Myocardial Remodeling in Chronic Porcine Model: a DT-MRI Study Using the Toroid-based Representation

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Introduction

Diffusion Tensor Magnetic Resonance Imaging (DT-MRI) is a non-invasive technique capable of characterizing myocardial fiber architecture and structural properties **[1]**, which may provide new insights about left ventricular (LV) remodeling after myocardial infarction (MI). The helical organization and anisotropic nature of cardiac myofibers require efficient strategies for visualization and investigation. The toroid-based representation of the DT has been shown to be less prone to visual ambiguity and offers two new quantitative scalar maps, TV and {1-TVR} **[2]**. These indices provide additional information of the subtle changes in diffusivity and degree of anisotropy compared to standard indices **[3]**. The purpose of this work is to evaluate the structure and fiber organization of normal porcine hearts and hearts 2- and 8-weeks post-MI using TV and {1-TVR} maps derived from DT-MRI. Results revealed that TV and {1-TVR} maps are sensitive to changes which occur due to cardiac remodeling post-MI.

Methodology

LV remodeling was evaluated using 5 normal porcine hearts and hearts 2- and 8-weeks post surgical ligation of marginal branches of left circumflex coronary artery. The toroid-based function of the DT allows the introduction of new indices, TV and {1-TVR}, which provides complementary scalar maps representing the tissue macrostructure. TV is defined by $TV = (\pi/3)\lambda_1\left[\lambda_2\lambda_3 + \lambda_3^2/2\right]$ and represents a measure of diffusivity; TVR is defined by the ratio of TV to the volume of a toroid scaled by $\langle\lambda\rangle$: $TVR = TV/TV_{\langle\lambda\rangle}$, $TV_{\langle\lambda\rangle} = \pi/2\langle\lambda\rangle^3$. Fiber inclination angles were defined using the orientation of the primary eigenvectors **[4]**. Derived from T2-weighted images and using the 16 segments of the standard cardiac polar map, tissue segments were classified into *Infarct (I)*, *Non-Infarct (NI)*, and *Border (B)* regions (see **Fig.1A** and **1B** for an example at 8-weeks post-MI). Within each region, structure and fiber organization were assessed using TV, the coefficient of anisotropy {1-TVR}, and fiber angle variance (FAV) that is employed to capture the degree of fiber angle spreading over the volume of interest. The mean values of TV (mm^6/s^3), {1-TVR}, and FAV (deg^2) indices were then computed, and compared between *I*, *NI* and *B* regions.

***Data acquisition*:** Animals were euthanized and hearts were excised and perfused with saline. Each heart was then placed in a container and filled with Fomblin (Ausimont, Thorofare, NJ). DT-MRI was performed on a 3.0T Siemens Trio scanner (Erlangen, Germany) using a segmented EPI sequence, 6 gradient directions; b-values=0 (T2-weighted) and 600s/mm^2; voxel-size=2×2×2mm^3; 50 short-axis slices; TR=5400ms; TE=84ms; 40 averages (EPI factor=7).

Results

The toroid-based maps, TV and {1-TVR}, as well as, the fiber angle map allows for the highlighting of the structural and geometrical properties of cardiac myofibers, as illustrated for one heart at 8-weeks post-MI in **Fig.1C**, **1D**, and **1E**, respectively. In addition, by thresholding the TV index above the NI and B values and using the nonlinear properties of the TV index, a three-dimensional delineation of the infarcted region was created (see **Fig.1F**). **Fig.2** depicts the quantification of myocardial remodeling using the FAV and toroidal indices.

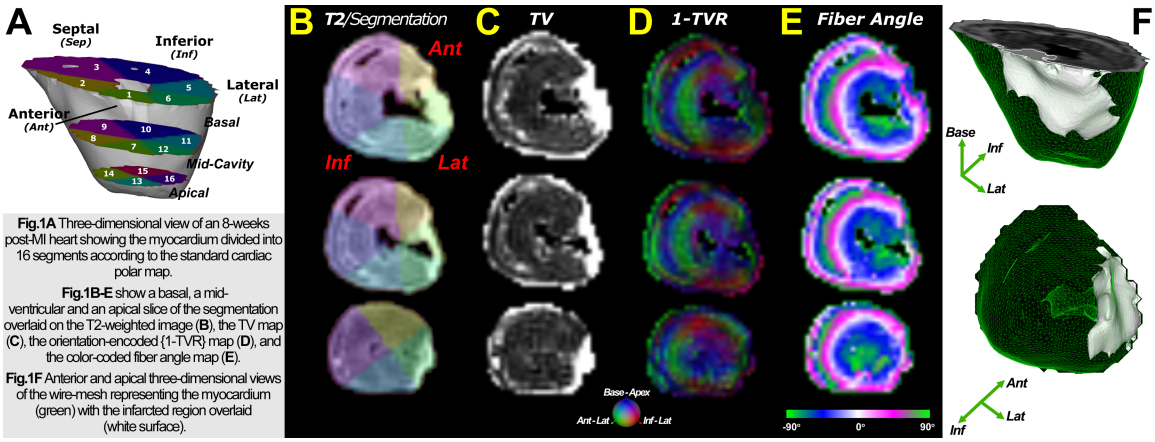

Fig.1A Three-dimensional view of an 8-weeks post-MI heart showing the myocardium divided into 16 segments according to the standard cardiac polar map.

