Mapping propagation of mechanical activation in the paced heart with MRI tagging

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Wyman, Bradley T., William C. Hunter, Frits W. Prinzen, and Elliot R. McVeigh. Mapping propagation of mechanical activation in the paced heart with MRI tagging. Am. J. Physiol. 276 (Heart Circ. Physiol. 45): H881–H891, 1999.—The temporal evolution of three-dimensional (3-D) strain maps derived from magnetic resonance imaging (MRI) tagging were used to noninvasively evaluate mechanical activation in the left ventricle (LV) while seven canine hearts were paced in situ from three different sites: the base of the LV free wall (LVb), the right ventricular apex (RVa), and the right atrium (RA). Strain maps plotted against time showed the evolution of shortening over the entire LV midwall and were used to generate mechanical activation maps showing the onset of circumferential shortening. RA pacing showed rapid synchronous shortening; LVb pacing showed a wave front of mechanical activation propagating slowly and steadily from the pacing site, whereas RVa pacing showed regions of rapid and slower propagation. The mechanical (M) activation times correlated linearly with the electrical (E) activation (M = 1.06E + 8.4 ms, R = 0.95). The time for 90% activation of the LV was 63.1 ± 24.3 ms for RA pacing, 130.2 ± 9.8 ms for LVb pacing, and 121.3 ± 17.9 ms for RVa pacing. The velocity of mechanical activation was calculated for LVb and RVa pacing and was similar to values reported for electrical conduction in myocardium. The propagation of mechanical activation for RVa pacing showed regional variations, whereas LVb pacing did not.

magnetic resonance imaging; magnetic resonance tagging; pacing; conduction abnormalities

Each year 123,000 pacemakers are implanted in the U.S. alone (1) to improve heart function and the quality of life for the recipients. Despite the extensive experience with implantable pacemakers, dating back to their introduction in 1958, only 43% of those under the age of 60 who had pacemaker implants reported an improvement in their quality of life (30). In addition, the application of pacing therapy for the treatment of heart failure has been controversial, with some researchers showing improvement in heart function (9, 21) and others claiming no improvement (17). The low satisfaction rate and controversy in assessing pacing in the diseased heart may partly be a consequence of our lack of understanding of how pacing affects cardiac mechanics. This study applies tagged magnetic resonance imaging (MRI) to gain a better understanding of the effects of pacing on the mechanics of the heart. This knowledge could then be used to evaluate and modify pacing protocols and to assist in decisions of when to use pacing therapy to treat heart failure.

It has been previously demonstrated that alterations in the electrical activation of the heart also alter the “mechanical activation,” defined as the onset of circumferential shortening. Previous studies have examined deformation and strain due to ventricular pacing at a few isolated sites using surface markers (12, 39), radiopaque implanted markers (4, 18, 45), or ultrasonic crystals (4, 35). Other studies have used phase-imaging radionuclide ventriculograms to obtain measurements of the sequence of shortening based on the ventricular blood pool (5, 15, 40). However, none of these studies has been able to map the entire left ventricular (LV) midwall.

MRI tagging has been used to evaluate systolic LV function in the healthy and infarcted heart (3, 31) and, more recently, to elucidate the differences in the LV during pacing (27). By using the methods of MRI tagging, the temporal evolution of local three-dimensional (3-D) strain of the entire LV under pacing conditions can be evaluated (28). From the data for strain versus time, both the mechanical activation times and the velocity of the propagation of mechanical activation can be computed. MRI has several advantages over other methods for evaluating myocardial mechanics because it is noninvasive, measures local strains over the whole LV, measures the complete strain tensor, does not require exposure to ionizing radiation, and can be applied clinically.

In this study we successfully demonstrated that MR-tagged imaging can be used to noninvasively map the mechanical activity of the entire LV during pacing. We also mapped the regionally asynchronous spread of contraction across the LV during ventricular pacing. This technique has the potential to evaluate the effects of different pacing protocols such as electrode placement or the effects of pacing on the diseased heart.

