Regional Myocardial Function: Advances in MR Imaging and Analysis¹

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LEARNING OBJECTIVES

After reading this article and taking the test, the reader will be able to:

• Identify advances in and limitations of cine MR imaging for the evaluation of regional myocardial function.

• Discuss the principles of myocardial strain imaging and recent developments in image analysis.

Describe current velocity-encoded MR imaging techniques for assessment of regional myocardial function. Ernesto Castillo, MD • João A. C. Lima, MD • David A. Bluemke, MD, PhD

Cardiovascular magnetic resonance (MR) imaging can provide threedimensional analysis of global and regional cardiac function with great accuracy and reproducibility. Quantitative assessment of regional function with cardiac MR imaging previously was limited by long acquisition times and time-consuming analysis. The use of steady-state free precession cine MR imaging substantially improves assessment of myocardial wall motion. Advances in gradient technology and reconstruction techniques have increased MR image acquisition speed and made real-time cine MR imaging possible. Myocardial deformation may be measured with cine MR tagging, and interpretation of the resultant tagged MR images by means of harmonic phase analysis enables prompt and precise strain measurements. Velocity-encoded and stimulated-echo techniques such as phase-contrast MR imaging and displacement encoding with stimulated echoes, or DENSE, provide highresolution strain maps. Clinical validation of these strain imaging techniques will depend on future assessments of their effect on the management of cardiac disease.

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¹From the Russell H. Morgan Department of Radiology and Radiological Sciences (E.C., D.A.B.), and the Department of Medicine, Division of Cardiology (J.A.C.L.), Johns Hopkins University School of Medicine, MRI-143 Nelson Basement, 600 N Wolfe St, Baltimore, MD 21287-0845. Presented as an education exhibit at the 2002 RSNA scientific assembly. Received February 26, 2003; revision requested April 28 and received May 16; accepted May 20. E.C. supported by a research grant from the Fundación Ramón Areces, Madrid, Spain. **Address correspondence to** E.C. (e-mail: *ecastillo@ihmi.edu*). Cardiac cine magnetic resonance (MR) imaging is considered the standard of reference for measurement of ventricular volume and various parameters of global ventricular function, such as ejection fraction and ventricular mass (1). Ventricular volumes and ejection fraction, however, may not correlate with myocardial contractility, because they are very sensitive to loading conditions (2). Interest in imaging of regional cardiac function has been driven by the fact that ischemic heart disease is the primary cause of death from cardiovascular disease worldwide (3). In ischemic heart disease, even a slight oxygen supply-demand imbalance that occurs as a result of coronary artery narrowing leads to contractile dysfunction of the specific territory involved (4). Regional ventricular function can be measured with the use of cine MR imaging and MR tagging techniques, although the image data analysis previously was too time consuming for these techniques to be useful in a routine clinical setting. The ongoing clinical need for objective, reproducible assessment of regional myocardial contractile function continues to make these techniques relevant (5), and new methods of analysis increase their appeal. This review describes current techniques for assessing regional myocardial function with MR imaging, including cine MR imaging, strain imaging, myocardial MR tagging and quantitative analysis of tagged images, realtime strain imaging, strain-encoded imaging, and velocity-encoded imaging.

Cine MR Imaging of Myocardial Wall Motion and Thickening

A major advance in cine MR imaging is the steady-state free precession (SSFP) pulse sequence (variants of which are known by the commercial names FIESTA [fast imaging employing steady-state acquisition], True FISP [true fast imaging with steady-state precession], and Balanced FFE [fast field echo]). The use of SSFP sequences in cine MR imaging results in a substantial improvement in the quality of images compared with those obtained with conventional segmented k-space fast gradient-echo (GRE) sequences (6,7) (Fig 1). SSFP requires high-speed gradients with extremely short repetition times of 3–5 msec. In SSFP sequences, equilibrium (ie, a steady state) is achieved and maintained between the transverse and the longitudinal magnetization while the magnetic field is exposed to a train of equally spaced radio-frequency pulses (8). The signal is thus acquired in a free precession mode. With the use of SSFP sequences, acquisition is less dependent on the inflow of fresh spins than it is with fast GRE sequences, and signal intensity is related mainly to inherent properties of the tissue (eg, T2/T1 ratio) (6,7).

