Remodeling of cardiac fiber structure after infarction in rats quantified with diffusion tensor MRI

Junjie Chen,1,2 Sheng-Kwei Song,3 Wei Liu,1,2 Mark McLean,1 J. Stacy Allen,1 Jie Tan,1 Samuel A. Wickline,1 and Xin Yu1
1Cardiovascular Magnetic Resonance Laboratories, Cardiovascular Division, Department of Medicine, 2Department of Biomedical Engineering, and 3Departments of Chemistry and Radiology, Washington University, St. Louis, Missouri 63110

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Structural remodeling of myocardium after infarction plays a critical role in functional adaptation. Diffusion tensor magnetic resonance imaging (DTMRI) provides a means for rapid and nondestructive characterization of the three-dimensional fiber architecture of cardiac tissues. In this study, microscopic structural changes caused by MI were evaluated in Fischer 344 rats 4 wk after infract surgery. DTMRI studies were performed on 15 excised, formalin-fixed rat hearts of both infract (left anterior descending coronary artery occlusion, n = 8) and control (sham, n = 7) rats. Infarct myocardium exhibited increased water diffusivity (41% increase in trace values) and decreased diffusion anisotropy (37% decrease in relative anisotropy index). The reduced diffusion anisotropy correlated negatively with microscopic fiber disarray determined by histological analysis (R 0.81). Transmural courses of fiber orientation angles in infract zones were similar to those of normal myocardium. However, regional angular deviation of the diffusion tensor increased significantly in the infract myocardium and correlated strongly with microscopic fiber disarray (R 0.86). These results suggest that DTMRI may provide a valuable tool for defining structural remodeling in diseased myocardium at the cellular and tissue level.

Ventricular function is influenced prominently by the unique three-dimensional organization of myocardial fibers. The mammalian ventricle is composed not only of circumferential and longitudinal fibers but also of obliquely running sheets of fibers that form a helical spiral from base to apex. When viewed from the apex, the orientation of left ventricular (LV) fibers changes smoothly from a left-handed helix in the epicardium to a right-handed helix in the subendocardium (1, 25). This structure is a key determinant of ventricular torsion, strain, and stress (2, 18, 27).

After acute myocardial infarction (MI), cardiac muscle undergoes a prolonged remodeling process that induces widespread structural changes (4). The most prominent and apparent are myocyte death and scar formation in the infract myocardium. However, this wound healing process is not limited to the infract area. Changes in noninfarcted myocardium include myocyte hypertrophy and apoptosis, fiber disarray, angiogenesis, and an increase in interstitial collagen, all of which can eventually lead to death from heart failure (26). As a consequence of the structural remodeling, regional and global myocardial functions are altered (31). However, the mechanism by which alterations in structural components contribute to progressive deterioration in cardiac function remains unknown. Accordingly, we propose that a three-dimensional depiction of myocardial microstructure after infarction could provide novel insights into the structure-function relationship in the postinfarct myocardium.

Early descriptions of myocardial fiber microstructure were based on histological measurements of fiber orientation (1, 24, 25). However, histological reconstruction of myocardial fiber structure is a very laborious and time-consuming process. In addition, simultaneous determination of the longitudinal (inclination angle) and transmural (transverse angle) components of the fiber orientation at the same location is difficult based on this two-dimensional technique. Furthermore, the exact orientation of myofiber near the endocardium and epicardium is subject to distortion during tissue preparation. As a result, this method has found limited applications in determining myofiber structure in diseased hearts. Thus a detailed and complete picture of ventricular fiber microstructure after MI has not been developed.

Magnetic resonance imaging (MRI) provides an alternative method to study the remodeled myocardium and its microstructure. Contrast-enhanced perfusion MRI is a widely accepted method for noninvasive determination of infract location and size (13, 14). However, this method cannot provide information regard-

Address for reprint requests and other correspondence: X. Yu, Campus Box 8086, 660 S. Euclid Ave., St. Louis, MO 63110 (E-mail: xin@cvu.wustl.edu).

