

Mechanisms of arrhythmia

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Professor

Director of electrophysiologic laboratory

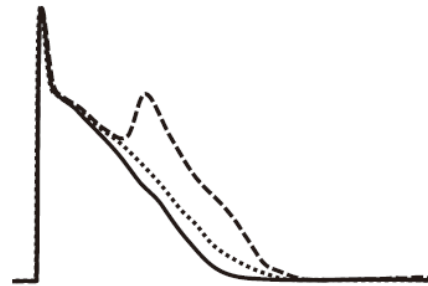
Yonsei Health System

Seoul, Korea

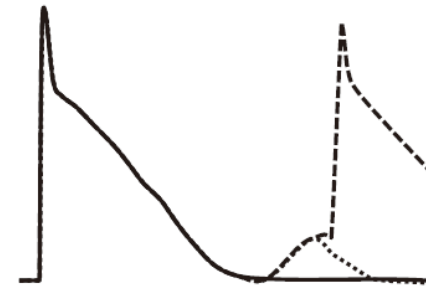


Major arrhythmogenic mechanisms

Focal Ectopic/Triggered Activity

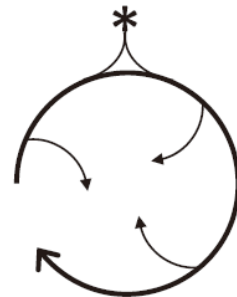


Early Afterdepolarizations (EADs)
Promoted by: Prolonged Repolarization



Delayed Afterdepolarizations (DADs)
Promoted by: Ca²⁺-Handling Abnormalities

Re-entry

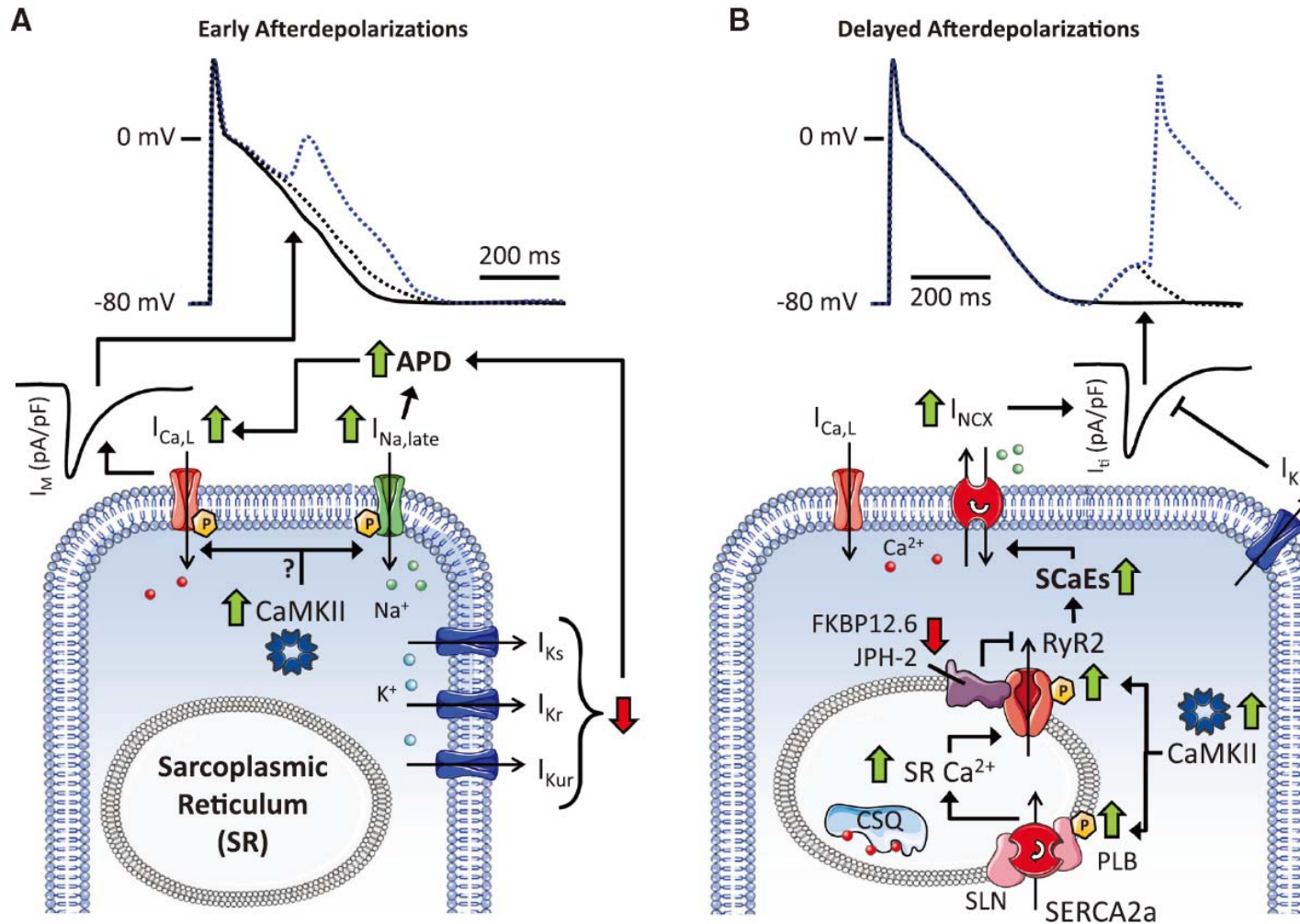


Leading Circle
Promoted by: Short ERP, Slow
Conduction, Long Circuit Pathways



Spiral Wave
Promoted by: Short ERP, Slow
Conduction, Rotor Stability

Mechanisms of EAD & DAD

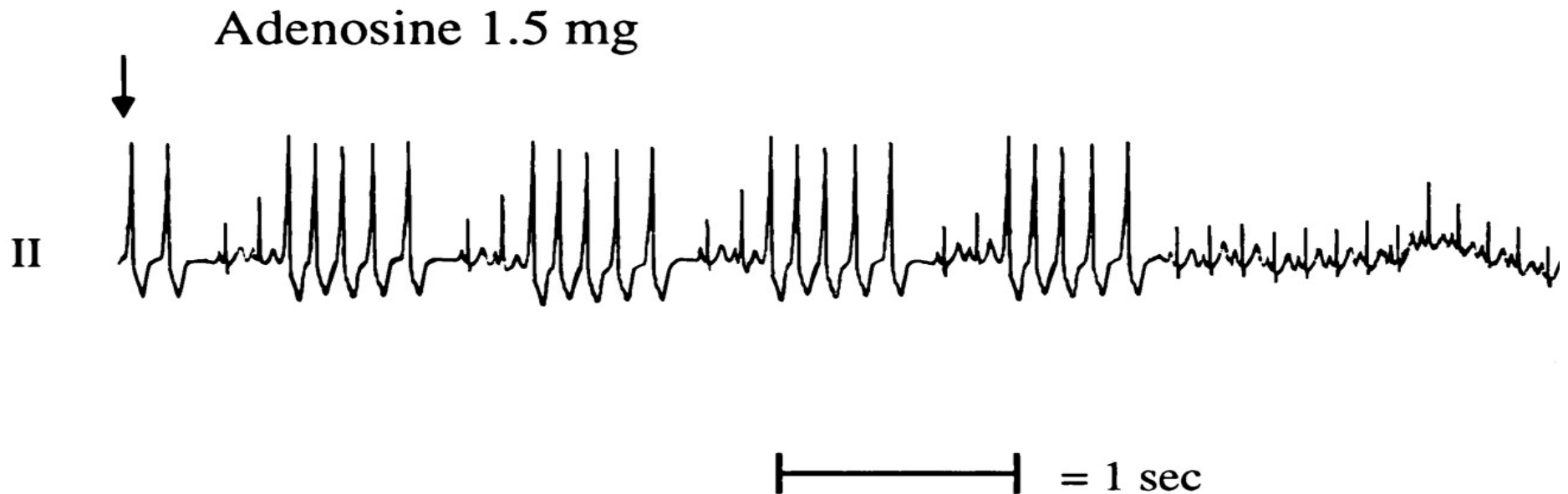


Idiopathic

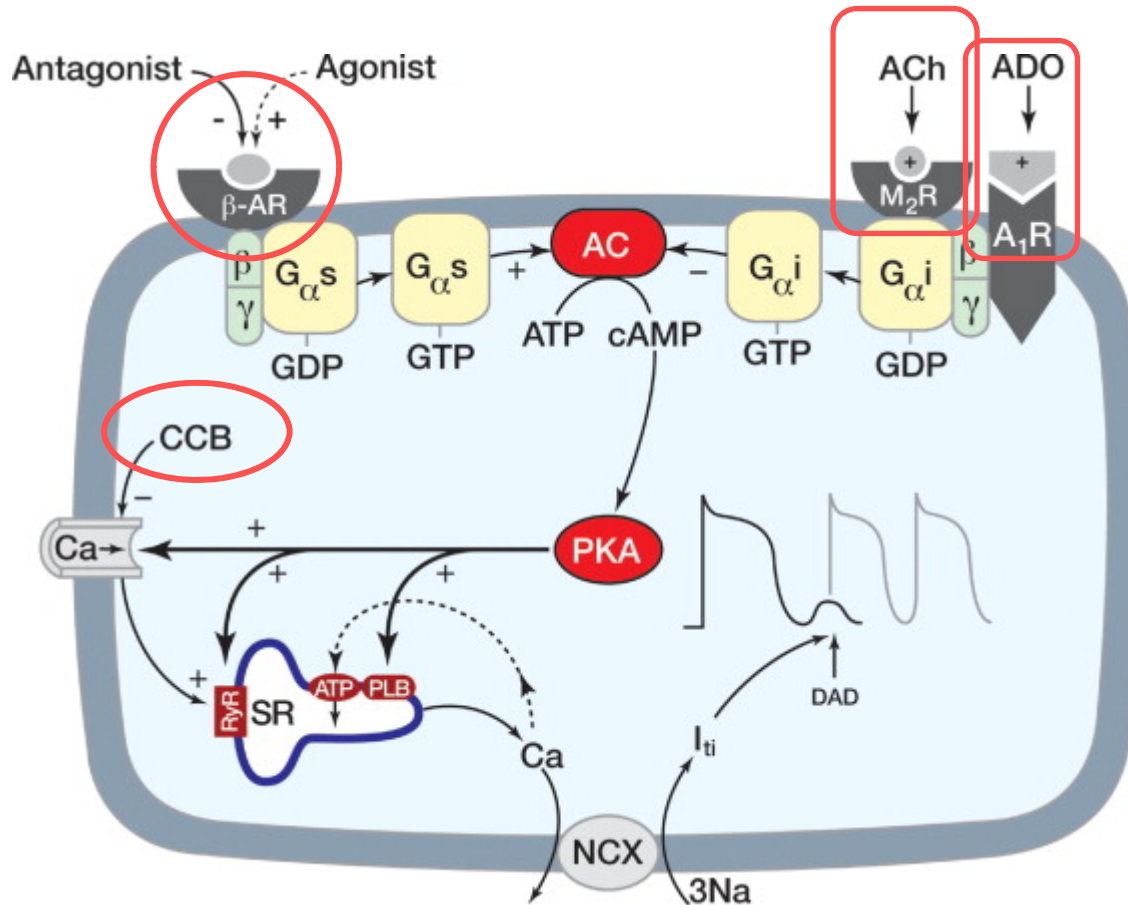
Idiopathic RVOT arrhythmias

Pharmacology

- β -blockers, Adenosine, Ca-channel antagonists, vagal maneuvers



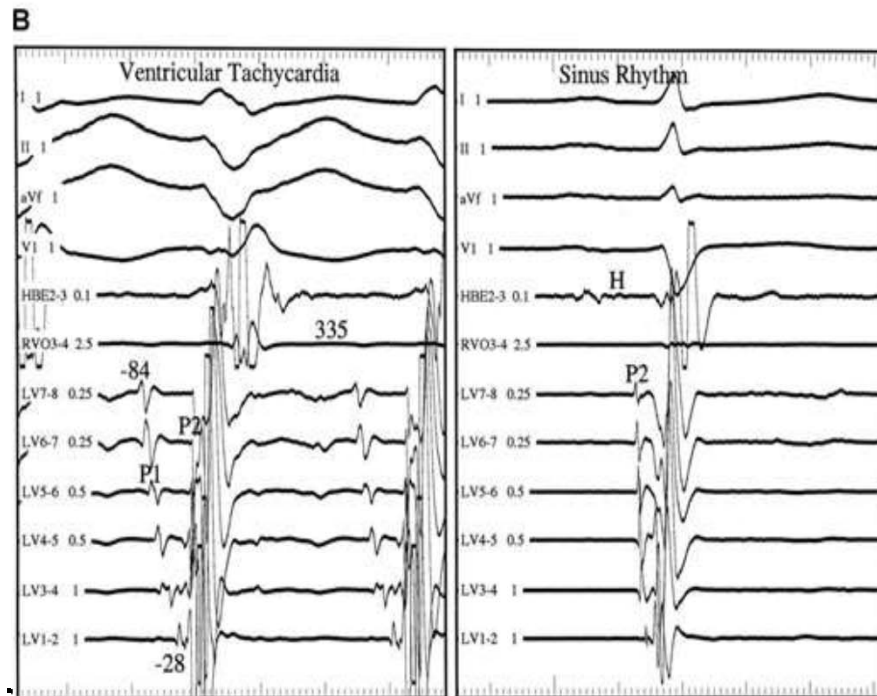
