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Regional Myocardial Three-Dimensional Principal Strains During Postinfarction Remodeling

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Background. **The purpose of this study was to quantify myocardial three-dimensional (3D) principal strains as the left ventricle (LV) remodels after myocardial infarction (MI). Serial quantification of myocardial strains is important for understanding the mechanical response of the LV to MI. Principal strains convert the 3D LV wall-based strain matrix with three normal and three shear elements, to a matrix with three nonzero normal elements, thereby eliminating the shear elements, which are difficult to physically interpret.**

Methods. **The study was designed to measure principal strains of the remote, border zone, and infarct regions in a porcine model of post-MI LV remodeling. Magnetic resonance imaging was used to measure function and strain at baseline, 1 week, and 4 weeks after infarct. Principal strain was measured using 3D acquisition and the optical flow method for displacement tracking.**

Results. **Principal strains were altered as the LV remodeled. Maximum principal strain magnitude decreased in all regions, including the noninfarcted remote, while maximum principal strain angles rotated away from the radial direction in the border zone and infarct. Minimum principal strain magnitude followed a similar pattern; however, strain angles were altered in all regions. Evolution of principal strains correlated with adverse LV remodeling.**

Conclusions. **Using a state-of-the-art imaging and optical flow method technique, 3D principal strains can be measured serially after MI in pigs. Results are consistent with progressive infarct stretching as well as with decreased contractile function in the border zone and remote myocardial regions.**

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After a myocardial infarction (MI), the left ventricle (LV) is at risk for remodeling. Infarct expansion has been implicated in sustaining LV remodeling after MI [1]. Immediately after ischemia, the infarct region ceases to contract and is subjected to mechanical loads produced by cavity pressure and the noninfarcted remainder of the ventricle. This abnormal loading results in stretching of the infarct and increased stress in the border zone (BZ) region adjacent to the infarct [2]. This dysfunctional BZ becomes more hypocontractile and progresses to involve additional perfused myocardium as remodeling continues.

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Tagged magnetic resonance imaging (MRI) is a method of tracking the myocardial displacement using noninvasive markers [3]. The development of three-dimensional (3D) tagging in a single acquisition makes regional LV measurements of the 3D strain possible [4, 5]. Principal strains derived from the strain tensor provide information on the magnitude and direction of the deformation that are more amenable to physical interpretation than LV wall-based strains. For LV wall-based strains, the strain matrix is oriented with respect to the left ventricular geometry. The coordinate system is rotated so that the x, y, and z directions align with the radial, circumferential, and longitudinal directions of the LV, respectively. Components of the normal and shear strains are expressed as magnitudes values in the given wall-based direction. Changes in cardiac strain during remodeling are reported as normal and shear values with constant orientation. Normal strains are easily interpreted whereas shear strains are more difficult to comprehend because of their definition and complex orientation (Appendix 1).

Studies using invasive methods and tagging have suggested that mechanical changes in the BZ and infarct regions are associated with remodeling [6–8]. These

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studies have shown that wall-based circumferential and longitudinal strain magnitudes are altered in the infarct and BZ regions. However, a complete understanding of the mechanical alterations in these regions has been limited by the inability to measure 3D strains during remodeling. The purpose of this study was to serially quantify myocardial 3D principal strains after MI to better understand the mechanism of post-MI remodeling.

Material and Methods

The study was designed to quantify the changes in regional principal strains in a porcine model of post-MI remodeling. Animals were treated under an experimental protocol in compliance with National Institutes of Health "Guide for the Care and Use of Laboratory Animals" (NIH publication 85-23, revised 1996) and approved by the University of Pennsylvania Institutional Animal Care and Use Committee. Five animals received a baseline MRI to access LV volume and regional principal strains before infarction. Subsequently, a posterolateral infarct was created by ligating the left circumflex artery distal to the first obtuse marginal artery branch, and markers were placed along the boundary of the infarct. The animals were recovered, and an MRI was performed at 1 week and 4 weeks after infarction.

