Neural Control of Ventricular Rate in Ambulatory Dogs with Pacing Induced Sustained Atrial Fibrillation

박형욱

전남대학교병원 순환기내과

Brain-Autonomic Nerves and the Heart

National Disaster

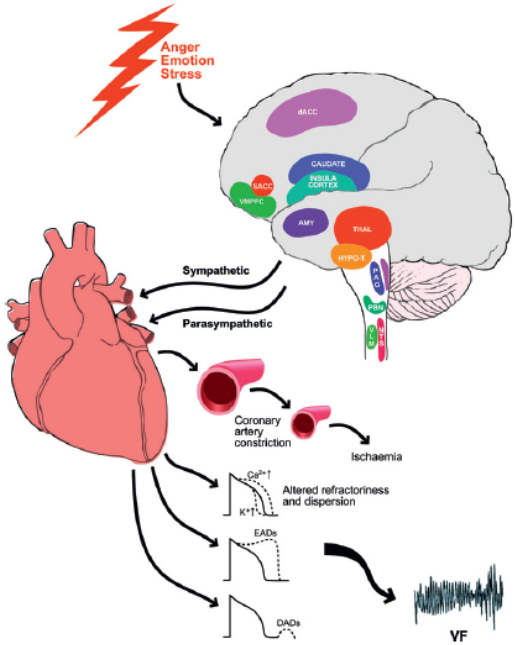
-- SCD increases at times of national disaster

Experimental models

-- VS protects against stress induced arrhythmia
Stress magnifies the proarrhythmic effects of ischemia

Humans

-- Stress induces coronary or microvascular constriction
Anger potentiates ventricular arrhythmias
Beta-blockade protective for SCD
Emotion precipitates VF in long QT patients



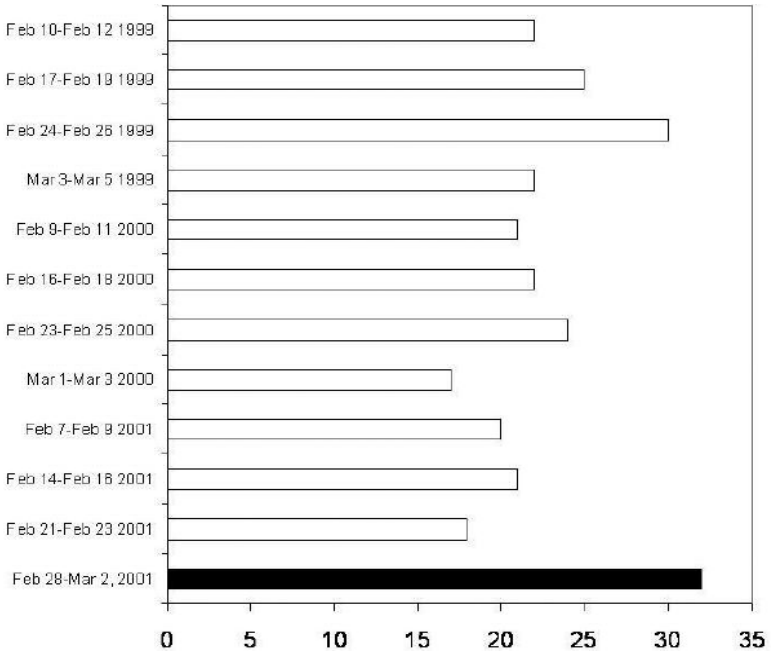
Socioeconomic influence

-- Chronic psychosocial factors influence rates of arrhythmia
and sudden death

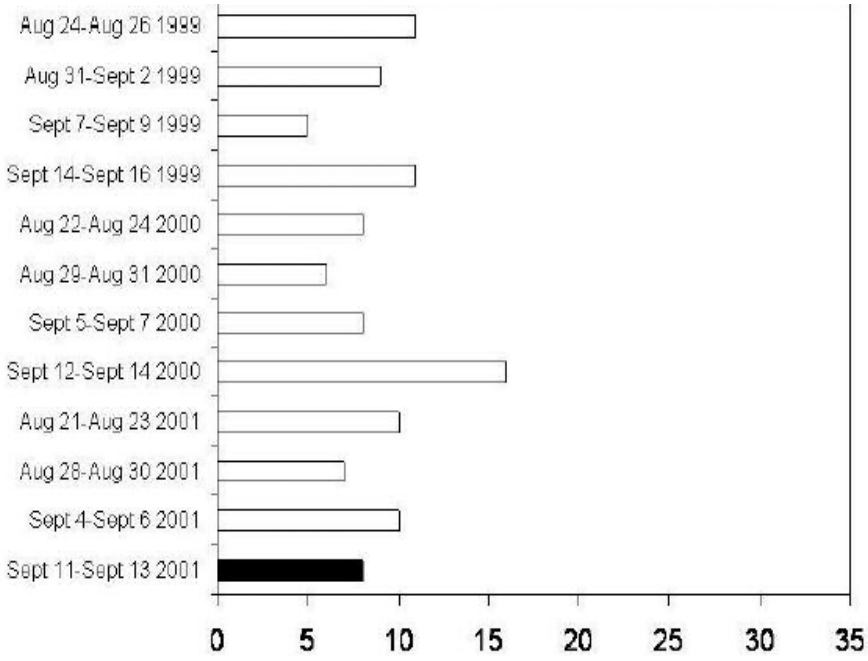
Taggart P et al. BMJ 2010

Brain-Autonomic Nerves and the Heart

National Disaster
-- Earthquake

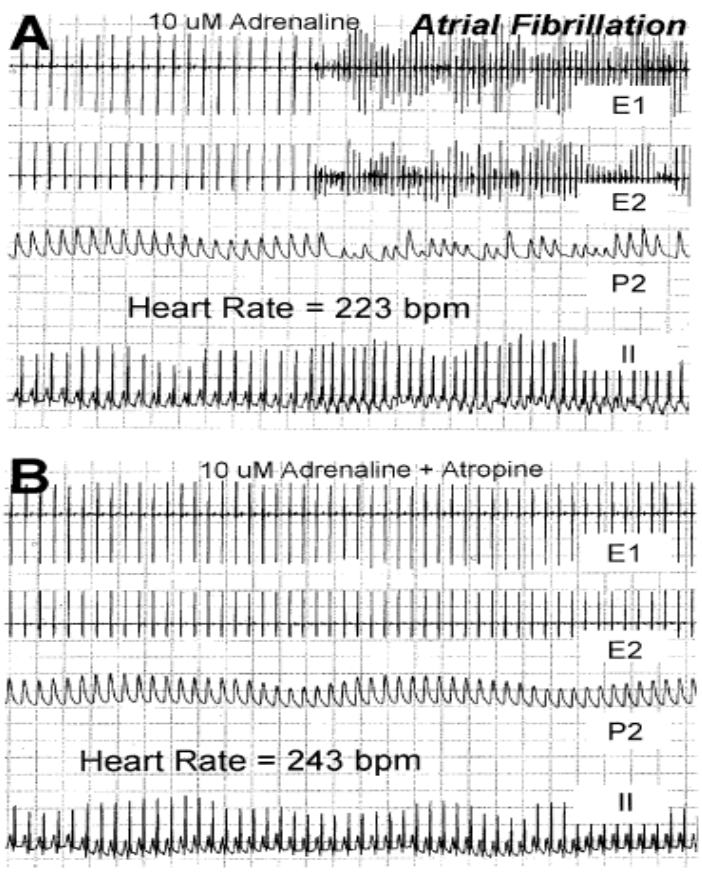


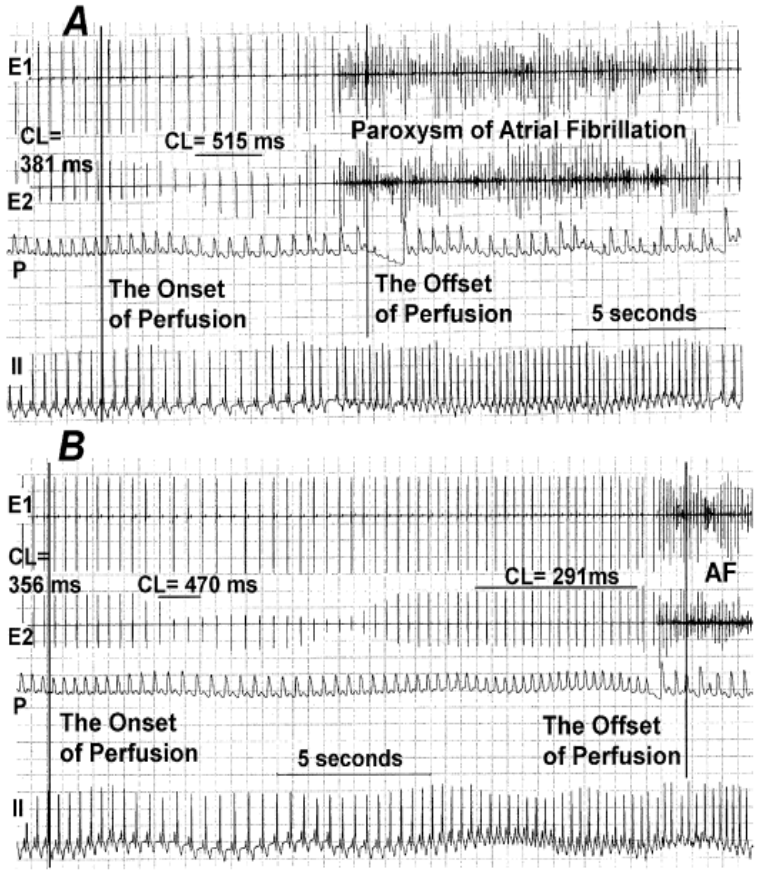
National Disaster
-- Terror



Gold LS et al. Prehospital Disast Med 2007;22(4):313–317

Role of adrenergic and cholinergic stimulation in spontaneous atrial fibrillation in dogs





