Circumferential Myocardial Shortening in the Normal Human Left Ventricle
Assessment by Magnetic Resonance Imaging Using Spatial Modulation of Magnetization

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Background. Conventional cardiac imaging methods do not depict true segmental myocardial shortening, since they cannot determine segment length between fixed points in the myocardium.

Methods and Results. We used electrocardiographically gated magnetic resonance imaging with spatial modulation of magnetization to noninvasively “tag” the myocardium with dark stripes at uniform 7-mm intervals center to center at end diastole. We then determined end-systolic stripe separation and thereby calculated circumferential shortening. When end systole was not reached in the first image series, a second temporally overlapped series starting in late systole was used to determine late-systolic shortening. Septal, anterior, lateral, and inferior segments were assessed at endocardium, midwall, and epicardium on five midventricular short-axis sections each in 10 normal volunteers. A transmural gradient in circumferential shortening was observed, with the percentage of endocardial segment shortening consistently greater than epicardial segment shortening (epicardial, 22±5%; midwall, 30±6%; and endocardial, 44±6%; p < 0.0001 by analysis of variance). Circumferential shortening varied from apex to base with slices closer to the base of the left ventricle showing less shortening at the midwall (28±9%) and endocardium (39±6%) than more apical slices at the midwall (34±13%) and endocardium (49±9%) (p<0.05 and p<0.01, respectively, by analysis of variance).

Conclusions. Transmural and longitudinal heterogeneity of circumferential shortening is present in the normal human left ventricle. Magnetic resonance imaging with spatial modulation of magnetization is a powerful new tool for assessment of circumferential shortening and provides information unobtainable with conventional imaging methods. (Circulation 1991;84:67-74)

Direct assessment of segmental myocardial shortening has required invasive methods, such as implanting pulse transit sonomicroscopy crystals or fluoroscopically trackable metallic markers within the myocardium. These techniques have limited applicability in humans. A method that noninvasively tags the myocardium can permit direct visualization of shortening within the left ventricular wall. Several approaches have been developed, using presaturation techniques, with spin-echo or cine magnetic resonance imaging (MRI) to accomplish such tagging. Spatial modulation of magnetization (SPAMM) is one such method. The technique permits tagging along two orthogonal sets of closely spaced parallel planes (7 mm center to center in this study) perpendicular to the image plane. Thus, it is particularly suitable for evaluation of segmental shortening. The method can depict both myocardial translation and transmural differences in shortening. The present study was designed to use SPAMM MRI to characterize circumferential myocardial shortening in the normal human left ventricle.

Methods

We studied fifteen randomly selected normal subjects, aged 23–34 years, five of whom were men. None had clinical evidence of any cardiovascular
abnormality or any abnormality on spin-echo MRI. All were in normal sinus rhythm. Ten studies, obtained in five men and five women, were chosen for quantitative evaluation based on image quality. MRI was performed on a 1.5-T Signa scanner (GE Co., Milwaukee, Wis.). To identify cardiac landmarks, a coronal, electrocardiographically (ECG) gated, spin-echo, multislice, single-phase scan was performed using 5-mm-thick slices with 5-mm skips, an echo time of 20 msec, and a repetition time equal to the RR interval. ECG gating was done prospectively on RR intervals with a cycle length lasting at least 85% of the subject's mean cycle length, which was determined in the scanner just before imaging. Hardware and software design permitted scanner triggering without time jitter after R wave peak recognition. The long axis of the left ventricle was prescribed from the coronal plane images by identifying a point on the left edge of the aortic wall at the base of the aortic root and the most leftward and anterior point on the left ventricular apex. Compound oblique short-axis SPAMM images were then obtained perpendicular to that axis. Parameters for SPAMM imaging were as follows: 256×128 matrix, 24-cm field of view, 0.88-mm² final pixel size, and slice thickness 5-mm with 5-mm slice separations. To optimize the method, we initially explored protocols varying stripe number, orientation, thickness, separation, pulse sequence, and SPAMM flip angles. The optimal protocol consisted of two binomial sequences of nonselective radio frequency pulses separated by magnetic field gradient pulses oriented to produce orthogonal sets of parallel planes of reduced signal in three-dimensional space perpendicular to the imaging plane (Figure 1). In the imaging plane these appeared as orthogonal sets of dark stripes at 45° to the x and y axes of the image, with a 7-mm initial dark stripe separation center to center. Initial stripe spacing is constant throughout the cardiac volume. Two averaged signals, flow compensation, and a SPAMM flip angle of 130° were used to enhance myocardial signal and stripe persistence.

