Variability of the body surface distributions of QRS, ST-T and QRST deflection areas with varied activation sequence in dogs

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SUMMARY Distributions of QRS, ST-T and QRST areas of 192 lead body surface ECG's were measured in dogs for multiple activation orders. Qualitatively, the distributions of QRST area were found to be strikingly similar over all activation orders in contrast to the distributions of QRS or ST-T areas. Quantitative results showed that variability of the QRST areas over all activation orders was consistently less than those of either QRS or ST-T. The factor responsible for the QRS deflection is ventricular activation sequence while those responsible for the ST-T deflection are both activation sequence and ventricular recovery properties. Since the total QRST deflection area was largely independent of activation sequence it is likely the quantity is an index of ventricular recovery properties. The significance of this relation is that QRST deflection area may permit evaluation of intrinsic ventricular recovery properties in the presence of abnormal ventricular activation as occurs with intraventricular conduction disorders and ectopic origin of excitation. Evaluation of intrinsic ventricular recovery properties may also permit recognition of states at risk of ventricular arrhythmias due to increased disparity of these properties.

The QRS complex of the electrocardiogram reflects ventricular excitation while the ST-T deflection represents combined effects of excitation and recovery. Excitation sequence is represented in the ST-T deflection because it determines the sequence of onset of recovery. That is, the action potential upstroke determines not only the time of activation but also the beginning of repolarisation. Excitation sequence together with intrinsic ventricular recovery properties, which are determined by action potential form and duration, are responsible for ST-T deflection waveform. The effects of activation sequence on the ST-T deflection limit the utility of the deflection as an index of ventricular recovery properties. Alteration of these properties is one of the most frequent effects of myocardial disease and it is likely that the recognition of disease could be improved if the effects of recovery properties and excitation sequence on ST-T waveform could be differentiated.

During the QRS complex, myocardium is changing from the resting to excited state while events during the ST-T deflection consist of a return to the resting condition. Effects of activation sequence on the ST-T deflection are therefore of opposite polarity to those on the QRS complex, and it is likely that effects of that sequence are cancelled by algebraic addition of the deflections. Addition of instantaneous QRS and ST-T deflections involves uncertainty as to the proper time phase of the deflections, but the area of QRS and ST-T deflections can be added without ambiguity to provide an index of ventricular recovery properties. This possibility was first recognised by Wilson et al who expressed the QRST area from limb leads in vector form and titled that quantity the "ventricular gradient." Wilson et al reported evidence that the ventricular gradient was independent of activation sequence but later studies yielded conflicting findings. Despite those results, it remains possible that the QRST deflection area is an index of recovery properties. Evidence has been obtained that ventricular recovery properties are altered by different electronic interactions during varied activation sequence. Such alterations of recovery properties are small and would be expected to result in small changes of the QRST area with respect to changes in the QRS and ST-T deflection areas considered separately.

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Qualitative evidence that the QRS deflection area in extensively sampled body surface ECG's and cardiac surface electrograms is largely independent of ventricular activation sequence has been previously published. Evidence that induced changes of ventricular recovery properties in localised cardiac regions were associated with changes of QRS deflection areas in electrograms from these regions has also been published. In that study, the distributions of QRS deflection areas on the cardiac surface showed only minor differences during supraventricular and ectopic ventricular pacing but the differences were not evaluated quantitatively. Quantitative evaluation of the independence of QRS deflection area from ventricular activation sequence is desirable to confirm previous qualitative impressions and to establish the extent to which the quantity can be used as an electrophysiological marker of changes in ventricular recovery properties in the presence of conduction delays or ectopic activation. In light of recent theoretical evidence establishing the independence of QRS area and activation sequence, we here report experimental confirmation of the prediction. In this study we determined the variability of QRS, ST-T and QRS deflection areas in extensively sampled body surface electrocardiograms during varied activation sequences. Results showed the QRS area to be markedly less influenced by activation sequence than either QRS or ST-T deflection areas. This finding is compatible with the QRS deflection areas reflecting ventricular recovery properties.

Methods

Experiments were performed on 12 closed chest dogs anaesthetised with pentobarbital 30 mg·kg⁻¹. Animals were maintained on artificial respiration using a respirator that could be halted at a fixed phase of the respiratory cycle. Bipolar pacing catheters were placed in the right atrium and right and left ventricles and used to pace the heart regularly at a rate faster than the spontaneous rhythm. Two to 25 different ventricular activation sequences were produced including ones resulting from atrial and simultaneous atrial and ventricular stimulation. Additional activation sequences were produced by varying the time phase between stimuli at two or more sites in 10 ms steps. These included atrial stimulation with delay of right or left ventricular stimulation, simultaneous atrial and right ventricular stimulation with delay of left ventricular stimulation and simultaneous atrial and left ventricular stimulation with delay of right ventricular stimulation.