Sharifov OF, et al. J Am Coll Cardiol 2004; 43:483-90

Autonomic AF - Differentiation

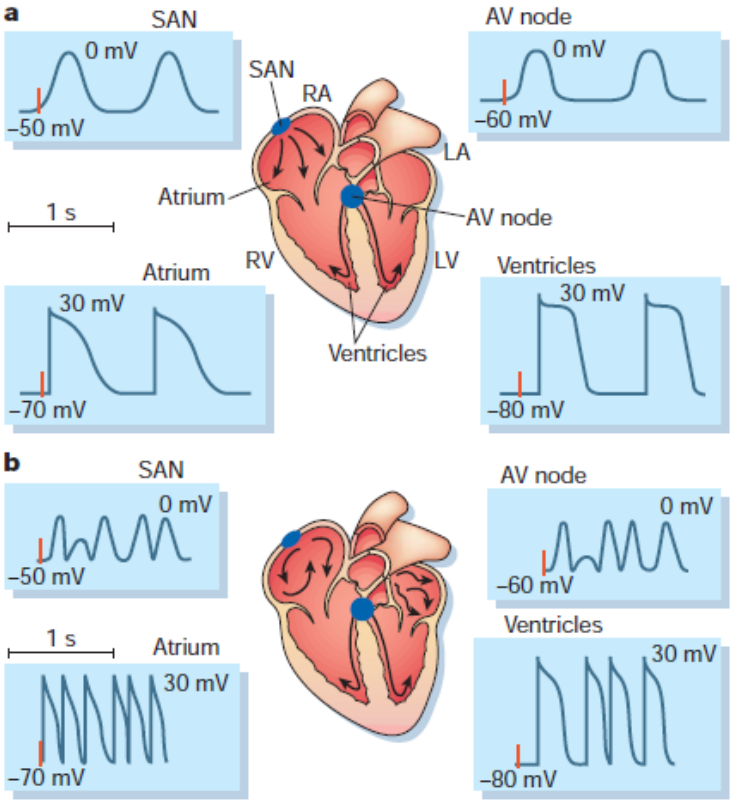
- Adrenergic AF

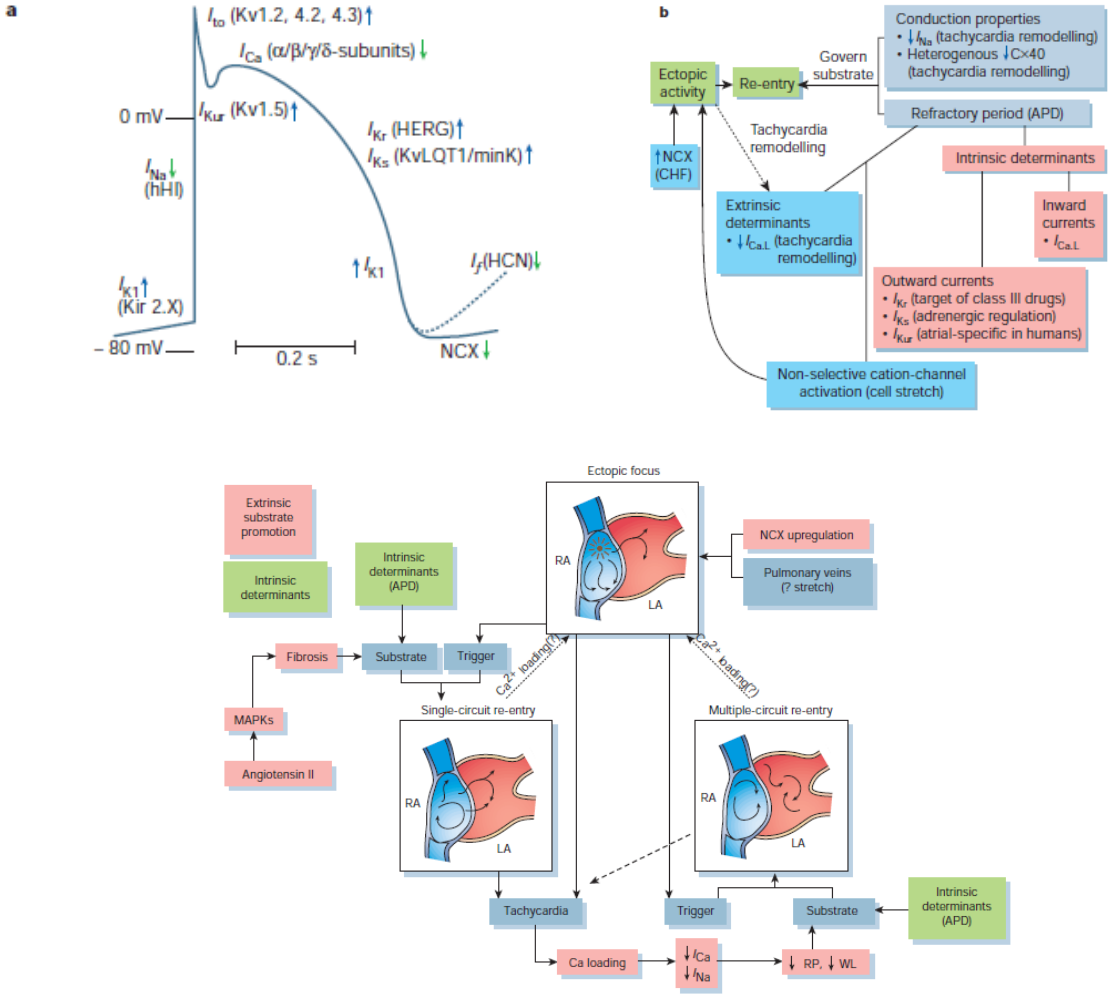
-- Tachycardia
-- Postoperative
-- Alcohol
-- Exercise
-- Emotional stress
-- Polyuria
-- Better with BB
-- More common with heart disease

- Cholinergic AF

-- Male predominance
-- Age at onset 40-50
-- Bradycardia
-- Vomiting
-- Severe constipation
-- After large meal
-- Cold carbonated beverages
-- Rest
-- Coughing
-- Diving into cold water
-- Valsalva
-- Exacerbated with digoxin, beta-blockers
-- More common without heart disease

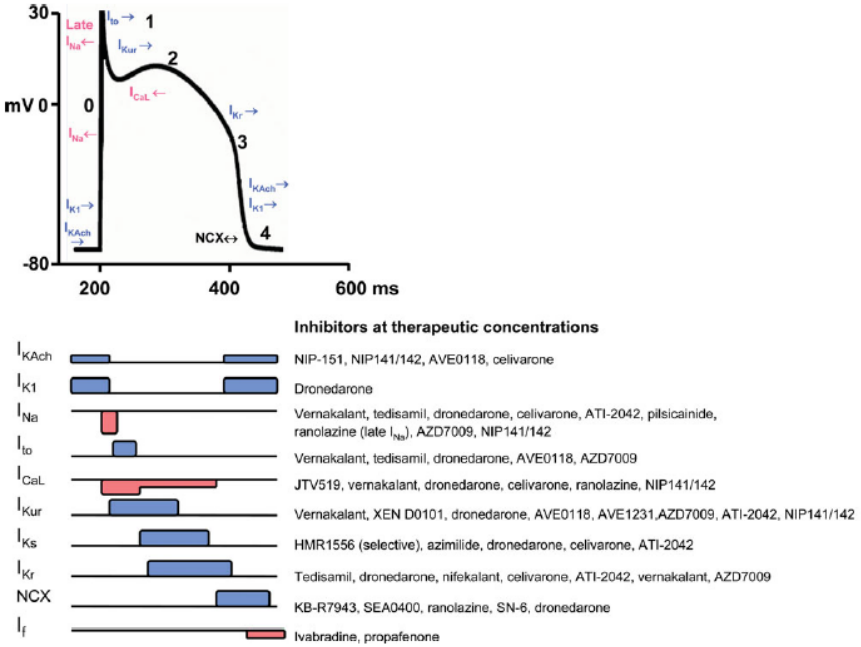
Electrical and Structural Remodeling During Atrial Fibrillation

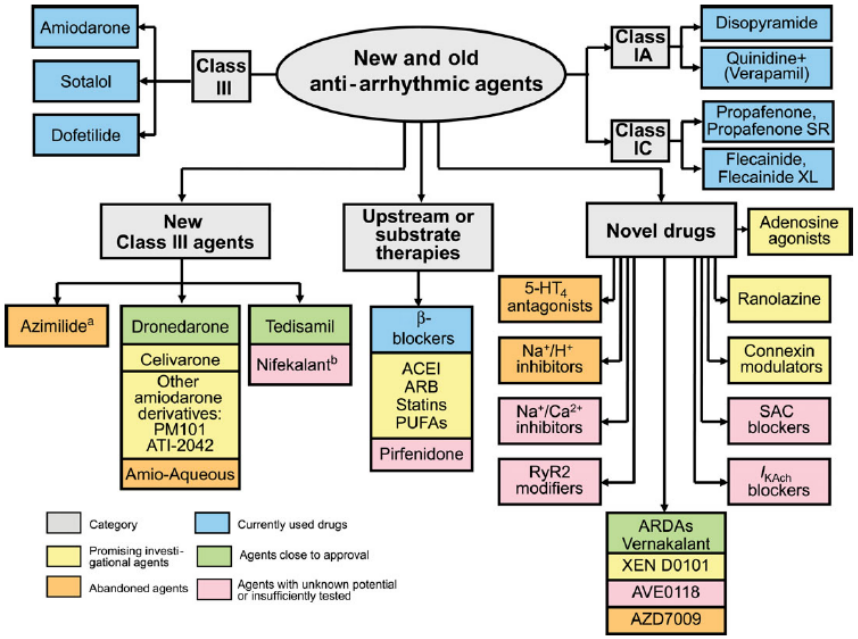




Nattel S. Nature 2002: 415; 219-226

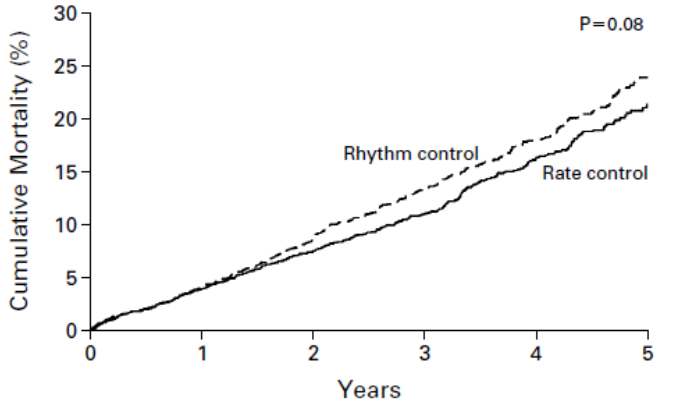
Anti-arrhythmic drug therapy for atrial fibrillation: current anti-arrhythmic drugs, investigational agents, and innovative approaches



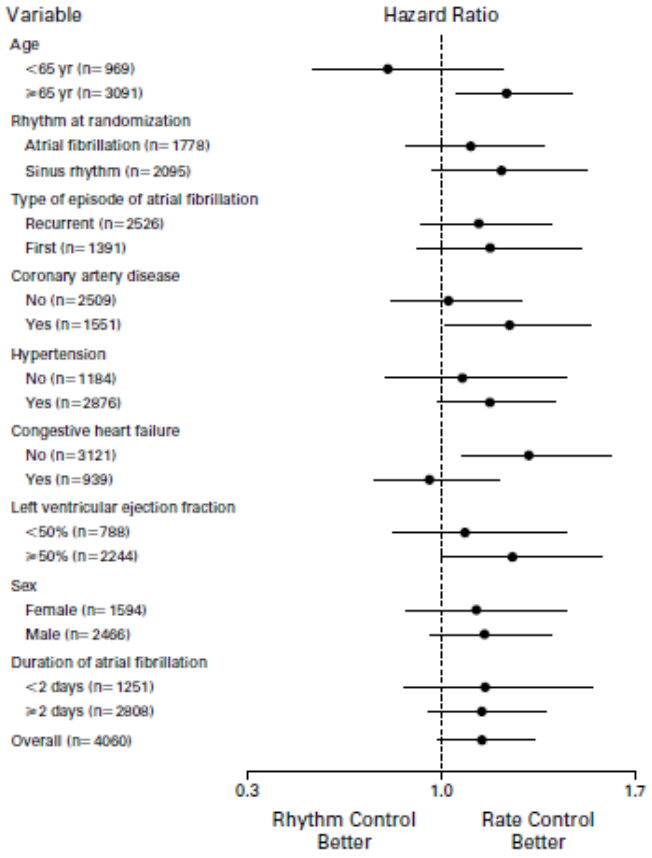


Savelieva I, et al. Europace 2008; 10: 647-65

A Comparison of Rate Control and Rhythm Control in Patients with Atrial Fibrillation: Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)

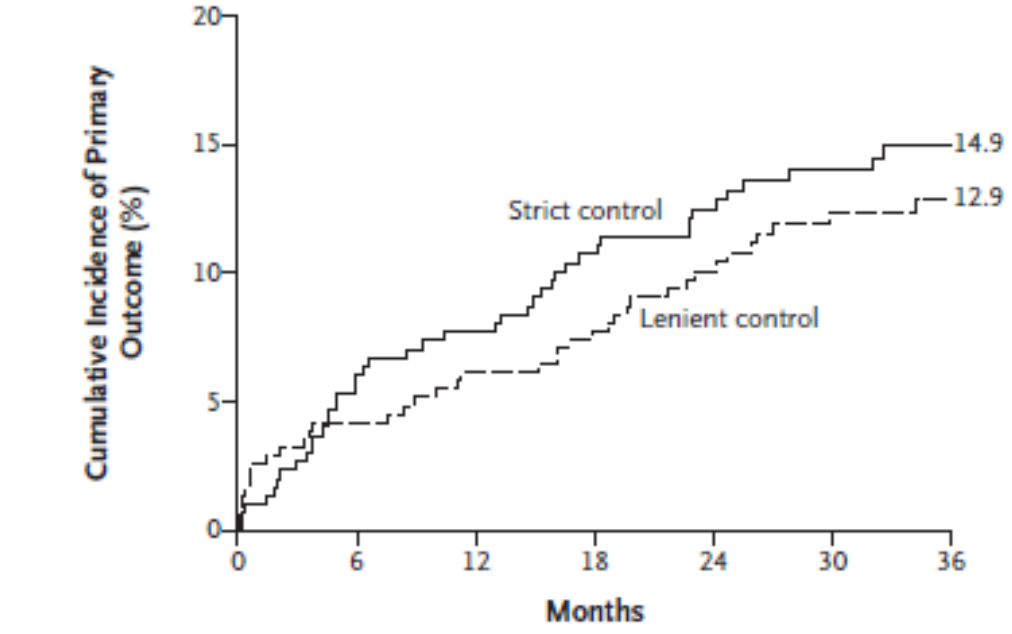


No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)



AFFIRM Investigators. NEJM 2002; 347:1825-33

Lenient versus Strict Rate Control in Patients with Atrial Fibrillation: RACE II



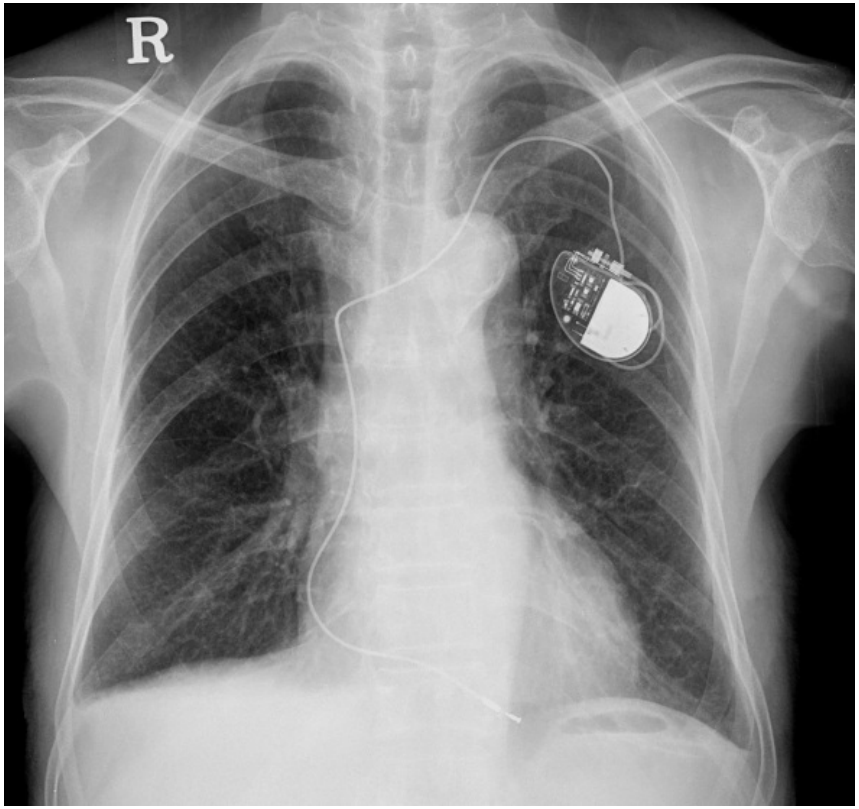
No. at Risk							
Strict control	303	282	273	262	246	212	131
Lenient control	311	298	290	285	255	218	138

Van Gelder IC, et al. NEJM 2010; 362:15

What does AV node do?
What happens to AV node?

