

## Ultrastructural Imaging of Collagen Fibrils in Mouse Model of Abdominal Aortic Aneurysm

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Abdominal aortic aneurysms (AAA) are a leading cause of death in the US. An aortic aneurysm is a persistent abnormal dilatation of the aorta that usually has no symptoms until it ruptures, which is a serious medical emergency. The specific cause of aortic aneurysms is still enigmatic, but it is believed to be initiated by degradation of elastin in the aortic wall. This degradation leads to weakening of the aorta, and in response the aorta is remodeled by degradation and deposition of collagen.

An open question in AAA pathology is: what is the quality of the collagen deposited in the AAA remodeling process and is this quality related to the risk of rupture. Previous studies of collagen in AAA have found defects in the organization and micro-architecture of collagen within AAA, and have correlated these defects with differences in aortic stiffness[1–3]. In terms of ultrastructural information, only limited information has been gathered of collagen within AAA[4]. This study aimed to determine if AAA contains ultrastructural defects in collagen.

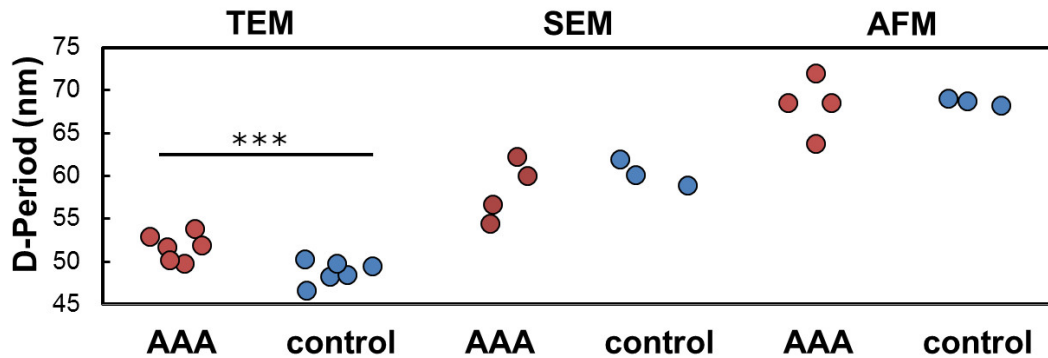
To investigate the ultrastructural features of collagen in AAA, we imaged collagen *in situ* using transmission electron microscopy (TEM), scanning electron microscopy (SEM), and atomic force microscopy (AFM). A standard mouse model for AAA was used, which involves the infusion of angiotensin-II in ApoE KO mice[5]. Saline-infused ApoE KO mice were used as controls.

SEM and AFM images showed no difference in length of d-period for AAA collagen fibrils (Fig.1). However, TEM images revealed a significant difference in length of d-period (Fig.1). These measurements were significantly smaller than the standard d-period value of 67 nm; therefore, these observations may be an artifact of the dehydration and resin embedding processing of the tissue. On the other hand, because both the AAA and control aortas were processed in parallel, these different responses to TEM processing could be due to structural differences, other than d-period, in the collagen fibrils.

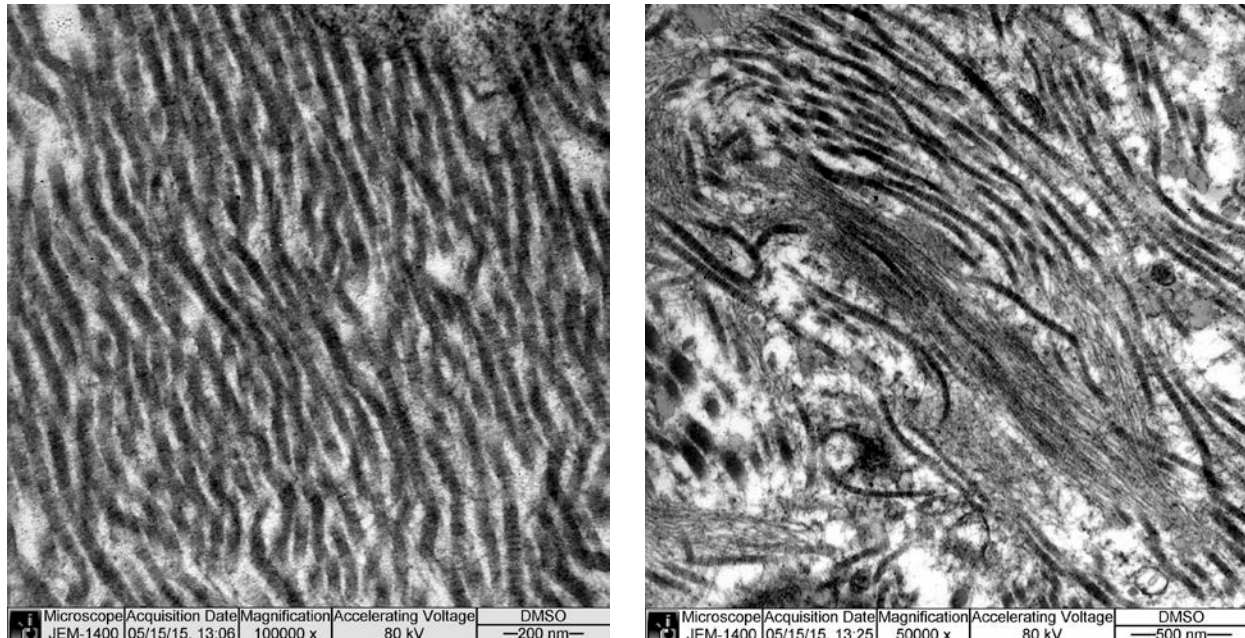
Additionally TEM and AFM images revealed AAA collagen fibrils with weakened or no banded structure (Fig. 2). TEM images showed no difference in average fibril diameter, but AAA mice contained a subset of very small collagen fibril cross sections (~20 nm). In this study, using multiple imaging modalities, ultrastructural defects were observed in collagen from mice with AAA. Understanding collagen ultrastructure could lead to critical insights into the specific pathology of AAA.

## References:

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**Figure 1.** Measurements of collagen fibril d-periods from AAA and control mice. Each dot is the mean value for a mouse. \*\*\*  $p < 0.006$



**Figure 2.** TEM images of collagen fibrils with weakened or no periodic structure. Left panel shows a bundle of fibrils with weakened banded structure. Right panel shows small fibrils, exhibiting no banded structure, amongst normal fibrils. Scale bars are shown in each image.