Computer Modeling of Cardiac Repolarisation for the Analysis of the Electrocardiogram

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Abstract

This paper describes the methods and techniques used to develop a computer model of left ventricular repolarisation, and the results obtained using the model to investigate cardiac repolarisation and its manifestation on the surface electrocardiogram. We showed that normal T waves can be generated by the model for a normal repolarisation of the left ventricle, with a physiological value of dispersion of repolarisation of 20 ms. The time course of body potentials agrees with published experimental results. Increasing dispersion to a pathological value 100 ms, T waves became symmetric. The model was able to simulate normal U waves correctly.

1. Introduction

Heart disease and associated arrhythmias are the most common cause of death in Europe and United States. Research to improve their diagnosis, treatment and prevention has made huge progress in the recent years. It is now clear that inhomogeneities in the repolarisation of the ventricles are responsible for re-entrant type arrhythmias[1]. A robust non-invasive measure of repolarisation inhomogeneities has not been found yet. Also the genesis of the electrocardiographic T and U waves associated with ventricular repolarisation, are not fully understood.

The work described in this paper was prompted by the problem of finding new ways to measure repolarisation abnormalities from the 12-lead electrocardiogram, and in so doing also gain a better understanding of the genesis of T waves and U waves. In particular, we studied the body potential distribution during repolarisation, the 12-lead ECG T wave shape in physiological conditions, the effect of increased dispersion of repolarisation on the T wave shape, and the genesis of the U waves.

2. Methods

A novel computational model of left ventricular repolarisation[2] has been developed. It uses an experimentally derived repolarisation sequence in a 3-dimensional left ventricle, embedded in a 3-dimensional torso, to reproduce the 12-lead ECG and associated potentials on the torso surface. The model is original because it can simulate repolarisation independently of repolarisation.

2.1. Geometric model

The torso surface was represented by a cylinder 50 cm tall with an elliptic cross-section (major diameter 34 cm, minor diameter 26 cm) as shown in fig. 1.

The dimensions of the cylinder were chosen as in Gelernter et al[3]. The torso was considered electrically homogeneous and isotropic with a conductivity equal to 0.3 S/m.

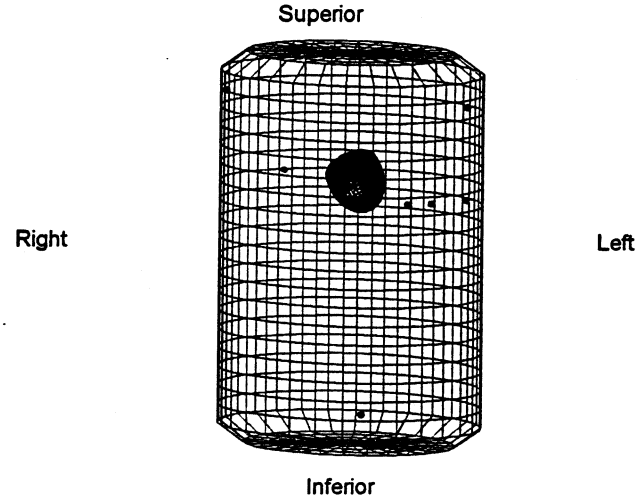

Figure 1. Geometric model of the torso, and the left ventricle. Dots indicate the location of the virtual electrodes used to compute the 12-lead electrocardiogram.

The surface describing the left ventricle comprised both epicardial and endocardial surfaces and is shown in fig.1. It was modelled by a truncated ellipsoid representing the epicardium with dimensions: height 10.6 cm truncated at 7.0 cm, major diameter 7.0 cm, minor diameter 6.6 cm. An approximately ellipsoidal cavity represented the endocardium. This cavity had an height of 4.8 cm. The left ventricle (LV) was considered electrically homogeneous and isotropic: the intracellular

conductivity was 0.1 S/m, the extracellular conductivity 0.2 S/m.

2.2. Action potential

A template of a myocardial cell transmembrane action potential (AP) was associated with each point in which the left ventricle had been subdivided.

To reproduce left ventricular repolarisation, only the repolarisation phase of the AP was modeled. Figure 2 shows the template used in the model. The shape and duration of phase 3 is the same across all the left ventricle. While the plateau phase (phase 2) has a constant value(+20 mV) and its duration varies across the left ventricle.

