

Session 2. New Concepts in Risk Stratification of Sudden Cardiac Death

## Sudden Death Risk in Patients with PVCs

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## Possible cause of SCD in patients with PVC

- Malignant arrhythmogenic PVC itself → fast VT to VF
- Benign PVC but malignant condition – inherited arrhythmia syndrome
- Progressive PVC induced CMP (HF pump failure)
- Ischemic PVCs or DCMP

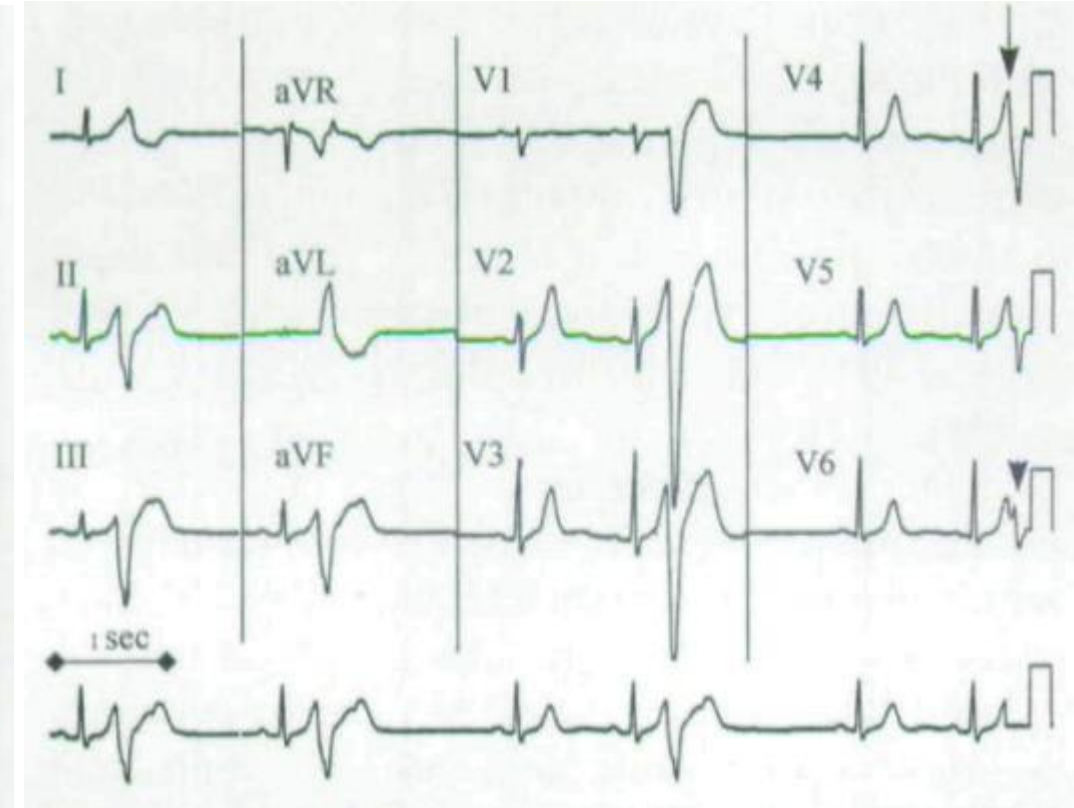
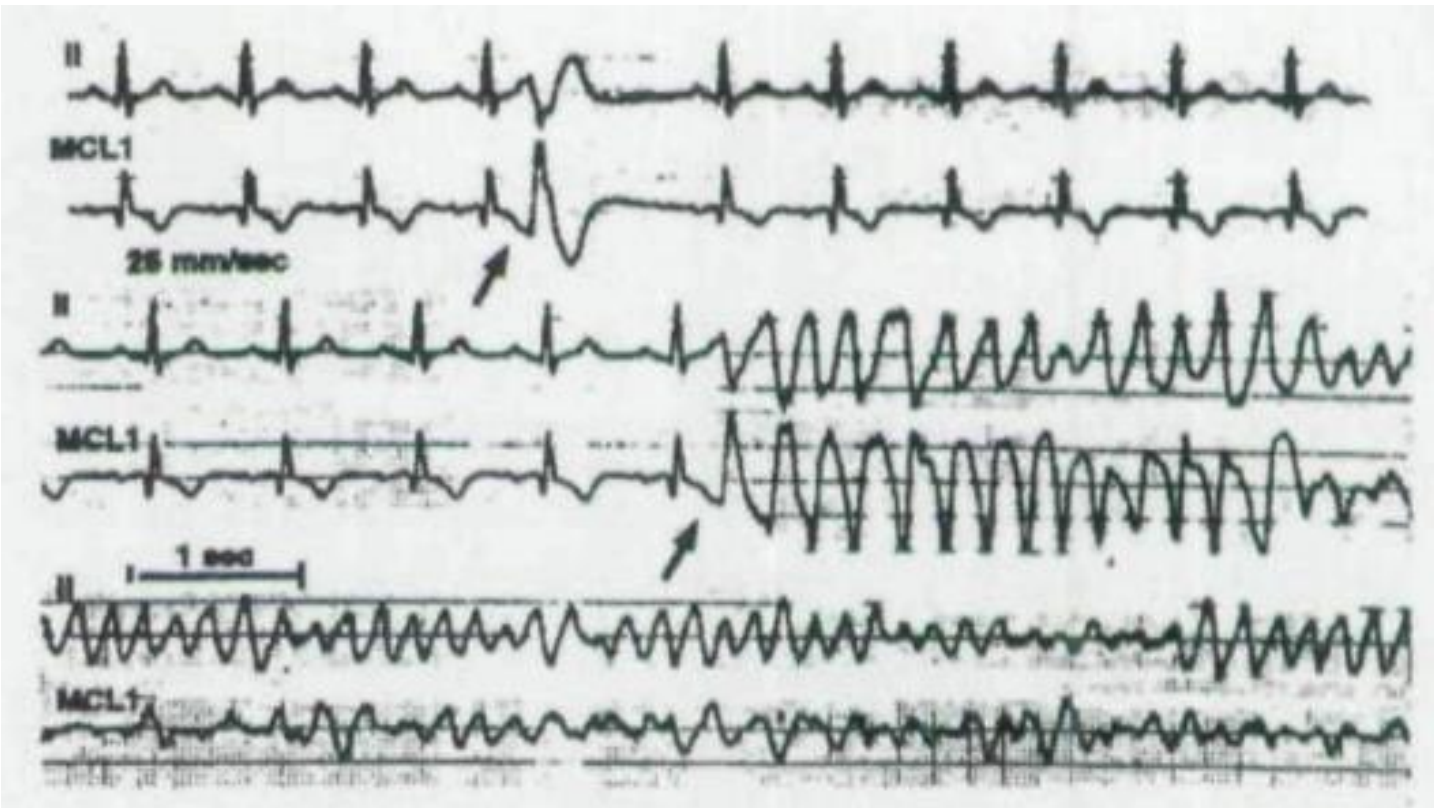


## Focus to...

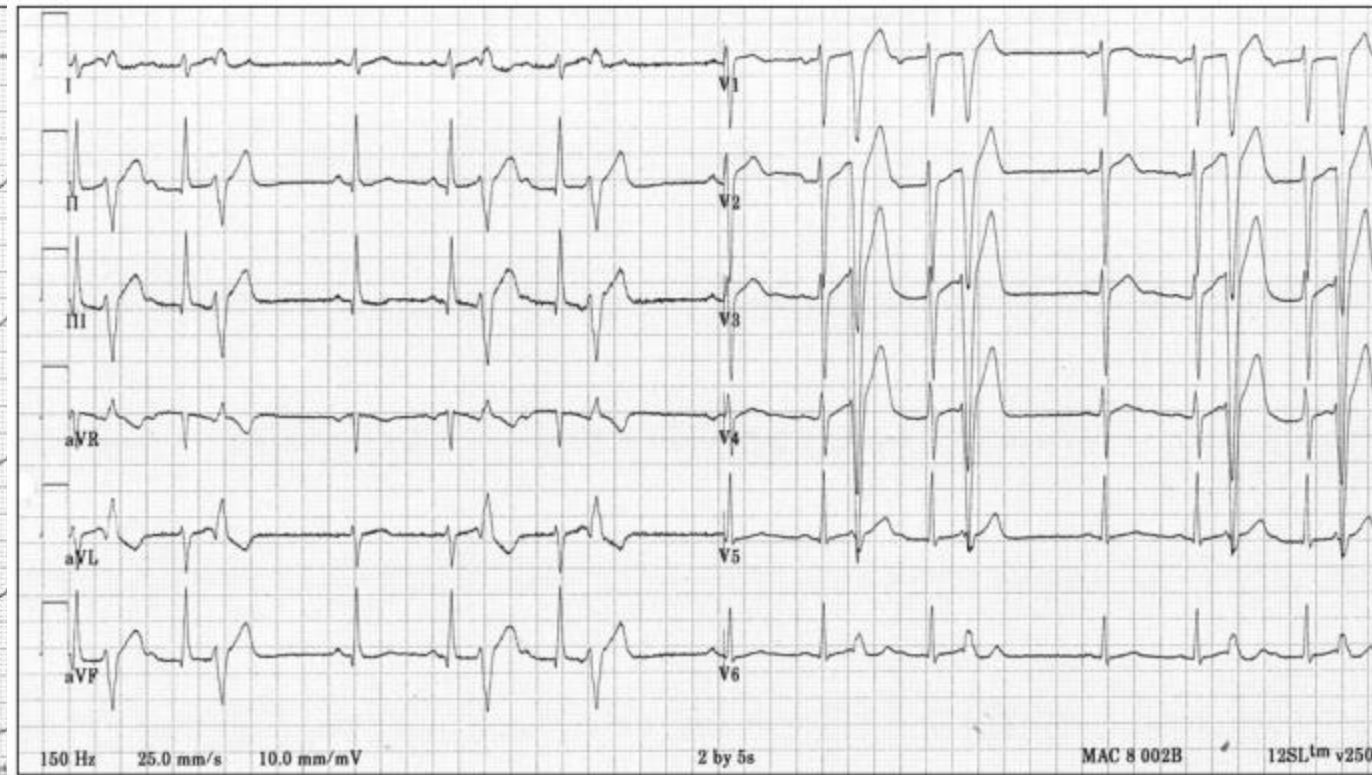
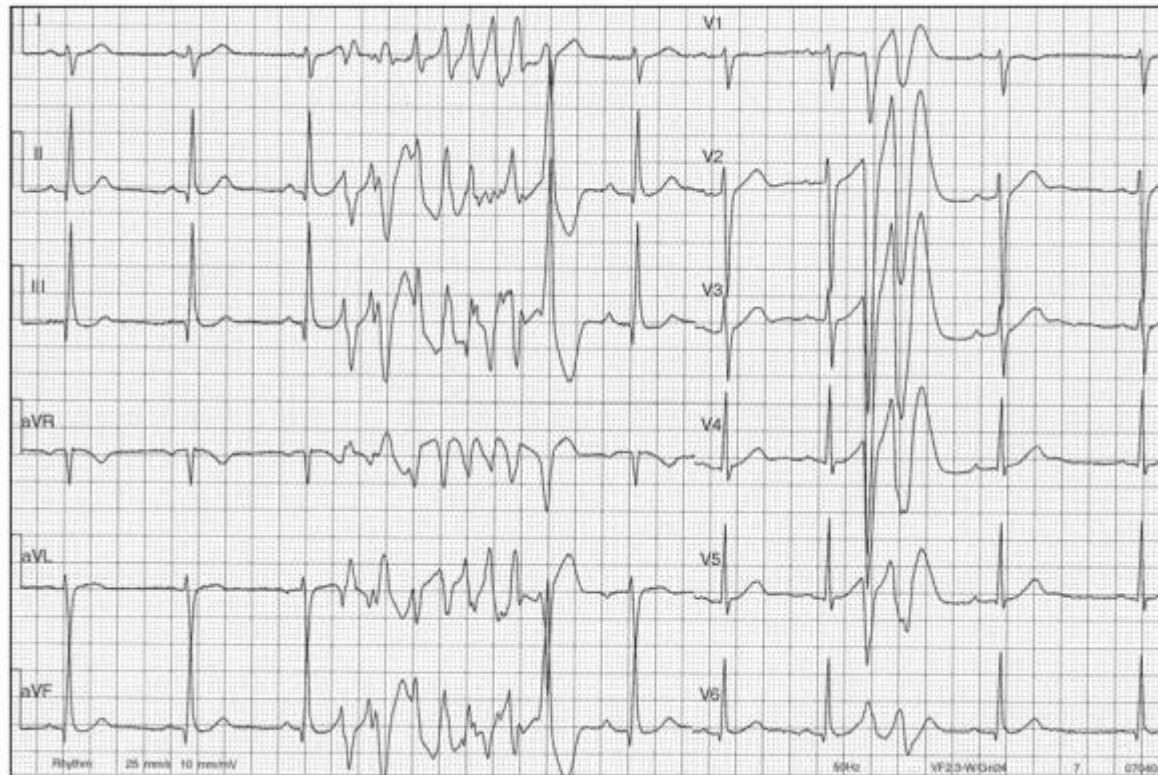
- Malignant PVC
  - PVC from conduction system (Purkinje system)
  - PVC from myocardium (outflow tract)
  - PVC on inherited arrhythmia syndrome
- PVC induced CMP (LV dysfunction → HF, pump failure)
- Ischemic or DMCP PVC (arrhythmogenic substrate+)



