Effect of Epicardial Adipose Tissue–Derived Secretome on Atrial Fibrillation Vulnerability

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Introduction: Epicardial adipose tissue (EAT) may promote arrhythmogenesis through secretome-mediated electrophysiological effects that increase myocardial heterogeneity. However, the spatial extent of these effects remains unclear, particularly whether they are confined to the epicardium or penetrate toward the endocardium. In particular, the role of EAT penetration depth in sustaining atrial fibrillation (AF) requires further investigation.

Methods: In this study, we used a computational framework to investigate the effect of EAT distribution and penetration on AF window of vulnerability. A 3D anatomical biatrial model was discretized with a multilayer hexahedral mesh (average edge length 300 μm). Atrial wall thickness ranged from 600 to 900 μm, corresponding to 2–3 element layers. Electrical activity was simulated using the Courtemanche model, remodeled for persistent AF. EAT-related electrophysiological changes were incorporated based on prior studies, including a 40% reduction in I_{Na} and I_{K1} conductances and a 20% increase in I_{Ks} and I_{Kr}. Ten patients with persistent AF undergoing de novo ablation were analyzed. Both atria and EAT were segmented from CT images. EAT burden was quantified as percentage of epicardial surface for left (LA) and right atria (RA). Two representative patients with distinct distributions were selected (Patient P1: 9.1% LA, 11.7% RA; Patient P2: 19.2% LA, 29.5% RA), and their EAT patterns were mapped onto the biatrial model (panel A in Figure). Simulations were performed for three penetration scenarios: epicardial layer only, two layers, and three layers. AF was induced using a S1–S2 protocol.

Results: At the cellular level, EAT induces an increment of the resting membrane potential, prolongs action potential duration, and reduces upstroke velocity (panel B in Figure). Preliminary results at the atrial level, show tat these alterations promote conduction slowing and the formation of more refractory and heterogeneous regions, facilitating the maintenance of reentrant activity.

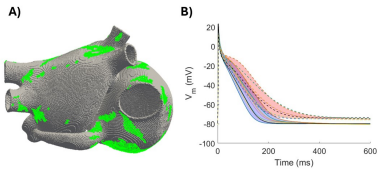

Figure 1. A) atria with fat representation (green); B) APD traces in atrial regions (EAT in red, control in blue)