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Experimental Measures of Cardiac Electrical Activation

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Abstract

Background—The purpose of this study was to conduct a detailed experimental investigation of total ventricular activation time, determine how to measure it accurately, and compare it to the commonly used measure of QRS width. In addition we investigated a measure of electrical synchrony and determined its relationship to the duration of ventricular activation.

Methods—Unipolar electrograms were recorded from the myocardial volume using plunge needle electrodes, from the epicardial surface using “sock” electrode arrays and from the surface of an electrolytic torso-shaped tank. Electrograms were analyzed to determine a root mean square (RMS) based measure of ventricular activation and electrical ventricular synchrony.

Results—The RMS-based technique was found to be an accurate means of measuring total ventricular activation time (TVAT) from unipolar electrograms recorded from the heart, the entire tank surface or the precordial leads. The 3- and 12-lead electrocardiograms provided statistically poor indications of TVAT. In normal canine hearts, a quantification of ventricular electrical synchrony (VES) for normal ventricular activation showed that the ventricles activate, on average, within 3 ms of each other with the left typically activating first. VES was not strongly correlated with TVAT.

Conclusion—Conclusions from this study are 1) ventricular activation was reflected accurately by the RMS width obtained from direct cardiac measurements and from the tank surface with measures similar to the precordial leads, but not from a single 3- or 12-lead ECG; and 2) current proposed measures of electrical synchrony are not strongly correlated with TVAT.

INTRODUCTION

Over the past decade, cardiac resynchronization therapy (CRT), a ventricular pacing treatment aimed at restoring synchronous contraction of the ventricles, has been shown to improve outcomes for heart failure patients.^{1–3} CRT utilizes ventricular stimulation, an electrical therapy, in response to mechanical insufficiency. A primary indication for CRT is a widened QRS complex, taken as a measure of increased duration of the electrical activation of the ventricles.^{4, 5} This clinical emphasis on electrical therapeutic approaches has created a need for a basic understanding and detailed quantification of electrical activation of the ventricles,

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as well as a need to define the associated concept of electrical synchrony. Despite a widely accepted relationship between QRS width and ventricular synchrony, there is little data on how well the QRS width relates to total ventricular activation time (TVAT) and the implications toward electrical synchrony. In addition, there is no validated measure of synchrony that can be related to total ventricular activation time. Therefore, the purpose of this study was to conduct a detailed experimental investigation of total ventricular activation time, determine how to measure it accurately, and compare it to the commonly used measure of QRS width. In addition we investigated a recently published measure of electrical synchrony applied to patients undergoing CRT that looks at the differences in the mean activation times between the left and right ventricles⁶ and determined its relationship to ventricular activation time.

Experimental data was obtained from high-resolution electrical imaging, achieved by recording unipolar electrograms from throughout the myocardial volume using plunge needle electrodes, from the epicardial surface using “sock” electrode arrays, and from the surface of an electrolytic torso-shaped tank. A maximum curvature algorithm was applied to a computed root mean square (RMS) signal from multiple, simultaneously collected electrograms (EGs) from the heart or torso surface to investigate accurate measures of ventricular activation. These results were compared with measures of total ventricular activation time obtained from high-resolution electrical recordings directly from the myocardial volume and with QRS width measured from the ECG. Also using electrograms measured directly from the myocardial volume, we carefully computed the average activation times of each ventricle and investigated how the difference was related to TVAT.

By establishing accurate measures of ventricular activation time and ventricular electrical synchrony, this study endeavors to use experimental measurements to give more definitive understanding of the effectiveness and accuracy of the measure of QRS width as a surrogate for total ventricular activation time and a quantitative definition to electrical synchrony.

METHODS

Experimental Preparation

All experiments were conducted in accordance with the University of Utah Institutional Animal Care and Use Committee and conformed to the Guide for the Care and Use of Laboratory Animals. A total of 24 mongrel dogs (13 males, 11 females, 25.4 ± 5.1 kg), were anesthetized with 30 mg/kg pentobarbital I.V. with additional amounts administered as needed and included in one of three separate experimental protocols.