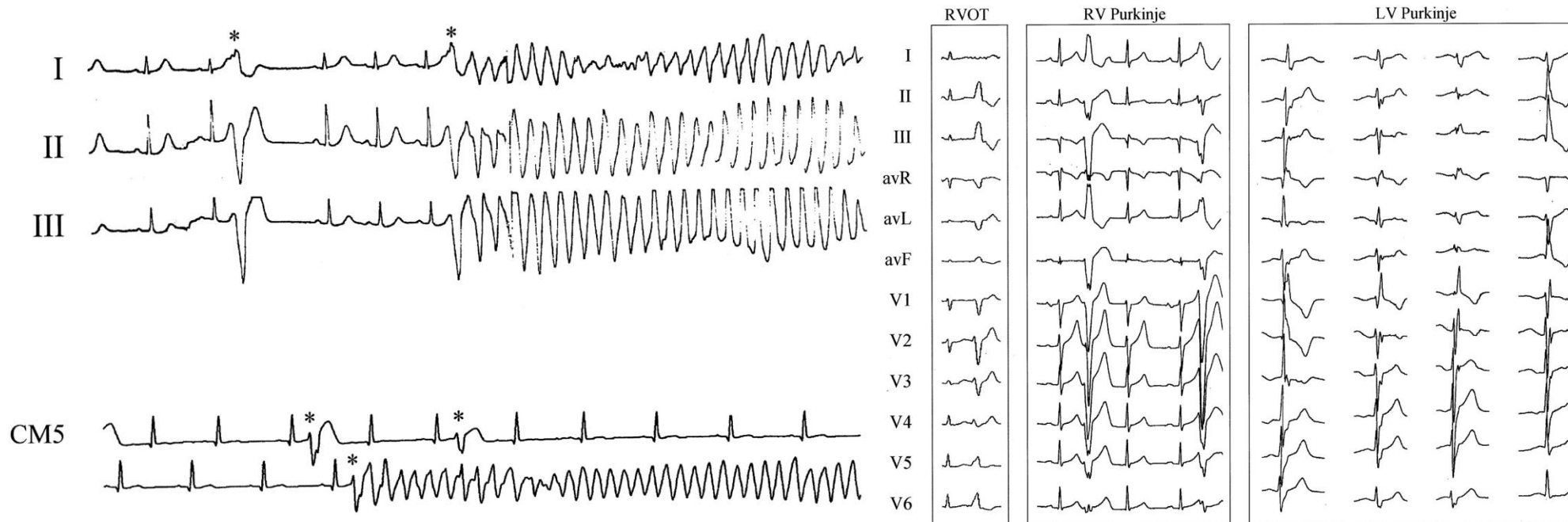
# Mode of onset of malignant VA in iVF



# Short-coupled variant of TdP (RV fascicle)



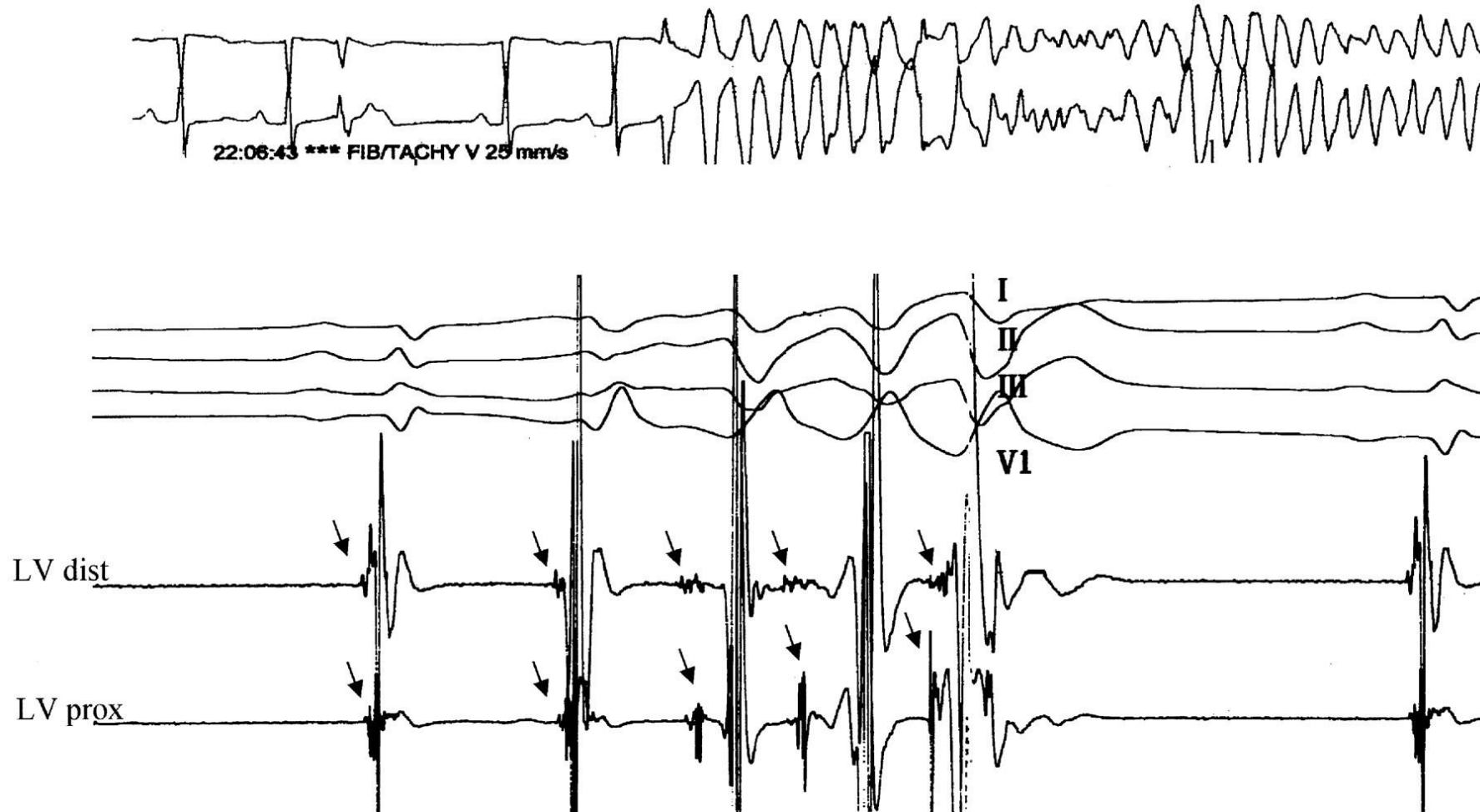
# Mapping and ablation of iVF (27 patients)



	Sex, Female/Male	Age, y	Family History of Sudden Death	Number of VF Before Ablation	Persistent/ Episodic Arrhyth- mias	Polymorphic/ Monomorphic Premature Beats	Ectopic QRS Durations, ms	Coupling Interval Initiating VF or Polymorphic VT, ms
RVOT (n=4)	3/1	27±8	0	2±2	4/0	1/3	145±12	355±30
Purkinje (n=23)	11/12	43±14	6	10±13	4/19	18/5	126±18	280±26
<i>P</i>	NS	0.02	NS	0.03	<0.01	0.06	0.04	0.01