From patient's EP strip

한강다리 폭파, 방실결절 절제

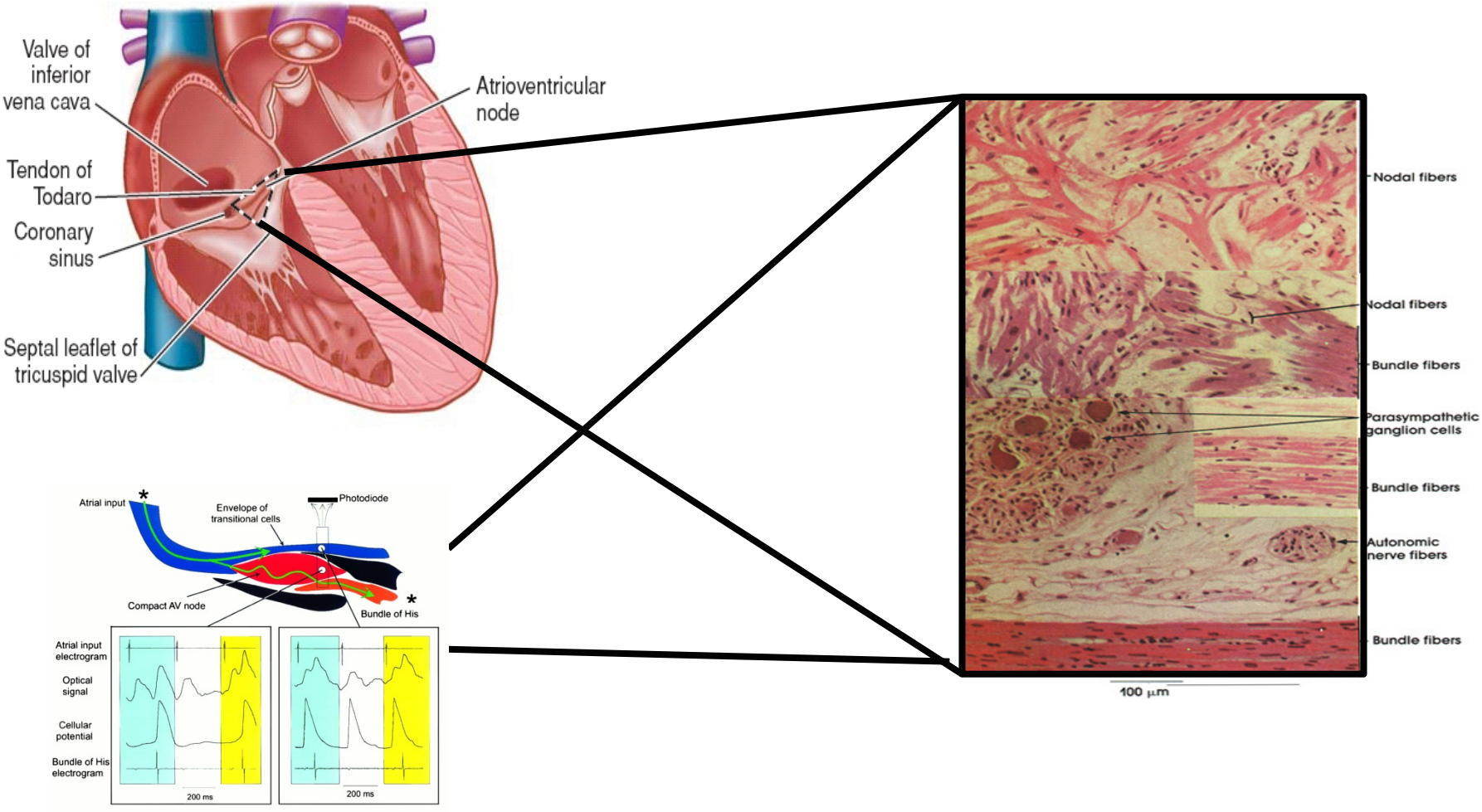


Photographs from google.com

AV node

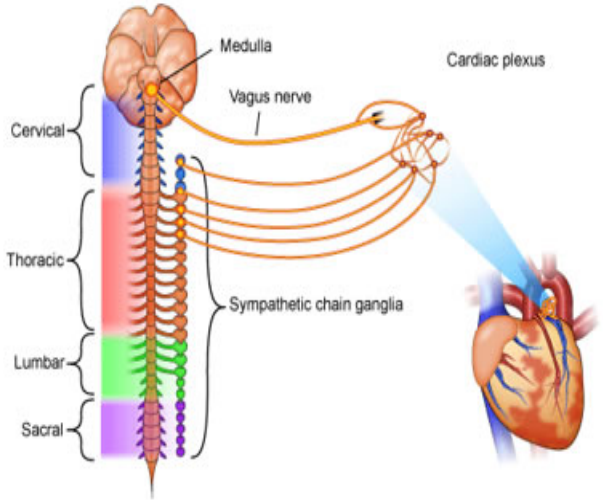
" 줄을 서시오"

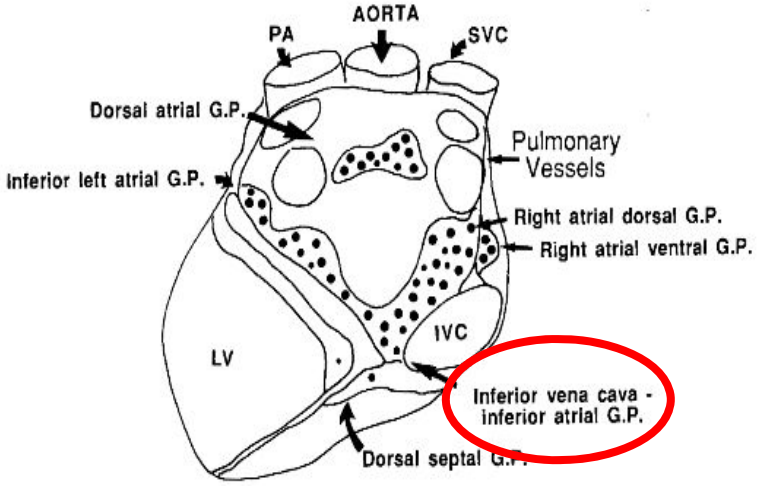
AV Node
- Mystery of conduction delay -

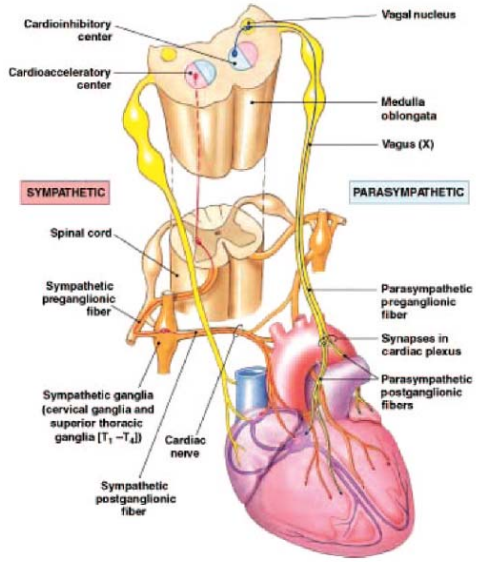


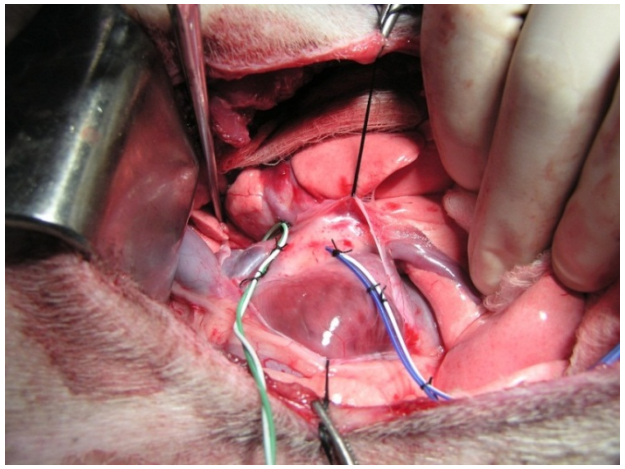
Anatomy Atlases. Bergman RA.
Medkour D et al. Circulation 1998;98:164-74