Body surface electrocardiograms from 192 sites were recorded simultaneously on magnetic tape. Electrodes were stainless steel needles placed subcutaneously in 16 vertical columns of 12 electrodes each. Columns were uniformly spaced around the thoracic circumference and electrodes in each column were uniformly spaced between the levels of the upper abdomen and cervicothoracic junction. Electrocardiograms were recorded using a multiplexing system consisting of six time division multiplexers each of which switched 32 signals onto a single channel once each millisecond. Each of the six multiplexer outputs was recorded on a single channel of a wideband FM instrumentation recorder at a tape speed of 120 ips. A seventh tape channel was used to record a clock signal synchronised to the multiplexers and used for later demultiplexing of the data. A real time display of all 192 leads permitted verification that all channels were operative. Leads were recorded from each thoracic electrode paired with a Wilson central terminal from three limb electrodes. Recordings were made for a period of 10 s for each activation sequence while respiration was halted in the expiratory phase.

Data were computer processed to yield scalar waveforms and isoarea maps of the QRS, ST-T and QRS deflection areas calculated by integrating the ECG's over the appropriate intervals. Data tapes were played back at 7½ ips, digitised and stored on digital magnetic tape. One or more cardiac cycles were chosen for analysis from each activation sequence. Each lead was baseline adjusted using linear interpolation between corresponding times of consecutive TP segments and gain corrected using a prerecorded calibration signal. When a recording was inadequate because of excessive noise or amplifier failure, potentials at that site were estimated as the average of potentials at neighbouring sites. The resulting data were permanently stored on tape and isoarea maps were calculated and plotted. The onset of QRS, end of QRS and end of T deflections were manually selected from an RMS voltage versus time curve for each complex analysed. This curve expresses the average signal voltage over the total thorax.

Since the main endpoint of this study was to quantitatively validate the hypothesis that the body surface distribution of QRS area was less "variable" than those of QRS and ST-T areas, a statistic of variability had to be defined. In light of the considerable spatial dependency of body surface potentials pooling variances from all 192 sites could not be used without the tedious removal of interdependent variance between leads. However, if the 192 variables in each distribution could be accurately represented by a smaller set of canonical (orthonormal) variables, then the variances of the
FIG 1  Body surface distributions of QRS, ST-T and QRST areas for supraventricular (SV), right ventricular (RV), left ventricular (LV) and simultaneous right plus left ventricular (RV + LV) paced beats. In each panel, isosurface contours are drawn at 10 mVms increments. QRS, ST-T and QRST areas in each ECG were obtained by integrating the waveforms over the QRS, S-T, and Q-T intervals respectively. The plus and minus signs identify electrode sites on the body surface and indicate area polarities. Top and bottom rows of sites correspond to levels of the suprasternal notch and umbilicus respectively. Central columns correspond to the anterior thoracic midline and the lateral columns correspond to sites just right and left of the spine.
canonical variables could be pooled directly since there would then be no inter-variable dependence. The method of principal components analysis provides such an orthonormal basis with which multivariate data with inter-variable correlation can be accurately represented in a space of smaller dimensionality. Specifically, all QRS and ST-T distributions (192 dimensional vectors) were used to estimate the 192 × 192 dimensional covariance matrix of areas. Eigenvectors of the covariance matrix and their corresponding eigenvalues were estimated using the power method which iteratively selects these in decreasing order of eigenvalue magnitude (Goertzel and Tralli). The eigenvectors, when normalised, form an orthonormal basis with which to represent the original distributions. The eigenvalues yield the variance of the area distributions along their respective eigenvectors in the multidimensional space. Each individual area distribution of 192 dependent areas, when represented along the basis vectors resulted in a vector of uncorrelated variables of dimension n < 192. For each experiment, area variability was determined by calculating variances of QRS, ST-T and QRST across all activation orders and along each of the independent dimensions and then pooling the variances over all dimensions. The justification for pooling is that the dimensions are independent.

Beat-to-beat variation was evaluated in one experiment. Three consecutive beats for each of four activation orders were analysed. These activation orders were induced by pacing from the right atrium, right atrium plus right ventricle, right atrium plus left ventricle, and right atrium plus simultaneous left and right ventricles, and the variability of the QRS, ST-T, and QRST areas were calculated as described above.

