Structural Basis for Regional Heterogeneity of Left Ventricular Function?

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INTRODUCTION: Structure-function relationships are essential to understanding biological performance. The complex, but highly ordered arrangement of myofibers in the ventricular wall is closely related to regional myocardial function. This work tests the hypothesis that midwall myofibers are not oriented in the circumferential direction in all regions of the left ventricle and furthermore that regional gradients in myofiber orientation are heterogeneous. Regional differences of myofiber arrangement should impact regional function in addition to having implications for the interpretation of MRI tissue tagging strains.

METHODS: Five sheep were euthanized with left ventricular (LV) pressure adjusted via central venous exsanguination to match *in vivo* LV end-diastolic pressure. The hearts were subsequently fixed *in situ* by injection of 5% buffered glutaraldehyde into left anterior descending and left circumflex coronary artery catheters, excised, and stored in 10% formalin. Mid-ventricular slices were imaged on a 1.5T GE Signa Excite scanner using a custom diffusion tensor weighted interleaved echo-planar imaging sequence. Scan parameters were: TE/TR=75ms/1000ms, BW=±62.5kHz, FOV=250mm, encoding matrix=256x256, 975x975x3000μm resolution, 32 interleaves, 3 averages, 5 b=0 s/mm^2, and 55 isotropically distributed diffusion encoding directions with b-value=1000 s/mm^2.

Reginal myofiber orientations were measured using a local cardiac coordinate system. A longitudinal axis was defined by a line passing from the LV apex to the mitral valve aspect of the left aortic valve commissure; the radial direction was defined as a vector from the geometric centroid of the slice to the point of interest; the circumferential direction was defined from the cross product of the longitudinal and radial directions. Local myofiber direction was defined as the angle (α) between the primary eigenvector of the diffusion tensor and the local circumferential direction. Epicardial and endocardial contours were defined by b-spline fits to threshold determined perimeter points. Papillary muscles were manually masked. The left ventricular midwall was defined as 50% radial wall depth between the epicardium and endocardium. Finally, a circumferential fiber contour was defined from a b-spline fit to all locations where -5°< α <5°.

RESULTS: Figure 1 shows a map of the myofiber angle within a representative mid-ventricular short-axis slice of ovine left ventricle. A contour of the circumferential fibers (α=0°) is a shown as a white line. The contour indicates that in the lateral wall there is a preponderance of negatively oriented (α<0°) epicardial fibers. Figure 2 demonstrates the transmural variation of the myofiber angle in the septal and lateral wall. The dark line indicates the group mean fiber angle as a function of normalized wall depth (0%–epicardium, 100%–endocardium) with the dashed lines indicating ±1 standard deviation. In the lateral midwall (50% depth), fibers are oriented at an angle of α=-14°±8°. In comparison, septal midwall fibers average 10°±12°. These plots demonstrate that circumferential fibers are not located at the midwall, but, instead, at 43±9% wall depth in the septum and 67±11% wall depth in the lateral wall. In addition, the septal wall has a steeper gradient in myofiber angle change, resulting in more fibers being oriented in an almost longitudinal direction (α ~±90°).

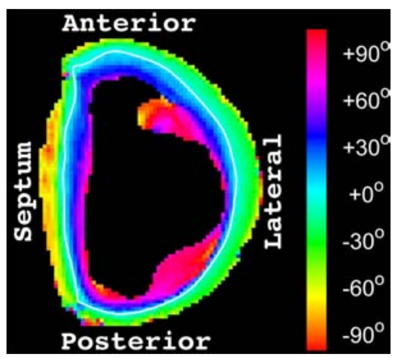

Figure 1

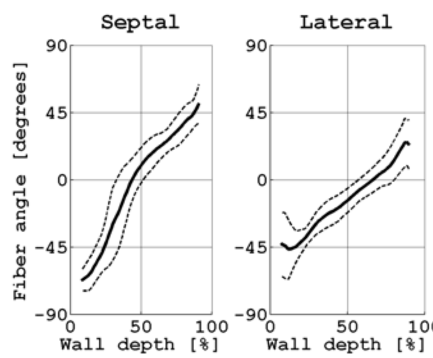

Figure 2

CONCLUSIONS: Midwall myofibers are not always oriented in the circumferential direction. When analyzing ventricular function using MRI tissue tagging or displacement imaging it is often assumed that midwall myofibers are oriented in the circumferential direction. The results herein, however, suggest that midwall myofibers can lie as much as -14°±8° oblique to the local circumferential direction which would result in underestimates of myofiber shortening by as much as 8%. Numerous studies have used MRI tissue tagging to demonstrate decreased circumferential shortening in the septum relative to the lateral wall [1-2]. This may, in part, be attributed to a greater fraction of myofibers oriented in the longitudinal direction. Recent MRI tissue tagging results also demonstrate a correlation between greater pre-stretch of the antero-lateral and infero-lateral wall and greater circumferential shortening[3]. This latter result implicates a hemodynamic driving force for variations in regional function. The results, herein, suggest that regional variations in myofiber arrangement may also play a role.

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