Published in final edited form as:

Am J Physiol Heart Circ Physiol. 2004 June ; 286(6): H2401–H2407. doi:10.1152/ajpheart.01013.2003.

Transmural mechanics at left ventricular epicardial pacing site

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Abstract

Left ventricular (LV) epicardial pacing acutely reduces wall thickening at the pacing site. Because LV epicardial pacing also reduces transverse shear deformation, which is related to myocardial sheet shear, we hypothesized that impaired end-systolic wall thickening at the pacing site is due to reduction in myocardial sheet shear deformation, resulting in a reduced contribution of sheet shear to wall thickening. We also hypothesized that epicardial pacing would reverse the transmural mechanical activation sequence and thereby mitigate normal transmural deformation. To test these hypotheses, we investigated the effects of LV epicardial pacing on transmural fiber-sheet mechanics by determining three-dimensional finite deformation during normal atrioventricular conduction and LV epicardial pacing in the anterior wall of normal dog hearts in vivo. Our measurements indicate that impaired end-systolic wall thickening at the pacing site was not due to selective reduction of sheet shear, but rather resulted from overall depression of fiber-sheet deformation, and relative contributions of sheet strains to wall thickening were maintained. These findings suggest lack of effective end-systolic myocardial deformation at the pacing site, most likely because the pacing site initiates contraction significantly earlier than the rest of the ventricle. Epicardial pacing also induced reversal of the transmural mechanical activation sequence, which depressed sheet extension and wall thickening early in the cardiac cycle, whereas transverse shear and sheet shear deformation were not affected. These findings suggest that normal sheet extension and wall thickening immediately after activation may require normal transmural activation sequence, whereas sheet shear deformation may be determined by local anatomy.

Keywords

epicardial pacing; transmural deformation; fiber; sheet

Cardiac Resynchronization Therapy (CRT) has proven to be effective in improving cardiac function in moderate-to-severe heart failure associated with an intraventricular conduction delay, most commonly of a left bundle branch block type (3,5,6,15,16,24,29). The advent of CRT has resulted in an increasingly frequent use of left ventricular (LV) epicardial pacing in clinical settings. Despite the clinical benefits of CRT, LV epicardial pacing is associated with detrimental effects on normal transmural function. Systolic wall thickening, which is an

important component of regional cardiac function, is significantly reduced at the pacing site (33). Furthermore, LV epicardial pacing reverses the normal activation sequence of transmural depolarization into the epicardial-endocardial propagation (11,12,19), which significantly increases QT interval and transmural dispersion of repolarization, and enhances susceptibility to torsade de pointes in a subset of patients (10,22). To design more effective and safe pacing therapies, it is of critical importance to understand the effects of epicardial pacing on normal transmural function.

Several lines of evidence support the concept that transverse shear deformation is required for normal systolic wall thickening (17,18,30). Because the LV myocardium consists of helically woven myofibers (25,31) that are arranged in transversely oriented myocardial sheets (17), transverse shear deformation is anatomically related to myocardial sheet shear, and sheet shear deformation contributes significantly to normal systolic wall thickening (8). Because LV epicardial pacing significantly reduces transverse shear deformation (33), we hypothesized that impaired end-systolic wall thickening at the epicardial pacing site is due to reduction in myocardial sheet shear deformation, resulting in a reduced contribution of sheet shear to wall thickening. We also hypothesized that LV epicardial pacing would reverse transmural mechanical activation sequence and thereby mitigate normal transmural deformation. To test these hypotheses, we investigated the effects of LV epicardial pacing on transmural fiber-sheet mechanics by determining three-dimensional (3-D) finite deformation during normal atrioventricular (AV) conduction and LV epicardial pacing in the anterior wall of normal dog hearts in vivo. Our measurements indicate that impaired end-systolic wall thickening at the epicardial pacing site was not due to selective reduction of sheet shear, but rather resulted from overall depression of fiber-sheet deformation, and relative contributions of sheet strains to wall thickening were maintained. Epicardial pacing also induced reversal of the transmural mechanical activation sequence, which significantly depressed sheet extension and wall thickening early in the cardiac cycle, whereas transverse shear and sheet shear deformation were not affected.