Anatomy of the Extrinsic and Intrinsic Cardiac Nervous System



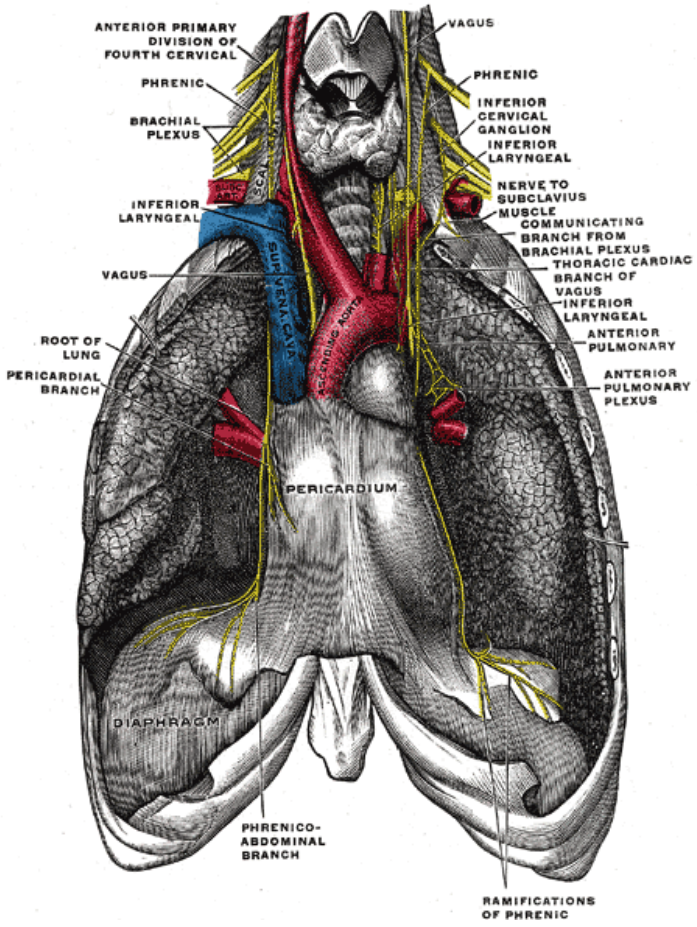


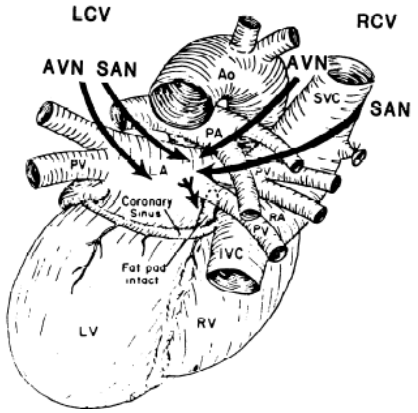


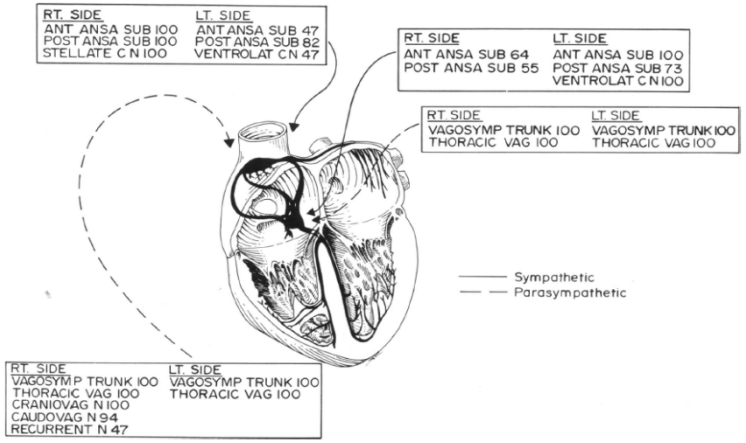


The Anatomical Record. Yuan BX et al. 1994; 239; 75-87

Selective innervation of SA and AV node and Little brain of the Heart

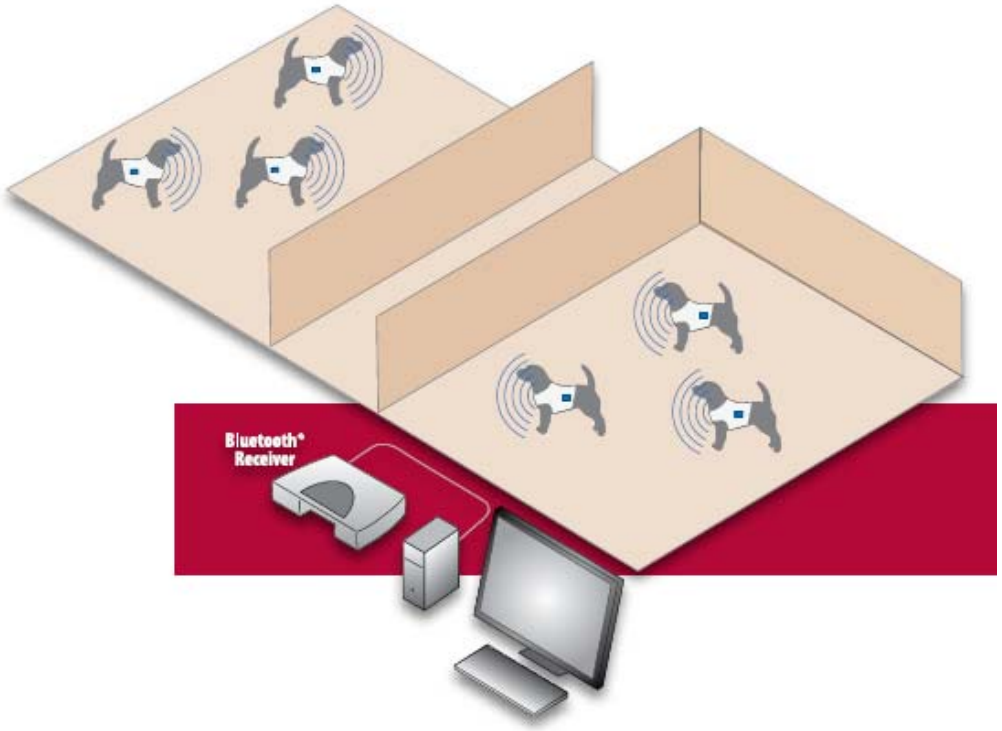


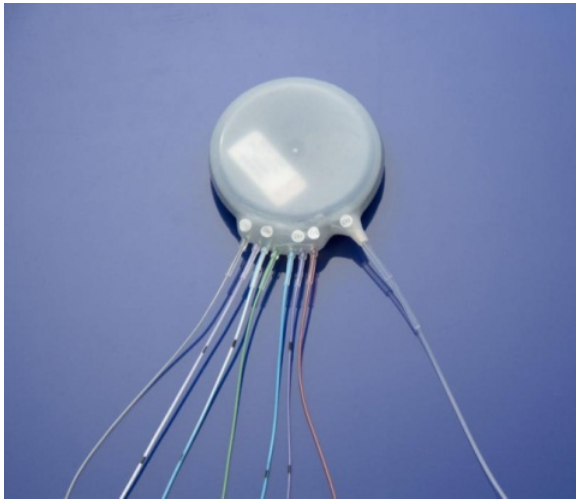


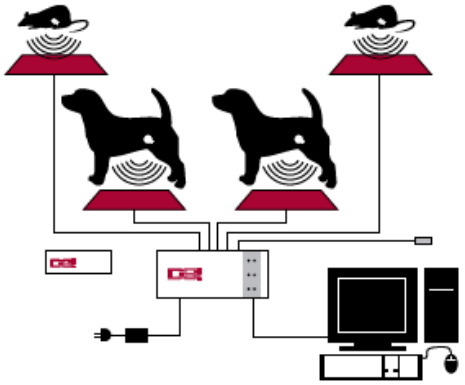


Ardell JL et al. Am J Physiol
DC Randall et al. Am J Physiol

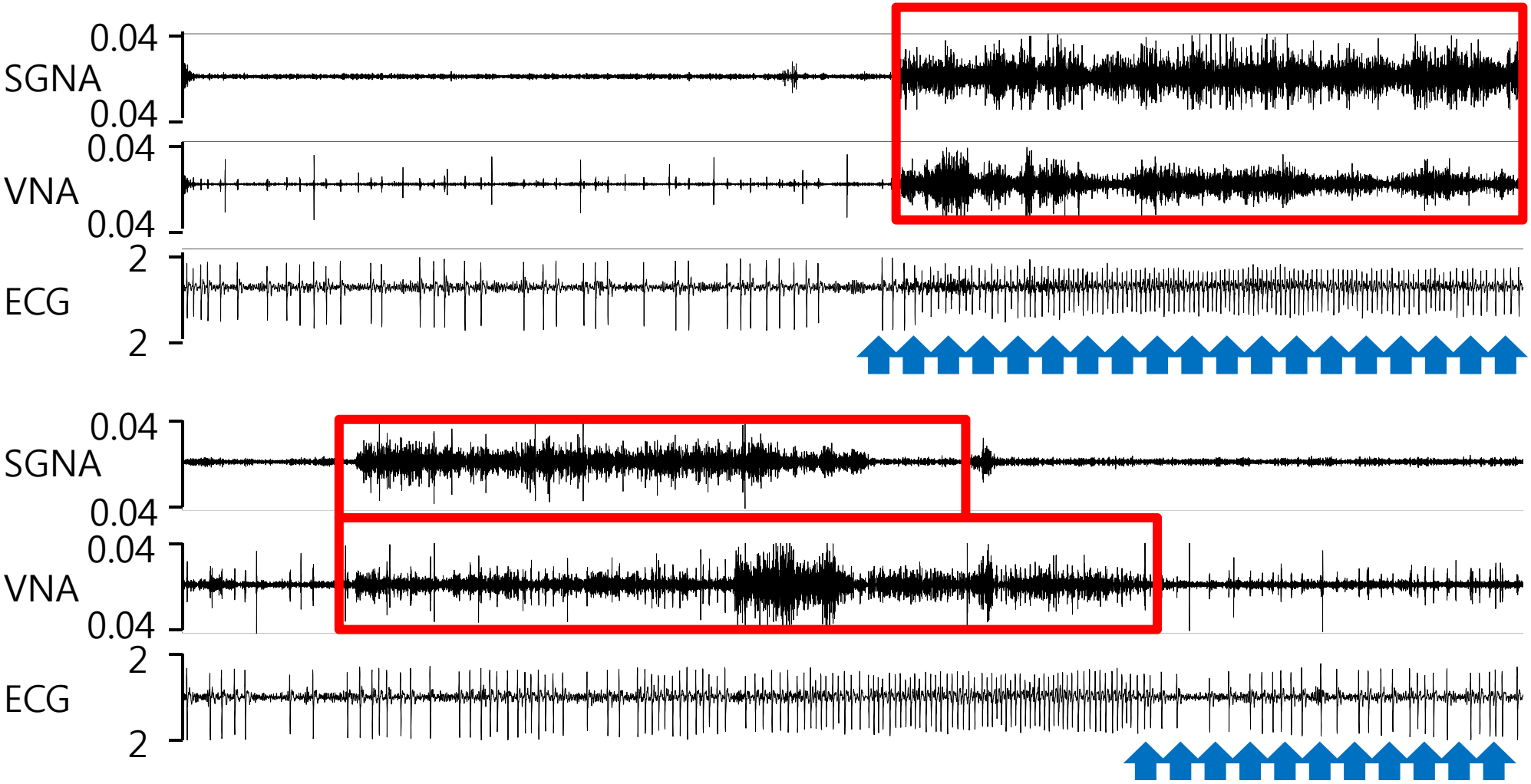
Direct evidence of nerve discharge and cardiac arrhythmia in ambulatory animal





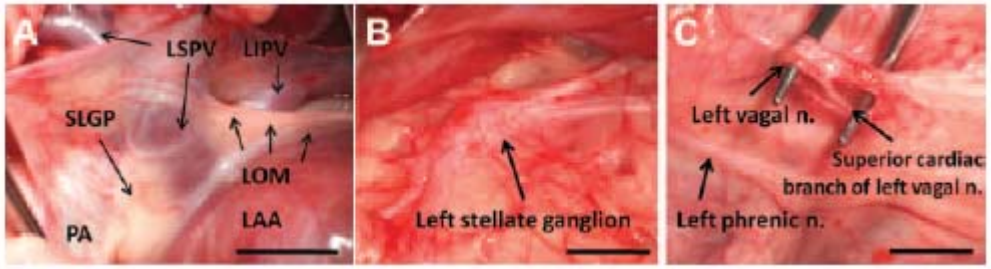


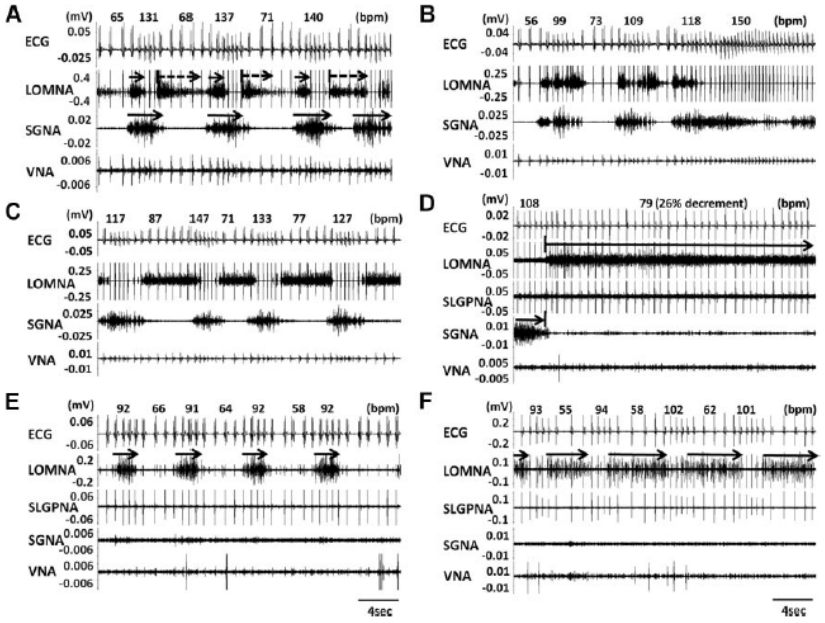
Sympathovagal coactivation associated with rapid VR during AF

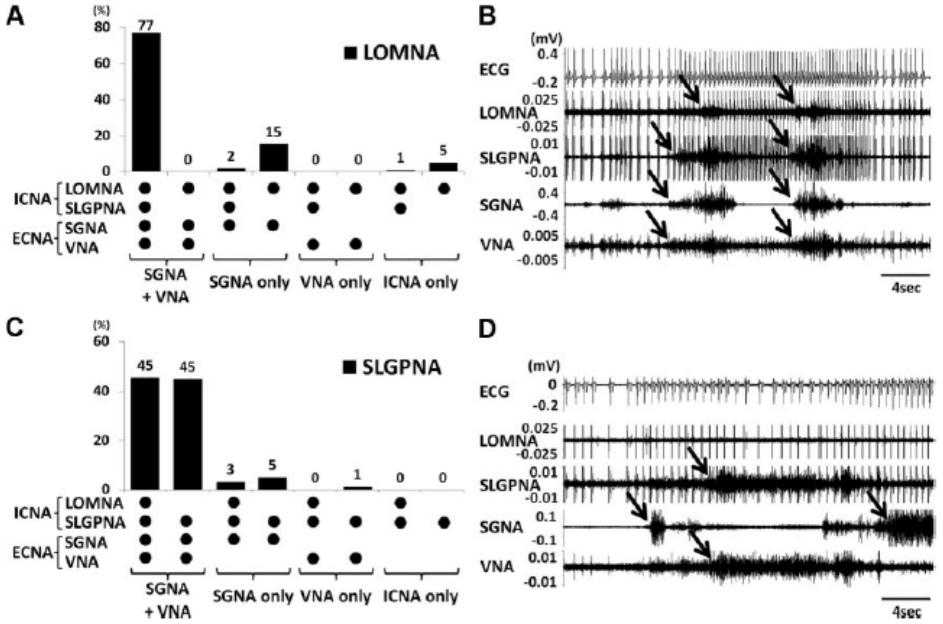


SGNA; Stellate ganglion NA, VNA; Vagal nerve activity

Intrinsic Cardiac Nerve Activity and Paroxysmal Atrial Tachyarrhythmia in Ambulatory Dogs







