

Assessment of Myocardial Systolic Function by Tagged Magnetic Resonance Imaging

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ABSTRACT

Tagged magnetic resonance imaging (MRI) can assess myocardial function by tracking the motion of the myocardium during the various phases of the cardiac cycle. In contrast to experimental methods, such as implantation of radiopaque markers or sonomicrometry, tagged MRI is noninvasive, carries no risk of radiation exposure, and can be used in the context of clinical routine. For the physician, using tagged MRI to its fullest potential requires an understanding of the technique and the derived parameters of myocardial systolic function. This work describes the tagged MRI technique and explains the quantification of systolic function with respect to the underlying theory of the mechanics of a continuous medium. The advantages of tagged MRI in coronary artery disease are emphasized, and currently available data on tagged MRI in coronary artery disease are reviewed.

KEY WORDS: Left ventricular systolic function; Tagged MR imaging.

TAGGED MAGNETIC RESONANCE IMAGING

The principle of tagged magnetic resonance imaging (MRI) is to selectively saturate spins of myocardial tissue. On electrocardiogram-gated MRI, the deformation of the saturation pattern (saturated tissue will give no signal on the MR image) and thus of the myocardial wall can be visualized. The assessment of myocardial mechanical

function by means of tagged MRI was first proposed by Zerhouni et al. (1) using selective radiofrequency saturation pulses to create a set of radially aligned tagging planes in the short-axis (SA) view. To improve detection of radial strains (e.g., wall thickening), Bolster et al. (2) implemented the STAG (striped radial tags) technique. STAGs can visualize radial thickening for separate layers of the myocardium, such as endocardium, midwall, and epicardium. The above techniques, however, necessitate

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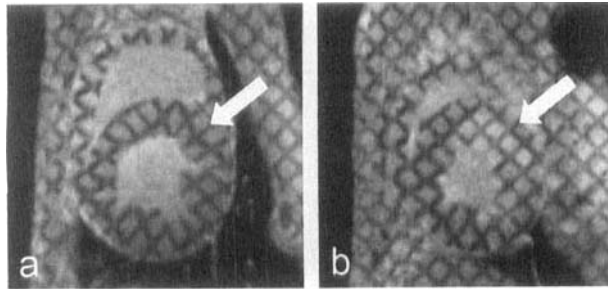


Figure 1. During systole, a tagged grid is deformed (a); however, after myocardial infarction, the deformation is attenuated or missing (b).

long tag generation times, because the time to create the tagging planes increases with the number of tags.

The SPAMM technique (*spatial modulation of magnetization*) implemented by Axel and Dougherty (3) overcomes the problem of long tag generation pulses. Using two nonselective saturation pulses separated by a magnetic field gradient (“wrap gradient”), a sinusoidal variation of transverse magnetization is obtained. This results in a sinusoidal variation of the signal intensity throughout the entire image. The tagging contrast was then improved by binomial SPAMM, where multiple saturation pulses with variable amplitudes, again separated by magnetic field gradients, were used (4). Binomial SPAMM, applied in two orthogonal directions, allowed Axel and Dougherty (4) to produce a tagging grid superimposed on the MR image. Figure 1 illustrates the deformation of the tagging grid in non-infarcted tissue (Fig. 1a) versus infarcted tissue (Fig. 1b) during systole.

CSPAMM (*complementary spatial modulation of magnetization*) has been proposed to prolong the tagging contrast (5). Because spin-lattice (T_1) relaxation of the tagged tissue causes the tagging planes to vanish after a period of 400–500 msec, the above-mentioned techniques can track the myocardium only in systole. CSPAMM uses a regular SPAMM sequence to obtain a tagging grid, followed by a second image acquisition where one saturation pulse is inverted to obtain a negative grid. Subtraction of both images delivers an image containing the tagging grid, independent of T_1 relaxation mechanisms. This technique requires longer imaging times but allows tracking of the myocardium into diastole. The DANTE (*delays alternating with nutations for transient excitation*) (6) tagging sequence, which uses multiple saturation pulses but with a continuous frequency encoding gradient, was introduced by Mosher and Smith (7). A tagging grid with low tag spacing is ob-

tained; however, tag attenuation at the edges of the field of view limits tag detection in these areas.