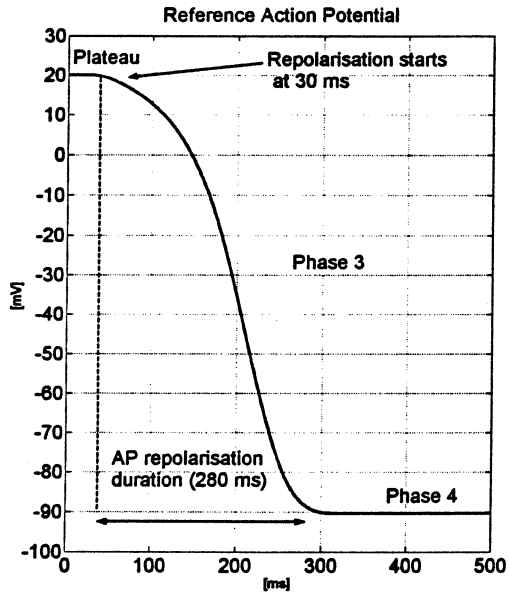

Figure 2. Template of action potential repolarisation used in the model.

To investigate the effects of alterations in the normal action potential shape by after-potentials, an additional template was generated as shown in fig. 3.

2.3. Computer simulations

Using the model of LV repolarisation, the potentials on the torso surface and the 12-lead ECG were computed by means of standard techniques[2,4].

T waves were simulated for a value of dispersion of repolarisation equal to 20 ms, corresponding to values found in normal subjects[5].

T waves in the 12-lead ECG were simulated again increasing the value of dispersion of repolarisation to 100 ms.

The action potential with after-potential in fig. 3 was then used to compute the 12-lead ECG, with a value of dispersion equal to 20 ms.

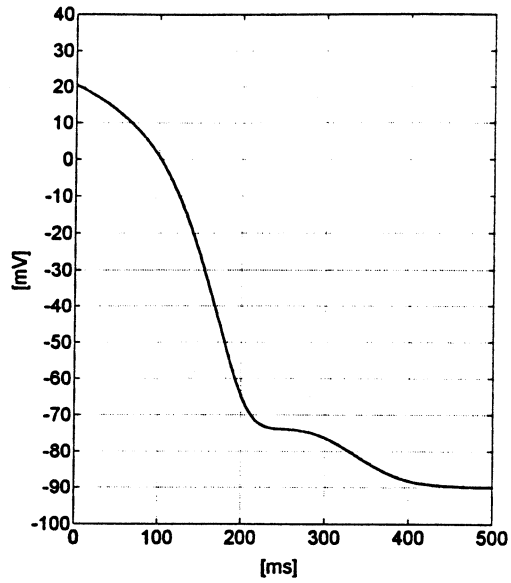

Figure 3. Template of action potential exhibiting an after-potential prolonging the repolarisation phase.

2.4. Repolarisation sequence of the left ventricle

To model repolarisation of the left ventricle, this was, initially, completely depolarized with all the action potentials in the plateau phase (phase 2).

A specific repolarisation starting time was set for each point on the left ventricular surface (both epi- and endocardium) according to a published experimental repolarisation sequence[5]. The repolarisation starting time for a given point was defined as the time when its action potential began the repolarisation phase (phase 3), completing repolarisation on reaching the resting potential. Figure 2 shows an AP with a repolarisation starting time equal to 30 ms. As this figure shows, the duration of the plateau phase (phase 2) determines the AP repolarisation starting time, i.e. the beginning of the AP repolarisation phase (phase 3). The time interval between end of repolarisation of the first and last AP in the left ventricle to repolarise is the dispersion of repolarisation in the model.

2.5. T wave shape feature

To quantify the shape of the T wave two features were computed: (1)Symmetry ratio of the area (SR area). Defined as the area from the beginning of the T wave to the peak divided by the area from the peak to the end; (2) Symmetry ratio of the time (SR time). Defined as the time interval from the beginning of the T wave to the peak divided by the interval from the peak to the end. A value of symmetry ratio close to one indicates a T wave with a symmetric shape.

