Inter-individual differences in cell composition across the ventricular wall may explain variability in ECG response to serum potassium and calcium variations

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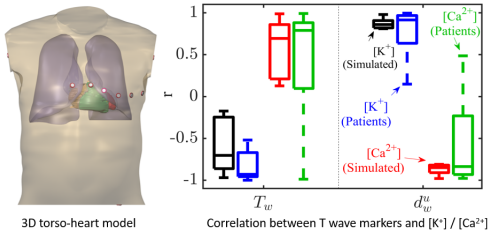
Background and Aim: Non-invasive monitoring of serum potassium and calcium concentration ($[K^+]$ and $[Ca^{2+}]$) can help to prevent arrhythmia in kidney patients. Current electrocardiogram (ECG) markers, including the width T_w and the time-warped temporal morphological variability d_w^U of the T wave, correlate significantly with $[K^+]$ and $[Ca^{2+}]$ but these relations are highly variable between patients. We hypothesized that inter-individual differences in cell type distribution across the ventricular wall can explain this variability.

Methods: We computed T_w and d_w^U in ECGs simulated with human heart-torso models with different proportions of endocardial, midmyocardial, and epicardial cells, while varying $[K^+]$ (3–6.2mM) and $[Ca^{2+}]$ (1.4–3.2mM). Electrical activity was simulated with a reaction-diffusion model with modified Ten Tusscher-Panfilov dynamics. Results were compared to measurements from 29 end-stage renal disease patients undergoing hemodialysis.

Results: T_w and d_w^U correlated strongly with $[K^+]$ (absolute median Pearson correlation coefficient r ranging from 0.70 to 0.93) and $[Ca^{2+}]$ (r ranging from 0.69 to 0.86) in the simulated cases and patients. Different cell type distributions reproduced inter-patient variability, with the same sign and magnitude of r in simulations as in patients.



3D torso-heart model and median, 25-th/75-th percentiles and min/max values of r between T_w and $[K^+]$ (black for simulations, blue for patients) and $[Ca^{2+}]$ (red for simulations, green for patients) and analogously for d_w^U.

Conclusion: Variations in the morphology and duration of the T wave were related to $[K^+]$ and $[Ca^{2+}]$ variations in our models and in the patients, with the observed high inter-individual variability in patients well reproduced by variations in cell type distribution across the ventricular wall.