BS-512-03

HIGH-RESOLUTION STRUCTURE-FUNCTION MAPPING OF INTACT HEARTS REVEALS ALTERED SYMPATHETIC CONTROL OF INFARCT BORDER ZONES

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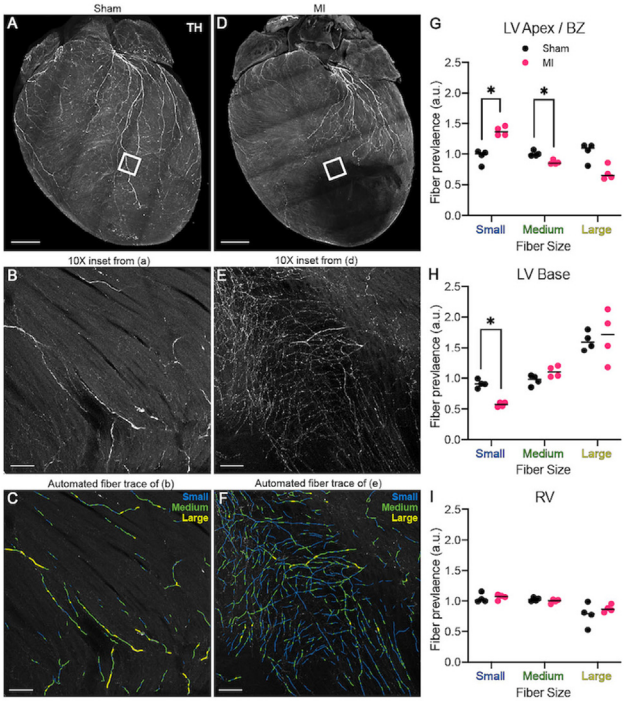
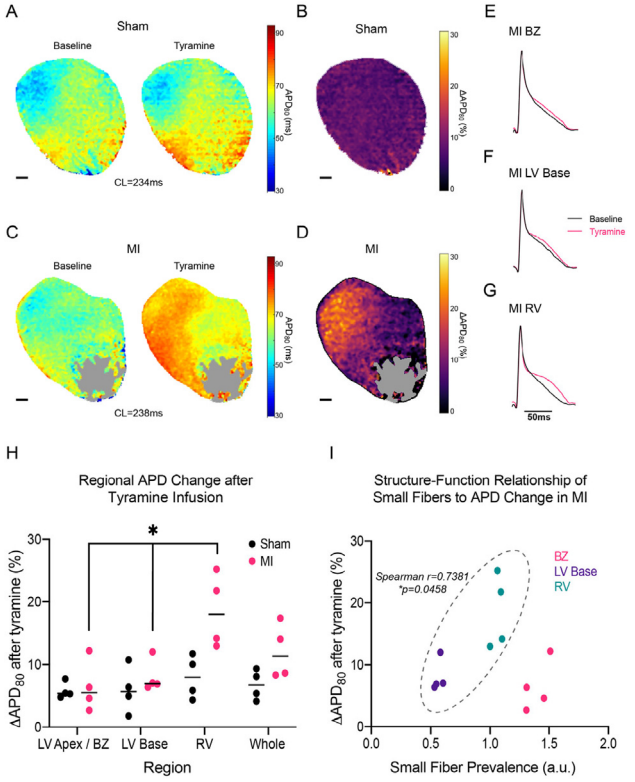
Background: Intramyocardial sympathetic nerve remodeling after myocardial infarction (MI) contributes to adverse outcomes such as sudden arrhythmic death, yet the underlying structural mechanisms are poorly understood. This is partly due to challenges in directly correlating high-resolution structural and electrical data from the same heart.
Objective: We sought to examine microstructural changes on the intact post-MI heart and to directly link these changes with electrical dysfunction.
Methods: We developed a high-resolution pipeline for anatomically precise alignment of electrical maps with structural myofiber and nerve-fiber maps created by customized computer vision algorithms.
Results: Using this integrative approach in a mouse model, we identified distinct structure-function correlates to objectively delineate the infarct border zone, a known source of post-MI arrhythmias. During tyramine-induced sympathetic nerve activation, we demonstrated regional patterns of altered electrical conduction aligned directly with altered neuroeffector junction distribution, pointing to potential neural substrates for cardiac arrhythmia.
Conclusion: This study establishes a synergistic framework for examining structure-function relationships after MI with microscopic precision, which has potential to advance understanding of arrhythmogenic mechanisms.





