The positive T wave

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Abstract

introduction The instant of maximum slope (T_{up}) of the T wave in the unipolar electrogram is a well-established measure of repolarisation time (T_{R}). Nevertheless, recent observations on positive T waves have caused a renewed debate. The purpose of this study was to elucidate the mechanism that leads to positive and negative T waves and to investigate which electrogram feature best predicts T_{R}.

methods We simulated propagating action potentials (AP) and electrograms with a bidomain reaction-diffusion model of the human heart including heterogeneous ion-channel properties. To explain positive T waves we compared results with those of a much simpler model, which predicts T waves from local and remote AP.

results T_{R} was defined as the instant of steepest downstroke of the AP. T-wave polarity was mostly determined by T_{R}. Positive T waves occurred at early-repolarising sites. Correlation between T_{up} and T_{R} was > 0.99, in both negative and positive T waves. T-wave area and peak value also correlated highly with T_{R}.

conclusion The polarity of the T wave is primarily determined by T_{R}. Positive T waves occur at early-repolarising sites. Local T_{R} is best estimated by T_{up}, also in positive T waves.

List of abbreviations

APD action potential duration, 5, 8

LV left ventricle, 5

RV right ventricle, 5

UE unipolar electrogram, 4, 5, 9

T_{down} instant of steepest downstroke of the T wave, 4, 8

T_{R} Repolarisation time, 6, 8

T_{up} instant of steepest upstroke of the T wave, 4, 8

ϕ_{e} extracellular potentials, 5

1 Introduction

Measurement of repolarisation time from the unipolar electrogram (UE) is important for clinical studies of repolarisation abnormalities, as well as for experimental studies. It is therefore necessary to understand how the T wave in the electrogram is generated, and how it relates to local repolarisation time. The recent debate on repolarisation measurement in positive T waves [1–3] demonstrates that this understanding is incomplete.

Wyatt et al. [4] proposed to use the instant of steepest upstroke (T_{up}) of the T wave in the UE as a measure of local repolarisation. Experimental and theoretical studies have confirmed the validity of this method [1]. Other authors have proposed that an exception should be made for positive T waves, using the instant of steepest downstroke (T_{down}) of the T wave in the UE instead of T_{up} [5, 6].

In this study, we used a detailed 3-dimensional computer model of the human heart to show how, according to existent biophysical knowledge, the shape of the T wave is determined. We used the simulated electrograms to evaluate T_{up} and relate it to repolarisation time as determined from the underlying action potentials.

2 Methods

V_m and extracellular potentials (ϕ_e) were simulated with a computer model of the human heart that has been described previously [7]. This model has anisotropic myocardium and heterogeneity of membrane properties (table 1). Propagating action potentials were computed by a monodomain reaction-diffusion model. Ionic currents were computed with the TNNP model for the human ventricular myocyte [8]. Some parameters of the ionic model were changed, and differences between the left ventricle (LV) and right ventricle (RV) were implemented according to published data (on canine hearts) [9, 10], as outlined in table 1. The types XL and XS (table 1) were used to implement abnormally long and short action potential duration (APD) in some experiments.

[Table 1 about here.]

Two different models were used for the computation of ϕ_e: a "realistic model" and a "simple model." The realistic model computed ϕ_e from V_m throughout the heart by solving

$$\nabla \cdot ((G_i + G_e)\nabla \phi_e) = -\nabla \cdot (G_i \nabla V_m) \tag{1}$$

where G_i and G_e are the intracellular and extracellular conductivity tensor fields, respectively [7]. The reference potential for electrograms was taken from the roof of the right atrium.

If it is assumed that the heart and intracavitary blood are uniformly isotropic and that the reference point is equally well connected with any position in the ventricles, then the UE at a point x is simply a scaled mirror image of the difference between the local V_m and the average V_m in the ventricular myocardium (V_{avg}):

$$\phi_{e,simple}(x) = -\frac{\sigma_i}{\sigma_i + \sigma_e}\left(V_m(x) - V_{avg}\right) \tag{2}$$

where σ_e and σ_i represent the conductivities of the extracellular and intracellular domains, respectively. The "simple model" used this formula. For the fraction $\sigma_i/(\sigma_i + \sigma_e)$ the value 0.25 was chosen.

Simulations were performed with a normal-heart model and models containing a modified zone of 10 mm radius located in the LV free wall. This zone had either abnormally short or abnormally long APD.

