Published in final edited form as:

Magn Reson Med. 1998 April ; 39(4): 507–513.

Imaging Asynchronous Mechanical Activation of the Paced Heart with Tagged MRI

Elliot R. McVeigh, Frits W. Prinzen, Bradley T. Wyman, Joshua E. Tsitlik, Henry R. Halperin, and William C. Hunter

*From the Departments of Biomedical Engineering (E.R.M., F.W.P., B.T.W., W.C.H.), Radiology (E.R.M.), and *Medicine (J.E.T., H.R.H.), Johns Hopkins University School of Medicine, Baltimore, Maryland, and the Department of Physiology (F.W.P.), Cardiovascular Research Institute Maastricht, University of Lirnborg, Maastricht, the Netherlands.*

Abstract

A method for imaging the rapid temporal-spatial evolution of myocardial deformations in the paced heart is proposed. High time resolution-tagged MR images were obtained after stimulation of the myocardium with an MR-compatible pacing system. The images were analyzed to reconstruct dynamic models of local 3D strains over the entire left ventricle during systole. Normal canine hearts were studied *in vivo* with pacing sites on the right atrium, left ventricular free wall and right ventricular apex. This method clearly resolved local variations in myocardial contraction patterns caused by ventricular pacing. Potential applications are noninvasive determination of electrical conduction abnormalities and the evaluation of new pacing therapies.

Keywords

pacing; heart; MRI; tagging

INTRODUCTION

In the normal heart, electrical activation spreads over the left ventricle (LV) rapidly through a specialized conduction system, which produces uniform contraction of heart muscle fibers. A disruption of this uniform contraction pattern is often the hallmark of cardiac disease; therefore, a method to measure the regional cardiac function precisely is critical in the detection of heart disease, and in the quantitative evaluation of the response to therapy. In particular, ventricular pacing has been demonstrated to immediately reduce ventriculoaortic pressure gradients in hypertrophic obstructive cardiomyopathy (1,2), and these improvements can be long term (3); however, the mechanical mechanism of this improvement is unknown, and it is therefore difficult to derive a rational approach for the application of this therapy. Determination of the optimal location of the pacing site, or sites, and the optimal pacing waveforms requires a quantitative metric to evaluate regional differences in ventricular function and activation. A noninvasive imaging method for measuring mechanical activation would also allow the evaluation of other pathologies such as bundle branch block and Wolff-Parkinson-White syndrome (4), or the ectopic excitation of the ventricle by a pacemaker, where the change of

Address correspondence to: Elliot R. McVeigh, Ph.D., Medical Imaging Lab, Department of Biomedical Engineering and Radiology, Johns Hopkins University School of Medicine, 407 Traylor Bldg., 720 Rutland Ave., Baltimore, MD, 21205.. J. Tsitlik is currently located at Cardio Technologies Inc., New York, New York.

normal conduction pathways leads to asynchronous activation and thereby induces large regional changes of heart muscle contraction (5-7).

In this paper we present a noninvasive, high-resolution myocardial tagging method, coupled with an MR-compatible electrical stimulation and sensing apparatus to capture the very rapid and spatially heterogeneous contraction patterns in the ectopically paced LV. Image analysis methods are used to produce strain evolution maps of myocardial contraction of the entire LV, and these maps show the very large inhomogeneities in myocardial muscle contraction associated with ectopic pacing. Although asynchronous activation has been observed before with nuclear medicine (8) and direct video imagery of physical markers on the heart wall (5), the technique introduced in this paper represents the first time that local myocardial strains have been measured noninvasively over the entire LV during ectopic pacing.

MATERIALS AND METHODS

A series of seven experiments were performed in anesthetized dogs in which the contraction of the LV was induced by stimulation from pacemaker leads placed at three locations. One pacing lead was sewn onto the right atrium to create normal activation of the heart through the His-Purkinje system. Also, two ventricular pacing sites were investigated: the right ventricular apex, which is the normal position for a pacemaker lead placed chronically; and the left ventricular basal free wall. Only single-site pacing was performed in these experiments. (The experiments were performed in accordance with the guidelines set by the Johns Hopkins Animal Care and Use Committee.)