3. Results

3.1. General repolarisation features

Figure 4 shows the body surface potential generated by the model during repolarisation for a physiological value of dispersion equal to 20 ms. Body potential distributions are displayed at 0 ms, 100 ms and 200 ms from the beginning of repolarisation. At 200 ms the potential reaches its highest values.

The body surface potential distribution generated by the model is in qualitative agreement with the one experimentally observed in healthy human subjects.[6] As in the experimental sequence[6], at the beginning of repolarisation, the torso is equipotential.

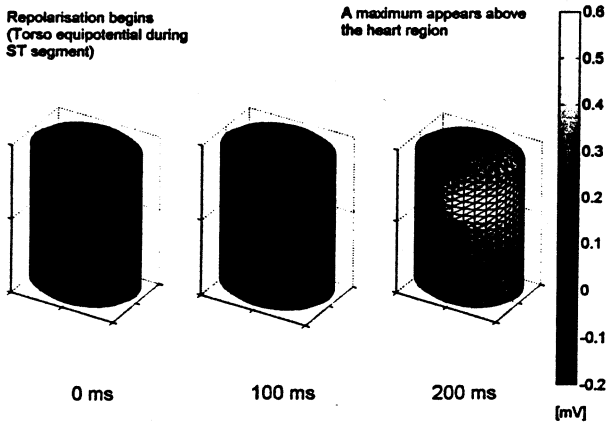

Figure 4. Body surface potentials generated by the model during left ventricular repolarisation with a value of dispersion equal to 20 ms.

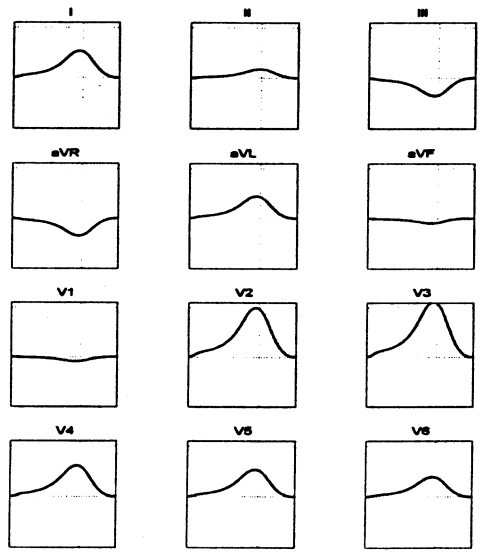

Figure 5. Simulated T waves in the 12 leads. In each graph, the y-axis varies from -0.5 mV to 0.5 mV, and the x-axis from 0 ms to 300 ms, in 200 ms steps.

Body potentials then show a dipolar distribution with a maximum in the left mammary region.

3.2. Simulation of normal T waves

Figure 5 shows the simulated T waves for a physiological values of dispersion of 20 ms. The asymmetrical shape, amplitude and orientation agree with normal ECGs. Simulated T wave amplitudes varied from –0.18 mV (aVR) to +0.56 mV (V3).

3.3. Effect of dispersion of repolarisation

Figure 6 shows the simulated T waves in lead V2 for a value of dispersion equal to 20 ms (left) and of 100 ms (right). The values of the symmetry ratios are reported in the same figure. For a physiological value of dispersion of 20 ms, simulated T waves in the 12 leads appear as in normal subjects. This is confirmed also by the value of the symmetry ratio of the area close to 1.5, in agreement with the published value for normal subjects.[7]

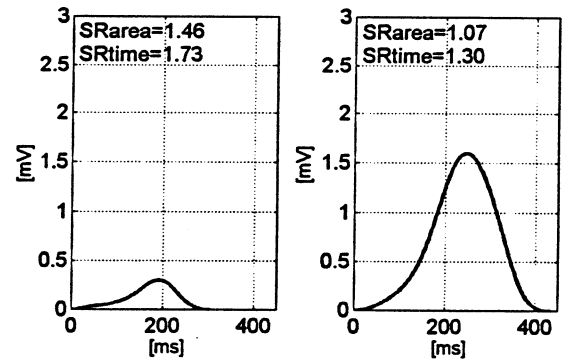

Figure 6. Simulated T waves in lead V4 for a value of dispersion equal to 20 ms (left) and of 100 ms (right), with corresponding values of the symmetry ratios.