T waves could be positive, negative, biphasic, or multiphasic. To allow a division into positive and negative T waves, we evaluated the areas enclosed by the zero line and the electrogram, from the instant 100 ms after local depolarisation to the end of the simulation. A T wave was defined as positive when the positive area exceeded the negative area. Repolarisation time (T_{R}) was defined as the instant of steepest downstroke of V_{m}. T_{R} and T_{up} were evaluated in the interval from 100 ms after local depolarisation to the end of the simulation (500 ms after the first activation). For positive T waves, T_{down} was evaluated in the interval from T_{up} to the end of the simulation. For negative T waves, T_{down} was not assessed.

3 Results

Figure 1, panel A, demonstrates the simple model for one site in the heart. In panel B, electrograms are compared that were computed with the "simple" and "realistic" models. These simulated electrograms were highly similar. The two models agreed on the polarity of the T wave in 90 % of the analysed positions (panel C, $N = 10^4$). Correlation between the T-wave area computed by the two models was 0.96 ($N = 10^4$).

These comparisons show that the T wave is essentially determined by the local V_m and by V_avg. The electrogram is positive when local V_m is lower than V_avg. This happens in particular for early-repolarising cells. The electrogram remains positive as long as there are depolarised cells elsewhere in the heart. This implies that all T waves, except for the latest repolarising area, must end positively. The examples in figure 1 illustrate this.

[Figure 1 about here.]

The simple model does not define electrogram shapes outside the myocardium. The realistic model reproduced the well-known shape of the cavity potential [11]. The simple model also failed to reproduce the low-amplitude electrograms that the realistic model predicted in thin trabeculae.

In the normal heart, positive T waves were found in 44 % of the analysed positions. Average T_R at locations with positive T waves was 40 ms earlier than at locations with negative T waves. In figure 2, panel A, T_R distribution is shown separately for positive and negative T waves. Most positive T waves were associated with T_R that were earlier than those of negative T waves, but some overlap between the two distributions was present. Figure 2, panels B and C, show that T-wave area and peak value correlate highly with T_R.

[Figure 2 about here.]

Figure 3 shows a sample of electrograms taken from various sites in the heart, selected to show the variation in T-wave shape from entirely positive through biphasic to negative. Local repolarisation times (T_R) are indicated with dots in the electro-

grams. These are invariably located on the upslope of the T wave. All T waves in this example end positively, and at the same time, as in the simple model.

[Figure 3 about here.]

Differences between repolarisation parameters were computed for $N = 10^4$ individual positions, and the average and standard deviation of the difference were computed. For positive T waves, T_{up} underestimated T_{R} by 0.1 ± 2.3 ms and T_{down} overestimated T_{R} by 28.7 ± 8.1 ms.

Figure 4 shows scatter plots comparing electrogram-based estimates of repolarisation with T_{R}. For negative T-wave morphologies, T_{up} correlated very well with T_{R}. The slope of the regression line was close to 1. For positive T waves the correlation was somewhat lower, but still very high. Correlation between T_{down} and T_{R} was much lower, and associated with a slope of only 0.65.

[Figure 4 about here.]

A simulation was performed with a small area in which cells had a very short APD (type XS in table 1). Statistics were compared with those of the normal heart. While differences in T_{up} (ΔT_{up}) correlated well ($r = 0.995$) with differences in T_{R} (ΔT_{R}), the differences in T_{down} (ΔT_{down}) were more weakly related ($r = 0.769$). Regression slopes were 1.015 for T_{up} and 0.392 for T_{down}. Analysis was limited to those waves that were positive both with and without XS zone ($N = 4280$).

4 Discussion

Our model predicts that 1) the polarity of the T wave is mostly determined by the difference between local membrane potential and the average of all membrane potentials in the ventricles. Positive T waves occur therefore at early-repolarising sites, negative T waves at late-repolarising sites. 2) Local repolarisation time is best estimated by the instant of maximum slope of the T wave, whatever its polarity. 3) Failure of this method is to be expected in thin isolated bundles. 4) All T waves end at the same time. 5) All but the very latest T waves end positively.

We have shown that at least for T waves in healthy tissue the UE can be understood as a downscaled and inverted difference between the local V_m and the average V_m in the heart. With this simple model, the meaning of the T wave in the UE is immediately clear. The signal is positive when the local V_m is more negative than the average, and negative when the local V_m is more positive. The most early-repolarising sites are therefore characterized by positive T waves. Later sites have an initially negative T wave, due to the decrease of the average potential caused by the earlier sites. When they repolarise themselves, their V_m quickly becomes more negative than the average, causing a rapid change in their UE from negative to positive. Only the latest repolarising sites have entirely negative T waves. In a computer model, not disturbed by noise and electrical interference, it is possible to see that all T waves are either positive or biphasic with a positive second phase, except at the very latest repolarising sites. In addition, all T waves end simultaneously. Both the "simple model" and the more realistic bidomain model demonstrate that the steepest upslope of the T wave is associated with the steepest downslope of local V_m.