Tag spacing determines the spatial resolution for calculation of the strain field. The smaller the tag spacing, the more accurate the determination of the inhomogeneous strain field. With small tag spacing, however, tag detection might be hindered due to convergence of neighboring tagging planes or truncation artifacts. In addition, a higher uncertainty in tag position estimation has been shown for a tag spacing of three to five pixels (8). Recent studies suggest adapting the tag spacing to the expected myocardial motion in systole (variable separation tagging) (9). If a set of parallel tagging planes is used in the SA view, systole will increase the tag separation in the regions where the tagging planes are perpendicular to the direction of wall thickening. However, the tag separation of the tagging planes parallel to the direction of wall thickening decreases. A series of specially designed radiofrequency pulses can produce a tagging pattern with low tag spacing in the areas sampling radial thickening and high tag spacing in the areas sampling circumferential shortening. The primary drawback of this technique is the longer tag generation radiofrequency pulse. Stuber et al. (10) suggested acquiring two or more MR images of one slice, however, with different tagging grid positions. This technique improves the spatial resolution for calculation of the strain field, but the imaging time is prolonged.

The optimum tag spacing is a trade-off between the need for high spatial resolution and technical considerations. Guidelines for tagged MRI have been elaborated by several authors. These authors suggested using a tag spacing of at least 5 pixels (8) and a tag thickness of 1.5 pixels to guarantee accurate tag delineation throughout systole (11). A long tag generation pulse should be avoided, and the tagging planes should be perpendicular to the highest resolution direction (11). When imaging is performed with a tag spacing of five pixels (equivalent to 6.25 mm, given a field of view of 32 cm and 256 frequency encoding steps), field-fitting analysis is applied to estimate the spatial strain distribution between the tagging planes and thus improve spatial resolution (12).

Our group uses a combination of the DANTE and SPAMM tagging sequence, followed by a segmented k-space spoiled gradient recalled acquisition in the steady state (SPGR) imaging sequence (13). Seven saturation pulses with varying amplitudes (similar to binomial SPAMM) and an underlying readout gradient (similar to DANTE) that is constant but decreased while saturation pulses are applied deliver a good tag profile of parallel tagging planes throughout the entire image. Two sets of

identical SA view images (the second set is rotated by 90 degrees) are used. The SA view images are later superimposed on each other to obtain a tagging grid. This technique maintains the tagging planes orthogonal to the readout direction, thus maximizing spatial resolution across the tag profile and minimizing tag blurring from motion. In addition, the tag generation pulse for each image is shortened to further reduce motion artifacts. The SPGR imaging sequence, with partial k-space filling and a fractional echo to reduce TE, allows imaging of five to seven SA and six to nine long-axis (LA) views for three-dimensional (3D) analysis within about four breathholds. When evaluating cardiac systole, usually 6–10 cardiac phases (time frames) of each slice from diastole to end-systole are imaged, thus covering 180–300 msec of systolic motion. Table 1 summarizes the imaging parameters of our SPGR sequence.

For image analysis and strain calculation, we use computers that support 3D texture mapping (Silicon Graphics) and in-house software programs ("Findtags" and "Tag Strain Analysis"). At first, the contours of the myocardium (endo- and epicardium) and the positions of the tags are defined. Performing this in SA and LA views of the heart allows us to calculate the tag displacements and strains in three dimensions (see following section). Although semiautomated interactive analysis is applied, it typically takes 3–4 hr to obtain one 3D data set of the heart. Future improvements are therefore directed toward a more efficient contour detection, tag detection, and strain calculation process: Denney (14) has introduced a

technique to perform strain calculation without the need of user-defined contour detection. Osman et al. (15) obtained strain calculations using the *harmonic phase* (HARP) angle of tissue, which was tagged with the SPAMM sequence (15). The HARP angle is thought to represent a material property of tissue and can therefore be used to determine tissue displacements over time and calculate strains. The technique does not require user-defined contour and tag definition. It has, however, not been validated for 3D application.

