QUANTIFYING THE IMPACT OF ANTI-ARRHYTHMIC THERAPY IN ATRIAL FIBRILLATION PATIENTS USING COMPUTATIONAL WHOLE-HEART MODELS

R. K. Barrows[1,2], C. M. Augustin, M. F. Gsell, C. H. Roney, J. A. Solís-Lemus, H. Xu, A. A. Young, R. Rajani, J. Whitaker, E. J. Vigmond, M. J. Bishop, G. Plank, M. Strocchi, S. A. Niederer

[1]King's College London
[2]National Heart and Lung Institute, Imperial College London (72 Du Cane Road, W12 0NN, London, UK)

Atrial fibrillation (AF) is the most common cardiac arrhythmia with more new cases of AF diagnosed each year in the NHS than the four most common types of cancer combined. It is associated with a significantly increased risk of stroke, heart failure, and mortality, and represents a major burden on healthcare systems. AF is characterised by a rapid, irregular heart rate with impaired atrial contraction and can cause a deterioration in left ventricular (LV) function. Management strategies include slowing the ventricular rate (rate-control) or aiming to restore healthy sinus rhythm (rhythm-control). Large randomised controlled trials have not reached a consensus on the optimal treatment strategy. Quantifying the relative contributions of heart rate, regularity, and atrial contraction to LV function could clarify the benefits of these approaches.

We developed a cohort of 3D patient-specific computational models of the heart using CT scans from 10 AF patients. The models incorporated muscle fibre orientations in the ventricles and atria, spring boundary conditions simulating the pericardial sac, and were coupled with an ODE-based closed-loop model for the circulatory system. Equations governing both the electrical and mechanical behaviour of the hearts were solved using finite element methods. Machine learning techniques including Gaussian process emulators and Bayesian history matching were employed to calibrate the models. A factorial study assessed the impact of heart rate, regularity, and atrial contraction on LV function. The results were then used to compare simulations of untreated AF (a rapid, irregular heart rate with no atrial contraction), pharmacological/paced rate-control (a slower, irregular/regular heart rate with no atrial contraction), and rhythm-control (a slower, regular heart rate with effective atrial contraction). LV function for each simulation was evaluated using ejection fraction (the percentage of blood volume ejected from the chamber) and compared with simulations of untreated AF.

Our models predict that rhythm-control provides superior improvements in LV function compared to rate-control. However, they also suggest that in patients with a high fibrosis burden or ablation scarring, where atrial contraction is unlikely to be effective, restoring sinus rhythm may not improve LV function beyond that achieved with pharmacological rate control. Lastly, paced and pharmacological rate control resulted in equivalent improvements in LV function.

By leveraging mathematics, computational modelling, and machine learning, this study demonstrates the potential to revolutionise arrhythmia therapy trials through in-silico simulations. While exploring different treatment options for AF in vivo is not feasible, these models offer a unique opportunity to tailor treatments to individual patients, paving the way for more targeted and effective therapeutic strategies.

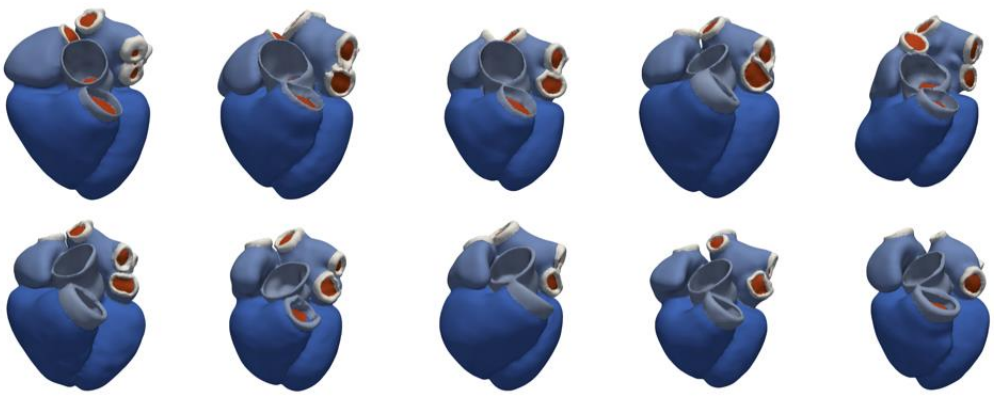

Figure 1: A cohort of computational AF patient models.