The first experimental protocol consisted of nine studies where each heart was rapidly excised and perfused using a modified Langendorff procedure.⁷ Ninety-six ($n = 6$), 147 ($n = 2$), or 152 ($n = 1$) transmural plunge-needle electrodes with 10 electrodes along each shank were then placed throughout the entire ventricular myocardial volume (Figure 1A).⁸ Endocardial data sets were obtained by selecting EGs recorded from electrodes 1 and 2 from each needle. Similarly, epicardial data sets were defined as electrodes 9 and 10 from each needle. Unipolar EGs were referenced to a remote electrode placed at the aortic root. Recordings were made during different activation sequences: atrial drive, anterior left and right ventricular endocardial and epicardial pacing under normal conditions. In six of the experiments, after conducting the pacing protocol, both ventricular cavities were flushed with Lugol solution for three to five minutes to inactivate the specialized Purkinje conduction system and the pacing protocol was repeated.⁹ Four additional isolated Langendorff-perfused experiments were conducted to study LV activation and the timing of the activation of the septal wall. In this preparation, previously described¹⁰, the right ventricular wall was removed to expose the septum. Intramural needles were inserted in the LV free wall as well as the exposed septal wall.

The second set of six experiments used isolated hearts perfused with oxygenated blood provided by a support dog. The hearts were placed in the appropriate anatomical position in a small human torso-shaped electrolytic tank described in detail previously.^{11, 12} Unipolar ECGs were recorded from a 490-electrode sock array placed over the ventricular surface and from the entire surface of the torso-tank (384 electrodes) (Figure 1B & C) with respect to Wilson's central terminal. The Lead II, three bipolar limb leads, precordial leads and the 12-lead ECGs were derived from selected electrodes sites located on the torso-tank surface (Figure 1C). Activation sequences included right atrial pacing as well as anterior left and right ventricular epicardial pacing under normal conditions.

In a third set of five experiments, the hearts were exposed via a medial thoracotomy and suspended in a pericardial cradle.¹³ A 247-electrode sock array was placed over the heart covering the surface of both ventricles. Unipolar ECGs were recorded from the heart with respect to a remote lead placed on the left leg. A three-lead or a single Lead II ECG was simultaneously recorded during various activation sequences, including atrial drive, left and right ventricular pacing and biventricular pacing.

Data Collection and Analysis

Signals, amplified and bandpass filtered from 0.03 to 500 Hz, were either simultaneously recorded ($n = 20$),¹⁴ or recorded in consecutive banks of 192 ($n = 4$)¹⁵ at a 1 kHz sampling rate with 12-bit resolution and stored on a Macintosh computer. Potential values were gain-adjusted and linear base lines were established between consecutive T-P intervals. Signals with an activation down-stroke characterized by a substantially smaller modulus of the derivative than the other signals from the same needle, suggesting they were located outside the myocardium, or with poor signal quality were removed from the data set.

Local activation time was estimated as the time of the minimum derivative of the unipolar electrogram.^{13, 16, 17} All activation times were referenced to the time of the pacing artifact or the onset of ventricular electrical activity for non-ventricularly-paced beats. Activation time (AT) was defined as the difference between the earliest and latest measured activation times from any set of ECGs. As shown in Figures 2A–B, with the earliest activation time of 13.1 ms on the anterior epicardium and latest activation time of 86.8 ms on the postero-basal epicardium, the AT is 73.7 ms as measured on the epicardial surface. Ideally defined as the duration from the time of the first depolarizing (activating) ventricular cell to that of the last depolarizing ventricular cell, total ventricular activation time, or TVAT, provides a quantitative representation of the timing of the spread of activation throughout the ventricles.¹⁶ We estimated TVAT as the latest minus the earliest activation time as measured from 92 to 150 plunge needle electrodes evenly distributed throughout the ventricular free walls. Activation time irregularities were identified and eliminated from the data set using the arrival of the depolarization wave front seen in the time series of isopotential maps¹³ visualized using Map3D software (<http://www.sci.utah.edu/ncrr/software/map3d.html>).¹⁸