KINEMATICS OF A CONTINUOUS MEDIUM

The kinematics of a continuous medium can be used to determine important parameters of myocardial mechanical behavior (16). Based on the theory of the mechanics of a continuous medium, the kinematics of a continuous medium deals with motion (displacement) of particles in space. Particles, or material points, are (in theory) infinitesimal elements of the geometric body they form (e.g., the heart). During contraction, the particles of the myocardium move within a reference coordinate system and relative to each other. It is the task of the kinematics of a continuous medium to describe and quantify this motion. Examples of such different types of motion are given in Fig. 2. For the purpose of clarity, examples are illustrated in a two-dimensional (2D) coordinate system.

Rotation and translation (Fig. 2, a and b, respectively) describe rigid-body motion without change of shape of a geometric body. In these cases there is no movement of the particles relative to each other. Strains include frac-

Table 1

Imaging Parameters for a Segmented k-Space Spoiled Gradient Recalled Acquisition in the Steady State

Imaging Parameter	Typical Value
Tag thickness	1.5 pixels
Tag spacing	5–6 pixels
Slice thickness	7 mm
Field of view	28–36 cm
Views per segment	7–15
Frequency encoding steps	256
Phase encoding steps	100
TR	3.1 sec
TE	1.1 sec
Flip angle	10 degrees
Time frames	6–10*

* The number of time frames should be adjusted to image from end-diastole to end-systole.

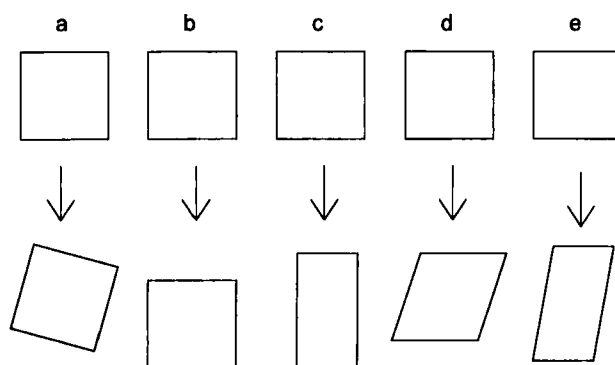


Figure 2. Different modalities of motion as described by the mechanics of a continuous medium: rotation (a), translation (b), fractional change in length (c), shear (d), and a combination of fractional change in length and shear (e).

tional change in length and shear (Fig. 2, c and d, respectively). The particles move relative to each other and transform a geometric body from its initial state to a transformed state (shape). Strain assessment factors out rigid-body motion. The strains will not change, regardless of what kind of additional rigid-body motion a geometric body is exposed to. It is important to note that such different types of motion will be combined during normal and abnormal cardiac contraction (Fig. 2e).

Fractional change in length is, by definition, the change of length per unit of initial length. If a line segment of 1 cm is stretched to a final length of 1.01 cm, the strain is 0.01 cm/1.00 cm, or 0.01 (=1%). In the context of left ventricular (LV) systolic function, a negative value usually represents compression of a line segment between two material points and a positive value represents elongation. Theoretically, one can look at the fractional change in length in any arbitrary direction, but usually the circumferential, longitudinal, and radial direction is chosen with respect to the heart's geometry (17). In systole, these strains are then called circumferential and longitudinal shortening (E_{cc} , E_{ll}) and radial thickening (E_{rr}). As an example, it can be seen in Fig. 3 that a tagging grid will be deformed during cardiac contraction. The tagging planes perpendicular to the endocardial wall motion will move further apart (E_{rr}), whereas those parallel to it will come closer together (E_{cc}).