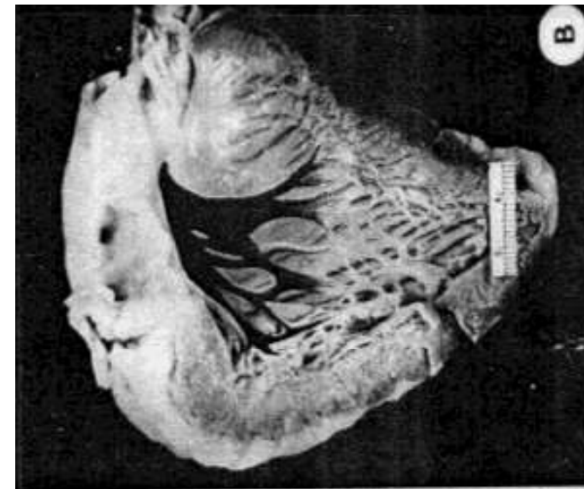
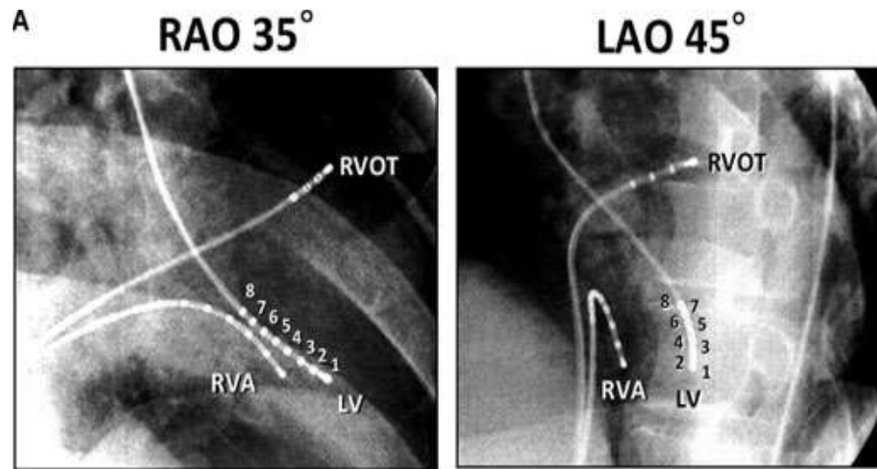
Signal transduction schema for initiation and termination of cAMP-mediated triggered activity



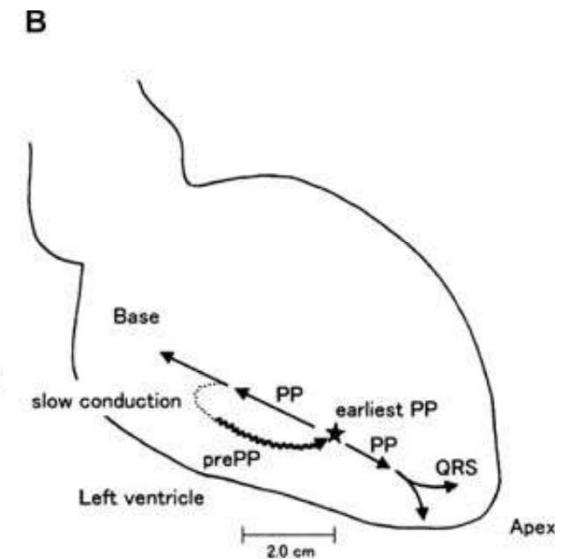
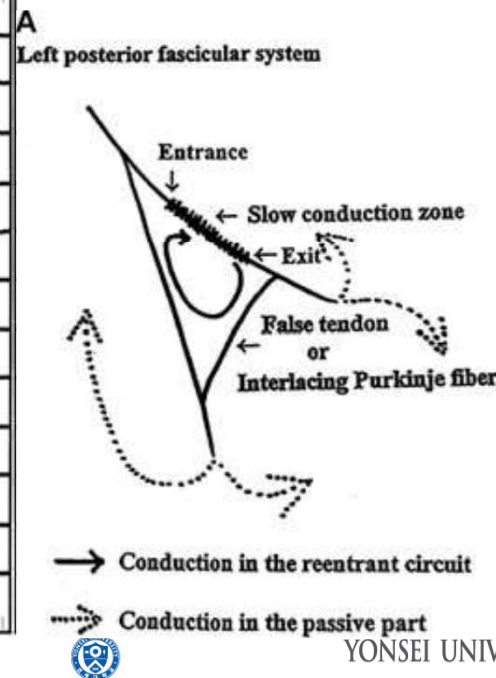
Lerman B. Heart Rhythm
2007;4:973-976

AC = adenylyl cyclase; ACh = acetylcholine; ADO = adenosine; A_1R = A_1 -adenosine receptor; β -AR = β -adrenergic receptor; CCB = calcium channel blocker; DAD = delayed afterdepolarization; I_{ti} = transient inward current; M_2R = muscarinic receptor; NCX = Na^+/Ca^{2+} exchanger; PLB = phospholamban; PKA = protein kinase A; RyR = ryanodine receptor; SR = sarcoplasmic reticulum.

Idiopathic LV fascicular VT



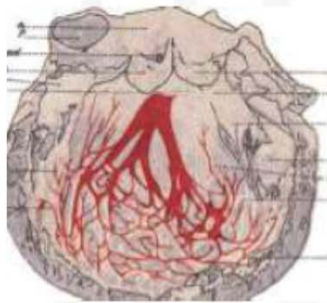
SEVERANCE CARDIOVASCULAR HOSPITAL



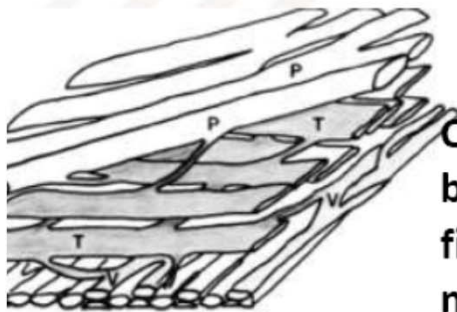
NOGAMI A. PACE 2011

YONSEI UNIVERSITY COLLEGE OF MEDICINE

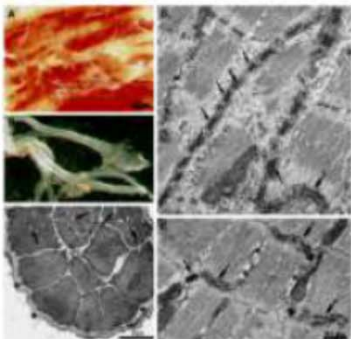
Complex Structure and Function of Purkinje Cells



