The U Wave Explained as an Intrinsic Part of Repolarization

JA Kors, HJ Ritsema van Eck, G van Herpen

Erasmus University Medical Center, Rotterdam, The Netherlands

Abstract

In the ECG the U wave follows the T, which is considered to reflect ventricular repolarization. Several hypotheses about the genesis of the U wave have been put forward, but a satisfactory explanation is still outstanding. We present a simple digital model of the left ventricle that simulates the formation of the U wave on the basis of known electrophysiological processes responsible for the electrical sources in the myocardium, and of the physical laws, embodied in the lead vector concept, which link the potentials in or on the body to these sources.

The repolarization waves constructed by the model reproduce the natural aspects of a T wave followed by a U wave. The creation of a U wave appears to be conditional on small voltage differences between the tail ends of the action potentials assigned to the myocardial cells. No fundamental demarcation exists between U wave and preceding T wave.

1. Introduction

In the ECG the U wave follows the T, which is considered to reflect the repolarization of the cardiac ventricles. Three hypotheses are being entertained about the genesis of the U wave:

(1) Hoffman and Cranefield [1] conjectured that the Purkinje system is the origin of the U wave. Purkinje action potentials have a duration that is prolonged beyond that of the endocardial and epicardial cell layers. Objections against this theory have been that the inconsiderable mass of the Purkinje network or its partial and patchy endocardial distribution would not produce detectable signals on the body surface [2]. Also, amphibia are not in the possession of Purkinje fibres but do show U waves [3].

(2) Antzelevitch and Sicouri [4] reported that cells in the mid-myocardium (M cells) have action potentials that last well beyond the end of the T wave. It was, therefore, very attractive to credit this terminal activity with a function in the formation of the U wave. In 1992, Nesterenko and Antzelevitch [5] concluded on the basis of experiments with a linear cable model of cells (Luo-Rudy model) that the U wave may indeed be generated, at least in part, by the delayed repolarization of M cells. However, in later work from the same group the model did not produce the desired U waves [6]. This explanation was then abandoned in favor of the Purkinje theory for the normal U waves while the M cells were still kept responsible for pathological U waves [6]. This distinction seems rather artificial and has to rely again on the disputed role of the Purkinje system.

(3) Surawicz advanced a mechano-electrical hypothesis of U-wave genesis [7]. In this proposition the effect of mechanical stretch of the myocardial cells on the transmembrane potential is to produce an after-potential, which coincides, and might be causally connected, with the occurrence of the U wave. Di Bernardo and Murray [8] also introduce after-potentials, of substantial size, which they assign to the endocardial and epicardial boundaries of their model to produce U waves. Such huge after-potentials as they bring into play, however, are unrealistic as they would be associated with the occurrence of serious ventricular arrhythmias, the incidence of which in the normal population is entirely negligible in comparison to the occurrence of U waves.

None of these hypotheses has received general acceptance [2], and a satisfactory explanation of the origin of the U wave is still outstanding. Here we present a simple digital model, which explains the formation of the U wave on the basis of known electrophysiological processes responsible for the electrical sources in the myocardium, and of the physical laws, embodied in the lead vector concept, which link the potentials in or on the body to these sources.

2. Methods

A slice of the left ventricular myocardium is mapped out in a hexagonal grid with an inter-knot distance of 1 mm. Each grid point can be thought of as the center of a small "volume" of myocardium or "cell". The boundaries of the myocardial slice are drawn in such a fashion that the wall contains 12 cell layers, 1 layer representing the endocardium, 10 layers the mid-myocardium, and 1 layer the epicardium. Each layer is an assembly of identical cells. The 12 layers thus fill a cross section of the ventricle with a wall thickness of approximately 1 cm.

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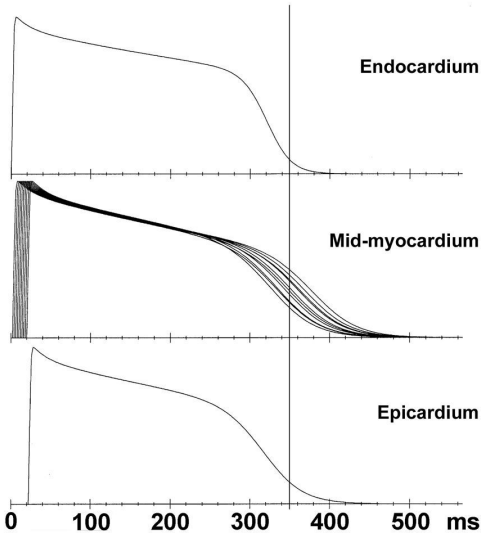

Figure 1. Action potentials as assigned to the different myocardial layers. The vertical marker at 350 ms coincides with AP_{90} of the endocardial layer.