Shear strain changes the shape of a geometric body but does not cause compression or elongation. For example, in Fig. 2d it can be seen that shear strain transforms a square into a rhomboid. This process causes the sides of the quadrangle to subtend different angles, which are unchanged in the case of fractional change in length. With respect to myocardial geometry, shear strains are usually viewed in the circumferential-longitudinal plane (E_{cl}), in the circumferential-radial plane (E_{cr}), and in the longitudinal-radial plane (E_{lr}). As an example, it can be

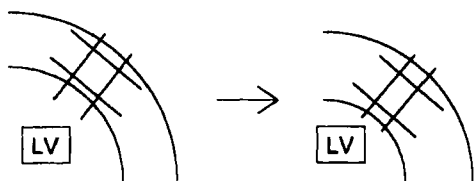


Figure 3. With cardiac contraction, tagging planes perpendicular to endocardial wall motion will move further apart (radial thickening), whereas those parallel to wall motion will come closer together (circumferential shortening). Note that the impact of shear strains is neglected and a homogeneous transmural strain distribution is assumed.

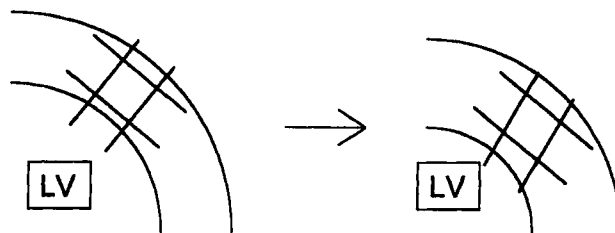


Figure 4. Cardiac contraction includes rotation of the myocardium, which is higher for the endocardial layers than for the epicardial layers. A square will be transformed into a rhomboid. Note that the impact of fractional change in length is neglected and a homogeneous transmural strain distribution is assumed.

seen in Fig. 4 that systolic rotation of the myocardium, which is physiologic and higher for the endocardial layers than for the epicardial layers (see below), transforms a square into a rhomboid.

Because contraction of the LV includes rotation and shear, E_{cc} , E_{ll} , and E_{rr} do not represent the maximum strains. The maximum strains are called the principal strains or eigenvectors in the circumferential, longitudinal, and radial direction. Quantification of maximum strains is expressed using the eigenvalue of the "associated" eigenvector. In the normal LV, the principal radial strain is usually referred to as maximum principal strain, because it is a fractional increase in length ("thickening"). The principal circumferential strain is usually referred to as minimum principal strain, because it is a decrease in length ("shortening"). The maximum strains subtend variable angles with respect to the heart's epicardial surface, whereas radial thickening is always perpendicular to and shortening is always parallel to the heart's epicardial surface.

To describe myocardial motion during contraction in an accurate and realistic manner, it is convenient to define a model, including the cardiac geometry and an algorithm to calculate the parameters of LV systolic function. By using the same model in population-based or longitudinal studies, the impact of disease or therapy on myocardial performance can be evaluated. The main models used are variations of three different approaches and these are elaborated in the following section.

ASSESSMENT OF LV SYSTOLIC FUNCTION

One Dimensional

Measuring the distance between tagging planes at end-diastole and at various time points during systole allows

calculation of the fractional change in length, such as circumferential shortening. This method can only estimate fractional change in length in the direction perpendicular to the tagging planes. It does not take into account the complex motion and deformation of the heart, such as rotation and shear, and cannot track myocardial tissue through systole. It has been widely used, however, to determine circumferential shortening with high spatial resolution in the radial direction.

Two Dimensional

Using the intersection points of the tagging grid as landmarks, the myocardium can be decomposed into several geometric areas (e.g., squares or triangles). During systole, these areas undergo rigid-body rotation and deformation. Figure 5 shows the deformation of a tagging grid (basal slice, midwall) during systole, as viewed from the apex. If one approximates the motion within these areas as homogeneous, the deformation can be quantified by two principal strain components. For example, a circle placed into a triangle (Fig. 5, bottom left) will be deformed into an ellipse during contraction (Fig. 5, bottom right). The major and minor axes of the resulting ellipse are perpendicular to each other and are a representation of the principal strains or orthogonal eigenvectors (18,19).