Complex arborization of Purkinje network

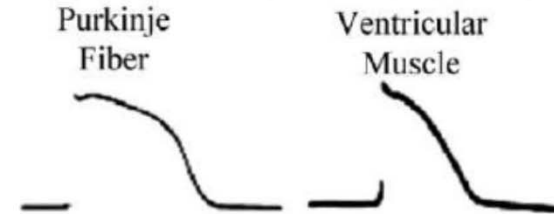


Complex junctions between Purkinje fibers and ventricular muscle

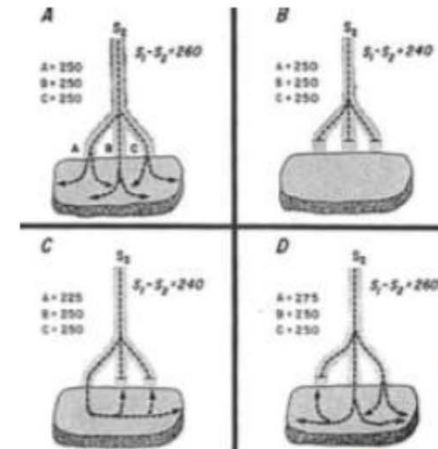


Specific cellular architecture of Purkinje fibers

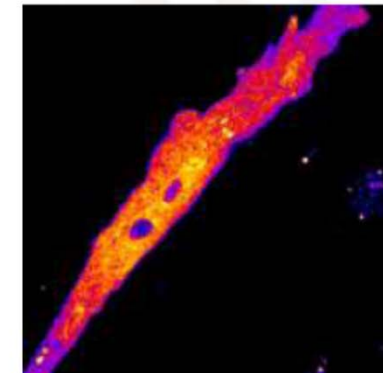
Longer APD



longest APD at junction



Spontaneous Ca²⁺ waves can occur spontaneously

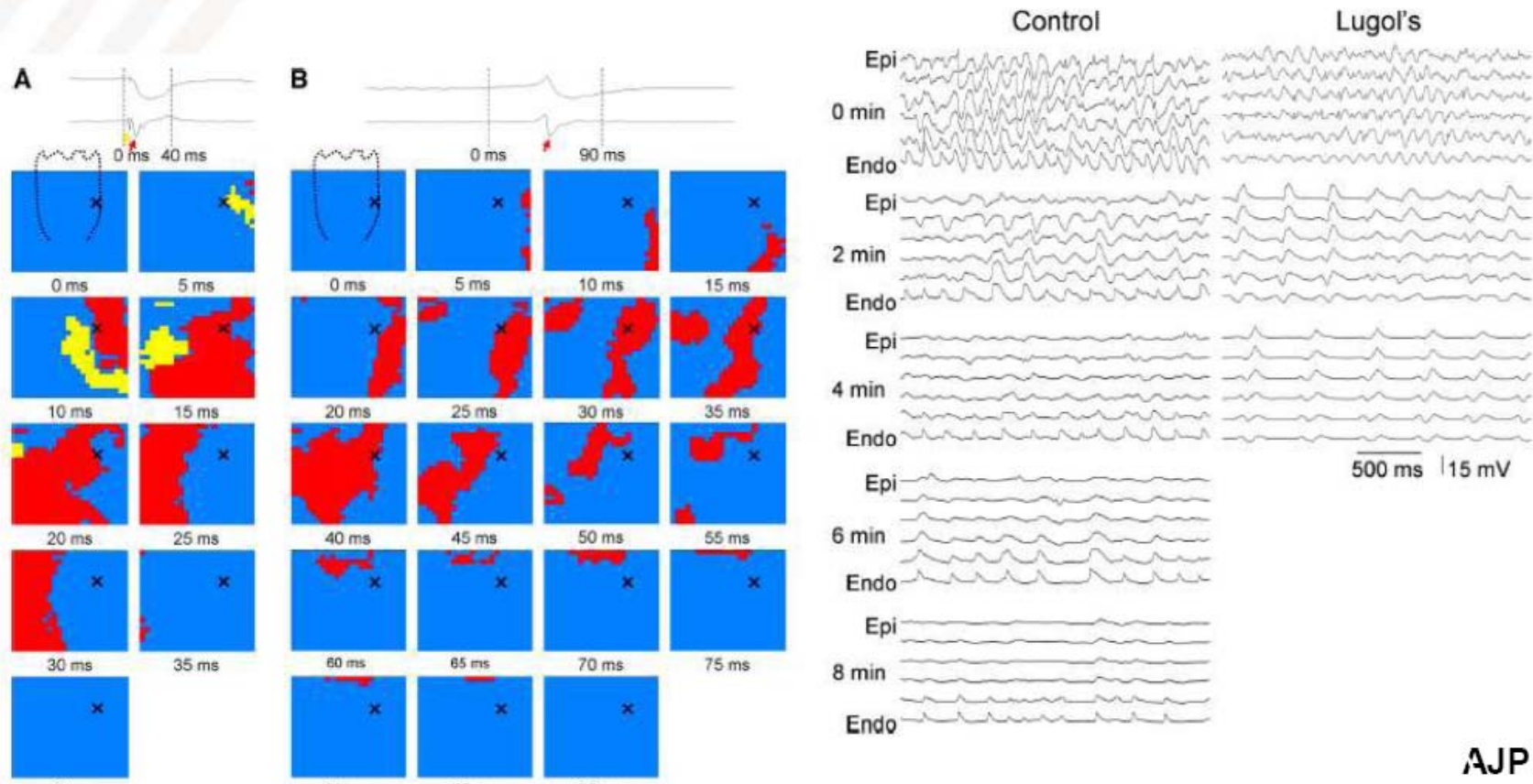


Role for Purkinje network in VF maintenance

Derek J. Dossall,¹ Paul B. Tabereaux,² Jong J. Kim,¹ Gregory P. Walcott,² Jack M. Rogers,¹
Cheryl R. Killingsworth,² Jian Huang,² Peter G. Robertson,²
William M. Smith,^{1,2} and Raymond E. Ideker^{1,2,3}

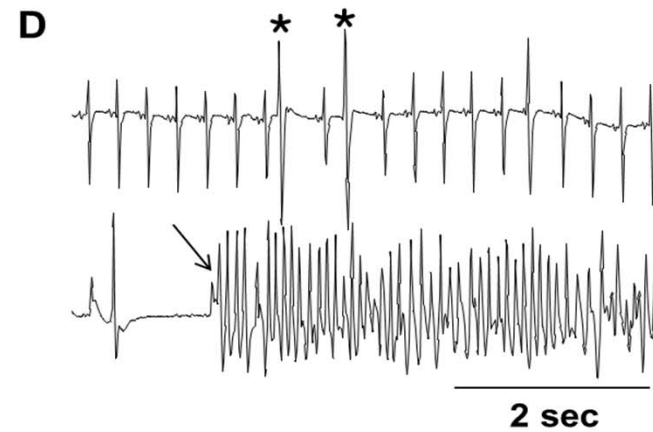
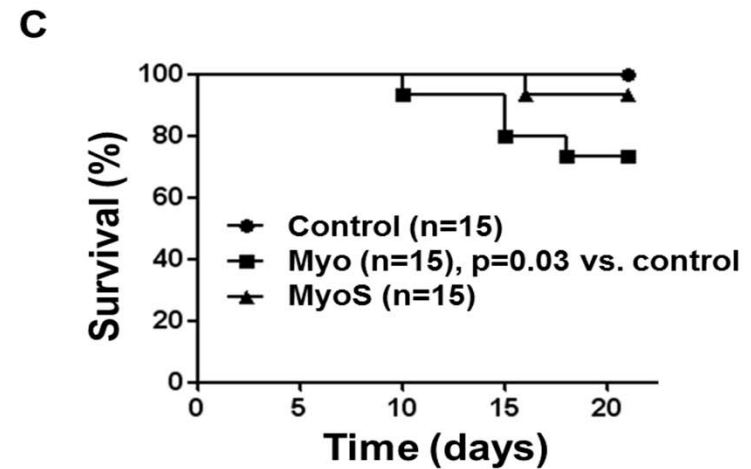
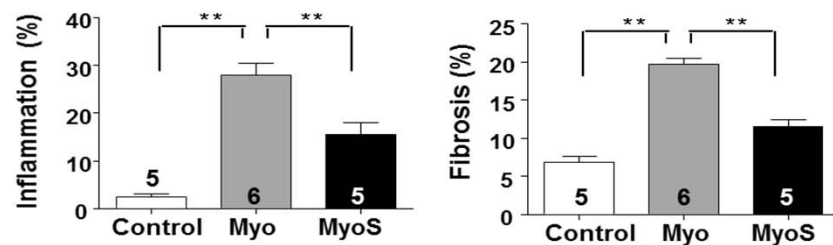
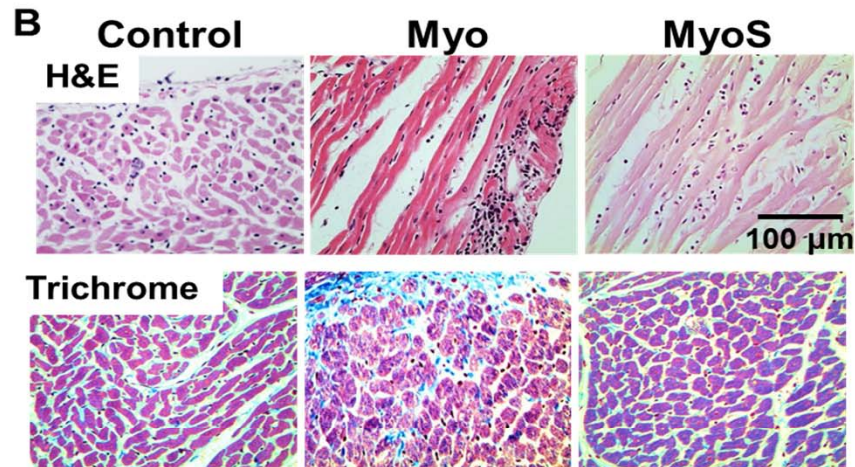
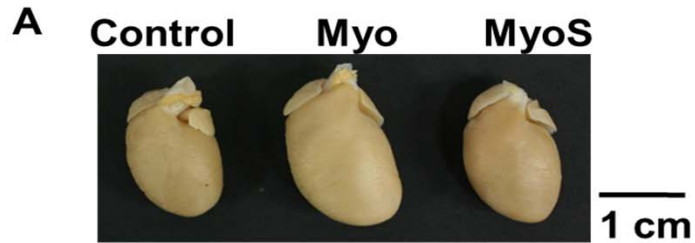
Departments of ¹Biomedical Engineering, ²Medicine, and ³Physiology, University of Alabama at Birmingham,
Birmingham, Alabama

