Virtual antiarrhythmic drug tests in computational atrial modeling reflecting patient specific anatomy, histology, and electrophysiology: retrospective feasibility test

**Introduction**: Since cardiac anatomy, histology, and ion channel characteristics differ from patient to patient, thus the effect of antiarrhythmic drug (AAD) is also variable with each patient. We evaluated the feasibility of virtual AAD test (V-AAD) by utilizing computational atrial modeling in patients with AAD resistant atrial fibrillation (AF).

**Methods**: We retrospectively conducted V-AAD in 10 patients (5 male, 59.4±9.5 years old, 70.0% persistent AF) with AAD resistant AF (5 flecainide, 2 amiodarone, 1 sotalol, and 2 dronedarone resistant) who underwent catheter ablation. To conduct realistic V-AAD, we integrated patients’ cardiac computed tomogram image, endocardial bipolar voltage, fiber orientation, and estimated ion current characteristics to in-silico modeling of AF. Ion current characteristics were deducted by reverse engineering of rate dependent monophasic action potential duration (MAPD) adaptation. After induction of virtual AF, we conducted dose-dependent V-AAD (amiodarone 2 and 10µM; flecainide 1 and 5µM; sotalol 1 and 10µM; dronedarone 3µM and 7µM) with observing wave-dynamics and AF termination.

**Result**: In this realistic model of AF, spatial distribution of fibrosis was 64.4±9.4%, and AF was induced and maintained > 30sec in 100.0%. After V-AAD intervention, AF was terminated by at low-doses amiodarone (20.0%), flecainide (10.0%), sotalol (0%), and dronedarone (10.0%), but was terminated at high-doses amiodarone (60.0%), flecainide (10.0%), sotalol (10.0%), and dronedarone (10.0%), respectively. Correlation rate of clinically resistant AAD with V-AAD was 80.0%. Patients with Smax higher than 1.0 showed that their clinical findings were well correlated with V-AAD results. After adding V-AAD, dominant frequency (DF; 10.2±4.4 Hz to 4.8±1.2 Hz, p<0.001), number of phase singularities (PS; 44603.1±51135.9 to 615.2±983.4, p<0.001), and maximal slope of restitution (Smax; 2.0±2.2 to 0.5±0.8, p<0.001) changed significantly in dose dependent manner.

**Conclusion**: V-AAD intervention is feasible in realistic computational modeling of AF that is integrated patient specific atrial anatomy, endocardial voltage, and electrophysiology. V-AAD clearly shows dose-dependent antiarrhythmic effects.