The combined use of multishot echo-planar and SSFP imaging techniques reduces acquisition time by a factor of 2-3 for single-section or multisection acquisition, compared with acquisition time with the use of SSFP sequences alone (9). This combination of techniques enables imaging of the left ventricle in less than 2 minutes. A further reduction in the total number of breath-holds needed for complete coverage of the left ventricle can be achieved with four-dimensional (ie, involving three spatial dimensions and the temporal dimension) cine SSFP acquisitions (10). Other methods for decreasing acquisition time involve the use of noncartesian (eg, spiral or radial) kspace sampling instead of cartesian (ie, rectilinear) schemes. Different reconstruction schemes and parallel acquisition of image data with sensitivity encoding (or SENSE) and simultaneous acquisition of spatial harmonics (or SMASH) also increase time efficiency (11,12). With sensitivity encoding, it is possible to achieve real-time cine imaging with a temporal resolution of 13 msec at a spatial resolution of approximately 4 mm (11).

Cine MR imaging pulse sequences allow direct qualitative and semiquantitative assessment of myocardial regional function. Image data acquired with SSFP sequences in cine MR imaging are substantially improved over those obtained with conventional GRE sequences for visual and semiautomated endocardial contour detection (6,7). Interstudy variability with SSFP is excellent, and interobserver variability is also improved over that achieved with cine GRE techniques (6,7,13). However, in healthy volunteers and patients with heart disease, several authors have measured higher end-diastolic and end-systolic left and right ventricular volumes with SSFP pulse sequences than with conventional cine GRE techniques (7, 14, 15). The values measured for

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Figure 1. Long-axis cine MR images obtained with a fast GRE sequence (repetition time msec/ echo time msec = 8.1/4.5, angle of 20°) (**a**, **b**) and an SSFP sequence (3.7/1.5, angle of 45°) (**c**, **d**) in a 68-year-old man with coronary artery disease. The heterogeneous blood-pool signal intensity seen in the GRE images, which was caused by slow blood flow, is not present in the SSFP images.

ejection fraction and left ventricular mass were lower (by 10% and 19%, respectively) with SSFP than with GRE cine imaging. High-resolution SSFP MR images (with an isotropic voxel size of 0.8 mm) demonstrate a complex border between blood pool and endocardial trabeculae and papillary muscles that is not evident on conventional GRE images (16). In other words, the precise location of the endocardial border is depicted differently on images acquired with SSFP sequences than on those acquired with GRE and real-time cine MR techniques (13–16). The use of automated methods for myocardial border detection may enable more reliable quantitative analysis based on cine MR images (17).

Clinical Significance of Wall Motion and Thickening

The most important clinical application of regional functional analysis is in the assessment of reversibly injured yet viable myocardium in ischemic heart disease (Fig 2) (18,19). Quantitative measurement of wall thickening provides a more **Radio**Graphics

Figure 2. Wall thickening analysis of short-axis cine MR images obtained in a 71-year-old man with chronic myocardial infarction in the region of the left anterior descending artery. (a) Delayed-enhancement short-axis image obtained with gadolinium-based contrast material shows transmural hyperenhancement (arrows) in the thinned myocardial wall of the septum and in the anterior wall corresponding to scar tissue. (b) The endocardial and epicardial contours are diagrammed on the SSFP image. Chords for measuring wall thickness are shown along the left ventricular circumference. (c) Bull's-eye plot shows the extent of wall thickening. The smallest ring represents the apical region, and the largest ring represents the basal region. There is reduced thickening (from 0%-30%) in the scar tissue and surrounding myocardium (arrowheads) compared with thickening of more than 200% in the remote myocardium (arrows).





a.

precise indication of regional function than does visual estimation of wall motion (20). Measurement of wall thickening, however, accounts for cardiac motion only in the radial direction, whereas contraction takes place also in the circumferential and longitudinal directions (21). With the use of myocardial strain imaging, all the components of myocardial contraction can be measured at once. This imaging technique therefore can provide a more accurate assessment than measurement of wall thickening alone (22).