12 Dog hearts endocardium treated with Lugol's solution



AJP 2008

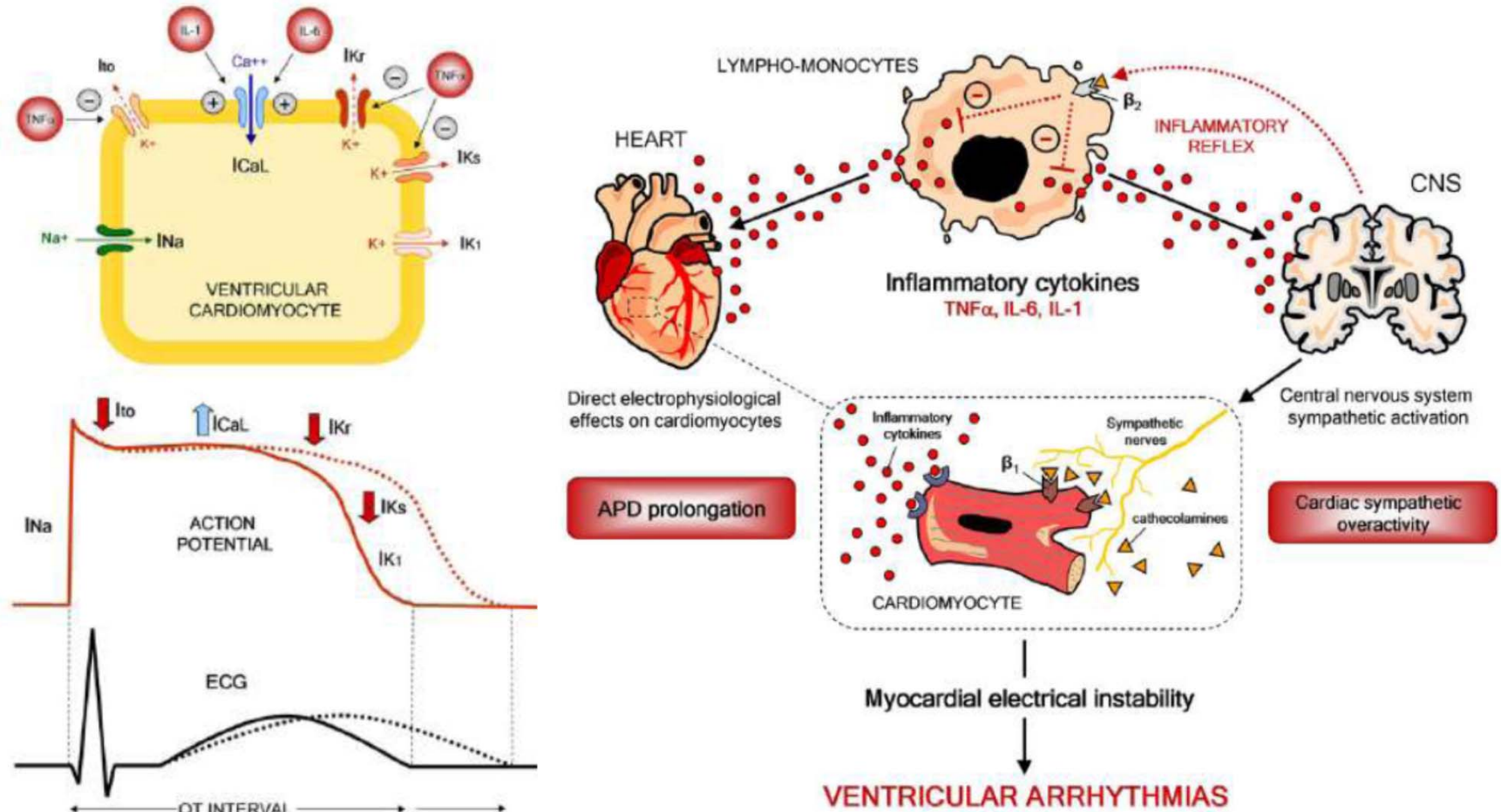
Myocarditis and arrhythmia



Park H, et al. Circ J. 2014;78(9):2292-301

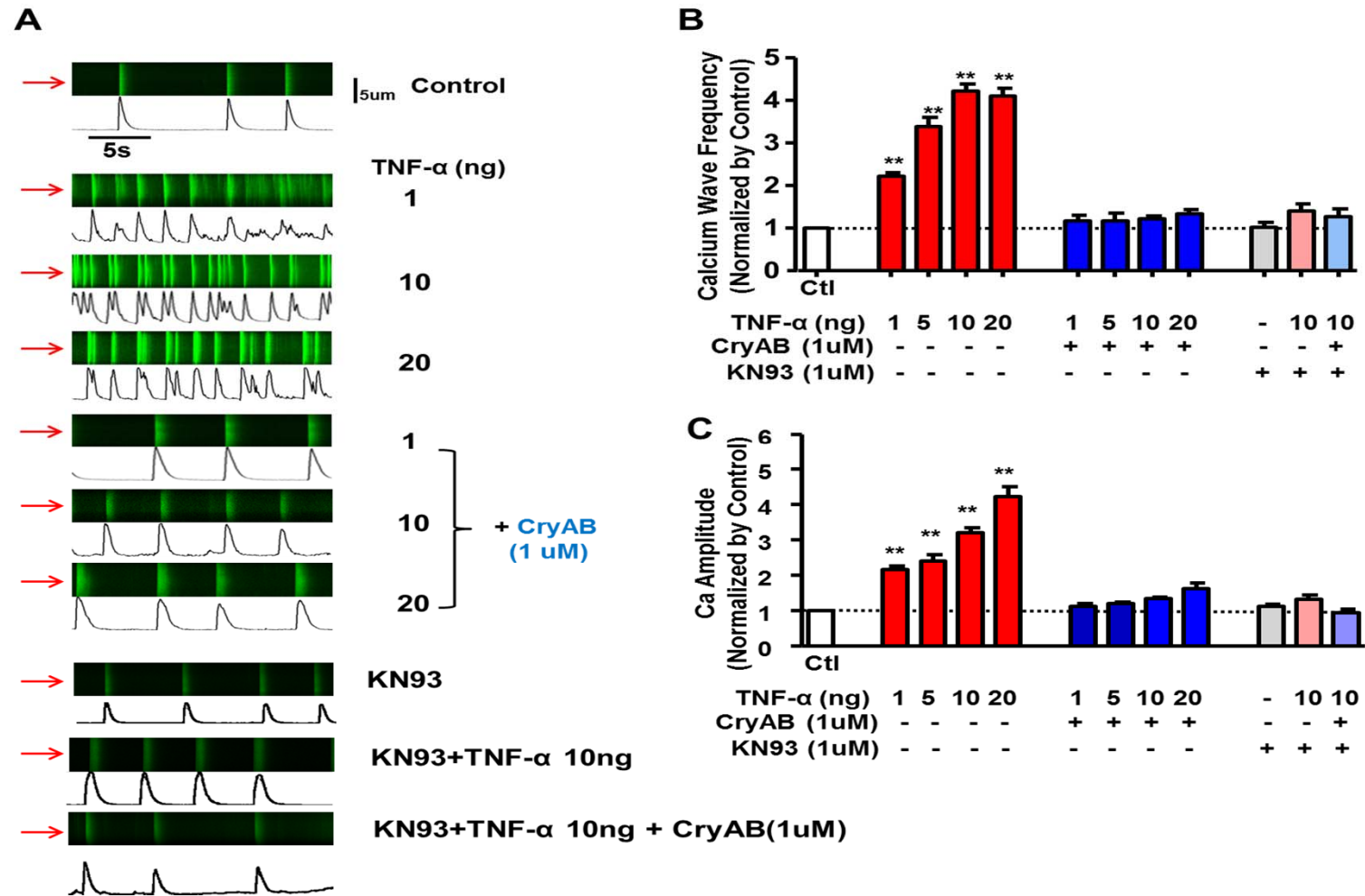
Systemic Inflammation and Ventricular Arrhythmias

Potential Pathways and Mechanisms



from Lazzarini et al, Eur Heart J 2016 Jun 1. pii: ewh208

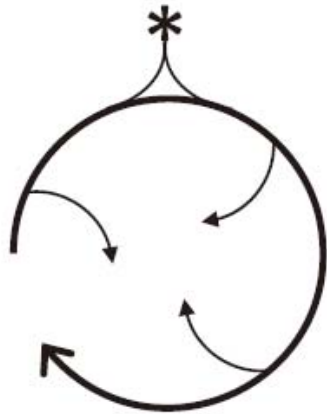
Spontaneous Ca²⁺ release in rat neonatal myocytes treated with TNF- α



Park H, et al. Int J Cardiol. 2015;182:399-402.

Ischemic VT

Re-entry



Leading Circle

Promoted by: Short ERP, Slow Conduction, Long Circuit Pathways

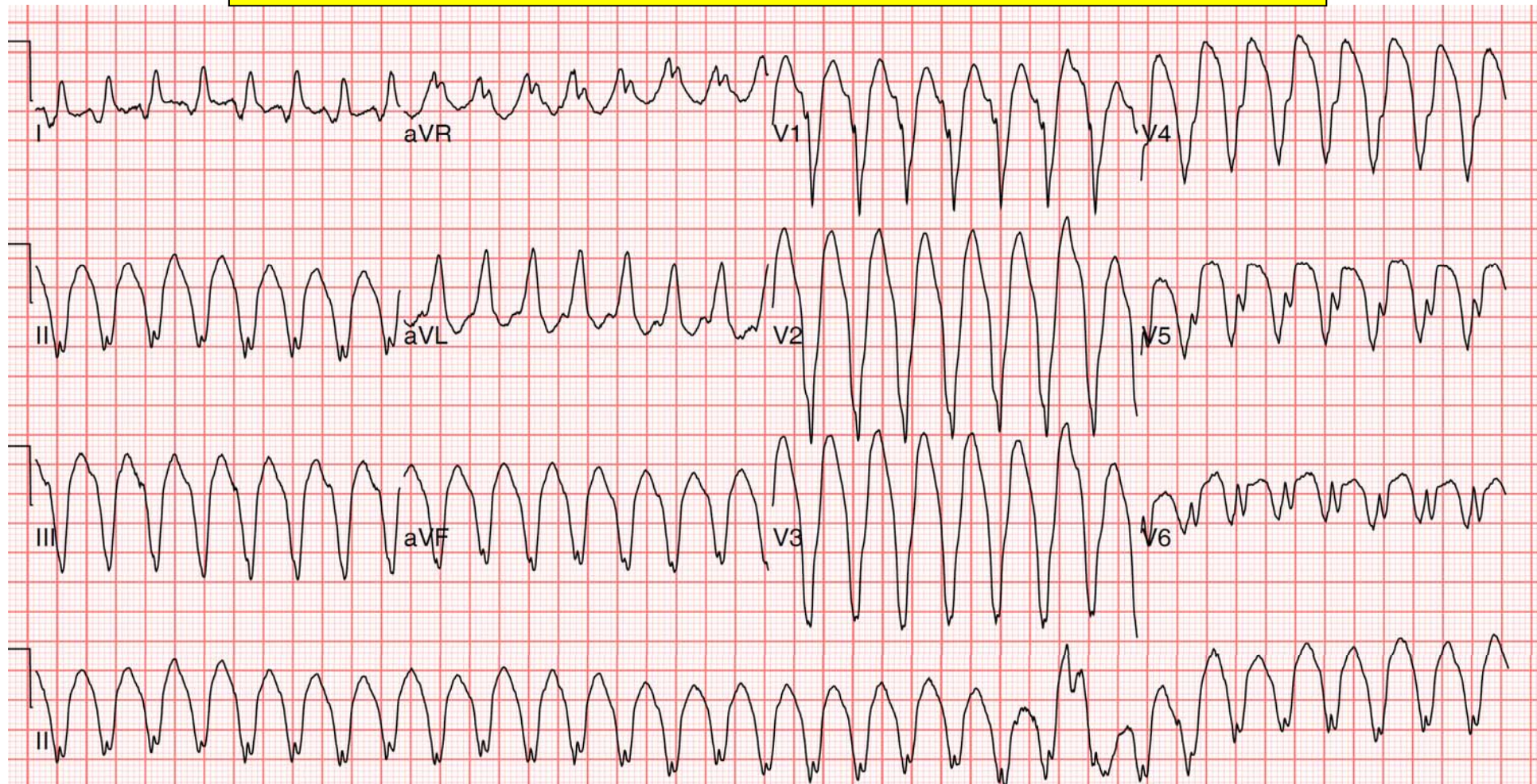


Spiral Wave

Promoted by: Short ERP, Slow Conduction, Rotor Stability

M/55, Gardener, s/p PCI at p-LAD for Ant MI Palpitation, dyspnea, dizziness for 1 hour

