

The Diagnosis of Aorta and Marfan Syndrome

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DESCRIPTION

The flexibility required for reducing stroke pressure and pushing blood downstream is conferred by highly organized aortic wall components. Biomechanical and/or biochemical equilibrium can be disrupted by mutations in the genes encoding elastic lamellae proteins, which can lead to vascular diseases. Mutations in fibrillin-1 cause both abnormal lamellae construction during development and an increase in bioactive TGF- in the mature animal. Marfan syndrome (MFS) is a multi-system condition characterized by cardiovascular (thoracic aorta aneurysm), ocular (Ectopia lentis), and musculoskeletal (tall stature with arachnodactyly) abnormalities. Aortic dilatation that is irreversible frequently results in life-threatening dissections and ruptures.

Aortic aneurysms (both thoracic and abdominal) are a serious health problem in the ageing population of developed countries due to their high incidence (4.8% of the population will develop an aneurysm over their lifetime) and possibly lethal consequence. Invasive surgery is now the most effective treatment. Characterizing the progressive micro-structural remodeling of the vessel wall as a result of both heritable disease and ageing is critical for preventing aneurysms and/or developing less invasive treatments.

Historically, the predominant approach for examining vascular tissue structure has been microscopic imaging of two-dimensional sections using optical or transmission electron microscopy. These methods indicated significant artery wall alteration in the tunica media, including elastic lamellae fragmentation and the loss of vascular smooth muscle cells. Despite their widespread usage in pathological diagnosis, these methods are susceptible to artifacts (primarily because of mechanical sectioning). Furthermore, despite the fact that serial sectioning (combined with optical or electron microscopy), serial block-face scanning electron microscopy, and confocal microscopy can all be used to visualise three dimensional micro and Nano-structures of small tissue volumes, they are not well suited to resolving the three-dimensional structure of large tissue volumes. When compared

to previous methods, X-ray computed micro-tomography (micro CT) can examine the 3D structure of relatively large samples (up to cm^3) at high resolutions (sub). This non-destructive method has been applied to cardiovascular samples using synchrotron-based phase-contrast micro CT and can capture interior tissue characteristics in unstained cardiovascular tissues.

Stergiopoulos and colleagues used micro CT imaging with poor resolution to photograph aorta tissue for histological inspection and to define aortic form for numerical simulations. Finally, we demonstrated that phase-contrast micro CT (which does not use exogenous contrast agents) can quantify differences in the sub-micron structure of rat carotid arteries as a result of intra-luminal pressure and collagen orientation within the annulus fibrosus of native (unfixed and unstained) intervertebral discs using a high-flux synchrotron X-ray source.

This technique is gaining popularity in cardiovascular research due to its potential therapeutic use. Despite its ability to detect the inside microstructure of blood vessel walls, high-resolution micro CT imaging has yet to be used to describe 3D remodelling caused by MFS-related aneurysms and/or ageing. We show how a synchrotron-based phase-contrast micro CT scan can image intact, large-volume vascular systems at micrometre scale resolutions in this work. Using micro CT images of WT and MFS mouse aortae at various ages, we created new image processing and analysis techniques for analysing critical histological characteristics in 2D and 3D. We were able to characterise the similarities and differences between age-related (from 3-9 months) and MFS-related aortic wall remodelling using this approach.

Aortic wall remodelling is a typical feature of both ageing and hereditary connective tissue diseases connected to vasculopathies, such as Marfan Syndrome (MFS). Despite the fact that the aorta has a three-dimensional structure, due to the limits of current imaging methods, volumetric assessment has received little attention. A novel imaging tool known as phase-contrast micro CT can discern the 3D micro-scale structure of large materials without staining or sectioning them.

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