In-silico 2D Atrial Tissue Modelling on a Population: Impact of Fibrosis in Arrhythmogenesis

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Introduction: Cardiac fibrosis (FB) is the main anatomical obstacle leading to Atrial Fibrillation (AF) treatment efficacy.

Aims: To evaluate the impact of inter-subject variability in myocyte-fibroblast interaction at the electrophysiological level.

Methods: A population consisting of 127 different ionic profiles based on the Koivumaki chronic AF cardiomyocyte (CM) model was tested for three concentrations of diffuse cardiac FB (0%, 5% and 10%). The Maleckar model of active fibroblast was used model fibroblasts. It resulted in 381 simulations of 4 seconds performed in plane with 40000 cells (2cmx2cm). APD90, CV, AP peak and RMP were measured and compared. According to the value of these markers the population was divided in three groups: (1) Cond, i.e. conductive for every level of FB; (2) NCond10, i.e. non-conductive for 10%FB and (3) NCond5_10, i.e. non-conductive for 5 nor 10%FB.

Results: From the total population, 35, 27 and 65 models resulted in Cond, NCond5 and NCond5_10 groups respectively. Attending to the conductive models, CV and APD90 of the CM lower for increasing concentrations of FB. Also, RMP slightly increases for higher levels of FB (Fig. 1C). When groups were compared in terms of conductances, two parameters showed statistical differences between groups ($p<0.05$) (Fig. 1A). Lower values of I_{KCa} are observed to correspond to conductive profiles, while higher g_{K1} values are observed in conductive profiles (Fig. 1E).

Conclusions: The multivariable study proposed, allowed the identification of I_{KCa} and I_{K1} as determinant currents involved in myocyte-fibroblast electrophysiological interaction. The population tested reproduced the behavior described in the bibliography reducing CV.