Myofiber Orientation in the Normal and Infarcted Heart, Assessed with MR-Diffusion Tensor Imaging

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Abstract

Cardiac fiber orientation is one of the main determinants of fiber stress and strain during ejection [1, 2, 3]. We measured fiber orientation using MR-DTI. Traditional methods to quantify the cardiac fiber field rely on the definition of the coordinate system. We propose to use the entity divergence for characterization of the continuity of the myocardial fiber structure. The entity divergence is a scalar quantity with a value independent of the actual choice of the coordinate system. Moreover, the divergence value of the fiber field expresses the degree of uniformity of stress along the fiber direction [4]. The divergence of the myofiber field appeared to be $< 0.08\ mm^{-1}$ *in the midwall for all normal hearts. At the insertion sites of the papillary muscles and the anterior RV fusion site the divergence of the fiber field is elevated to values above* $0.3\ mm^{-1}$. *In the infarcted hearts, divergence values in the unaffected tissue are similar to the values observed in healthy hearts. In and adjacent to the infarcted region, no significant differences in the divergence values were observed. This indicates that continuity of the fiber structure remains preserved in the presence of a transmural myocardial infarction.*

1. Introduction

Cardiac fiber orientation is one of the main determinants of fiber stress and strain during ejection [1, 2, 3]. Recently a technique called Magnetic Resonance Diffusion Tensor Imaging (MRDTI) has been introduced which enables determination of the 3-dimensional myofiber direction throughout the intact heart [5, 6, 7, 8]. Cardiac myofiber orientation is usually characterized by the helix angle and the transverse angle. Determination of these angles however, requires a well defined local wall-coordinate system [9]. Definition of such a wall-coordinate system is often difficult due to the fact that cardiac geometry is not rotationally symmetric and the endocardial wall is irregular. We propose the use of the divergence of the myofiber field as a characteristic of local myofiber orientation. The entity divergence is a scalar quantity with a value independent of the actual choice of the coordinate system. Moreover, the divergence value of the fiber field expresses the degree of uniformity of stress along the fiber direction [4]. In healthy hearts, non-uniformities in the cardiac stress distribution may be expected at the insertion sites of the papillary muscles and at the RV fusion sites.

In hearts with a cardiac infarction, local mechanics in the normally perfused region adjacent to the infarction is disturbed [10]. The disturbed mechanics may be related to changes in fiber orientation.

We investigate whether divergence-patterns in the region adjacent to the infarction deviate from normally observed patterns. To this end, fiber orientation was measured in both normal hearts and hearts with a chronic transmural infarction. Subsequently, divergence values were calculated throughout the heart.

2. Methods

Animal handling was performed according to the Dutch Law on Animal Experimentation (WOD) and the European Directive for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (86/609/EU). The protocol was approved by the Animal Experimental Committee of the University of Maastricht.

2.1. Animal model

In seven female goats, weighing 25 to 50 kg, anesthesia was induced with thiopental 15 mg/kg IV and maintained by ventilation with halothane (1 to 2 %) in a 2:3 mixture of O_2 and N_2. The ECG was recorded from the limb leads. During sterile surgery the thorax was opened and an infarction was created by ligation of one of the descending branches of the left circumflex coronary artery (LCx)(figure 1). Ten weeks after infarct induction the

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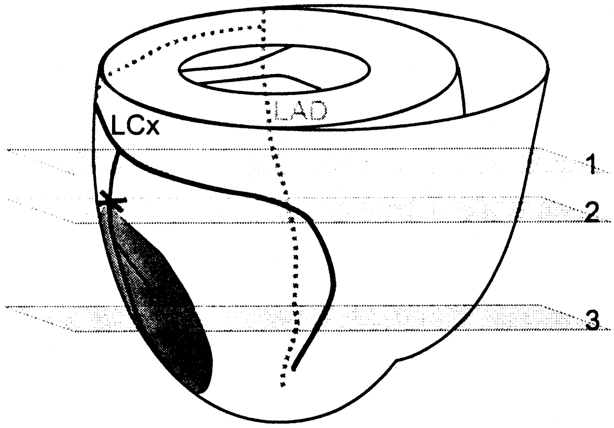

