Introduction: Mechanisms that sustain persistent atrial fibrillation (PeAF) remain poorly understood. Recent human data from activation mapping have suggested focal breakthroughs from endocardial-epicardial dissociation to maintain PeAF by constant multiplication of sources. However, detailed analyses of signal and driver characteristics and phase mapping from an endo-epicardial perspective has not been described before. We tested the hypothesis that there will be endo-epicardial electrical dissociation on phase mapping PeAF and intended to study the driver characteristics and signal complexities.

Methods: Simultaneous intra-operative mapping of endo- and epicardial lateral RA wall was performed in patients with PeAF using two HD Grid catheters (Abbott, 16 electrodes, 3mm spacing). Filtered uni- and bipolar electrograms (EGM's) of continuous 2 minutes AF recordings and electrodes locations were exported onto MATLAB for phase analyses. Signal phase at each location of the endocardial surface was compared to phase timing at the opposing epicardial surface. Difference of ≥20ms between paired endo- and epicardial electrodes defined dissociation. Activation patterns were simultaneously compared between endo- and epicardial surfaces on dynamic phase maps and were characterized into single or multiple wavefronts, rotational circuits, focal sources or disorganized activity based on standard criteria. Bipolar EGM's with ≥5 directional changes were classified fractionated.

Result: Fourteen patients with PeAF undergoing cardiac surgery (57.1% valvular, 42.9% ischemic) were included. Mean AF cycle length was 178±47ms. Endo-epicardial dissociation was seen in 50.3% of activations. The most common patterns seen were disorganised activity (Endo: 36.5±11.2% vs Epi: 41.7±9.1%, p=0.0194) and single wavefronts (Endo: 31.3±10.6% vs Epi: 28.1±12.6%, p=0.129). Transient rotors (median revolutions: 2, mean duration: 590±140ms) were seen on phase mapping but were non-sustained (Endo: 14.8±1.9% vs Epi 15.6±3%, p=0.669). Transmural migration of rotors (n=6) from the epi- to the endocardium were noted in 2 patients. No focal activations were seen. Simultaneous comparison of endo-epicardial wavefront patterns showed significant heterogeneity (McNemar’s test,
p<0.0001 (two-tailed). Fractionation of bipolar EGM's was significantly higher in the epicardium than endocardium (81.2% vs 72.1%, p<0.0001).

**Conclusion**: Simultaneous endo-epicardial phase mapping of human PeAF shows significant electrical dissociation, wavefront heterogeneities and complex fractionations. No focal activations were seen in our cohort and for the first time were able to demonstrate transmural migratory rotors. Such complex 3D-interactions provides compelling evidence to explain why current endocardial treatment approaches have suboptimal outcomes.