To calculate the RMS of potentials (V_{RMS}) from the heart or body surface an analysis tool was developed utilizing MATLAB® (MathWorks, Inc., Nattick, MA) using Equation (1),

$$V_{\text{RMS}}(t) = \sqrt{\frac{\sum_{i=1}^n v_i^2(t)}{n}} \quad (1)$$

where n is the number of electrograms sampled and $v_i(t)$ is the potential of electrogram i at time t .¹⁹

Curvature of the RMS waveform was calculated by Equation (2),

$$\text{Curvature}(t) = \left| \frac{d^2 V_{\text{RMS}}}{dt^2} \right| / \left[1 + \left(\frac{dV_{\text{RMS}}}{dt} \right)^2 \right]^{3/2} \quad (2)$$

where V_{RMS} is the RMS potential and t is time.¹³ 20 Peaks in the curvature waveform represented significant deviations from baseline in the RMS signal allowing regions of the RMS waveform to be selectively marked. The onset and end of ventricular activation was marked using the first and last peaks associated with ventricular electrical activation exceeding a threshold of three standard deviations above the noise level in the RMS-based curvature signal as shown in Figure 2C.²⁰

Ventricular electrical synchrony (VES) was measured as the mean RV activation time minus the LV mean activation time.⁶ Each ventricular mean activation time was calculated as the average activation times from all electrograms recorded within the respective ventricular freewalls.

Statistical Analysis

Statistical calculations were made using Graphpad Instat® to compute both the repeated measures analysis of variance (ANOVA) with Tukey-Kramer multiple comparisons, and the nonparametric Spearman's correlation coefficient, R , via simple linear regression. For each test, p -values less than 0.05 were considered significant. All values are expressed as mean $\pm$ standard deviation.

RESULTS

Quantifying Total Ventricular Activation Time from the Heart

Figure 2 shows an anterior view (panel A) and posterior view (panel B) of an epicardial activation time map computed from EGs recorded from electrode 10 (outermost) of 96 plunge needles for a beat paced from the anterior LV epicardium. For this example, both the earliest (indicated by a white star) and the latest (indicated by a black star) activations measured from all 960 electrodes occur on the epicardial surface, resulting in the same value for epicardial AT and TVAT of 73.7 ms. Panel C shows the RMS curve for the same beat computed from the 960 EGs recorded from the myocardial volume. Under the RMS curve are histograms of the associated activation times from the entire ventricular volume. Panel C demonstrates that activation times begin and end with the onset and end of the portion of the RMS signal relating to ventricular electrical activity as marked with vertical bars in the figure using the maximum curvature technique. Throughout this paper we will refer to this marked region as the RMS width for brevity.

Accuracy of activation times estimated from EGs recorded from the left and right ventricular free walls with only a few EGs from the septal wall (those which were accessible from the epicardium at the interventricular groove) as a representative of TVAT, was assessed first. We used four isolated hearts with the RV free wall removed and placed needles in both the LV free wall and the exposed septal wall. Results showed that total septal activation time measured in this way begins and terminates within the activation time of the LV free wall following atrial stimulation (see example Figure 3A). On average, the LV free wall activated 2.1 ± 4.0 ms

before the septal wall and final activation of the septal wall preceded the final activation of the LV free wall by 3.5 ± 4.0 ms. For epicardial and endocardial LV pacing, the septal wall began activation 28.5 ± 11.7 ms before the LV free wall. The latest septal activation time as measured from the needles was very close to that of the latest activation for the LV free wall for both LV epicardial and endocardial pacing sequences (average difference, 0.4 ± 0.8 ms) in 3 of 4 hearts. For a single heart, there was additional time required for the septum to finish activating of 14 ms and 12 ms for epicardial and endocardial pacing, respectively. In this heart, the pacing site was directly opposite the septal wall on the left lateral free wall, leaving the septum as the last area to be reached by the excitation wave front. An example of the timing of the septum and LV freewall activation for LV epicardial pacing is shown in Figure 3B.

