AF, VT, VF
Summit 2019

Friday & Saturday
December 5-7, 2019
Sofitel Chicago
Magnificent Mile

ABLATION/MAPPING OF VENTRICULAR FIBRILLATION

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DISCLOSURES

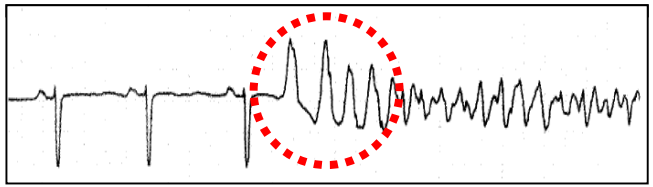
- Biosense webster: speaker fees, research grant
- Medtronic: speaker fees, research grant
- Boston scientific: speaker fees, research grant

INDICATIONS

2017- AHA/ACC/HRS Guidelines:

‘Catheter Ablation is an option for selected patients with polymorphic VT/VF only if an initiating PVC focus or substrate can be identified’

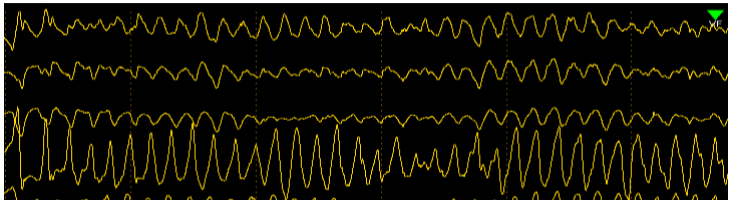
Ventricular Fibrillation : Initiating Triggers



Rare PVCs but predominantly monomorphic when they are present

12 lead documentation of VPBs is essential

Ventricular Fibrillation : Maintaining Substrate



Well identified in the RVOT/Ant RV

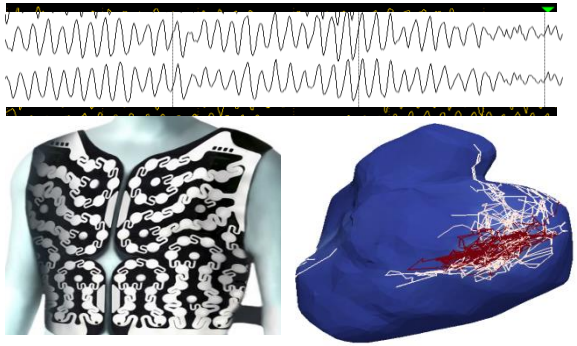
Non-invasive characterisation of human VF drivers

Structural Heart Diseases	Apparently normal Hearts ('primary electrical diseases')
• Ischemic Heart Disease +++ • Cardiomyopathies++ • ARVD • Valvular • Others...	• Brugada syndrome • Long QT /short QT syndromes • Early Repolarisation/J wave syndromes • Catecholaminergic polymorphic VT (CPVT) • **Idiopathic VF defined by exclusion of the above**

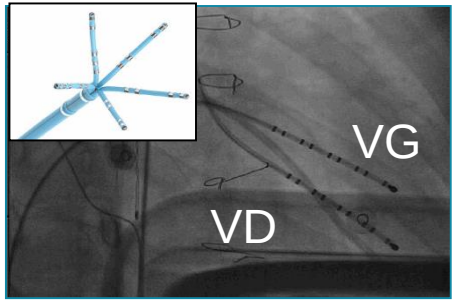
ACC/AHA/HRS Guidelines 2017- Europace 2017

High density mapping in patients victims of Sudden cardiac Death - methods

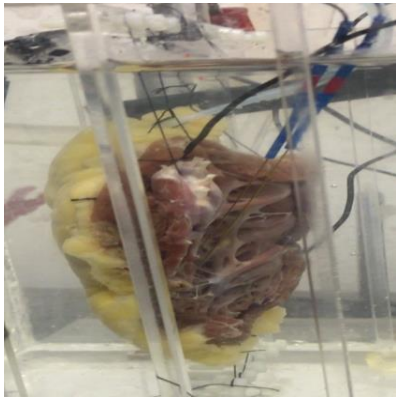
Localization of main drivers (spontaneous or induced VF)



ElectroGram Mapping (in sinus rhythm)



Ex vivo human hearts optical-microelect-Histology



Program 'Isolated Human Heart' donation or transplantation– Bioethical agreement 2014

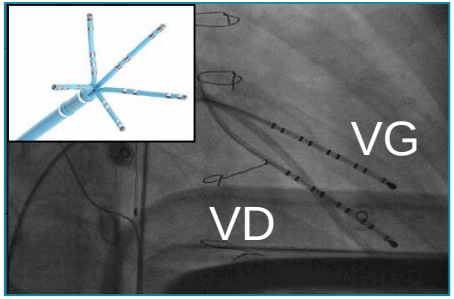
65% reproductibility of driver locations (when VF induced from RV then LV

View projections

High density mapping in patients victims of Sudden cardiac Death - definition of criteria

EGM CRITERIA – COMPARED to CONTROLS

ElectroGram Mapping (in sinus rhythm) using 2mm bipole spacing

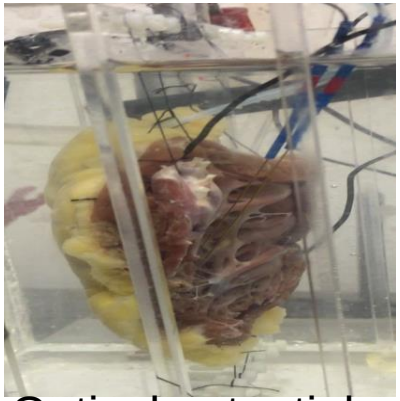


Abnormality of myocardial depolarization : presence of prolonged egms (> 70ms- >3 components-split and late) *

Abnormality of myocardial repolarization : heterogeneity of repolarization maps - lesser knowledge

*Criteria defined with ≥5mm bipole spacing-
*paucity of control patients

Ex vivo human hearts optical-microelect-histology

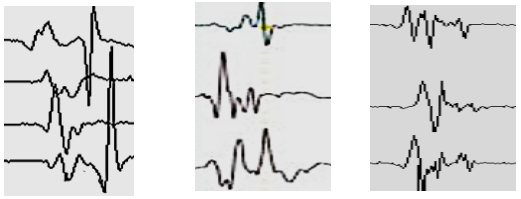


Optical potentials

Precise repolarization mapping (endo - and epicardial)

Hsia..Marchlinski et al- Soejima..Stevenson et al- Cano et al- Nademanee et al- Anter et al

FRAGMENTED ELECTROGRAMS



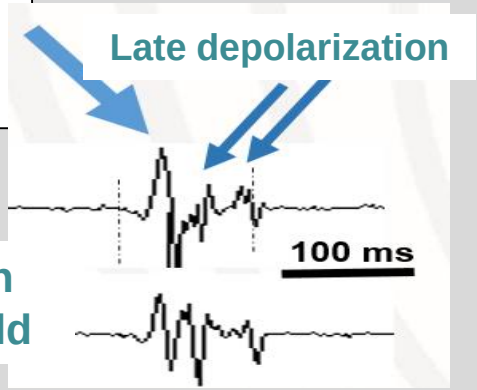
No disease specificity of EGM fragmentation

(can be BrS- IVF-J wave-CMD-ARVD-Inflammatory..)

‘Fragmented’ potentials : Depolarization vs Repolarization

Local Depolarization
(activation map)

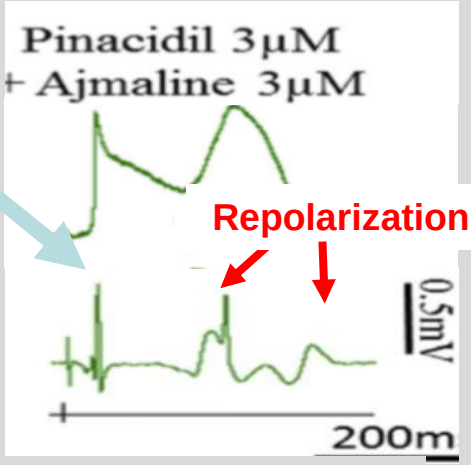
In continuity with depolarization field



Mapping in Humans

Local Depolarization
(Phase 1 AP)

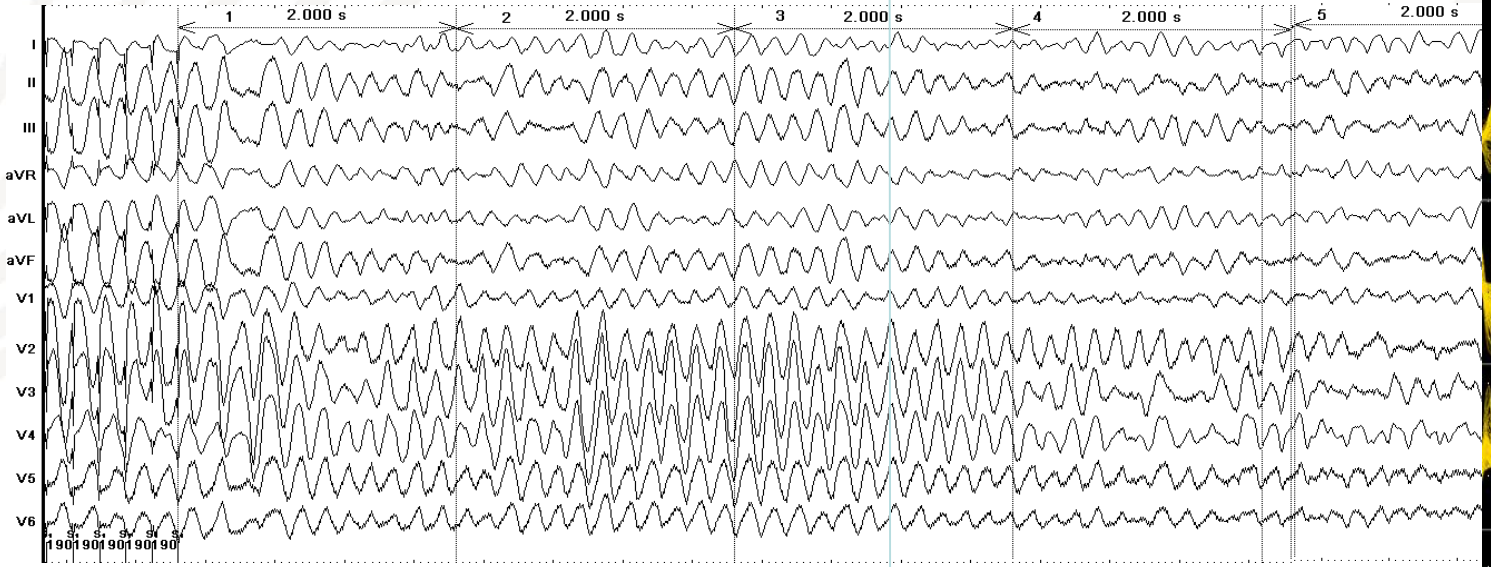
Gap with depolarization

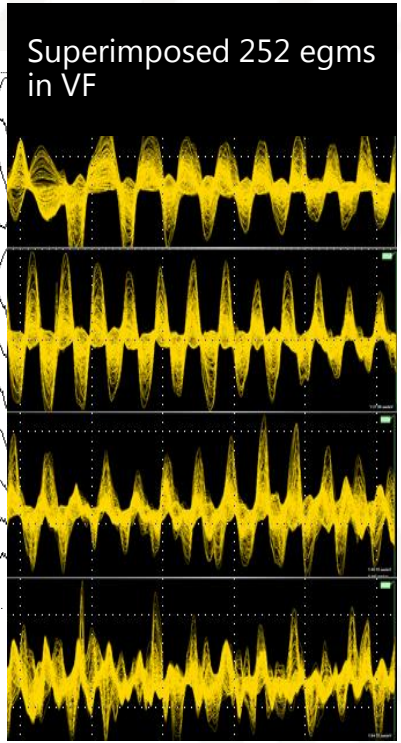


Mapping in Wedge-Dogs

VF EARLY (ORGANIZED) AND LATER (DISORGANIZED)

Case: patient 47 yrs- Brugada syndrome





Electrograms not altered

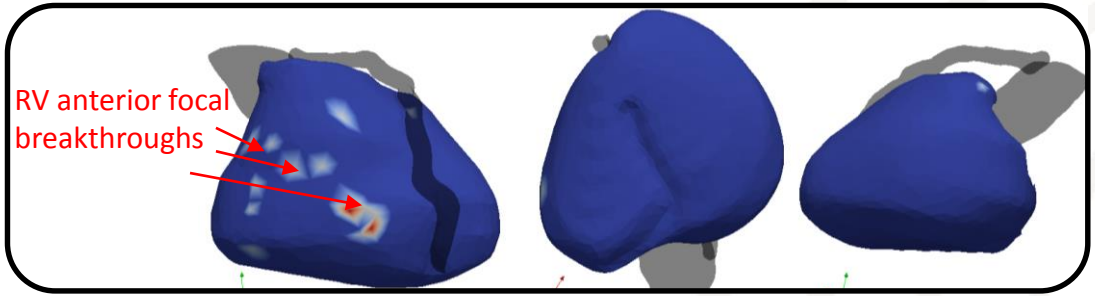
High similarity of endocardial and epicardial VFCL (suggesting transmurality of activities)

Electrograms Fragmented (unreliable annotation)

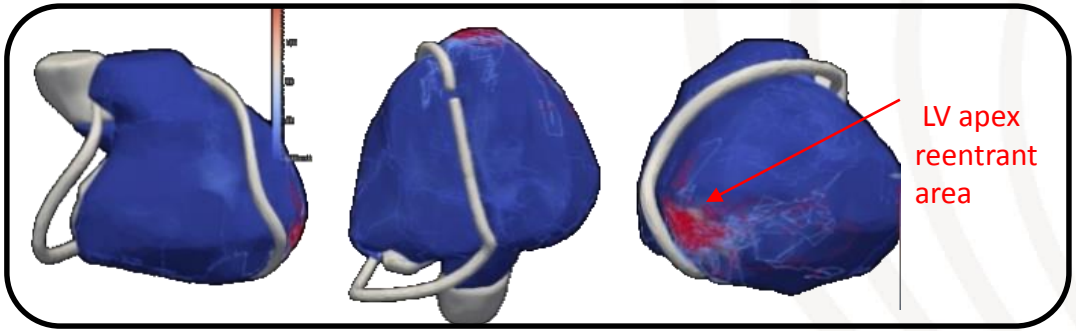
Lesser similarity of endocardial and epicardial VFCL