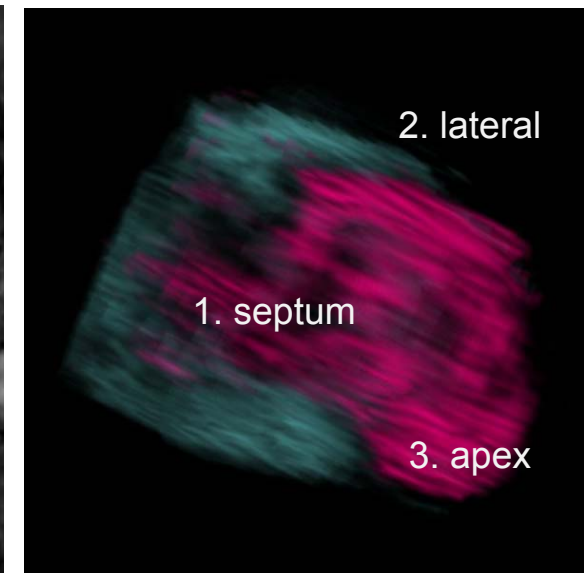
HR 188 bpm, Negative concordance, LAD, BP 70/40 mmHg



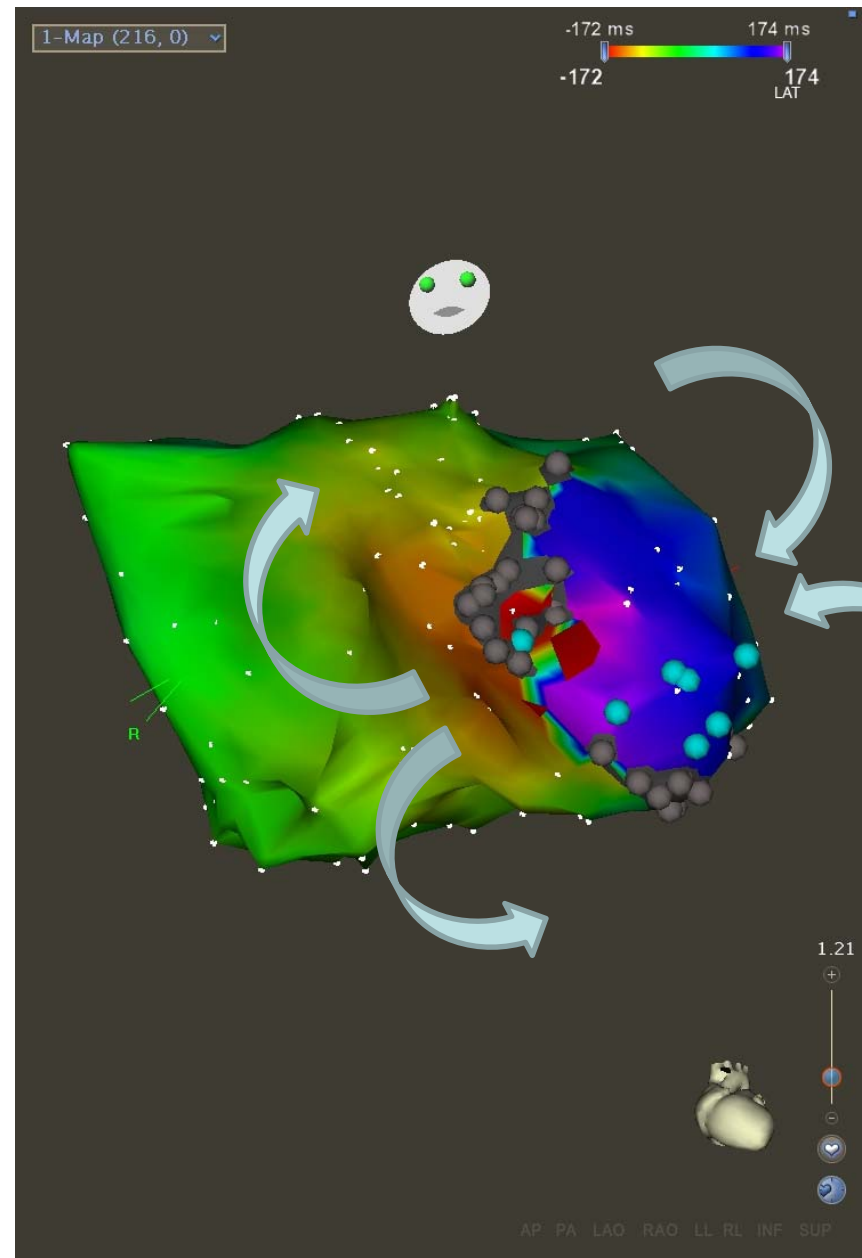
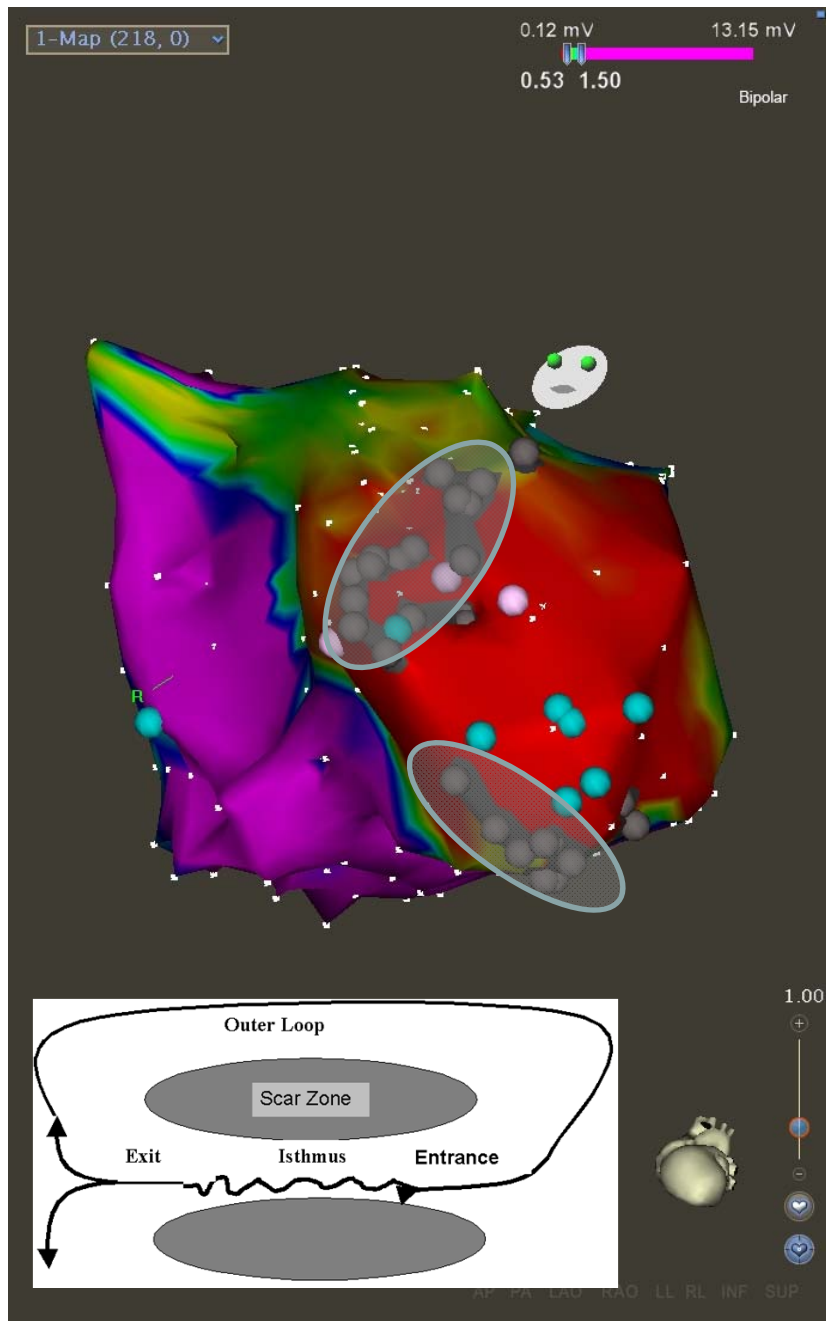
→ Patent stent, IABP, DC shock (x 25)

ECHO & MRI

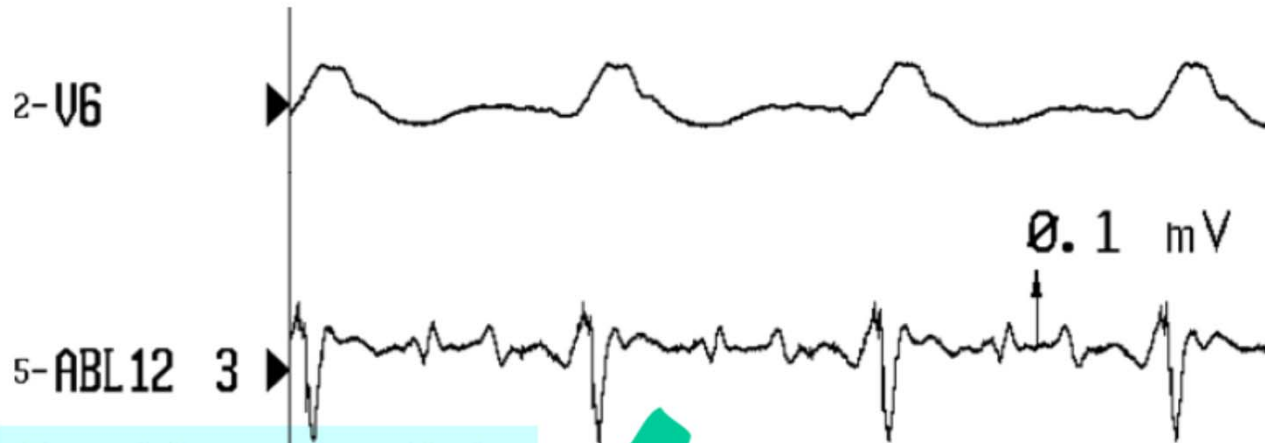
- TTE: Akinesia with thinning and scarring at LAD territory, aneurysmal change in apex - LVEDD=65mm, LVEF=20%



Q. Exit site ?

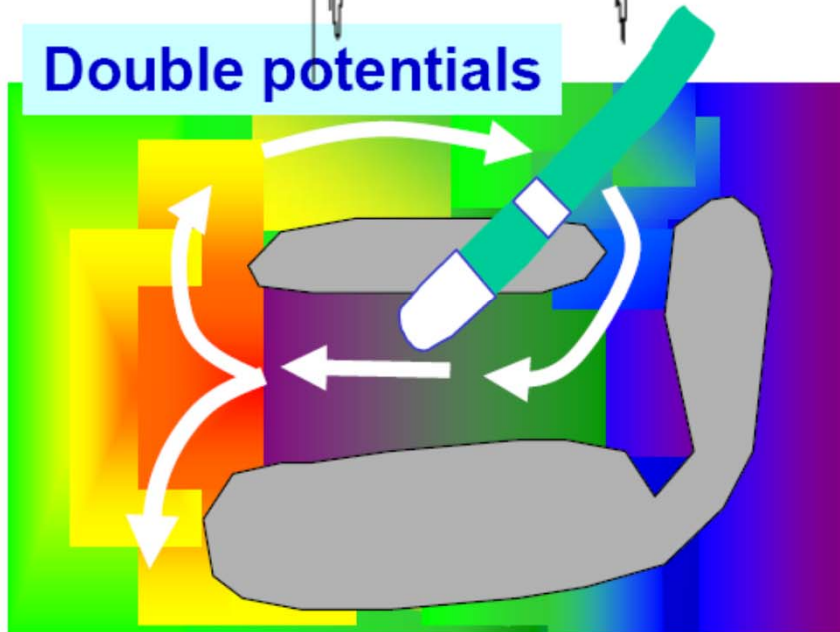


**Post-pacing Interval Fundamental assumption:
The potential used for measurement indicates
depolarization at the pacing site.**



