# Aortic Flow Assessment Using Phase Contrast MRI in Mice with Aortic Regurgitation

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## Introduction:

Hemodynamic wall shear stress (WSS) has been related to atherosclerosis development in both humans and animal models. However, the association between salient characteristics of flow patterns and localization of atherosclerotic lesions is still not fully understood. Our recent study [1] with low density lipoprotein receptor-deficient (*Ldlr*$^{-/-}$) mice has found that, following the surgical induction of aortic valve regurgitation (AR), atherosclerotic plaques developed extensively along the thoracic and abdominal aorta, which were normally lesion free (Figure 1). By using this mouse model with significant flow alternation (induction of diastolic retrograde flow), this study was to develop a phase contrast MRI technique for investigating the relationship between flow WSS and atherogenesis in the mouse aorta.

## Methods:

**AR creation**: AR on *Ldlr*$^{-/-}$ mice fed with high-fat diet [2] was created by catheterization under real-time ultrasound guidance via the right common carotid artery and by puncturing the aortic valve using the guide wire. Following the procedure, the catheter was removed and the right common carotid artery was ligated.

**Phase contrast MRI (PCMRI)**: Imaging was performed on a 7.0 T MR system (Varian Inc.) using a 3 cm diameter millipede radiofrequency (RF) coil (Varian Inc.) [3] and a 6 cm diameter insert gradient system. The experimental protocol was approved by the Animal Care Committee of the Hospital for Sick Children in Toronto. Mice were anesthetized using isoflurane and body temperature was measured and maintained using circulating warm air. Two subcutaneous electrocardiogram leads and a respiratory monitor (SA Instruments) were used for prospective triggering off of the R-wave during exhalation only. A CINE through-plane 2D gradient echo PCMRI sequence was implemented to acquire time resolved velocity images at multiple oblique slices [4]. Some of the sequence parameters are TR/TE=5/1.6ms, FOV=3cm$^2$, matrix size: 200x200, slice thickness: 1 mm, flip angle: 8$^o$, VENC are 200 and 320 cm/s for control and AR mice respectively. Partial Fourier acquisition with 70% partial fraction was used in the readout direction to reduce TE. Velocity images were calculated after phase subtraction of the two acquisitions and background phase correction.

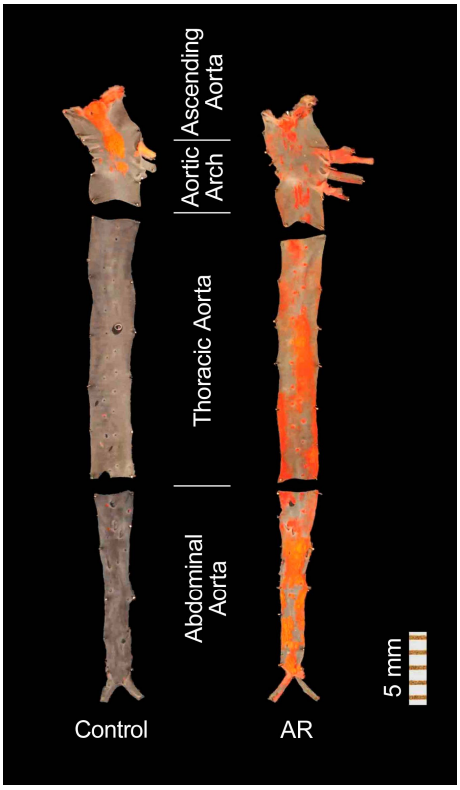


Figure 1: En face topography of oil red O stained atherosclerotic lesions in a typical control Ldlr-/- mouse and an aortic regurgitation mouse.

## Results:

Figure 2 illustrates the blood flow distribution during systole at ten prescribed planes covering the ascending aorta, aortic arch and descending aorta. Note the velocity in AR mouse is higher than in control mouse. In both control and AR mice, the descending aorta shows skewed velocity profiles due to vessel curvature. Figure 3 shows the blood flow distribution during diastole at the same planes. Only AR mouse shows retrograde flow during diastole at the descending aorta.

## Conclusion and discussion:

Phase contrast MRI was able to elucidate blood flow in the aorta of control and AR mice. Retrograde flow during diastole was present in the AR mouse, which has been observed previously using Doppler ultrasound [1]. Furthermore, WSS can be derived either from PCMRI measurement or *in vivo* measurement driven computational fluid dynamics (CFD) to find the correlation between atherosclerotic plaque severity and hemodynamics.

**References:** 1. Zhou Y.Q. et al., Arterioscler Thromb Vas Biol (2010)30:1181-1188; 2. Won D. et al., Am J Pathol (2007)171:1691-1704; 3. Wong W.H. et al., Proc ISMRM (2000)1399; 4. Nayler G.L. et al., J Comput Assist Tomogr (1986)10:715-722

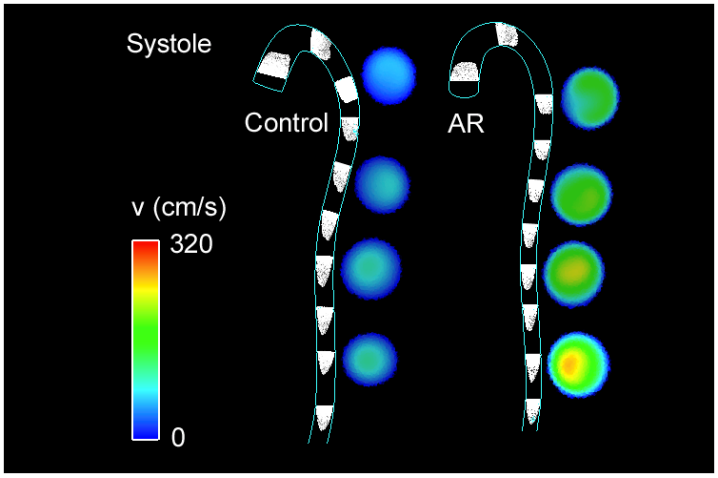


Figure 2: Vector arrow and cross-sectional velocity distribution at 10 prescribed planes during systole (t=20ms).

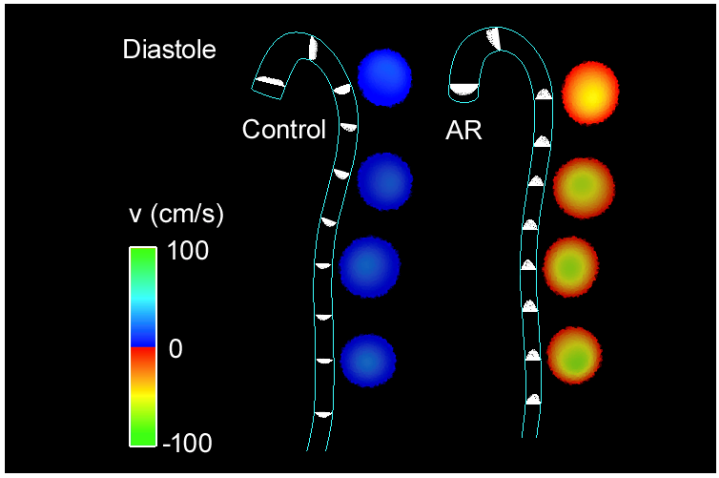


Figure 3: Vector arrow and cross-sectional velocity distribution at 10 prescribed planes during diastole (t=70ms). Note the discontinuous colormap at zero velocity to discriminate antegrade flow in control mouse and retrograde flow in AR mouse. Positive velocity starts from blue whereas negative velocity from red.