RESULTS 1 – VF MAPS SHOW THE MAIN DRIVER AREAS IN AN INDIVIDUAL

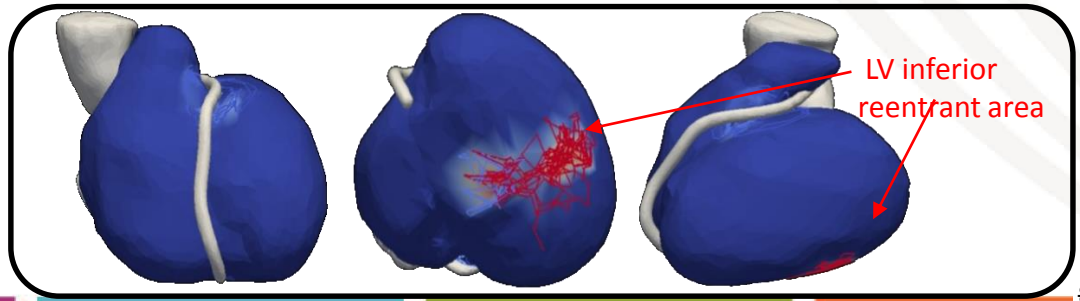
Brugada syndrome



Ischemic Heart disease



Dilated cardiomyopathy



RESULTS 2: Human VF dynamics Depend on the underlying HD

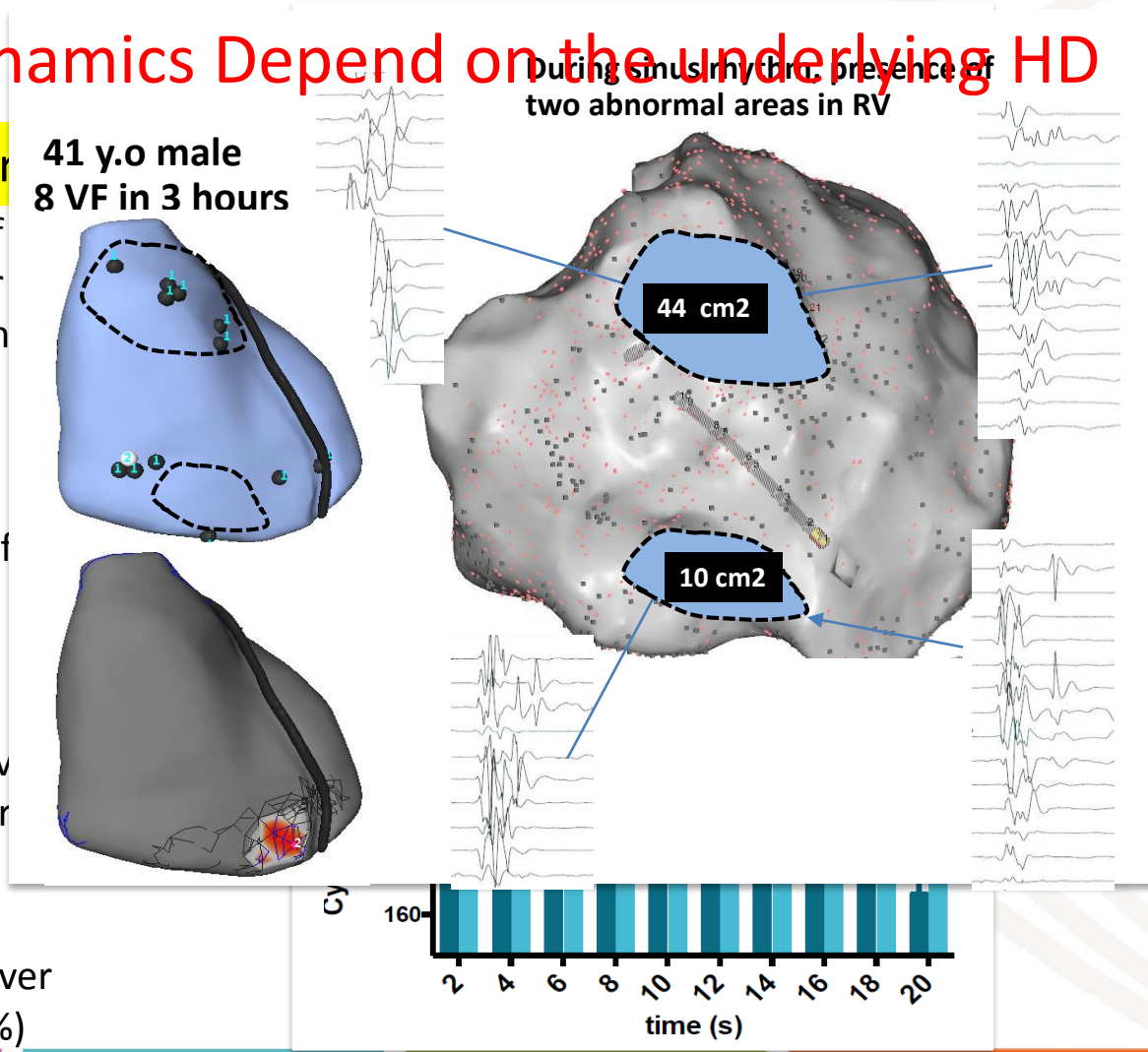
VF associated with Brugada Syndr

1. RV is the dominant driver source in 30 of (81%) patient during organized/early VF for 4,64±3.25s particularly focal breakthrough figure-of- 8 reentries and LV is passively activated

2. RV wavefronts invade LV and produce in f seconds secondary drivers associated with higher LV DF

3. Location of drivers includes constantly RV But extends frequently to anterior and infer RV walls

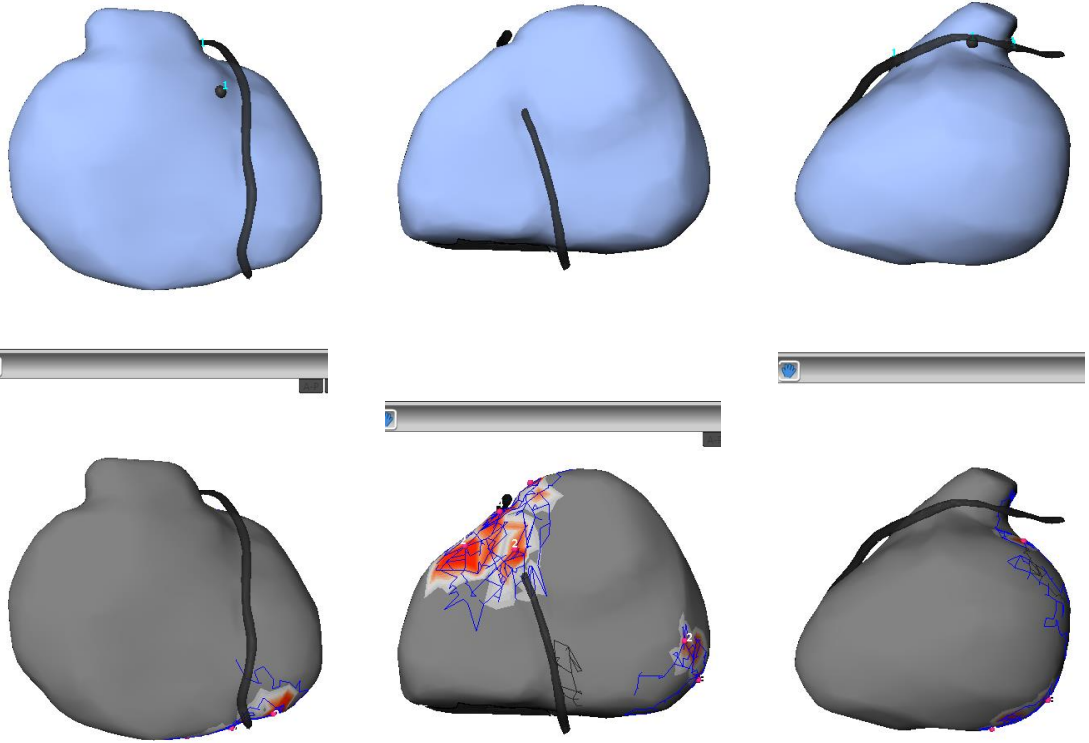
4. Abnormal electrograms in SR at most driver areas: typically at epicardial site (18cm2/9%)

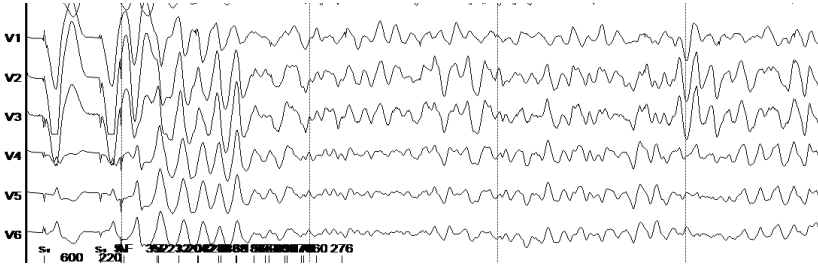


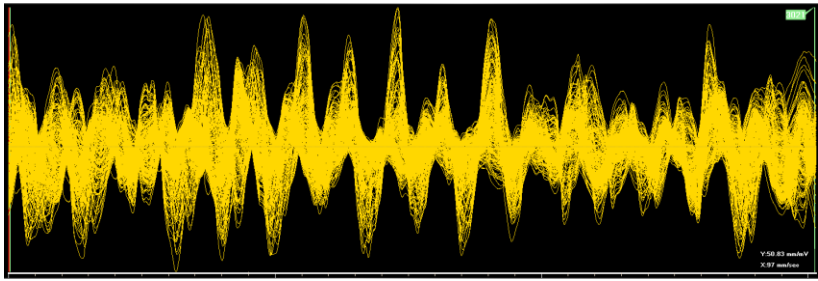
M 33 y

- SCD in 2013 with diagnosis of Brugada Syndrome. Family history of Brugada (Father and Brother).
- ICD Vr implant Secondary prevention in 2013. ICD Change in 2017
- 13 VF since 2013
- First Procedure in 2017 Endo+Epi ablation.
- New VF storm in June 2018.
- Second procedure with complete endo+epi maps and Ajmaline challenge. No abnormal Egms observed Endo+Epi.
- New VF after this procedure.

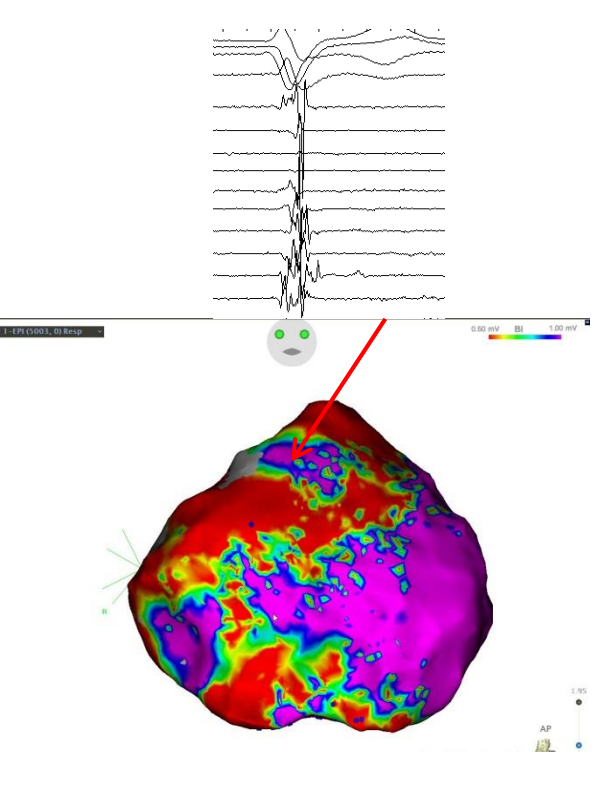
M 33 y, 2 failed previous epicardial ablation, last ablation in Bx