**Local vs
Far-field
potentials**

Double potentials

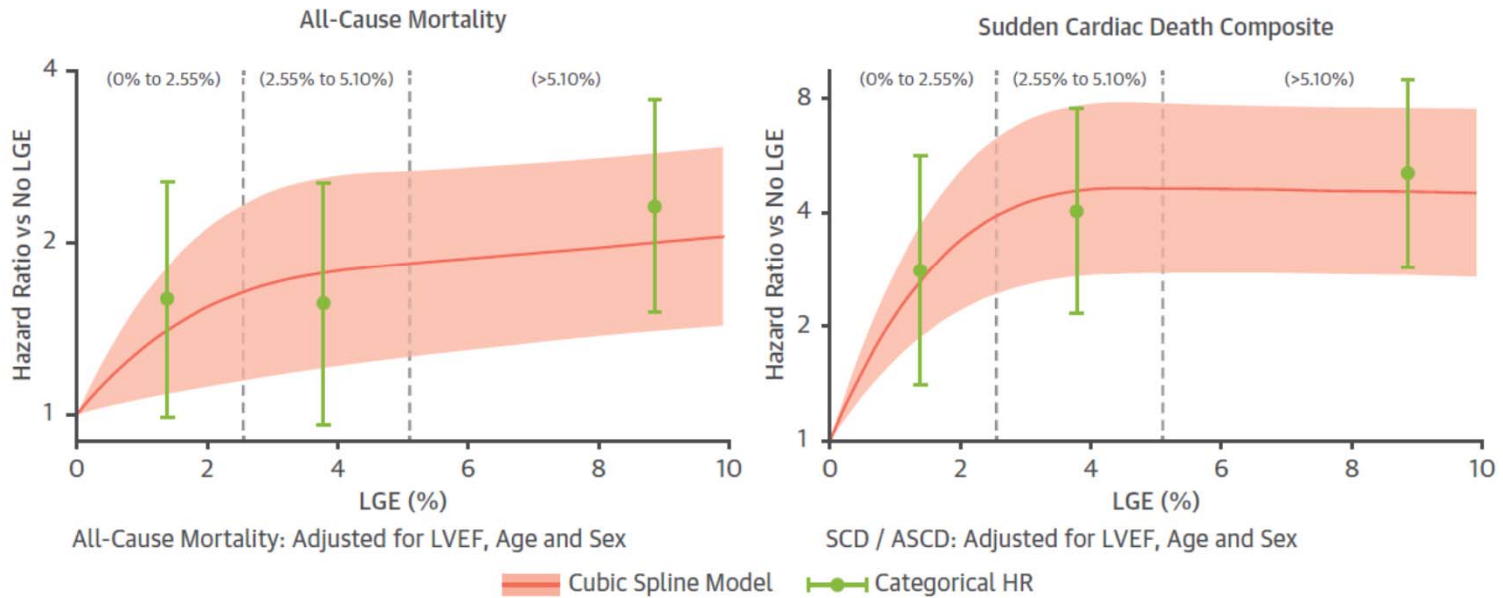


Tung et al. Recognition of far-field electrograms during entrainment mapping of VT. JACC 2003;42:110-5.

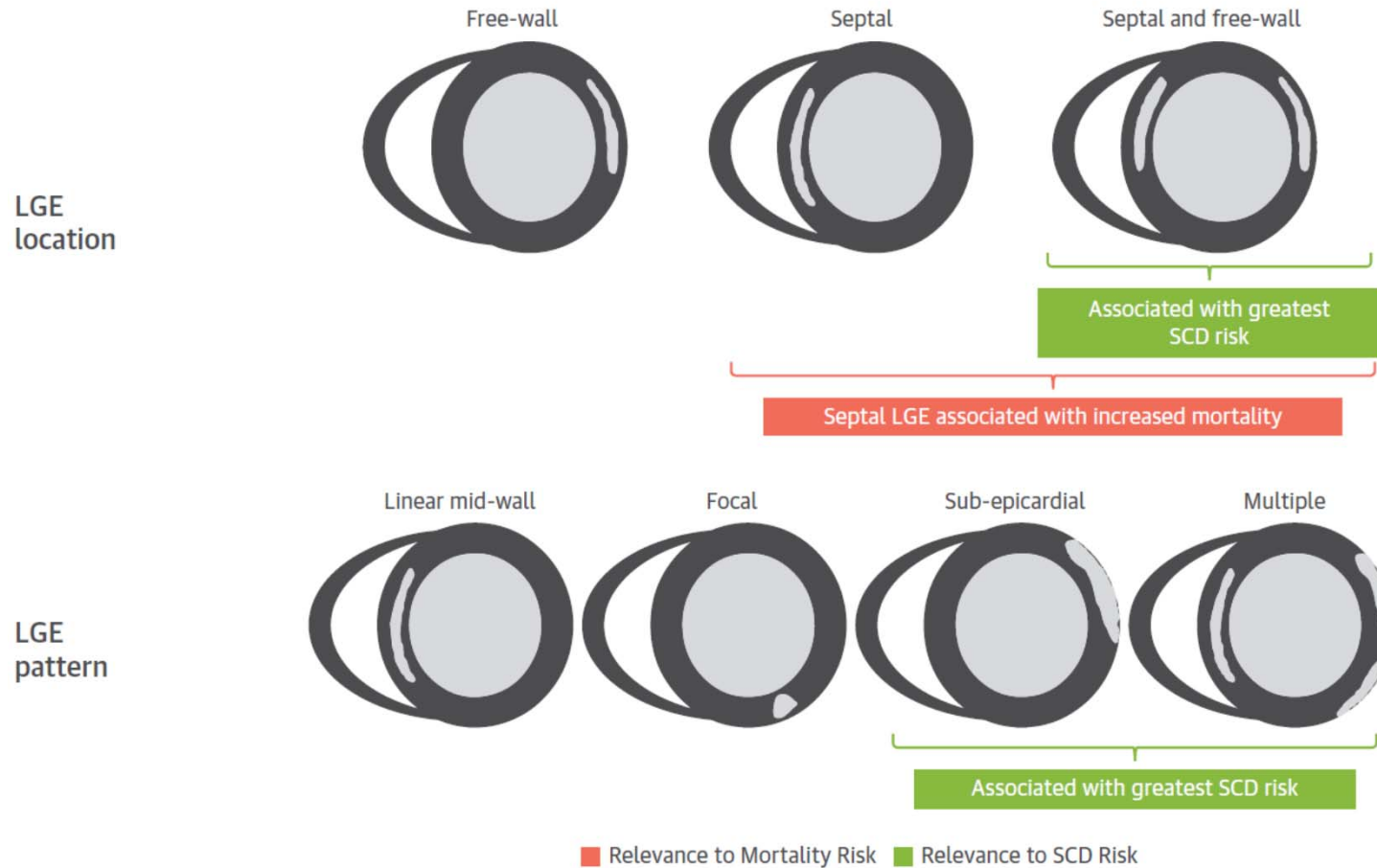
LGE extent



LGE extent



LGE location and pattern



Pattern of late gadolinium enhancement predicts arrhythmic events in patients with non-ischemic cardiomyopathy

Dong Geum Shin ^{a,1}, Hye-Jeong Lee ^{b,1}, Junbeom Park ^c, Jae-Sun Uhm ^a, Hui-Nam Pak ^a, Moon-Hyoung Lee ^a, Young Jin Kim ^{b,*}, Boyoung Joung ^{a,*}

^a Division of Cardiology, Yonsei University College of Medicine, Seoul, Republic of Korea

^b Department of Radiology, Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Republic of Korea

^c Department of Cardiology, School of Medicine, Ewha Womans University College, Seoul, Republic of Korea

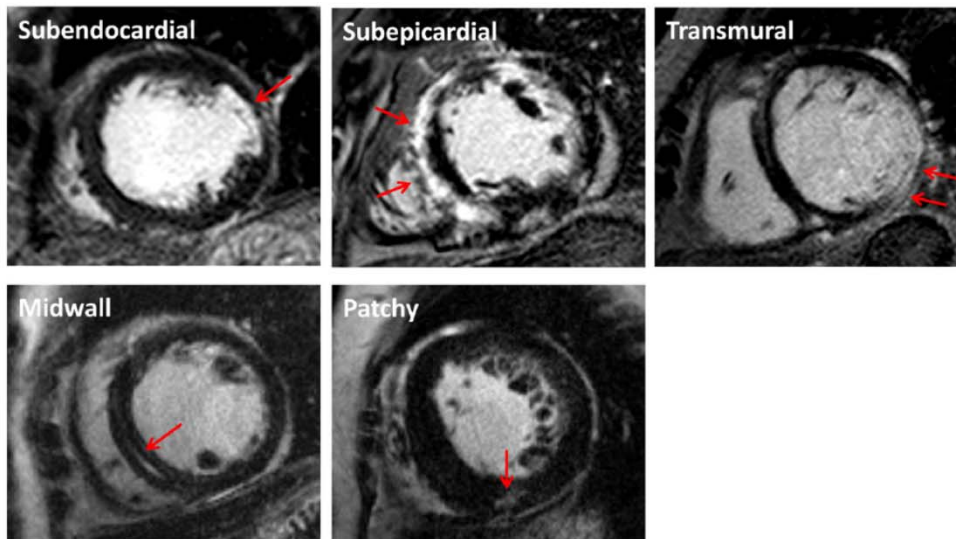
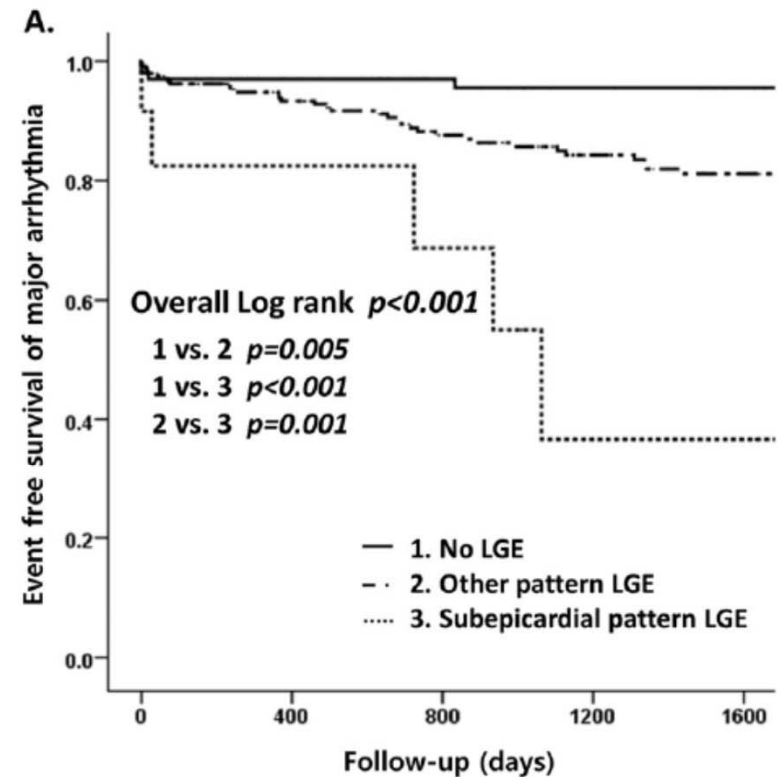
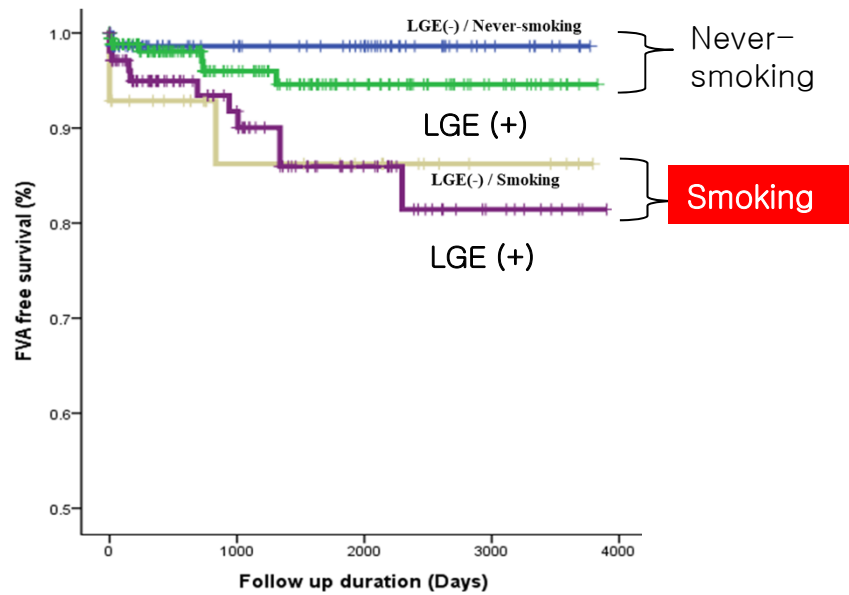