METHODS

In these experiments the canine heart was paced from one of three locations: the right atrium (RA), the base of the LV free wall (LVb), or the apex of the right ventricle (RVa). These sites were chosen for the following reasons. First, the RVa site is commonly used in patients and results in a sequence of activation resembling that of left bundle branch block (44). Second, the LVb site can be reached clinically by routing the pacemaker leads through the coronary sinus, and the sequence of activation resembles, at least partially, Wolf-
Parkinson-White (WPW) syndrome. Finally, RA pacing was used to stimulate intrinsic pacing at the same heart rate as the RVa- and LVb-pacing protocols. Tagged MR images were acquired during each of the pacing protocols and then processed to determine the temporal evolution of myocardial strain during systole, the mechanical activation times, and the velocity of the propagation of mechanical activation.

Animal Preparation

Seven mongrel dogs (weight 20–25 kg) were initially anesthetized with thiopental sodium (20 mg/kg), and then anesthesia was maintained with an infusion of midazolam (0.1 mg·kg\(^{-1}\)·h\(^{-1}\) iv) and sufentanil (0.1 µg·kg\(^{-1}\)·h\(^{-1}\) iv). Animals were ventilated with room air supplemented with O\(_2\) by a Harvard respirator. Tygon catheters were inserted into the jugular vein and the femoral artery for administration of fluid and drugs and arterial sampling of the blood gases. An MR-compatible Millar catheter-tip micromanometer (model SPC-350MR; Millar Instruments, Houston, TX) was inserted into the LV via the carotid artery to monitor pressure. The chest was opened, and nonferromagnetic bipolar pacing leads were sewn onto the heart at the RA, LVb, and through the RV wall on the endocardial RVa. Throughout the experiments, the stability of the animal preparation was monitored with recording of arterial blood pressure and blood gases and with observation of the end-diastolic LV volume and ejection fraction as estimated from the MR images. After the experiment, the animal was killed with an overdose of pentobarbital sodium. The experiments were performed with approval of the Johns Hopkins Animal Care and Use Committee.

Pacing Protocol

In the MR environment, strong electromagnetic fields are induced by the scanner from both the radio-frequency (RF) field used to excite the nuclear spins and from the magnetic field gradient switching needed for imaging. As a result of these fields, the electrode wires in the scanner room become potential antennas and, hence, must be protected to prevent spurious currents, which could induce arrhythmia or tissue heating. Current induction on the pacing wires also leads to spurious currents, which could induce arrhythmia or tissue heating. These fields, the electrode wires in the scanner room become potential antennas and, hence, must be protected to prevent spurious currents, which could induce arrhythmia or tissue heating. Current induction on the pacing wires also leads to spurious currents, which could induce arrhythmia or tissue heating. These fields, the electrode wires in the scanner room become potential antennas and, hence, must be protected to prevent spurious currents, which could induce arrhythmia or tissue heating. Current induction on the pacing wires also leads to spurious currents, which could induce arrhythmia or tissue heating.

Each electrode was passed through a two-stage passive low-pass LC filter designed to attenuate signals at the operating frequency of the MRI scanner (64 MHz) and at the frequencies induced by gradient switching (42). The filters and other circuitry were encased in a shielded box. Electrode leads were twisted together to minimize the possibility of creating inductive loops. The electrodes were then passed through shielded cable to an additional three-stage filter (43) positioned outside the 5-gauss line inside an RF-shielded box. After filtering was completed, the pacing leads were passed outside the scanner room, where they were simultaneously recorded on a Gould four-channel recorder (TA240S) and sampled at 200 Hz using an M10-16 data-acquisition card (National Instruments, Austin, TX) and LabView software running on a Macintosh Quadra computer. The pressure information from the Millar catheter in the LV and the pacing signal were also recorded. Pacing was performed using a Grass stimulator (model S48; Grass Instruments, Quincy, MA) connected to an isolation stimulus unit (SIUS; Grass). The stimulus level was set high enough to ensure consistent capture as verified by electrocardiogram (ECG), LV pressure, and the cine MR data. The normal electrical activation of the heart was suppressed by using atrioventricular (AV) synchronous pacing at a rate above the spontaneous rate.