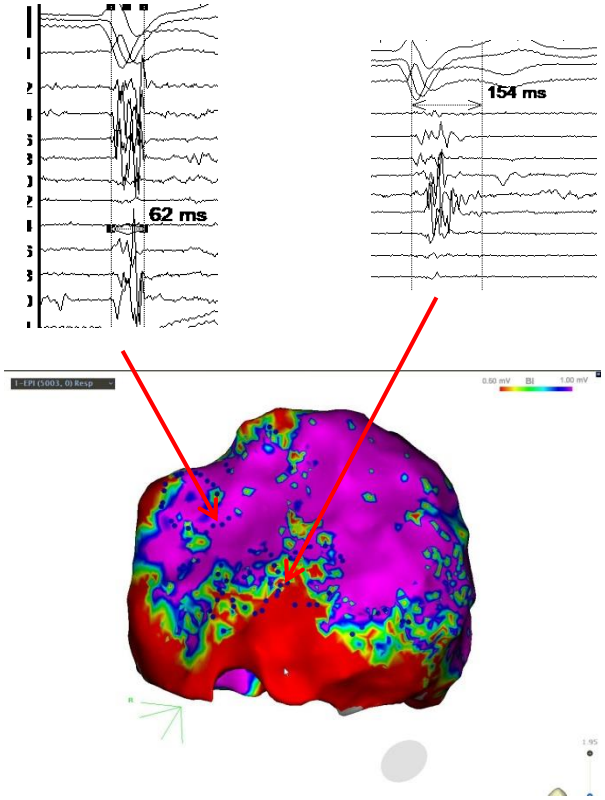


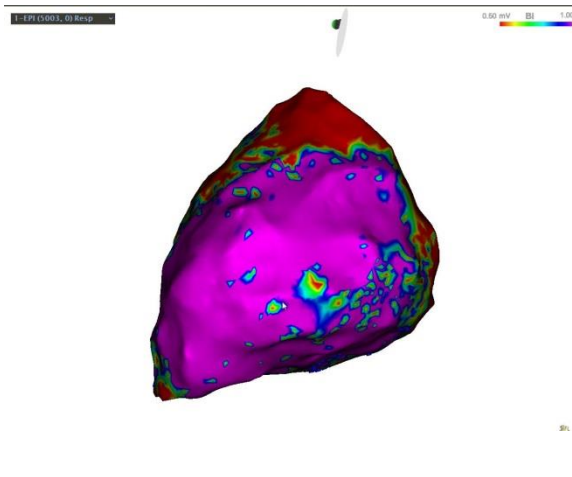




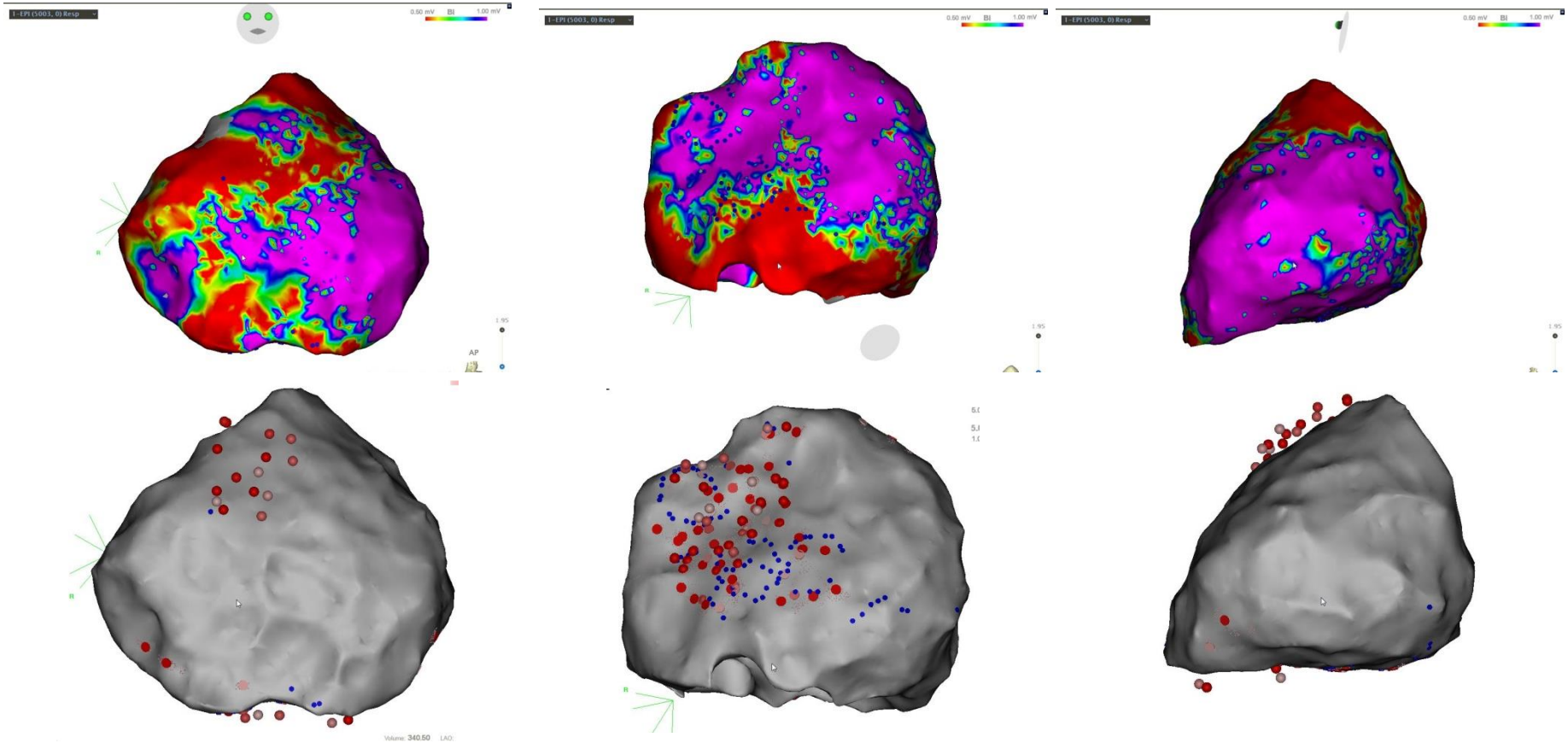
Epicardial Mapping





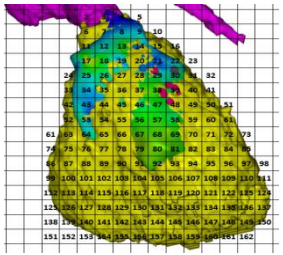


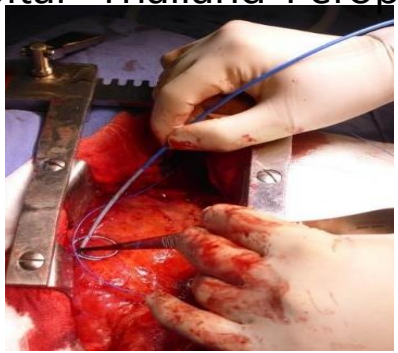
Epicardial Mapping and ablation sites

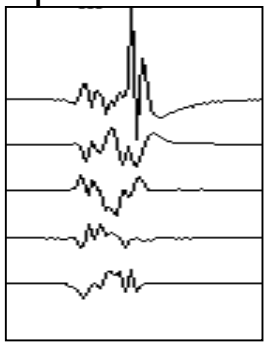


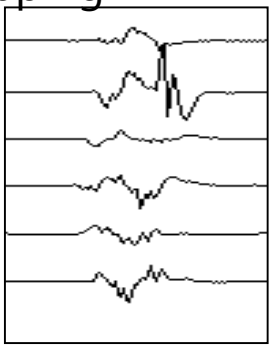
Brugada substrate

Bumrungrad Hospital- Thailand-Perop epicardial mapping

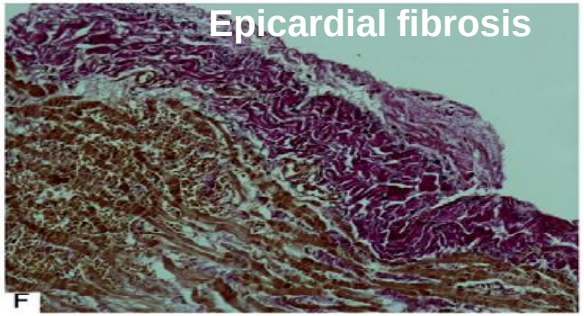






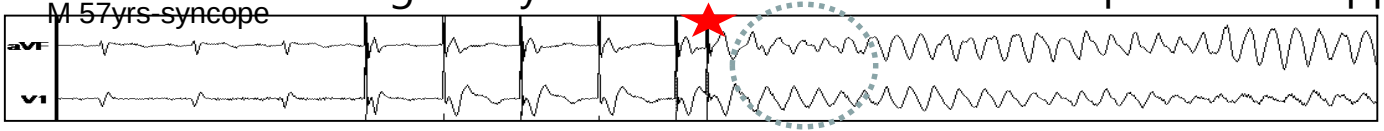


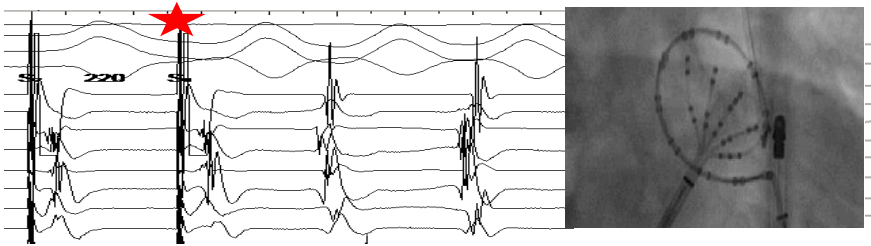
Targeted Biopsy



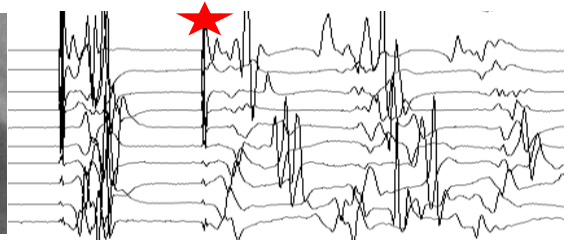
Brugada syndrome – Endocardial and epicardial mapping

M 57yrs-syncope





ENDOCARDIAL



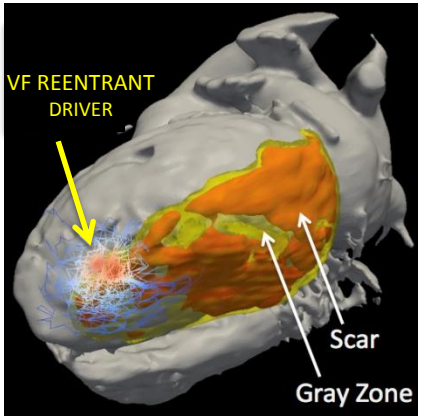
EPICARDIAL

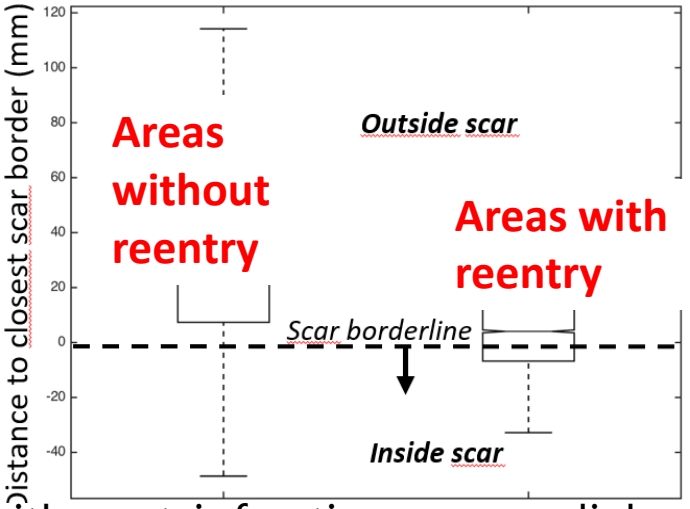
Brugada Sd is an affection dominantly affecting the RVOT epicardium

Brugada Sd is primarily an abnormality of myocardial depolarization, (with secondary repolarization changes)

Results 2- Main Drivers co-locate with markers of abnormal substrate

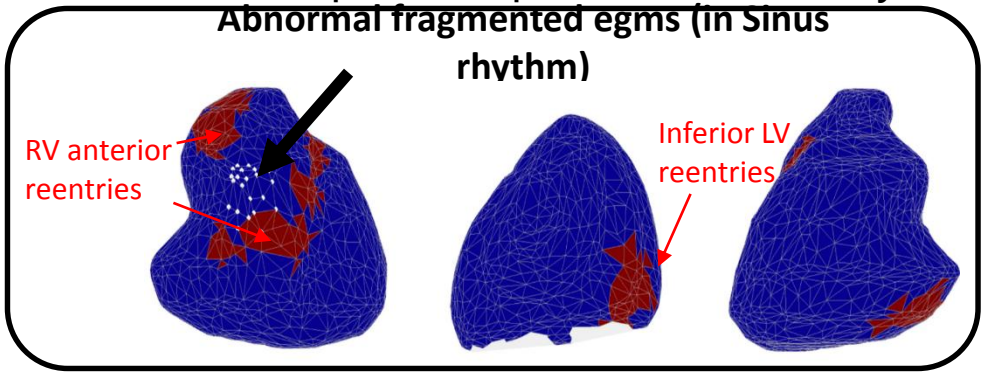
Myocardial scar on Imaging





n= 12 pts with post-infarction myocardial scar

Abnormal Egms on mapping in SR

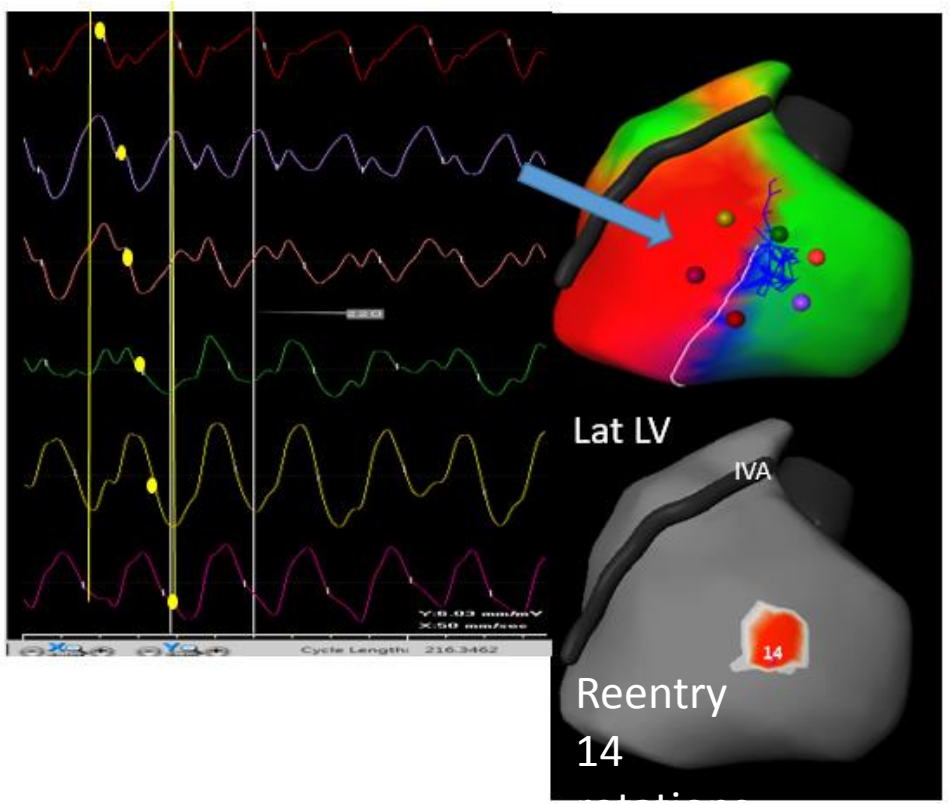


geodesic distances of VF driver areas to abnormal egm areas

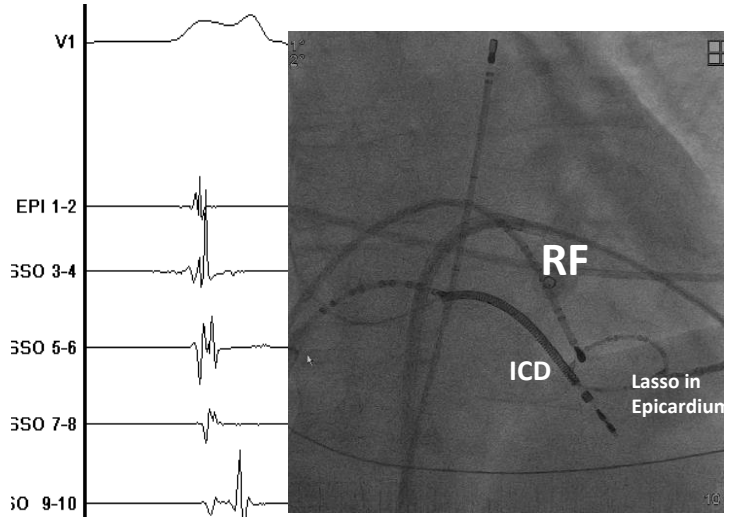
VF in Dilated Cardiomyopathy - M 52 yrs – 5 VF episodes - no Scar on MRI