LV freewall and septal activation times obtained from the exposed septum model were then compared with those from intact isolated hearts under both LV and atrial stimulation in six separate experiments. Beats were matched for pacing site, activation onset and offset for comparability with the exposed septum model experiment. Figures 3C and D show an example of RV activation times that were later than LV activation times for both atrial stimulation and LV epicardial pacing respectively in intact isolated hearts. On average, the latest RV activation times following LV pacing of the epicardium and the endocardium were 32.6 ± 9.6 and 23.7 ± 8.7 ms longer than latest the LV activation times, respectively. From these six hearts, results always showed an increased time of RV free wall activation that followed the LV free wall activation in excess of any times seen in the exposed septal studies. Therefore, we concluded that the inclusion of only a few EGs from the septal wall would not significantly affect the measured value of TVAT in these studies.

In the first set of experiments with transmural needle recordings from the total ventricular volume, electrograms were recorded when pacing from the right atrium, LV or RV. RMS widths were computed from RMS signals generated from EGs measured from the epicardial and endocardial surfaces as well as from the total ventricular volume. TVAT was computed from the latest minus the earliest activation times measured from the entire myocardial volume. The mean RMS widths and TVATs for various activation sequences are provided in Table 1. It can be seen from this table that calculating the RMS width from EGs recorded from the entire myocardial volume, only epicardial, or endocardial surfaces can accurately reflect TVAT. A multivariate repeated measures ANOVA yielded no significant differences between measured TVAT and RMS widths from the epicardium, endocardium, and myocardial volume ($p = 0.4562$, ns). Figure 4 shows an example in which histograms of the activation times from all ventricular needle electrodes are plotted under the RMS curves generated from the ventricular volume (panel A), epicardial surface (panel B), and endocardial surface (panel C). For the three panels in Figure 4, the histograms remained the same while the subset of EGs used for RMS calculation varied. The marked duration of the ventricular electrical activity from the RMS waveform is equal to the span of the activation times in all three cases.

Table 2 shows how activation times obtained from either the endocardial or epicardial surfaces can differ significantly from TVAT for various activation sequences. However, activation time calculated from a dataset combining EGs from both the epicardial and endocardial surfaces provided a statistically accurate estimate of TVAT. When activation time of either the epicardial or endocardial surface was compared to TVAT the greatest mean difference was 21.5 ms (see Table 2, LV epicardial pacing) compared to a maximum difference of 7.1 ms when the RMS widths were used (see Table 1, RV epicardial pacing). Results from a multivariate repeated measures ANOVA with post tests showed endocardial and epicardial activation times to be significantly different from TVAT ($p < 0.0001$).

To illustrate neither epicardial nor endocardial activation times alone can reflect TVAT adequately, Figure 5 depicts activation times measured from an anterior, left ventricular,

endocardially paced beat. Figure 5A shows an activation time histogram from myocardial volume EGs overlaid with an RMS signal computed from the same EGs depicting the alignment of earliest and latest activation with the width of the RMS signal as indicated by curvature peaks. Figures 5B and C show the volume RMS signal overlaid on the histograms of activation times obtained only from the endo- or epicardial surfaces, respectively. For the three panels in this figure, the RMS signal was held constant while the dataset used to calculate the activation time histograms varied. Epicardial (panel B) and endocardial (panel C) activation time histograms are subsets of the entire myocardial volume histograms (panel A). The epicardial surface activation time histogram (panel B) reveals a 19 ms delay between the peak curvature marker in the RMS signal and the earliest measured activation on the epicardium (start of the histograms). This gap results from the time required for transmural propagation of this endocardially-paced beat to reach the epicardial surface. Similarly, Figure 5C shows the latest endocardial activation (last histograms) to occur 13 ms prior to the second peak curvature marker in the RMS signal, again due to timing of transmural conduction. The gaps revealed in these figures indicate the inability of the activation times from either surface alone to accurately reflect TVAT.

