

Figure 1: (A) LV wedge preparation of endocardium for optical mapping with infarct region highlighted in yellow. (B) 2D AP duration and (C) amplitude alternans maps. (D) Representative AP traces demonstrating alternans prior to onset of VT. (E) Spatial evolution of amplitude alternans with increase in pacing frequency.

B-PO02-027

RIGHT PREDOMINANT ELECTRICAL REMODELING IN A PURE MODEL OF PULMONARY HYPERTENSION PROMOTES REENTRANT ARRHYTHMIAS

Benjamin Strauss PhD, Emerson Obus MS, Michael G. Katz MD PhD, Anthony Fargnoli PhD, Marine Cacheux PhD, Joseph G. Akar MD, PhD, James P. Hummel MD, Yassine Sassi PhD and Fadi G. Akar PhD

Background: Electrophysiological (EP) properties have been studied mainly in the monocrotaline (MCT) model of pulmonary arterial hypertension (PAH). Findings from these studies however are confounded by major extra-pulmonary toxicities, including liver failure and direct myocardial damage. This has precluded the ability to draw definitive conclusions regarding the role of PAH *per se* in EP remodeling.

Objective: To investigate the EP substrate in a new model of PAH that avoids extra-cardiopulmonary toxicities.

Methods: Sprague Dawley rats underwent surgical left pneumonectomy (Pn) followed by injection of the VEGF inhibitor Sugen 5416 (Su/Pn). 5 wks later, hemodynamic measurements and cardiac MRI were performed *in vivo*, optical action potential (AP) mapping *ex vivo* and molecular analyses *in vitro*. The control (CTRL) group consisted of age matched rats.

Results: Su/Pn rats exhibited substantial RV hypertrophy and were prone to pacing induced VT. Underlying this differential susceptibility was disproportionate RV sided prolongation of AP duration in Su/Pn hearts. This, in turn, promoted the formation of right-sided AP alternans at physiological rates in Su/Pn but not CTRL. Correspondingly, key K channel transcripts were downregulated in the RV of Su/Pn rats. While propagation was impaired at all rates in Su/Pn, the extent of conduction slowing was most severe immediately prior to the emergence of inter-ventricular lines of conduction block and onset of sustained VT. Measurement of the cardiac wavelength at elevated rates revealed a decrease in Su/Pn relative to CTRL. Nav1.5 and total Cx43 expression were not altered while Cx43 phosphorylation was markedly decreased in PAH. Col1a1 and Col3a1 transcripts were upregulated coinciding with myocardial fibrosis. Once generated, VT was sustained by multiple reentrant circuits likely facilitated by the short wavelengths with lower frequency of activation in RV corresponding to wave break formation in that chamber.

Conclusion: In this pure model of PAH, we document RV-predominant EP remodeling that facilitates the initiation of multi-wavelet reentry underlying VT. The Su/Pn model represents a severe form of PAH that allows the study of EP properties without the confounding influence of extra-pulmonary toxicity.

B-PO02-029

REDUCED ATRIAL FIBRILLATION DRIVERS IN RESPONSE TO REACTIVE OXYGEN SCAVENGING - A NOVEL THERAPEUTIC TARGET IN ATRIAL FIBRILLATION?

Markus Rottmann, Anna Pfenniger MD, PhD, Shin Yoo PhD, David Johnson, Beth Elizabeth Geist, Suman Mandava, Wenwei Zhang, Amy Burrell, Andrew J. Wasserstrom, Bradley P. Knight MD, FHRS, Rod S. Passman MD, FHRS and Rishi Arora MD, FHRS

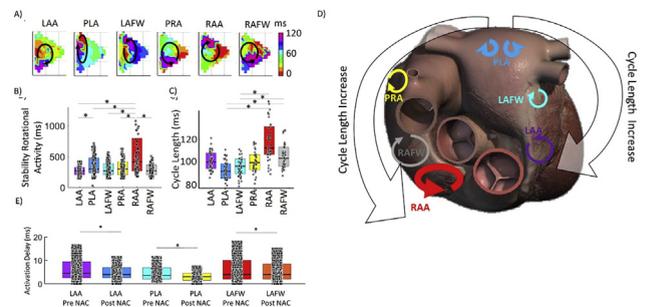
Background: Oxidative Stress (OS) is thought to be a mediator of atrial fibrillation (AF), but the precise role of OS in AF is unknown. We assessed reactive oxygen species (ROS) scavenging on slow conduction and maintenance of rotational drivers.

Objective: We hypothesized that ROS are dynamically involved in a vulnerable substrate and that ROS scavenging reduces AF drivers and arrhythmogenic slow conduction zones.

Methods: AF was induced in 48 dogs by rapid atrial pacing (RAP) for 3-14 weeks. Epicardial high-density mapping was performed (130 electrodes, dist. 2.5mm) in the atrial regions: posterior left atrium (PLA), left atrial free wall (LAFW), left atrial appendage (LAA), posterior right atrium (PRA), right atrial free wall (RAFW), right atrial appendage (RAA). N-acetylcysteine (NAC) was given intravenously (100mg/kg) in 15 AF dogs. We mapped all atrial regions pre and post NAC. We detected rotational activity in activation time maps and quantified slow conduction as activation delay in neighboring electrodes.

Results: We detected rotational activity in all regions (Figure A) with the stability of 376 ± 255 ms in the LAA, 422 ± 174 ms in the PLA, and 317 ± 174 ms in the LAFW (Figure B). The cycle length of rotational activity was shorter in the PLA (CL 94 ± 7 ms) compared to other regions ($P < 0.05$) (Figure C) and increased in remote regions with increasing distance to the PLA (Figure D). After providing NAC, rotational activities reduced in the left atrium by 40% in the LAFW, by 39% in the PLA, and by 12% in the LAA (Figure E).

Conclusion: Acute scavenging of ROS reduces arrhythmogenic slow conduction and AF triggers. These results show that ROS is dynamically involved in the maintenance of AF.



B-PO02-030

ELECTROPHYSIOLOGICAL CHANGES IN PERSISTENT ATRIAL FIBRILLATION IN A CHRONICALLY PACED CANINE MODEL

Eugene Kwan, Bram Hunt BS, Robert Schwartz, Yuki Ishidoya MD, Wilson W. Good, Mark McMillan, Orvelin Roman, Jason Mendes, Edward DiBella, Rob S. MacLeod, Derek J. Dosdall PhD, FHRS and Ravi Ranjan MD, PhD, FHRS

Background: Previous studies have described slowly conducting regions in patients experiencing atrial fibrillation (AF).