Externally pacing the heart and sensing the electrocardiogram during MRI presents a challenge because of the voltages induced in the pacing leads by the radiofrequency (RF) pulses and the magnetic field gradient pulses. Specialized filters were designed to eliminate these voltages (9-11). The leads were connected to the pacing and monitoring system through filter connectors on the penetration panel of the RF-shielded scanning room. The electrical stimulation pulses to pace the heart were generated by an electrical stimulator (Model 248G, GRASS Medical Instruments, Quincy, MA) and passed through isolation units and specially designed RF filter units before being delivered to the pacing leads on the heart. Electrograms and left ventricular pressure were similarly passed through an RF filter before being amplified and recorded on a four-channel recorder (Model TA240S, Gould, Inc., Cleveland, OH), and sampled at 200 Hz with eight bits using the LABVIEW (National Instruments, Austin, TX) program on a Macintosh computer. Measurements of the electrical conduction delays and left ventricular pressures were made during stimulation from each of the three pacing sites to confirm capture of the pacing stimulation.

MRI was performed on a standard Signa 1.5 T scanner with software release 4.7 (General Electric Medical Systems, Milwaukee, WI). The spin-tagging pattern in the myocardium was produced with a 6-ms RF/gradient tagging pulse that was designed to produce parallel plane saturation bands of 1.5-mm thickness and 5.5-mm separation throughout the imaging volume. The tagging pulse was triggered by a signal from the pacemaker, and image acquisition commenced 3 ms after the tagging pulse was completed. A sequence of images was obtained with a time separation of 19.5 ms in six dogs and 13.0 ms in one dog. The MRI-tagged images were acquired during breath-hold periods with a segmented *k*-space acquisition (12,13). The scanning parameters were: TR = 6.5 ms, TE = 2.1 ms, readout-bandwidth = ± 32 kHz, 320-mm field of view, 256×96 acquisition matrix, fractional echo, three readouts per movie frame (in one dog, this was reduced to 2), and 6- to 7-mm slice thickness. A presaturation pulse preceded the tagging pulse to saturate the blood in the ventricle. For a heartrate of 120 beats per minute, a 16- to 20-s breath-hold was required; each breath-hold was followed by a recovery period of 45 to 60 s. For each pacing site, a set of seven to nine contiguous short axis sections were

obtained with the tags at 0° followed by the same sections with both tags and readout gradient direction rotated to 90° (12). Finally, a set of nine long axis sections, oriented radially at 20° intervals around the long axis, were imaged with the tags oriented perpendicular to the long axis. Imaging of all sections for one pacing mode required approximately 30 to 40 min. Stability of the preparation was monitored with LV blood pressure (MRI-compatible catheter model SPC-350MR, Millar Instruments, Inc., Houston TX) and arterial blood gases and by visually checking the end-diastolic LV volume and ejection fraction in the collected images.

Figure 1 shows the timing diagram for this protocol. Only one of the three orthogonal tag orientations used to obtain a complete sampling of the 3D myocardial motions is shown in this figure. Figure 2 shows a stack of short axis slices with both horizontal and vertical motions sampled at a single end-systolic time frame and a set of long axis images that sample the “through plane” motion in the orthogonal direction at this same time frame. This combination of three 1D tagging orientations with the 320-mm field of view has been shown to yield estimates of the tag line location that have a precision of 0.13 mm (0.1 pixels) (14). Because the effective sampling window for the position of the tags is the time for a single echo readout (2.5 ms), there is very little blurring from motion (13).

Image analysis techniques were applied to sets of images such as those shown in Fig. 2 to reconstruct a full 3D displacement field and calculate a model of the strain in the LV at 10 to 12 time points within systolic contraction. In the first step of the analysis, the position of the central spine of each tag line was tracked using detection methods optimized for the signal profile of the tag lines, and a semiautomated myocardial boundary algorithm was used to estimate the position of the endocardial and epicardial surfaces in the images (15,16). The set of orthogonal 1D displacements Obtained from the three tag Orientations were used simultaneously in a least-squares fitting method to obtain an analytical function describing the 3D displacement field in the myocardium (17). It is important to note that only tag position information was used in this fitting process; the less precise myocardial boundary estimates were used only to define the domain of the calculation. The function describing this displacement field gives the trajectory of material points, which represent particles of myocardial tissue tracked through space and time. The 3D displacement field was then used to compute the Lagrangian strain tensor at each material point in the myocardium as a function of time. The myocardial strain represents the fractional change in length of the tissue; if the strain is positive, this represents thickening, and if the strain is negative, this represents shortening. The strain in any direction can be computed from the 3D strain tensor; the strain in the circumferential direction is of particular interest because it represents myocardial shortening in the myocardial fiber direction at the mid wall. The values of the strain tensor were mapped as color onto a dynamic, interactive 3D model of the beating LV for observation of mechanical activation. This visualization tool, called a dynamic heart modeler, can be used to explore the temporal/spatial dependence of any component of the myocardial motion or strain.