MRI Protocol

Cine images were acquired on a GE Signa 1.5 T scanner using segmented k-space acquisitions during breath-hold periods (26). Breath holds (16–24 s) were accomplished by stopping the respirator at an identical point in the cycle. Each breath hold was followed by a recovery period of 45–60 s. The pacing signal was used to trigger the tagging pulse at end diastole. For the ventricular pacing experiments, tagging took place at 45 ms after the pacing signal; for the atrial pacing experiments, the tagging occurred at end diastole as determined from the cine sequence of MR images. In each case, the first image occurred 6 ms after tagging. A total of 12–20 images were taken through systole at 20-ms intervals, except in one study in which a higher time resolution of 13 ms was used. On the average, 270 ms of systole were imaged with the data acquisition stopping at end systole. The magnetic tags were placed on the myocardium by saturating the proton spins in evenly spaced planes. When the images were subsequently taken perpendicular to the tag planes, these tags were seen on the images as dark lines. The inverting proton spins move with the heart and served as material point markers, which were used to determine the tissue displacements orthogonal to the tags (25, 29). The tagging pattern produced 1.5-mm-thick saturation bands spaced at 5.5-mm intervals. The scanning parameters used were a 28- to 32-cm field of view, a time to repetition of 6.5 ms, a time to echo of 2.1 ms, a 256 × 96 acquisition matrix, a ± 32-kHz bandwidth, two to three readouts per movie frame, an in-plane spatial resolution of 1.25 × 3 mm, and a slice thickness of 6–7 mm.

For each of the three pacing sites, seven to nine short-axis slices were taken using a parallel line tagging pattern, with the tags perpendicular to the frequency-encoding direction, followed by the same set of short-axis slices with both the tags and readout gradient rotated 90° (25, 26). Nine long-axis slices, with the slices oriented radially from the center of the RV, right ventricle; LV, left ventricle.

Fig. 1. Sample tagged magnetic resonance (MR) images showing a short-axis slice (short axis 0), same short-axis slice with tags rotated 90° (short axis 90), and a long-axis slice (long axis). Images in columns at left, middle, and right were taken at early systole shortly after tagging, mid-systole, and late systole, respectively. Orientation of tags in 3 orthogonal directions permits calculation of displacement and strain in 3 dimensions. RV, right ventricle; LV, left ventricle.
LV cavity and spaced 20° apart, were imaged with the tags parallel to the short-axis imaging planes. The complete acquisition took ~40–50 min. Examples of the tagged images for the same orthogonal short-axis slice and one long-axis slice are shown in Fig. 1 at different times in systole.

Data Processing

Calculation of myocardial strain with field fitting. The tagged MR images were analyzed by delineating the contours and the tags using a semiautomated software package (19, 20). The 3-D Lagrangian strain tensor was calculated by field fitting the displacements in prolate-spheroidal coordinates using the method of O’Dell et al. (33). Field fitting uses the three orthogonal sets of one-dimensional displacements measured from the tags to generate an analytical solution of the 3-D displacement field, which interpolates across the heart, permitting the calculation of displacement and, hence, strain at any location. The displacement field is evaluated on a regularly spaced mesh that represents the material points of the heart. Strains are computed on the material point mesh. Whereas the full 3-D strain tensor was calculated on a mesh of 3 radial, 7 or 8 longitudinal, and 24 circumferential points, in this study only the circumferential strain \( \varepsilon_{c} \) at the midwall was used. Analysis was done at the midwall for several reasons. First, the myocardial fibers run predominantly in a circumferential direction in the midwall (41); thus \( \varepsilon_{c} \) becomes a measure of fiber shortening or stretching. Second, it has been shown, at least in the middle third of the heart, that maximal shortening in the midwall occurs in the fiber direction (16). Finally, the precision of the \( \varepsilon_{c} \) calculation using the field-fitting method is higher at the midwall than at the endocardial or epicardial wall (33). Figure 2A shows an example of an 8 x 24 mesh at the midwall of the LV for a single time point. Figure 2B shows the two-dimensional (2-D) “bull’s-eye” representation of the grid of Fig. 2A used for the presentation of the data.

Fitting strain versus time. The field-fitting technique was performed on each time frame independently. Because this study investigates the evolution of strain over time, additional temporal interpolation was used. The midwall \( \varepsilon_{c} \) data at each material point were interpolated across time using a seventh-order polynomial fit to all of the data points. The seventh-order polynomial was chosen over other orders of polynomial fits and local cubic splines because it provided a good trade-off between accuracy of the fit and noise reduction of the data.