Quantifying Total Ventricular Activation Time from the Body Surface

Having established that the width of the RMS signal from cardiac EGs is an accurate measure of TVAT, we next evaluated the ability of RMS signals generated from recordings from the body surface to represent TVAT by comparing RMS widths computed from epicardial and tank surface EGs. Results of repeated measure ANOVA followed by multiple comparisons showed significant differences in measures of the RMS widths for the 12-lead, 3-lead and lead II ECGs (Table 3) when compared to the measures from epicardial EGs, while measures from the full set of tank surface leads or precordial leads showed no significant differences. Table 3 also summarizes the results of linear regression comparisons between RMS widths computed from epicardial surface EGs and various sets of tank surface EGs. As the number of tank surface EGs included in the RMS decreased, generally the accuracy of tank-surface estimates of TVAT decreased, with the exception of the precordial leads which exhibited the lowest mean difference (highest accuracy) when compared to the RMS widths computed from the epicardial surface EGs.

To further test the relationship between the QRS width and TVAT, 3-lead ECGs were recorded from an *in situ* preparation and compared with the RMS width measured from simultaneously recorded epicardial EGs during varied pacing regimens. The basis for this comparison is shown in Figure 6A, which displays the RMS widths obtained from the epicardial surface electrograms versus the TVAT calculated from transmural needle EGs from the myocardial volume. Building on this relationship, using data from separate studies in which EGs were not recorded from transmural needle electrodes but from epicardial “sock” electrodes, RMS widths computed from epicardial EGs were compared with RMS widths calculated from the 3-lead ECG (Figure 6B). The resulting correlation ($R = 0.42$) is weaker (panel B) than that seen between TVAT and epicardial surface RMS width ($R = 0.90$, panel A). Using a linear fit forcing the intercept to be zero, the resulting slope for panel B has a much smaller value (0.784 vs. 0.994) compared to panel A, indicating that the 3-lead ECG tends to underestimate TVAT. On average, errors in the estimates of TVAT based on the 3-lead ECG were 10.06 ± 12.26 ms, ranging from a maximal overestimation of up to 9 ms to a maximal underestimation of 47 ms ($n = 101$ sequences).

Measuring Ventricular Electrical Synchrony

Measurements of VES were obtained from the EGs recorded from plunge needles distributed throughout the ventricular volume. For electrical sequences initiated via atrial stimulation ($n = 6$), VES ranged from -2.48 ms to 8.74 ms (mean 2.68 ± 4.31 ms). Mean VES values were

36.0 ± 8.7 ms and -39.2 ± 9.8 ms for left ventricular (n = 25) and right ventricular (n = 16) pacing sites, respectively. Figure 7 shows the VES values from epicardial and endocardial surfaces versus those from the myocardial volume for several types of activation sequences (n = 47). The results from atrially-paced beats were grouped near the origin reflecting small values of VES and ventricular synchrony. The left ventricular paced beats were grouped in the upper right quadrant reflecting LV followed by RV activation. Likewise, the right ventricular paced beats were in the lower left quadrant (negative values), indicating RV activation prior to LV activation.

Although values for VES obtained from the endocardial surface were statistically different ($p < 0.001$) from the values derived from the myocardial volume, they exhibited a small mean difference (1.739 ms) and high correlation ($R = 0.9987$). VES values from the epicardial surface were statistically similar to the myocardial volume ($p = \text{NS}$) and produced a smaller mean difference (0.4235 ms) and high correlation ($R = 0.9980$).

Relationship of Ventricular Electrical Synchrony to Total Ventricular Activation Time

Comparisons of volume RMS-based widths and VES values (Figure 8) showed a correlated trend with some outliers ($R = 0.825$, $p < 0.0001$). Besides having different ventricular activation times, beats with small values of VES typically produced narrow, monophasic RMS waveforms while dyssynchronous beats showed wider RMS signals that were often multiphasic in shape.

DISCUSSION

The study addressed the assumption that QRS width is an accurate measure of ventricular activation time. The technique of measuring the duration of ventricular activation in an RMS signal from unipolar EGs recorded from the heart and body surface was found to be an extremely accurate means of determining TVAT. This technique, as introduced by Fuller et al. as a means to measure repolarization dispersion from the cardiac and body surfaces,^{19, 20} provides a powerful means to sum all of the information recorded from multiple unipolar electrograms in a way that makes detection of slight deviations from baseline accurate. The results of this study suggest that cardiac mapping techniques, which measure electrical signals directly from the heart, may provide accurate measures of TVAT if the RMS technique is applied. From body surface measurements studied here, it appears that the use of a single lead ECG may provide the least accurate measure of TVAT. Results showed large differences between measured TVAT and the QRS width measured from one lead. Additionally, the results showed 3- and 12-lead ECGs provided statistically poor indications of TVAT. However, QRS widths from the precordial leads and entire tank surface did provide reasonably accurate measures of TVAT.