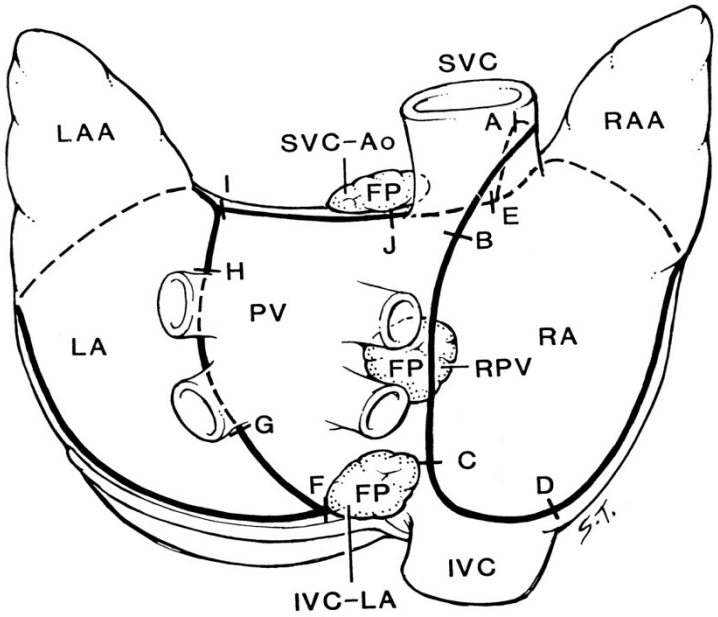
EK Choi, et al. Circulation 2010; 121: 2615-23

Purpose

- Relative importance of RVNA and LVNA
- Relation of IVC-IAGPNA and VNA
- Sole role of IVC-IAGPNA without VNA

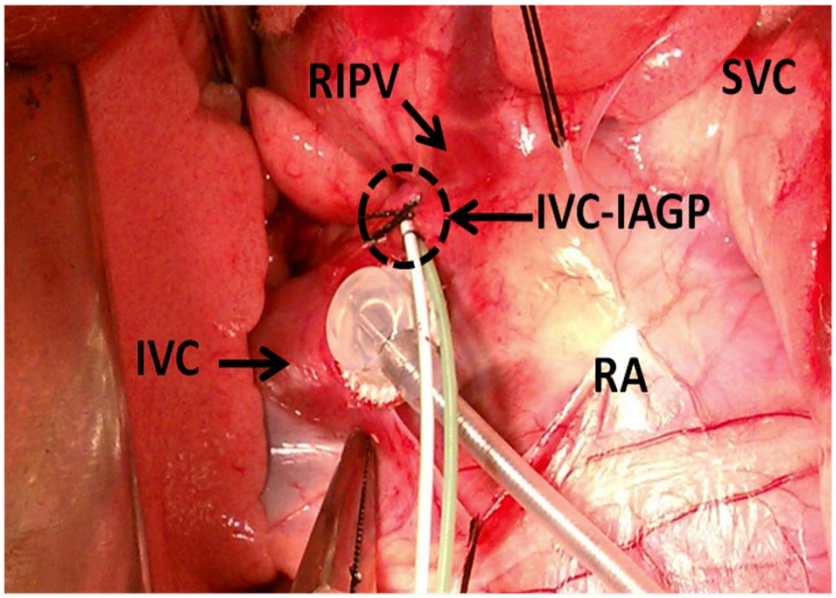
IN AMBULATORY DOGS WITH PACING INDUCED SUSTAINED ATRIAL FIBRILLATION

Posterior view of the atria and GP



CW Chiou et al. Circulation 1997;95:2573-2584

Operation view of the atria and GP



Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

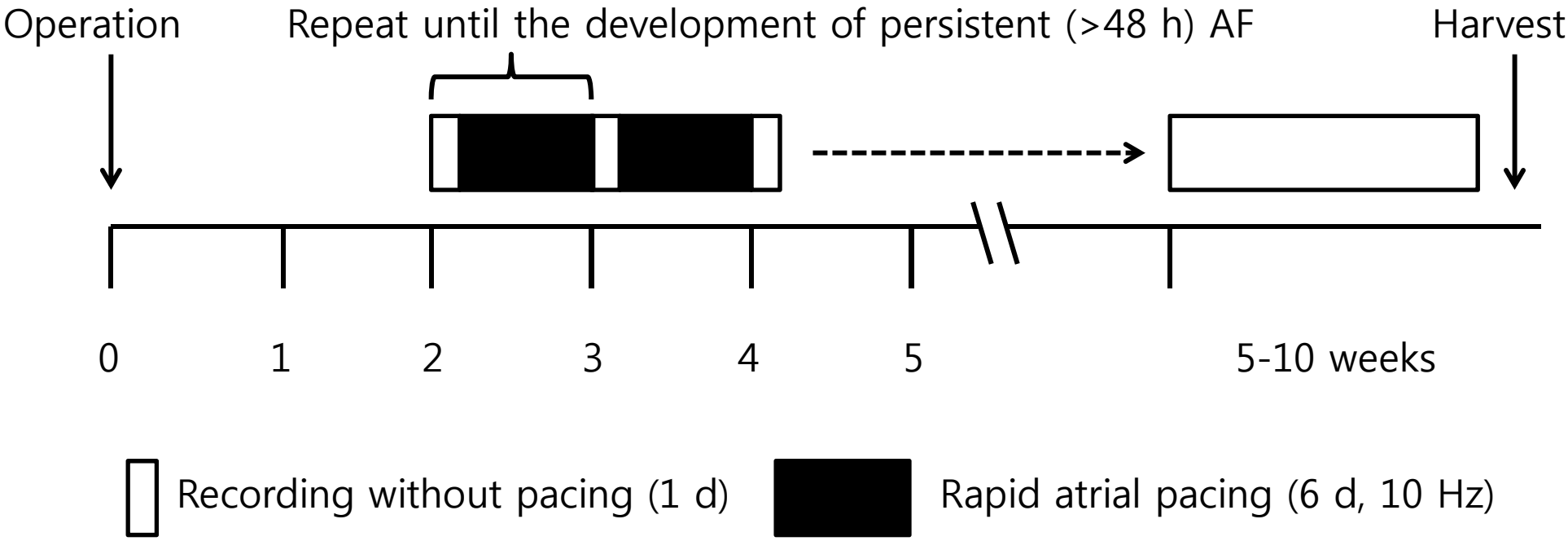
Methods

- Bilateral vagus nerve activity (VNA) and IVC – inferior atrial ganglionated plexus nerve activity (IAGPNA) rec ording during sustained (>48 hours) AF in ambulatory dogs.

- NAs were integrated over 10-s segments, resulting in 8640 data points/24 hours. We also determined the a verage VR during AF for that 10-s period.

Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

Methods – Study protocol



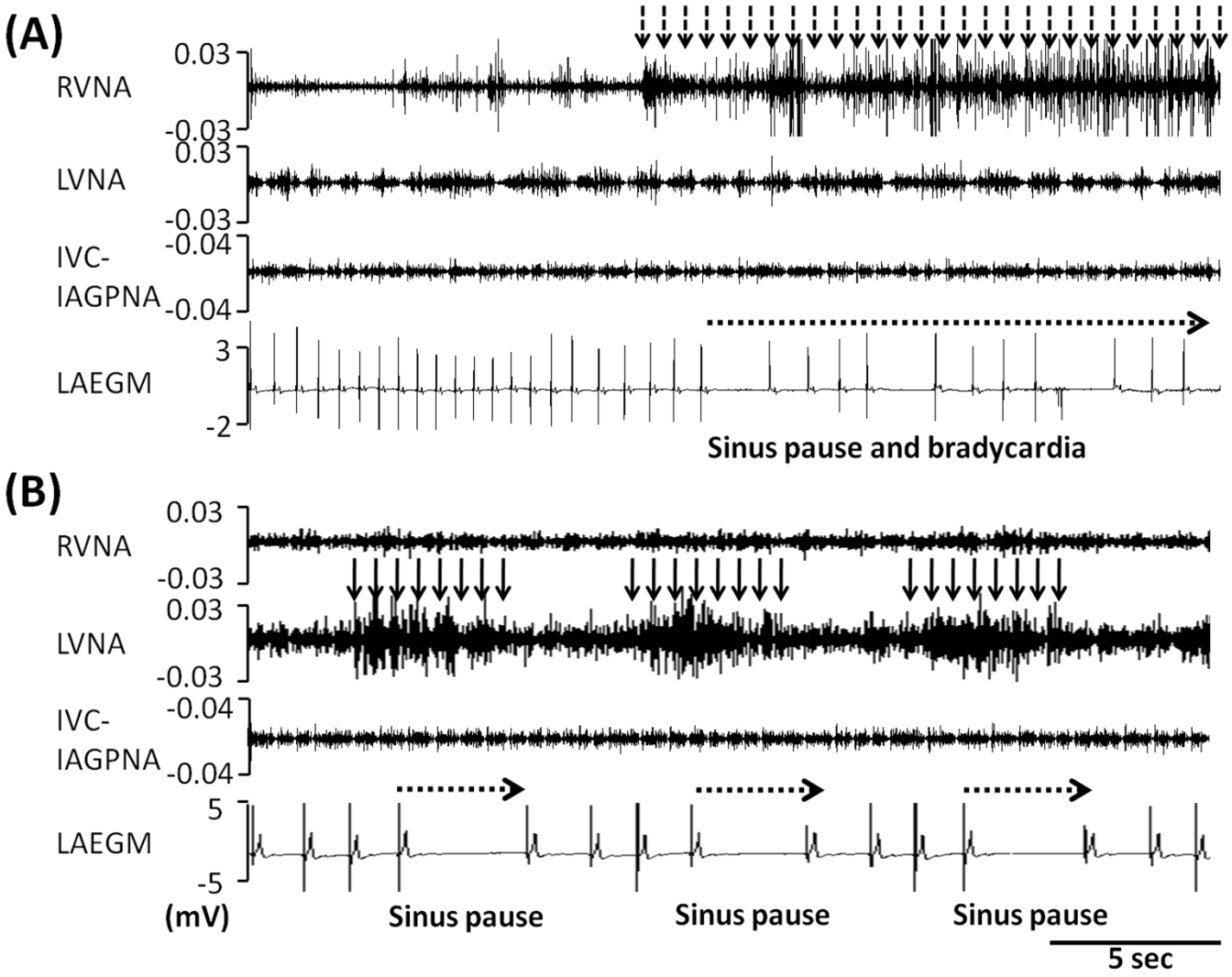
Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

