# Aberrant Myocardial Sheetlet Orientation in Hypertrophic Cardiomyopathy detected using *In Vivo* Cardiovascular Magnetic Resonance Diffusion Tensor Imaging

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**Target audience:** Scientists and clinicians working in the field of cardiac diffusion MRI.

**Purpose:**

Cardiac Diffusion Tensor Imaging (cDTI) provides information on cross-myocyte components of intramyocardial water diffusion. Assuming these to be constrained by the sheetlet and shear-layer microstructure of left ventricular myocardium [1], we investigate if *in vivo* cDTI could identify changing sheetlet orientations and abnormalities in hypertrophic cardiomyopathy (HCM).

**Materials and Methods:**

We performed cDTI *in vivo* at 3T (Siemens Skyra) at end-systole and late-diastole in 8 healthy controls and 4 patients with HCM in 3 short-axis slices. Diffusion was measured with a monopolar STEAM-EPI sequence as previously described in [2,3]: 6 diffusion encoding directions, b=350s/mm$^2$, spatial resolution = 2.7×2.7×8mm$^3$. Additionally 3D cine DENSE [4] scans were performed at 1.5T (Siemens Avanto) to analyse the effect of myocardial strain on the diffusion tensor at both cardiac phases. Diffusion analysis was performed with in-house developed software. Voxel-wise calculation of the diffusion tensor before and after a previously suggested strain correction [5] was performed before calculating the Helical Angle (HA), and the secondary-eigenvector angle (E2A) defined as the angle between the secondary eigenvector and the LV epicardial wall in the cross-myocyte – radial plane.

**Results:**

Voxel-wise analysis of diffusion tensors relative to ventricular coordinates showed the expected transmural progression of HA, with no significant differences between phases or between HCM and controls before and after strain correction.

In both controls and HCMs, E2A values before strain correction changed from more wall-parallel in diastole (low angles) to more wall-perpendicular in systole (higher angles), although no significant differences were encountered between the two phases once the tensor was strain corrected (controls p=0.96, HCMs p=0.11) (Figure 1). Figure 2 shows the effect of strain on the orientation of the secondary eigenvector for a systolic diffusion tensor. Before and after strain correction, HCM hearts showed consistently higher E2A values at both cardiac phases (p=0.004 for both phases after strain correction) (Figure 1).

Figure 3 shows the histogram of myocardial E2A values. Before strain correction, the histogram of E2A values differed between controls and HCMs mainly at diastole, where controls showed a significant peak at angles close to 0. After strain correction the differences between the two cohorts and between cardiac phases are reduced but controls showed higher frequencies at angles close to zero. In contrast the HCM patients showed E2A values more towards a perpendicular to the LV wall conformation (Figure 3).

**Discussion:**

*In vivo* cDTI quantifies cross-myocyte diffusion. Applying the previously suggested myocardial strain correction [5] to diffusion measured *in vivo* does not significantly affect the orientation of the primary-eigenvector and therefore HA, but results in substantial changes of E2As measured, especially in volunteers with normal strains. Although such correction has been advocated prior to analysis of the secondary eigenvector of the diffusion tensor acquired with a monopolar STEAM sequence, the limitations of the correction model should be considered. It assumes similarly homogeneous deformation at the microscopic as well as the macroscopic scale measured by DENSE. This fails to recognise the different, more complex deformations and realignments occurring at the microscopic scale of sheetlets and shear layers - the scale likely to result in anisotropies of diffusion. Further insight is needed to assess what type of correction is appropriate for analysis of cross-myocyte components of diffusion. Nevertheless, with or without correction, the larger median value of E2A in HCM is in keeping with the more wall-perpendicular sheetlet orientations expected in hyper-contracted myocardium. This may provide a novel phenotypic insight into diastolic abnormalities arising from genetic sarcomeric dysfunction, with potential therapeutic implications. It is hoped that further microstructural as well as cDTI investigation will clarify these relationships.

**References**

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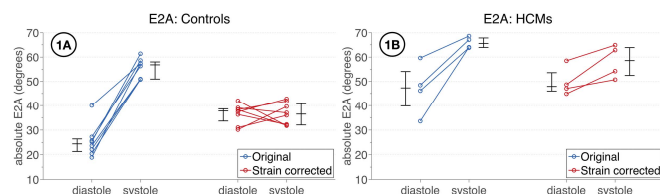[5] Reese, et al, J Magn Reson B, 34:253 1996.

Figure 1: Scatter plots showing the mean myocardial E2A values for all subjects (A-controls, B-HCMs) at the two imaged cardiac phases before (blue) and after (red) strain correction. In all plots the median and interquartile range are shown.



Figure 3: Histogram of myocardial E2A values for all subjects (A,B-controls, C,D-HCMs) at the two imaged cardiac phases before and after strain correction. The thick lines represent the inter-subject average.
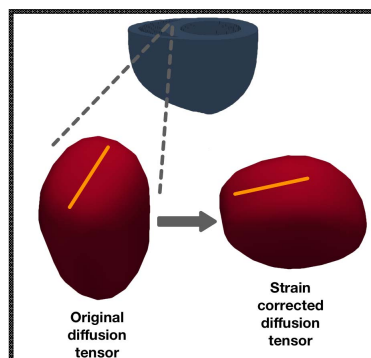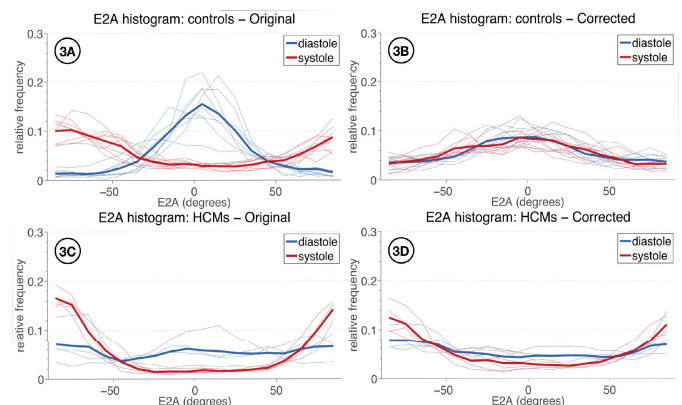


Figure 2: Systolic mid-septal diffusion tensor represented by a superquadric glyph before and after strain correction. The orange line represents the orientation of the secondary eigenvector.