Circumferential shortening was assessed by acquiring multislice, multiphase, short-axis SPAMM spin-echo images at five (n=9) or six (n=1) short-axis locations imaged at five or six points during systole, starting 13 msec after the R wave, with 60-msec intervals between images. The levels selected represented the middle 50% of the base-to-apex length of the left ventricle. In patients in whom only five time points were imaged initially, a second SPAMM-imaging sequence on these same slices was performed. This second series was delayed after the R wave, such that it began at the time of the last image in the first series and extended into diastole. The temporally overlapped images from the second series were used to identify end systole and, if necessary, to measure interstripe distances from late to end systole. Thus, end systole could be defined as the time of maximal shortening in each subject. In five subjects, additional systolic shortening occurred between the first two images of the second series (end systole, 313 msec), whereas in one subject, additional shortening occurred until the third image of the second series (end systole, 373 msec). As in all spin-echo MRI-gated cardiac imaging, data used to calculate each image is derived from many cardiac cycles. During each cardiac cycle, data are acquired on one of 128 lines in the phase-encoding directions on each of five imaging planes. Thus, with two averaged signals, 256 cycles are required to obtain five different image slices. To obtain all five image slices at the same five time intervals during systole, as done in this study, required five times 256 (1,280) cardiac cycles.

Figure 1. Three-dimensional geometric representation of magnetic resonance imaging with spatial modulation of magnetization. Two orthogonal sets of dark (saturated) planes lie parallel to the long axis of the left ventricle in three-dimensional space. The intersection of these planes with short-axis image planes results in a grid of dark stripes. Measurements were made at four sites on the left ventricle where the stripes were perpendicular to the endocardium at end diastole. In spin-echo magnetic resonance imaging, data used to calculate each image is derived from many cardiac cycles. During each cardiac cycle, data are acquired on one of 128 lines in the phase-encoding directions on each of five imaging planes. Thus, with two averaged signals, 256 cycles are required to obtain five different image slices. To obtain all five image slices at the same five time intervals during systole, as done in this study, required five times 256 (1,280) cardiac cycles.
into account in-plane translation using a region-of-interest module of the Volumetric Image Display and Analysis (VIDA) package running on a Sun Workstation, which is shown in Figure 2. A line was specified normal to the SPAMM stripes of interest, and the pixel brightness profile along the line was displayed graphically. The user could point to the graph of the line profile while a cursor would mark the corresponding location on the original cross-sectional image. On end-diastolic images, a dark stripe center is denoted by a narrow peak in pixel intensity within a trough. On subsequent systolic images, the nadir of pixel value occurs at the center of the stripe. Over time, in an immobile object, the $T_1$ relaxation reduces the difference in signal amplitude between bright and dark stripes, but the location of the center of the dark stripes remains invariant. The thickness and separation of the tag lines are limited by the resolution of the images, not the stripe production technique. Point loci at dark stripe centers were stored, and point-to-point distances, equal to stripe separation, were calculated. Circumferential segment shortening was calculated from measurement of segment length ($L$) at the endocardium, midwall, and epicardium and at end diastole (ED) and end systole (ES). Percent segment shortening ($\% SS$) was calculated as $\% SS = 100 \left( \frac{L_{ES} - L_{ED}}{L_{ED}} \right)$. Endocardial measurements were made at the endocardial edge of the myocardial stripes. Midwall measurements were made at 50% of the wall thickness at end diastole, and end-systolic midwall measurements were made at the same loci using the change in position of orthogonal stripe pairs to account for intramural displacement due to thickening. Epicardial measurements were made at the epicardial edge of the myocardial stripes. When orthogonal dark stripes obscured the correct measurement site, the nearest available location was used. When stripes were bent at measurement sites during systole, the minimum separation was measured. Intraobserver variability of interstripe distance was determined from blinded paired measurements. Interobserver variability of percent segment shortening was also determined using blinded paired measurements and the same analysis tool in another patient population.

For statistical analysis, systolic segment shortening was compared at multiple sites using analysis of variance with Scheffe’s test. To account for variations in slice location along the long axis of the left ventricle, four of the five slices obtained in each subject, corresponding to the middle half of the long axis, were selected for analysis in each subject. Analyses were performed comparing endocardial, midwall, and epicardial sites. We also compared anterior, lateral, inferior, and septal sites and compared basal with more apical sites globally and for each region.

