Renewal rate constants of phase singularity formation and destruction in atrial fibrillation are temporally stable measures of fibrillatory dynamics

**Background:** The optimal approach for atrial fibrillation (AF) ablation is unknown, with a subset of patients unresponsive to current strategies. In such patients, development of novel mechanism-based approaches could be needed, but this requires a stable, robust and easily measurable marker of underlying AF dynamics. We hypothesized that renewal rate constants $\lambda_f$ and $\lambda_d$, previously shown to quantify rates of phase singularity (PS) formation and destruction during fibrillation, could be used as such a marker.

**Objective:** We hypothesised $\lambda_f/\lambda_d$ are temporally stable and can be used as robust markers of underlying fibrillatory dynamics.

**Methods:** Basket recordings from $n=20$ patients (43 epochs) and $n=12$ sheep (20 epochs) were studied. Temporal stability of $\lambda_f/\lambda_d$ was analyzed by investigating if averages created using 20 second windows (i) have a stable mean, ii) time-independent autocorrelation functions, and iii) if coefficient of variation (CV) of $\lambda_f/\lambda_d$ over time are lower than for established measures (dominant frequency (DF) and AF cycle length (AFCL)).

**Results:** Mean $\lambda_f/\lambda_d$ estimated from 20 second windows was constant ($R^2_{\lambda_f}=0.97; R^2_{\lambda_d}=0.99$), with time-invariant autocorrelation functions. CV was also lowest for $\lambda_f$ (3.7% (95%CI,1.6,5.9)) and $\lambda_d$ (2.6% (1.5,3.8)) compared to DF (16.3% (95%CI,2.5,30)) and AFCL (12.2% (95%CI,6.7,17.7)), and also significantly different to DF ($P < 0.001$) and AFCL ($P < 0.001$).

**Conclusions:** $\lambda_f/\lambda_d$ are temporally stable, providing a robust and clinically usable mechanistic tool to directly quantify AF dynamics, mechanistically connected to rotor regeneration that is the key to underlying AF perpetuation.