MATERIALS AND METHODS

All animal studies were performed according to the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*. All protocols were approved by the Animal Subjects Committee of the University of California, San Diego, which is accredited by the American Association for Accreditation of Laboratory Animal Care. A subset of data from the five animals included in this study has been presented previously in our report (2), which described local ventricular deformation during early relaxation under normal AV conduction.

Experimental protocol

The protocol for surgical preparation was described in detail previously (2). Briefly, five adult mongrel dogs (19–28 kg) underwent median sternotomy under general anesthesia, with the LV pressure, central aortic pressure, and the surface ECG monitored throughout the study. Low-dose dopamine ($2.5\text{--}5.0\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) was administered intravenously to maintain blood pressure in two animals. To measure 3-D myocardial deformation, three transmural columns of four to six 0.8-mm-diameter gold beads and a 1.7-mm-diameter surface gold bead above each column were placed within the anterior wall between the first and the second diagonal branches of the left anterior descending coronary artery (LAD) (Fig. 1A). To provide end points for a LV long axis, 2-mm-diameter gold beads were sutured to the apical dimple (apex bead, Fig. 1A) and on the epicardium at the bifurcation of the LAD and left circumflex coronary arteries (base bead, Fig. 1A). Pacing wire pairs were sutured to the left atrium (LA) and the LV epicardial surface across the triangle of the surface gold beads (Fig. 1A). Atrial pacing was performed by stimulating LA electrodes, and LV epicardial pacing was performed by

stimulating both LA and LV electrodes (LA-LV delay = 20–40 ms), via a square-wave, constant-voltage electronic stimulator at a frequency 20% above baseline heart rate to suppress native sinus rhythm. Stimulation parameters (voltage 10% above threshold, duration 8 ms, and frequency) were kept constant in each animal. Each animal was positioned in a biplane radiography system, and synchronous biplane cineradiographic images (125 frames/s) of the bead markers were digitally acquired with mechanical ventilation suspended at end expiration. Image acquisition for the two pacing modes (atrial pacing and LV epicardial pacing) was performed consecutively at the same heart rate to minimize variation in hemodynamic conditions. At the end of the study, the animals were euthanized with pentobarbital sodium and the heart perfused fixed with 2.5% buffered glutaraldehyde at the end-diastolic pressure measured in the study (2,39). Because the heart was fixed at end-diastolic pressure, fiber and sheet orientations in the fixed hearts were assumed to represent the fiber-sheet structure in the end-diastolic reference configuration in vivo (2,8,32). To avoid the distortional effects of dehydration and shrinkage associated with embedding, histological measurements were obtained using freshly fixed heart tissue. In the transmural block of tissue within the implanted bead set, the mean fiber (α) and sheet angles (β) were determined from epicardium to endocardium at every 1-mm-thick section sliced parallel to the epicardial tangent plane (Fig. 1B) (2,8). The digital images from the biplane X-ray were spherically corrected (2) to reconstruct the 3-D coordinates (20) of the gold bead markers. Continuous, nonhomogeneous transmural distributions of 3-D finite strains were computed (2). Six independent finite strains [circumferential strain (E_{11}), longitudinal strain (E_{22}), radial strain (E_{33}), circumferential-longitudinal shear (E_{12}), longitudinal-radial shear (E_{23}), and circumferential-radial shear (E_{13})] were computed in the local cardiac coordinate axis (circumferential, longitudinal, and radial, respectively) system (X_1, X_2, X_3) (23), which were subsequently used to compute another set of six finite strains [fiber strain (E_{ff}), sheet strain (E_{ss}), strain normal to the sheet plane (E_{nn}), shear within the sheet plane (E_{fs}), sheet shear (E_{sn}), and fiber-normal shear (E_{fn})] in the local fiber-sheet coordinate system (X_f, X_s, X_n) (7) through an orthogonal transformation to convert the strain tensor using α and β at each depth. Finite strains were calculated for each frame (125 frames/s) as a deformed configuration with end diastole as the reference state at three wall depths: 25% (subepicardium), 50% (midwall), and 75% (subendocardium) wall depth from the epicardial surface. End diastole was defined as the time of the peak of the ECG R-wave for atrial pacing and the ventricular pacing artifact (V-spike) for LV epicardial pacing. We chose the V-spike rather than the peak of R-wave as the reference state for LV epicardial pacing because the former reflects the timing of the activation of the pacing site, as opposed to the latter, which represents the timing of activation of the whole ventricle. End systole was derived from the nadir of the dicrotic notch of the central aortic pressure.