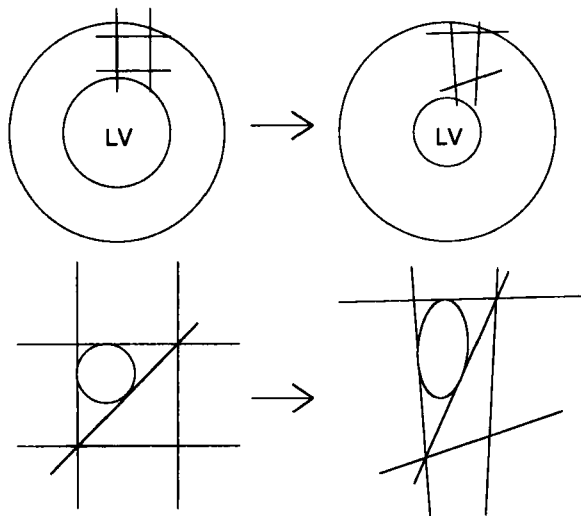


Figure 5. During systole a tagging grid (top) undergoes rigid-body rotation and deformation (here at midwall, as viewed from the apex). A circle placed in the tagging grid (bottom, left) will be deformed into an ellipse (bottom, right). The major and minor axes of the ellipse represent the maximum principal strain and minimum principal strain, respectively.

The 2D model can accurately determine strains in 2D imaging. However, it is unable to detect through-plane motion. Therefore, myocardial tissue cannot be tracked from end-diastole to end-systole, and the temporal evolution of strains at a given material point cannot be evaluated over time. This problem has been addressed in the models of 3D analysis.

Three Dimensional

In addition to the SA views, 3D analysis necessitates LA view imaging. Note that the imaging itself remains 2D, only the combination of 2D images in the SA and LA views allows calculation of motion in 3D.

Because of through-plane translation, a given tag point of an end-diastolic image cannot be tracked prospectively through systole. Conversely, for tag points in images at a later time frame (e.g., end-systole), the material coordinates for the baseline image (at end-diastole when the tags have been set) are known. By combining the information about contraction (SA views) and through-plane motion (LA views), one can calculate the displacement for material points from end-diastole to each time frame after the baseline image and obtain the strain values of myocardial deformation in three dimensions (20,21).

NORMAL LV SYSTOLIC FUNCTION

During contraction, the myocardium experiences a global rotational movement around the central axis. When viewed from apex to base, the basal slices initially rotate counterclockwise and then clockwise by end-systole. The apical slices rotate counterclockwise. Rotation of the endocardial layer is greater than the epicardial rotation. Translation in the longitudinal direction is oriented from base to apex and increases with distance from the apex.

The distribution of E_{cc} and E_{ll} is quite homogeneous, with the circumferential component slightly exceeding the longitudinal component. In contrast, E_{rr} is highest at the base, with decreasing values for the midventricle and apex. E_{cl} shear strains are rather homogeneously distributed and E_{lr} and E_{cr} shear strains seem to be negligibly low. E_{cc} , E_{ll} , and E_{rr} strain values for a population of 31 normal human hearts (3D analysis) are given in Table 2. Additional 3D strain values for normal human hearts are published in references 21 and 22.

Figure 6a illustrates the tag displacement of a patient with myocardial infarction (MI) of the septal wall. Systolic tag displacements are significantly reduced in the

Table 2

Average End-Systolic Values for Fractional Change in Length, as Determined by 3D Analysis in 31 Normal Human Hearts (Midwall About the Heart Equator)

Strain	Septal	Anterior	Lateral	Inferior
E_{cc}	-0.17 ± 0.04	-0.24 ± 0.07	-0.23 ± 0.05	-0.17 ± 0.05
E_{ll}	-0.16 ± 0.04	-0.16 ± 0.04	-0.15 ± 0.05	-0.16 ± 0.04
E_{rr}	0.28 ± 0.12	0.29 ± 0.12	0.26 ± 0.18	0.22 ± 0.1

Values are means $\pm$ SD.
From Ref. 22.

septal areas (9 o'clock) when compared with the lateral wall. Circumferential shortening (E_{cc}) is reduced in these areas, as shown in Fig. 6b. The temporal evolution of strains during the process of ventricular contraction is illustrated in Fig. 6c. In a patient with inferior MI, E_{cc} (black line) is within the mean ± 1.64 SD of 31 normal

human hearts (gray lines) in the septal, anterior, and lateral region. However, E_{cc} deviates from normal subjects in the inferior infarcted region.

