Analytic description of MR diffusion indices in ex-vivo human hypertrophic cardiomyopathy

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Purpose: We propose to describe diffusion-related properties of hypertrophic cardiomyopathy in humans in comparison to normal.

Introduction:
Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease and the leading cause of sudden death in the young [1]. HCM is well known to contain major changes at the structural level with myocytes disarray, increase in collagen content and modification of the extracellular matrix (ECM), that can only be determined using invasive focal myocardial biopsy or after death. In-vivo Diffusion Weighted Imaging (DWI) of the heart remains very challenging due to cardiac and respiratory motions. Most of the cardiac DWI studies have been performed with animals using a high-field scanner or extra-long time acquisition [2-3] but that will never be applicable to in-vivo imaging. Our objective is therefore to study hypertrophic cardiomyopathy in humans and to find MR diffusion indices that could reflect the myocardial fiber disarray and ECM changes. To set apart motion-related technical challenges but investigate the potential clinical value this technique could have in humans, we studied hypertrophic and control ex-vivo human hearts with spatial resolution that can be reproduced for in vivo cardiac studies. Imaging was performed within a few hours after sudden death and after forensic expertise.

Theory: Quantitative comparison between healthy and hypertrophic myocardial fiber organization remains difficult and dependent on the fiber tracking algorithm applied to Diffusion Tensor (DT) data. Consequently, we decide to base our analysis on parametric maps of MR diffusion indices. We consider the following MR diffusion indices (each providing different information about water diffusion in the myocardium): Fractional Anisotropy (FA[4]), which measures deviation from isotropy and reflects the degree of alignment of cellular structures within fiber tracts ; Mean Diffusivity (MD[4]), which measures average molecular motion and fiber Coherence Index (CI[5]), which estimates the smoothness of the principal diffusion direction field.

Method: 22 ex-vivo human hearts (HTM:18, normal:6) were studied after data acquisition on a 1.5 T clinical scanner (Siemens, Avanto), using 12 direction Spin-Echo/Echo-Planar diffusion imaging sequence (resolution: 2x2x2mm^3, matrix: 128x128, DW parameters b: 0 and 1000s/mm²) and anatomical T1 and T2 weighted MR sequences. Hypertrophic hearts were selected from forensic cases with sudden death, macroscopic and microscopic evidence of hypertrophic cardiomyopathy, whereas normal hearts were selected after exclusion of any cardiovascular disease.
T1 and T2-weighted image data were used as a reference to determine the distribution of hypertrophic regions (see Figure 1(a) and 2(a)). To assess DT-MRI data, we selected three short-axis slices of interest (basal/medium/apex) and segmented, in each slice, the left ventricle in four segments (w.r.t. histopathological studies: inferior/lateral/septal/anterior). The segmentation step is illustrated for the medium slice in Figures 1(c) and 2(c). Finally, after computing the respective MR diffusion indices for each slice, we displayed the results using histograms: the four masks resulting from the segmentation step (inferior/lateral/septal/anterior) were used to plot the distribution of each MR diffusion index in each histopathological segment (see Figure 1(d) and 2(d)).

Results and Discussion:
Figure 1(d) and 2(d) show the distribution of each MR diffusion index (FA, MD and CI) in each histopathological segment for the medium slice of a healthy and a HCM heart. As shown here, the shape of CI and FA histograms were different when comparing normal to the hypertrophic hearts. First, the hypertrophic myocardium presents a more dispersed CI histogram with a lower mean value (0.83 vs. 0.95(normal)) in accordance with rearrangement and fiber disarray observed in [6]. Second, compared to the healthy case, the FA histogram of the hypertrophic heart shows greater variance and a larger mean value (0.32 vs. 0.23(normal)). This could be related, if one assumes that DWI measures mainly extra-cellular water diffusion, to myocytes swelling in the pathologic hypertrophic regions. Finally, note that MD was not significantly different between hypertrophic and normal cases. As a preliminary result, FA and CI appear to be good MR diffusion-related candidates to help in identifying myocardial fiber disarray.

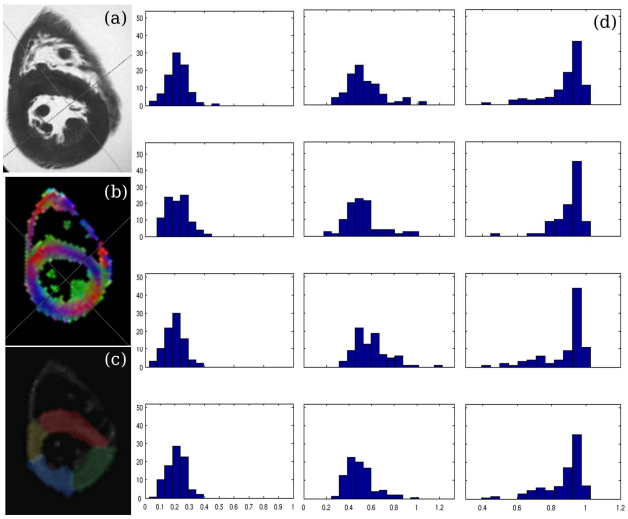

Figure 1: Healthy human heart (290g). ***(a)*** *T2 weighted image..****(b)*** *Fiber directionality map.* ***(c)*** *Anatomical segment masks (green: anterior, red: septal, yellow: inferior, blue: lateral).* ***(d) Top to bottom,*** *Anatomical segments ordered as follows: anterior, inferior, lateral and septal.* ***Left to right,*** *diffusion indices ordered as follows: FA, MD and CI.*

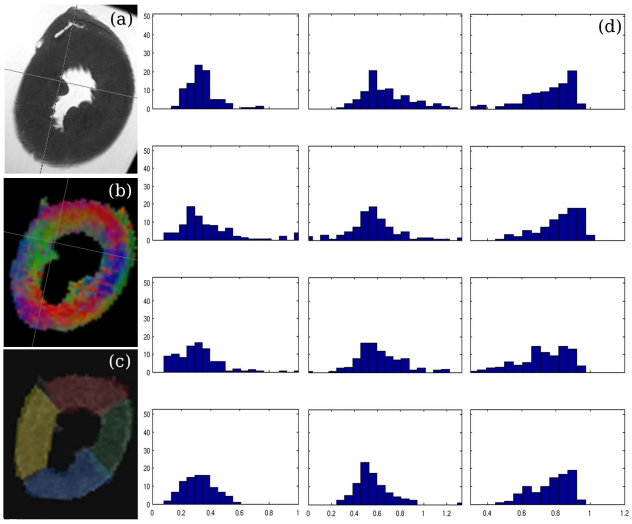

Figure 2: Hypertrophic human heart (630g). ***(a)*** *T2 weighted image.* ***(b)*** *Fiber directionality map.* ***(c)*** *Anatomical segment masks (green: anterior, red: septal, yellow: inferior, blue: lateral).* ***(d) Top to bottom,*** *Anatomical segments ordered as follows: anterior, inferior, lateral and septal.* ***Left to right,*** *diffusion indices ordered as follows: FA, MD and CI.*

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