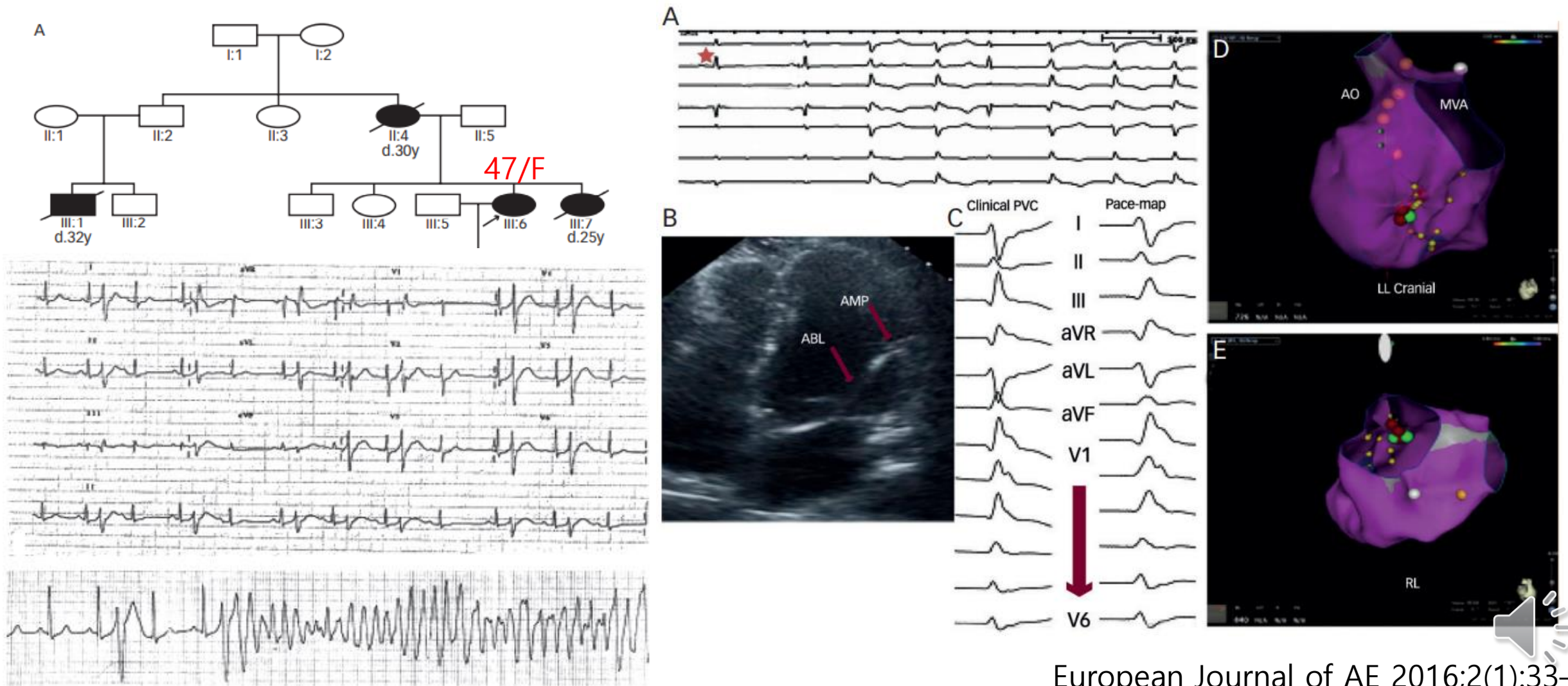


# PVC originating from LV Purkinje system



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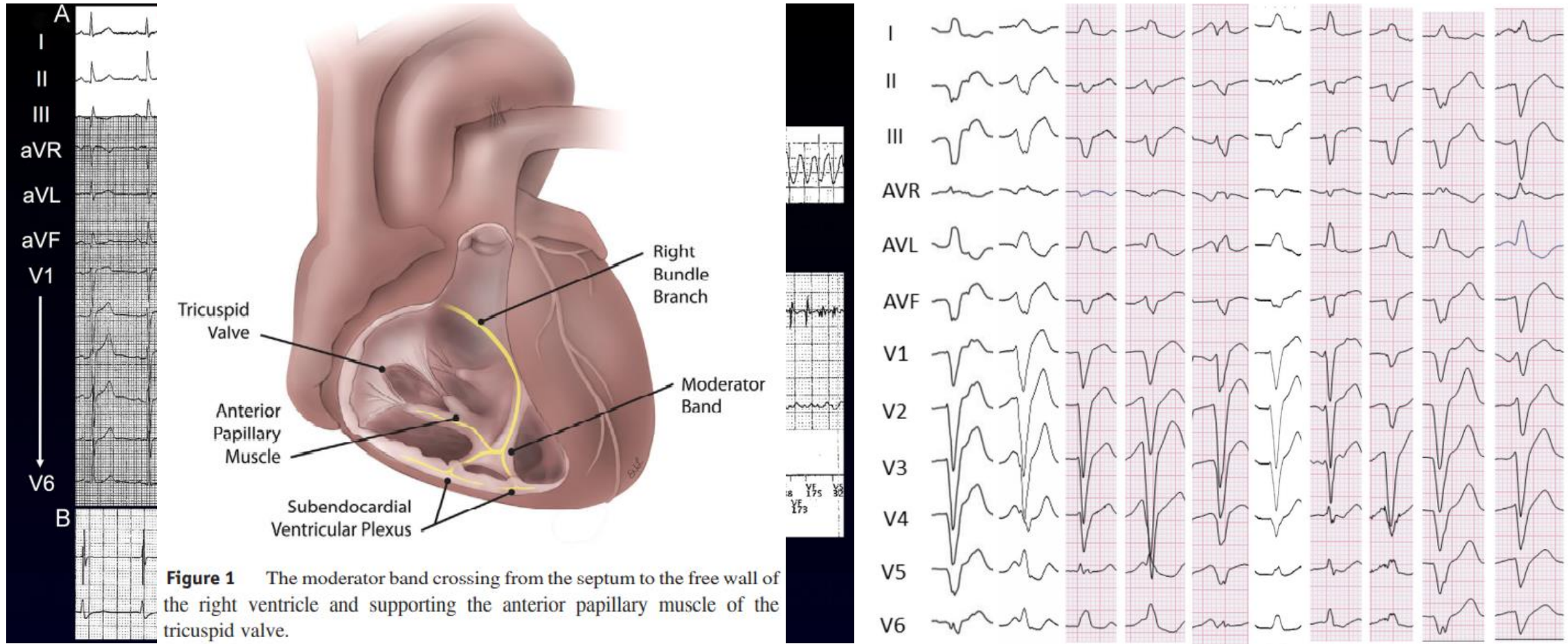
## PVC arising from the anterolateral PM





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## PVC originating from moderator band



# Catheter ablation of VF triggers

Authors	Year of publication	Number of patients	Aetiologies of VF	Ablation site	Follow-up duration	Outcome
Non-structural heart disease						
Nademanee <i>et al.</i> <sup>36</sup>	2011	9	Brugada syndrome	Areas of delayed depolarization over RVOT (anterior aspect)	20 ± 6 months	No recurrent VF/VT in all patients off medication (except for one patient on amiodarone)
Knecht <i>et al.</i> <sup>41</sup>	2009	38	Idiopathic VF	Targeted PVCs originating from Purkinje system	63 months (median)	Seven patients (18%) experienced VF recurrence at median of 4 months. Five of these seven patients underwent repeat ablation without VF recurrence
Haissaguerre <i>et al.</i> <sup>40</sup>	2008	8	Idiopathic VF (with early repolarization)	Purkinje tissue, ventricular myocardium or multiple sites	Specific follow-up of these patients not given	All PVCs eliminated in five patients; unsuccessful in three patients
Haissaguerre <i>et al.</i> <sup>44</sup>	2003	7 (three with Brugada syndrome; four with LQTS)	Brugada syndrome and long QT syndrome	Targeted PVCs originating from Purkinje system (1 Brugada syndrome and three LQTS) or RVOT	17 ± 17 months	No patient had recurrence of symptomatic ventricular arrhythmia but one had persistent PVC
Haissaguerre <i>et al.</i> <sup>39</sup>	2002	27	Idiopathic VF	Targeted Purkinje-like potentials originating from distal Purkinje system	24 ± 28 months	Twenty-four patients (89%) had no recurrence of VF off medication
Haissaguerre <i>et al.</i> <sup>38</sup>	2002	16	Idiopathic VF	Earliest site of PVC activation at Purkinje system	32 months	Successful in 13 patients—no VF recurrence or syncope

Number of patients In catheter ablation for VF triggering PVC

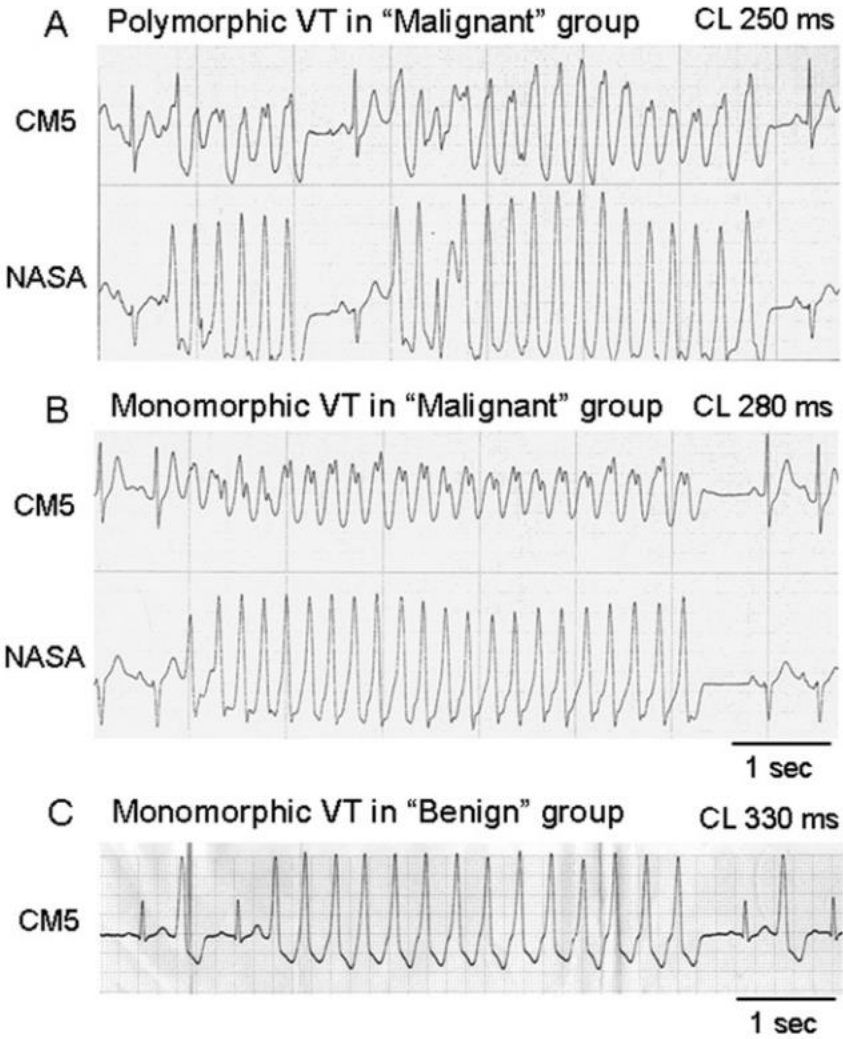
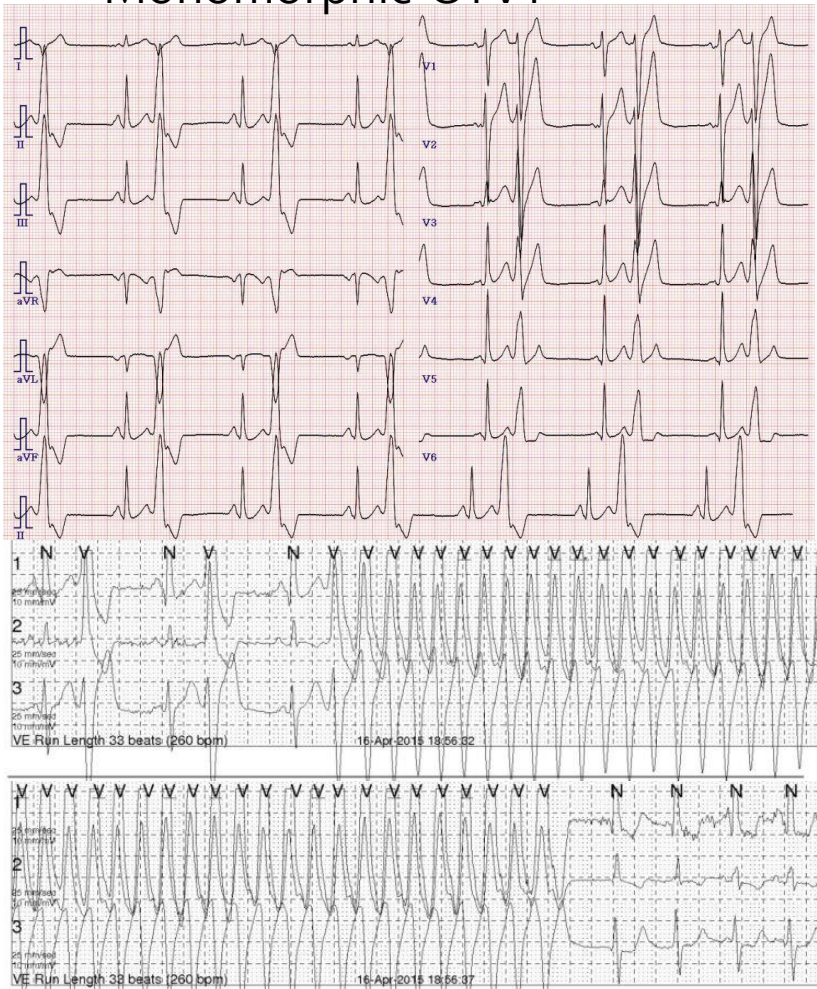
Outflow tract: 9+3 =12  
mainly BrS or LQTS