Fig.1B-E show a basal, a mid-ventricular and an apical slice of the segmentation overlaid on the T2-weighted image (**B**), the TV map (**C**), the orientation-encoded {1-TVR} map (**D**), and the color-coded fiber angle map (**E**).

Fig.1F Anterior and apical three-dimensional views of the wire-mesh representing the myocardium (green) with the infarcted region overlaid (white surface).

TV, {1-TVR} and FAV were uniform in normal hearts, and significantly ($p<0.05$) altered in the infarct regions at 2- and 8-weeks post-MI. TV, {1-TVR}, and FAV were also altered ($p<0.05$) in *NI* and *B* regions at 2-weeks post-MI with normalization by 8-weeks. This suggests the ongoing tissue reorganization process, which is underscored by a concomitant alteration in diffusivity, anisotropy and myocardial fiber inclination in the remote territory between 2- and 8-weeks post-MI. The LV remodeling process is also reflected by an expansion of the infarcted region *(I)*, which evolves from 2 to 8-weeks post-MI (see **Fig.2D**). These changes in TV, {1-TVR} and FAV are in agreement with previously observed spatial and temporal changes in regional activation of matrix metalloproteinase's **[5]**.

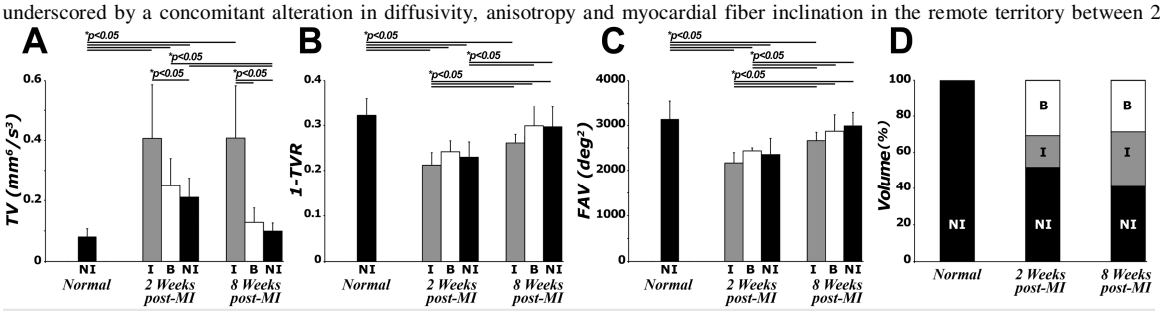

Fig.2 Mean TV (**A**), {1-TVR} (**B**), FAV (**C**), and regional *(NI, B, I)* volume *(expressed as a percentage of total volume)* (**D**) computed from the 16 regions of the standard cardiac polar map for normal, 2- and 8-weeks post-MI hearts. The structural alteration observed with diffusivity (**A**), anisotropy (**B**) and FAV (**C**) demonstrates that the toroidal model is able to characterize the remodeling process.

Discussion

The toroidal model yields two quantitative scalar maps, TV and {1-TVR} that were applied for the characterization of temporal changes in myocardial structure post-MI. Diffusivity (TV), anisotropy ({1-TVR}) and fiber angle variance (FAV) were altered 2-weeks post-MI, but showed a tendency to return to the original basal values at 8-weeks post-MI. These parameters revealed a structural dynamic modification (*i.e.* LV remodeling) as a function of time post MI. This suggests that structural changes attributed to LV remodeling, which involve both the infarcted and non-infarcted LV myocardium, were quantifiable by the toroid-based indices. In conclusion, toroidal DT-MRI indices provide a means for a non-destructive, regional quantification of hearts post-MI, which in turn, may enhance the understanding of myocardial macrostructure and temporal changes involved in the post-MI remodeling process.

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References: **[1]** Helm PA *et al.* Circ Res 2006; 98:125-32 **[2]** Mekkaoui C *et al.* SCMR 2008 **[3]** Mekkaoui C *et al.* ISMRM 2008 **[4]** Scollan *et al.* Am J Physiol. 1998; 275:2308-18 **[5]** Vanhoutte D *et al.* Cardiovasc Res. 2006; 69:604-13