The location of VF reentries points to areas of interest

Sequential activation of egms (in VF)



Local Epicardial Egms in Sinus Rhythm



Idiopathic Ventricular Fibrillation defined by ‘no phenotype’

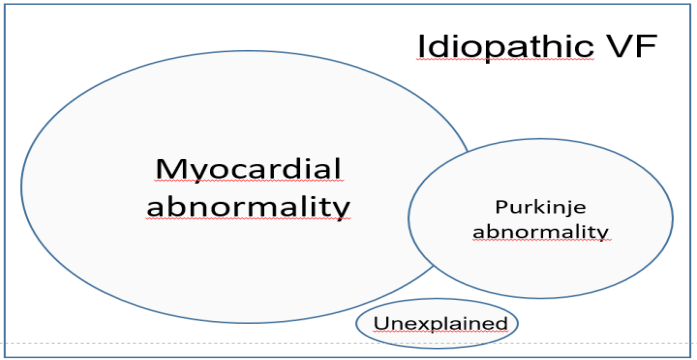
Inclusion of 51 pts (29±12 yrs, 13 women) with IVF **excluding Abnormal Repolarizations and SHD (**Coronary arteries- MRI- Ajmaline- Adrenaline- Isoprenaline)

Results – two major substrates can be found in IVF

Patients with altered depolarization in localized myocardial areas (34/51: 67%)

Patients with abnormal Purkinje activity : 22%

No explanation for sudden death : 11%

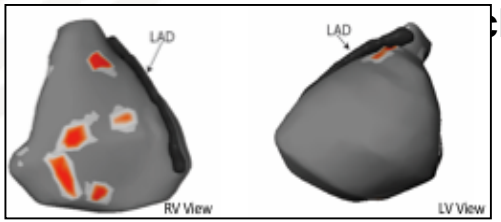


A spectrum of substrates underlie IVF in Man

Circulation EP, 2018
Localized Structural Alterations Underlying a Subset of Unexplained Sudden Cardiac Death

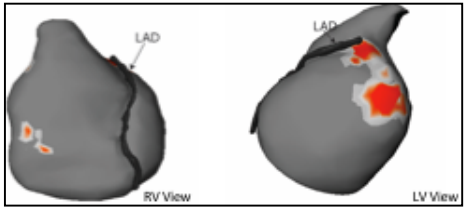
IVF – LOCATION OF VF DRIVERS

Dominant RV



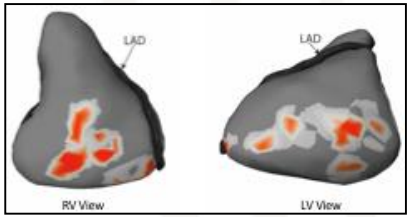
Patients confirmed having no Brugada pattern nor ARVD

Dominant LV



A dominant driver region is observed in ~ half of IVF

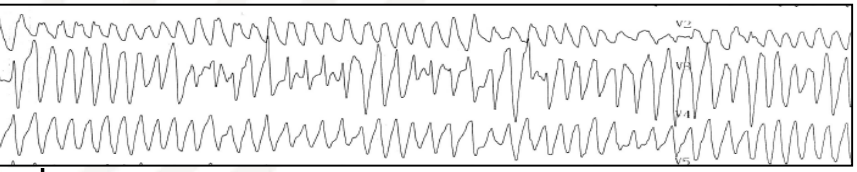
No

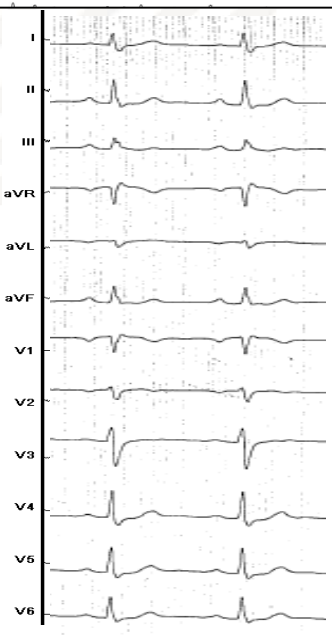


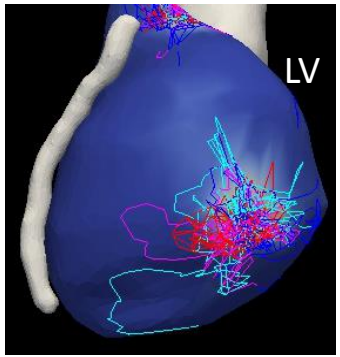
The location of main driver areas appears not dependent on induction site (similar maps with VF induced from LV in 12 pts)

Haissaguerre, Hocini et al Circulation EP, July 2018,
Localized Structural Alterations Underlying a Subset of Unexplained Sudden Cardiac Death

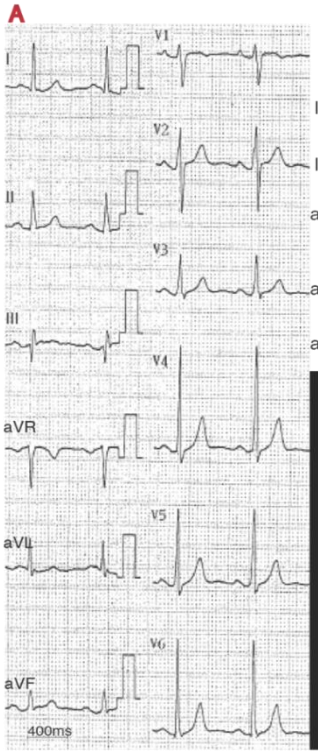
F 50 yrs Induced VF-
driven dominantly from LV

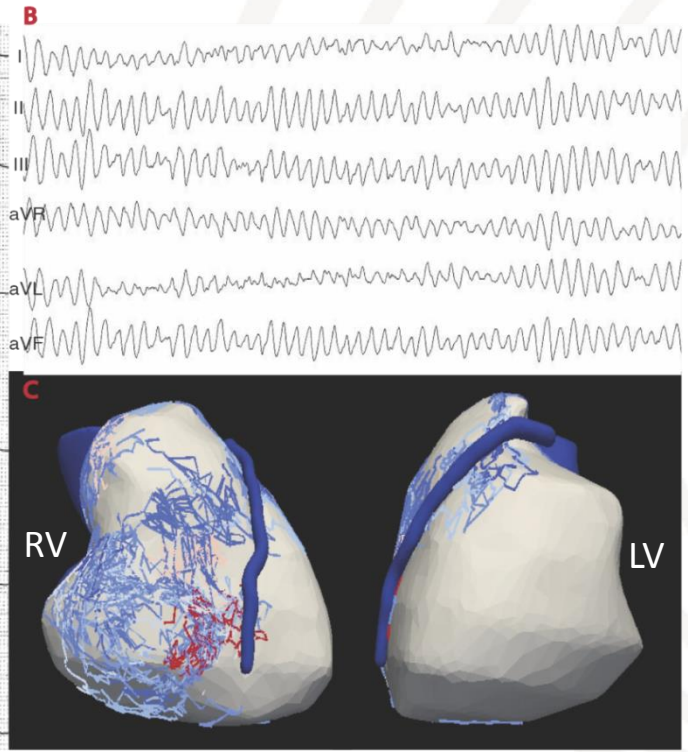




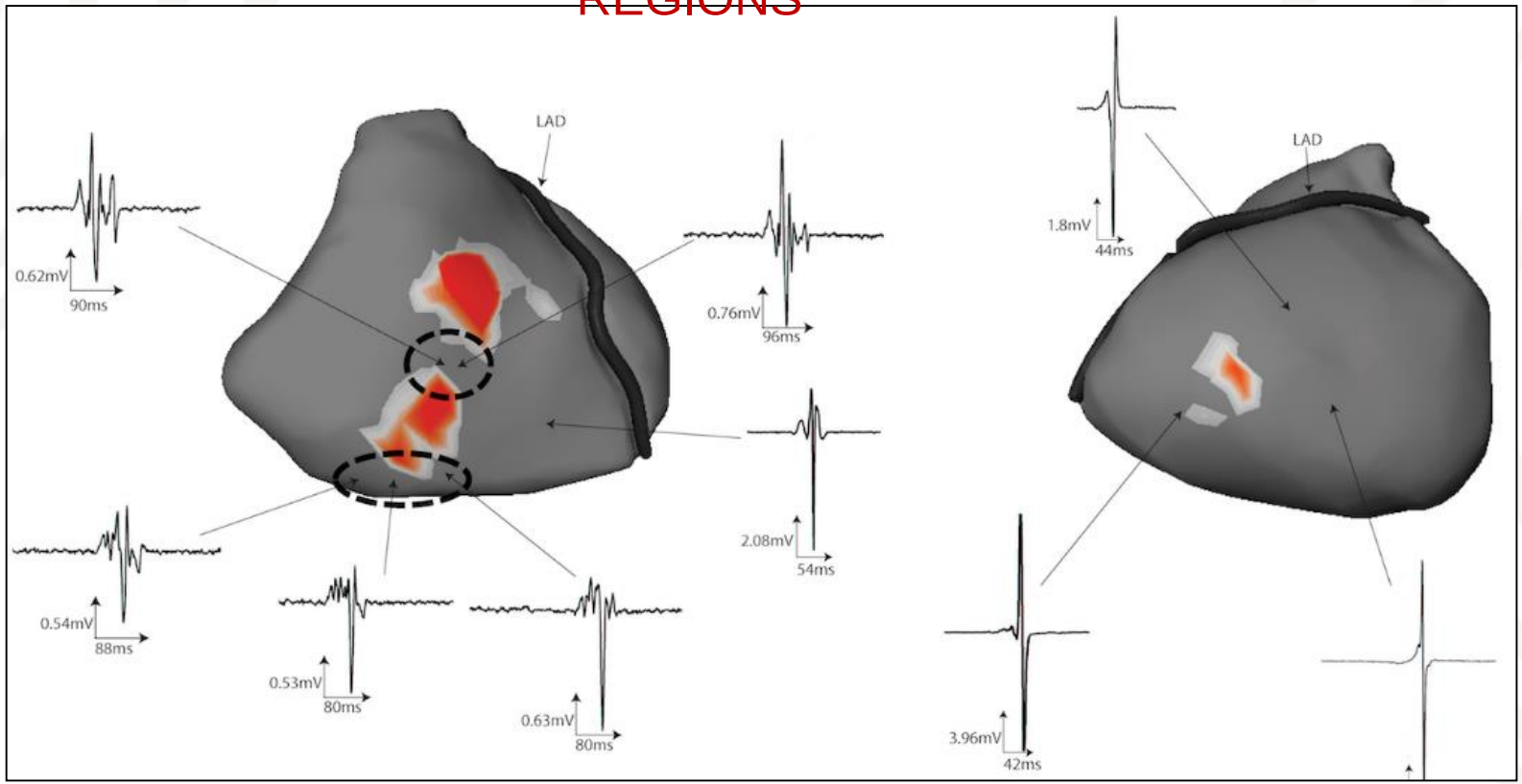


M 47yrs –Induced VF
Driven dominantly from RV





ABNORMAL ELECTROGRAMS CO-LOCATE WITH MAIN DRIVER REGIONS



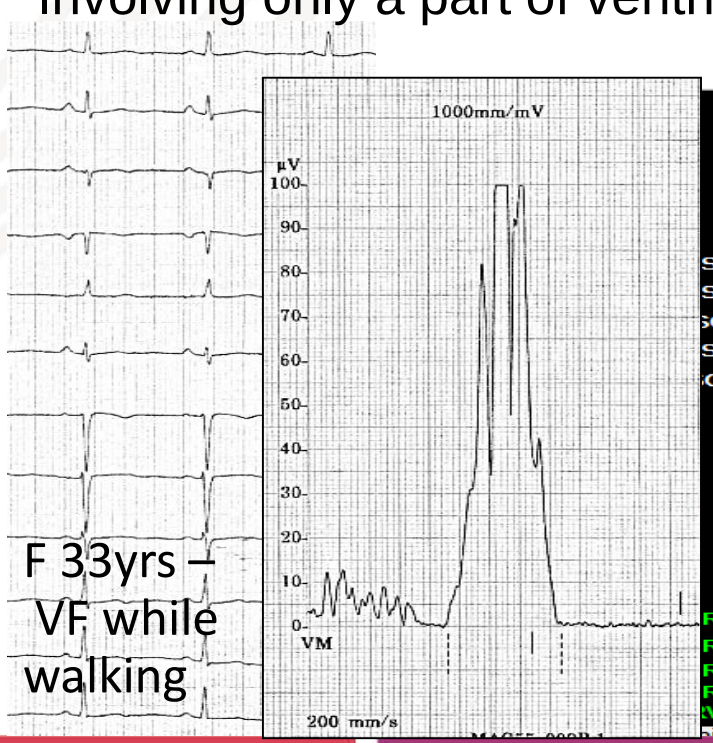
82% of areas displaying abnormal electrograms ,
were localized in contiguity with the highest density of VF driver activities