Three phases were defined in the cardiac cycle: early contraction phase [beginning at end diastole and ending at the peak positive ($dP/dt_{\max}$)], ejection phase (beginning at $dP/dt_{\max}$ and ending at end systole), and early relaxation phase (beginning at end systole and ending at minimum LV pressure) (2,13) (Fig. 2). The QT interval was defined as the time interval between the initial deflection of the QRS complex and the point at which a tangent drawn to the steepest portion of the terminal part of the T wave crossed the isoelectric line (22). Corrected QT was calculated using Bazett's formula (4). Transmural dispersion of repolarization was defined as the interval between the peak to the end of the T wave on the surface ECG (1,37).

To assess the fiber-sheet mechanics of impaired wall thickening (E_{33}) during epicardial pacing, the contribution of each term on the right-hand side of the following equation was investigated (8)

$$E_{33} = 2E_{sn} \sin \beta \cos \beta + E_{ss} \cos^2 \beta + E_{nn} \sin^2 \beta \quad (1)$$

It is evident from Eq. 1 that in terms of fiber-sheet coordinates, E_{33} depends only on the sheet angle (β) and the fiber-sheet strain components in the (X_s, X_n) plane normal to the local fiber axis, namely E_{sn} , E_{ss} , and E_{nn} (8).

To assess transmural mechanical activation sequence with both pacing modes, mechanical activation time (t_m) was defined as the time to reach 10% of the maximum fiber shortening (E_{ff}) at each transmural depth. To evaluate the effect of reversed transmural mechanical activation sequence on transmural deformation, transmural mechanical activation strains (E') were defined in both the local cardiac and fiber-sheet coordinate system. With atrial pacing, the reference configuration was t_m at subendocardium and the deformed configuration was mechanical activation time at subepicardium. Conversely, with epicardial pacing, the reference configuration was t_m at subepicardium and the deformed configuration was t_m at the subendocardium. Because transmural mechanical activation sequence propagates from subendocardium to subepicardium with atrial pacing, and from subepicardium to subendocardium with epicardial pacing (see RESULTS), E' strains describe mean transmural myocardial deformation when mechanical activation travels between subendocardium and subepicardium.

Statistical analysis

Values are means $\pm$ SE unless otherwise specified. A paired t -test was used to compare atrial pacing and LV epicardial pacing for global hemodynamic parameters, time intervals, and each strain component. Two-factor repeated-measures ANOVA was used for the time course analysis, with the effects of pacing mode (atrial vs. LV epicardial pacing) and time on each strain component determined at three depths (subepicardium, midwall, and subendocardium) individually. Statistics were performed using SigmaStat version 3.0 (SPSS; Chicago, IL). Statistical significance was accepted at $P < 0.05$.

RESULTS

Anatomic measurements for these five animals were described previously (2). Briefly, the mean fiber angle ranged approximately from -60° (epicardium) to $+60^\circ$ (endocardium). The mean sheet angle was predominantly negative with smaller variations across the wall (-36° to -2°). The centroid of the bead set was $65 \pm 1\%$ of the distance from base bead to apex bead, in the anterior LV free wall 1–1.5 cm lateral from the LAD. Mean wall thickness at the bead set location was 10 ± 1 mm, and the deepest bead was located at $91 \pm 2\%$ wall depth. Global parameters are summarized in Table 1.