TAGGED MRI IN CORONARY ARTERY DISEASE

The detection of wall motion abnormalities in coronary artery disease might become the predominant application for tagged MRI, because of the segmental distribution of coronary artery disease; the ability of tagged MRI to assess a variety of myocardial strains, their inhomogeneous regional distribution, and temporal evolution; and the possible combination of tagged MRI with other MRI techniques to provide a comprehensive cardiac examination.

Coronary Artery Stenosis

In dogs with partial occlusion of the left anterior descending coronary artery (LAD) and dobutamine stress, the minimum principal strain revealed less shortening in the anterior region when compared with the posterior region. The maximum principal strain, however, did not show significant changes in this area. Thus, only the minimum principal strain provided a measure for differentiation of regions supplied by normal versus stenotic vessels (23). Kraitchman et al. (23) suggested that the determination of maximum principal strain with stress may be a poor measure for predicting stenotic vessels. Alternatively, the larger variance in the maximum principal strain data, and thus a technical reason, might have made the maximum principal strains indistinguishable from noise (23). Because radial thickening is usually supported by the lowest density of tag data, Moore et al. (24) suggested calculating novel parameters of systolic function,

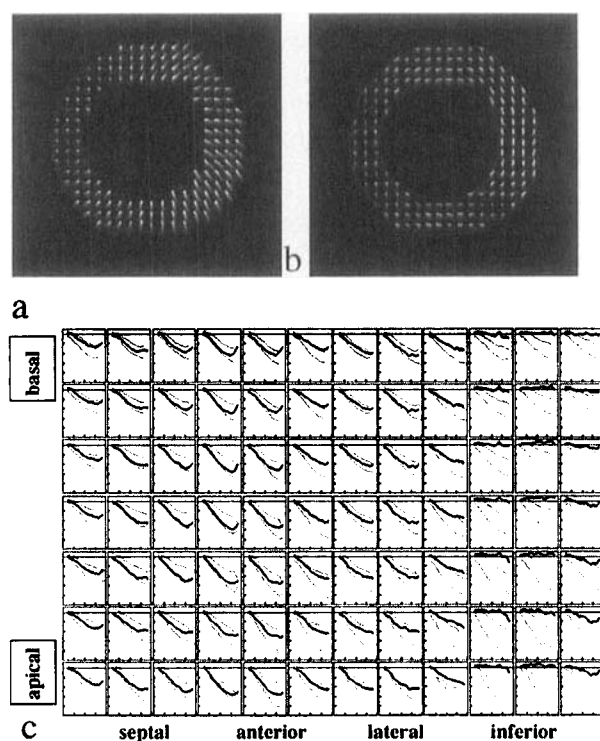


Figure 6. Tag displacements (a) and circumferential shortening (b) are reduced in an example showing MI of the septal wall (9 o'clock). The temporal evolution of circumferential shortening during contraction is shown in c in a patient with inferior MI. In the inferior region, E_{cc} (black line) is outside the range of mean ± 1.64 SD of 31 normal human hearts (gray lines).

the “shortening index” and “radial function.” To calculate these parameters, tissue incompressibility must be assumed. Both parameters are based on the high density tag information of longitudinal shortening and circumferential shortening only.

Coronary Occlusion and MI

Coronary occlusion has been shown to alter the rotational deformation of the heart in dogs (25), and in 7-day-old nonreperfused transmural infarcts a marked reduction and reorientation of the principal strains was detected in sheep (26). Azhari et al. (27), using a 3D model of cardiac geometry, found the shrinkage of the endocardial area, defined by the intersection points of the tagging planes with the endocardial borders, to be the most sensitive parameter for detecting systolic dysfunction in acute coronary occlusion. Similarly, Lima et al. (28) used a 3D volume element approach combined with tagged MRI to improve the quantification of percent wall thickening. The positive predictive value of strain assessment for the detection of MI has been shown to be significantly improved when tagged MRI is combined with contrast-enhanced MRI perfusion analysis (29).