Purkinje: 38+ 8+ 27 +16 = 56

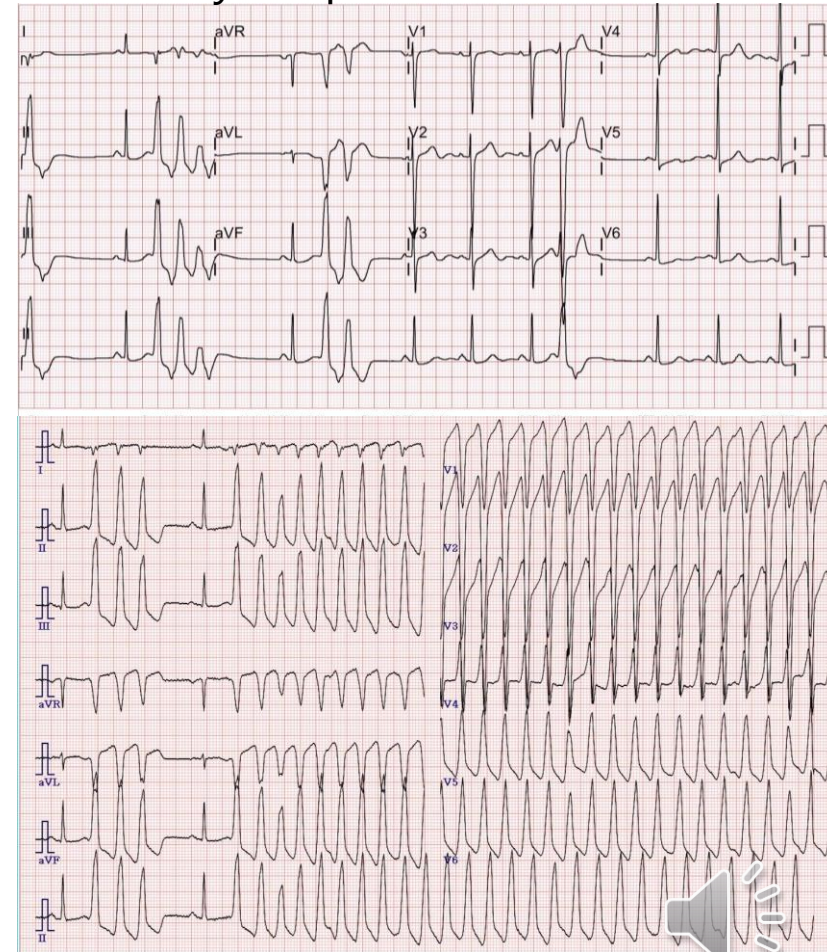


# PVC originating from RVOT

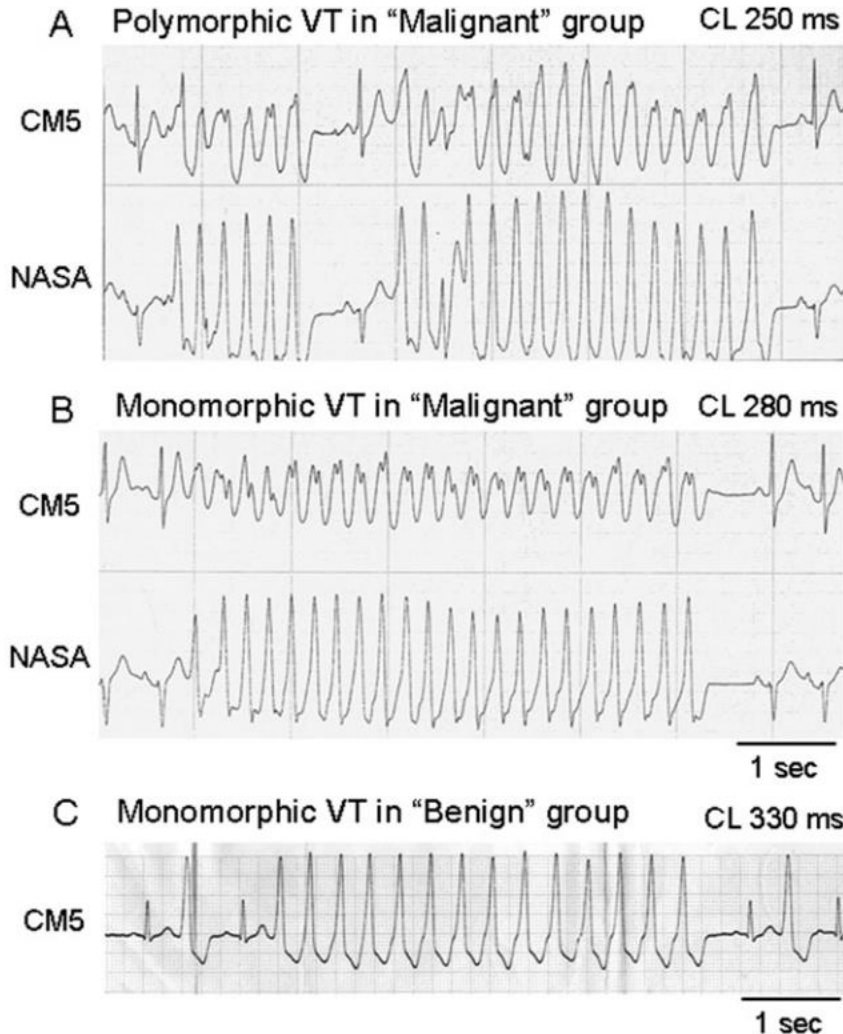
Monomorphic OTVT



Polymorphic OTVT



# PVC originating from RVOT

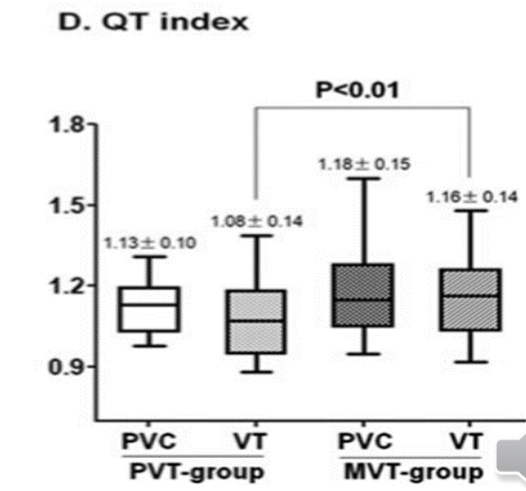
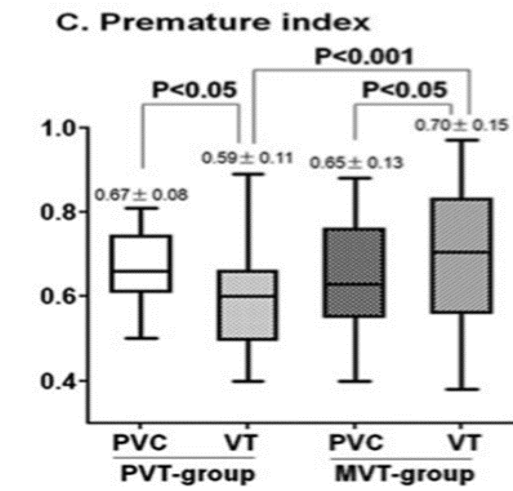
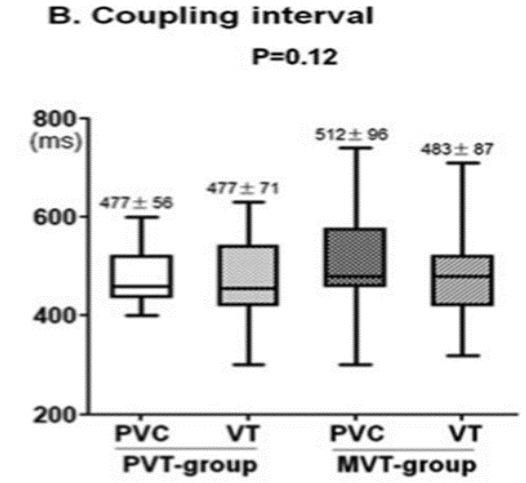
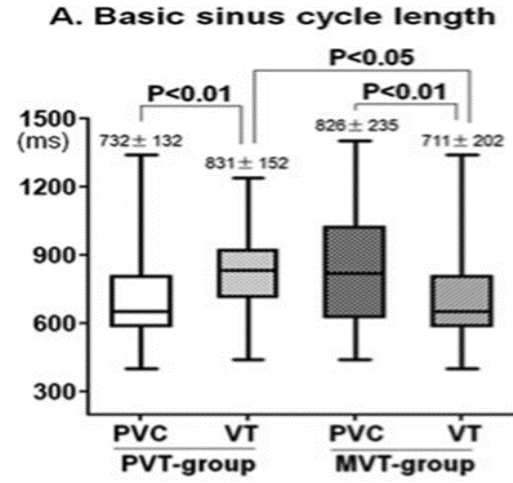
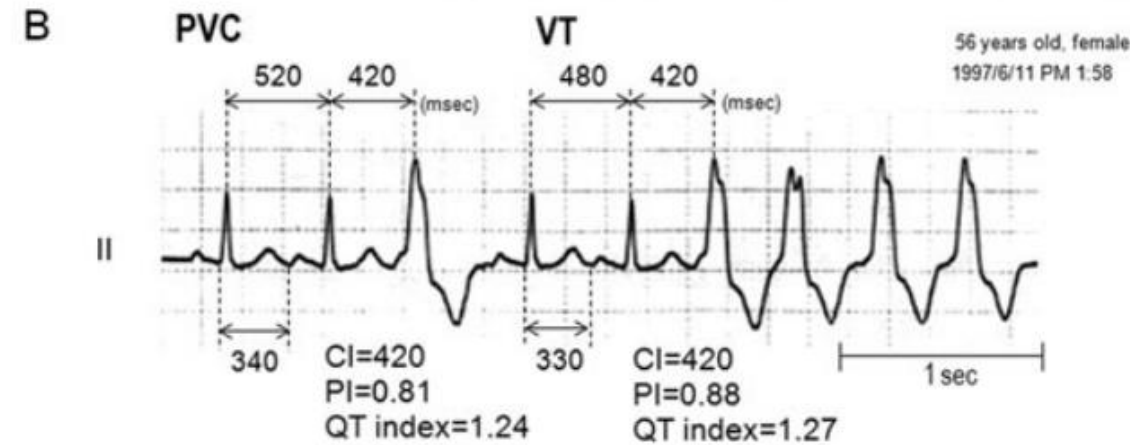
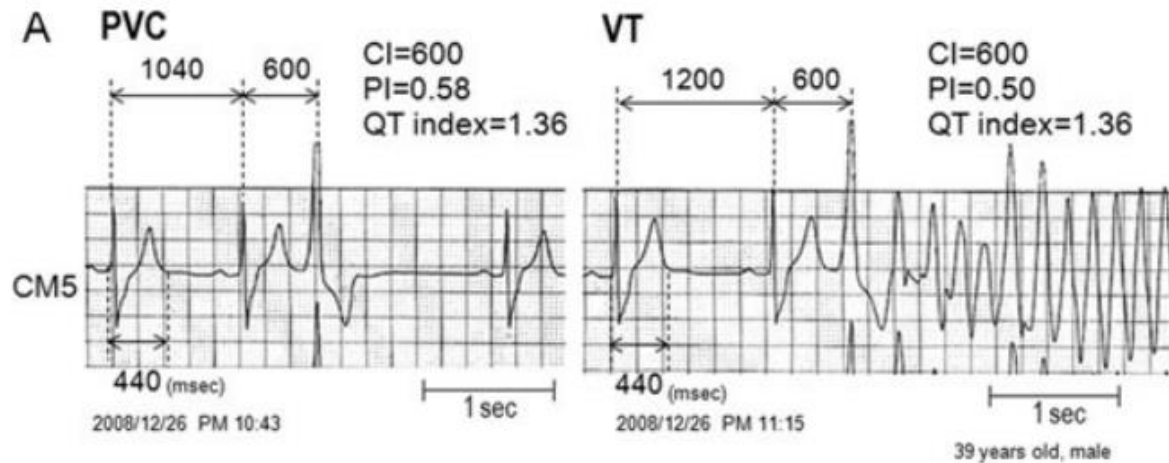


**Table 1** Comparison of ECG characteristics between malignant RVOT VT, benign RVOT VT, and idiopathic VF

	Malignant RVOT VT	Benign RVOT VT	Idiopathic VF	<i>P</i>
CI, ms:				
Haissaguerre et al.	355 ± 30	—	280 ± 26	.01
Viskin et al.	340 ± 30	427 ± 76	300 ± 40	<.001
Noda et al.	409 ± 62	428 ± 65	—	.27
QRS duration, ms:				
Haissaguerre et al.	145 ± 12	—	126 ± 18	.04
Noda et al.	148 ± 8	142 ± 12	—	.03
Cycle length of VT, ms:				
Noda et al.	245 ± 28	328 ± 65	—	<.0001



