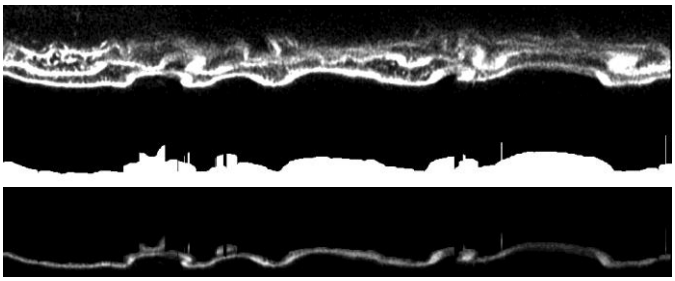

Fig. 6 Top: resliced of original stack of images; Middle: binary mask created by MATLAB script; Bottom: combination of original stack and mask stack, where the luminal elastin layer is isolated from the rest.

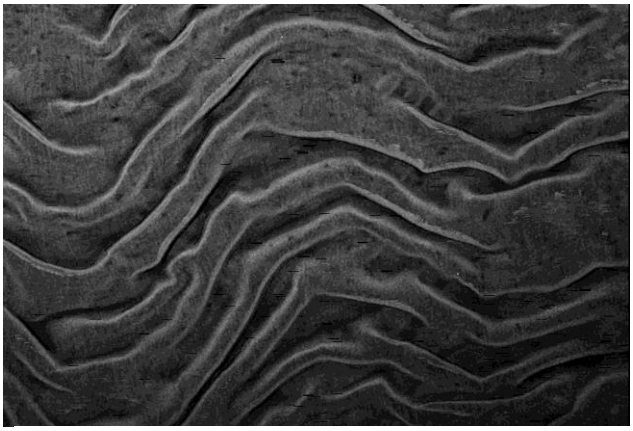

Fig. 7 Z-projected image stack of the arterial wall, with the luminal elastin layer isolated from the rest.

Conclusion

Future outcomes will further inform tortuosity data, though the small sample size of current aneurysm-based deaths shows promise for tortuosity as an important metric in understanding aneurysm severity.

Image processing techniques developed give clear images that could be used to quantify organization of a single elastic laminae in the arterial wall.

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