Strain Imaging

Myocardial strain imaging involves the assessment of local tissue deformation as an indicator of myocardial contractile function. Strain measurements are expressed as the fractional change in b.



c.

length (in percent) from the resting state (end diastole) to the state following myocardial contraction (23). By convention, contraction or shortening of the myocardial fibers yields negative strain values, and lengthening results in positive



Figure 3. Scheme of coordinate systems for measuring myocardial strain defined by the finite strain tensor E. Normal strains (black arrows) are defined in relation to the circumferential, or short-axis, plane: Circumferential shortening (E_{cc}) occurs parallel to the tangent of the myocardium with respect to the epicardial surface (shown here as the endocardial surface for space reasons); radial thickening (E_{RR}) occurs perpendicular to the circumferential direction, toward the ventricular centroid; and longitudinal shortening (E_{LL}) occurs perpendicular to the other two components and parallel to the longitudinal axis of the left ventricle. Principal strains (white arrows) are defined in relation to the direction of movement in the main myocyte fiber bundles during systolic deformation. The maximal principal strain is the greatest elongation (E_1) orthogonal to the fiber direction. The minimal principal strain is the greatest shortening (E_2) parallel to the fiber direction. Principal strains are referred to the major and minor axes of an ellipse resulting from the deformation of a circle during systole because of wall shear. Strain that occurs perpendicular to these two principal strains is labeled E_3 . The angles between E_{cc} - E_2 and E_{RR} - E_1 are defined as α and β , respectively.

values (23). Strain is a tensor and is characterized not only by the magnitude of the length change but also by the direction of the change. Two frames of reference are used in calculating the strain tensor—one related to a local cardiac coordinate system, and the other related to the local fiber orientation. Changes during the cardiac cycle in any of the three spatial dimensions relative to the circumferential (or short-axis) plane are considered *normal* strains (Fig 3). During systole, circumferential shortening occurs in the short-axis plane along curved lines parallel to the epicardial surface, directed counterclockwise as viewed from the base. Wall thickening is an indication of strain that occurs radially, proceeding in a direction from the long axis toward the epicardium. Base-to-apex shortening occurs longitudinally, parallel to the long axis. Strain changes that occur in a plane between two of these three initially orthogonal normal directions are called shear strains. The greatest systolic compression and expansion in the left ventricular wall occur in the planes parallel and perpendicular to the direction of the principal local myocardial fibers (24). Changes in these dimensions, referred to as principal strains, represent the greatest shortening and the greatest elongation, respectively. Another parameter that is measured during the assessment of myocardial function with MR tagging is left ventricular systolic torsion, or twist, and the subsequent diastolic "untwist" (23). Torsion involves motion between short-axis planes that occurs simultaneously with differential rotation around the long axis; in other words, it involves motion between the heart base (clockwise rotation) and the apex (counterclockwise rotation).

Myocardial MR Tagging

Short-axis and long-axis two-dimensional tagged images allow the tracking of myocardial strain in three dimensions (23,25). MR tagging is performed with cine MR imaging by applying a special radio-frequency pre-pulse immediately following detection of the R wave on the ECG tracing (26). The pre-pulse is oriented perpendicular to the imaging plane and induces a local saturation that is depicted on images as a dark line superimposed on myocardial tissue. The multiple lines produced by successive applications of the pre-pulse are observed as parallel stripes or as a grid on cine MR images of the cardiac cycle. MR tagging is performed by using segmented k-space GRE pulse sequences with spatial modulation of magnetization (SPAMM) or delays alternating with *n*utations for *t*ransient *excitation* (DANTE) (27, 28).