Results

RVNA, LVNA and bipolar left atrial electrogram in sinus rhythm

RVNA associated with SB and pause

LVNA associated with SB and pause



Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

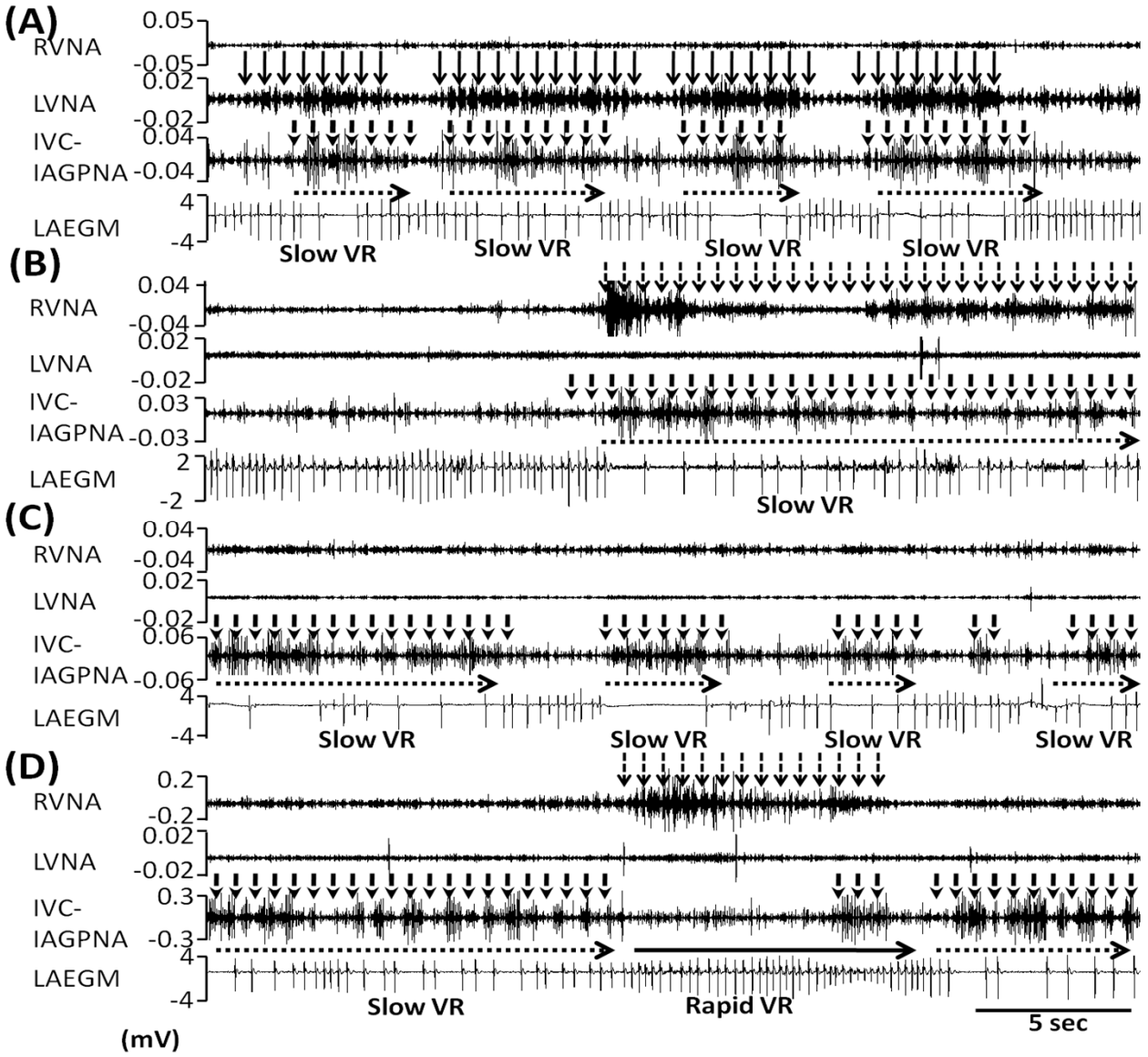
RVNA, LVNA, IVC-IAGPNA during sustained AF

IVC-IAGPNA with LVNA (+)

IVC-IAGPNA with RVNA (+)

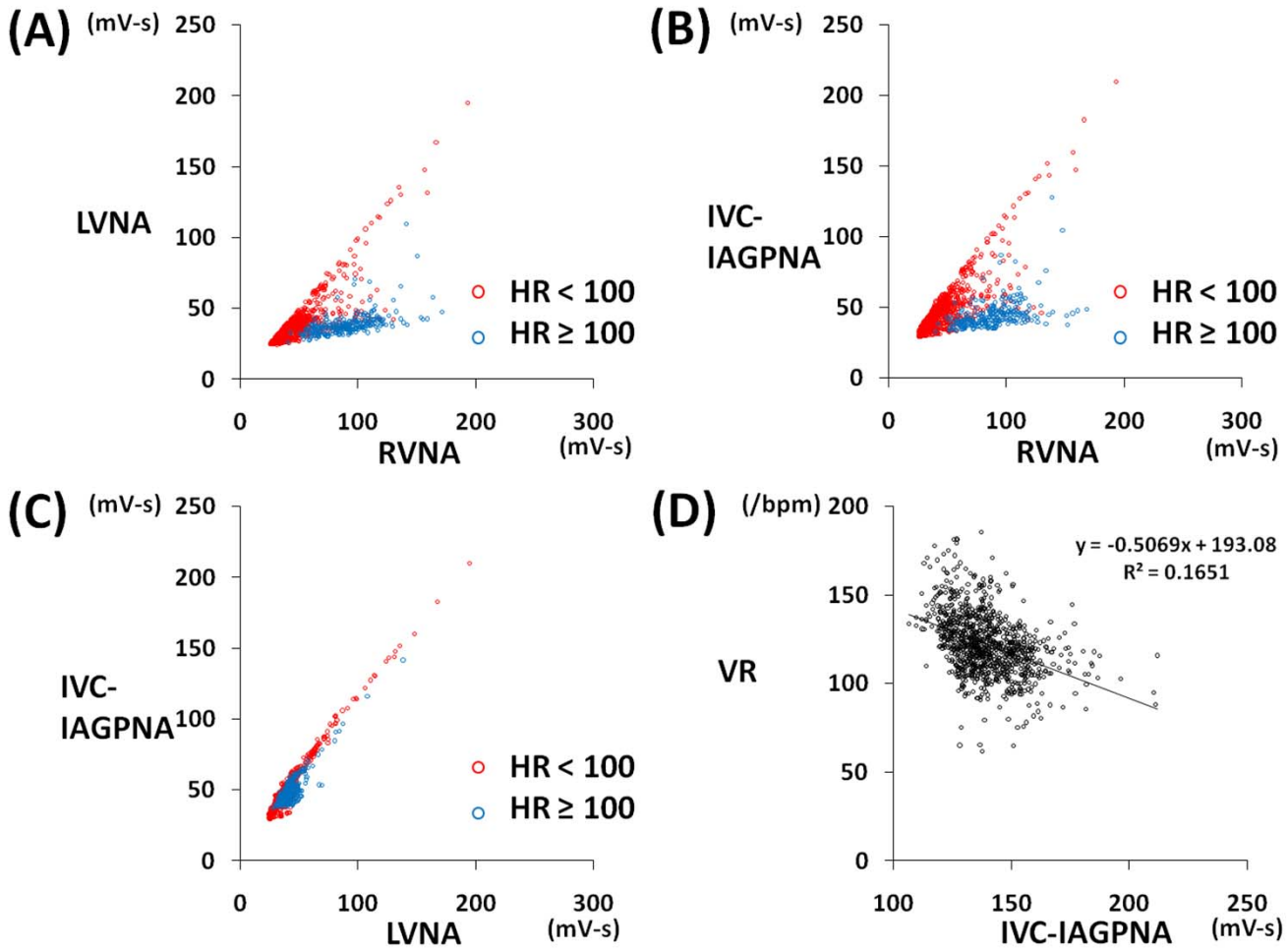
IVC-IAGPNA independent with VNA

RVNA activation after IVC-IAGPNA withdrawal



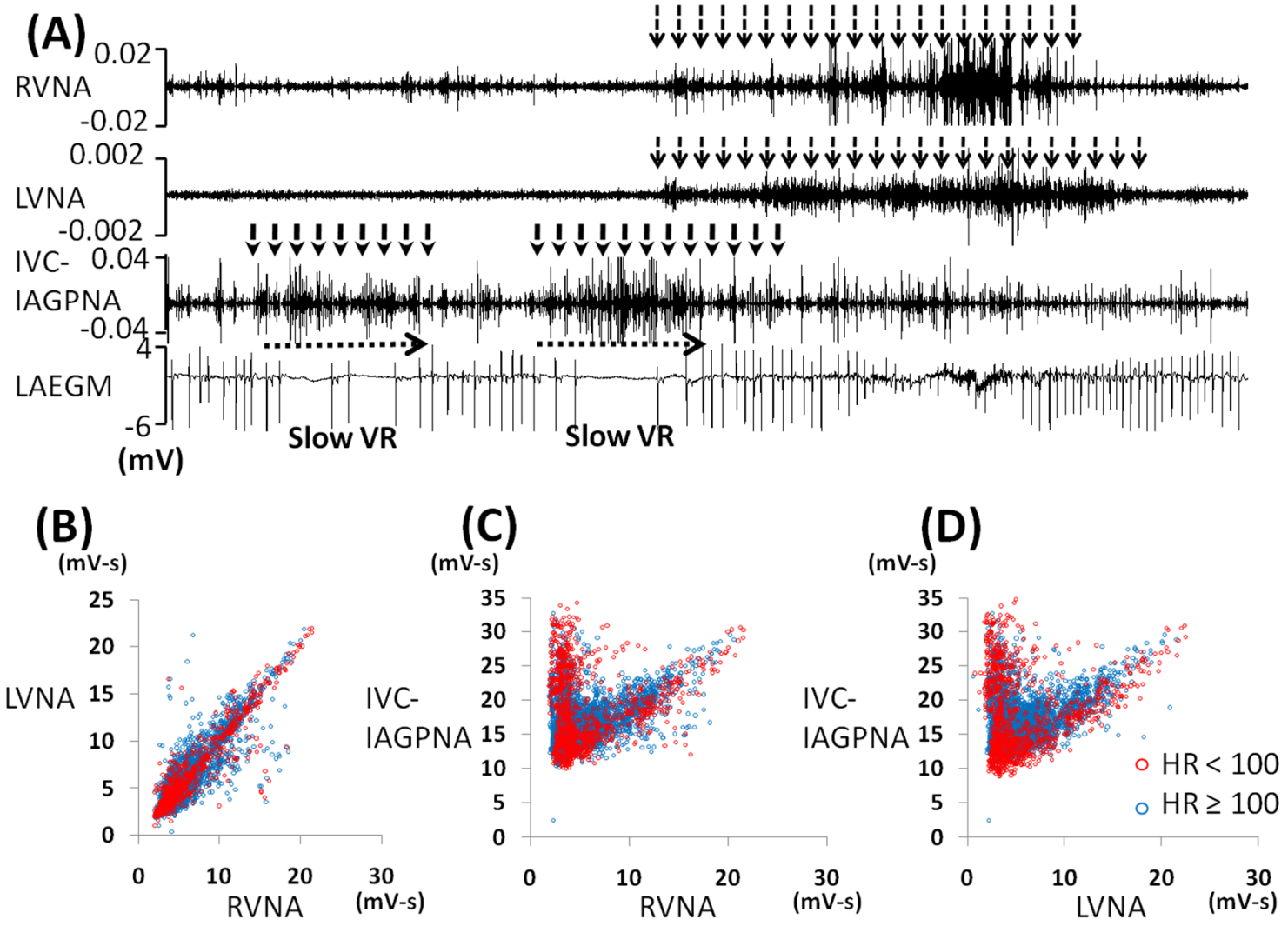
Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

10-s integrated NA and ventricular rate: "L" shape relationship



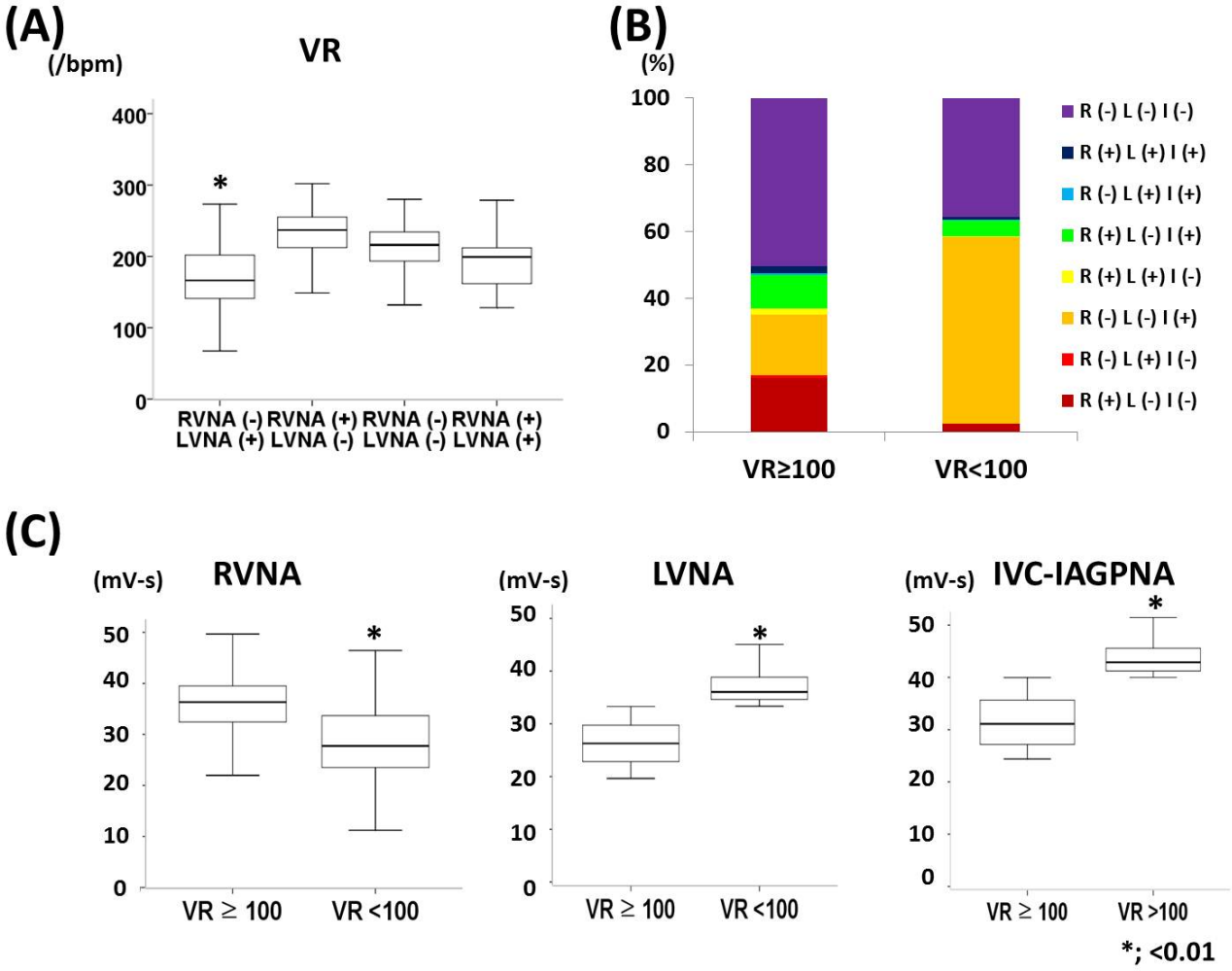
Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