Mechanical activation time. Three basic temporal patterns were observed during pacing: prestretched regions (Fig. 3A), early shortening (Fig. 3B), and relatively no shortening (Fig. 3C).
Prestretch is defined as lengthening that takes place after normal diastole due to contraction of other parts of the heart. Because imaging in this study occurred during systole, any observed stretching would be prestretching. In regions with a positive strain peak above the noise level (E_{cc} > 0.02), the onset of activation was determined from the point of maximum stretch (Fig. 3A, arrow).

In regions without a peak, a different method was required for determining the mechanical activation times. Because the signals showed a smooth progression of shape from one location to the next, the methods of time-delay estimation were employed (7). Time-delay estimation calculates the time offset between two similar signals by shifting one of the signals in time until the mean-squared difference between the two signals is minimized. A similar method of maximizing the cross-correlations was used by Augustijn et al. (2) to calculate the time difference between adjacent strains. When the time-delay estimation algorithm was used in regions with E_{cc} peaks, it yielded the same results as determination of the point of maximum stretch.

A region was classified as akinetic if the difference between maximum and minimum strains was \( \leq 0.04 \). In akinetic regions, as shown in Fig. 3C, the mechanical activation time was computed from bilinear interpolation of the neighboring locations to preserve continuity in the mechanical activation maps. Only 9% of the regions in the paced hearts were classified as akinetic.

Velocity. Mechanical activation maps were computed for each pacing site in the seven hearts from the activation times at each material point as determined by one of the above-described methods. These mechanical activation maps were used to calculate the speed and direction of the propagation of mechanical activation at each material point in the midwall of the heart using the forward-backward differences for both time and mesh distance. Because the velocity calculations were calculated across three mesh locations, erroneous values occurred at locations where waves of shortening either diverged, such as at the pacing site, or converged, such as on the opposite side of the heart. To eliminate these discretizing errors, material points that had neighbors with a wave propagating at an angle of \( \geq 90^\circ \) difference, indicating a second activation wave front, were eliminated from the collective velocity statistics. This method of calculating velocity was found to be inappropriate for the RA-paced hearts because the activation did not progress as a single wave front but, rather, as multiple wave fronts due to the complex underlying Purkinje system.

Cumulative LV activation plots. To pool the data for calculation of collective statistics, plots of the cumulative fraction of mechanically activated LV midwall was generated. The percentage of LV myocardium activated in the midwall was calculated by weighting each material point by the relative volume represented by that material point and then summing across all activated regions to determine the fraction of activated myocardium. For the RA-paced hearts, there was a delay from the pacing spike to ventricular contraction as the electrical conduction passed through the AV node, and this delay varied in each heart. To compare RA-paced hearts, which have varying AV delays, with the ventricularly paced hearts, the AV delay was subtracted from the RA activation times so that the earliest point of activation was at time 0.

Electrical Activation

Measurements of electrical activation were made to verify the correlation between mechanical activation times and the underlying electrical activation times. The goodness of fit was determined by the correlation coefficient (R) and the standard
errors of the slope, which were calculated and compared with unity slope using the t-test (47). Electrical measurements were recorded from the bipolar electrodes that were not serving as the pacing site. For example, during RA and RVa pacing, the LVb electrodes were used for electrical measurements, whereas, during RA and LVb pacing, the RVa electrodes were used for electrical measurements. The bipolar electrodes were registered with the MR images by determining the location of earliest contraction in the ventricular pacing experiments. In one pacing study, 12 additional unipolar monitoring electrodes were placed throughout the LV free wall to measure the electrical activation times. Electrical activation at the bipolar electrodes was taken as the zero crossing after deflection (38), and in unipolar electrodes it was the point of maximum deflection. Unipolar electrode placement was registered with the MR images by using a string to measure the following distances on the surface of the excised, preserved heart: circumferential distance from both RV attachments and the distance from the fibrous ring at the base of the LV. The RV attachments served as a landmark on the MR images, and the fractional distance of the electrode between the two RV attachments, along with the absolute distance from the base of the LV, was then used to register the location of the electrode in the MR images. This method was not effective, however, for localizing electrodes near the apex of the heart, so these measurements were excluded from the analysis. Some electrical measurements were also excluded from the study when the time of activation could not be determined due to system noise or recording failure. After the position of the electrodes on the MR images was located, the mechanical activation time at the electrode location could be determined. The correlation between electrical activation and mechanical activation times served to validate the methods.

