

Permutation Test for Arrhythmia Survival Models based on Cardiac Anatomical Shape

A Caponio, N El-Ganainy, C Asher, P Lamata, MM Maleckar, G Balaban
Kristiania University College, Oslo, Norway

Introduction. Anatomical shape features derived from cardiac MRI are increasingly used as biomarkers in survival models for time-to-event outcomes such as arrhythmic risk. However, assessing the statistical significance of such models is challenging: shape representations are high-dimensional, events are rare, and there is a lack of formal hypothesis tests. We introduce a permutation testing framework to address this gap.

Methods. Left ventricular (LV) end-diastolic shapes were reconstructed from short-axis CMR contours for two cohorts of patients with non-ischemic dilated cardiomyopathy: 156 patients from Royal Brompton Hospital (RBH) with 25 major arrhythmic events and 102 patients from Guy's and St Thomas' NHS Trust (GSTT) with 12 events. Statistical shape models were built using principal component analysis (PCA). The first 10 PCA modes were used as predictors in a Cox regression model with Lasso regularization, selecting the optimal model via cross-validated log-likelihood. To test significance, outcome labels were randomly permuted 200 times and the Cox–Lasso model was refitted for each permutation, generating an empirical null distribution of the C-index. The permutation p -value was estimated as the proportion of null C-index values exceeding the observed value.

Results. In the RBH cohort, cross-validation selected PCA modes 5, 6, and 10, yielding an observed C-index of 0.74. This exceeded the null distribution median (0.63; 95% CI: 0.55–0.72), with a permutation p -value of 0.030. In the GSTT cohort, PCA modes 8 and 10 were selected, yielding a C-index of 0.69 that did not exceed the null median ($p > 0.05$).

Conclusion We present the first permutation testing framework for time to arrhythmia models based on cardiac shape features. The framework revealed significant prognostic value in the RBH cohort and no significant association in the GSTT cohort.

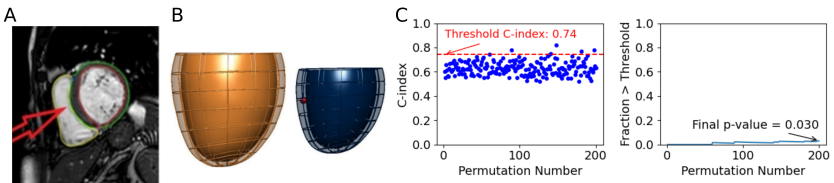


Figure 1: **A** Example CMR slice. **B** Example extreme shapes (± 2 std) along mode 1 of the RBH PCA model. **C** Permutation C-index distribution and P-value convergence with the RBH data.