Cardiac Digital Twins: Ready for the Clinic or Premature Translation?

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Aims: Cardiac digital twins (CDTs) are increasingly used to predict clinical outcomes, including risk stratification and ablation targeting for ventricular tachycardia (VT) therapies. CDTs are governed by a high-dimensional parameter space, predicting VT behaviour relies on the implicit assumption that the parameter space is constrained so that simulated and real physiology are in close agreement. We aim to evaluate the validity of this assumption.

Methods: We used local activation time (LAT), action potential duration (APD), and ECG to compare outcomes in three common modelling configurations: (i) an infarct border-zone left ventricular (LV) model at a medium resolution of $400\,\mu\mathrm{m}$ (MR-M); (ii) the same model at higher resolution of $200\,\mu\mathrm{m}$ (HR-M); and (iii) the $400\,\mu\mathrm{m}$ model augmented with a fast-conducting layer (FL-M). Model predictions were compared under (i) sinus rhythm (SR), initiated by pacing at ventricular earliest activation sites, and (ii) VT, induced via unidirectional block within a scar-related isthmus.

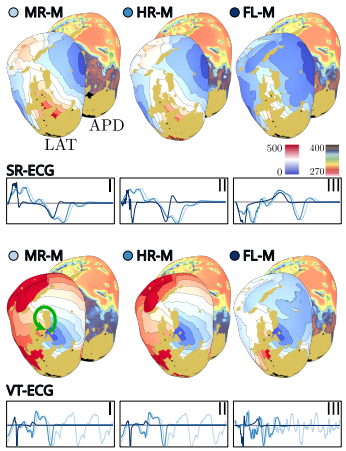

Fig.1 Model predictions for SR (top) and VT (bottom) in tested models.

Results: All three model configurations produced different outcomes in both SR and VT (see Fig.1). In SR, the FL-M model yielded a QRS duration of approximately $150\,\mathrm{ms}$, whereas the other models exhibited substantially prolonged QRS durations of $\approx 300\,\mathrm{ms}$. In sustained VT simulations, circuit length was insufficient to maintain reentry the FL-M and HR-M models, stable reentry was observed in the MR-M model. Repolarization dynamics were comparable, as action potential duration remained unchanged.

Conclusion: CDT predictions are highly sensitive to modelling choices, raising concerns regarding their validity. Further investigation is warranted, particularly for studies that do not directly compare simulated and clinical observations, to quantify bounds of confidence for CDT-based predictions.