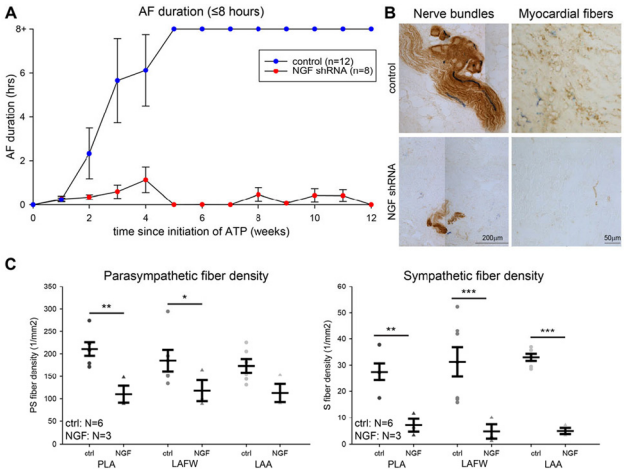
BS-512-04

TARGETED ATRIAL EXPRESSION OF NGF SHRNA ATTENUATES NEW PARASYMPATHETIC AND SYMPATHETIC NERVE SPROUTING AND RESULTING DEVELOPMENT OF PERSISTENT ATRIAL FIBRILLATION IN A CANINE MODEL - A NOVEL GENE THERAPY APPROACH TO ATRIAL FIBRILLATION

Anna Pfenniger MD, PhD; Shin Yoo PhD; David Johnson; Markus Rottmann PhD; Rod S. Passman MD, FHRS; Bradley P. Knight MD, FHRS and Rishi Arora MD, FHRS

Background: The autonomic nervous system plays an important role in development of atrial fibrillation (AF). We previously showed marked autonomic remodeling in a canine rapid atrial pacing (RAP) model of persistent AF. Nerve growth factor (NGF), a neurotrophin essential for the growth and survival of peripheral neurons, was upregulated in fibrillating atria. However, the role of NGF in the development of autonomic remodeling in AF remains to be demonstrated.
Objective: To prevent autonomic remodeling and development of persistent AF in a canine RAP model of AF.
Methods: NGF shRNA was injected in the atria of 8 dogs followed by electroporation to facilitate atrial gene delivery. The animals were then subjected to RAP for up to 12 weeks. Time to AF onset was determined. At the terminal EP study, episodes of AF were recorded with high-density mapping in the posterior left atrium (PLA), left atrial free wall (LAFW) and left atrial appendage (LAA) for offline analysis of AF characteristics. Tissue of each atrial region was harvested and used for immunohistochemistry with markers for parasympathetic (acetylcholinesterase, brown) or sympathetic nerves (dopamine beta-hydroxylase, blue).

Results: After initiation of RAP, control animals developed persistent atrial fibrillation (>8 hours) after a median of 14 days. In contrast, NGF shRNA animals never developed this burden of AF over the duration of the study. Residual AF recorded at time of terminal EP study was slower (lower dominant frequency; PLA: 10.5±0.8Hz Vs 11.0±0.7Hz; LAFW: 9.7±0.8Hz Vs 10.4±0.7Hz; LAA: 8.8±0.5Hz Vs 9.9±0.5Hz; two-way ANOVA $p<0.001$), less fractionated (longer fractionation interval; PLA: 80.4±8.1ms Vs 68.1±5.2ms; LAFW: 79.3±9.3ms Vs 70.9±3.1ms; LAA: 87.9±7.8ms Vs 80.3±2.0ms; two-way ANOVA $p<0.001$) and more organized (higher organization index and lower Shannon's entropy). Tissue analysis showed that RAP induced hypertrophy of nerve bundles was significantly attenuated in dogs receiving NGF shRNA. This decrease in bundle size was accompanied by a significant decrease in parasympathetic and sympathetic fibers in the atrial myocardium.
Conclusion: Targeted inhibition of atrial autonomic remodeling by NGF shRNA prevents development of persistent AF. Future optimization of this approach may lead to a novel, mechanism-guided therapy for AF.