1- IVF Patients with Localized myocardial alteration: 67%

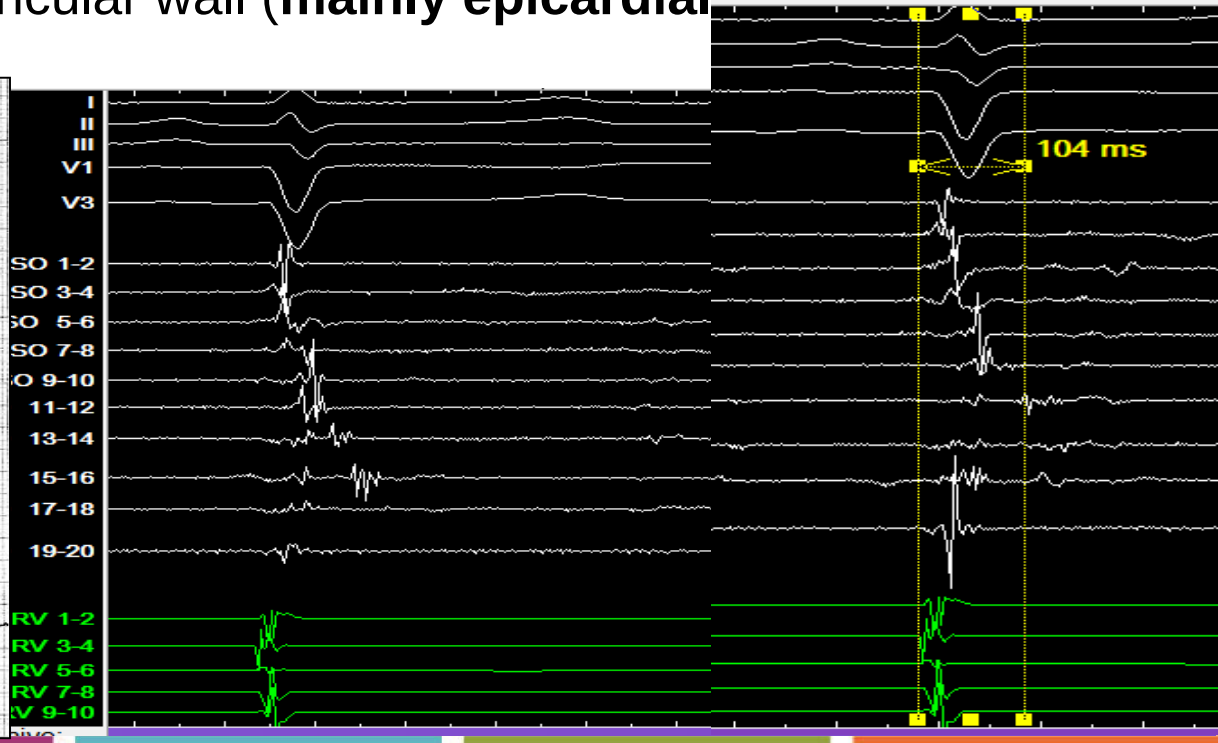
Areas of abnormal egms indicating localized myocardial alteration in 34/51 pts

‘Small’ size (area surface = 14 ± 6cm2 – 4.3% of total surface)

Involving only a part of ventricular wall (**mainly epicardial**)

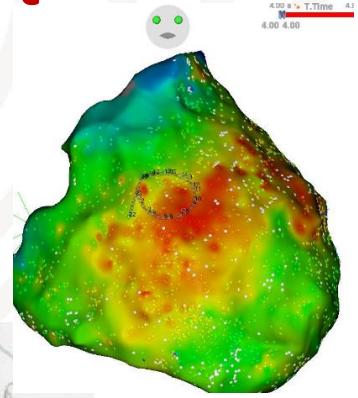


F 33yrs – VF while walking

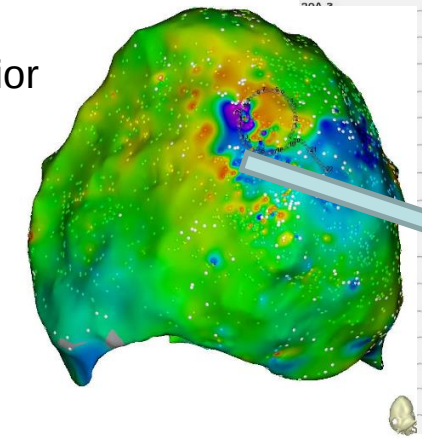


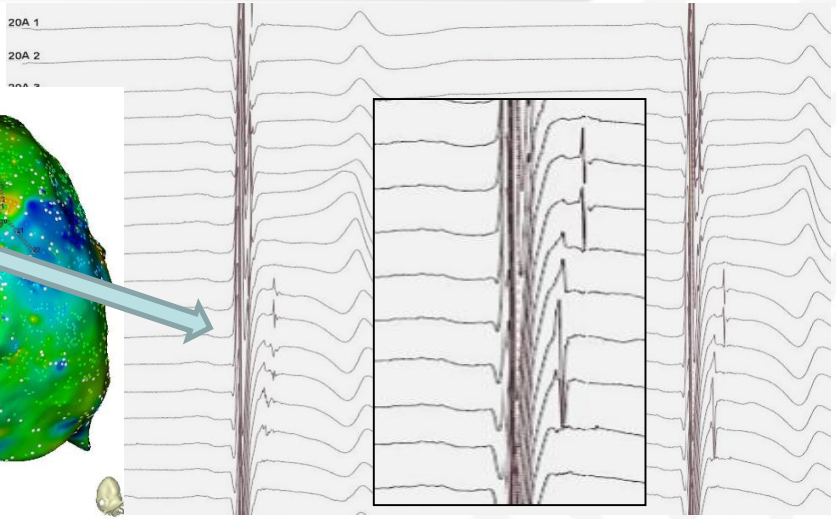
M 34 yrs – VF during sport

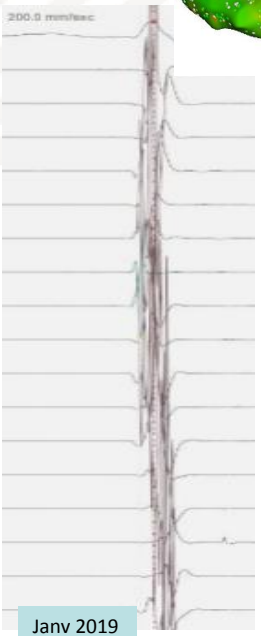
RV Anterior view



Inferior view

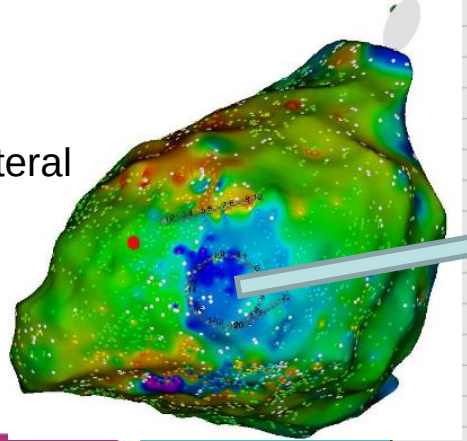


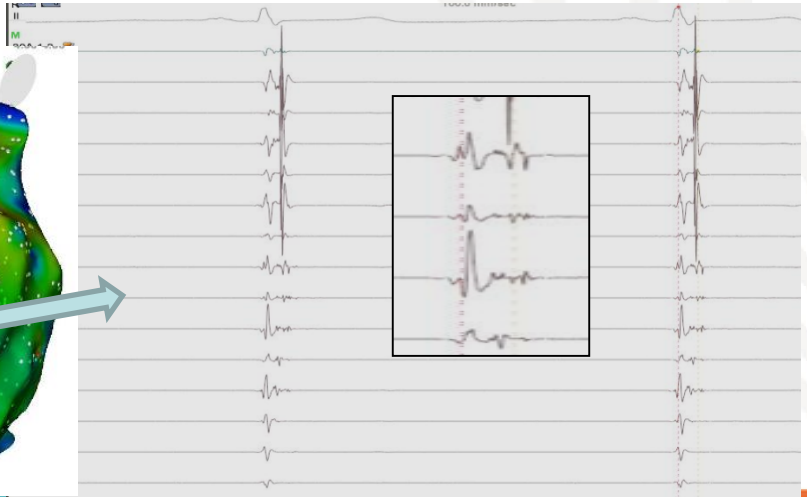




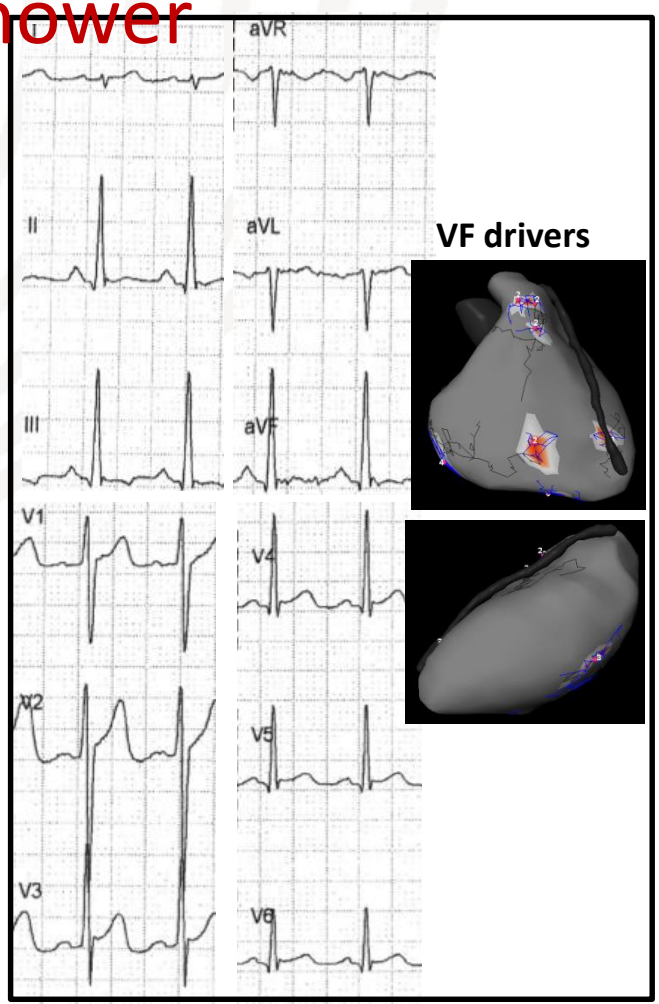
EPICARDIAL MAP 6083 PTS

LV lateral view



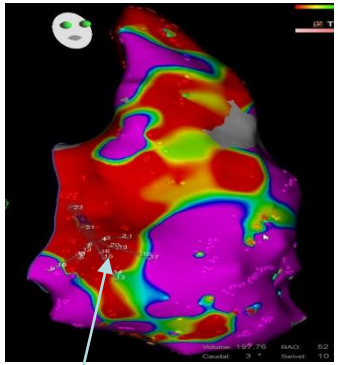


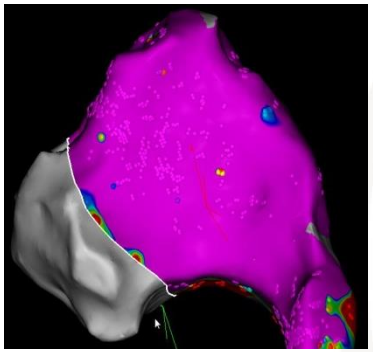
M 19yrs – VF when taking a shower

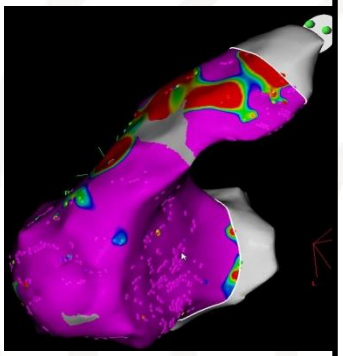


VF drivers

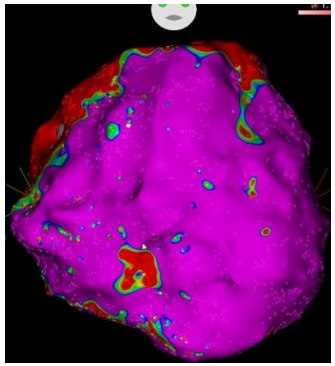
RV Endocardium – 2601 pts – Bipole 2mm-Volume 168ml - low voltage

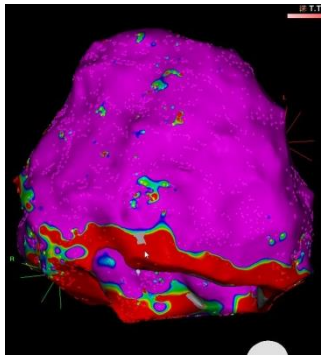


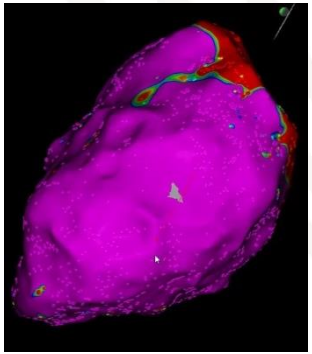




Epicardium – 6227 pts – Bipole 2mm



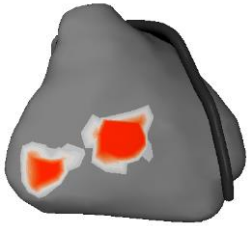




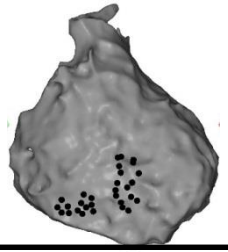
ABLATION TARGETING THE MYOCARDIAL SUBSTRATE

