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Action potential duration gradients in the heart ventricles and the cardiac electric field during ventricular repolarization (a model study)☆

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Abstract

Background: We simulated contributions of transmural, apicobasal, anteroposterior and interventricular action potential duration (APD) gradients to the body surface potential distribution (BSPD) with constant or varied magnitudes of the transmural and apicobasal gradients.

Methods: Simulations were done in the framework of the discrete computer model of the rabbit heart ventricles on the basis of realistic activation sequence and APDs. The APD gradients were set constant at 20 ms or varied in the range of ±80 ms.

Results: The apicobasal, transmural and interventricular APD gradients of 20 ms produced similar BSPDs, whereas the BSPD inversion was caused by the inverted apicobasal or transmural 80 ms gradients. The transmural APD gradient produced transversal and mainly apicobasal T-wave vectors due to wall curvature and cancellation effects. The "normal" transversal and apicobasal repolarization gradients were decreased and increased by activation sequence, respectively.

Conclusion: The different APD gradients contributed consistently to the development of BSPD.

Keywords: APD gradient; Activation; Repolarization; *T*-vector; Body surface potential distribution; Rabbit

Introduction

On the basis of biophysical principles, any wave on the body surface ECG represents a resulting voltage gradient generated by cellular electrical activity within the heart. In the period of repolarization, the voltage gradients in the heart ventricles resulted from the differences in action potential duration (APD) and the differences in activation times between the different parts of the ventricles [1]. Experiments revealed transmural, apicobasal, left-to-right and anterior–posterior APD gradients in the heart ventricles with the magnitude of these gradients being different in various species or conditions [2–6]. All these gradients could contribute to the *T*-wave; however, there is no consensus on which one is the most significant in the development of the *T*-wave.

The measurements in the normal human and animal hearts *in vivo* showed the negligible if any transmural repolarization gradient. Accordingly, it was suggested that the *T*-wave results primarily from the apicobasal differences in repolarization times [3,4,7,8]. On the other hand, the measurements *in vitro* detected no notable apicobasal repolarization gradient but a significant transmural gradient. Consequently, the conclusion was that the transmural gradient plays a predominant role in the genesis of the *T*-wave [2,9–12]. However, the most studies were devoted to the transmural gradient in the left ventricular wall while it is also presented in the right ventricle as well as in the interventricular septum [13–15]. In view of the fact that the mass of the septum is comparable with the left ventricular free wall mass, the septum could contribute much to the resulting repolarization gradient. The experiments, as well as computer simulations, showed that both the transmural and the apicobasal APD gradients can generate concordant *T*-waves and body surface potential distributions [5,12,16]. However, it remains unclear how the two different gradients can produce the similar electric field.

The objective of the present study was to simulate the contribution of the transmural, apicobasal, anterior–posterior and left-to-right APD gradients and their combinations to the *T*-vector and the body surface potential distribution in two conditions: when the magnitudes of each gradient were the

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same and under the changes of the apicobasal or transmural APD gradients. Though the magnitudes of APD gradients in different directions can vary substantially in the real heart, this simplification allows us to make an objective comparative analysis of the significance of separate APD gradients. Further, we examined the effect of the activation sequence as the other contributing factor to the cardiac electric field in the period of repolarization.

Materials and methods

Model description

Simulations were carried out in the framework of the so-called cellular automaton, a discrete computer model of the rabbit heart ventricles on the basis of the recent experimental measurements reported from our group [17]. The shape of the model was reconstructed from the transversal and longitudinal cross-sections of the rabbit ventricles. The model had a hexagonal structure and consisted of ≈100,000 cells with intercellular space of 0.25 mm [18]. Each model cell had 12 equidistant "neighbors". The input of the model was: (1) the APD and (2) the values of activation times in 20 nodal points distributed over the epi- and endocardium of the model. The values of APD and activation time in each model cell were simulated on the basis of the values in the nodal points by interpolation [17]. The morphology of the action potentials was simulated using the rabbit ventricular action potential model [19] and was modified by lengthening/shortening the repolarization phase depending on the duration value in each model cell. Activation times in the model corresponded to the experimental data [17,20]. The APD values and the APD gradients were set in the physiological range. The outputs of the model were the (1) APD distribution, (2) activation and repolarization sequences, (3) resultant electrical *T*-vector and (4) the body surface potential distribution.

Body surface potentials calculation

The body surface potentials were calculated as:

$$V_{\text{obs}} = -K^{*}\sum_{i=1}^{N}\mathbf{Grad}_i{}^{*}\mathbf{R}/R^3,$$

where V_{obs} is the potential value in the observation point, located on the body surface; K is the volume conductor property factor; $\mathbf{R}$ is the vector, directed from the ith model cell into the observation point; $\mathbf{Grad}_i$ is the gradient of the action potential value in the ith model cell; and N is the total number of model cells.

The value of $\mathbf{Grad}_i$ in each time moment was calculated as:

$$\mathbf{Grad}_i = \sum_{k=1}^{12}\mathbf{R}_k{}^{*}(p_i - p_k),$$

where $\mathbf{R}_k$ is the vector, directed from the ith model cell to one of 12 neighboring model cells; p_i is the potential value in the ith model cell; and p_k is the potential value in one of 12 neighboring model cells in the given time moment. Potential values in each model cell varied in the range from −85 to 17 mV according to the given AP morphology.

The realistic geometry of the rabbit torso and the heart orientation parallel to the cranial-to-caudal axis were used in the simulation of the body surface potentials.

T-vector calculation

The *T*-vector in each time moment was calculated as the sum of action potential gradients in all model cells:

$$T = \sum_{i=1}^{N}\mathbf{Grad}_i,$$

The *T*-vector was calculated in the Cartesian coordinate system bounded to the ventricles. The apicobasal axis was directed from the base to the apex; the anterior–posterior axis was directed from posterior to anterior, and the left-to-right axis was directed from the right to the left ventricle. The *T*-vector was simulated for the whole model as well as for its separate parts: the left and the right ventricular free walls, interventricular septum, and the apex.

APD distributions

Nine APD distributions produced by single APD gradients (transmural, apicobasal, anterior–posterior and left-to-right) as well as by the combinations of these gradients were simulated (Fig. 1). Each single APD gradient had the same value of 20 ms. The transmural APD profiles in the model were set linear with the progressive increase from the epicardium to the endocardium and no M-cell-like behavior according to the previously obtained experimental data [17] (Fig. 1, A). Modeling the apicobasal gradient, we set the basal APD 20 ms longer than the apical ones (Fig. 1, B). Modeling the anterior–posterior gradient, we set the APD of the posterior epicardium of the ventricular base 20 ms longer than that on the anterior epicardium (Fig. 1, C), and the left-to-right gradient was simulated by setting the APD of the lateral epicardium of the right ventricular base 20 ms longer than that of the lateral epicardium of the left ventricular base (Fig. 1, D). In other simulations (Fig. 1, E–I), the model included two to four APD gradients simultaneously.

In addition, we simulated a set of combinations of transmural and apicobasal APD gradients, where one of the gradients was varied from −80 to 80 ms while the other was kept constant at 20 ms. The negative value of the transmural and the apicobasal APD gradients meant that the epicardial APD was longer than the endocardial APD, and the apical APD was longer than the basal APD, respectively.

Results

Activation sequence

The activation sequence of the rabbit heart ventricles (Fig. 2) was simulated on the basis of experimental data [20]. Activation spread from the apex to the base of the ventricles and from the endocardium to the epicardium. The right