End-systolic wall thickening and fiber sheet strains during epicardial pacing

Epicardial pacing significantly reduced wall thickening (E_{33}) and transverse shear (E_{23}), and E_{13} ($P < 0.05$; see Table 2). Epicardial pacing also depressed all the fiber-sheet strains, and all the terms on the right-hand side of Eq. 1 ($2E_{sn} \sin \beta \cos \beta$, $E_{ss} \cos^2 \beta$, and $E_{nn} \sin^2 \beta$). As a result, the relative contribution of each term to wall thickening ($2E_{sn} \sin \beta \cos \beta / E_{33}$, $E_{ss} \cos^2 \beta / E_{33}$, and $E_{nn} \sin^2 \beta / E_{33}$) was not significantly affected by epicardial pacing ($P = \text{NS}$). With either atrial or epicardial pacing, the relative contribution of the sheet shear term ($2E_{sn} \sin \beta \cos \beta$), sheet extension term ($E_{ss} \cos^2 \beta$), and sheet-thickening term ($E_{nn} \sin^2 \beta$) was fixed at 48–63%, 33–44%, and 4–8%, respectively.

Time course of finite strains at the pacing site

With atrial pacing, most strain components underwent a simple contraction-relaxation pattern with the peak deformation near end systole, reflecting synchronous contraction within the LV (see Fig. 3). Epicardial pacing markedly changed the time course of all strain components in both cardiac and fiber-sheet coordinates, indicated by a significant interaction between the

effects of pacing mode and time ($P < 0.05$). The hallmark effect of epicardial pacing was multiple phases of deformation, which are exemplified by E_{ff} . The myofibers started to shorten immediately after the epicardial pacing pulse, whereas the LV was still in diastole. This early shortening occurred before ventricular ejection and was at its maximum before dP/dt_{max} . The myofibers subsequently underwent elongation during the ejection phase, followed by shortening, which reached the next peak near end systole. The myofibers then underwent stretch and shortening again, followed by another peak shortening during the early relaxation period and subsequent stretch. Although the early peak shortening near dP/dt_{max} ($E_{ff} = -0.091 \pm 0.018$) was comparable to the end-systolic shortening with atrial pacing [$E_{ff} = -0.124 \pm 0.009$, $P = \text{not significant (NS)}$], it clearly preceded aortic valve opening and did not contribute to ejection. The wall thickening that occurred at this time point also did not contribute to ejection. The subsequent peak shortening near end systole ($E_{ff} = -0.055 \pm 0.031$) was significantly decreased ($P < 0.05$). The peak shortening during early relaxation ($E_{ff} = -0.053 \pm 0.016$) was significantly decreased compared with end-systolic shortening with atrial pacing ($P < 0.05$). Most strains exhibited multiple peaks of deformation similar to E_{ff} .

Transmural mechanical activation sequence at the pacing site

Epicardial pacing reversed the normal transmural sequence of fiber shortening at the pacing site (see Fig. 4 and Table 3). With atrial pacing, t_m was 30 ± 8 ms earlier in subendocardium than in subepicardium ($P < 0.05$), reflecting the normal electrical activation sequence in the endocardial-epicardial direction. Epicardial pacing significantly reduced t_m in subepicardium ($P < 0.05$), whereas subendocardium was unaffected ($P = \text{NS}$). The net result was reversal of the transmural sequence of fiber shortening; subepicardial fiber shortening occurred 19 ± 5 ms earlier than subendocardial counterpart ($P < 0.05$; Fig. 4).

Because the reference and deformed configurations of E' strains were defined by transmural changes of fiber strains, fiber shortening (E'_{ff}) was not affected by reversal of transmural mechanical activation sequence ($P = \text{NS}$). Despite normal fiber shortening, most E' strains were significantly reduced ($P < 0.05$), including wall thickening (E'_{33}), sheet extension (E'_{ss}), and sheet thickening (E'_{mn}). However, transverse shear (E'_{23}) and sheet shear (E'_{sn}) were not significantly altered by reversal of transmural mechanical activation sequence ($P = \text{NS}$).