Figure 1. Schematic illustration of infarct location. A descending branch of the LCx is ligated, resulting in a lateral transmural infarction. Planes used for analysis are indicated, 1: equatorial, 2: basal to infarction, 3: through the infarcted region. LAD: Left anterior descending coronary artery

animals were anesthetized again. The thorax was re-opened and a clamp was placed around the aorta. The heart was arrested with an injection of 1M KCl into the left ventricular cavity, rapidly excised and rinsed in cold saline. After the removal of the atria the heart was casted in a 20 % gelatin substance in order to maintain shape, and subsequently stored at 4°C. MR Diffusion Tensor Imaging measurements were performed within 3 days. Control measurements were performed on 5 healthy female goats weighing 26-55 kg that were sacrificed for unrelated orthopedic experiments. After an overdose of Euthasate the goats were bled to death. The hearts were excised and the same procedure as for the infarcted hearts was followed.

2.2. Measurement of fiber orientations

Magnetic Resonance Diffusion Tensor Imaging (MR-DTI) is a technique which has been developed to measure the diffusion tensor for water in biological tissues [5]. In muscular tissue diffusion of water along the myofiber direction is about 1.6 times faster than perpendicular to the myofiber. Diffusion properties of tissue are described by a diffusion tensor with 6 independent components. These components can be determined if diffusion is measured in at least 6 directions . The principal direction of the diffusion tensor corresponding to the largest diffusivity closely coincides with the myofiber direction [6, 7, 8, ?].

MR-Diffusion Tensor Imaging (MR-DTI) measurements were performed at a 4.7 Tesla, 200 MHz Varian (Palo Alto, USA) NMR Spectrometer. We measured diffusion properties in 10 directions in 3mm thick adjoining slices covering the whole heart. The long axis of the left ventricle was visually aligned with the axis of the magnet bore. Image resolution was 0.78×0.78 mm^2, resulting in a voxel size of 1.8 mm^3. The diffusion tensor was reconstructed by fitting the diffusion data to a 6 component diffusion tensor in a least squares approach. The principal directions of the tensor were calculated with respect to the magnet coordinate system, in order to identify myofiber orientation.

2.3. Divergence of the fiber field

We described the fiber field by a unit vector $\vec{e_f}$ pointing in the fiber direction. The divergence of the fiber field was defined as:

$$\vec{\nabla} \cdot \vec{e_f} = \left|\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z}\right| \quad (1)$$

where u is the x-component, v is the y-component and w is the z-component of the fiber direction. We calculated the divergence of the cardiac myofiber field on a pixel-by-pixel basis. In the normal hearts the equatorial slice was selected as the slice that was positioned at one-third of the long axis length from the base of the heart [11]. A typical value for the divergence was obtained by selecting the midwall pixels of this slice and calculating the mean value for the divergence in these pixels. Divergence plots were created for several slices. It was investigated whether characteristic patterns could be observed.

In the infarcted hearts the infarcted region was characterized by local wall thinning. It was investigated whether in regions adjacent to the infarction divergence values were elevated when compared to the same region in normal hearts.

3. Results

In three goats a transmural infarction was properly induced, two goats died due to induction of the infarction, and in two goats the infarction appeared not to be transmural. Although there was substantial variation in infarct size and location, all infarctions were located below the equator at the lateral side of the heart.

Fiber orientation was measured post-mortem using MR-DTI. Fiber orientation as measured within the magnet-coordinate system is visualized for the equatorial slice in figure 2. The midwall fibers run predominantly in the circumferential direction. More axially oriented fibers are found in the papillary muscles and near the endo- and epicardial surfaces.

In normal goat hearts the divergence value in the midwall region of the equatorial slice averaged 0.064 ± 0.009 mm^{-1} (mean $\pm$ sd). In the (not affected) equatorial slice of the infarcted hearts this value was the same: $0.064 \pm$

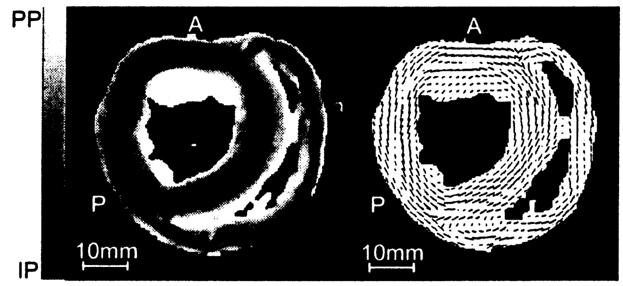

Figure 2. Visualization of the fiber field in the equatorial slice (slice 1, fig 1) of a normal heart with respect to the magnet coordinate system, A: Anterior, P: Posterior. Left: Out-of-plane component of the fiber direction. Black indicates in-plane (IP) fiber direction, white indicates fiber direction perpendicular to the plane (PP). Right: Projection of the fiber direction onto the imaging plane.