RESULTS

When systolic contraction was evoked by right atrial pacing, the LV was excited via the normal pathway of the Purkinje system, and the pattern of mechanical activation was found to be very uniform as a function of position. However, when the heart was paced from a ventricular site, significant asynchronous and spatially heterogeneous contraction was observed. The abnormal contraction pattern associated with ventricular pacing was immediately obvious when the sequences of tagged MR images were viewed in a movie loop. Figure 3 compares a sequence of short-axis, tagged MR images of a midventricular slice when paced from an atrial site and from pacing sites on the basal freewall with right ventricular apex. The asymmetry in the

deformation of the myocardium during ventricular pacing is clearly demonstrated in this figure by the asymmetric deformation of the tag lines throughout systole.

The asynchronies in the evolution of strain during ventricular pacing were clearly visible when the paced ventricles were viewed with the dynamic heart modeler. Figure 4 shows the evolution in time of the circumferential component of the 3D strain tensor (E_{cc}) evaluated at the mid wall for the three pacing sites; as stated above, this component of the strain tensor closely matches muscle fiber shortening at the mid-wall of the LV. For atrial pacing, muscle shortening evolves relatively homogeneously over the ventricle; this is shown as the uniformly increasing blue color over the ventricle in the top row of Fig. 4. With ventricular pacing, a clear focus of early mechanical activation was observed at the pacing site, followed by the propagation of a contraction wavefront to the opposite side of the heart. This is seen as the blue “wave” of muscle shortening emanating from the LV freewall pacing site (10 o'clock) in the middle row of Fig. 4 and from the RV apex site (5 o'clock) in the bottom row of Fig. 4. A second interesting observation was the significant “prestretch” of the late activated myocardium remote from the pacing site. This prestretch was quite pronounced (15–20%) and occurred in the first 100 ms after the ventricular pacing pulse. This prestretch is visualized as the bright yellow color on the heart model.

An alternative way of visualizing the contraction pattern is to graph the time course of strain for each material point of the LV. Each graph can be mapped to a position in an array that corresponds to a position in the LV. An example of such an LV strain evolution map is shown in Fig. 5 in which the sequence of mechanical shortening (mid-wall E_{cc}) for the left ventricular base and right ventricular apex pacing sites are plotted. The LV strain evolution maps are an excellent method for observing the rapid rate of prestretch in the passive, late activated regions (see columns 1–4 and 12 for LV base pacing and columns 4–9 for RV apex pacing) and the rapid contraction at the pacing site (see columns 5–9 for LV base pacing and columns 1,2,11, and 12 for RV apex pacing). Also demonstrated directly from these plots is the increased “stroke” or total dynamic range of the strain in the prestretched region. Because the majority of this shortening occurs during the ejection phase (with high ventricular pressure), the prestretched region is performing increased contractile work (18).

Although asynchronous mechanical activation was obvious from both the dynamic heart modeler and the LV strain evolution map showing E_{cc} versus time, we also sought a parameter that could be used to accurately map the onset of contraction; this parameter could be used for localization of ectopic foci and quantitative characterization of mechanical asynchrony. If we define the mechanical activation time as the time at which the muscle begins to undergo shortening, this will correspond to the time at which the prestretch reaches a peak, as shown in E_{cc} versus time curves of the LV strain evolution maps of Fig. 5. For those curves in Fig. 5 that have an easily detectable maximum in the prestretch of the tissue, this definition works well. Note that some prestretched regions will begin to shorten from a stretched condition. Table 1 shows the time delay between the earliest and latest activated regions over the entire LV during the three pacing modes. This is a very simple parameter to describe the asynchrony found in ectopically excited hearts: its value will be high when there is a large delay between the mechanical activation of early activated regions close to the pacing site and the late activated regions that are distant from the pacing site.