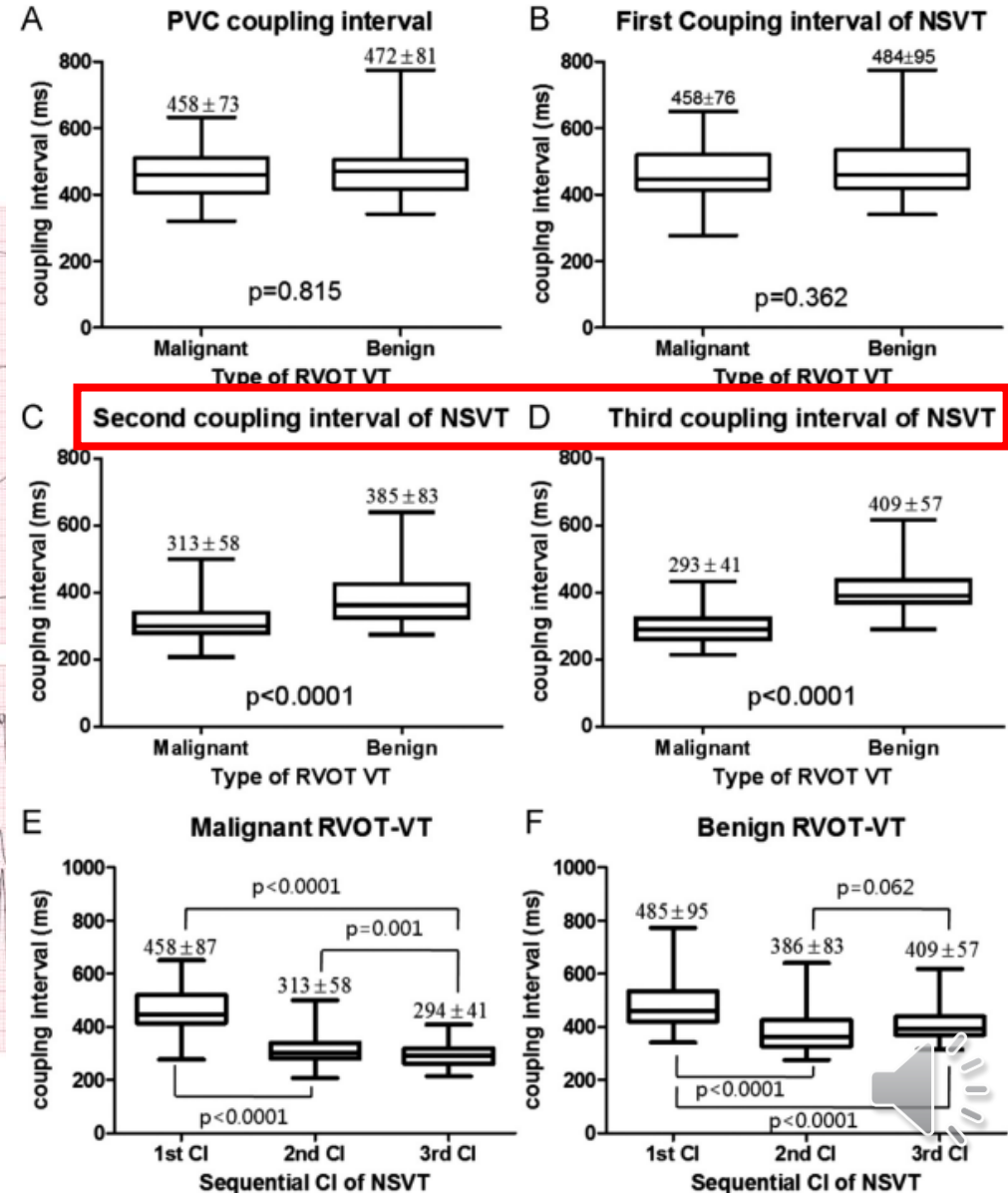
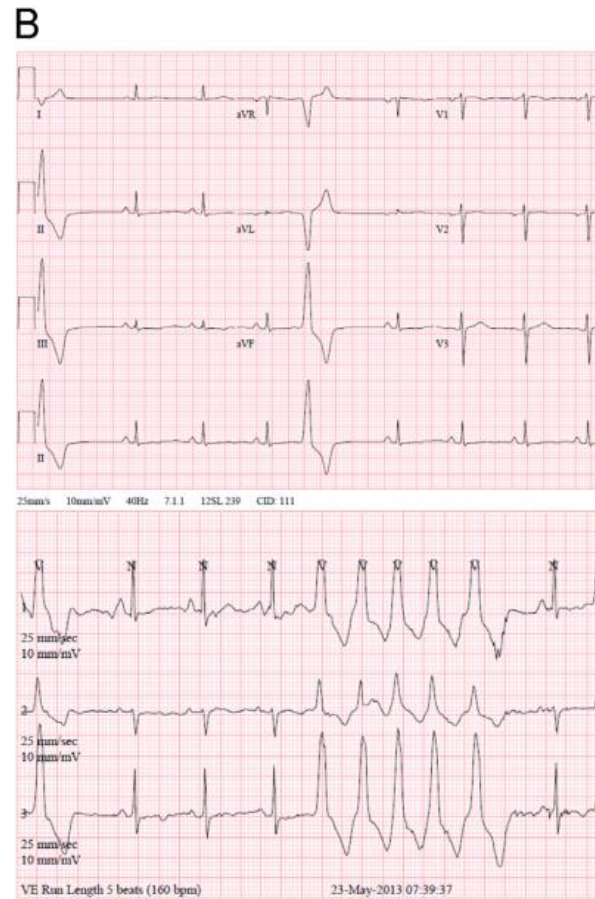
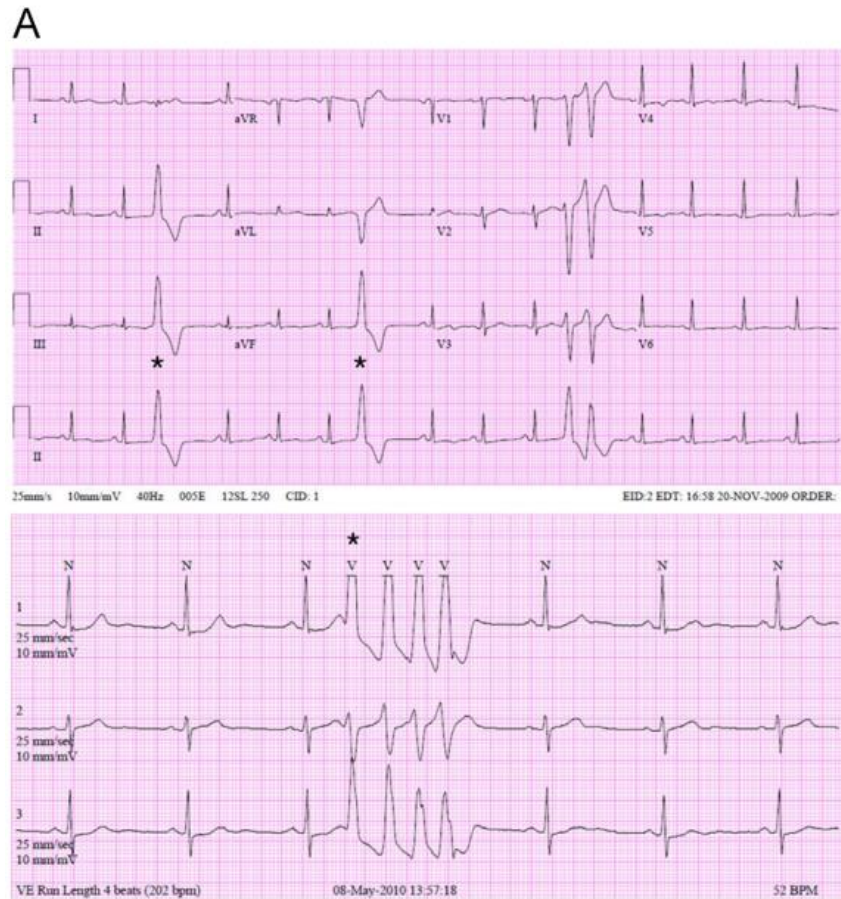
# Malignant vs. Benign OT PVC



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## Sudden Death Risk in Patients with PVCs

### Accelerating PVC coupling interval



# Clinical outcomes of malignant OT VT

Study	Case Presentation	Procedure	Outcomes
Haïssagurre M. (Cir 2002)	4/27 VF (3 F, 1M)	Idiopathic VF 23/27 ICD, 4/27 early RFCA without ICD OT PVC – acutely elimination of 4~7 energy application	24±28 months Free from VF in 24/27 (89%) Recurrent VF in 2, PMVT in 1 ¼ recurrent PVC in ROVT VT
Viskin S. (JCE 2005)	Case 1 F/35	Recurrent syncope EPS – negative PACE map: anteroseptal of RVOT->ICD	8 years FU Free from VT without drug
	Case 2 F/54	Palpitation -> SCD EPS – negative -> ICD	2 years FU Free from VT without drug
	Case 3 F/65	Palpitation -> presyncope EPS – NSVT induction RFCA : midseptal of RVOT	5 months FU Free from VT
Noda T. (JACC 2005)	16 OTVT (9F, 7M) 39±10	11 Syncope 5 Presyncope 5 VF 16/16 – induction (2 ISP, 1Epi, 1 ME) 3/16 Partial success -> BB 13/16 Success but 1 VF with PES->ICD 1 PMVT with PES -> BB	54±39 months Free from VF, SCD in all 16 10 years FU 1 ARVD
Igarashi M. (JCE 2012)	18 PVT/VF (7M,38.9%) 43±14	11 Syncope 5 Presyncope 2 SCD 17/18 EPS – no induction in 1 -> ICD 1/18 refused EPS -> ICD with BB	63±19 months Free from syncope, SCD, VF 2/17 recurrent PVC- redo
Kurosaki K. (Cir J 2013)	14 PVT (12F, 86%) 45±11	8 syncope 2 presyncope 4 VF 13/14 (93%) – success 1/14 (7%) – partial success	68±23 months Free from VT/VF No recurrent syncope or SCD
Kim Y. (HR 2009)	36 OTVT (18F, 50%) 43±16	36 Syncope 6 VF 21/36 (62%) – success 7/36 (21%) – partial success 6(17%) – failed	48±35 months 1 SCD



## Long term outcome of RFCA for malignant OT PVC

### EPS results (52 patients)

Successful ablation of VT/PVC focus, n (%)	37 (71.3)
Partial modification of VT/PVC focus, n (%)	9 (17.0)
Failed induction or ablation, n (%)	5 (10.6)
Single focus of VT/PVC, n (%)	30 (65.2)
Acute complications of EP procedure, n (%)	0 (0)

### Long-term clinical outcomes (19/52 patients)

Recurrent VT, n (%)	5 (9.6)
Recurrent VF, n (%)	9 (17.3)
Recurrent SCD, n (%)	2 (3.8)
Redo ablation, n (%)	3 (5.8)
Channelopathy(LQTs, BrS), ARVD, n (%)	2 (4.0)
Antiarrhythmics, n(%)	22 (42.3)



