Evaluating Aortic Valve Remodeling in a Rabbit Model Using High Resolution MRI

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Introduction: Aortic valve sclerosis (AVS) is a common inflammatory disorder defined by generalized thickening of one or more of the three aortic valve leaflets.[1] Approximately 25% of the human population over age 65 is affected by AVS.[2] The disease usually progresses slowly, with 3% of patients over 75 years of age developing aortic stenosis, which necessitates valve replacement. Currently the integrity of the human aortic valve is investigated using transthoracic or transesophageal echocardiography.[3] The quality of echocardiographic images is dependant on transducer placement at the tip of the valvular cusp.[4] This proves difficult due to longitudinal motion of the valve during the cardiac cycle. Image quality is also greatly reduced by valvular calcification, which causes large shadows in the echocardiographic images. Magnetic resonance imaging (MRI) is a noninvasive method for aortic valve evaluation that allows visualization of the valve in any chosen plane and provides high resolution images that cannot be obtained by echocardiography.[5] We propose that MRI can be used quantitatively to monitor changes in the progression of the sclerotic disease process.

Methods: Male New Zealand White rabbits (n=29) were fed a cholesterol-supplemented diet to promote the formation of aortic valve sclerosis. Six additional rabbits were fed a cholesterol-free diet and served as controls. The aortic valves of all 35 rabbits have been examined using MRI every 3 months, starting at 6 months. Images were obtained using a 1.5 T GE MR clinical scanner interfaced with a customized two-channel phased array RF coil. A retrospectively gated cine fSPGR sequence (FOV=8 cm, Matrix 256x128, Slice thickness=2 mm, NEX=6, FA=20 deg., BW=31.25 kHz) was used. A plethysmograph attached to the rabbit's ear provided the gating signal. Oblique sagittal images were acquired of each valve cusp. Image analysis was performed off-line using the OCCI Viewer.[6] Images were reviewed by three independent blinded observers and valve thickness was measured in the middle third of the cusp using digital calipers. Measurements from all three cusps were averaged to generate average valve thickness measurement for control and cholesterol-fed rabbits. Results are shown as mean +/- SEM and were assessed by one-way ANOVA followed by a Tukey-Kramer post hoc test.

Results: Using retrospective peripheral gating we acquired high quality images in which the aortic valve is clearly measurable (Figure 1). The valve leaflets were best visualized during the diastolic phase, when the valve was closed. Valve leaflets were observed to thicken over time, to a greater degree in rabbits on cholesterol-supplemented diet compared to control (Figure 2). The most significant difference was observed at 15 months when cholesterol-fed rabbit cusps measured 25% more than control rabbit cusps.

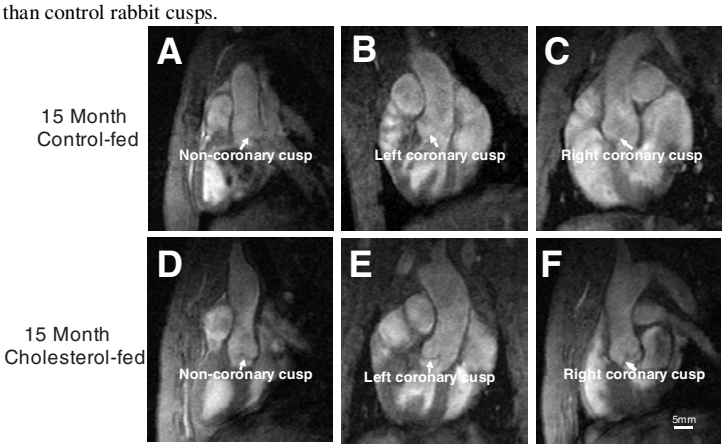

Figure 1: Retrospectively gated cine fSPGR oblique sagittal images of rabbit aortic valve cusps. A-C: Control rabbit. D-F: 15-Month Cholesterol-fed rabbit. A, D: Non-coronary cusp. B, E: Left coronary cusp. C, F: Right coronary cusp.

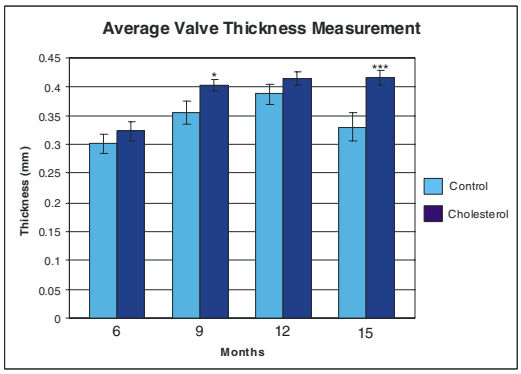

Figure 2: Average valve thickness of control and cholesterol-fed rabbits at 6, 9, 12 and 15 months. *P<0.05, ***P<0.001

Discussion and Future Directions: Here we show the first evidence that increasing valve thickness can be measured *in vivo* using high resolution MRI. Retrospective peripheral gating couples image acquisition to the cardiac cycle thereby generating images during diastole when the valve is closed and relatively still, resulting in high quality images in which the aortic valve is clearly distinguishable and measurable. Increased valve thickness was observed for both control and cholesterol-fed rabbits. Greater thickening was evident in rabbits on the cholesterol-supplemented diet when compared to control. Variations in control thickness measurements were observed and may be due in part to motion artifacts and spatial resolution limitations. Currently we are unable to gate the respirations of rabbit subjects; the clarity of valve images is significantly influence by respiratory motion. Choppy breathing produces motion artifacts and reduces image quality. This limitation is of no consequence in human subjects where respiratory gating is feasible. The healthy rabbit valve is extremely small and thin, hence MR image quality is also limited by the spatial resolution of the 1.5T MR scanner. Although higher field strength improves spatial resolution it also increases the prevalence of motion artifact. Development of rabbit cardiac and respiratory gating at higher field strengths would allow us to overcome motion artifacts while increasing resolution. Despite these limitations, rabbit aortic valve thickness is measurable using a 1.5T MR scanner. Since the rabbit aortic valve is approximately one tenth the size of a human valve we are confident that differences in human valve thickness over time would be evident at 1.5T. Our current MRI technique, which allows us to examine the progression of the sclerotic process on a case by case basis, can also be used to investigate the efficacy of disease treatments *in vivo*. Here we present the initial findings of a 3 year study which is using MRI techniques to examine whether dietary modification or the application of a lipid lowering agent can modify the sclerotic process in aortic valves. All diseased rabbits will be subdivided into 5 treatment groups and monitored for a year to examine the effect of dietary and pharmacological intervention.

References:

1. Rosenhek R *et al*, (2004). Mild and moderate aortic stenosis. Natural history and risk stratification by echocardiography. Eur Heart, 25: 199-205. **2.** Otto CM *et al* (1999). Association of aortic valve sclerosis with cardiovascular mortality and morbidity in the elderly. N Eng J Med, 241: 142-7. **3.** Bonow RO *et al*, (1998). Guidelines for the management of patients with valvular heart disease: executive summary. Circulation, 98: 1949-84. **4.** Hoffmann R *et al*, (1993). Planimetry of orifice area in aortic stenosis with multiplane transesophageal echocardiography. J Am Coll Cardiol, 22: 529-34. **5**. Debl K *et al*, (2005). Planimetry of aortic valve area in aortic stenosis by magnetic resonance imaging. Invest Radiol, 40(10): 631-6. **6.** http://cardiacimaging.ca/technical_resources/occi_viewer/