**Results**

Figure 3 depicts end-diastolic and end-systolic short-axis spin-echo images obtained using SPAMM. A presaturation sequence of nonselective radio frequency and gradient pulses produces a grid of dark lines across acquired images, which are actually localized alterations of tissue magnetization and thus move with the tissue in subsequent images. When the heart is serially imaged through systole, the stripes of magnetically tagged myocardium move and change.
shape. Changes in interstripe distances during systole reflect circumferential myocardial shortening. Note that, at end systole, stripes throughout the left ventricle tend to converge at the endocardium. This pattern, which was consistently found on all slices imaged in the short-axis plane, indicates that circumferential shortening is greater at the endocardium than at the epicardium. Where stripes are initially aligned perpendicular to the endocardium, circumferential shortening can be quantitated at epicardial, midwall, and endocardial sites. Circumferential segment shortening within the wall can also be measured wherever a line joining a pair of intersections of orthogonal lines lies parallel to the endocardium. Components of motion unrelated to myocardial shortening, such as in-plane rigid body motion, can be readily distinguished. Rotational motion of the myocardium tends to be clockwise at the base and counterclockwise at the apex, when viewed from the apex.

The value \( n=10 \) for stripe separation, specified as 7 mm, was determined to be \( 7.08\pm0.34 \) (mean\pmSD) mm. Analysis of intraobserver variability of interstripe distance demonstrated good reproducibility \( (r=0.92) \) (Figure 4). As reported elsewhere, interobserver variability using this analysis tool in human subjects is also quite good \( (r=0.92) \).  

A transmural gradient in systolic shortening was found, as depicted in Figure 5, that shows the mean percent circumferential shortening for the endocardial, midwall, and epicardial segments for all slice levels analyzed. Shortening at the endocardium is twice that at the epicardium, with midwall shortening intermediate in value. Differences between epicardium and midwall and between midwall and endocardium were both significant at \( p<0.001 \), confirming the gradient seen visually on end-systolic images. There were no statistically significant differences in circumferential shortening among the anterior, lateral, inferior, and septal regions.

Figure 6 depicts the behavior of the transmural gradient in circumferential shortening along the left ventricular long axis, from the most basal to the most apical short-axis slice analyzed. An endocardial-to-epicardial gradient in shortening is evident at all levels studied. Comparison between levels shows significantly greater shortening on more apical slices at the midwall and endocardium. At the midwall this gradient is complex, with less shortening at the second slice location than the first but more shortening at the more apical third and fourth image slice locations (Figure 6). To determine whether there were differences in the base-to-apex gradient between anterior, lateral, inferior, and septal regions, midwall shortening data from each region were compared (Table 1). Differences in shortening from base to apex were significant only in the inferior region \( (p=0.010) \). There were no statistically significant differences in circumferen-
tial shortening between the anterior, lateral, inferior, and septal regions of the ventricle.

**Discussion**

Conventional cardiac imaging methods cannot directly depict intramural myocardial shortening. Instead, ventriculographic methods depend on changes in the shape and size of the ventricular cavity silhouette to assess regional myocardial function. Tomographic methods, such as two-dimensional echocardiography, ultrafast computed tomography, and conventional spin-echo and cine MRI can also be used to evaluate systolic changes in left ventricular wall thickness to assess systolic function. However, these approaches cannot show transmural differences in segmental function. Further, they cannot measure distance and distance changes between fixed points in the myocardium or depict rigid body motion of the heart. Assessment of true segmental shortening has required implantation of pulse transit somomicroscopy crystals or fluoroscopically trackable metallic markers within the myocardium. These techniques have been invaluable, but they have limited applicability because of their invasive nature. The ability to noninvasively assess shortening at various depths across the thickness of the left ventricular wall is a unique capability of myocardial tagging with MRI techniques. Therefore, we mea-

**FIGURE 5.** Bar graph showing mean±SD of percent circumferential shortening for endocardium (Endo, n=40), midwall (Mid, n=40), and epicardium (Epi, n=40) for all segments measured. Note that shortening at endocardium is twice that at epicardium. ANOVA, analysis of variance.

**FIGURE 6.** Graph showing transmural gradient in circumferential shortening along left ventricular long axis from most basal to most apical short-axis slice imaged. Endocardial (endo) to epicardial (epi) gradient in shortening is evident at all levels studied. Comparison between levels shows significantly greater shortening on more apical slices at midwall (mid) and endocardium (p<0.05 and p<0.01, respectively, by analysis of variance).
TABLE 1. Percent Circumferential Midwall Shortening by Segments

<table>
<thead>
<tr>
<th>Region</th>
<th>Segment shortening (%)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>22±7</td>
<td>22±13</td>
<td>29±8</td>
<td>31±15</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>32±8</td>
<td>27±12</td>
<td>28±10</td>
<td>33±12</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>32±12</td>
<td>28±14</td>
<td>40±14</td>
<td>35±14</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>23±6</td>
<td>27±8</td>
<td>36±10</td>
<td>37±13</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SD. Segments 1–4, basal (1) to apical (4) segments at the midwall (n=10).