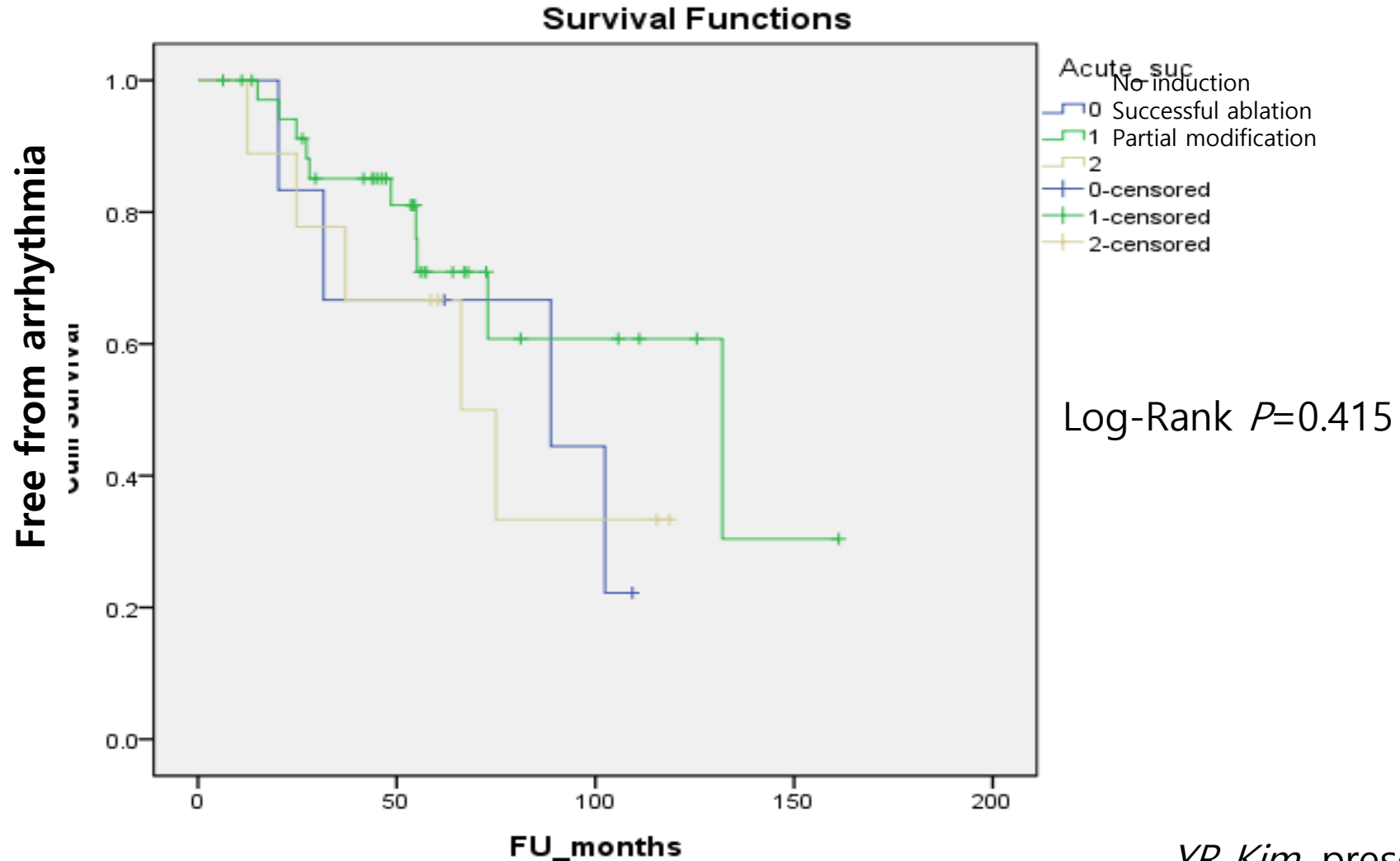


# Long term outcome of RFCA for malignant OT PVC

	Total (52)	No Recurrence (33)	Recurrence (19)	P Value
<b>RFCA result</b>				
Success	37 (71.2%)	27 (73.0%)	10 (27.0%)	0.070
Partial success	9 (17.3%)	4 (12.1%)	5 (26.3%)	
Fail or no induction	6 (11.5%)	2 (6.1%)	4 (21.1%)	
Number of VT Foci	1.39±0.58	1.35±0.55	1.47±0.64	0.543
Complication	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
<b>Antiarrhythmics</b>	21 (42.0%)	9 (26.5%)	12 (75.0%)	0.002*
<b>ICD therapy</b>				
inappropriate	1	1 (3.3%)	0 (0.0%)	<0.001*
appropriate	13	0 (0.0%)	13 (68.4%)	



# VT/VF free survival according to ablation success

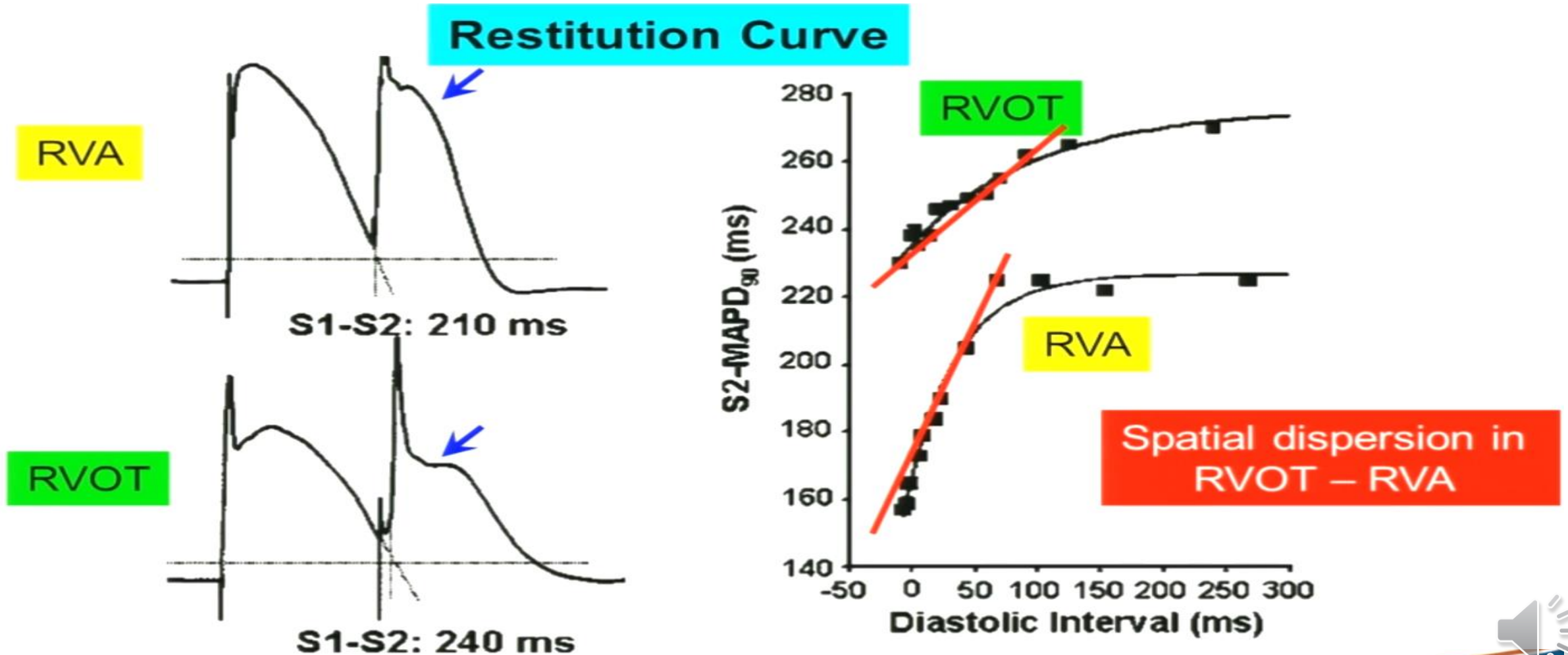


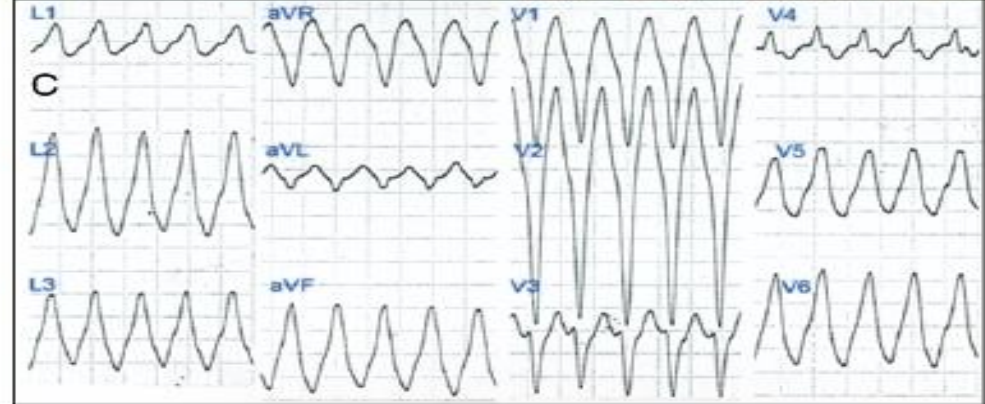
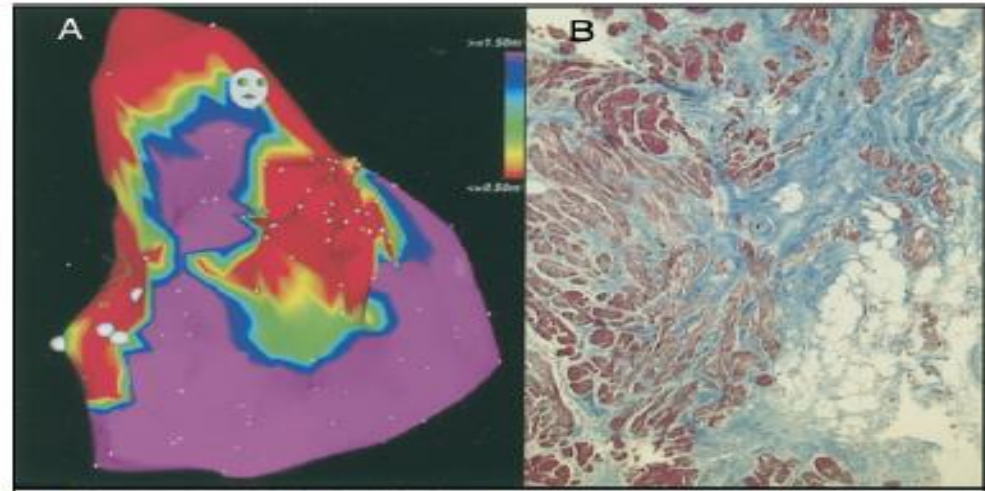
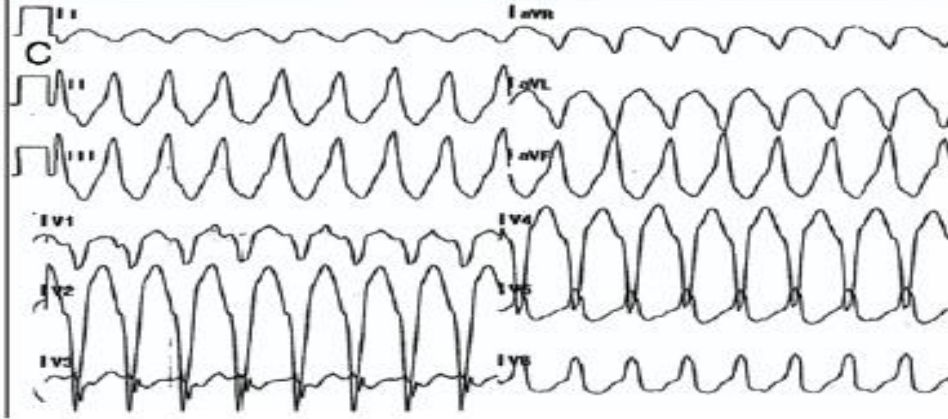
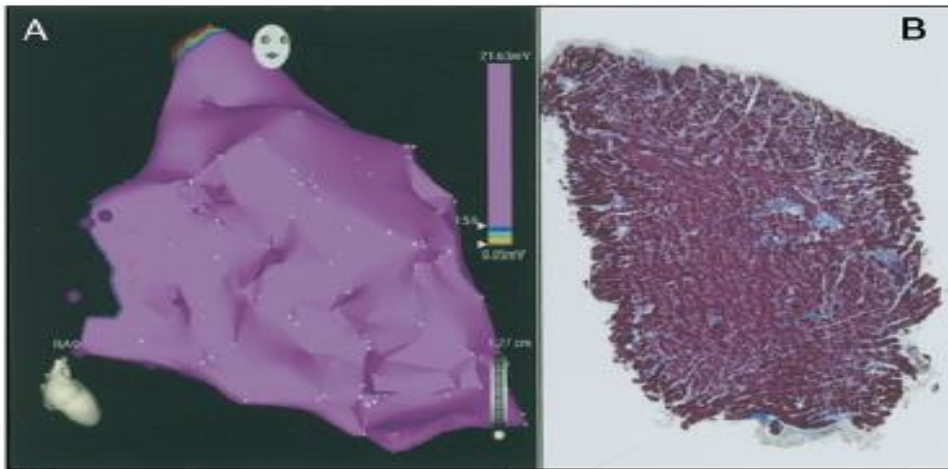
## Possible mechanisms of malignant OT-VT

- Triggering activity secondary to cAMP-mediated DAD
- Intracellular  $\text{Ca}^{2+}$ 
  - Altered positive feedback of  $\text{Ca}^{2+}$  induced  $\text{Ca}^{2+}$  release.
  - Dispersion of refractoriness in ventricular myocardium by functional block or delayed conduction d/t rapid firing triggered activity
  - Up-regulation of the beta-adrenergic receptor system
  - Genetic mutation of RyR2
    - Excessive release of SR  $\text{Ca}^{2+}$  by RyR2 phosphorylation
- Ventricular substrate
  - Alternation of QRS, more than one focus and lower success rate
  - Multiple myocardial foci or substrate-based micro-reentry
  - VT arising from the pulmonary artery