DISCUSSION

Although the effect of LV epicardial pacing on fiber strain has been described at single selected layers at the pacing site, including the subepicardium (9,27) and midwall (21,28,35,36), the present study is the first to examine the transmural gradient of fiber-sheet strains at the pacing site.

Mechanism of impaired endocardial wall thickening at the epicardial pacing site

On the basis of reduced transverse shear deformation at the epicardial pacing site, we hypothesized that impaired end-systolic wall thickening results from reduction in myocardial sheet shear. However, our results indicate that impaired end-systolic wall thickening at the epicardial pacing site was not due to selective reduction of sheet shear but rather resulted from overall depression of sheet deformation. In fact, all end-systolic fiber-sheet strains were significantly depressed by epicardial pacing (Table 2). Relative contributions of sheet shear, sheet extension or sheet thickening to wall thickening were consistent with the results of Costa et al. (8) and were not altered significantly by epicardial pacing. These findings imply that impaired wall thickening results from lack of effective myocardial deformation, most likely due to insufficient calcium levels at end systole at the pacing site. Intracellular calcium levels at the pacing site may be depleted by the time LV reaches end systole because the pacing site

initiates contraction earlier than the rest of the ventricle, and the time interval from electrical activation to end systole is significantly increased (ED-ES duration, Table 1). Moreover, early myofiber shortening at a pacing site is unloaded (14,28), and unloaded shortening is associated with increased rates of decay of intracellular calcium transient (38).

Reversal of transmural mechanical activation

Our measurements demonstrate that epicardial pacing reversed the transmural mechanical activation sequence, resulting in an earlier onset of myofiber shortening in the epicardium. Notably, this is the first study to show that the onset of fiber shortening in the subendocardium leads that of the subepicardium and that this mechanical sequence is reversed when the transmural sequence of activation is reversed with epicardial pacing. To assess the effect of reversed transmural mechanical activation sequence on transmural deformation, we defined E' , which describe mean transmural myocardial deformation when mechanical activation travels between subendocardium and subepicardium. Because E'_{23} and E'_{sn} were not affected by epicardial pacing, these shear deformations do not depend on the transmural sequence of mechanical activation but depend on the magnitudes of fiber shortening. This finding implies that the direction and the magnitude of sheet shear deformation may be determined by local anatomy and supports the concept that sheet shear deformation is required for normal systolic wall thickening (8,17,18,30). In contrast, other E' strain components were significantly depressed by epicardial pacing. For example, E'_{ss} and E'_{33} were significantly reduced when “after-load” was low. These results suggest that a normal transmural mechanical activation sequence may be required for normal sheet extension and therefore wall thickening. Normal endocardial-epicardial activation sequence may allow optimal co-ordination of sequential fiber shortening and sheet mechanics across the wall to maximize wall thickening.

Limitations

Our data describe transmural mechanics in the LV midanterior wall from the epicardium to 90% wall depth. Regional and transmural variations should be taken into consideration when these results are extrapolated to other regions of the LV, such as the lateral, posterior wall and the septum. In addition, the 3-D finite strains that we measured in open-chest, anesthetized dogs may not accurately reflect the transmural mechanics in closed-chest, conscious animals. Finally, the magnitude of baseline dp/dt_{max} and dp/dt_{min} was relatively high for open-chest dogs in this study, most likely due to dopamine use in two of five animals during surgical procedure, which may have affected the normal transmural mechanics. To minimize the confounding effects of surgery, anesthesia, and dopamine between normal AV conduction and epicardial pacing, two pacing modes were studied consecutively in a short period of time.

In conclusion, we demonstrate that impaired end-systolic wall thickening at the epicardial pacing site was not due to selective reduction of sheet shear but rather resulted from overall depression of fiber-sheet deformation, and relative contributions of sheet strains to wall thickening were maintained. These findings suggest lack of effective end-systolic myocardial deformation at the pacing site, most likely because the pacing site initiates contraction significantly earlier than the rest of the ventricle. Epicardial pacing also induced reversal of the transmural mechanical activation sequence, which significantly depressed sheet extension and wall thickening early in the cardiac cycle, whereas transverse shear and sheet shear deformation were not affected. These findings suggest that normal sheet extension and wall thickening immediately after activation may require normal transmural activation sequence, whereas sheet shear deformation may be determined by local anatomy.