$0.014\ mm^{-1}$. In figure 3 typical divergence patterns in the equatorial slice are shown for both normal (left) and infarcted (right) hearts. These patterns are similar for healthy and infarcted ventricles: In major parts of the myocardial wall the divergence values are $<0.08\ mm^{-1}$. However, at the anterior fusion of the left and right ventricular walls, and at the insertion sites of the papillary muscles the divergence values significantly exceeded the level of $0.3\ mm^{-1}$.

Figure 3. Divergence pattern in the equatorial slice (slice 1, fig 1) of a normal heart (left) and a heart containing a transmural infarction (right). White arrows indicate the regions in which the divergence values significantly exceed the level of $0.3\ mm^{-1}$.

In figure 4, typical divergence patterns of an infarcted heart are shown for the slice just basal to the infarction and for a slice through the mid-infarct region. Corresponding slices in a normal heart are shown for comparison.

The infarct region is characterized by substantial wall thinning. The divergence pattern is not significantly different for the normal and the infarcted hearts.

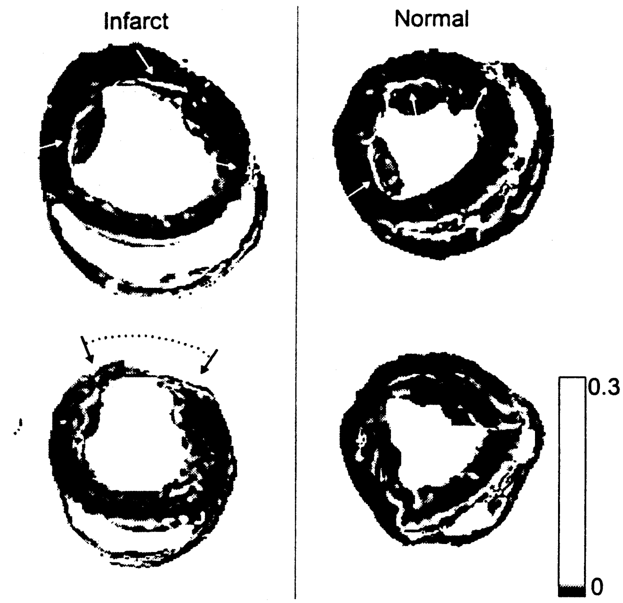

Figure 4. Left: Divergence patterns in the infarcted heart. Upper panel: Slice basal to the infarction (slice 2, fig 1). The white arrows indicate the regions in which the divergence values significantly exceed the level of $0.3\ mm^{-1}$. Lower panel: Slice through the mid-infarct region (slice 3, fig 1). Substantial wall-thinning is observed in the region indicated by the dotted line spanned between the two black arrows. Right, upper and lower panel: Corresponding slices in a normal heart.

4. Discussion and conclusion

The entity divergence is a coordinate free measure, which expresses the uniformity of stress along the fiber direction. In a normal cardiac fiber field, divergence values are expected to be zero [4]. Divergence values rise significantly when fibers are discontinuous or when tapering occurs. Also, merging of fibers may be associated with elevated divergence values ($>>0\ mm^{-1}$).

We calculated the divergence of the cardiac fiber field on a pixel-by-pixel basis, a method which is relatively sensitive to noise. Divergence values were $<0.08\ mm^{-1}$, throughout most of the cardiac muscle. At the insertion sites of the papillary muscles and the anterior RV fusion site divergence values were significantly larger ($>0.3\ mm^{-1}$). Apparently, at these sites, fibers merge with other fibers over a distance of 3 mm. The results indicate that the divergence value can be used to detect stress non-uniformities in the cardiac fiber field.

In and adjacent to a transmural cardiac infarction, the divergence pattern in three infarcted hearts showed no significant deviations from the pattern in normal hearts. Potential stress non-uniformities that occur due to the presence of an infarction are not observed. We therefore conclude that myocardial fiber structure remains quite well preserved in the presence of a transmural myocardial infarction.

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