# Spatial dispersion of APD

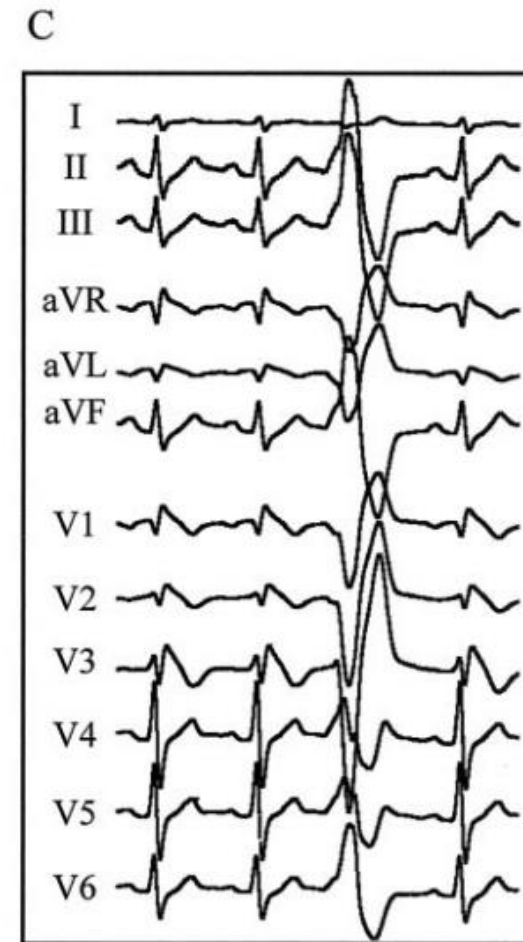
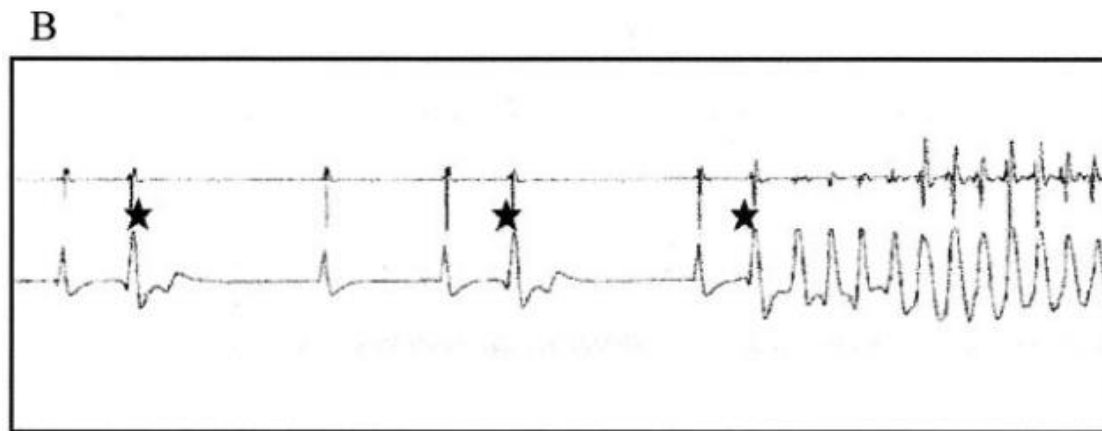
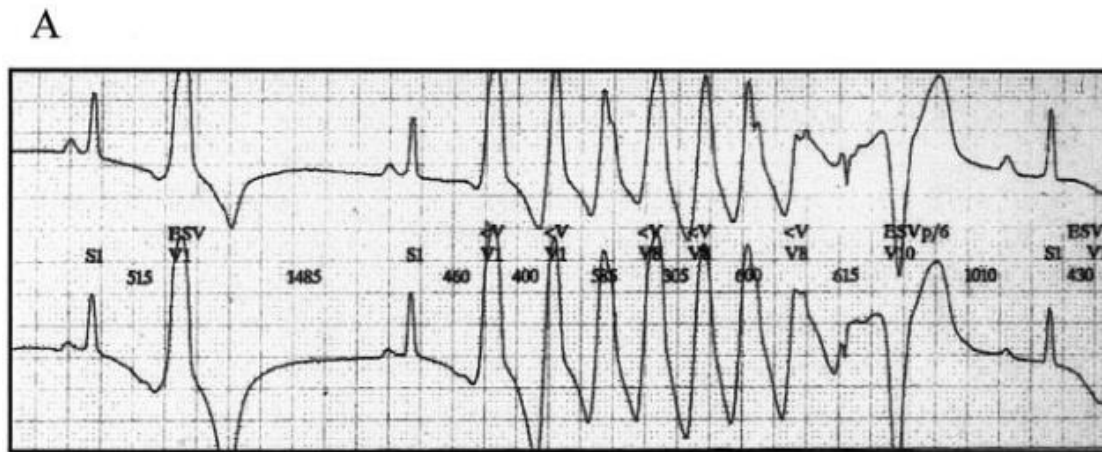




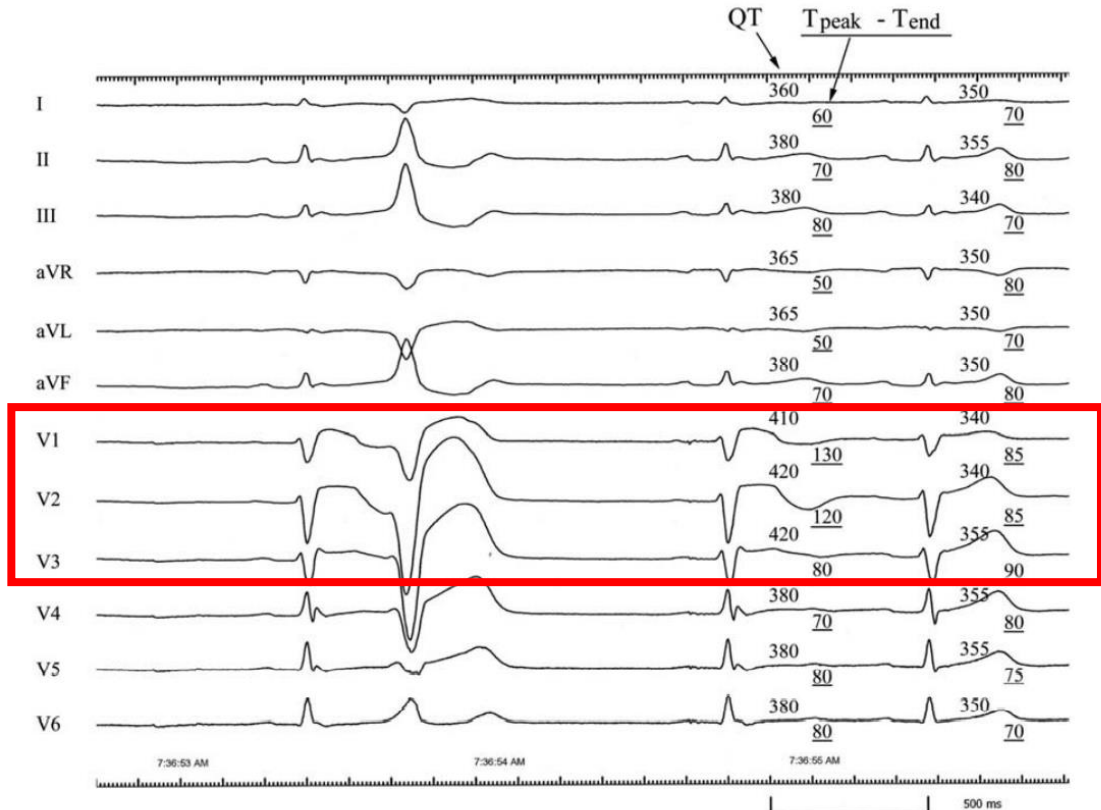
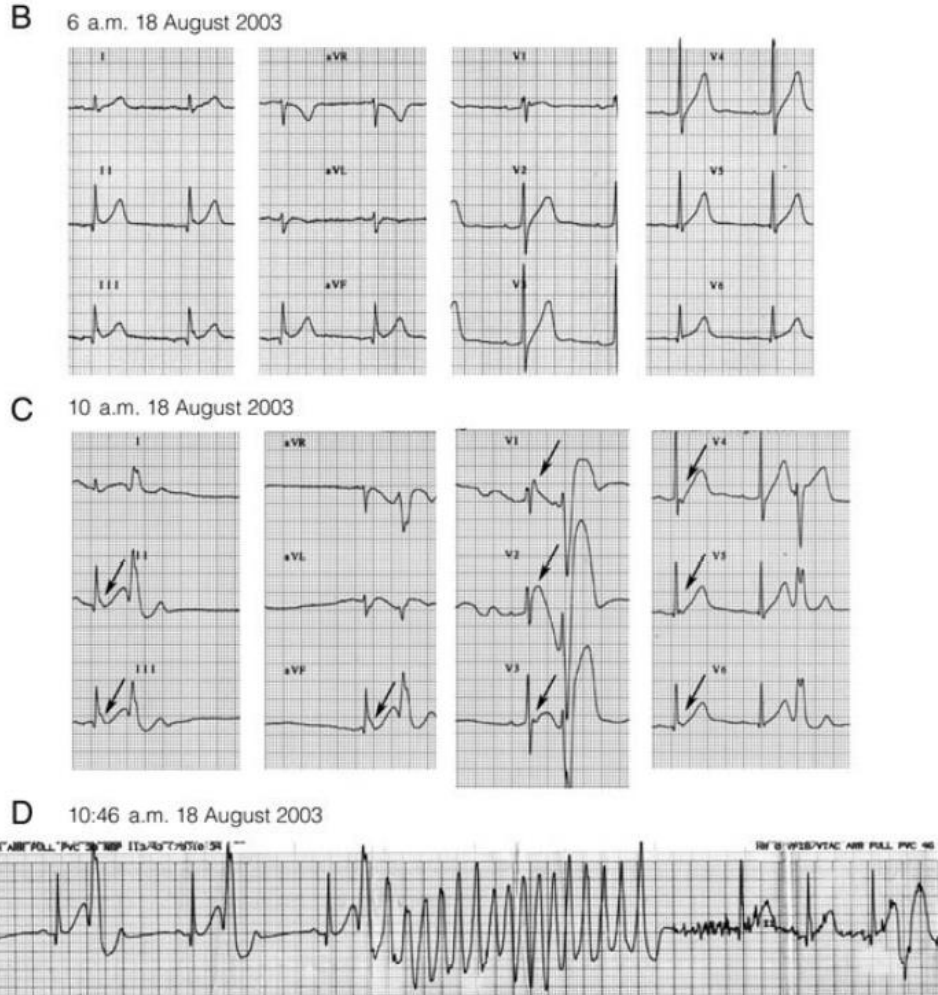
Clinical Characteristics	Overall Sample (n = 27)	Normal EVM Group A (n = 20)	Abnormal EVM Group B (n = 7)	p Value
Age (yrs)	33.9 ± 8	33.6 ± 6	34.1 ± 3	0.91
Gender (male)	15 (55)	12 (60)	3 (43)	0.66
Family history of sudden death	3 (11)	2 (10)	1 (14)	1.0
Clinical symptoms	25 (92)	19 (88)	6 (86)	0.46
<b>Pre-syncope</b>	7 (26)	4/19 (21)	<b>3/6 (50)</b>	0.30
Palpitations	18 (72)	15/19 (79)	3/6 (50)	0.30
Competitive athletes	9 (33)	7 (35)	2 (28)	1.0
Interval between symptom onset and EVM (months)	35 ± 8	35 ± 9	36 ± 4	0.9