We also investigate a difference between the mean activation times of both ventricles as introduced by Jia et al.⁶ as a measure of synchrony. In normal canine hearts, a quantification of VES for normal ventricular activation determined that the LV and RV activate, on average, within 3 ms of each other with the LV typically activating slightly before the RV although they are nearly simultaneous. Published CRT studies have suggested optimal LV pacing sites range from the lateral to the posteriolateral aspect of the LV for improving synchrony.^{1, 2} Pacing from the anterior endocardial LV, far from these suggested locations, in a heart following Purkinje inactivation, exhibited a VES value of 59 ms (right-most data point in Figure 6) and QRS width of 122 ms indicating an electrically dyssynchronous beat. This specific case exemplifies the more general result that VES values were consistent with expected values based on the applied pacing sequence. Jia et al.⁶ used only epicardial activation times to compute VES, our results suggest that this is sufficient to get an accurate estimate of the volume VES.

This work may provide some practical insight as to why measures of QRS width have not always been a strong predictor for synchrony and enables us to begin to reflect on how we may better use clinical electrical measures in the future to provide more accurate measures of ventricular activation time and synchrony. While, the ECG is the most widely used clinical electrical measure, the results from this study shows that measures of QRS widths from the single-, 3- or 12- ECG do not provide accurate measures of total ventricular activation time. Results showed that a full body surface map or even the just the precordial leads may provide a better measure of TVAT. The fact that the precordial leads are a component of the 12-lead ECG would explain why the correlation with TVAT was higher for the 12-lead over the 3- or single-lead measurements. These findings may raise the question as to whether the precordial leads might be investigated for a more consistently accurate measure of ventricular activation.

In this experimental study, TVAT was not strongly correlated with measures of synchrony. This suggests that we must consider seeking new measures of synchrony from clinical data.

High-resolution electrical measurements are requisite to defining and understanding electrical activation and synchrony but only have value if we can extrapolate these defined quantities from clinically available measurements. There are other methods for obtaining electrical data in the clinic that, although may be less common than the ECG, are still feasible. These include endocardial potential mapping using catheter based techniques^{4, 21–25}, epicardial potential mapping^{6, 12, 26–28} and endocardial and epicardial activation mapping^{21, 29, 30} via inverse solutions from body surface potential measurements.

Based on the results of this study, endocardial potential mapping may potentially provide an accurate measure of TVAT using the RMS technique from the potentials. However, traditional activation time measurement of the endocardial surface would provide a poor surrogate measure for TVAT. Also, accurate measure of VES may be obtained from the endocardial activation times if both ventricles are mapped, however, this is not usual practice in a clinical setting.

Indirectly determining the epicardial potentials from inverse calculations based on body surface potential measurements is still experimental, but has achieved some success in the clinic and has been applied to CRT patients.⁶ The work presented here suggests that this technique may provide feasible measures of TVAT and VES. TVAT could be computed from the RMS width from the epicardial potentials and VES could be determined from the activation times on the epicardial surface provided the data from the left and right ventricles can be properly distinguished. A different approach to solving the inverse solution estimates activation times on the endocardial and epicardial surfaces from body surface potentials.³⁰ While this technique does not compute potential values, only activation times, our results suggest that TVAT could be determined from the combined activation times both the epicardial and endocardial surfaces. In addition, VES may also be determined from these two surfaces with accuracy, again, provided the geometry can accurately distinguish the LV from the RV.

