3D MR Microscopy Rendering with Non-Uniformity Correction and a Non-Linear Adaptive Noise Filter for Studies of a Transgenic Mouse Heart Model of Myxomatous Valvular Disease

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INTRODUCTION

3D MR microscopy was used to image isolated hearts to study myxomatous valvular disease (MVD) in a unique transgenic mouse model [1]. MVD encompasses several genetic entities that show a common set of degenerative alterations in valvular histology and function. The mitral valve is most frequently affected; however, the involved human genes have yet to be identified. The *Hs3st1* gene codes for the enzyme 3-*O*-sulfotransferase-1 (3OST1), which regulates production of certain heparan sulfate molecules (HS^{AT+}). *Hs3st1*$^{-/-}$ mice have significant chances of developing mitral or aortic valve leaflet thickening. However, MVD produces focal lesion of only ~50-150μm thickness, which greatly hampers the study of this disease in mice. Echocardiography can only provide a qualitative assessment of leaflet thickening; whereas, histologic sectioning can miss the small focal lesions. MRI has the advantage that some soft tissues can be observed in 3D without the destruction associated with sectioning, allowing for visualization of the valves in situ. It also has the advantage that 2-3 hours of imaging can provide enough data for a full 3D reconstruction, leaving the sample intact for specific histological or molecular studies that would not be conducive to obtaining 3D information.

METHODS

Mice *Hs3st1*$^{-/-}$ and wild type (n=4) were developed and raised at Dartmouth Medical School. After ultrasound imaging, animals were sacrificed and the hearts were perfusion fixed in 10% formalin. After shipping to Calgary, hearts were immersed 1:40 Gadolinium (Magnevist) in 20% formalin for 24 hours before imaging. MRI was undertaken at 9.4T using a Bruker Avance console and a 2cm volume coil. Gradient echo FLASH 3D images were collected with TR/TE/α=50ms/5.4ms/30º, NT=1, matrix of 256x256x256 and a pixel resolution of 50x50x78μm. Images were first processed with a non-uniformity correction to remove the RF bias. There was second order non-uniformity in the z direction and little non-uniformity in the xy plane. A nonlinear adaptive noise filter was applied [3]. 3D visualization was done on desktop workstations using custom software with real-time interactive rendering [2].

RESULTS

The mitral valve in the knockout mouse is approximately twice as thick as the wild type (Fig. 1). Volume and surface renderings from MRI data are shown in Fig. 2,3.

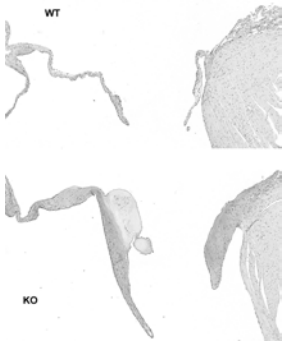


Figure 1: Histology of mitral valve. H&E stained sections of cross-sections of mitral valve from wild type (WT, Top) and knockout (KO, Bottom) mouse hearts.

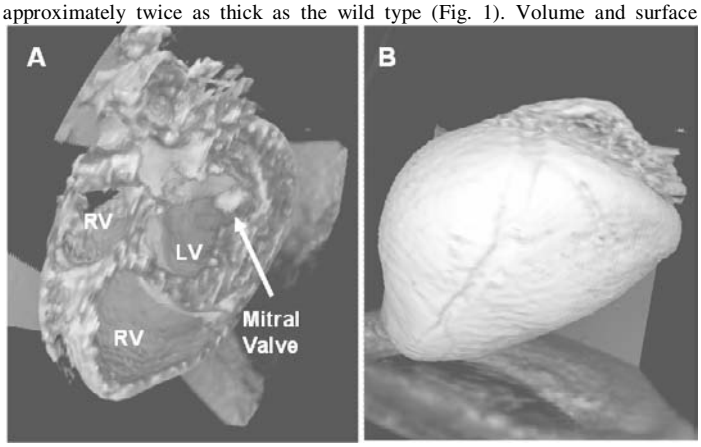
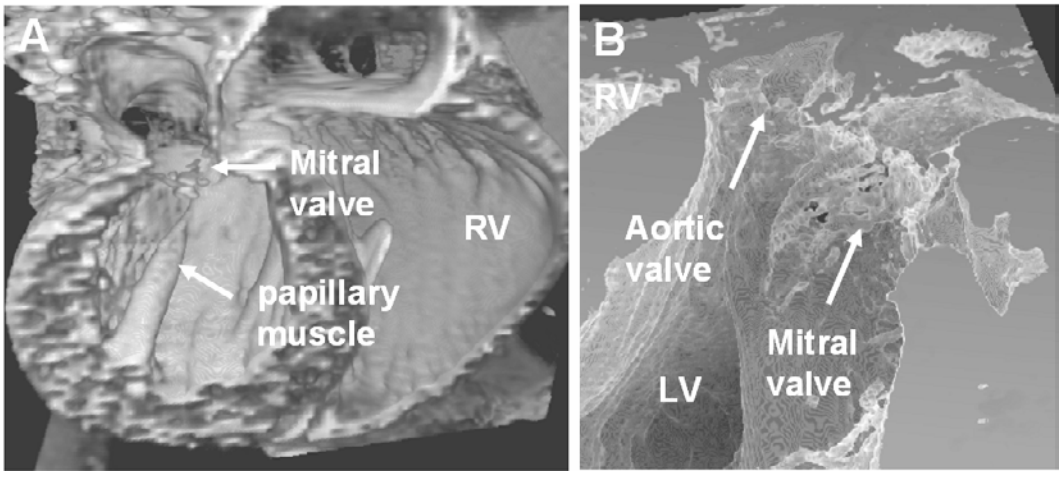


Figure 2: MRI surface rendering A) 3D rendering with close surface cut away to show cavities of the right ventrical (lower and left openings) and left ventrical (upper right opening); and B) Surface rendering of total heart showing quality of background and noise reduction and RF correction.

Figure 3: Virtual "cut away" of a heart with valve disease. A) cross section looking "up" showing a thick left ventricle wall and enlarged papillary muscle leading to the mitral valve; and B) Cut away of the mitral and aortic valves.

DISCUSSION

The 3D rendering provides excellent information on the location and integrity of the valves and the overall integrity of the structure such as the ventricle thickness. The ability to interact with the data volume with interactive 3D visualization provides significant additional information for interpretation of the structure of the heart. Valve thicknesses were visually smaller in the wild type vs. the transgenic mouse hearts.



REFERENCES

1. HajMohammadi S et al. *J Clin Invest* 2003; 111(7):989-999.
2. Kniss J, Premoze S, Hansen C, Ebert D. *13th IEEE Visualization* 2002.
3. Black MJ, Sapiro G, Marimont D, Heeger D. *IEEE Trans Image Process* 1998; 7(3):421-432.