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ing ongoing microscopic structural changes. Recent studies have demonstrated that diffusion tensor MRI (DTMRI) may provide an alternative method for rapid and nondestructive reconstruction of the three-dimensional fiber structure throughout the ventricles at high spatial resolution (7, 9, 10, 22, 23). This method is based on the assumption that water diffusion along the myocardial fiber is the greatest, and therefore the primary eigenvector of the diffusion tensor coincides with the local fiber orientation. By comparing DTMRI and conventional histological results, recent reports (9, 10, 22) have demonstrated a direct correlation between MRI and histological fiber angle measurements, thereby validating the DTMRI approach for complete characterization of myofiber architecture.

Although DTMRI has been used to delineate myofiber architecture in normal myocardium, its utility for quantifying structural changes in diseased myocardium has not been demonstrated. The principal goal of this study was to elucidate microscopic structural changes in postinfarct remodeling myocardium with DTMRI. Cardiac structure in Fischer 344 rats was characterized using DTMRI 4 wk after infarction. Quantitative histological analysis was performed to identify cellular processes responsible for changes that occurred in DTMRI measurements. Our results suggest that DTMRI has the potential to noninvasively locate MI and to detect changes in the myocardial structure that occur at cellular levels.

MATERIALS AND METHODS

Animal model. Transmural infarction in the anteroseptal region was created in 12- to 24-mo-old Fischer 344 rats (280–360 g) by permanent occlusion of the left anterior descending (LAD) coronary artery (n = 8). Briefly, the animal was anesthetized, intubated, and attached to a ventilator. Via a thoracotomy, the proximal LAD was permanently occluded with a surgical suture. The infarction was confirmed by regional cyanosis. The surviving rats were given buprenorphine for pain relief and maintained under physiological conditions in a pathogen-free environment for 4 wk. Additional sham-infarct procedures (thoracotomy and pericardial incision) were performed in seven age-matched rats as the controls. All the procedures conformed to the guidelines set forth by the Washington University Animal Care Committee.

Four weeks after the surgery, the rat was heparinized (100 units) and anesthetized with isoflurane, and the heart was excised and cannulated for retrograde perfusion at 100 cm hydrostatic pressure with a modified Krebs-Henseleit buffer equilibrated with 95% O₂-5% CO₂ at 37°C. The buffer contained (in mM) 118 NaCl, 4.7 KCl, 1.2 KH₂PO₄, 1.2 MgSO₄, 2.5 CaCl₂, and 25 NaHCO₃. After an equilibration period of 5 min to wash out residual blood, the perfusate was switched as described to the LV long axis. A multislice spin-echo sequence with diffusion-sensitizing bipolar gradient was used to acquire short-axis, diffusion-weighted images. Imaging parameters were the following: echo time, 45 ms; repetition time, 3.0 s; diffusion time, 20 ms; diffusion-gradient on time, 10 ms; and field of view, 2.0 × 2.0 cm²; slice thickness, 1.0 mm; and number of averages, 4. Images were acquired with a 128 × 128 data matrix and zero filled to 256 × 256. These parameters yielded an in-plane resolution of 78 × 78 μm². A total of 11 short-axis images covering the whole LV were acquired. For each short-axis slice, two sets of diffusion-sensitizing gradients (G₁ = 2 G/cm and G₂ = 8 G/cm) were applied along six independent directions. The corresponding b values were 48 and 764 s/mm², respectively. Total image acquisition time was about 5 h.