MR tags usually fade in early diastole (approximately 400–500 msec) because of T1 relaxation. For imaging of diastolic function, the tagging pulse may be applied in late systole and followed by the imaging sequence in diastole (29). **Radio**Graphics



Figure 4. Early-systolic (a, d), end-systolic (b, e), and end-diastolic (c, f) short-axis tagged MR images were obtained by using CSPAMM with spiral readout. Spiral readout is a very efficient k-space sampling method that allows high temporal resolution (a-c) or high isotropic spatial resolution (d-f). The high-temporal-resolution images were acquired with 12 interleaved spiral readouts in 13 msec (45 heart phases) at a tag spacing of 8 mm. The high-spatial-resolution images $(1.5 \times 1.5 \text{ mm})$ have a tag spacing of 4 mm and a temporal resolution of 35 msec (16 heart phases). (Courtesy of S. Ryf, MSc, ETH Zürich, and M. Stuber, PhD, Johns Hopkins University, Baltimore, Md.)

Another technique that can be used for tagging in both systole and diastole is *c*omplementary SPAMM (CSPAMM) (30). With the CSPAMM method, two acquisitions are subtracted one from the other: one obtained with a SPAMM technique and a second obtained with a saturation pre-pulse that is inverted with respect to the SPAMM sequence. The primary drawback of the CSPAMM technique is that it doubles the acquisition time and thus the breath-holding time, which may result in the misregistration of the images to be subtracted. However, a reduction of imaging time with CSPAMM is possible by applying a segmented echo-planar imaging sequence that allows the acquisition of systolic and diastolic grid-tags within a single breath-hold (31). Recent implementations of CSPAMM have included the use of spiral k-space sampling for either higher tag resolution (4-mm tag spacing instead of the usual 7–8 mm) or higher temporal resolution (13 msec instead of the usual 30–40 msec) (32) (Fig 4). A new method for three-dimensional image acquisition also has been described recently (33). Other efforts to improve tagged MR image quality have included the use of undersampled projection-reconstruction (34) or of SSFP (35).



c.

d.

Figure 5. HARP image analysis. The HARP technique enables measurement of motion from a series of tagged MR images (such as that in **a**) by filtering selected peaks in the k-space representation of the image (circle in **b**). The resulting image can be decomposed into a harmonic magnitude image (**c**) or a HARP image (**d**). The magnitude image shows anatomic detail and can be used for segmentation. In contrast, the HARP image contains myocardial motion information. Because the value of a material point on a HARP image is invariant over time, this technique can be used to track the trajectory of a given point or points and to compute either lagrangian or eulerian measurements of strain.

Quantitative Analysis of Regional Wall Motion on Tagged MR Images

Several semiautomated methods have been developed to detect the tagging lines on images of the myocardium and to quantify three-dimensional myocardial strain with extreme precision (25). With use of these methods, the position of a tag may be estimated to within approximately 0.12 mm. This level of accuracy allows strain in the subendocardial, midwall, and subepicardial layers to be identified and measured. Until recently, quantitative analysis of tagged MR images has been extremely time-consuming. A new technique that overcomes this limitation is harmonic phase (HARP) analysis (36). HARP analysis involves less user intervention and faster processing time than previous techniques. HARP analysis enables the tracking of phase changes from one of the off-center spectral peaks in the Fourier domain (Fig 5). The phase change is related to the in-plane motion of the myocardial tags. If there is no motion, the phase of the sinusoidal tag pattern remains linear. If there is motion, the sinusoidal tag pattern deviates from linearity in its phase. **Figure 6.** HARP analysis of short-axis tagged MR images. (a) A circular grid that contains a variable number of segments of equal size (in this case, 12) is defined by the user to represent the region of measurement within the left ventricular wall (green = subendocardial layer, red = midwall, blue = subepicardial layer). Points on the grid are then automatically tracked through all the image sections in the data set, and strain values are calculated from the trajectory of each point. (b) Calculated strain values are displayed as a color-coded map superimposed on the tagged images. (c) Strain plots show circumferential shortening in every segment and in all three layers (color coded as in **a** and **b**). The x axis represents the number of imaged phases of the cardiac cycle (20, up to a maximum of 670 msec), and the y axis is the percentage of change in circumferential shortening.





a.