During a 6-month follow-up, LAD ligation in sheep was associated with an initial decrease of circumferential and longitudinal shortening in infarcted and noninfarcted areas. However, partial functional improvement was seen in the infarct-adjacent noninfarcted areas (30). The decrease of circumferential shortening in the infarct-adjacent areas was significantly less with angiotensin-converting enzyme inhibitor therapy (31). Further, iodine-123 meta-iodobenzylguanidine uptake was found to correlate with decreased circumferential shortening in the infarct-adjacent noninfarcted regions after 8 weeks of coronary ligation in sheep, suggesting that sympathetic denervation may contribute to LV remodeling after MI (32). Finally, abnormal circumferential lengthening was observed during isovolumic systole in the border zone of LV aneurysms after long-term coronary occlusion (33).

Clinical studies 5 days after anterior MI revealed reduced circumferential shortening throughout the LV, including noninfarcted and remote areas (34), whereas the principal radial strains were shown to be decreased in infarcted areas but increased in remote areas (35). In patients after a first anterior MI, regional systolic function as determined by circumferential shortening and ejection fraction improved during 8 weeks follow-up, however, only at the expense of an increased LV end-diastolic volume index (36).

Assessment of Myocardial Viability

Parallel tagging planes applied in LA views of the heart visualize systolic base to apex translation. Sayad et al. (37) applied this technique to quantitatively predict improvement of wall thickening after revascularization. Croisille et al. (38) reported that regional strain analysis, especially radial thickening, can identify viable myocardium when tagged MRI is performed at rest and during low-dose dobutamine infusion (5 μ g/kg/min, MRI after 90-min LAD occlusion and 48-hr reperfusion in dogs). Geskin et al. (39) performed tagged MRI during low-dose dobutamine infusion in patients and found that an increase of circumferential shortening in dysfunctional epicardial and midwall layers early after acute MI can predict functional recovery at 8 weeks in these areas. In a recent study, Bogaert et al. (40) combined positron emission tomography with tagged MRI and showed that recovery of viable subepicardial myocardium can contribute to regional and global functional improvement post-MI.

MRI VELOCITY-ENCODING TECHNIQUES

An alternative MRI approach to analyze myocardial systolic function is based on the velocity-encoding technique. The velocity of the transverse magnetization is encoded using phase-sensitive gradient pulses (41). Four acquisitions are performed to yield each 2D velocity-encoded image. The 3D trajectory of material points can be obtained by integrating these velocities (42,43). Alternatively, the spatial gradients of the velocity fields (strain rates) can be directly computed (44). The advantage of these techniques is the insensitivity to T1 relaxation mechanisms, which affords the evaluation of the entire cardiac cycle. Further, the spatial resolution does not depend on tag density but on pixel size, and no image segmentation is required for quantitative analysis. Velocity-encoding techniques are, on the other hand, very sensitive to motion artifacts and flow. The temporal resolution is comparatively low (45). Wedeen et al. (46) used a stimulated echo technique to create “motionless movies” of strain rates. All images are acquired at a fixed delay after the electrocardiogram trigger. Whereas velocity-encoding is progressively varied to obtain the movie frame, the resulting sequence of images is always derived from the same tissue slice; however, each slice is velocity encoded at a different time within the cardiac cycle. This tech-

nique can overcome the problem of through-plane motion for strain rate imaging. It is still susceptible to systematic phase errors, induced by global motion and tissue deformation (47). Strain rates were determined in the ischemic canine model by Arai et al. (48). Ischemic myocardium due to prolonged coronary occlusion could then be discriminated from normal myocardium using this technique. Reference data on strain rates in normal human subjects can be found in reference 49.

SUMMARY

Tagged MRI provides a novel technique for the assessment of LV systolic function. The technique is non-invasive and without radiation exposure. Tagged MRI detects a variety of dynamic functional parameters, including radial distribution and temporal evolution. These parameters can now be uniquely assessed in a clinical setting. However, there are drawbacks, such as patients with the contraindications for MRI, the relatively high cost, and limited availability of the MR technology. The role of tagged MRI is evolving and broadens the diagnostic spectrum of experimental and clinical cardiology.

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