Data analysis. A MATLAB-based software was developed for image analysis and visualization (The MathWorks, Natick, MA). For each slice, the diffusion tensor at each voxel was calculated by solving the equation

\[
\ln \frac{S(b_1)}{S(b_2)} = \sum_{i=1}^{3} \sum_{j=1}^{3} (b_{ij} - b_{ij}) D_{ij}
\]

where \(S(b_1)\) and \(S(b_2)\) are the signal intensity recorded in the presence of diffusion gradients \(G_1\) and \(G_2\), respectively, and \(b_{ij}\) and \(b_{ij}\) are components of the corresponding b matrices. \(\overline{D}_{ij}\) is a component of the effective self-diffusion tensor D. Consequently, the three eigenvalues of the diffusion tensor, \(\lambda_1\), \(\lambda_2\), \(\lambda_3\), and their corresponding eigenvectors were calculated. A map of the diffusion tensor trace (i.e., the sum of all three eigenvalues at each voxel) and a map of relative anisotropy (RA) were generated. RA was calculated as (8)

\[
RA = \frac{\sqrt{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}}{\sqrt{3}\bar{\lambda}}
\]

where \(\bar{\lambda}\) is the mean (trace/3) of the three eigenvalues. All three eigenvalues and the trace of diffusion tensor were further normalized to \(\lambda\) of the surrounding solution to minimize the effect of diffusivity variations due to temperature fluctuation.

The orientation angles of the myocardial fiber were calculated by transforming the primary eigenvector from MRI Cartesian coordinates to a local cylindrical myocardial coordinates proposed by Scollan et al. (22). This coordinate system was also similar to that developed by Geerts et al. (7) but differed from the wall-bound myocardial coordinates used in histological studies (24). To define this local coordinate system, epicardial and endocardial borders were outlined by 20 control points and fitted with smooth curves using cubic spline method. The papillary muscles were excluded from endocardial tracing by visual inspection. The LV long axis planes were perpendicular to the LV long-axis imaging plane and originated at the center of LV cavity. Subsequently, a circle centered at the LV center was fitted to the epicardial surface. The epicardial tangent planes were defined as the planes tangent to the epicardial circle and parallel to the LV long axis. After the determination of the local
myocardial coordinate system, two angles, the inclination angle and the transverse angle, were calculated to uniquely specify the orientation of a fiber in three dimensions. The inclination angle, or the helix angle, was defined as the angle between the projection of the primary eigenvector onto the tangent plane and the short-axis imaging plane. The transverse angle was defined as the angle between the projection of the primary eigenvector onto the short-axis imaging plane and the tangent plane.

The LV was further divided into four segments: septum, anterior, lateral, and inferior. The intersection of the interventricular septum with the right ventricle was manually identified. The remaining LV wall was then divided evenly into three segments as anterior, lateral, and inferior. Wall thickness in each segment was also calculated. The transmural shifts of inclination and transverse angles from endocardial to epicardial borders were evaluated at these segmented regions, as well as in infarct zones. The infarct region was located at the anterolateral region of the heart. Angular deviation of the inclination and transverse angles, which is defined as the regional standard deviation of the inclination and transverse angles, respectively, was calculated to evaluate the coherence of fiber orientation in a given region.

**Histological analysis.** Histological analysis was performed following the DTMRI study. Hearts were sliced at 2 mm thickness from base to apex along the LV long axis to enable direct correlation of slice locations between the MRI and histological analysis. Each slice was embedded in paraffin and sectioned at 4 μm. The tissue sections were stained with Masson’s trichrome for the identification of infarct myocardium. Regions that failed to demonstrate red staining of cardiac myocytes were considered to represent infarcted myocardium. The infarct ratio was calculated using the method proposed by Pfeffer et al. (17). Briefly, in each slice, the infarct ratio was defined as the ratio of the length of the endocardial circumference made up by the infarct area to the entire endocardial circumference. Infarct area in each slice was calculated by multiplying the infarct ratio by the LV area of the whole slice. Infarct ratio of the entire LV was obtained by calculating the ratio of the total infarct area to the sum of LV areas in all slices analyzed.