DISCUSSION

These data highlight the ability of MRI tagging to measure heterogeneous local muscle contraction patterns throughout the LV with high time resolution. They demonstrate that large regional differences in muscle contraction are induced when activation is asynchronous. The MRI images and strain analysis reveal a clear transition in contraction pattern from earliest- to

latest-activated regions. Previous studies, using invasive techniques to quantify strain, could only visualize small patches of this global transition (5-7). A simple parameter describing the range of mechanical activation times was reported in Table 1. Although this single value characterizes the range of activation delays found over the entire LV, it does not characterize the spatial relationships between these delays. Obviously, the data allow us to analyze more detailed dynamics such as the anisotropy of the velocity of the mechanical activation through the myocardium and the variability of strain rates with respect to proximity to the pacing site; however, these analyses are beyond the scope of this communication.

As a consequence of the inhomogeneous contraction pattern revealed by MRI, a number of physiological sequelae are anticipated. First, the increased systolic shortening seen in late-activated regions has been shown to induce a rise in regional myocardial blood flow and oxygen consumption (5,18). This concept of work redistribution may have an impact in the choice of pacing paradigms for therapy. Such increased flow demand could be deleterious if the late activated region were downstream from a coronary stenosis. Second, the prestretch occurring in late-activated regions could produce a hypertrophic response through stretch-stimulated gene expression (19,20). This is supported by the asymmetric ventricular hypertrophy observed after chronic ectopic pacing (21,22). Finally, rapid prestretch of cardiac muscle is implicated in arrhythmogenesis (23,24). Reduced local work, blood flow, and oxygen demand are expected in early-activated regions (5,18,21). The present technique can make noninvasive measurements to predict the outcome of these mechanical changes and evaluate potential therapies.

In this communication, we have demonstrated that pacing can be successfully applied during MRI, and the mechanical consequences to LV contraction can be measured with high spatial and temporal resolution. Although curves such as those shown in Fig. 5 have been measured for isolated regions of the heart, these data represent the first time that a complete mapping of asynchronous mechanical activation of shortening has been achieved over the entire LV. This has the potential to change the way cardiac electrophysiology treatments are delivered; on-line measurements of the mechanical consequences of pacing or RF-ablation could be used to direct therapy.

Acknowledgements

This research was supported by a grant from the NHLBI, HL45683, and a Whitaker Biomedical Engineering Research Grant. F. Prinzen was a visiting professor at Johns Hopkins, partially funded by Medtronic. E.R. McVeigh is an Established Investigator of the American Heart Association.

The authors would like to thank Suribhotla Rajasekhar, Ken Rent and Scott Reeder for assistance in performing the experiments; Chris Moore and Michael Guttman for assistance in data analysis.

REFERENCES

1. Jeanrenaud X, Goy JJ, Kappenberger L. Effects of dual-chamber pacing in hypertrophic obstructive cardiomyopathy. *Lancet* 1992;339:1318–1323. [PubMed: 1349992]
2. Fananapazir L, Cannon RO III, Tripodi D, Panza JA. Impact of dual-chamber permanent pacing in patients with Obstructive hypertrophic cardiomyopathy with symptoms refractory to verapamil and beta-adrenergic blocker therapy. *Circulation* 1992;85:2149–2161. [PubMed: 1350522]
3. Fananapazir L, Epstein ND, Curiel RV, Panza JA, Tripodi D, McAreavey D. Long-term results of dual-chamber (ddd) pacing in obstructive hypertrophic cardiomyopathy: evidence for progressive symptomatic and hemodynamic improvement and reduction of left ventricular hypertrophy. *Circulation* 1994;90:2731–2742. [PubMed: 7994815]
4. Parks WJ, Pettigrew RI, Ngo TD, Hulse E, Campbell R. Identification of preexcitation sites in Wolff-Parkinson-White syndrome using magnetic tagging. *Soc. Magn. Reson. Med* 1993;1:274.[Abstract]