Slowing of VR associated with IVC-IAGPNA without RVNA or LVNA



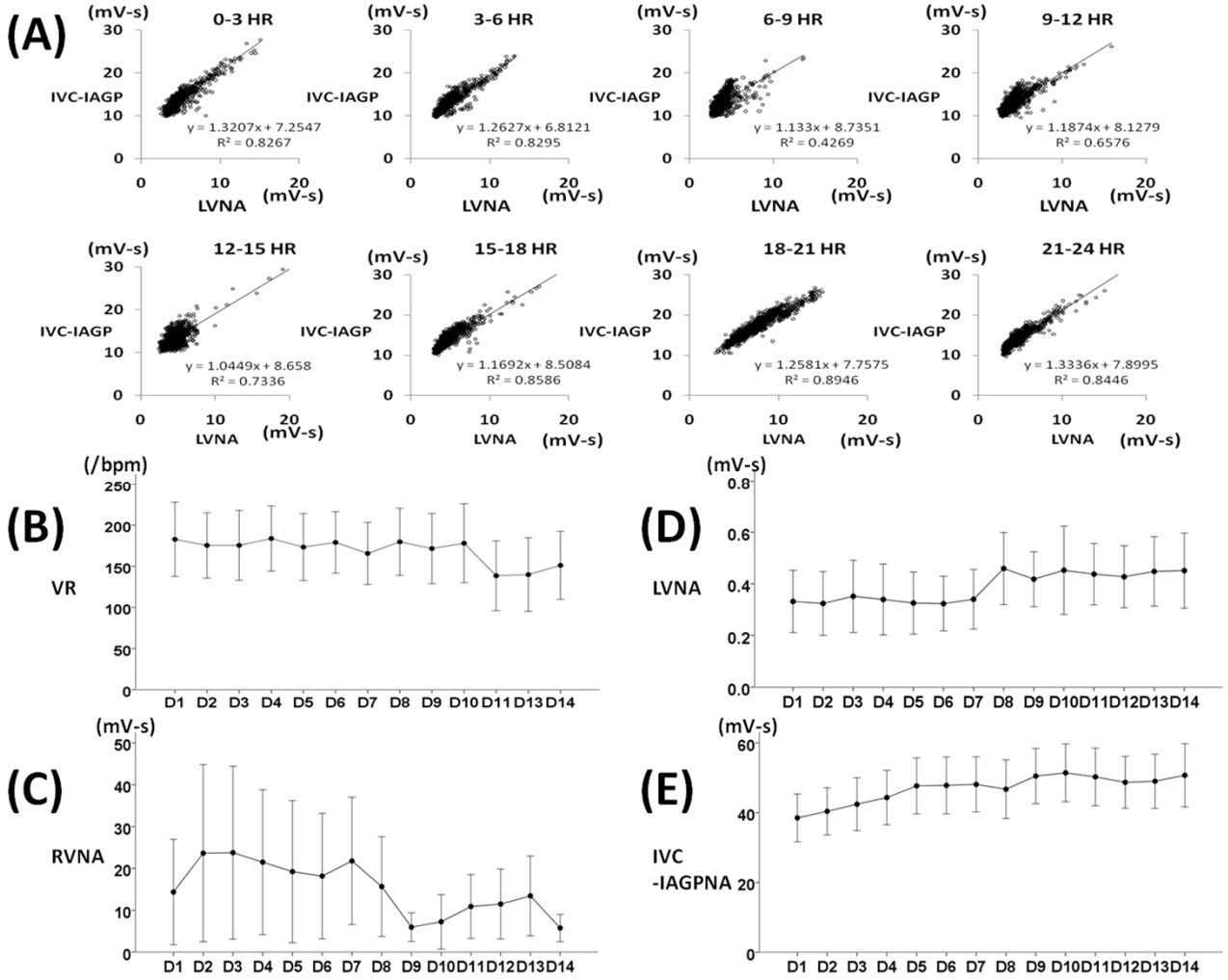
Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

Relationship between RVNA, LVNA, IVC-IAGPNA and VR



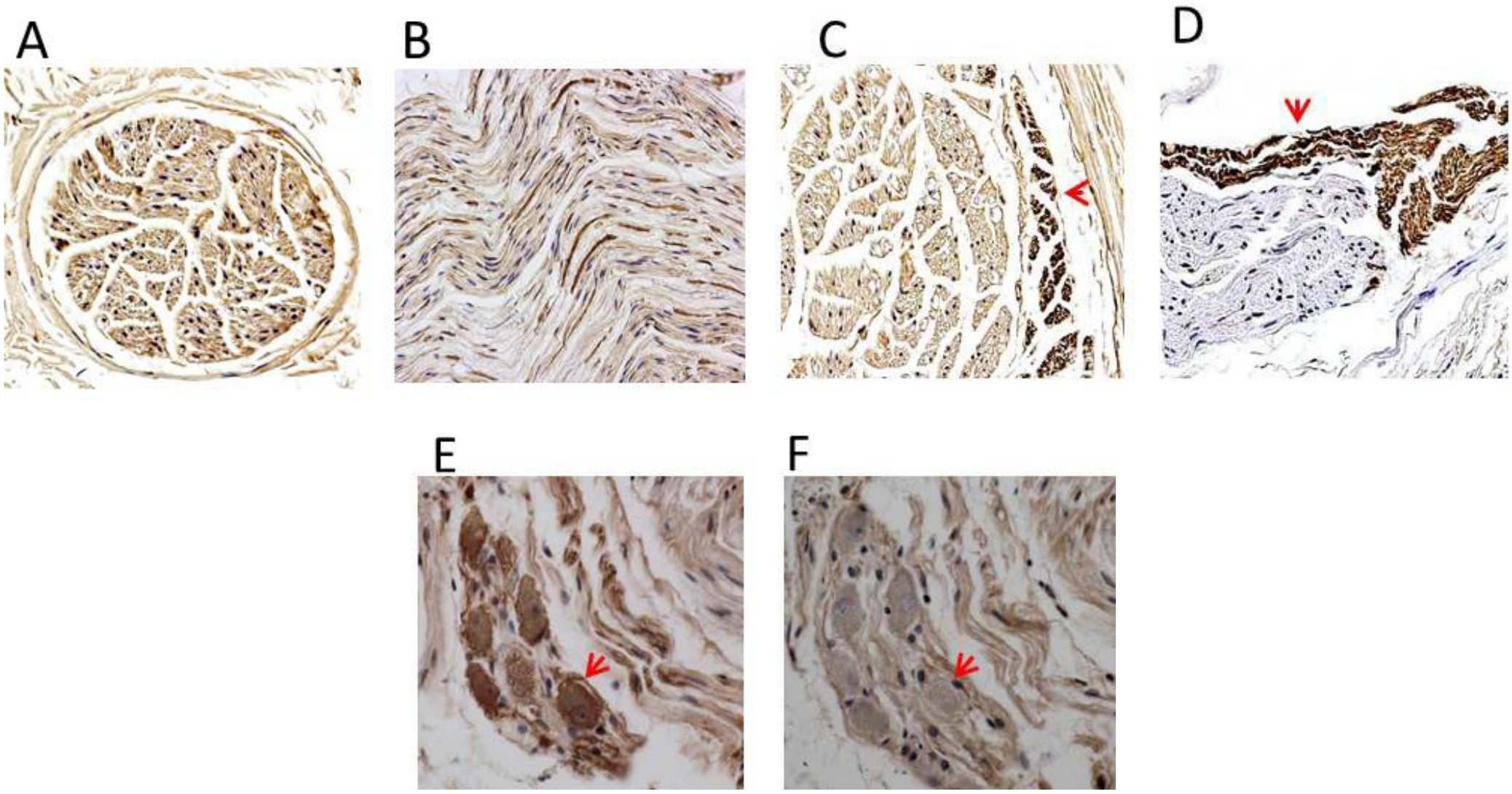
Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

Circadian variation of linear correlation of LVNA, IVC-IAGPNA



Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

Immunocytochemical staining of the cervical vagus nerve



Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

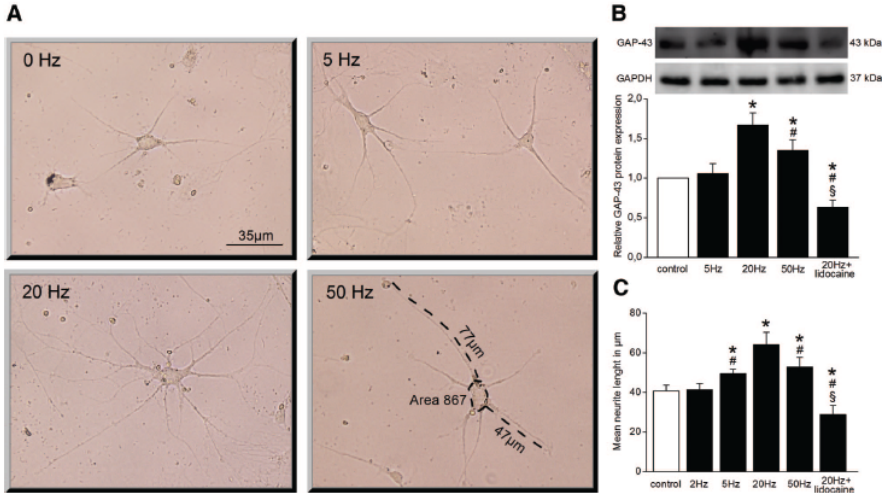
Conclusions

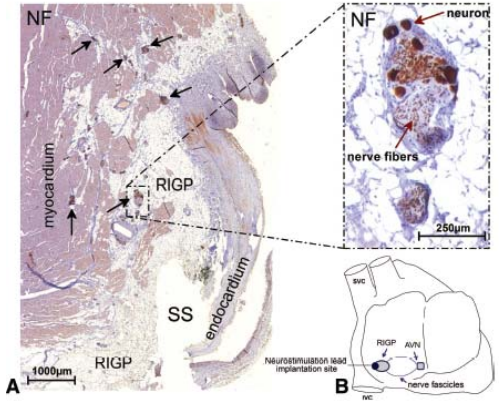
- IVC-IAGPNA and LVNA, but not RVNA, is associated with a reduction of VR to <100 bpm during AF in am bulatory dogs.

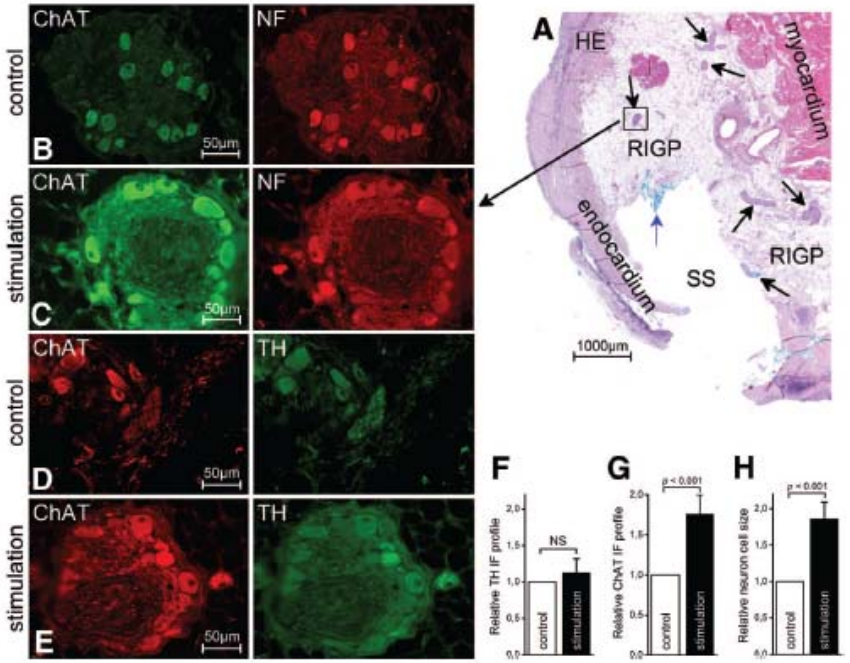
- It is possible that IVC-IAGP relays LVNA to atrioventri cular node, resulting in VR reduction during sustaine d AF.