Picrosirius red staining was also performed to characterize collagen fiber structure. Angular deviation of myocardial and collagen fibers in tissue specimens from the midwall was evaluated in selected histological sections of normal (n = 20) and infarct (n = 29) myocardium from all 15 hearts using an “intensity gradient” technique proposed by Karlon et al. (12). Digitized images of picrosirius red-stained sections were obtained using a Nikon Optiphot 2 upright microscope at ×200 magnification. The acquired images were of 640 × 480 pixels in an area measuring 600 × 500 μm. Local fiber orientation was determined with custom-designed software in each 20-pixel-square subregion by calculating the largest accumulator of the intensity gradient. Figure 1 shows an example of such calculation in normal myocardium. Consequently, angular deviation in the whole region, an index of local fiber disarray, was calculated as the standard deviation of the fiber orientation angles in those 20-pixel-square subregions (32 × 24 subregions in total).

To determine whether changes in angular deviation of the transverse angle and the relative anisotropy of diffusion tensor reflect changes occurred at microscopic levels, angular deviation of the transverse angle and relative anisotropy were determined in regions of interest at the same locations.
as the chosen histological sections. These regions of interest were of 8 × 6 imaging voxels in an area of 625 μm × 469 μm, similar to those of histological sections (Fig. 1). DTMRI measures were directly compared with histological analysis.

Statistics. Data are presented as means ± SD. An unpaired Student’s t-test was used for intergroup comparison of the parametric variables. A two-tailed value of P < 0.05 was considered significant. Correlations between DTMRI data and histological analysis were performed using the linear regression method.

RESULTS

Morphological and histological analysis. Infarct size calculated from Masson’s trichrome-stained slices ranged from 10% to 19% of the LV. Infarct zones typically showed significant wall thinning compared with sham-operated hearts. In sham-operated rats, average anterior wall thickness was 2.91 ± 0.25 mm, and the anterior-to-septum wall thickness ratio was 1.07 ± 0.19. In the infarct area, average wall thickness was 1.91 ± 0.75 mm, and the infarct-to-septum wall thickness ratio was 0.80 ± 0.22 (P < 0.05). The gross structure of remote noninfarct areas and myocardium in sham-operated rats appeared normal.

Water diffusivity and relative anisotropy. Figure 2 shows the trace map image (Fig. 2A), the RA map image (Fig. 2B), and Masson’s trichrome-stained images (Fig. 2, C and D) of an infarct heart slice. Infarct myocardium exhibited increased trace values and decreased relative anisotropy. After being normalized to λ of the surrounding solution, the mean trace value was 1.43 ± 0.06 in the normal myocardium and 2.02 ± 0.21 in the infarct zone (P < 0.001).

Further analysis revealed that all three eigenvalues increased in the infarct area (Fig. 3). The primary, secondary, and tertiary eigenvalues normalized by λ of the surrounding water were 0.63 ± 0.02, 0.45 ± 0.03, and 0.35 ± 0.05, respectively, in the normal myocardium and 0.82 ± 0.08, 0.68 ± 0.09, and 0.56 ± 0.08, respectively, in the infarct region (P < 0.00005 for infarct vs. control). These data suggest that the magnitude of water diffusion along each eigenvector was increased in the infarct myocardium as was the mean diffusivity.

In addition to increased water diffusion, infarct area also exhibited decreased RA (Figs. 2 and 3). Mean RA
in the normal myocardium was 0.27 ± 0.03. It was decreased by 37% in the infarct area (0.17 ± 0.05, \( P < 0.005 \)). This value, although small, is well above that of the surrounding water (0.10 ± 0.04, \( P < 0.0005 \)), which is considered isotropic.

**Myocardial fiber orientation.** Figure 4 shows the inclination and transverse angles of the primary eigenvector in normal hearts. The inclination angle of the primary eigenvector shifted linearly from +80° at the endocardium to −50° at the epicardium. The average transverse angle was within 20° from the tangent plane of the short-axis view, indicating that myocardial fibers are circumferentially oriented within the short-axis plane. No significant difference was observed in the transmural courses of the inclination and transverse angles among different anatomic locations.