# PVC initiated VF in LQTs and BrS



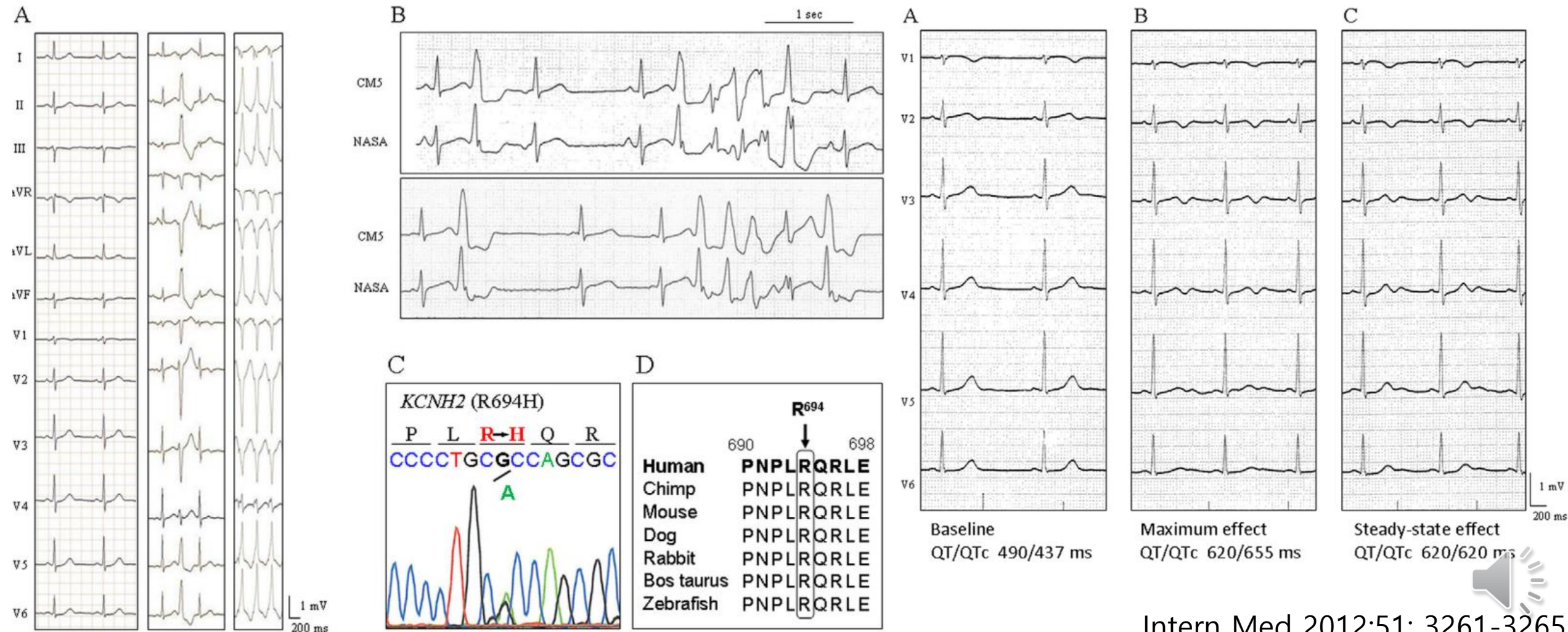
# PVC initiated VF in ERS



PVC initiated VF in ERS vs. BrS  
**More Short long** short sequence: 72% vs. 15%  
**Shorter** coupling interval :328ms vs. 395ms  
 Right precordial QT spatial dispersion >>



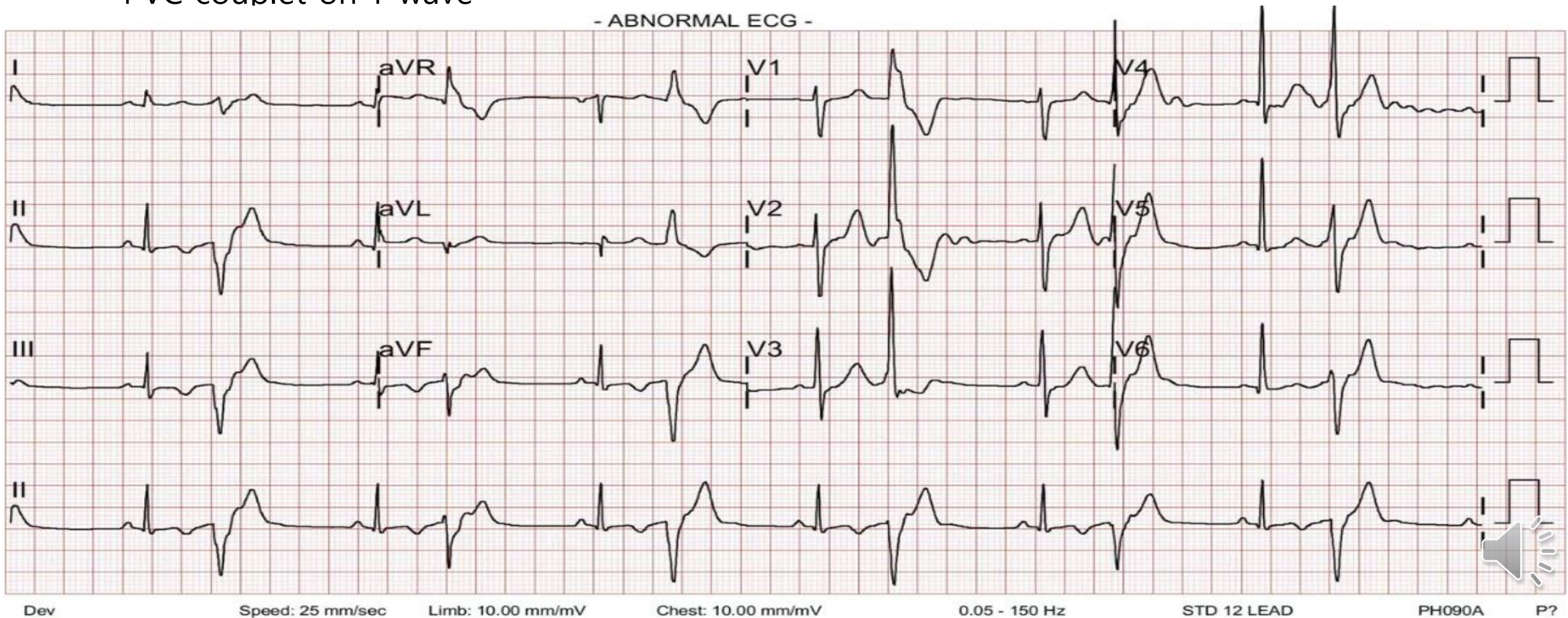
# Benign RVOT PVC trigger polymorphic VT in LQT 2





# Clinical outcomes of malignant OT VT

- s/p ICD d/t VF-SCD 2016.7.20
- LQT – epinephrine provocation (+)
- PVC couplet on T wave



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# Sudden Death Risk in Patients with PVCs

**Episode: VF (315 bpm / 190 ms)**

22 Oct 2018 6:53

VT/VF Episode 3 of 3  
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**Episode: VF (315 bpm / 190 ms) (Continued)**

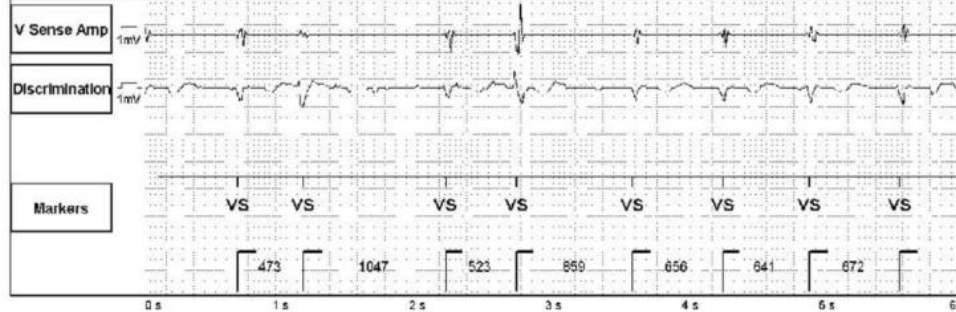
22 Oct 2018 6:53

VT/VF Episode 3 of 3  
Page 3 of 3

1: V Sense Amp AutoGain (0,5 mm/mV)  
2: Discrimination AutoGain (1,3 mm/mV)

3: Markers

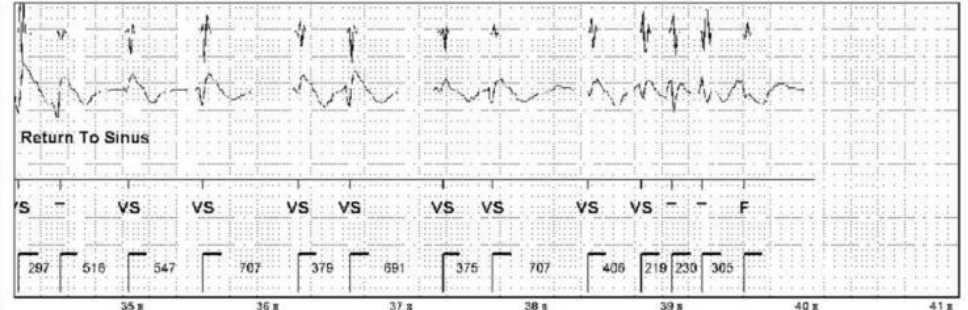
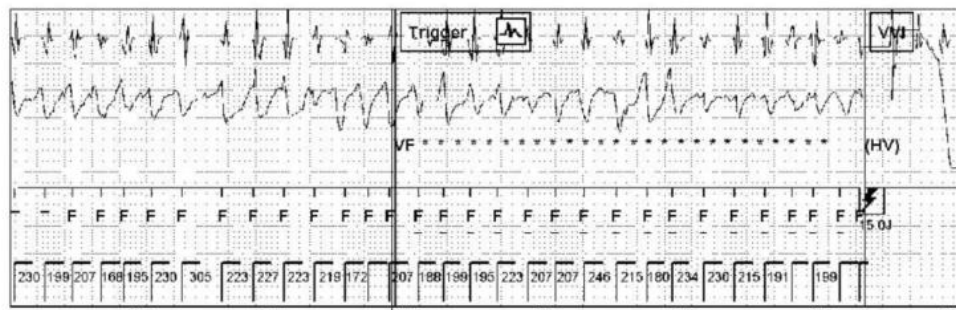
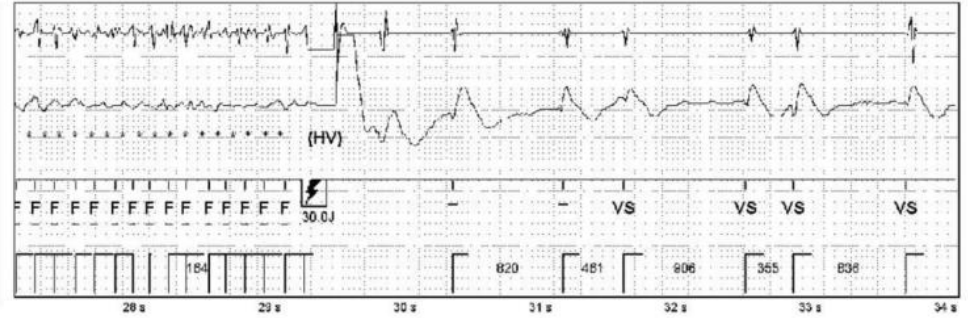
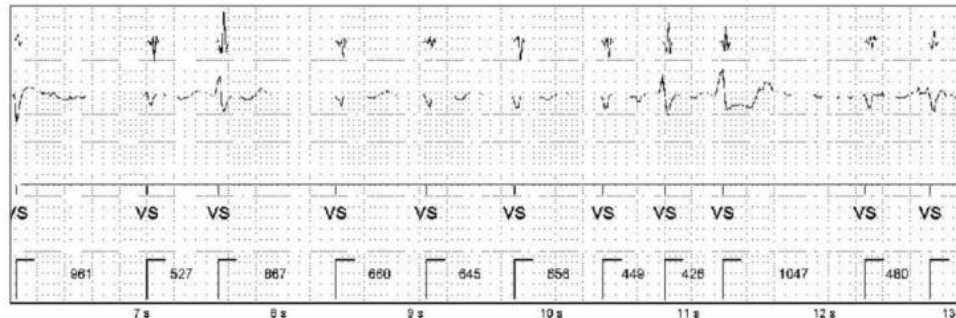
Sweep Speed: 25 mm/s



1: V Sense Amp AutoGain (0,5 mm/mV)  
2: Discrimination AutoGain (1,3 mm/mV)

3: Markers

Sweep Speed: 25 mm/s



## Who's the enemy? What is the target?

### • PVC itself?

- If monomorphic fast VT, **yes!**
- If polymorphic VT, don't think so...but **can be targeting to treatment**

### • PVC on the bad timing?

- **short coupled PVC (1<sup>st</sup> CI)** – originating from Purkinje
- **accelerated TCL (2<sup>nd</sup> CI)** – Outflow tract
- If presentation with SCD d/t VF - **ICD back up**

### • PVC with a latent inherited arrhythmia syndrome

- **continuous FU**
- If presentation with SCD d/t VF - **ICD back up**



**감사합니다**

**Thank you!**

