

## BS-512-03

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

Ching Zhu MD; Pradeep S. Rajendran MD, PhD; Peter Hanna MD, PhD; Guy Salama PhD, FHRS; Igor R. Efimov PhD, FHRS and Kalyanam Shivkumar MD, PhD, FHRS

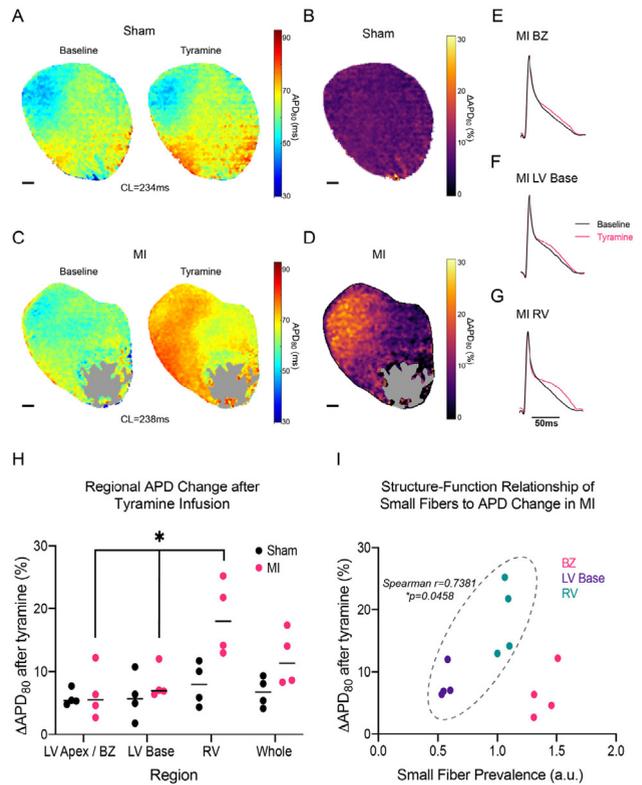
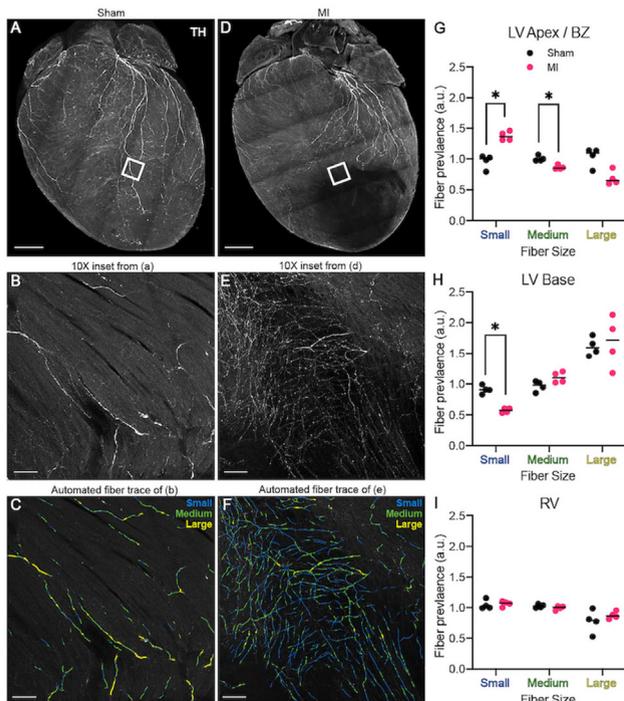
**Background:** Intramyocardial sympathetic nerve remodeling after myocardial infarction (MI) contributes to adverse outcomes such as sudden arrhythmic death, yet the underlying structural mechanisms are poorly understood. This is partly due to challenges in directly correlating high-resolution structural 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).