Error Analysis

The precision in the interpolated strain estimate was calculated as the root-mean-squared error (RMSE) between \( E_{cc} \) calculated at the imaging times and the polynomial fit of \( E_{cc} \) over time. A good fit of the data would yield an error comparable to the strain errors previously reported using the field-fitting method (33). Using the standard deviation found in the \( E_{cc} \) measurements, we performed 50 Monte Carlo simulations on each of a subset of studies to determine the precision of the mechanical activation times. The number of Monte Carlo simulations was then doubled to confirm convergence of the error estimate. Using the standard deviation for the mechanical activation times, we also used Monte Carlo simulations to calculate the standard deviation of velocity. Again, 50 simulations were used and then doubled to verify convergence.

RESULTS

Circumferential Strain

The strain maps of Fig. 4 clearly demonstrate the regional differences between RA pacing and RVa or LVb pacing of the heart over the entire LV. Under RA pacing
the heart contracted in a relatively uniform manner throughout the midwall (Fig. 4A). With few exceptions, the shortening was uniform and synchronous, as demonstrated by the similar values of both $E_{cc}$ and the temporal derivative of $E_{cc}$ at each location. Significant differences were seen in the strain maps for the ventricularly paced hearts. The strain maps for the LVb-paced heart (Fig. 4B) show that the tissue shortened rapidly at the pacing site with a steep temporal derivative and 100 ms from pacing. The contraction in these prestretched regions did not begin until a delay of $>100$ ms from pacing. The contraction in these prestretched regions then required approximately another 100 ms to return to the starting zero-strain condition. Near the pacing site, the rapid shortening phase was often followed by a “rebound” stretch (see Fig. 4B), which occurred as the load increased due to the start of contraction by regions on the opposite wall. The strain map for RVa pacing (Fig. 4C) has characteristics similar to those shown in the LVb strain map except that the regions of rapid shortening and prestretch have changed, reflecting the change of pacing site.

Mechanical Activation Time

Representative activation maps for three studies are shown in Fig. 5 for RA, LVb, and RVa pacing. Each row represents a different heart. The RA-paced hearts show a rapid spread of activation as indicated by the more narrow range of color. For the LVb-paced hearts, a wave of mechanical activation emanates from the pacing site and travels around the heart in both directions until it converges at the opposite wall. The RVa-paced hearts also show a wave of propagation starting near the pacing site and moving to the free wall.

The cumulative LV mechanical activation plots are shown in Fig. 6 for each of the hearts and for each of the three pacing protocols. From the cumulative LV mechanical activation plots, two parameters were calculated to characterize the speed of activation. The time to 90% activation (Act90) represents the time for 90% of myocardium to begin contracting. Act90 was used instead of complete activation time to eliminate the effects of a few late-activated outliers. The activation rate (Rate20–90) was calculated as the slope of the cumulative LV mechanical activation plots between 20 and 90% activation. The range of 20–90% activation was used because the cumulative LV mechanical activation plots were generally found to rise at an approximately constant rate over this range. Table 1 summarizes these parameters for each experiment along with the mean and standard deviations across all experiments for each pacing protocol.

The time for contraction, indicated by the mean of the Act90 values, shows RA pacing ($63 \pm 24$ ms) to be much faster than RVa ($121 \pm 18$ ms) and LVb pacing ($134 \pm 9$ ms). The mean Rate20–90 was $1.9 \pm 0.9$% activation per millisecond for RA pacing and $0.8 \pm 0.1$% activation per millisecond for both LV and RV pacing.

Fiber orientation assumptions. The mechanical activation times were calculated from the strain in the circumferential direction; however, at the midwall the fiber direction may vary from the circumferential direction (32, 34). If the fibers or shortening were not aligned in the circumferential direction, we would still expect that the projection of shortening in the circumferential direction would lead to the same results for activation time as long as the shortening was not orthogonal to the circumferential direction. To test this assumption the strain was calculated in one LVb-paced heart at a 30° angle above $E_{cc}$ ($E_{cc+30}$) and at a 30° angle below $E_{cc}$ ($E_{cc-30}$), representing a fiber direction of 30° in the

![Mechanical Activation Time](image-url)