Idiopathic VF with localized myocardial abnormality

Location of VF reentries in the RV

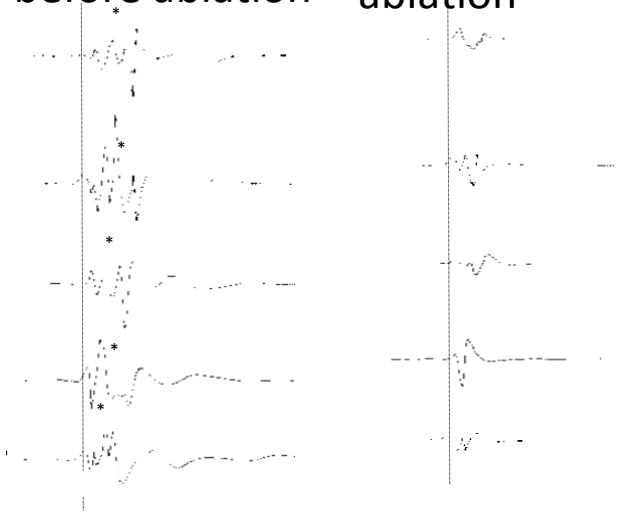


Sites of abnormal signals in Epicardial RV



Local signal before ablation

Signal after ablation



N° of VF : 7±3 episodes

MEDIAN 19min RF

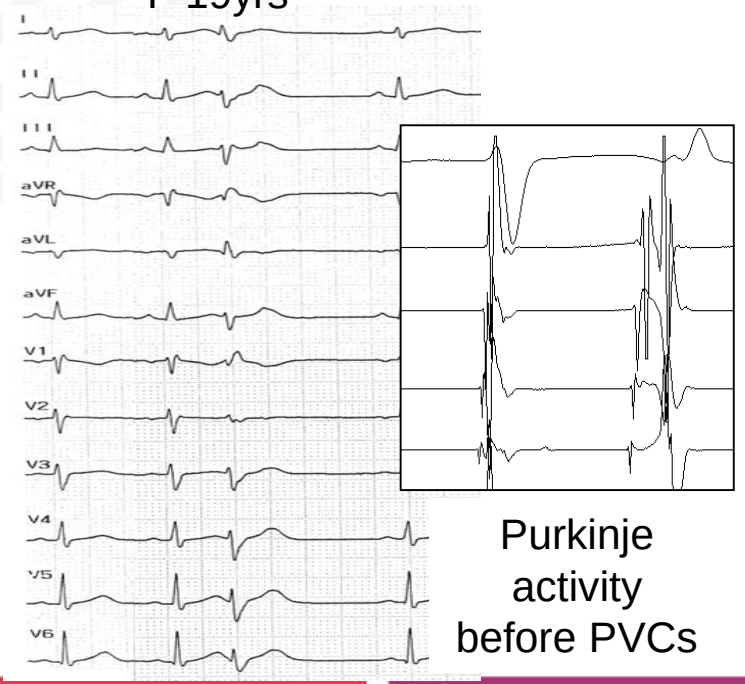
IQR 17- 22

RF Delivery on Substrate, min
18
27
24
21
9
17
20
9
22

2- IVF Patients with Purkinje abnormal activity: 22%
(and no area of myocardial alteration)

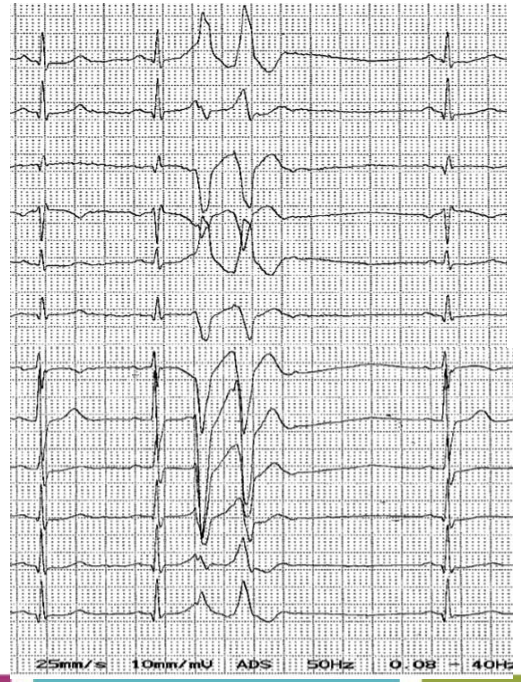
<u>With documented ectopy</u>

F 19yrs

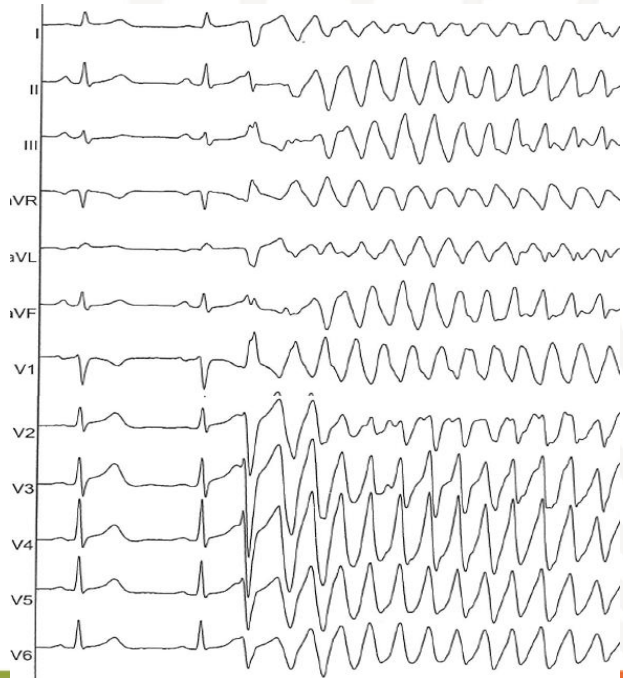


Purkinje activity before PVCs

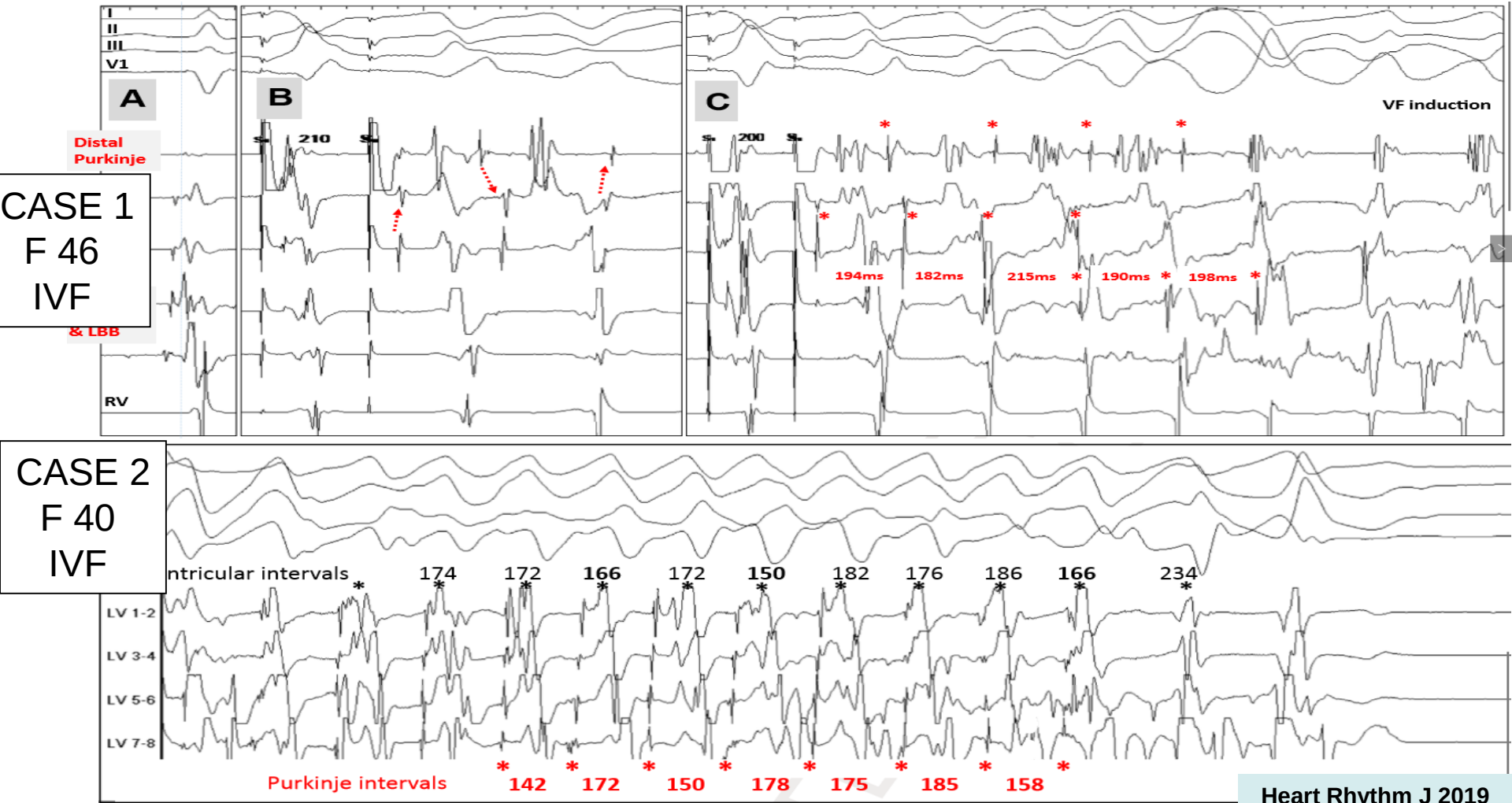
H 36 ans



F 47ans

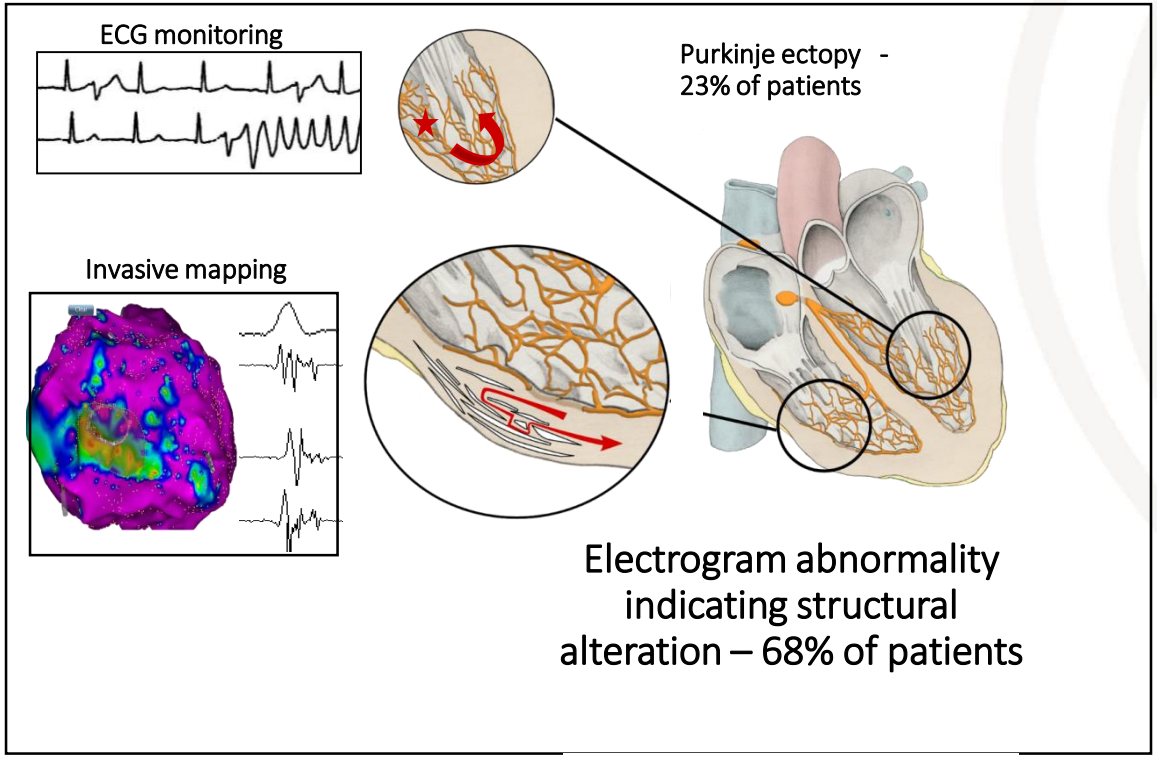


Idiopathic VF with Inducible Purkinje reentry

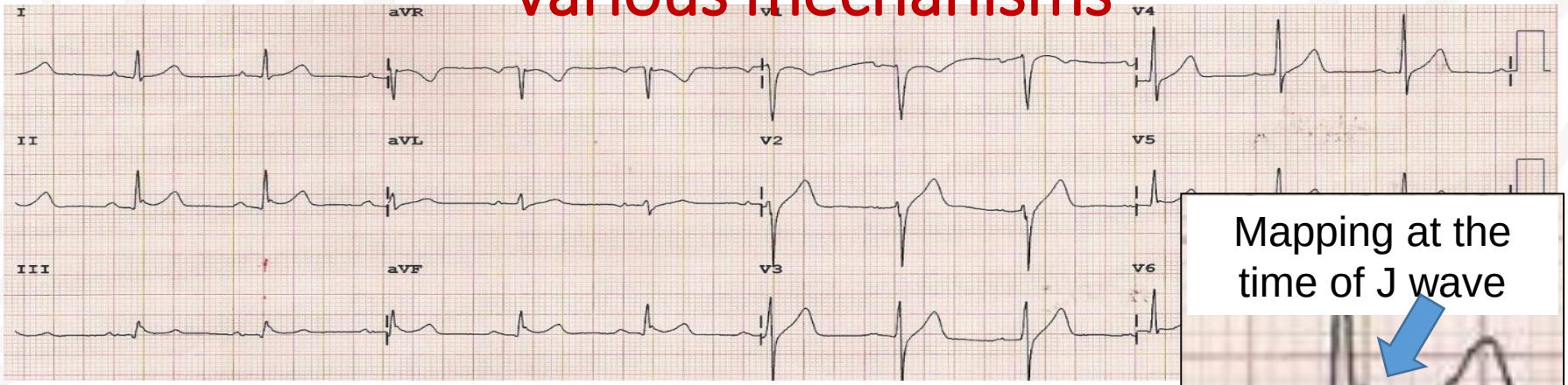


Heart Rhythm J 2019

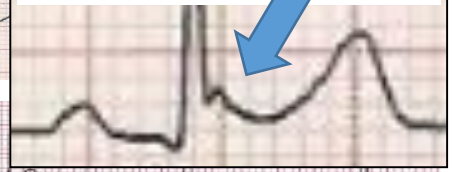
Comprehensive mapping shows that ~ 90% of Idiopathic VF /Unexplained SCD have phenotype abnormalities explaining VF