Transmural variations of the fiber orientation angles in the infarct zones are shown in Fig. 5. In the infarct myocardium, average inclination and transverse angles deviated only slightly from that of control myocardium from endocardial to epicardial borders (Fig. 5, A and B). However, the angular shift per millimeter transmural depth in infarct region was much larger than that of the normal myocardium (42 ± 14°/mm in infarct zones and 29 ± 5°/mm in normal myocardium, \( P < 0.05 \)). In addition, the angular deviation in the infarct area was significantly larger than that of control myocardium at the same transmural location. Angular deviation of the inclination angle was about 10° in the normal myocardium and increased to 20° in the infarct region (\( P < 0.05 \) from 25% to 95% transmural depth). For the transverse angle, angular deviation in the infarct area was also doubled from the midwall to epicardial region (\( P < 0.05 \) from 55% to 95% transmural depth). These data suggest that the infarct area may have greater regional variations in fiber orientation.

**Comparison between histological and DTMRI measurements of myofiber disarray.** Quantitative histological analysis was performed on 20 areas from the normal myocardium and 29 areas from the infarct myocardium at the midwall region where myocardial fibers were circumferentially orientated. In the normal myocardium, angular deviation calculated from Masson’s trichrome-stained tissue sections was 8.4 ± 1.6°. Angular deviation of the transverse angle in the same

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**Fig. 4.** Myocardial fiber orientation in normal rat hearts. A: representative map of inclination angle; B: transmural variations of inclination angle at anterior, lateral, inferior, and septum regions at midventricular level; C: transmural variations of inclination angle of the whole short-axis slice at basal, midventricular, and apical levels; D: representative map of transverse angle; E: transmural variations of transverse angle at anterior, lateral, inferior and septum regions at midventricular level; F: transmural variations of transverse angle of the whole short-axis slice at basal, midventricular, and apical levels. In inclination angle (also called helix angle) maps, red color at endocardium represents a right-handed helix, and blue color at epicardium represents a left-handed helix.
area calculated from DTMRI data was 6.1 ± 1.6° comparable to that calculated from histological measurements. In the infarct myocardium, angular deviation from both histological analysis and DTMRI measurements increased to 27.3 ± 5.4° and 22.7 ± 5.4°, respectively (P < 0.00001 compared with normal myocardium). Angular deviation calculated from the DTMRI data demonstrated strong correlation with that from histological quantification (R = 0.86, Fig. 6A). In addition, decreased RA in the infarct region was found to

Fig. 5. Cardiac fiber structure in infarct and control myocardium. A: transmural variations of the inclination angle at control and infarct regions; B: transmural variations of the transverse angle at control and infarct regions; C: angular deviation (AD) of the inclination angle at control and infarct regions; D: AD of the transverse angle at control and infarct regions.

Fig. 6. A: correlation of the AD measured from diffusion tensor MRI (DTMRI) and histology; B: correlation of RA measured from DTMRI and AD measured from histology.
DISCUSSION

In this study, changes in myocardial fiber structure after infarction in rat hearts were characterized using diffusion tensor MRI. To our best knowledge, this report presents the first study that characterizes the three-dimensional microscopic features of myocardial remodeling after infarction using DTMRI. The main observations were that infarct zones manifest increased water diffusivity and reduced diffusion anisotropy. These changes correlate strongly with histological methods. In addition, collagen fiber orientation in the scar tissue was preserved but with a greater angular deviation than that in normal viable tissue.

The infarct myocardium exhibited significantly reduced diffusion anisotropy. Two factors contribute primarily to diffusion anisotropy: cell morphology and fiber orientation within the imaging voxel. If all myocytes were oriented at the same direction within the imaging voxel, RA would be a measure of cell dimension, i.e., the longitudinal-to-transverse aspect ratio of myocytes. Thus changes in RA reflect changes in tissue composition. It is possible that the reduced RA in infarct zones is in part associated with the influx of inflammatory cells (e.g., neutrophils and macrophages) and myofibroblast because these cells are of spherical morphology instead of rod shaped. In reality, because myocardial fibers shift orientation continuously across the ventricular wall, an imaging voxel will always include a sampling of fibers that are oriented in different directions. Hence, changes in RA may also reflect changes in myofiber orientation within the imaging voxel. The significant negative correlation between RA and histological measures of fiber disarray supports this point.