Figure 7. Myocardial infarction in the left anterior descending coronary artery in a 40-year-old man. (a) Shortaxis delayed-enhancement image shows extensive hyperenhancement in the anterior wall and septum, which corresponds to an extensive infarction. Nonenhanced subendocardial areas (arrows) correspond to microvascular obstruction after acute infarction. (b, c) Color-coded maps superimposed on tagged MR images acquired in early systole (b) and end systole (c) show the regional extent of circumferential shortening. Contraction, indicated in blue, is evident mainly in the remote myocardial areas (arrowheads). In the infarcted region, virtually no contraction is evident, as is indicated by green; a slight myocardial lengthening, indicated by red, is evident in the area of microvascular obstruction (arrows in c).



The HARP method enables measurement of these deviations to track motion and to compute two-dimensional myocardial strain parameters. Strain values are displayed as temporal plots (Fig 6).

HARP analysis of myocardial strain on tagged MR images is 10 times faster than conventional tag analysis and almost as accurate (for pooled data, regression coefficient r = 0.93 for each strain, and P < .001) (37). In addition, subtle changes that occur in myocardial strain during stress testing or after infarction can be measured with HARP analysis (37,38) (Fig 7).





Real-Time Strain Imaging

HARP analysis is typically used for postprocessing of tagged images, but HARP principles also can be incorporated into an MR pulse sequence. Direct near-real-time depiction of myocardial strain has been obtained with a hybrid GRE– echo-planar pulse sequence (39). The temporal resolution achieved by using this approach is approximately 40 msec. Real-time strain imaging reduces the burden of breath holding for the patient. Regional strain changes caused by acute coronary ischemia can be detected significantly



Figure 8. Depiction of myocardial ischemia with a real-time pulse sequence based on HARP imaging principles. Color map superimposed on short-axis, end-systolic, tagged cine MR images of acute ischemia in a canine model shows the extent of circumferential shortening. On the color scale, green indicates no change, blue indicates contraction (negative values), and red indicates stretching (positive values). On the first image, which was acquired at 1 second of imaging, before coronary artery occlusion, the strain values are uniform. On the second image, acquired about 10 seconds after coronary artery occlusion (ie, at 28 seconds of imaging), an area in the anterior wall near the left anterior descending coronary artery shows stretching secondary to ischemia (arrows). This area increases over time until 120 seconds of imaging, when deflation of the balloon catheter occurs. In the remote area of the opposite wall, shortening appears to have increased (arrowheads) compared with the baseline. After deflation (at 125-135 seconds), the ischemic region recovers and again shows contraction.

earlier with this technique than with nontagged cine MR imaging (9.5 sec \pm 5 vs 33 sec \pm 14, P < .01) (39) (Fig 8). These methods may be particularly useful in the MR imaging assessment of myocardial contraction during dobutamine stress testing.

Strain-encoded Imaging

By orienting tags in parallel with the imaging plane instead of orthogonal to it, the imaging specialist can measure through-plane strain information (40). The acquisition of two images with a modified SPAMM tagging pulse sequence but with different phase encoding along the z axis (ie, in the section-select direction) allows pixel-bypixel calculation of a high-resolution map of longitudinal strain in the underlying myocardium. Because signal intensity on these images is directly proportional to local strain, the images are described as *strain encoded* (Fig 9). No postprocessing of the resultant maps is needed when this method is used. This technique may be useful for evaluating the right ventricle with short-axis images. The use of conventional methods of MR tagging in imaging of the right ventricle is limited because of the thinness of the myocardium and the orientation of the myocardial strain in the right ventricle.