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Table 1: *Selected parameters of the ionic model.*

	LV epi	LV M	(LV&RV) endo	**RV M**	**RV epi**	**XS**	**XL**
G_{to} (nS/pF)	0.294	0.294	0.073	**0.504**	**0.882**	0.294	0.073
G_{Ks} (nS/pF)	0.245	0.062	0.245	**0.112**	**0.490**	**0.735**	**0.010**
G_{Kr} (nS/pF)	0.096	0.096	0.096	0.096	0.096	0.096	**0.020**

Parameter values that are different from the original TNNP model [8] are printed in bold type. Units are nS = nanoSiemens, pF = picoFarad.

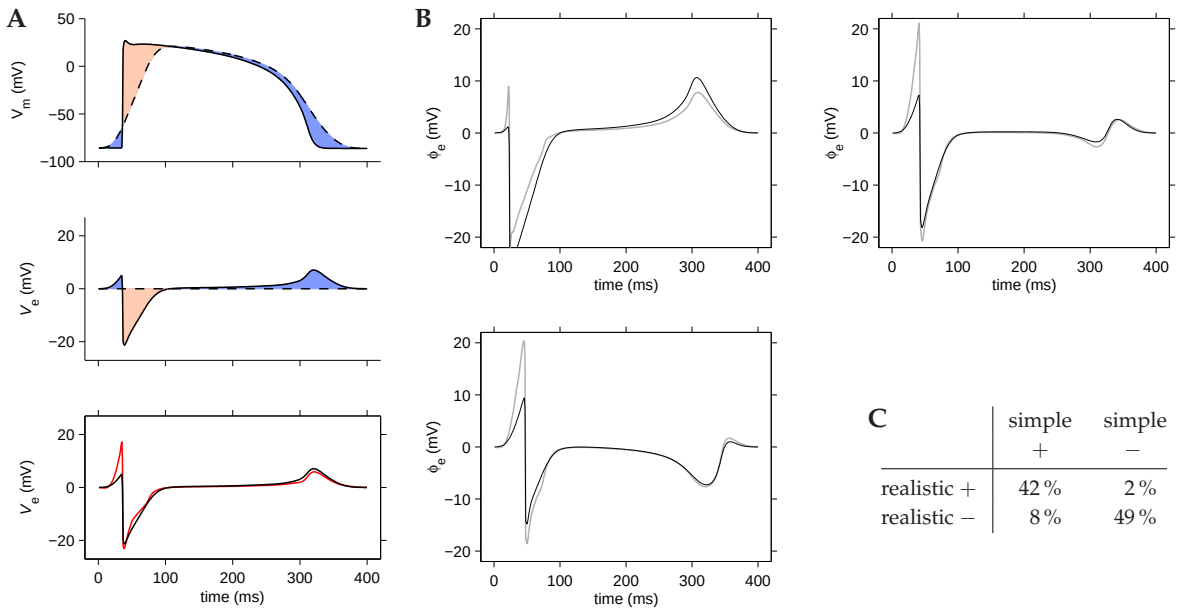

Figure 1: *Comparison between the simple and realistic models of the UE.* ***Panel A*** *shows how an electrogram is reconstructed according to the "simple model." The top panel shows V_{avg} (dashed line) and local V_{m} (drawn line) at a position in the right-ventricular subepicardium. The middle panel shows their temporal derivatives (dashed for dV_{avg}/dt). The lower panel shows the reconstructed electrogram. In* ***panel B****, electrograms according to the simple model (black lines) are compared to the realistic model (gray lines). In* ***panel C****, T-wave polarity according to the two models is compared for a sample of 10^4 positions randomly distributed in the ventricles.*