ABSTRACT CA-528:
Experimental and Clinical Research into Esophageal Protection from Ablation Related Injury

Friday, April 29, 2022
9:15 AM - 10:15 AM

CA-528-01

PATTERNS OF ESOPHAGEAL TEMPERATURE CHANGE PREDICT ESOPHAGEAL THERMAL INJURY IN CATHETER ABLATION FOR ATRIAL FIBRILLATION

Tanzina Afroze; Yaacoub Chahine; Fima Macheret; Mahbod Jafarvand; Patrick Boyle and Nazem Akoum

Background: Esophageal luminal temperature (ELT) monitoring during catheter ablation for atrial fibrillation (AF) is widely used to reduce the incidence of esophageal thermal injury (ETI).
Objective: We investigated whether specific patterns of temperature variation are associated with ETI.
Methods: We conducted an observational study on patients with paroxysmal or persistent AF undergoing radiofrequency (RF) or cryoballoon ablation (CBA) at the University of Washington between September 2019 and November 2021. The CIRCA-S multi-sensor probe (Circa Scientific) (panel A) was used to record high-fidelity ELT. Patients underwent upper endoscopy one day after ablation. ELT data were analyzed for patterns associated with ETI, including maximum and minimum temperature, number of peaks above 37°C (panel B), troughs below 30°C (panel C), number of spikes, area under the temperature curve (panel D).
Results: A total of 78 patients (61.5% paroxysmal AF; 30.8% female) were included. Among them, 61 patients underwent RF, and 17 patients CBA. ETI was detected in 10 patients (12.8%). Patients with ETI had a higher number of peaks or troughs recorded (3.3±1.7 vs. 2.25±1.11, $p=0.041$) and a lower area under the curve (632.9±681.27 vs. 1393.44±1761.97, $p=0.038$). Logistic regression analysis revealed that the total number of peaks/troughs was associated with an odds ratio [OR]: 1.78 for increased risk of ETI (confidence interval [CI]: 1.1 - 2.87; $p=0.02$), while the area under the curve's OR was 1.65; ([CI]: 1.01 -2.72; $p=0.048$).
Conclusion: The number of peaks/troughs and the area under the temperature curve recorded during ELT are associated with an increased risk of ETI. Prospective studies guided by these parameters are needed to demonstrate their efficacy in reducing ETI.

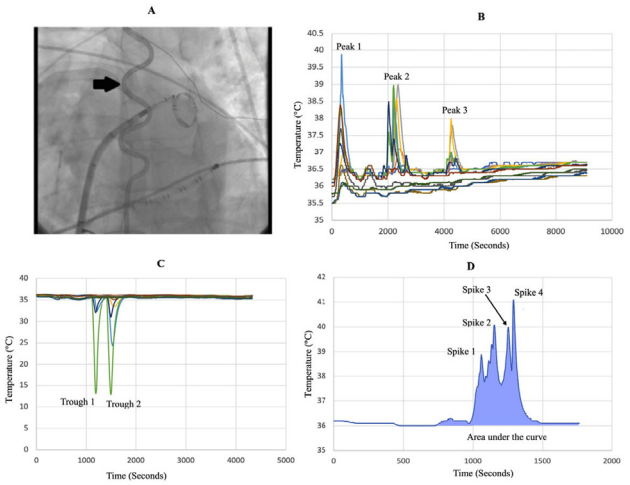


Figure 1: Fluoroscopic image of CIRCA-S multi-sensor probe and esophageal luminal temperature patterns. Fluoroscopic image of CIRCA-S multi-sensor probe **(A)**; peaks (fluctuation of temperature above 37 °C in RF, recorded by multiple thermistors) **(B)**; troughs (fluctuation of temperature below 30 °C in CBA, recorded by multiple thermistors) **(C)**; spikes (number of times temperature fluctuates before reaching the baseline, recorded by single thermistor) **(D)**.

CA-528-02

SHORT-TERM NATURAL COURSE OF ESOPHAGEAL THERMAL INJURY AFTER RADIOFREQUENCY CATHETER ABLATION FOR ATRIAL FIBRILLATION

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Background: Although esophagogastroduodenoscopy (EGD) is a good modality for assessing post ablation esophageal thermal injury (ETI), few details are known about the short-term healing or progression of esophageal injury.
Objective: Provide further insight into the short-term natural history of ETI and clinical outcome based upon repeated EGD imaging with use guided by late-gadolinium enhancement magnetic resonance imaging (LGE MRI).
Methods: A retrospective analysis of 378 patients who underwent EGD based on the findings on the esophagus by post-ablation LGE MRI imaging after left atrium radiofrequency ablation for atrial fibrillation from 2010-2019 at our institution. We defined ETI according to the Kansas City classification (type 1: erythema, 2a: superficial ulcers, 2b: deep ulcers, 3a: perforation without communication with the atria, 3b: perforation with