Although RA was reduced in infarct zones, water diffusion remained anisotropic because RA was still significantly higher than that in isotropic media. Furthermore, infarct zones maintained a similar transmural angular shift of the primary eigenvector as that in the control myocardium despite the greater angular deviation. The anisotropic water diffusion in infarct zones undoubtedly reflects structural features of the newly formed scar tissues. In infarct myocardium, collagen accumulation and cross-linking occurs as early as 2–3 days after infarction (4). At 4 to 6 wk, collagen concentration in scar tissue may increase by a factor of six (21, 30), which implies that collagen concentration can be as high as 30% in these scar tissues. Hence, collagen fiber organization may assume a significant role in restricting water diffusion and be the main contributor to the persistence of diffusion anisotropy in scar tissues. The newly formed collagen fibers were found to have maintained the original orientation of those myocardial fibers they replace (30). It is possible that the existing extracellular matrix network plays the role of scaffolding in organizing the collagen deposition in scar tissues. The wall stress produced by the remaining muscle may also be responsible for the alignment of fibers in the scar. This preservation of collagen fiber structure may explain why there was little deviation in the orientation of the primary eigenvector from that of control myocardium. The strong correlation between the angular deviation of the primary eigenvector of the diffusion tensor and the angular deviation of collagen fibers determined by histology provides further evidence that collagen fiber organization contributes to measured diffusion anisotropy in scar tissues.

In this study, myofiber orientation was quantified by using local myocardial coordinate system similar to that proposed by Scollan et al. (22, 23). Although our study was performed on formalin-fixed rat hearts, the measured transmural courses of inclination angle in our study are in agreement with the findings of several other DTMRI studies on either perfused or formaldehyde-fixed rabbit hearts, which were validated by histological measures (9, 22). In addition, the ratios among primary, secondary, and tertiary eigenvalues were also similar to those in perfused hearts (Fig. 3), indicating that the morphology and structure of myocardial fibers were preserved during fixation. Transverse angles were found within a ±20° range of variation. The large variation of the transverse angle at subendocardial region was attributable to the irregularities in the shape of the endocardial contour, such as the presence of papillary muscles and trabeculations. Finally, the increase in angular shift per millimeter transmural depth is likely attributable to the wall thinning during heart remodeling.

Geerts and colleagues (7) observed a difference in the transmural courses of inclination angle at selected anatomic locations in goat hearts, a finding that deviates somewhat from our observations of equivalent fiber angles within various segments. However, the regional mean angles in their study were calculated from user-selected 20° wide sectors, whereas the four segmented regions in our current study encompassed the entire heart. In addition, they used a more complicated approach to determine the myocardial coordinate system and calculated the inclination angle with a slightly different definition. These differences in species, methods, and definitions prevent strict comparisons between the two data sets. Nevertheless, these modest variances suggest that issues such as the particular myocardial coordinate system used can affect outcomes and require careful a priori consideration and meticulous description.

The calculation of inclination and transverse angles can be critically dependent on the specific choice of the LV long axis and the LV center. In histological studies, LV long axis was defined as a chord passing through anatomic landmarks such as the LV apex and the mitral aspect of the left aortic valve commissure (25).
Geerts et al. (7) described a method of fitting the ventricular midwall with a series of circles and then establishing the LV long axis as a chord traversing the center of these circles. Such an approach assumes that the left ventricle is axially symmetric. This assumption also has been utilized in several studies involving mathematical modeling of the heart (3). In the present study, the LV long axis was determined as the line bisecting the left ventricle in both four-chamber and two-chamber views under the same assumption that the left ventricle is axially symmetric.