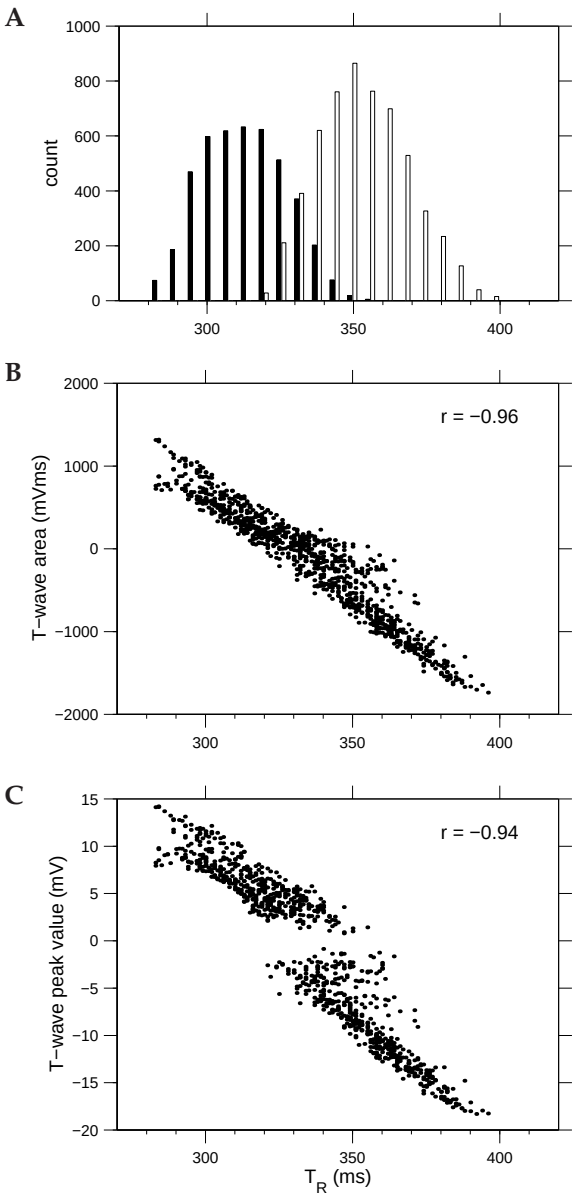

Figure 2: ***Panel A:*** *Distribution of T_R for positive T waves (black bars) and for negative T waves (white bars); $N = 10^4$.* ***Panel B:*** *scatter plot demonstrating the correlation between T_R and T-wave integral; $N = 1000$ for clarity.* ***Panel C:*** *scatter plot demonstrating the correlation between T_R and T-wave peak value; $N = 1000$.*

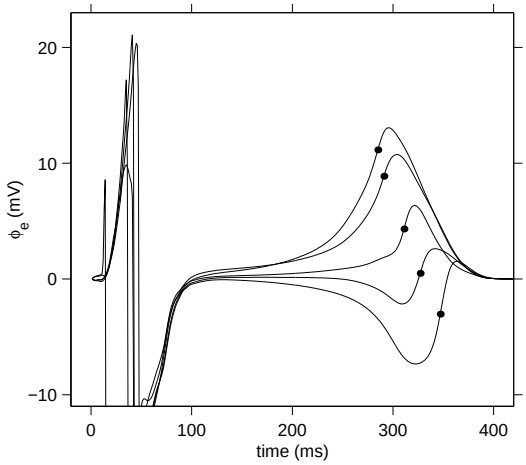

Figure 3: *Simulated electrograms from various sites in the ventricles, selected to show a variety of T-wave shapes from positive through biphasic to negative. Local* T_R *are indicated with dots.*

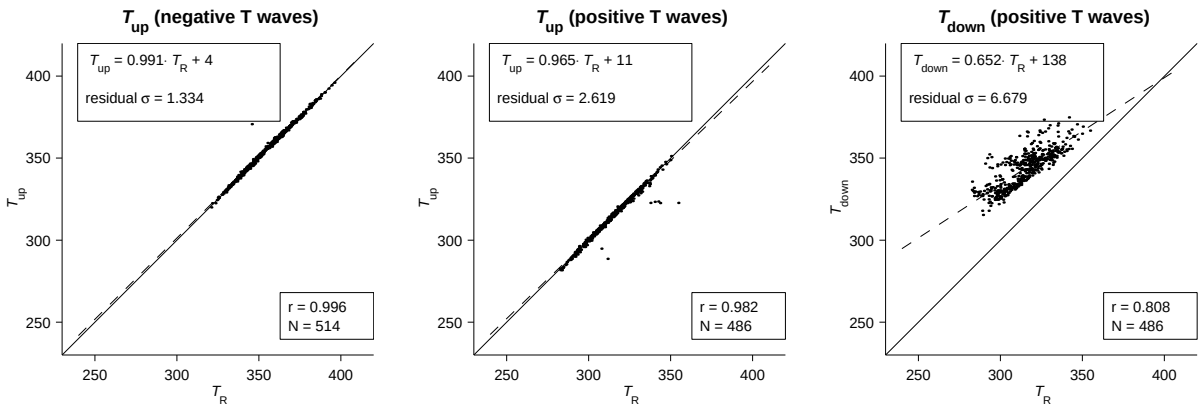

Figure 4: *Correlation between T_R and electrogram-based estimates. T_{up} was compared with T_R, for negative T waves (left) and for positive T waves (middle). T_{down} was only evaluated for positive T waves (right). Insets show parameters for a linear fit, correlation coefficient (r) and number of sites included (N). The dashed line in each panel shows the linear fit; solid lines show the identity relation.*
Zoom in if the data points are invisible on screen.