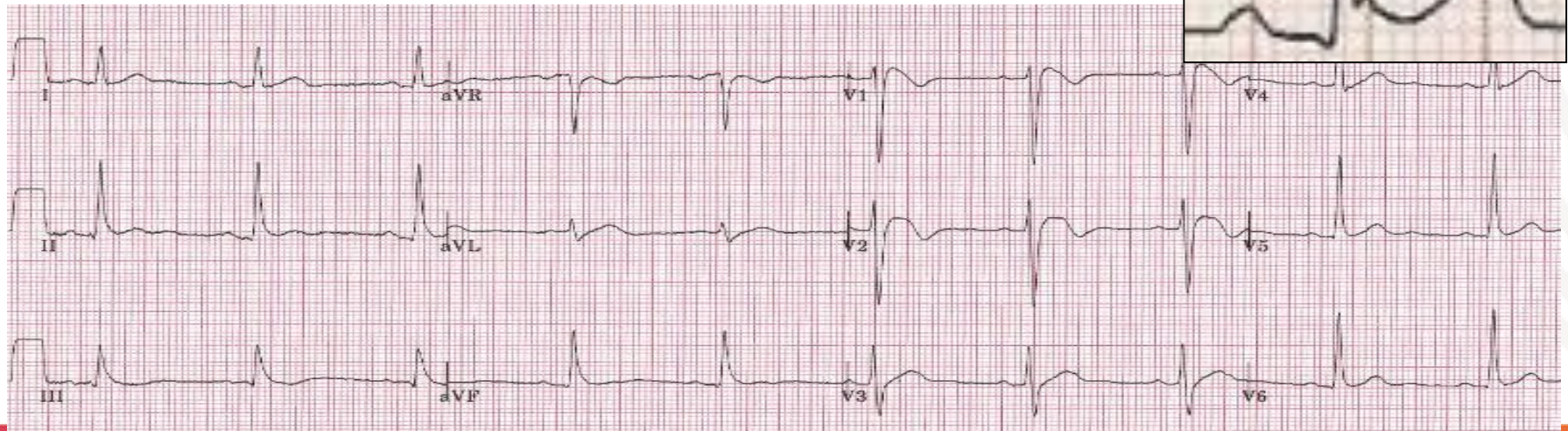


Inferolateral J wave –Early Repolarization: Various mechanisms



Mapping at the time of J wave





Differentiation of two distincts substrates underlying inferolateral J wave -

- J wave due to delayed depolarization
- Delayed activation with localized fragmented (> 3 spikes) egms of prolonged duration (> 70ms)
- Timing coincident with J wave on the ECG
- Accentuation with INa blocker in some patients

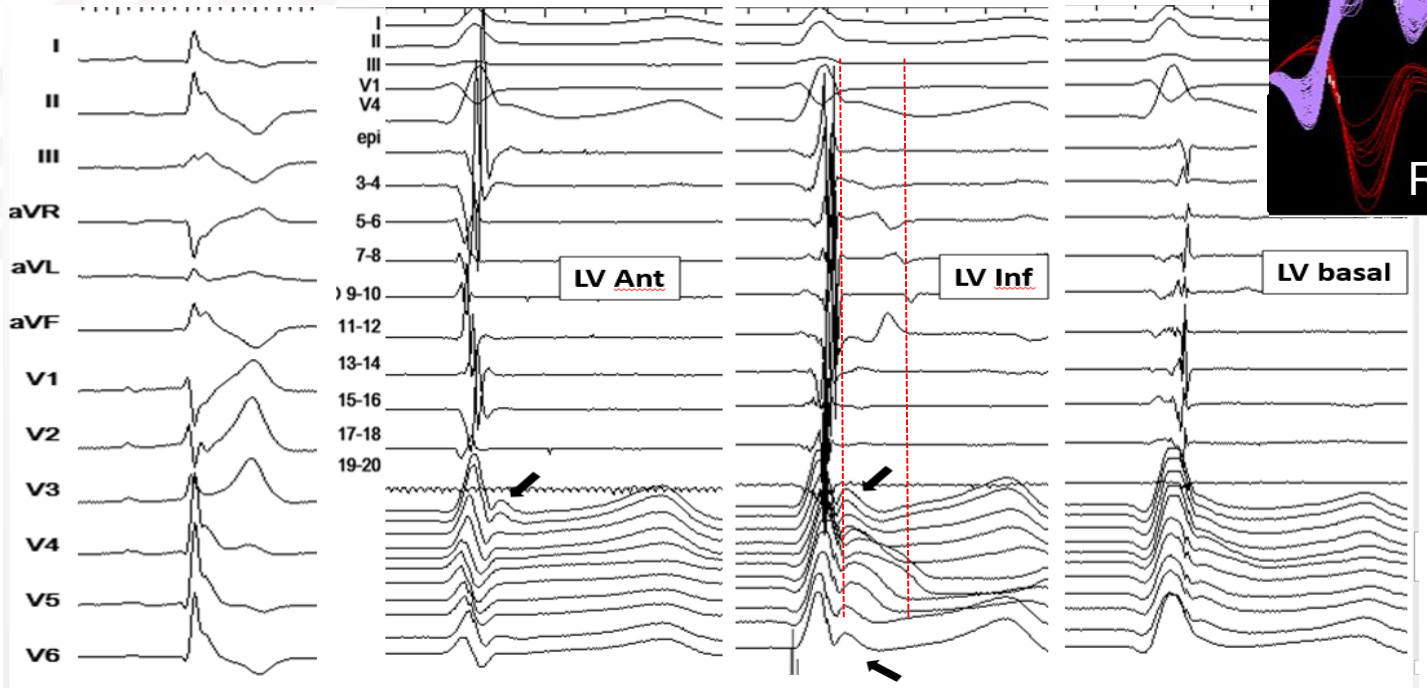
- J wave due to true early repolarization :
- Defined by the absence of delayed activation at the time of J wave
- no direct proof/argument of repolarization abnormality (short MAPs ~ in 3 pts)
- Attenuation with INa blocker

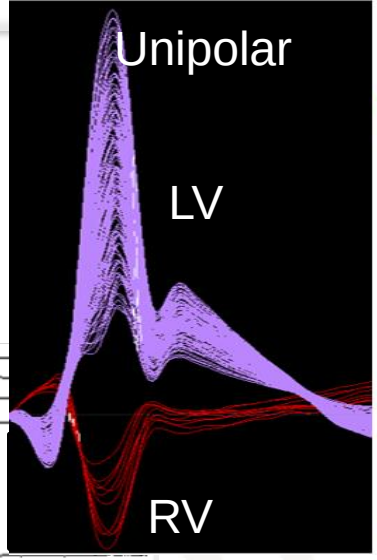
Comparison of Group 1 versus Group 2 with Respect to Clinical and Electrophysiologic Characteristics

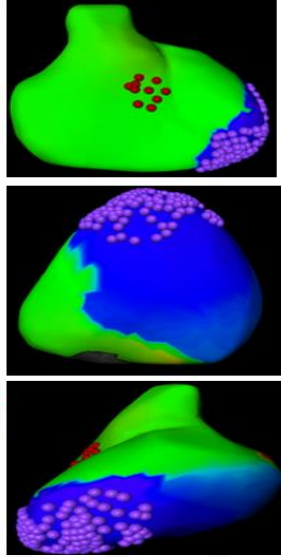
	Group 1: Late Depolarization. (n=40)	Group 2: J wave without late Depolarization. (n=11)	P value
Age	38.4 ± 13	29.3 ± 16	0.051
Female Gender	0 (0%)	4/11 (36%)	0.001
Presence of BrS ECG	33 (82.5%)	0 (0%)	<0.0001
Locations of J-Wave Elevation	26 inferior only (65%) 11 inferolateral (28%) 3 lateral only (7%)	2 inferior only (18%) 9 inferolateral (82%)	0.009
Family History	14 (35%)	4 (36%)	1.000
SCN5A Positive	4 of 21 (19%)	0 of 11 (0%)	0.272
VF Storms	21 (54%)	5 (41%)	0.679
VF Cycle Length (msec)	205 ± 20	147 ± 19	<0.0001
Location of Drivers	Right ventricle (100%) Inferior RV Epi (88%)	Inferior ventricular wall (100%): both interventricular groove and LV inferior wall	-----
#Treated with Quinidine/ # Response to Quinidine	14/0 (0%)	8/4 (50%)	<0.0001
# Treated with Ablation	36 (95%)	6 (55%)	0.015
Ablation Location	Predominantly epicardium of the RV	Left Purkinje system for VF triggers	
Ablation areas	20 ± 6 cm^2	4 ± 0.7 cm^2	<0.0001
Number of Ablation (Mean ± SD)	1.4 ± 0.65 (range 1-3; median 1)	1.2 ± 0.41 (range 1-2; median 1)	0.289
Complications of Ablation	1 hemopericardium	None	------

M 23 yrs - J wave caused by early repolarization

12 lead ECG

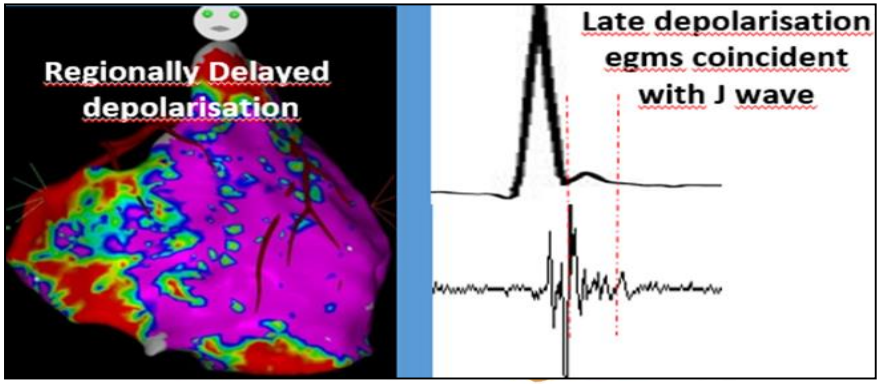






Extent of Epicardial Early repolarisation potentials

J-wave phenotype can be also caused by delayed activation - that can occur at any inferior region