5. Prinzen FW, Augustijn CH, Arts T, Allessie MA, Reneman RS. Redistribution of myocardial fiber strain and blood flow by asynchronous activation. *Am. J. Physiol* 1990;259:H300–H308. [PubMed: 2386214]
6. Badke FR, Boinay P, Covell JW. Effects of ventricular pacing on regional left ventricular performance in the dog. *Am. J. Physiol* 1980;238:H858–H867. [PubMed: 7386645]
7. Miyazawa K, Honna T, Haneda T, Shirato K, Nakajima T, Arai T. Dynamic geometry of the left ventricle during ventricular pacing: correlation with cardiac pumping action. *Tohoku. J. Exp. Med* 1978;124:261–266. [PubMed: 635900]
8. Bashore TM, Stine RA, Shaffer PB, Bush CA, Leier CV, Schaal SF. The non-invasive localization of ventricular pacing sites by radionuclide phase imaging. *Circulation* 1984;70:681–694. [PubMed: 6206965]
9. Halperin, HR.; Levin, HR.; McVeigh, ER.; Cho, P.; Curtis, W.; Moore, CC.; Acker, M.; Tsitlik, JE.; Belfer, P. New techniques for the study of cardiomyoplasty; *Proc. Annual International Conference of the IEEE Engineering in Medicine and Biology Society*; 1992. p. 2794-2795.
10. Tsitlik JE, Levin HE, McVeigh ER, Rogers W, Perry L, Halperin H. Safe and reliable pacing in dogs during MRI in a 1.5T magnet. *PACE* 1992;15:561.[Abstract]
11. Tsitlik JE, Levin HR, Herskowitz A, McVeigh ER, Moore CC, Halperin HR. Magnetic resonance imaging-induced myocardial injury can be prevented during cardiac pacing. *PACE* 1995;18:830.
12. McVeigh ER, Atalar E. Cardiac tagging with breath-hold cine MRI. *Magn. Reson. Med* 1992;28:318–327. [PubMed: 1461130]
13. McVeigh ER. MRI of myocardial function: motion tracking techniques. *Magn. Reson. Imag* 1996;14:137–150.
14. Atalar E, McVeigh ER. Optimum tag thickness for the measurement of position with MRI. *IEEE Trans. Med. Imag* 1994;13:152–160.
15. Guttman M, Prince JL, McVeigh ER. Contour estimation in tagged cardiac magnetic resonance images. *IEEE Trans. Med. Imag* 1994;13:74–88.
16. Guttman MA, Zerhouni EA, McVeigh ER. Analysis and visualization of cardiac function from MR images. *IEEE Comput. Graph. Appl* 1997;17:30–38.
17. O'Dell WG, Moore CC, Hunter WC, Zerhouni EA, McVeigh ER. Displacement field fitting for calculating 3D myocardial deformations from tagged MR images. *Radiology* 1995;195:829–835. [PubMed: 7754016]
18. Delhaas T, Arts T, Prinzen FW, Reneman RS. Regional fibre stress-fibre strain area as an estimate of regional blood flow and oxygen demand in the canine heart. *J. Physiol. (Lond)* 1994;477:481–496. [PubMed: 7932236]
19. Sadoshima JI, Takahashi T, Jahn L, Izumo S. Roles of mechano-sensitive ion channels, cytoskeleton, and contractile activity in stretch-induced immediate-gene expression and hypertrophy of cardiac myocytes. *Proc. Natl. Acad. Sci. USA* 1992;89:9905–9909. [PubMed: 1384064]
20. Sadoshima J, Xu Y, Slayter HS, Izumo S. Autocrine release of angiotensin II mediates stretch-induced hypertrophy of cardiac myocytes in vitro. *Cell* 1993;75:977–984. [PubMed: 8252633]
21. Prinzen FW, Cheriex EC, Delhaas T, Van Oosterhout MFM, Arts T, Wellens HJJ, Reneman RS. Asymmetrical thickness of the left ventricular wall due to asynchronous electrical activation. *Am. Heart J* 1995;30:1045–1053. [PubMed: 7484735]
22. Van Oosterhout MFM, Prinzen FW, Reneman RS. Chronic ventricular pacing induces local differences in myocardial wall thickness (WT) and changes in blood flow distribution. *J. Am. Coll. Cardiol* 1966;27:344A.[Abstract]
23. Franz MR. Bridging the gap between basic and clinical electrophysiology: what can be learned from monophasic action potential recordings? *Cardiovasc. Electrophysiol* 1994;5:699–710.[Review]
24. Wang Z, Taylor LK, Denney WD, Hansen DE. Initiation of ventricular extrasystoles by myocardial stretch in chronically dilated and failing canine left ventricle. *Circulation* 1994;90:2022–2031. [PubMed: 7522991]

FIG. 1.

Myocardial tagging of heart wall motion during pacing. The pacing signal triggers a sequence of (RF) and magnetic field gradient (Gx) pulses to first saturate the blood in the LV chamber (Presat. pulse), then to produce a set of parallel planes of saturated magnetization in the body (Tagging pulse). After the tagging pattern is placed in the tissue, a sequence of images are obtained during the contraction of the heart. Each rectangular box represents a signal readout period, and three readout periods are used to make a single movie frame. In this figure, every second time frame of the movie sequence is shown for clarity. The same procedure is performed with orthogonal tag line orientations to obtain the data for 3D displacements.