Park HW et al. Circ Arrhythm Electrophysiol 2012 In press

Chronic Electrical Neuronal Stimulation Increases Cardiac Parasympathetic Tone by Eliciting Neurotrophic Effects

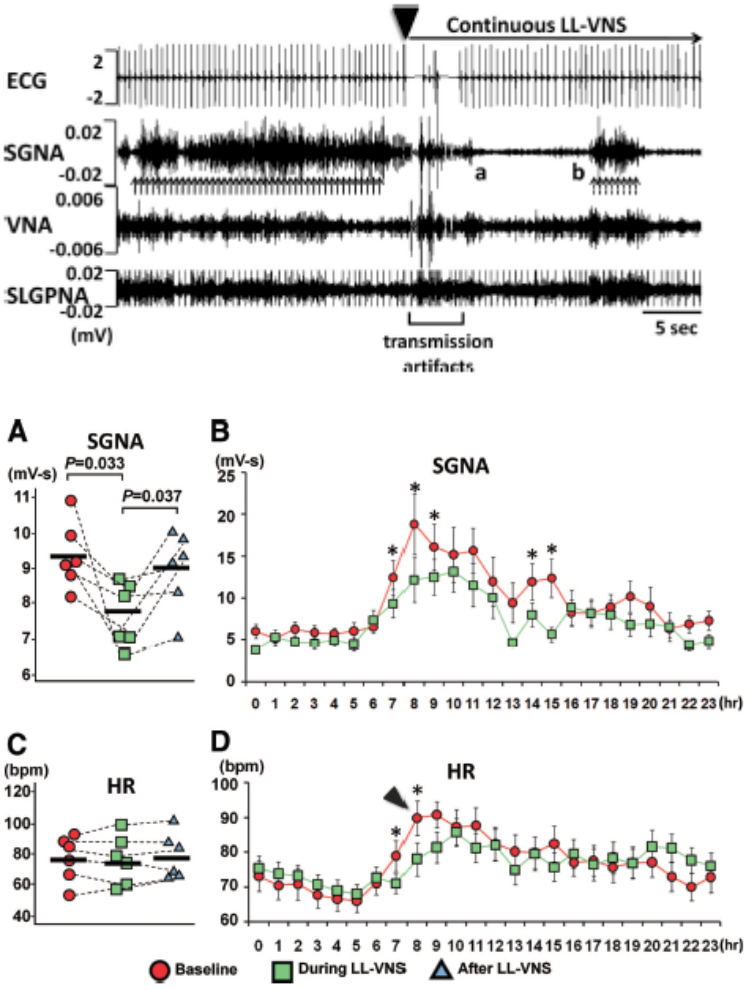


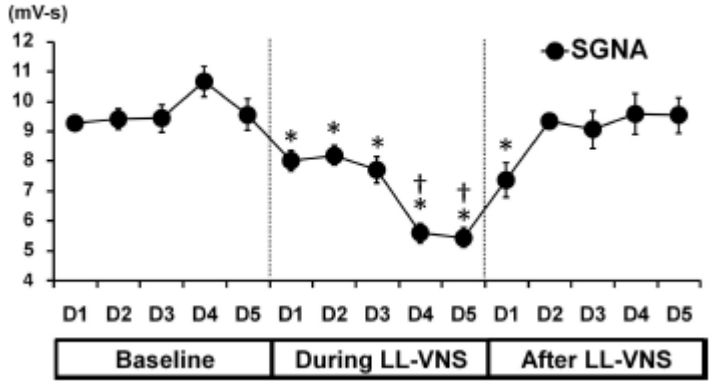


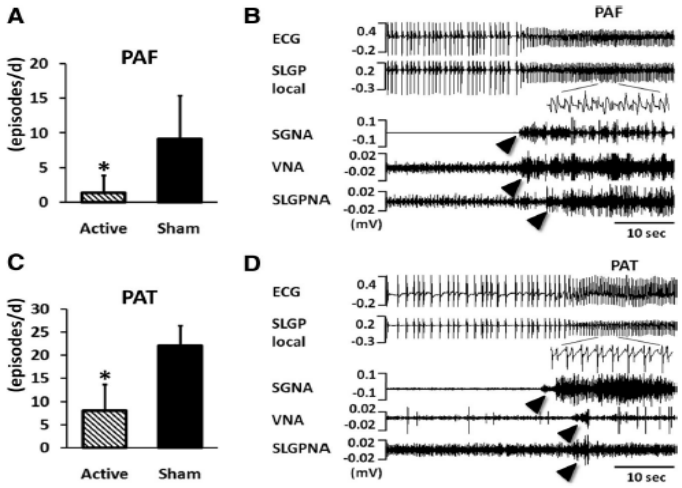


OR Rana, et al. Circ Res 2011;108:1209-19

Continuous Low-Level Vagus Nerve Stimulation Reduces Stellate Ganglion Nerve Activity and Paroxysmal Atrial Tachyarrhythmias in Ambulatory Canines



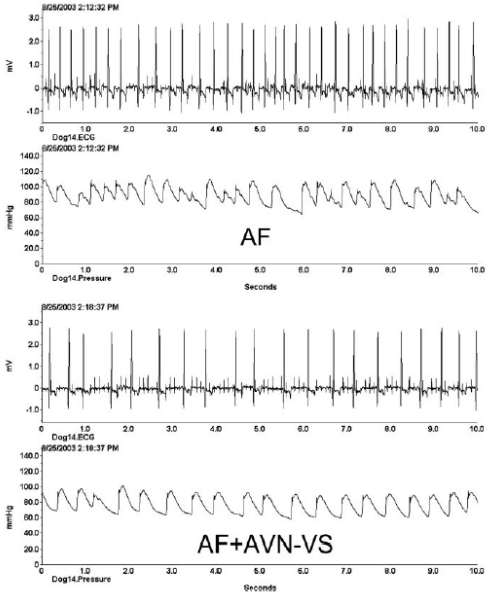


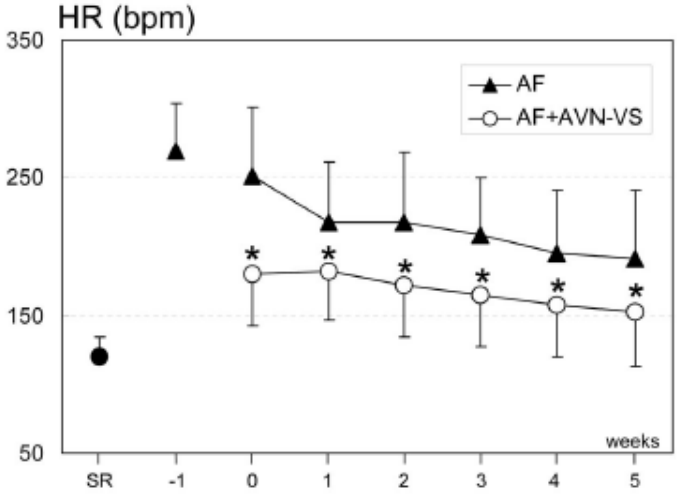


MJ Shen, et al. Circulation 2011;123

Chronic Atrioventricular Nodal Vagal Stimulation First Evidence for Long-Term Ventricular Rate Control in Canine Atrial Fibrillation Model

- Long-term ventricular rate slowing during AF can be achieved by implantation of a nerve stimulator attached to the epicardial AVN fat pad. This novel concept is an attractive alternative to other methods of rate control and may be applicable in a selected group of patients.

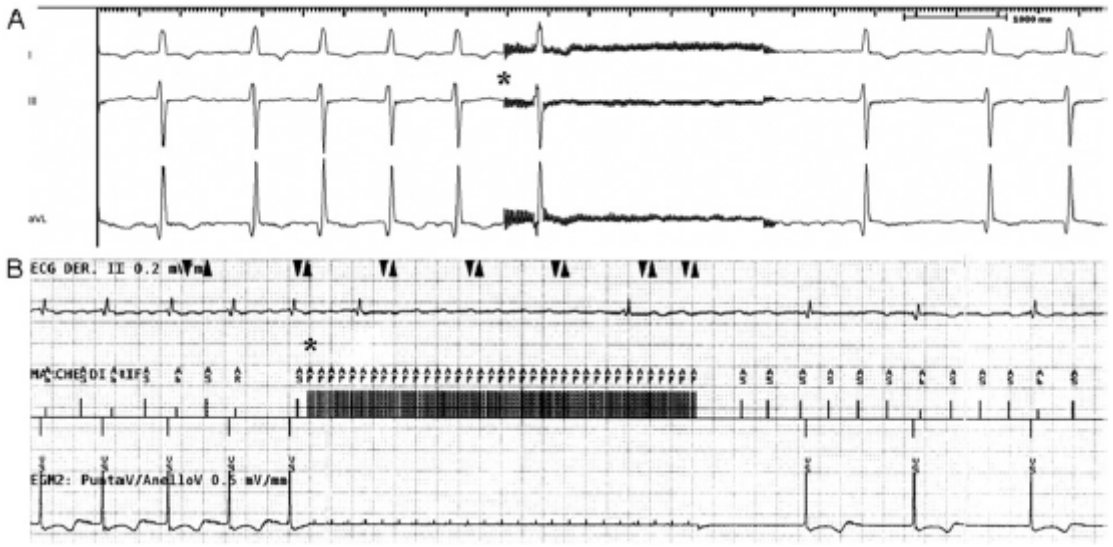




Zhang Y, et al. Circulation. 2005;112:2904-2911

Atrioventricular (AV) node vagal stimulation by transvenous permanent lead implantation to modulate AV node function: safety and feasibility in humans

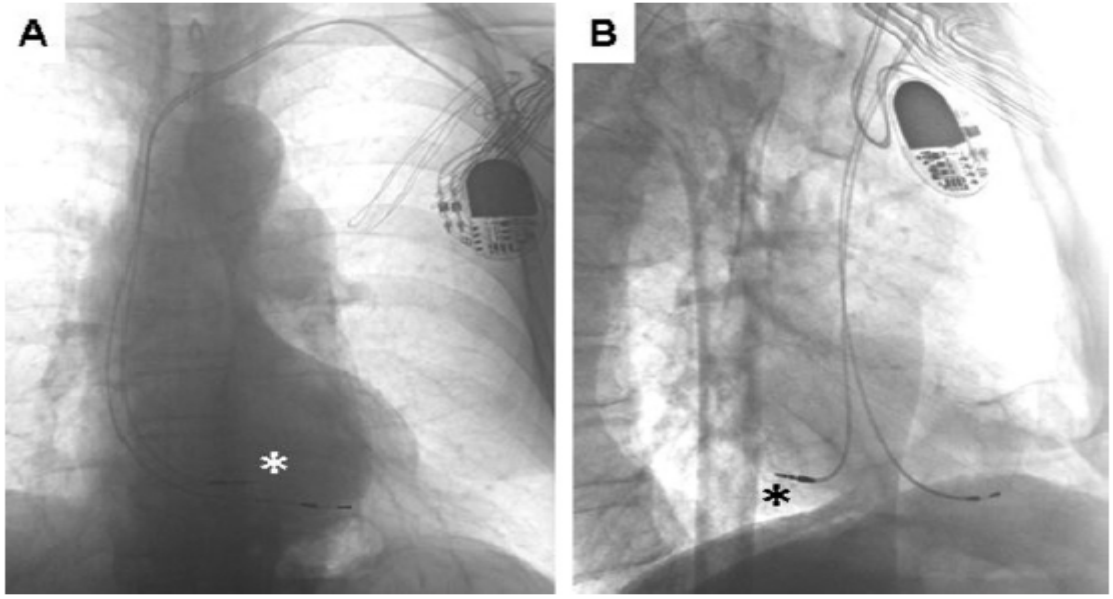
- Selective placement of the atrial lead yields electrical characteristics suitable for permanent pacing and enables VR to be significantly reduced under HFS.



Bianchi S, et al. Heart Rhythm 2009;6:1282–1286

Vagal tone augmentation to the atrioventricular node in humans: Efficacy and safety of burst endocardial stimulation

- Endocardial right atrial burst AVNS reduces ventricular rate during AF.
- Burst AVNS delivered during SR in the effective atrial refractory period allows optimization of lead positioning for AVNS



Rossi P, et al. Heart Rhythm 2010;7:683– 689

Therapeutic Intervention of Autonomic Nervous System

- Reduce incidence of arrthythmia
- Modulation of contribution of each nerve activity to arrhythmogenesis
- Device able to modify autonomic nerve activity by feedback