### Table 1. Mechanical activation parameters

<table>
<thead>
<tr>
<th>Study</th>
<th>Act90, ms</th>
<th>Rate20–90, %activation/ms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA</td>
<td>LVb</td>
</tr>
<tr>
<td>1</td>
<td>49.2</td>
<td>141.2</td>
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<td>2</td>
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<td>6</td>
<td>79.8</td>
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<tr>
<td>7</td>
<td>26.2</td>
<td>121.0</td>
</tr>
<tr>
<td>Means</td>
<td>63.1</td>
<td>130.2</td>
</tr>
<tr>
<td>±SD</td>
<td>±24.3</td>
<td>±9.8</td>
</tr>
</tbody>
</table>

Mechanical activation parameters are derived from cumulative left ventricular base (LVb) mechanical activation plots shown in Fig. 6. Act90, time for 90% of myocardium to become mechanically activated; Rate20–90, rate of activation measured as percentage of myocardium activated per ms and representing slope of cumulative LV mechanical activation plots between 20 and 90% activation. Region between 20 and 90% activation was used because rate of rise in cumulative LV mechanical activation plots was approximately linear in this range for most experiments. RA, right atrium; RVa, right ventricular apex.
circumferential-longitudinal plane above and below the circumferential direction. The strain maps and the mechanical activation maps of $E_{CC-30^\circ}$, $E_{CC}$, and $E_{CC+30^\circ}$ were qualitatively very similar. The Rate 20–90 values derived from the $E_{CC-30^\circ}$, $E_{CC}$, and $E_{CC+30^\circ}$ activation maps were 0.71, 0.77, and 0.83% activation per millisecond, respectively. The variation resulting from the change in the direction of calculation was within the standard deviation of $\pm 0.1\%$ activation per millisecond calculated for the set of LVb-paced hearts. The values for Act$_{90}$ for $E_{CC-30^\circ}$, $E_{CC}$, and $E_{CC+30^\circ}$ were 125, 121, and 118 ms, respectively. Thus the calculation of the onset of shortening from the circumferential strain is valid even if the direction of shortening is within $30^\circ$ of the circumferential direction.

Velocity of Mechanical Activation Propagation

From the mechanical activation maps, the velocity of the propagating wave front of mechanical activation was calculated at each material point. The velocity histograms for LVb- and RVA-pacing experiments are shown in Fig. 7. For LVb pacing, the velocity calculations were made at 963 of the 1,344 locations, representing 72% of the myocardial mass, and the remaining locations were eliminated due to quantization problems resulting from converging or diverging wave fronts. The median velocity for LVb pacing was $0.42 \pm 0.07$ m/s. For RVA pacing, the velocity calculations were made at 778 of the 1,344 locations, representing 56% of the myocardial mass. The median velocity for RVA pacing was $0.35 \pm 0.05$ m/s. Because these median velocities represent different proportions and locations of the myocardium, direct comparisons between LVb and RVA velocity measurements should not be made. For both LVb and RVA pacing, the bulk of velocity measurements (88%) were in the range from 0.2 to 1.0 m/s.

Electrical Activation

The mechanical (M) activation times correlated linearly with the electrical (E) activation (Fig. 8). The relation between electrical and mechanical activation was $M = 1.06E + 8.4$ ms, with a correlation coefficient of 0.95. The slope of the regression line ($1.06 \pm 0.54$) was not significantly different from unity according to Student's t-test. The y-intercept ($8.4 \pm 3.67$ ms) was significantly $>0$ ($P = 0.0275$) according to Student's t-test.

Error Analysis

The RMSE between the $E_{CC}$ data at the imaging times and the polynomial fit was $\pm 0.0095$ (with absolute values for $E_{CC}$ ranging from $\pm 0.2$). This is comparable to strain errors previously determined using the field-fitting method in normal hearts (33). Using this standard deviation for the $E_{CC}$ data, we ran Monte Carlo simulations on each of five different pacing experiments to determine the error in mechanical activation time. The standard deviation for all mechanical activa-
tion times converged to \( \pm 5.1 \) ms. The deviation was found to be higher for regions for which the shifting method was used \((\pm 6.1)\) and lower for the regions for which the peak-stretch method was used \((\pm 4.6)\). Examination of the cross-correlation matrix showed that the variance of the time measurements at each location were independent of the variance at other spatial locations.