Acknowledgments

We thank Rish Pavelec and Rachel Alexander for excellent managerial and surgical assistance. We also acknowledge outstanding technical assistance of Satoko Nagato for data analysis.

GRANTS

This work was supported by National Heart, Lung, and Blood Institute Grants HL-29589 (to N. B. Ingels, Jr.) and HL-32583 (to J. W. Covell). H. Ashikaga is a recipient of the American Heart Association Postdoctoral Fellowship (Western States Affiliate).

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Fig. 1.

A: schematic representation of the left ventricle (LV). X_1 , circumferential axis; X_2 , longitudinal axis; X_3 , radial axis; LAD, left anterior descending; LCx, left circumflex; D_1 , D_2 , first and second diagonal branch of LAD, respectively. *B:* schematic representation of local fiber-sheet axes. Fiber angle (α) was measured in the X_1 - X_2 plane at each wall depth with reference to positive X_1 . Sheet angle (β) was measured in the plane perpendicular to the fiber angle at each wall depth with reference to positive X_3 . X_f , fiber axis, X_s , sheet axis, X_n , axis oriented normal to the sheet plane. The X_f , X_s , and X_n axes present a Cartesian system (for details, see Ref. 2).

Fig. 2.

Three cardiac phases are shown. dP/dt_{max} , LV peak positive developed pressure over time; EC, early contraction phase; Ejection, ejection phase; ER, early relaxation phase; ED, end diastole; ES, end systole; LVP_{min} , minimum LV pressure.

Fig. 3.

Temporal sequence of each strain component. Values are means $\pm$ SE ($n = 5$). Subepicardium, midwall, and subendocardium represents 25%, 50%, and 75% wall depth from the epicardial surface, respectively. The reference state for strain calculation was end diastole for both atrial pacing (peak of the ECG R-wave) and LV epicardial pacing (V-spike). Note different scales for shear and normal strains. *A*: Cardiac strains; *B*: fiber-sheet strains.

Fig. 4.

Transmural delay in mechanical activation time (t_m). Values are means $\pm$ SE ($n = 5$).

Subepicardium and subendocardium refer to 25% and 75% wall depth, respectively. End diastole was used as the reference state (*time 0*) for both atrial pacing and LV epicardial pacing. Maximum fiber shortening in atrial pacing and LV epicardial pacing was found near end systole and $dP/dt_{\max}$, respectively. * $P < 0.05$ vs. subepicardium of the same pacing mode; † $P < 0.05$ vs. subepicardium of atrial pacing.

Table 1

Hemodynamic parameters and time intervals

	Atrial Pace	Epicardial Pace
Heart rate, beats/min	133 ± 12	133 ± 12
Peak LV pressure, mmHg	119 ± 9	109 ± 10*
dP/dt _{max} , mmHg/s	3,436 ± 858	2,754 ± 791*
dP/dt _{min} , mmHg/s	-2,105 ± 325	-1,680 ± 219
LVEDP, mmHg	8 ± 2	5 ± 1
LVESP, mmHg	99 ± 6	89 ± 7
τ, ms	23 ± 5	25 ± 5*
Early contraction, ms	34 ± 5	102 ± 14*
Ejection, ms	186 ± 34	174 ± 23
Early relaxation, ms	134 ± 15	138 ± 15
ED-ES, ms	219 ± 35	277 ± 36*
QT, ms	204 ± 16	248 ± 16*
QTc, ms	446 ± 36	539 ± 21*
TDR, ms	30 ± 3	63 ± 10*

Values are means ± SE; *n* = 5 dogs.

LV, left ventricle; dP/dt_{max}, peak positive developed pressure over time; dP/dt_{min}, peak negative dP/dt; EDP, end-diastolic pressure; ESP, end-systolic pressure; τ, the time constant of LV isovolumic pressure decay (logarithmic method) (26,34); ED-ES, time interval from end diastole (ED) to end systole (ES); QT, QT interval on surface ECG; QTc, corrected QT interval; TDR, transmural dispersion of repolarization.

