the lesions matured over time (Fig. 2). No significant difference in mean PFA lesion depth between 1 week and 6 weeks suggests lesion stabilization.

**Conclusion:** MRI demonstrates significantly different tissue responses to PFA when compared to RFA, with implications for PFA protocol and associated MRI monitoring optimization.

**References:**

**CA-534-04**

UNDERSTANDING THE RISK OF CORONARY ARTERY SPASM DURING PULSED FIELD ABLATION

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**Background:** Pulsed Field Ablation (PFA) has gained prominence by virtue of its proclivity to preferentially ablate myocardial tissue. Based on its safety, efficacy and efficiency, after regulatory approval of one multielectrode PFA catheter, there has been rapid uptake into clinical practice in various European centers. In addition, multiple other PFA catheters are under investigation. While the overall safety profile of PFA is quite favorable compared to conventional thermal ablation, it is possible that PFA may yet result in unusual complications. Indeed, a recent case of coronary spasm during off-label ablation along the mitral isthmus was recently reported.

**Objective:** To study the potential for coronary spasm during focal endo- or epicardial PFA in swine ventricles

**Methods:** During a series of endocardial and epicardial dose-finding evaluations, 2 kV bipolar/biphasic PFA pulses were delivered using an 8 Fr focal catheter (Farapoint, Boston Scientific). To evaluate vasospasm, we performed coronary angiography (CAG) after purposefully delivering PF in close proximity to epicardial coronary arteries. After sub-xiphoid pericardial access, the catheter was positioned immediately adjacent to the left anterior descending artery (LAD) in one swine. In two other swine, the catheter was positioned endocardially, immediately above the right coronary artery (RCA) at the proximal cavotricuspid isthmus in one swine and in the pulmonary artery trunk near the LAD in the other swine.

**Results:** In the swine with epicardial PFA, immediately after the ablation pulses, ST-elevation in the precordial leads was observed. Repeat CAG revealed spasm along the length of the catheter-tip. The spasm gradually recovered over 50 minutes and the animal was successfully survived. In the other 2 swine with endocardial PFA, no ST-changes were observed for either applications. However, CAG demonstrated coronary spasm of the RCA, but not in the LAD. Resolution of RCA spasm was not documented by repeat CAG. These swine was also successfully survived.

**Conclusion:** Coronary spasm can occur when PFA is performed in close proximity to large epicardial vessels in swine. Further detailed assessments in different animal models are needed to understand its incidence, dependence on proximity and location as well as therapeutic approaches.

**ABSTRACT BS-526:**

Extrinsic factors and mechanisms contributing to cardiac arrhythmias

Sunday, May 1, 2022
8:00 AM - 9:00 AM

**BS-526-01**

THE EFFECT OF CHRONIC NICOTINE EXPOSURE ON CARDIAC ELECTROPHYSIOLOGY IN THE RABBIT HEART
ROLE OF THE SUCCINATE PATHWAY IN THE ELECTROPHYSIOLOGICAL PROPERTIES OF RIGHT ATRIA IN A PERSISTENT ATRIAL FIBRILLATION SHEEP MODEL

Bastien Guillot; Girish Singh Ramlugun PhD; Guido Caluori PhD; Nestor Pallares Lupon MSc; Richard D. Walton PhD; Pierre Jais MD; Philippe Pasdois PhD and Olivier Bernus PhD

Background: The progression from paroxysmal to persistent atrial fibrillation (AF) is still a poorly understood process. Succinate levels are increased in AF patients indicating a potential role for metabolic remodeling in this transition process.

Objective: To assess the impact of the succinate pathway on the electrophysiological properties of right atria (RA) in a persistent AF sheep model.

Methods: Optical mapping was performed on ex vivo RA from a burst pacing AF sheep model, including 8 sham, 7 persistent AF, and 3 resistant animals. RA were perfused by Tyrode solution with glucose (5.6mM), subsequently replaced by succinate (10mM), known to increase mitochondrial Reactive Oxygen Species (ROS). An activator of the succinate [l]-adrenergic receptor (GPR91), cis-eptoxysuccinic acid (300mM), was also used to study the GPR91 involvement in atrial electrophysiology and AF (N~6). Action potential duration at 80% of repolarization (APD80) were assessed from 2 to 5Hz pacing frequency and during sinus rhythm (SR). We used an S1S2 pacing protocol to determine effective refractory period (ERF) and a burst pacing protocol (30Hz) to assess ex vivo AF vulnerability. Finally, an organ donation program allowed us to investigate these properties in a human RA from an AF patient.

Results: During succinate perfusion SR is decreased in Sham (1.5 vs 1.2 Hz; p=0.03), AF (1.5 vs 1 Hz; p=0.003) and resistant (1.3 vs 1 Hz; p=0.01) sheep. ERF is increased in AF sheep (184 vs 344 ms; p=0.0007) and APD80 is increased in Sham (217 vs 264 ms; p=0.0004) and AF sheep (195 vs 275 ms; p=0.003). We also observed an increase in amplitude alternans and decrease in frequencies at which alternans was observed. These results appear to be confirmed in a human AF RA where succinate increased APD80 (257 vs 309 ms), ERF (260 vs 330 ms) and the occurrence of spontaneous arrhythmias. Finally, in sheep, GPR91 activation led to a slowing of SR (1.7 vs 1.3 Hz; p=0.03) a shortening of APD80 (200 vs 170 ms; p=0.007) and an increase in spontaneous arrhythmias.

Conclusion: Succinate induces significant electrophysiological modifications, especially in persistent AF, and increases vulnerability to AF. We have shown that the GPR91 pathway is involved in atrial electrophysiology and succinate-induced arrhythmogenesis, most likely in combination with increased ROS production.

REVERSAL REMODELING IN CHRONIC SLEEP DISORDERED BREATHING

Li-Wei Lo MD, PhD; Yu-Hui Chou MS; Chin-Huei Liu MD; Wen-Han Cheng MD; Wei-Lun Lin PhD and Shih-Ann Chen MD

Background: Obstructive sleep apnea (OSA) has been associated with increased cardiovascular morbidity and mortality, including sudden cardiac death. Sympathetic overactivity has been reported in OSA.

Objective: The study aimed to investigate the effect of renal artery denervation (RDN) on OSA rabbits in preventing ventricular arrhythmias.

Methods: Eighteen rabbits, randomized to sham control (Gr1), OSA (Gr2) and OSA receiving RDN (Gr3). All rabbits were injected at the tongue base under endoscopic guidance with normal saline (Gr1) or liquid silicone (Gr2 & 3) 1 month prior to the experiment (Fig A & B). Combined surgical and chemical RDNs were approached through bilateral retroperitoneal flank incisions in Gr 3 two months prior to the experiment. Electrophysiologic properties were evaluated during sleeping. Immunoblots of ion channel protein and immunohistochemistry (IHC) were evaluated after experiment.

Results: During sleep, the arterial PCO2 was higher in Gr 2 (69.3±±3.4 mmHg), when compared to Gr 1 (50.5±±8.0 mmHg, p=0.006) and 3 (47.6±±2.9 mmHg, p=0.004) respectively. There were no differences of ventricular effective refractory periods of both RV and LV among 3 groups (Table). The VF inducibility was elevated in Gr 2 (21.3±±3.5%), when compared to Gr 1 (8.3±±0.3%, p=0.03) and 3 (8.0±±0.4%, p=0.02), respectively. There was a decrease of renal noradrenaline in Gr.