Limitations of Study

The use of plunge needle electrodes introduces another consideration involving the injury sustained by the heart due to needle insertion. However, in addition to our own validation studies, other investigations have shown that the insertion of these needles has no significant effect on myocardial function, structure, and activation sequence.^{31, 32} Finally, an important limitation of this study is that the electrical synchrony measurements presented were not compared with measures of mechanical synchrony or hemodynamics. This work has established accurate measures of the electrical parameters and future work will be necessary to compare these parameters with measures of mechanical synchrony. It is worth noting however, that results from recently published randomized clinical trials have demonstrated

heterogeneity of mechanical synchrony³³ and challenges associated with a lack of measurement standards for mechanical synchrony and dyssynchrony³⁴.

CONCLUSION

Through the findings of this study, some electrical measures central to our understanding of CRT and other pacing strategies have been defined and characterized in an experimental model. As QRS width is often assumed to represent ventricular activation timing³ and synchrony, it was necessary to assess these assumptions experimentally. There are two conclusions from this study; the first is that ventricular activation was reflected accurately by the RMS width obtained from direct cardiac measurements and from the tank surface with measures similar to the precordial leads, but not from a single, 3-, or 12-lead ECG. The second is that measures of synchrony are not strongly correlated with TVAT. This experimental work serves to provide an improved understanding of the electrical foundation for cardiac events, which may ultimately help improve the ability to properly proscribe and evaluate pacing therapies.

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Figure 1.

Graphical representations of the various experimental protocols employed. (A) Schematic of plunge-needle electrodes oriented in the myocardium. (B) Geometric mesh of a 490-electrode epicardial sock electrode covering both ventricles. (C) Torso tank geometric mesh with the pseudo-12-lead ECG electrodes marked.

Figure 2.

Isochronal maps of (A) anterior and (B) posterior aspects of the epicardial surface with the onset and termination of activation marked by a white and black star, respectively. (C) The resultant RMS signal generated from 960 EGs with ventricular activation time marked, overlaid on a histogram of activation time from each EG in the ventricular myocardial volume. Below the RMS signal is the computed curvature showing the marking of the earliest and latest peaks. Data shown in all panels is from the same anterior left ventricular epicardially-paced beat.

Figure 3.

Summed activation time histograms from left ventricular free wall (black) and septal wall (white) during (A) atrial drive, and (B) LV pacing. Similar histograms for the left ventricular (black) and right ventricular (grey) freewalls during (C) atrial drive and (D) LV pacing.

Figure 4.

Activation time histograms from the myocardial volume overlaid on RMS curves with marked widths. Histograms remain constant for all 3 panels while the calculated RMS signals are derived from the (A) myocardial volume, (B) epicardial surface, and (C) endocardial surface. All 3 panels are from the same anterior left ventricular endocardially paced beat.

Figure 5.

Myocardial volume RMS signal, overlaid on activation time histograms. The RMS signal remains the same in each panel while the histograms are determined from the (A) myocardial volume, (B) epicardial surface, and (C) endocardial surface. All 3 panels are from the same anterior left ventricular endocardially paced beat.

Figure 6.

(A) RMS width calculated from epicardial electrograms plotted against TVAT obtained from plunge needle electrograms ($n = 50$). (B) RMS widths from the body surface 3-lead ECG versus RMS widths determined from epicardial electrograms ($n = 101$).

Figure 7.

VES calculated from the myocardial volume plotted versus the VES from the epicardial and endocardial surfaces with pacing types delineated into three groups: right ventricular pacing, atrial drive, and left ventricular pacing.

Figure 8. RMS width measured from the myocardial volume plotted versus the absolute value of VES from the myocardial volume.

TABLE 1

Average RMS widths in ms from the myocardial volume, epicardial and endocardial surfaces with the total ventricular activation time (TVAT) in ms for various activation sequences plus or minus standard deviation. Ventricular pacing sites were located on the anterior aspect of the heart. (n=47) PPI = Post Purkinje Inactivation, NS = Not significantly different ($p>0.05$).