*By analysis of variance.

sured circumferential shortening at the epicardium, midwall, and endocardium at each site evaluated. The results demonstrate a consistent transmural gradient in circumferential shortening, with endocardial shortening nearly twice as great as epicardial shortening on all slices studied. These findings are consistent with previous animal studies using sonomicrometry data,14,15 which have also shown greater shortening at the endocardium than the epicardium. Since subendocardial ischemia can occur in both ischemic heart disease and marked concentric hypertrophy of any cause, it is possible that alteration of this transmural gradient will prove to be a useful marker of abnormal myocardial function. Although only the middle half, not the full long-axis length, of the left ventricle was evaluated, it was possible to demonstrate an apex-to-base gradient in midwall and endocardial shortening, with more shortening on more apical slices. This gradient was complex and differed layer to layer, but our results are in keeping with those obtained using echocardiography and ultrafast computed tomography.11,12

Rigid body motion and segmental shortening, with resultant thickening of the wall, are both important components of motion that contribute to the images obtained with conventional tomographic imaging techniques. Rigid body motion is itself complex, including in-plane, through-plane, linear, and rotational components. It is not possible by conventional techniques to differentiate these components of motion to identify true segmental shortening. Myocardial tagging with the SPAMM method permits direct assessment of circumferential shortening. Motion of the heart within the plane of the image does not affect the measurement of circumferential shortening, since shortening is only reflected by change in interstripe distances.

MRI tagging can also be used to assess and compensate for through-plane motion of the myocardium.16 When performing short-axis imaging with any conventional tomographic method, the myocardium within the imaging plane changes through the cardiac cycle. This phenomenon complicates assessment of wall thickening in the short-axis plane using conventional tomographic techniques since end-diastolic and end-systolic wall thicknesses are determined on different slices of myocardial tissue. In this study we did not attempt to evaluate through-plane motion. However, our segment shortening data are not invalidated by this phenomenon, since the myocardial stripes actually represent the intersection with the image plane of two sets of orthogonal planes of altered signal in three-dimensional space, which are themselves perpendicular to the image plane. Thus, stripe separation is the same initially at end diastole in all short-axis sections of the left ventricle. Therefore, on a single series of images, measurement of end-systolic stripe separation permits calculation of segmental shortening in the myocardium found in the image plane at end systole, even if the end-diastolic location of that slice of myocardium along the long axis of the ventricle is not known. When a second series of temporally overlapped images was used to determine late-systolic shortening, a small amount of late-systolic through-plane translation is not accounted for by our method. This limitation has been overcome subsequent to the studies described herein (see below). If measurements were made at each time interval during systole, different myocardium would be measured on each image, since long-axis translation moves tissue through the fixed tomographic short-axis plane. Hoffman et al17 have demonstrated in the mid–left ventricle that the long-axis translation can be significant, ranging from 0.5 to 1.5 cm or one to three slice thicknesses. In contrast, the epicardial apex remains fixed in space.17

The methods used in this study do not permit serial quantification of shortening at multiple time points on the same myocardial segment. To do so requires three-dimensional tracking of segment location. Such tracking can be achieved with multiplanar SPAMM imaging, although this currently requires considerably longer scanning times to acquire the necessary long-axis and short-axis images. Alternative approaches to three-dimensional tracking using SPAMM include the use of triplanar tags with one set oblique to the image plane16 and determination of myocardial through-plane velocity using phase information from gradient echo images.18

The SPAMM method differs in several important respects from the earlier magnetic tagging technique developed by Zerhouni et al.4 Their method uses conventional presaturation pulse techniques and, in short-axis imaging, generates eight 3.5-mm-thick equiangular radial stripes, intersecting at the center of the left ventricle across the short-axis tomographic image. The most striking differences between the two methods are the timing, arrangement, and number of lines that appear on the image. SPAMM lines are laid down in a square grid with operator-selectable stripe separations. Application of the preimaging SPAMM sequence takes only 10 msec; thus, the first image can be obtained 13 msec after the R wave is detected. The larger number of lines and closer spacing are suited to more detailed evaluation of myocardial motion in small segments but also create a formidable problem in data analysis.