FIG. 2.

A set of tagged MRI images of the heart shown at a single midsystolic time frame. The left box shows a parallel stack of nine short axis slices with vertical tags (sampling horizontal motion), the center box shows the same nine short axis slices with horizontal tags (sampling vertical motion). The nine short axis slices sample the heart from the base (top left image in each box) to the apex (bottom right image). The right box shows nine long axis slices (sampling “through plane” motion perpendicular to the short axis plane), which are rotated at 20-degree increments around the central long axis of the LV. Similar image sets are obtained at multiple time frames through the heart cycle to reconstruct the full 3D motions of the heart.

FIG. 3.

Three time sequences of tagged MR images in a short axis view of the same heart after stimulation from pacing leads at different locations. Each frame moving from left to right is an increment of 19.5 ms. The top row shows the myocardial motion after atrial pacing (normal activation sequence); the deformation of the tag lines is highly symmetric around the vertical axis at all time frames showing synchronous contraction. The middle row shows the response to pacing at the basal left ventricular free wall (pacing site is at ~3 o'clock); notice the early bending of the tag lines toward the left demonstrating early thickening in the free wall and compression in the septum. The bottom row shows the response to pacing at the right ventricular apex (pacing site at ~9 o'clock); in this case, there is early thickening in the septum and compression in the freewall. The asynchrony is particularly evident when viewed as a movie loop. In the interests of space, only one of the three tag orientations is shown (see http://www.mri.jhu.edu/mrm_pace/).

FIG. 4.

The paced LV for three different pacing sites viewed with the dynamic heart modeler. The color represents values of the circumferential strain; blue represents muscle shortening (blue saturates at -0.1), yellow represents muscle stretching (yellow saturates at 0.1). There are 19.5 ms between each reconstructed model. A line drawn between the gray and green circles marks the mid-septum; for optimal visibility of the pattern of shortening, the ventricle is viewed base-to-apex, with the right ventricle (RV) to the right. The endocardial layer of the model has been stripped away to expose the value of circumferential strain at the mid-wall. Atrial pacing (top row): After pacing the heart from the right atrium, the normal sequence of ventricular activation from the Purkinje system occurs, and the muscle contracts uniformly, as shown by the homogeneous development of the blue color in the top row. LV base pacing (middle row): When the ventricle is excited from the basal left ventricular free wall, early mechanical activation is seen emanating from the pacing site (marked by the red asterisk at ~ 10 o'clock) and propagating both in the longitudinal and circumferential directions. Notice the significant prestretch (yellow color) of the septal region remote from the pacing site. RV apex pacing (bottom row): When the ventricle is excited from a site at the apex of the RV (marked by the red asterisk at ~ 5 o'clock), the activation pattern is similar to that seen with LV base pacing, but the origin of the activation wavefront is changed (see the movie at http://www.mri.jhu.edu/mrm_pace/).

FIG. 5.

Two LV strain evolution maps in the same heart for different pacing sites. Each graph in the array represents the circumferential strain versus time for a specific material point at the mid wall of the LV. The entire LV is displayed by cutting down the septum and folding the surface out onto the page. Rows represent different levels from base of the heart (top row) down to apex (bottom row), and columns are circumferential position. Every second material point from the dynamic heart modeler is shown on this plot in the interest of space. The strain is plotted between -0.2 to 0.2 on the vertical axis, and from 50 to 300 ms on the horizontal axis. The E_{cc} versus time for LV base pacing is shown in (a) with the pacing site marked with an asterisk in column 7. The E_{cc} versus time for right ventricle apex pacing is shown in (b), with the pacing site marked with an asterisk in column 11. The positive peaks represent rapid prestretch of the passive myocardium.

Table 1
Mechanical Asynchrony and Prestretch for Each Pacing Site

Pacing site	Range of mechanical activation delays (ms)	Maximum E_{cc} prestretch
LV base	137 (18)	0.18 (0.04)
RV apex	125 (19)	0.17 (0.03)
RA	90 (29)	0.09 (0.04)

The average range of mechanical activation delay measured in the LV for different pacing sites. This time represents the difference between the earliest and latest activation times. The maximum prestretch measured in the LV is given in the second column. The standard deviation around the mean over the seven hearts for both parameters is given in parentheses.

Abbreviations: RV, right ventricle; RA, right atrium; LV, left ventricle.