An action potential (AP) is assigned to each cell layer. The shape of these APs is based on the functions proposed by Wohlfart [9]. Fig. 1 shows the APs as they were assigned to the endocardium, mid-myocardium, and epicardium.

The AP durations, given at 90% repolarization (AP_{90}), are 350 ms at the endocardium, and 342 ms at the epicardium. The mid-myocardium is assumed to contain a certain proportion of M cells with prolonged repolarization. In the first approximation we gave all 10 mid-myocardial layers M-cell characteristics. Their AP_{90} values range from 372 ms (subendocardial) over a maximum of 378 ms to 352 ms (subepicardial). These various figures are comparable to the AP durations reported by Drouin et al. [10] for human myocardial APs.

The timing of the APs follows a simulated excitation sequence. The excitation starts at the endocardial layer of the mid-septum where the left bundle inserts, and spreads from knot point to knot point. Conduction through the mid-myocardium and the epicardium occurs in steps of 2 ms (Fig. 2a). Conduction between neighboring endocardial cells, however, is 6 times as fast, in steps of 0.33 ms, to account for their activation by the fast Purkinje network. The transmural excitation in this manner takes approximately 22 ms, which corresponds with a myocardial conduction velocity of 40-60 cm/s. The endocardial excitation, spreading at a velocity of about 300 cm/s, reaches the outermost endocardial cells in 28 ms. Total activation time of the slice is 46 ms.

Repolarization times, defined as activation time plus AP_{90}, of the cells in the myocardial slice are shown in Fig. 2b. It can been seen that endocardial cells repolarize before epicardial cells, with a bulge in repolarization times in the mid-myocardium.

The model premises that a current dipole is generated between each pair of adjacent myocardial cells. The magnitude of this dipole is given by the instantaneous potential difference between their APs [11], as they are given in Fig. 1. Its direction is given by the axis connecting the centers of the 2 cells. For each cell the sources it generates, with respect to its six neighboring cells, are vectorially summed and the resultant vector is assigned to the grid point representing the cell. In this way the dipole source vectors $\mathbf{D}_1$, …, $\mathbf{D}_N$ are obtained (N=1328, the total number of cells in the model).

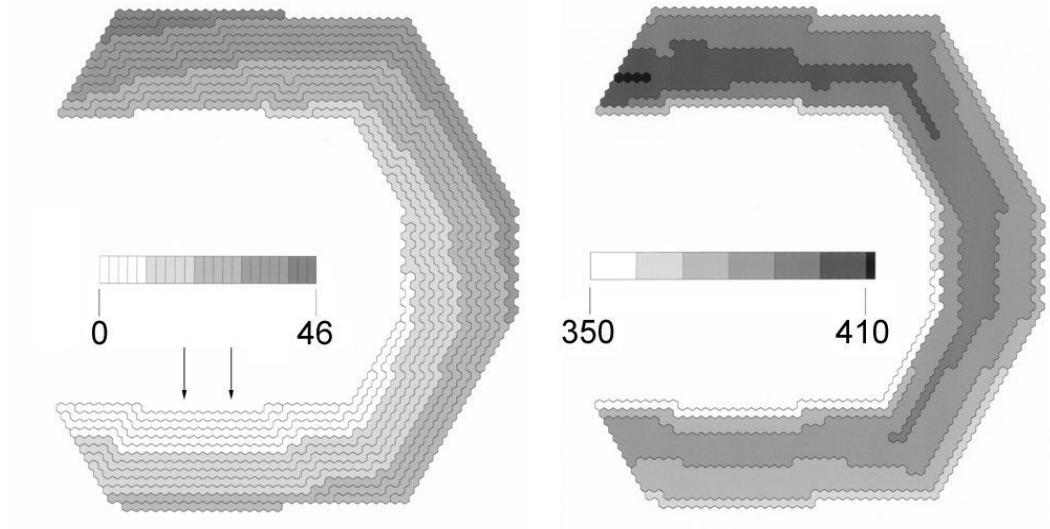

Fig. 2. (a) Excitation sequence of the myocardial slice. Isochrones are 2 ms apart. Start is at the arrows. (b) Repolarization times, defined as the summation of activation time and AP_{90} of the cells in the slice. Isochrones are 10 ms apart.