Pacing Location (Number of Runs)	TVAT	Volume RMS Width	Epicardial RMS Width	Endocardial RMS Width
Right Atrium (6)	37.7 ± 4.1	37.5 ± 3.1	36.7 ± 2.1	38.2 ± 3.3
LV Epi (6)	84.7 ± 8.9	84.8 ± 8.9	83.5 ± 9.1	83.5 ± 10.6
LV Endo (7)	81.6 ± 9.5	81.6 ± 8.0	83.1 ± 8.1	83.6 ± 8.6
LV Epi PPI (6)	96.8 ± 13.3	93.8 ± 12.8	95.5 ± 13.0	93.5 ± 15.6
LV Endo PPI (6)	101.0 ± 10.9	100.5 ± 11.5	100.0 ± 11.1	100.3 ± 15.5
RV Epi (6)	93.9 ± 14.3	88.8 ± 15.3	93.3 ± 20.0	86.8 ± 12.8
RV Endo (4)	84.5 ± 14.1	86.3 ± 12.6	86.3 ± 11.6	85.0 ± 11.4
RV Epi PPI (4)	108.8 ± 15.1	104.5 ± 21.8	103.5 ± 23.1	101.8 ± 23.3
RV Endo PPI (4)	99.4 ± 23.4	105.3 ± 24.5	103.5 ± 23.1	101.0 ± 23.2
Mean Difference from TVAT	—	2.3 ± 2.3, NS	2.0 ± 1.6, NS	2.6 ± 2.6, NS

TABLE 2

Average activation times (AT) in ms from the epicardial and endocardial surfaces with the total ventricular activation time (TVAT) for various activation sequences plus or minus standard deviation.

Pacing Location (Number of Runs)	TVAT	Epicardial AT (ms)	Endocardial AT (ms)	Endo + Epi AT (ms)
Right Atrium (6)	37.7 ± 4.1	30.8 ± 3.8	28.4 ± 3.8	36.4 ± 2.9
LV Epi (6)	84.7 ± 8.9	84.4 ± 9.3	63.2 ± 5.4	84.4 ± 9.3
LV Endo (7)	81.6 ± 9.5	69.7 ± 7.6	73.1 ± 5.6	80.9 ± 9.7
LV Epi PPI (6)	96.8 ± 13.3	95.1 ± 13.9	83.0 ± 13.0	95.1 ± 13.9
LV Endo PPI (6)	101.0 ± 10.9	89.5 ± 15.1	96.2 ± 12.8	100.1 ± 10.4
RV Epi (6)	93.9 ± 14.3	93.9 ± 14.3	75.7 ± 9.6	93.9 ± 14.3
RV Endo (4)	84.5 ± 14.1	76.3 ± 13.7	75.3 ± 10.2	84.5 ± 14.1
RV Epi PPI (4)	108.8 ± 15.1	108.2 ± 15.0	96.0 ± 10.3	108.8 ± 15.1
RV Endo PPI (4)	99.4 ± 23.4	91.2 ± 22.3	97.7 ± 25.1	98.8 ± 24.1
Mean Difference from TVAT	—	5.8 ± 4.9, **	11.3 ± 6.2, **	0.8 ± 0.6, NS

Ventricular pacing sites were located on the anterior aspect of the heart. (n=47) PPI = Post Purkinje Inactivation,

**
p<0.001

NS = Not significantly different (p>0.05).

TABLE 3

Linear regressions and ANOVA comparisons results of RMS widths obtained from the Epicardial Surface tested against those from the Tank Surface, 12 lead ECG, Precordial Leads, 3 Lead ECG, and Lead II ECG. (N=20)

RMS Comparison	Mean Difference ($\pm$ St. Dev.)	P-Value	Correlation (<i>R</i>)	Slope	Intercept
Epicardial Surface vs Tank Surface	7.15 $\pm$ 9.90	NS	0.9046	0.9364	11.804
Epicardial Surface vs 12 Lead ECG	8.70 $\pm$ 10.68	p < 0.05	0.8944	0.8760	17.578
Epicardial Surface vs Precordial ECG	5.50 $\pm$ 9.90	NS	0.9094	0.8894	13.770
Epicardial Surface vs 3 Lead ECG	11.40 $\pm$ 17.98	p < 0.01	0.7485	0.6430	36.001
Epicardial Surface vs Lead II ECG	11.25 $\pm$ 16.63	p < 0.01	0.7805	0.6813	33.257