Ionic Determinants of Conduction Velocity Drop and Propagation Failure During Pacing Stress Protocols

Alejando Liberos[1], Hector Martinez-Navarro[1], Duna de Luis-Moura[1], Saman Golmaryami[2], María Termenón-Rivas[1], Giada S Romitti[1], Ignacio García-Fernández[1], Miguel Lozano[1], Etel Silva[2], Juan Fernandez-Armenta[2], Miguel Rodrigo[1]

[1] CoMMLab, Universitat de València, Valencia, Spain
[2] Department of Cardiology, Hospital U. Puerta del Mar, Cádiz, Spain

In atrial fibrillation ablation, increasing stimulation frequencies have been investigated to unmask regions prone to arrhythmia initiation and maintenance. Ionic mechanisms underlying conduction velocity drop and propagation failure, which may be associated with the abnormal electrograms observed under these protocols, are investigated in this work.

A tissue model (0.3 × 2 × 0.025 cm; inter-node distance: 0.25 mm, a) was used to simulate paced activity across 2100 different ionic profiles generated by randomly sampling values between −50% and +100% of baseline for eight ionic currents (b). Pacing protocol consists of 7 stimuli followed by three premature stimuli with progressively decreasing coupling intervals (b). Models that successfully propagated all stimuli were analyzed to quantify conduction velocity (CV) across different stimulation intervals. Models exhibiting a CV drop between first and third extra stimuli (DropPop) were compared with those that did not (NonDropPop). Additionally, models which failed to propagate at least in once of the extra stimuli were also identified (FailPop).

Ionic differences between NonDropPop (N = 1328), DropPop (N = 270) and FailPop (N=70) are presented in (b). The baseline model exhibited a conduction velocity of 62.5 cm/s at long intervals and 57,7 cm/s during the three extra stimuli (NonDropPop). In DropPop, CV drop values between first and third extra stimuli were -7.12 cm/s ± 0.48 cm/s.

Sodium- and calcium-related currents (g_{Na}, g_{CaL}, j_{Rel}) determine the presence of conduction velocity drop at high stimulation rates, calcium- and potassium-related currents (g_{CaL}, I_{NCX}, g_{K1} and g_{Ks}) determine propagation failure. Tissue heterogeneity, including patches with CV drop or propagation failure, should be explored as a mechanism for abnormal conduction and fractionated electrograms.