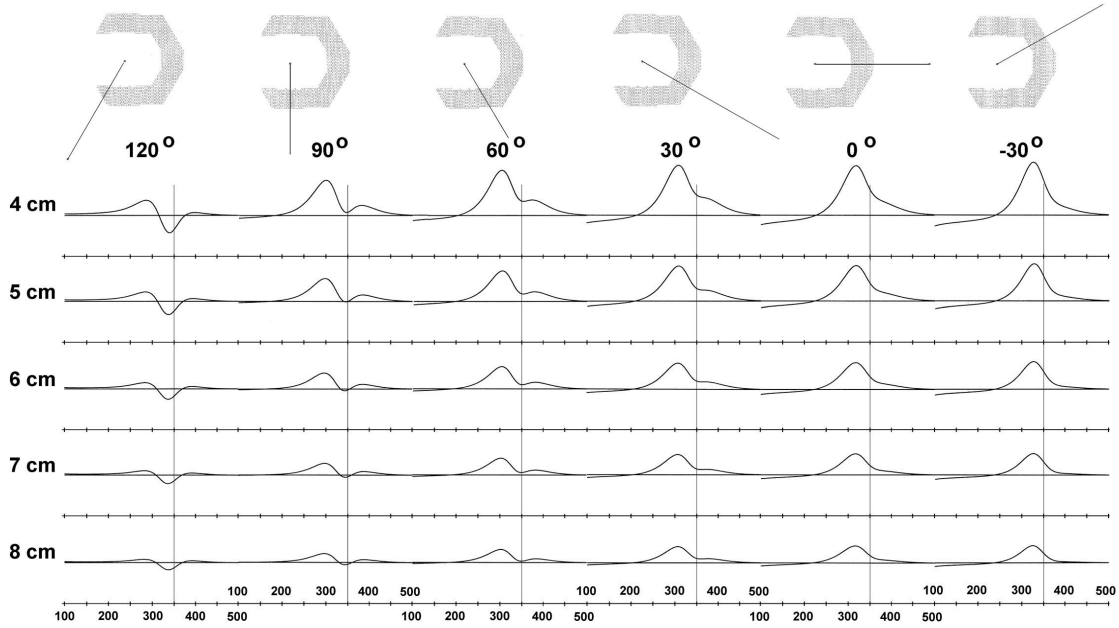

Figure 3. Repolarization patterns as computed for the model. The observation point P is moved around a mid-cavitary point in steps of 30°. For each direction the distance of P is varied from 4 to 8 cm. The time scales are in ms after start of the excitation process.

A potential will be generated at a given point P on the body by each dipole source **D**. This potential is a function of the magnitude of the dipole vector **D** and the so-called lead vector. This lead vector **L** of P is determined by the geometrical position of P relative to the location of **D** and by the electrical properties of the interposed tissues [12]. The potential at point P is then given by:

$$V_P = \mathbf{D} \cdot \mathbf{L} = |\mathbf{D}|\,|\mathbf{L}| \cos \alpha$$

where α is the angle between **D** and **L**. Each single dipole $\mathbf{D}_i$ has its own lead vector $\mathbf{L}_i$ and will, therefore, make a differently weighted contribution to V_P. The closer P is to the source $\mathbf{D}_i$, the larger $\mathbf{L}_i$ becomes; in a homogeneous infinite conducting medium the lead strength is inversely proportional to the square of the distance of the source to the measuring point. In addition, V_P is maximal for α = 0, but zero for lead vectors perpendicular to the dipole axis.

