ECG Patterns of Early Repolarization Attributable to Increased Transient Outward Current in the Subepicardial Region. A Simulation Study.

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BACKGROUND. An association between the presence of ECG patterns of early repolarization (prominent J wave and/or QRS slurring) and occurrence of malignant ventricular arrhythmias has been reported.

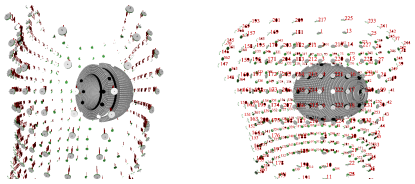

Figure 1. Anatomic model and placement in the thorax-shaped electrode system.

METHODS. We built a finite element model of the ventricles with 27000 elements organised in six myocardial strata for both the left and right ventricle (figure 1). The shape of the action potential was computed for the elements in each stratum using a modified Luo Rudy dynamic model that includes parameters extracted from the literature for the human myocardium. Activation times were assigned with a cellular automaton model and tuned to reproduce the well known recordings of Durrer D. at al. Electrograms were computed for 370 electrodes positioned on a surface with the shape of a human thorax in a uniform volume conductor around the ventricle (electrode positions were kindly provided by R. Macleod from University of Utah, USA).

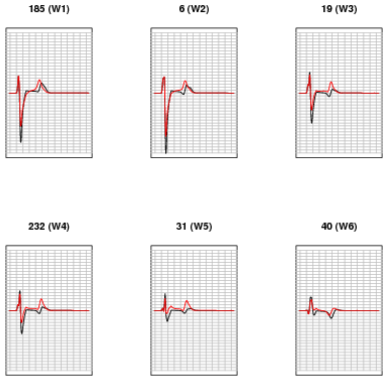

Figure 2. Simulated body surface electrograms without (black) and with (red) an I_{to} component, in one of the scenarios. The leads used are approximations of the precordials (identified with a corresponding 'W' instead of 'V'). In all leads either a degree of QRS slurring or a J wave is observed.

A pair of simulations were compared, one without an Ito current and one with a maximum transient outward conductance $\mathbf{g}_{to}$assigned randomly in the 0.076–0.190 nS/pF interval in the subepicardial layer. All other parameters were identical between the two simulations. An example is in figure 2.

The J point was taken as the instant where activation ended in the simulated myocardium. It was identical for all simulations, as activation was identical.

1000 such pairs of simulations were run, with maximal conductances for the rapid and slow K, the ATP-dependent K, plateau K, T and L-type Ca, Na/Ca exchanger currents in a range of 40–160% of the reference value from the literature.

The body surface effect of the Ito (ItoECG) was computed in each pair by substracting the ECG of the non-Ito case from that of the Ito case.

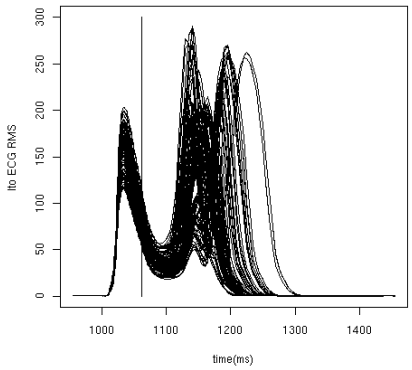

Figure 3. Simulated RMS of ItoECG graphs with various channel densities. The vertical bar represents the end of the QRS. The first deflection reflects the effect of the action potential notch on the ECG; beyond the vertical bar it leads to either QRS slurring or a J wave. The later deflections represent delayed differences in the T wave due to the fact that some early potassium outward currents had been prezent.

RESULTS.

The maximal amplitude of the root mean square (RMS) of the ItoECG was 28±4% of the maximal amplitude of the RMS of the non-Ito QRS. The ItoECG reached this maximum 28 ms before the J point It was correlated (R=0.97) and linearly related with the Ito maximal conductivity but not with any other maximal conductivities, except slightly with that of the plateau K current (R=-0.11, $p<0.001$).

At the end of ventricular activation (the J point) the ItoECG contribution to the RMS of the J point was 5.5±2.9% of the QRS RMS amplitude, then ItoECG continued to decrease for 21±2.4 ms. ItoECG was constant during the rest of the ST and then increased again in amplitude during the T wave (figure 3).

CONCLUSIONS. Parameters of the simulated effect of physiological levels of Ito on the body surface potentials are consistent with ECG observations of the early repolarization phenomenon. Most of the Ito effect was superimposed on the last part of the depolarization.