When dispersion was increased, T wave increased in amplitude and became symmetric in shape. These upright, symmetric T waves are observed in clinical practice in patients with ischemic heart disease[8]. Their origin has not been yet explained. The model suggests that this happens because of an increased dispersion of repolarisation in the left ventricle[9].

3.4. After potentials and U waves

We computed the 12-lead ECG using the model with a value of dispersion of 20 ms, but using the AP template with after-potential shown in fig. 3. The simulated 12-lead ECG, reported in fig 7, shows a normal T wave followed by a U-wave. Observe the polarity of the U wave, always concordant with the T wave, and its asymmetric shape, with a shorter ascent than descent. Simulated U waves duration was 228 ms, their amplitude was 18% of the amplitude of the preceding T wave. These values are in agreement with values reported by Surawicz for normal subjects.[10]

4. Discussion and conclusion

Complex and detailed computational models of the heart are being developed. Their aim is the modeling of all the different aspect of heart physiology, starting from the cellular level. In this work, however, we have shown that the investigation of some relevant clinical problems in cardiac electrophysiology and electrocardiography can be tackled using simplified models of the electrical activity of the heart. These models incorporate only the levels of detail necessary to describe the process of interest. A new model of left ventricular repolarisation was devised. The approach used is original, since it allowed the knowledge of the depolarisation sequence and of action potential duration gradients across the left ventricle to be ignored.

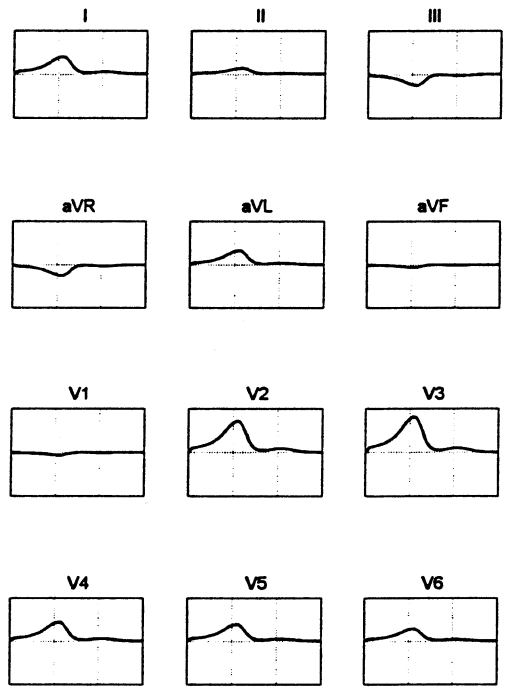

Figure 7. Simulated U waves in the 12 leads. In each graph, the y-axis varies from -0.5 mV to 0.5 mV, and the x-axis from 0 ms to 600 ms, in 200 ms steps.

We showed that T waves generated by the model for a simulated normal repolarisation sequence, are in agreement with T waves recorded from healthy subjects. It was thus possible to use the model to study the effect on the surface ECG of an increase in dispersion of repolarisation in the left ventricle. We were able to show that low dispersion is represented by asymmetrical T waves and high dispersion by increasingly tall, broad and symmetrical T waves. Results reported here indicate that there is a link between T wave shape and abnormal dispersion of repolarisation, and offer a theoretical framework in which to explain the occurrence of broad, tall and symmetric T waves in a variety of pathological conditions.

The same model was applied to the investigation of the origin of the U wave, which is still an unsolved problem in electrocardiology. The action potential was modified to include an after-potential prolonging its repolarisation phase. Our results show that an action potential exhibiting an after-potential prolonging its repolarisation phase is sufficient to generate normal U waves in the 12-lead ECG. The model suggests that one of the most favored theories[10] of U wave genesis may be indeed correct. This theory attributes U waves to after-potentials prolonging the action potential repolarisation phase. After-potentials are possibly caused by mechanical stretch.[10] This theory has never been verified experimentally for technical difficulties involved in recording the transmembrane action potential in vivo. To our knowledge, this is the first time such a theory has been verified in a computer model[11].

Acknowledgements

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