From the Monte Carlo simulations, using the variation determined for the activation times, we calculated the error in the velocity measurements. As expected, the error in velocity was a function of velocity, with greater accuracy for slower velocities. Table 2 shows the error as a function of velocity. The error at the LVb median velocity of 0.42 m/s was \( \pm 0.11 \) m/s, and the error at the RVa median velocity of 0.35 m/s was \( \pm 0.05 \) m/s. Although the error for velocities \( >1 \) m/s is \( \sim 50\% \), these velocities account for only a small portion of the data set.

**DISCUSSION**

This study represents the first time that mechanical activation maps have been obtained in the midwall throughout the entire LV during ventricular pacing. The maps indicate that the time for mechanical activation in the LV doubles with ventricular pacing at the RVa or LVb compared with RA activation. The velocity measurements as well as the cumulative myocardial activation plots imply limited involvement by the Purkinje system in conducting the electrical signal in the ventricularly paced heart.

Mechanical activation maps, generated from tagged MR images of the heart, provided an effective method for quantifying the asynchronous contraction that occurred during pacing. These methods permit the calculation of the strains and activation times where each material point has a myocardial volume of \( \sim 0.25 \) cm\(^3\).

**Comparison With Other Techniques**

Radionuclide phase-imaging studies have also been used to noninvasively determine the patterns of mechanical contraction of the ventricles from endocardial wall motion \((8, 24)\). However, this technique has lower spatial resolution, and the 2-D projections are difficult to reconstruct into a 3-D representation. Some errors in determining the sites of activation by radionuclide phase imaging, even from grossly separated pacing sites, have been reported \((24)\). A similar technique using turboFLASH MR imaging overcomes some of these limitations but still must infer activation from endocardial movement \((23)\).

Experimentally shortening has been measured with the use of a limited number of myocardial surface markers \((13, 38)\), radiopaque implanted markers \((4, 18, 45)\), or ultrasonic crystals \((4, 35)\). In these marker studies as well as the present study, the electrical activation correlated well with the mechanical activation time. The slope of the regression line in the present study was 1.06, which was not statistically different from unity. Other researchers have also reported a slope greater than unity \((4, 38)\). They attributed the increase over unity to a greater delay between electrical activation and the onset of shortening in later activated regions, because these regions are activated after an increase in pressure and, therefore, must contract against a greater load. The y-intercept of 8.4 ms represents the delay from electrical excitation to the start of contraction and is only slightly lower than the 17 ms reported by Badke et al. \((4)\). The present study, therefore, demonstrates the ability to obtain detailed mechanical activation maps noninvasively in the entire heart with an accuracy that, until now, was only possible with invasive experimental techniques.

Measurements of electrical activity of the heart are commonly used for diagnosis of heart disease. The ECG gives a quick, integrated indication of impulse conduction. Endocardial and epicardial electrical mapping techniques such as sock electrodes \((46)\) or basket electrodes \((22)\) can give precise measurements of impulse conduction. These, however, must be applied with caution due to their invasive nature. An additional advantage of the MRI-tagging approach is that it reveals the mechanical effects of asynchronous activation. This is important because the ultimate clinical evaluation involves the pump function of the heart. The present study and previous studies also show that the local contraction patterns are considerably more sensitive to abnormal conduction than measures of global cardiac function. However, before this method can be safely used to evaluate pacing in humans, it will be necessary to design an MR-compatible pacing system.

**Fitting Method**

To compare the seventh-order fit with other fitting methods, an interpolating B spline with eight knots was used for an LVb-paced heart \((37)\). Only small fitting

**Table 2. Standard error of velocity measurements as calculated from Monte Carlo simulations**

<table>
<thead>
<tr>
<th>Velocity, m/s</th>
<th>0–0.2</th>
<th>0.2–0.4</th>
<th>0.4–0.6</th>
<th>0.6–0.8</th>
<th>0.8–1.0</th>
<th>1.0–1.2</th>
<th>1.2–1.4</th>
<th>1.4–1.6</th>
<th>1.6–1.8</th>
<th>1.8–2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>31</td>
<td>263</td>
<td>200</td>
<td>140</td>
<td>84</td>
<td>49</td>
<td>27</td>
<td>29</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>Standard error</td>
<td>0.024</td>
<td>0.050</td>
<td>0.110</td>
<td>0.203</td>
<td>0.341</td>
<td>0.485</td>
<td>0.640</td>
<td>0.801</td>
<td>0.812</td>
<td>0.890</td>
</tr>
</tbody>
</table>