The methods used in the present study have a number of important real or apparent limitations.
ECG gated spin-echo MRI creates images from data obtained over hundreds of cardiac cycles. Thus, cycle length variability in stable normal sinus rhythm occurs mainly during diastole and since only systolic images were evaluated, the effect of this cycle length variability on our results is considerably less than that of total cycle length variability. Each image also represents a temporal average over many respiratory cycles. Therefore, respiratory effects on cardiac position and intracavity blood volume affect the results. Nonetheless, the quantitative reliability of such images has been demonstrated in studies showing the accuracy of spin-echo MRI estimates of left ventricular myocardial mass, which compare favorably in accuracy to single-beat methods, such as ultrafast computed tomography.\textsuperscript{19,20} Similarly, cine MRI, which also uses data from hundreds of cardiac cycles to create a given image, has proven to be an excellent method for determination of left ventricular ejection fraction.\textsuperscript{21} In addition, recent comparison of SPAMM and sonomicrometry determinations of circumferential shortening have shown good correlation between the two techniques in normal and ischemic myocardium.\textsuperscript{22} In the near future, we anticipate that it will be possible to perform SPAMM imaging with echo-planar\textsuperscript{23} or similar near–real-time single-beat MRI approaches, so that direct comparisons of results from single-beat and temporally averaged images should be possible.

The pixel size used in the present study also creates important limitations in the precision of measurement of segment shortening. Data were acquired in a 128$\times$256 matrix over a 24-cm field of view, so that raw pixel size was 1.88 mm (y axis) by 0.94 mm (x axis), interpolated to 0.88 mm$^2$. Initial stripe separation was only 7 mm, equal to less than 8 pixels. Despite this relatively limited resolution, interobserver and intraobserver reproducibility were quite good, and statistically significant differences in group data were obtained between epicardial, midwall, and endocardial shortening. There is no inherent limitation in SPAMM stripe spacing, but improved resolution will also require smaller pixel sizes. We anticipate that improved gradient amplifiers, system software revisions, and use of surface coils will facilitate reductions in pixel size in the future. This, in turn, will permit full use of the ability of the SPAMM approach to generate smaller interstripe separations than those in current use.

The 60-msec interval between images in this study could produce an error of up to 30 msec in the identification of the end of systolic shortening. This error is probably small. However, since these data were obtained, we have reduced this error further and eliminated the need for the overlapped image series in the following manner. First, improved pulse sequences have resulted in improved stripe persistence. Second, we have used a single-slice axial cine SPAMM MRI gradient echo acquisition, with a repetition time of 25 msec.\textsuperscript{7} Since cine SPAMM provides stripe persistence into diastole, one can identify end systole, identified as the time of minimal stripe separation, before multislice imaging with less than a 25-msec potential error in timing. With the time of end systole known, the intersequence delay can be adjusted so that the last SPAMM image time is at end systole.

The simple, operator-dependent measurement approach used in the present study is also a potential limitation. The images contain far more dimensional data than we used, since we limited our attention only to stripe pairs that initially were normal to the endocardium at end diastole. We did not track stripe intersections, the best-defined locations on the images. Further, we did not evaluate through-plane motion of myocardium. Finally, operator dependence introduces an additional element of variability into the measurement process. As discussed above, through-plane motion of myocardium does not affect validity of our segment shortening measurements, since initial stripe separation is uniform throughout the myocardium on all short-axis sections. More extensive use of dimensional information inherent in the images will ideally be performed using three-dimensional finite-element analysis of myocardial deformation, and operator-dependent measurements can be eliminated using automatic tracking approaches. Both of these approaches are presently under development.

SPAMM MRI shares the same limitations of all MRI techniques with regard to patient eligibility. Some patients produce images of poor quality for unknown reasons. This may be due to patient movement during scanning or to marked diaphragmatic motion. We estimate that, in all, 25% of unselected subjects do not produce adequate images for quantification by the techniques used in this study. Subjects who have pacemakers or implanted ferromagnetic objects or fragments cannot be imaged. Subjects who are markedly obese or claustrophobic cannot be imaged. Unstable patients cannot be observed closely in the scanner. When conventional gated imaging is used, patients with irregular cardiac cycle lengths due to atrial fibrillation or very frequent premature complexes cannot be imaged effectively. Single-beat imaging methods such as echo-planar MRI can obviate this problem as well as that of obtaining image data over many cardiac and respiratory cycles.

We believe that, despite the limitations cited, the measurements made in the present study and the interpretations made from those measurements are valid and add new information with respect to circumferential myocardial shortening in the normal human left ventricle. Application of SPAMM MRI to abnormal myocardium, particularly in the setting of ischemic heart disease, should enhance understanding of that disorder, since evaluation of transmural differences in function that are due to ischemia has, to this point, required use of highly invasive techniques. Further advances in imaging technology and
analytic software should greatly enhance the power of future applications of SPAMM MRI.

References


KEY WORDS • magnetic resonance imaging • left ventricle • myocardium
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