Considering that the potential field generated by the different sources is linear, by superposition the potential V_P at point P is obtained as the sum of the weighted contributions of all N source vectors. Since the dipole sources are time-varying and consequently also V_P, we write:

$$V_P(t) = \sum_{i=1}^{N} \mathbf{D}_i(t) \cdot \mathbf{L}_i = \sum_{i=1}^{N} |\mathbf{D}_i(t)|\,|\mathbf{L}_i| \cos \alpha_i$$

$V_P(t)$ is nothing else than the ECG recorded in a lead between the exploratory electrode at point P and an arbitrary zero.

3. Results

Fig. 3 illustrates the effect of varying distance and orientation of the observation point P on the appearance of the T and U wave. P is moved around a mid-cavitary orientation point, which is in the long axis of the ventricular slice. The rotation is performed in steps of 30°, from 120° to –30°, in analogy to the standard precordial leads. For each step the distance of P to the epicardium is kept the same for all directions. The direction at 90° is perpendicular to the ventricular axis. The signals may be read as ECGs with an exploratory electrode P and the opposing electrode at zero potential, at infinity. It can be seen that classical U waves are created in the directions at 90° and 60°. More to the left at 30° and 0° the terminal hump in the signal ceases to be clearly demarcated from the T wave but merges into it. Finally at –30° T and U coalesce into a single wave that conventionally would be called T, the last part of which, however, coincides with the U waves in the other leads and also concurs with the terminal T negativity which is observed at 120°. This suggests that this terminal part of the T is the equivalent of a U wave (or, for that matter, a U wave is the equivalent of the terminal part of an extended T). The overall amplitudes of the signals decrease with increasing distance of P from the epicardium, as they should. The U is largest at 30°, about the direction that a precordial lead V3 might have. Also, the amplitude ratio between T and U is highest at short distance, where the lead strength differences are most

pronounced, and diminishes the farther away P is. The T-U patterns vary with orientation and distance of P analogous to what is seen in reality in the precordial leads.

4. Discussion and conclusions

The U wave thanks its existence to potential differences occurring after AP_{90}. Such potential differences are a necessary, not a sufficient condition: they will produce a positive or negative prolongation of the T wave, but without lead vector differentials a body surface potential essentially will only show the differences between endocardial and epicardial potentials. This is what occurs in the models of Nesterenko [5], Di Bernardo [8], and Wohlfart [9]. However, the repolarization part of a normal action potential is a sigmoidally shaped curve. Two such functions will either not intersect or have only 1 intersection. Their difference values will thus be either positive or negative, or else biphasic (+/− or −/+), but cannot have 2 maxima with equal sign. Unless the endo- and epicardial repolarization curves are of very unusual appearance their differences, therefore, will not result in the double-humped deflection that ECG tradition labels as a separate T wave and U wave. If, on the other hand, lead vector differences are applied, the divergence in AP durations of the mid-myocardial layers is not nullified and a U wave appears.

The larger the lead vector differentials, the more conspicuous the U waves, such as in the central chest leads, where the wall thickness is far from negligible in proportion to the electrode distance. In certain leads of an ECG the U wave might not be observed as such in the repolarization part of the QRS-T complex. In such complexes the terminal part might be isoelectric due to perpendicular projection of the U vector on the lead axis, or the U wave is incorporated in the T wave, or it may be obscured by the following P wave.

The effect of lead vector differentials can further be illustrated by Fig. 2b, which shows a bulge in repolarization times centrally in the myocardial wall, with the endocardial cells repolarizing before the epicardial cells. This is contrary to the commonly held view that the course of repolarization should be inward, opposite to depolarization, in order to produce concordant T waves. However, when lead vectors are taken into account, concordant T waves can be produced very well even if the epicardial repolarization is later than the endocardial one. As long as the outwardly directed dipoles of the inward repolarization time shift, assisted by their lead vectors, are stronger than their opponents, we will have concordant T waves.

We conclude that U waves are an integral component of ventricular repolarization and can be expected to occur in every ECG. In our own material, through the use of a special measurement program [13], we found them present in every 12-lead ECG, in agreement with previous observations by other investigators. T and U together are the resultant of one and the same process of repolarization of the ventricular myocardium. This should have implications for the measurement of QT duration and for safety testing of drug-induced QT prolongation.

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Address for correspondence

Jan A. Kors
Medical Informatics
Erasmus University Medical Center
P.O. Box 1738
3000 DR Rotterdam
The Netherlands
j.kors@erasmusmc.nl