The variability in the calculation of fiber angles using different definitions of long axis was evaluated. In rat hearts, the left aortic valve commissure is positioned typically <1 mm from the center of the LV cavity at basal levels. Because the average LV length is ~11 mm, the deviation of MRI long axis from histological long axis is <5°. With the assumption that intramural fiber inclination angles change from +60 to −60° and that transverse angles range within ±15°, the differences in the calculation of fiber angles are within ±5° for inclination angle and ±9° for transverse angle. Such differences are smaller than the observed intersubject standard deviation for fiber orientation in the present study.

The LV center was defined as the center of the ventricular cavity in the present study. The difference in angle calculation by using the center of the epicardial border was also evaluated. In the rat hearts analyzed, average displacement of the epicardial center was 0.5 mm from the cavity center. The calculated difference in transverse angle was maximal at the endocardial border (13°) and minimal at the epicardial border (6°), indicating that endocardial transverse angle calculation is more sensitive to variations in the position of LV center. This large difference at the endocardial border may have contributed to the larger variations in the estimation of transverse angles at the endocardial region (Fig. 5D). Calculation of the inclination angle was minimally affected by the choice of the LV center. The difference was 0.6° at the endocardial border and 0.1° at the epicardial border.

The present study is the first to evaluate water diffusion in the postinfarct remodeled myocardium. Compared with the normal myocardium, the magnitude of water diffusion increased in the infarct zones. Histological examination revealed that few viable myocytes remained in the infarct tissue. The infiltration of fibroblasts, neutrophils, and macrophages was not sufficient to fill in the large space within the extracellular matrix left by the necrotic myocytes (Fig. 2D). As a result, increased extracellular space was present in infarct zones due to cell death and subsequent scar formation. Therefore, the increased water diffusivity in scar tissues is attributable to the increase in extracellular space as water diffusion becomes less restricted in the extracellular space. The association between increased water diffusion and tissue necrosis was also reported in animal studies of cerebral ischemia (29).

The acute effects of MI on water diffusion were evaluated by Hsu and colleagues (11) in isolated, perfused rabbit hearts. They observed a progressive decrease of the apparent diffusion coefficient within the first few hours of ischemia. Similar changes were found in brain ischemia in both animals and patients. Several studies (5, 15, 29) have shown that the apparent diffusion coefficient in infarct zones decreased immediately after stroke but gradually normalized and ultimately evolved into an increased apparent diffusion coefficient. Although our study was performed on formalin-fixed tissues, when taken together with Hsu’s data, it seems likely that changes in water diffusion in the infarct myocardium manifest a similar time course as that of brain tissue infarction.

Direct assessment of the location and extent of MI has significant clinical importance. Currently, the “delayed-enhancement” technique (DE-MRI) has gained the greatest acceptance in the assessment of myocardial damage in both acute and chronic MI (13). This technique identifies nonviable myocardium in patients with MI by imaging regions of delayed enhancement after the injection of Gd-DTPA. Although the precise mechanism of the differential contrast between viable and nonviable myocardium is not entirely clear, it has been suggested that the damaged microcirculation and increased interstitial space may play a role. In a time course study by Oshinski et al. (16), it was shown that imaging time after Gd-DTPA injection was critical in determining the infarct size by using this technique.

The significant increase of water diffusivity in the infarct zone as observed in the present study may provide an alternative way to delineate chronic MI. Similar to DE-MRI, good geometric correlation existed between the infarct zones that are delineated by DTMRI and by histological staining (Fig. 2). In addition, the negative correlation between RA and microscopic fiber disarray suggests that the technique can also be used to assess the structural integrity of the myocardium. Techniques for in vivo assessment of myocardial fiber architecture in humans have been proposed by Wedeen’s group (6, 20, 28). In a recent study, Wu et al. (32) used this in vivo technique to characterize disarrayed fiber architecture in postinfarct myocardium, and the results were found to correlate well with the viability map. These studies suggest that the multiparametric approach of DTMRI may lead to more comprehensive delineation of damaged myocardium without relying on exogenous contrast agent. When combined with other MRI techniques, such as MRI tagging (18) and phase-contrast strain-rate imaging (19), it will allow us to gain new insights into the physiological and pathological changes in the myocardial remodeling process.

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