Fig. 1. Examples of patterns of left ventricular late gadolinium enhancement (arrow) shown by delayed contrast-enhanced short-axis cardiac magnetic resonance imaging.

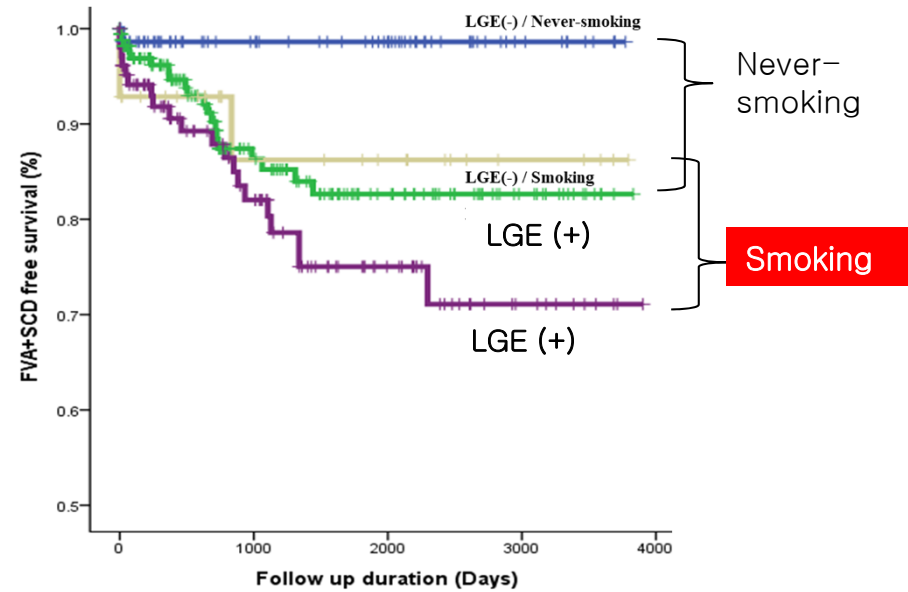


Fatal VA and SCD according to the LGE & Smoking

A. FVA free survival. $p=0.02$



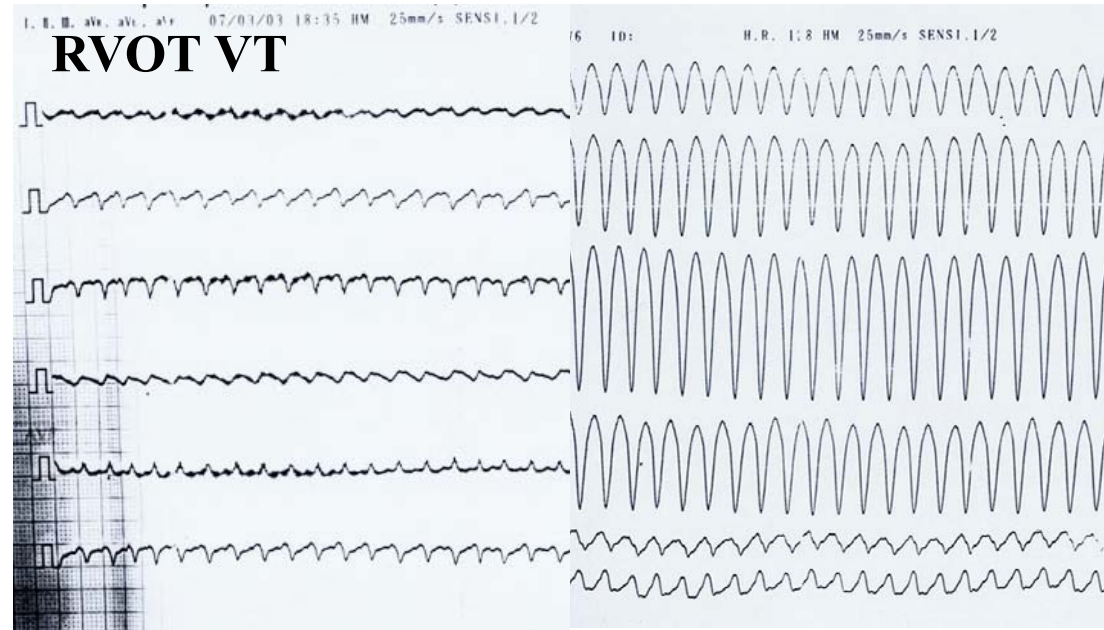
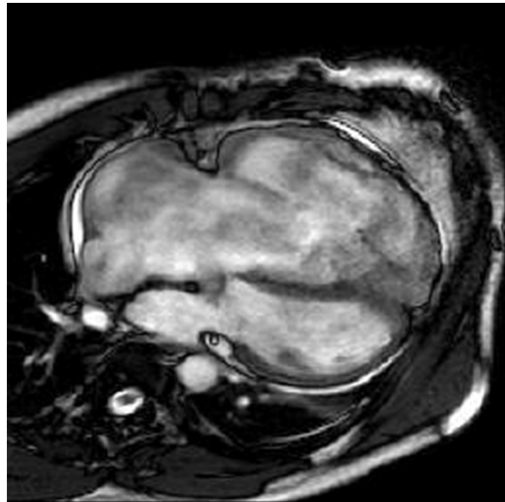
B. FVA+SCD free survival. $p=0.005$



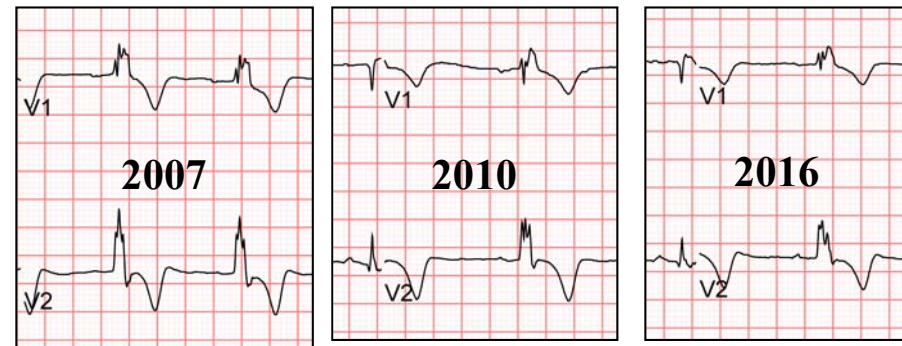
Park JB, Joung B, et al. Sci Rep 2018. in press