Results

One dog's body surface QRS, ST-T and QRST area maps for four different activation orders are shown in the fig. The QRST distribution for each activation order is obtained by adding the QRS and ST-T distributions for that activation order. The distributions of QRS and ST-T deflection areas differ markedly with activation order, whereas for distribution of QRST deflection areas remains nearly constant over the four activation orders. The striking similarity of QRST area distributions for varied activation was a consistent observation in all experiments. The area magnitudes seen in these examples were typical for all experiments which showed a range of ±200 mVms.

From calculations of the eigenvectors and eigenvalues of the area covariance matrix, it was determined that the first eight, in decreasing order of importance, accounted for 99.1% of the trace of the covariance. That is, the eight orthonormal basis vectors could be used to accurately represent the 192 dimensional area distributions. Alternatively, the coefficient of determination between measured areas and those represented on the 8 basis vectors was 0.991. In light of this result, each QRS, ST-T and QRST area distribution of 192 dependent measurements was represented by an eight dimensional vector of independent variables. Variances were calculated as described above by reducing each 192 dimensional area distribution to an eight dimensional vector of uncorrelated variables. Variances across activation orders of the eight variables were pooled separately for QRS, ST-T and QRST in each experiment and are tabulated in table 1. The number of activation sequences in each experiment are indicated. As shown in the table, the variability of QRST deflection areas was markedly less than that of either QRS or ST-T deflection areas.

As may be noted from table 1, there is considerable variability in the QRS, ST-T or QRST areas from experiment-to-experiment. This was not unexpected since no attempt was made to use dogs of the same breed, shape or weight. This lack of uniformity of experimental animals, plus the fact that different activation orders and numbers of activation orders were used would be expected to contribute to the observed differences. In spite of this inter-experiment variability, the high ratio of QRS or ST-T to QRST area variability (F statistics) over all experiments was a consistent finding. Within each experiment QRS and ST-T variabilities were significantly greater than QRST variability at the P < 0.01 level.

The variability of QRST deflection areas as well as those of QRS and ST-T deflection areas could not be accounted for on the basis of beat-to-beat variation.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>No of activations</th>
<th>Variability (mV²ms⁻² · 10⁴)</th>
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<tr>
<td></td>
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<td>QRS</td>
</tr>
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</tr>
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</table>
Beat-to-beat variability of body surface QRS, ST-T and QRST areas was assessed in a representative experiment using data from three beats for each of four different activation orders and are shown in table 2.

Discussion

This study quantitatively demonstrated that variability of the body surface distribution of QRST deflection areas with varied activation sequence was markedly less than the variability of either QRS or ST-T deflection areas. This finding is compatible with the theoretic possibility that algebraic addition of QRS and ST-T deflection areas results in cancellation of the effects of activation sequence. The cardiac factors responsible for the QRS and ST-T deflections are ventricular activation sequence and ventricular recovery properties. Since the QRST deflection area was found to be much less affected by activation sequence than either QRS or ST-T area, it is likely that the QRST area is largely determined by intrinsic ventricular recovery properties.

The study also demonstrated that although QRST area variability was small compared to that of QRS and ST-T deflection areas, the QRST area did vary with activation sequence. This variability could not be accounted for on the basis of beat-to-beat variation which includes measurement errors as well as physiological changes. The variability observed is compatible with previous evidence that intrinsic ventricular recovery properties are modified by activation sequence. The most likely mechanism for such modification is that of electrotonic interactions during repolarisation. Such interactions have been demonstrated in Purkinje tissue and in the atrioventricular node and Purkinje-papillary junction. Electrotonic interactions between the sinus node and adjacent cells during repolarisation have been reported and propagated repolarisation in ventricular fibres of dog and cat has been demonstrated. Alterations of refractory periods in the intact heart due to altered excitation sequence have been reported. The present study does not furnish direct evidence of modified recovery properties due to different electrotonic interactions during varied activation sequence. Since such modifications have been demonstrated in other studies however, they could be expected to modify the QRST deflection area if that quantity is an index of ventricular recovery properties. The small variations of QRST deflection area with varied activation sequence found in this study suggest that these areas reflect recovery properties.

Finally, findings in the study demonstrate that the relative independence of QRST deflection area from activation sequence is applicable to the extensively sampled body surface electrocardiogram. Since such an examination provides local cardiac information, this finding suggests it may be possible to evaluate ventricular recovery properties in local cardiac regions by means of the QRST area. This supports the conclusions of a previous study in which changes of the body surface distribution of QRST deflection areas were shown to be related to arrhythmia vulnerable states having greater than normal inequality of ventricular recovery properties.

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References

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