* *P* < 0.05 vs. atrial pacing.

Table 2

End-systolic strains

	Atrial Pace	Epicardial Pace
E_{11}	-0.154 ± 0.019	$-0.060 \pm 0.016^*$
E_{22}	-0.043 ± 0.009	-0.027 ± 0.012
E_{33}	0.235 ± 0.032	$0.085 \pm 0.023^*$
E_{12}	0.030 ± 0.006	0.027 ± 0.005
E_{23}	0.066 ± 0.014	$0.018 \pm 0.012^*$
E_{13}	0.067 ± 0.009	$0.040 \pm 0.009^*$
E_{ff}	-0.118 ± 0.010	$-0.040 \pm 0.015^*$
E_{ss}	0.121 ± 0.024	$0.034 \pm 0.014^*$
E_{nn}	0.036 ± 0.027	$0.004 \pm 0.015^*$
E_{fs}	0.065 ± 0.015	$0.028 \pm 0.012^*$
E_{sn}	-0.078 ± 0.038	$-0.026 \pm 0.022^*$
E_{fn}	-0.055 ± 0.013	$-0.031 \pm 0.010^*$
$E_{ss} \cos^2 \beta$	0.096 ± 0.021	$0.028 \pm 0.011^*$
$E_{nn} \sin^2 \beta$	0.020 ± 0.010	$0.008 \pm 0.006^*$
$2E_{sn} \sin \beta \cos \beta$	0.119 ± 0.020	$0.049 \pm 0.016^*$
$\frac{E_{ss} \cos^2 \beta}{E_{33}}$	0.438 ± 0.070	0.333 ± 0.091
$\frac{E_{nn} \sin^2 \beta}{E_{33}}$	0.082 ± 0.038	0.043 ± 0.063
$\frac{2E_{sn} \sin \beta \cos \beta}{E_{33}}$	0.481 ± 0.047	0.631 ± 0.077

Values are transmural means (subepicardium, midwall, and subendocardium) $\pm$ SE ($n = 5$).

E_{11} , circumferential strain; E_{22} , longitudinal strain; E_{33} radial strain; E_{12} , circumferential-longitudinal shear means; E_{23} , longitudinal-radial shear means; E_{13} , circumferential-radial shear means; E_{ff} , fiber strain; E_{ss} , sheet strain; E_{nn} , strain normal to the sheet plane; E_{fs} , shear means within the sheet plane; E_{sn} , sheet shear means; E_{fn} , fiber-normal shear means; β , sheet angle.

* $P < 0.05$ vs. atrial pace.

Table 3

Transmural mechanical activation strains

	Atrial Pace	Epicardial Pace
(E'_{11})	-0.042 ± 0.009	$-0.024 \pm 0.004^*$
(E'_{22})	-0.023 ± 0.007	$-0.002 \pm 0.002^*$
(E'_{33})	0.045 ± 0.008	$0.016 \pm 0.003^*$
(E'_{12})	0.019 ± 0.004	$-0.002 \pm 0.003^*$
(E'_{23})	-0.004 ± 0.006	0.007 ± 0.003
(E'_{13})	0.022 ± 0.005	$0.003 \pm 0.002^*$
(E'_{ff})	-0.024 ± 0.003	-0.020 ± 0.003
(E'_{ss})	0.029 ± 0.006	$0.006 \pm 0.004^*$
(E'_{nn})	-0.026 ± 0.009	$0.003 \pm 0.004^*$
(E'_{fs})	0.014 ± 0.005	$0.004 \pm 0.003^*$
(E'_{sn})	-0.017 ± 0.011	-0.006 ± 0.003
(E'_{fn})	-0.022 ± 0.005	$-0.005 \pm 0.003^*$

Values are transmural average (subepicardium, midwall, and subendocardium) $\pm$ SE; $n = 5$ dogs.

E' , transmural mechanical activation strains.

* $P < 0.05$ vs. atrial pace.