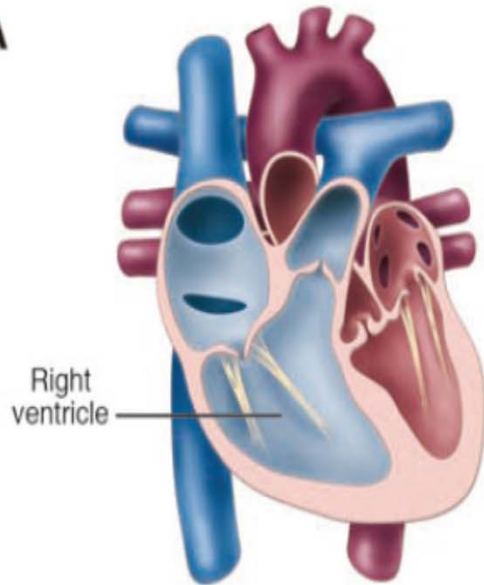
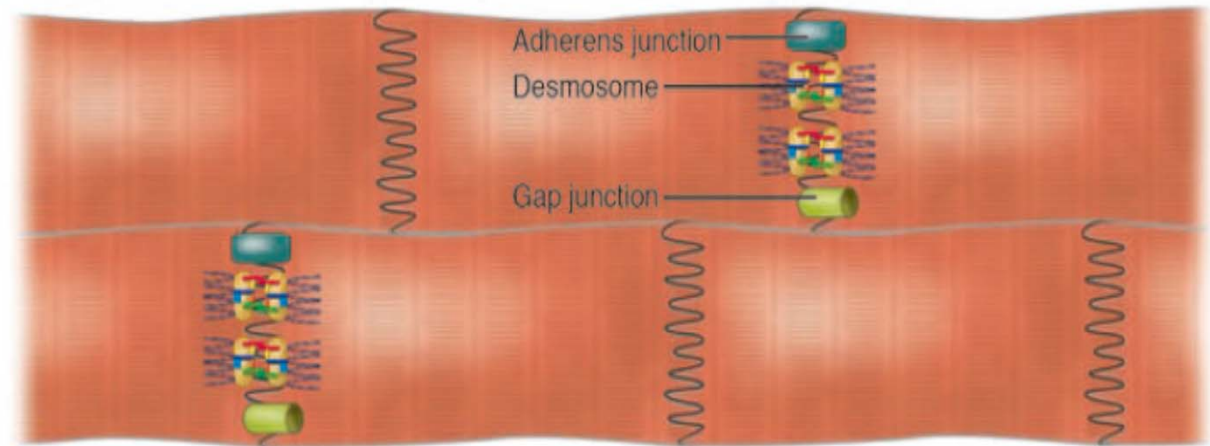
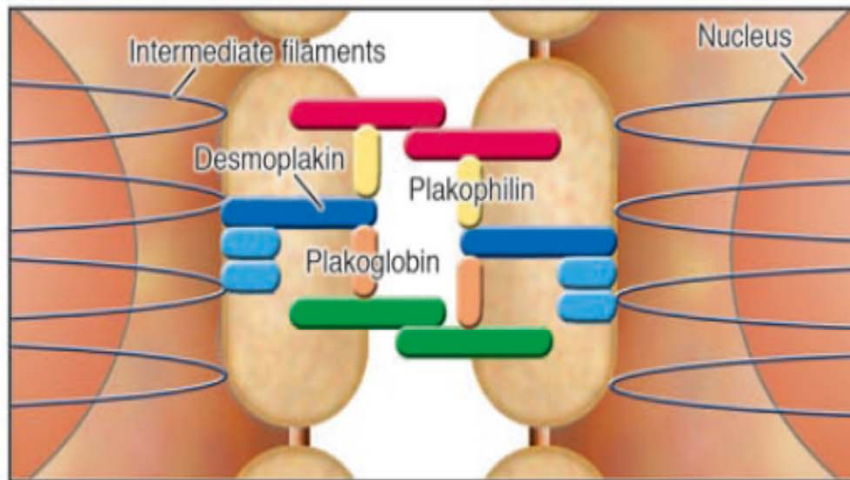
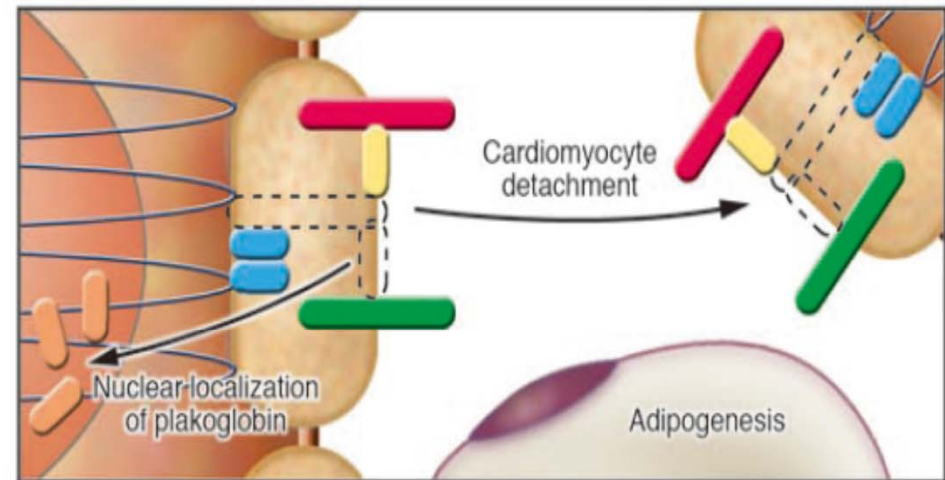
Non-ischemic

ARVD



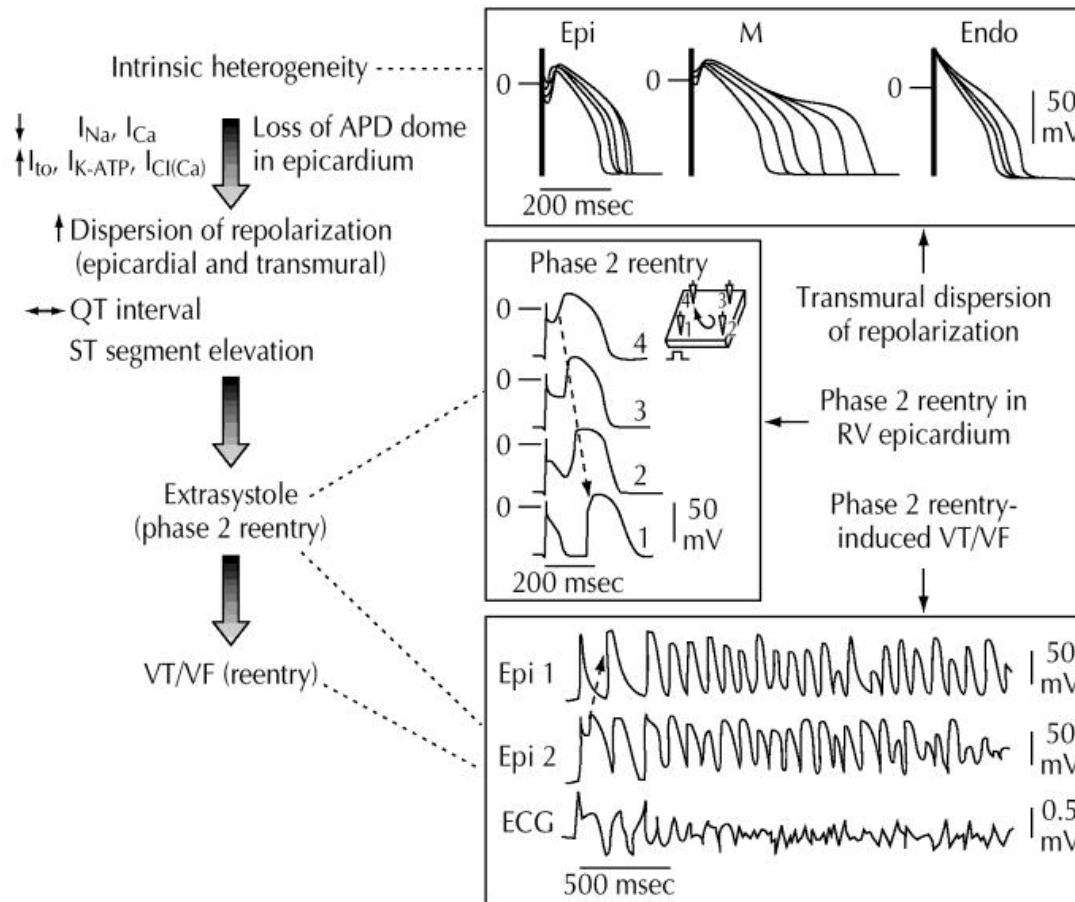
Epsilon wave



A**B** Cardiac myocytes**C** Desmosome**D**

Inhibition of Wnt/ β -catenin signaling
Increased number of adipocytes
Increased fibrosis and myocyte apoptosis
Ventricular arrhythmias and contractile dysfunction

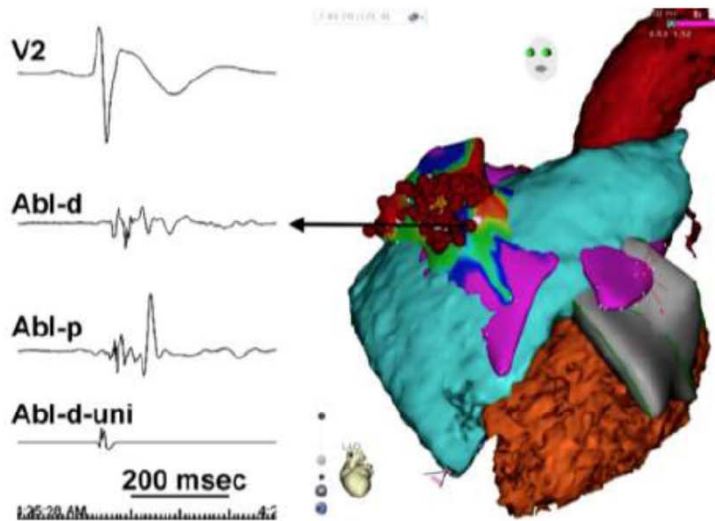
Brugada syndrome



Antzelevitch et al. JCE 2001;12:268-72.

The EGMs recorded from RVOT epicardium

Substrate ablation



Abnormal EGMs (n=9pts)

≤1mV, split or fractionated ≥2 distinct components, wide >80-120ms, beyond QRS

Endpoint

Elimination of all abnormal EGMs
24.8min RF

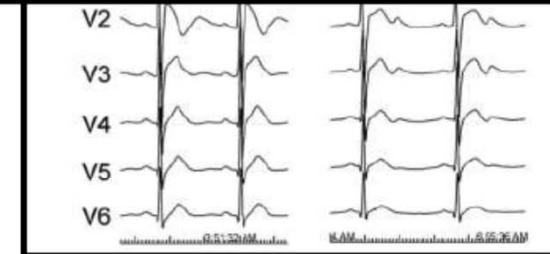
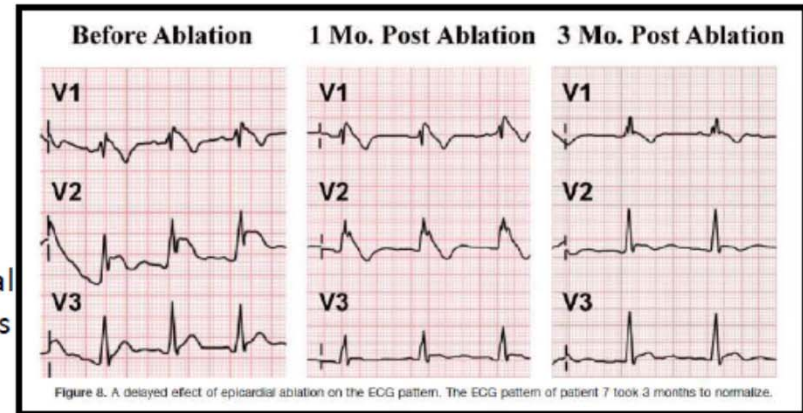
Non-inducibility of VF 7/9

Disappearance of type 1 Brugada ECG pattern
(5/9 acute, 3/9 delayed)

No complications

Follow-up 20 ± 6 months 1/9 VF recurrence

No use of sodium channel blocker during ablation



Nademanee K, et al. Circulation. 2011;123:1270–1279.

Nademanee et al. Heart Rhythm 2017;14:457–461

Summary

1. Idiopathic VT
 - Outflow tract VT는 cAMP-mediated triggered activity가 관여하며, 다른 이온 채널 구성을 보인다.
 - Purkinje cells are important arrhythmic triggers, Initiation and Maintenance of VF and PVT.
2. Ischemic VT는 slow conduction을 유발하는 substrate가 관여한다.
3. Non-ischemic VT
 - ARVC는 plakoglobin re-distribution, gap junction remodeling, apoptosis, inflammation 등이 특징이다.
 - Brugada syndrome은 RVOT epicardium EGM 이상과 연관된다.

Thank you for your attention!

