# Whole-body imaging of vascular pathology in fibulin-4 mice using Gd-liposomes and magnetic resonance angiography

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Introduction and purpose: Fibulins are a six-member protein family hypothesized to function as intermolecular bridges that stabilize the organization of extracellular matrix structures as elastic fibers and basement membranes. Previously, we generated a mouse model underexpressing Fibulin-4 and showed that reduced expression of Fibulin-4 leads to aneurism formation, dissection of the aortic wall and cardiac abnormalities. Mice homozygous for the Fibulin-4 reduced expression allele (Fibulin-4R/R) show dilatation of the ascending aorta and a tortuous and stiffened aorta, resulting from disorganized elastic fiber networks. The non-invasive and multi-contrast capabilities of magnetic resonance imaging (MRI) can aid tremendously in understanding this pathology and the effects of therapy.

Material and methods: In order to fully understand the complex nature of aortic vascular pathology in Fibulin-4R/R mice, we have used Gd-liposomes as an intravascular contrast agent to acquire high-resolution whole-body magnetic resonance angiograms (MRA) on a 3.0T MRI scanner with a 4-channel phased array interface (7 cm field-of-view). MRAs were processed using a 3D reconstruction platform to visualize the entire aorta from the aortic root until the branching of the iliac arteries.

Results and discussion: 3D MR angiographic reconstruction not only allowed accurate analysis of the thoraceous aortic aneurismal (TAA) lesions in Fibulin-4R/R mice, but also detailed examination of the surrounding aorta, collateral vessels and heart abnormalities (Figure 1). We observed variations in size and location of TAA in ascending aorta of Fibulin-4R/R mice. Strikingly, we also noticed incidental cases of aortic coarctation, a type of aortic pathology that in humans is also associated with aneurism formation.

Conclusions: We find combined manifestations of general aortic vascular pathology, including TAA, a tortuous descending aorta as well as aortic coarctation. In addition, using the fibulin-4R/R mouse model, we aim at molecular imaging of protease activity of MMPs upregulated during aneurism formation, using protease-activatable near-infrared fluorescence (NIRF) probes. We will test NIRF probes specific for MMPs in tissue sections from our aneurism mouse models. This multimodality approach will enable us to stitch function with anatomical detail.

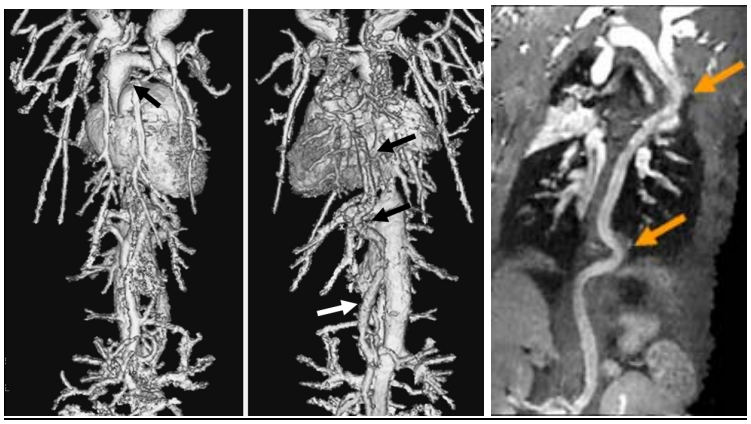

Figure 1:

Mouse underexpressing Fibulin-4 shows an aortic dilatation and a tortuous descending aorta. Surface rendering of a high resolution MRA acquired in a live mouse using an intravascular Gd-liposome formulation on a 3.0T clinical MRI scanner. Anterior and posterior views shown with arrows pointing at the course of the ascending and the descending aorta.