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Diffusion Tensor Magnetic Resonance Imaging of the Heart: Looking into the Layers of the Myocardium

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One of the fascinating features of cardiac contraction is that in the human left ventricle (LV), fibers shorten by ~15%, yet systolic thickening is ~55%, producing an ejection fraction of 60% to 65%. This efficiency is largely due to the anatomical fiber angles in the LV. Epicardial fibers spiral in a left-handed helix and endocardial fibers in a right-handed helix (1). It is known that fiber shortening in the epicardium (defined for the purpose of this paper as the outer one-third of the myocardium, and likewise for endocardium) is predominantly in the plane of the epicardial fiber direction (approximately 75^{o} from the circumferential plane); however, in the endocardium where the fibers are oriented at approximately -70^{o} from the circumference, maximal shortening is in the radial direction (0^{o}) (2,3). Thus, at the endocardium, maximal shortening is occurring at almost right angles to the plane of the anatomical fibers (cross-fiber shortening).

The consequence of the endocardium shortening in 2 directions (fiber and cross-fiber shortening) is that to preserve volume, it must thicken extensively in the third direction; explaining, at least in part, the marked systolic thickening produced by fiber shortening of 15%. It is thought that the epicardial fibers, as a consequence of their greater radius and thus mechanical advantage, cause the endocardial cross-fiber shortening, as this phenomenon has to be due to forces outside of the endocardium.

These functional characteristics have been largely elucidated in animal models and in humans using magnetic resonance tissue tagging. However, these data do not reveal to us the anatomical mechanism for this phenomenon. LeGrice et al. (4) have suggested in a canine model that rearrangement of myocytes by slippage along myocardial cleavage planes is in the correct direction and of sufficient magnitude in the endocardium to account for a substantial proportion (>50%) of systolic wall thickening. Diffusion tensor imaging (DTI) is a technique that relies on measuring restricted diffusion of water to reveal in vivo anatomical structures, and, in the current issue of the *Journal*, Nielles-Vallespin et al. (5) have now used this

technique to produce data further elucidating how the layers of the left ventricle behave during contraction.

In a series of animal and human experiments, they produced evidence that cardiac myocytes are organized in microstructures termed sheetlets that reorientate during LV thickening. They show that the DTI measurement of sheetlet orientation (the E2A or angle of the secondary eigenvector) moved in healthy humans by 45^{o} from a tangential plane (18^{o}) to a more radial direction during systole. This sheetlet redirection correlated closely with histology and radial thickening. Only small changes in the actual anatomical fiber angles were seen in systole. In hypertrophic cardiomyopathy, the sheetlet angle was more radial in direction in diastole, though changed less during systole compared to healthy subjects. In dilated cardiomyopathy, diastolic values were similar to those seen in the healthy subjects, although the redirection was significantly less in systole. Thus, these data provided a fascinating dynamic and microstructural view of how the LV and its layers change and realign during systole and may, in large part, explain the phenomenon of systolic wall thickening.

Some questions come to mind. First, the functional data with cross-fiber shortening mentioned previously are predominantly an endocardial phenomenon, although the sheetlet reorientation described in the current study seemed to be through the LV wall. We do not know if this is an issue of spatial resolution of DTI unable to focus on the endocardium, or perhaps there is indeed sheetlet reorientation through the thickness of the LV wall that would not have been previously predicted. The human data, while novel, are relatively limited. For instance, a significant proportion of the dilated cardiomyopathy patients have LV ejection fractions $\geq$50%, meaning a mild phenotype (**Figure 5B**). It would be very interesting to have a more comprehensive range of ejection fractions to see if there is a threshold effect, whereby below a certain level of ejection fraction (or even better, fiber shortening) the sheetlet

reorientation is severely limited. It would also be interesting to know, in the setting of hypertrophic cardiomyopathy, whether a patient's genotype predicts sheetlet behavior.

How will this affect the clinician in his or her day-to-day practice? Cardiac DTI is a complex technique that is unlikely to be taken up in clinical practice soon, despite recent innovations to reduce acquisition time (6,7). However, the significance of this study and the technique is that it will help us answer important and interesting questions about mechanisms of LV dysfunction. One of the consequences of the spiral orientation of the fibers is that the obliquely oriented epicardial fibers cause torsion of the LV during systole. During diastole, the recoil of this torsion occurs very rapidly, largely during isovolumic relaxation, and is thought to help in early diastolic filling of the LV (8,9). In a similar fashion, does sheetlet reorientation in diastole contribute to LV filling?

Another topical issue is how aging affects LV function. One feature that has been consistently seen in normal aging human subjects is a reduction in the ability of epicardial shortening (as measured by torsion) to influence the endocardium (as measured by endocardial circumferential shortening) (10,11), and this is related to the normal reduction in cardiac output seen with aging (12). Is this failure of epicardial-to-endocardial interaction due to reduction in sheetlet reorientation? Hopefully this paper by Nielles-Vallespin and colleagues will be the stimulus to answer these and other interesting and important questions.

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