# Effect of Blocking $I_{Kur}$ on the Genesis of Repolarisation Alternans in Canine Atrium

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**Aims**: This study aimed to investigate the effects of blocking the ultra-rapid delayed rectifier $K^+$ current ($I_{Kur}$) on the genesis of repolarisation alternans which was associated with arrhythmogenesis.

**Methods**: The canine atrial cell model developed by Ramirez *et al*. was used to examine the effects of blocking $I_{Kur}$ by various percentages on the action potential (AP). The action potential duration at 90% repolarization ($APD_{90}$) restitution curves were calculated using the dynamic pacing protocol and the standard S1-S2 protocol respectively to analyse the genesis of repolarisation alternans under control and $I_{Kur}$ block conditions. In addition, effective refractory period (ERP) restitution curves were also calculated using the combination of the two protocols described above. Furthermore, changes in the intracellular $Ca^{2+}$ transient amplitude ($CaT_{amp}$) and decay time (CaTD) were evaluated in the two conditions.

**Results**: Simulation results demonstrated that the $APD_{90}$ was prolonged by 7.0 ms to 84.0 ms, the $CaT_{amp}$ increased by 8.5 nM to 162.9 nM, and the CaTD increased by 3.2 ms to 57.5 ms when $I_{Kur}$ was blocked from 10% to 90% at 2 Hz pacing rate. APD and $Ca^{2+}$ transient alternans occurred when $I_{Kur}$ was blocked by 40% to 90%. Genesis of alternans was considered when the beat-to-beat variation > 10 ms in $APD_{90}$, ERP and CaTD or 10 nM in CaTamp at the longest pacing cycle length (PCL) (details in Table 1). Further analysis demonstrated that blocking $I_{Kur}$ promoted the genesis of APD alternans, via a mechanism of an increased APD that led to increased amplitude of $Ca^{2+}$ transient and prolonged $Ca^{2+}$ decay, which produced an increased $Na^+/Ca^{2+}$ exchange current, promoting the genesis of AP alternans.

Table. 1. The longest PCL for the genesis of alternans.

| Blocking $I_{Kur}$ | PCL (ms) | | | |
|---|---|---|---|---|
| | $APD_{90}$ | ERP | CaTD | $CaT_{amp}$ |
| 40% | 565 | 570 | 575 | 515 |
| 50% | 550 | 505 | 515 | 500 |
| 60% | 440 | 440 | 460 | 455 |
| 70% | 390 | 390 | 410 | 405 |
| 80% | 345 | 345 | 365 | 365 |
| 90% | 315 | 315 | 330 | 330 |

**Conclusion**: This study demonstrates that although prolonging the APD, blocking $I_{Kur}$ may promote the genesis of AP alternans at a lower pacing frequency, indicating a latent pro-arrhythmic of $I_{Kur}$ blocking.