Velocity-encoded Imaging

The other main method for measuring cardiac motion involves the use of velocity-induced phase shifts obtained with phase contrast pulse sequences (41-42). This approach enables the computation of trajectories of points within the myocardium. Myocardial motion is derived by

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Figure 9. Through-plane strain information obtained with strain-encoded MR imaging. (**a**-**c**) Longitudinal shortening is displayed on a composite short-axis image (**a**) obtained by combining an image with low tagging frequency (**b**) and an image with high tagging frequency (**c**). Dyskinetic tissue with stretching (1 in **a**) is represented by a hyperintense area on the low-frequency image and by a hypointense area on the high-frequency image. Akinetic myocardial tissue (2 in **a**), in which there is no contraction, has an appearance identical to that of surrounding static tissue (ie, chest wall or liver). Severely hypokinetic tissue (3 in **a**) and normally contracting subendocardial or midwall tissue (4 and 5 in **a**) show an inverse intensity pattern directly related to the strain values on a pixel-by-pixel basis. (**d**-**f**) Shortaxis strain-encoded MR images obtained in a 68-year-old woman after myocardial infarction. The low-frequency image (**d**) shows subendocardial hyperintense areas (arrows) that indicate myocardial dysfunction; the same areas are represented in red on the composite color-coded image (**e**). Delayed-enhancement image (**f**) shows a subendocardial area of hyperenhancement (arrows) in the region of the left anterior descending artery that represents chronic myocardial infarction and that corresponds with the areas of dysfunction depicted on the strain-encoded images.

integrating the myocardial velocities, which in turn enables the calculation of local strain. It is also possible to directly measure the temporal derivative of strain, the so-called strain rate (41). A major limitation of velocity-encoded imaging is its susceptibility to motion artifacts. In addition, the method cannot be used to measure large movements, because the tracking algorithms are based on the assumption of little spatial variation in the velocity field from one sampling position to the next. A recently developed technique for improving image quality involves the acquisition of two contiguous two-dimensional sections with a single-shot hybrid GRE–echo-planar sequence, which yields three-dimensional strain information (43). Automated processing without operator supervision is also possible with this technique.

Displacement *en*coding with stimulated *e*choes (DENSE) is a similar encoding technique that modulates the phase of each pixel according to its position rather than its velocity (44). DENSE has been used to obtain high-resolution phase maps

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Figure 10. Midventricular short-axis end-systolic cine MR images based on data obtained with the DENSE technique during a single breath-hold in a healthy volunteer. (a) Magnitude-reconstructed image. (b) Two-dimensional displacement map computed from a phase-reconstructed image. Each vector in the map represents the end-diastolicto-end-systolic motion of the myocardium as depicted in a single pixel. (c) Color-coded myocardial strain map shows circumferential shortening, which was computed from the displacement field. (Courtesy of D. Kim, W. D. Gilson, C. M. Kramer, and F. H. Epstein, University of Virginia Health System, Charlottesville, Va.)

of a 105-msec period during systole, but acquisition time was relatively long (4.3 minutes per image). The use of a STEAM (*st*imulated *e*cho *a*cquisition *m*ode) preparation pulse prior to the application of the DENSE sequence allows a reduction of acquisition time to 14 heartbeats per section (45). The high-density strain depiction (pixel size) provided by this technique without the need for user interaction is advantageous for quantifying myocardial function (Fig 10).

Conclusions

Cine MR techniques are currently the main MR imaging tools used to assess global and regional cardiac function. However, the analysis of cine MR images is only semiautomated and time consuming. Therefore, the clinical assessment of regional function-in particular, of myocardial viability and of stress-induced ischemia-is still based on the subjective assessment of wall motion. Recent advances in MR tagging with CSPAMM and in MR image analysis with HARP techniques nevertheless may encourage the clinical use of strain analysis and provide new insights into regional systolic and diastolic function. The utility of rapid analysis software for tagged MR images and of real-time strain image display will depend mainly on their effect on clinical evaluation of patients with acute myocardial infarction

or postischemic viable myocardium. Further potential applications of these techniques include the rapid acquisition and interpretation of myocardial strain measurements during stress testing. Strain-encoded and velocity-encoded MR imaging may become the new standard for the objective and reproducible assessment of regional myocardial function.

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