Magnetic resonance imaging was used to measure LV end-systolic volume (ESV) and end-diastolic volume (EDV), and regional principal strain at baseline, 1 week, and 4 weeks after MI using a 3T Scanner (Siemens, Malvern, PA). The LV volume imaging consisted of a cine cardiac acquisition followed by strain imaging using a 3D tag sequence [4].

Data Analysis

The LV volume data were obtained from the cine MRI scans. The endocardial contours were drawn for each slice and phase then imported into a custom program to calculate volumes. Systolic LV regional strain was assessed from tagged images using a method previously described and validated [7]. An optimized 3D optical flow mapping algorithm tracked the myocardium motion and produced displacement fields in the x, y, and z direction (Appendix 2). The Lagrangian Green's strain tensor was calculated from the displacement fields between the initial state of end diastole and the deformed state of end systole, and principal strains were determined from the strain tensor by solving the eigenvalue problem. Principal strains represent the magnitude (eigenvalue) and direction (eigenvector) of the maximum stretch (E_1), maximum shortening (E_3), and mutually orthogonal difference of the stretch and shortening (E_2) of the myocardium. They differ from wall-based strains by providing a means for tracking not only strain magnitude but also strain orientation as the heart remodels (Appendix 1).

A local wall-based coordinate system was established for eigenvector orientation [9]. The circumferential (*c*) direction was defined by a vector tangent to epicardial contour. Radial direction (*r*) was defined by a vector inward and normal to the local epicardial wall. The longitudinal direction (*l*) was defined to be in the direction of the vector cross product of *c* and *r*, tangent to the epicardial surface (Fig 1).

Three midventricular slices were selected for quantitative analysis for each animal. To investigate alteration of the principal strains during postinfarction ventricular remodeling, each slice was divided into three segments: infarct, BZ, and remote. Infarct regions were delineated using the markers. The BZ region was determined to be the myocardium encompassed by a 20-degree arc between the marker and the remote region [10].

Statistics

Data are presented as mean ± SEM. The LV volume data were assessed using one-way repeated measures analysis of variance with Tukey post-hoc evaluation. Two-way repeated measures analysis of variance with Tukey multiple comparisons was used to analyze the principal strain for differences between regions and timepoints. Pearson and Spearman's ranked-order correlation were used to analyze the relationship between the change in regional strain and LV volume. Strain magnitudes and directions in each segment were compared by paired Student's *t* test. A value of p less than 0.05 was considered statistically significant for all comparisons.

Results

Global LV Remodeling

Global LV remodeling occurred in all animals throughout the study period. Statistically significant and progressive

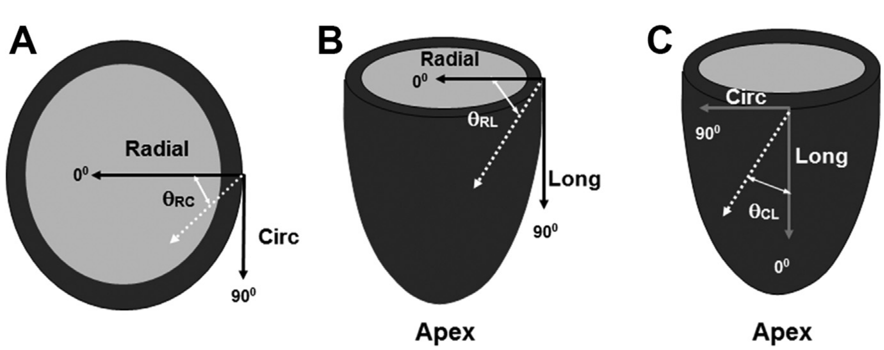

Fig 1. Coordinate system of principal strain vectors. (A) Radial-circumferential angle (θ_{RC}) is the principal strain vector projected on the radial-circumferential plane. Analogous descriptions are used for the (B) radial-longitudinal (θ_{RL}) and (C) longitudinal circumferential (θ_{CL}) planes. (Circ = circumferential; Long = longitudinal.)