Measurements were calculated from Monte Carlo simulations binned in 0.2 m/s intervals; n = no. of samples in each bin.
The mechanical activation maps, velocity data, and cumulative myocardium activation plots performed here provided a consistent view of the changes induced by ventricular pacing. First, maps of activation times enabled us to visualize the detailed evolution of activation under the various pacing protocols. Next, the velocity of mechanical propagation provided a measure, independent of the heart size, that contained information on impulse conduction. The local conduction velocity could be used to generate a velocity map that may be of interest in pathological hearts, because fibrosis (11) and ischemia (14) decrease conduction velocity. Finally, the cumulative myocardial activation plots summarized the rate at which the ventricle was activated.

From the measurements obtained in the paced hearts, several observations concerning the mechanical activation of the left ventricle are made. For the LVb- and RVa-paced hearts, the bulk of the material points had a velocity in the range of 0.2–0.8 m/s, which is on the same order as the velocities reported for conduction in myocardial fibers (6). Only a few material points showed conduction velocities in the 1–4 m/s range, which would be expected if conduction was dominated by the Purkinje fibers. However, the role of the Purkinje fibers could be underestimated because we determined only activation in the LV midwall, whereas the Purkinje fibers are found subendocardially, and because velocity measurements did not cover the entire left ventricle.

Whereas the LVb-pacing mechanical activation maps showed a steady and consistent propagation of activation, the RVa mechanical activation maps showed a more complex pattern of activation, especially around the septum. The septum in most of the RVa-pacing experiments was rapidly activated (for example, see RVa pacing in Fig. 5, last 2 rows), perhaps indicating some initial, but limited, involvement by the right bundle branch of the Purkinje system. This rapid septal activation was followed by a slower-than-average activation, perhaps due to slower transseptal electrical conduction. This pattern of activation was also indicated in the RVa cumulative activation histograms, in which a rapid rise in activation, consistent with the slope seen for RA pacing, is followed by a flatter region at ~50% activation (especially noticeable in Fig. 6, studies 2 and 7). There was one case in which this pattern was significantly delayed (Fig. 5, last row, and Fig. 6, study 7), but this can be explained by the electrode placement. In this study the RVa-pacing electrode was attached to the RV epicardium instead of being inserted through the RV free wall to contact the septum, as in the other experiments. Thus the activation wave front passed over the RV free wall before activating the LV at the interventricular attachments. This led to an initial delay followed by a rapid rise of the cumulative activation histogram as the activation occurred at multiple points along the RV attachment.

The RVa conduction patterns also frequently demonstrated an acceleration of shortening in the posterior-lateral wall near the base of the LV. This can be seen by the wider spacing of the isochrones (e.g., Fig. 5, last 2 rows), perhaps indicating limited activation of the left fascicular branch of the left bundle branch. This is also indicated by the higher-than-average slopes in the late-activated regions of the cumulative activation plots (Fig. 6, studies 2 and 7). The LVb-pacing experiments, on the other hand, showed no consistent regional trends in the spread of activation. The interpretation of the regional variations found in RVa pacing is not clear and, because the variations were not seen in all experiments, warrants further investigation.

It has been hypothesized that, during ventricular pacing, the electrical impulse travels through the myocardium until it reaches the Purkinje system, at which point the remainder of the ventricle quickly contracts due to rapid Purkinje activation (10). In these experiments there was never a flash of activation to indicate a sudden involvement by the Purkinje system. Although there may have been indications of limited Purkinje fiber activation during RVa pacing, as indicated by the regional increase in the slope of the cumulative activation plot, this increased slope was still far less than that during RA pacing, clearly demonstrating no cascade of activation.

In conclusion, the velocity of mechanical activation propagation during ventricular pacing was similar to the velocity of electrical propagation in myocardium. The propagation of mechanical activation for an LVb pacing site steadily encompassed the LV, whereas propagation for the RVa pacing sites showed regions of rapid and slower propagation. These results demonstrate the efficacy of MRI tagging as a tool for evaluating pacing protocols or locating ectopic sites noninvasively.

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