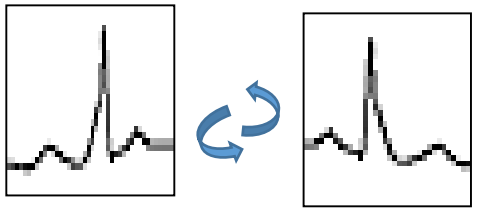
AREAS of TERMINAL ACTIVATION in SR

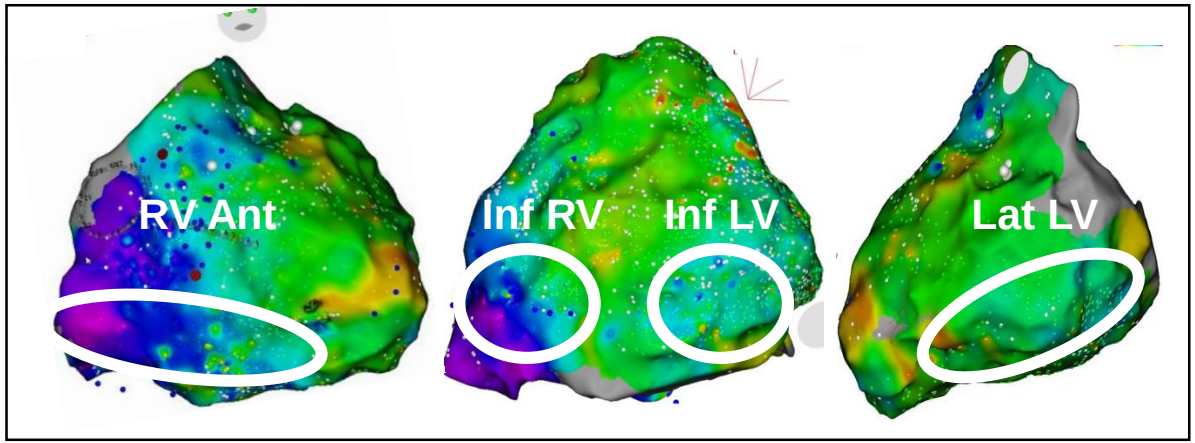
GREAT MAJORITY in EPICARDIAL AREAS

RV Anterior (lower half) or RV inferior

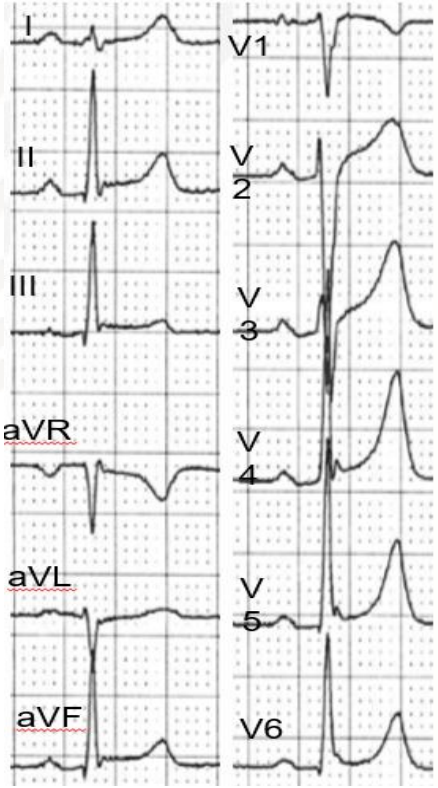
LV Inferior or inferolateral

Like a 'reversed' delta wave

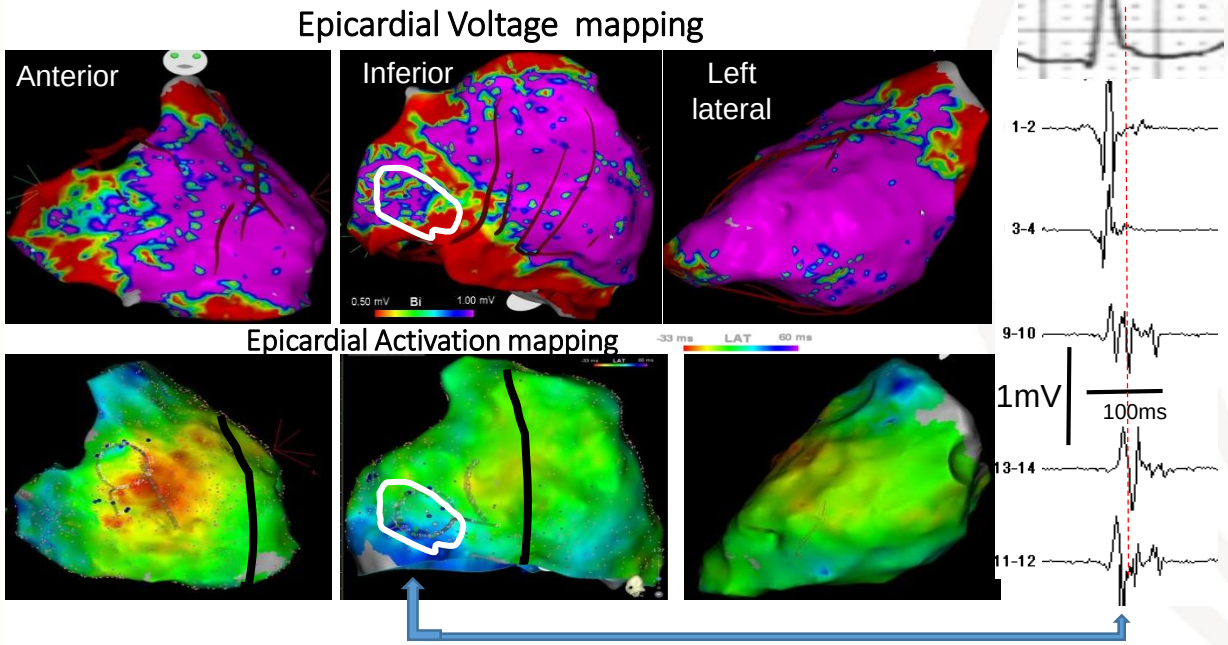




M 19yrs- J wave caused by abnormal depolarisation

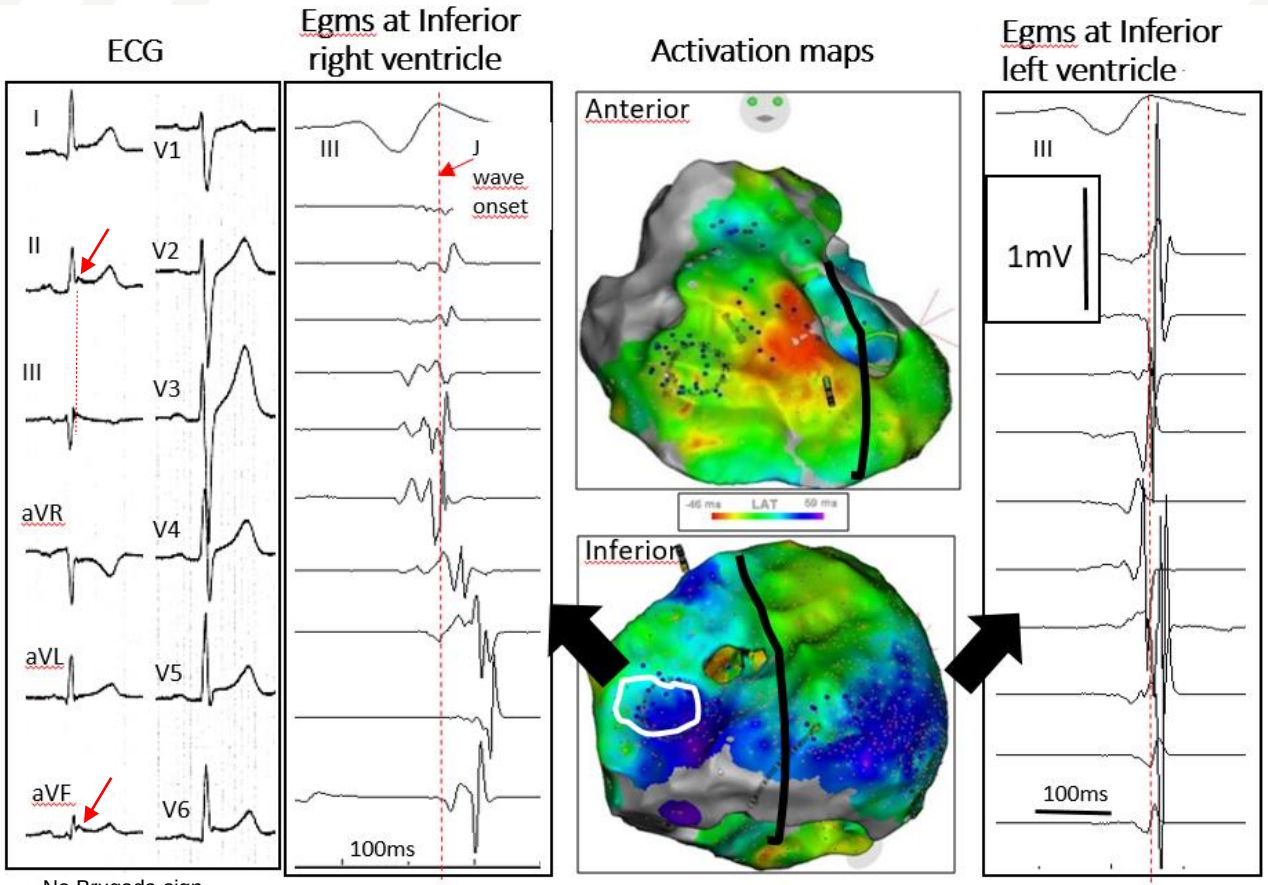


no Brugada pattern inducible by Ajmaline testing



Prolonged depolarisation is here the primary abnormality – which can be associated with secondary repolarization disturbances (ST+)

M 31yr- J-wave caused by abnormal delayed depolarisation (inf RV)



No Brugada sign induced on Ajmaline

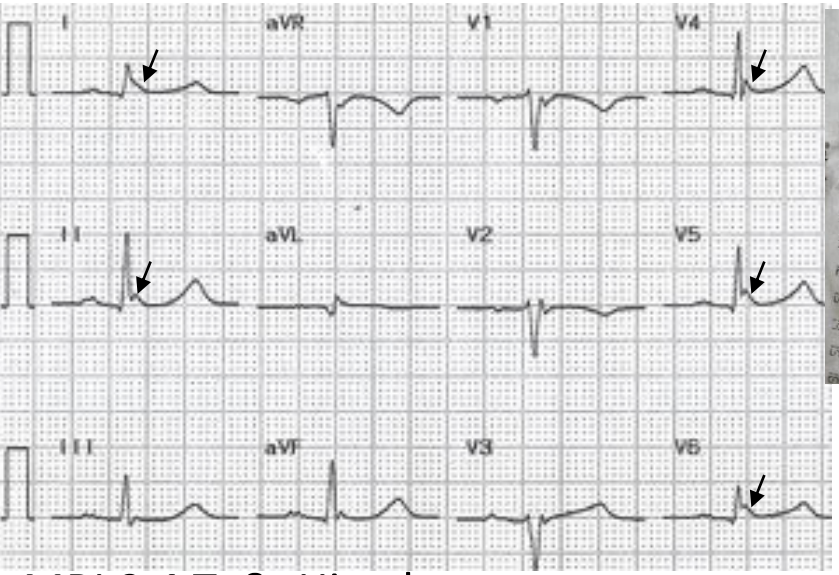
Bipolar Filters: 30-250 Hz

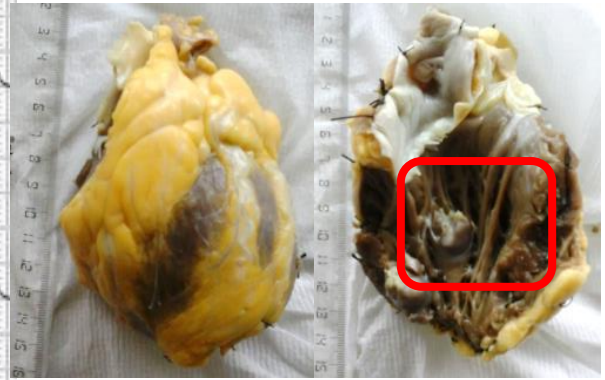
Terminology :

Early ‘repolarization’ is here inadequate

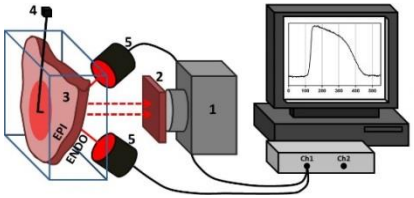
J wave – investigations of 4 *ex-vivo* human hearts confirms various mechanisms under the same phenotype

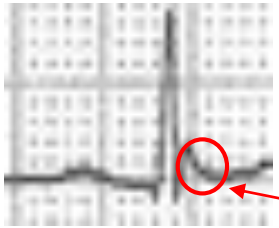
Ex Vivo Human heart programme F 64 yrs: Delayed Activation of basal LV



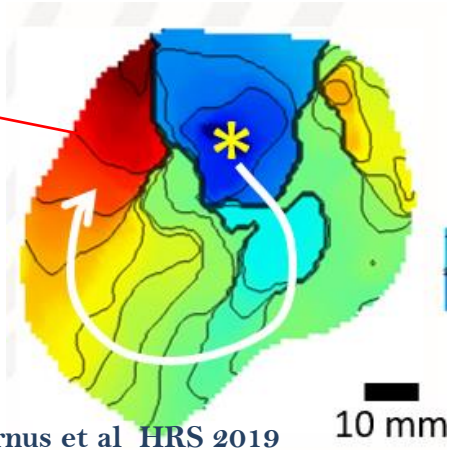


LV Optical mapping



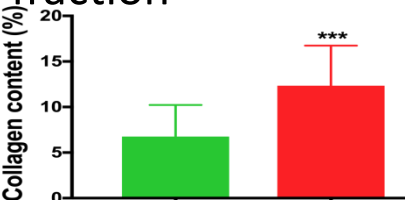


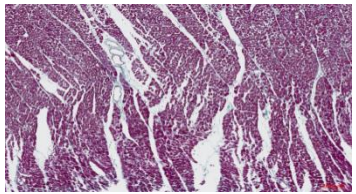
LV activation time



MRI 9.4 T & Histology :

increased extracellular collagen fraction





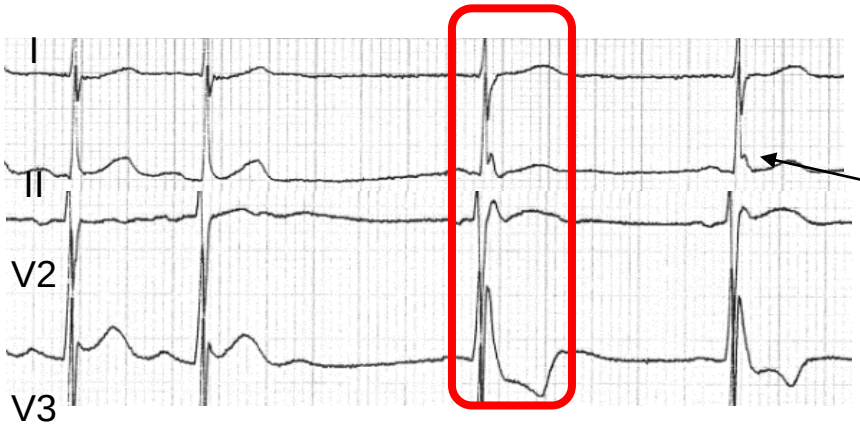
Prolonged conduction in the LV with the latest region coinciding in time with the J wave

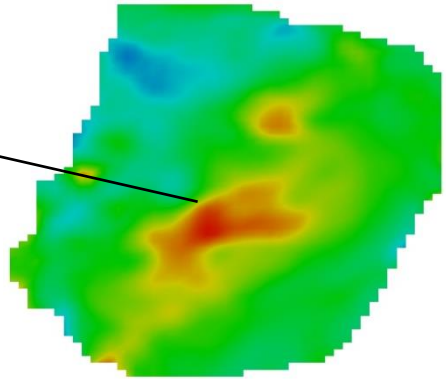
A wide spectrum of substrates underlie J-Wave Syndromes O Bernus et al HRS 2019

J wave – investigations of 4 *ex-vivo* human hearts confirms various mechanisms under the same phenotype

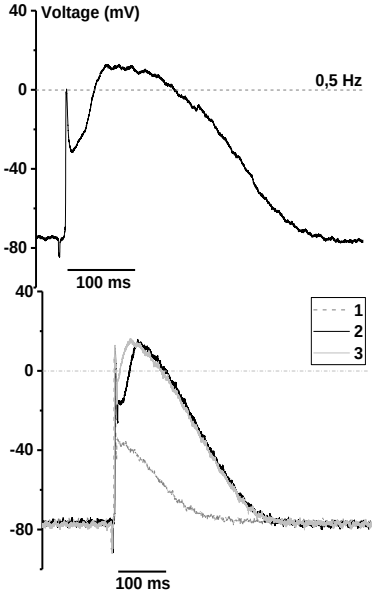
No depolarization abnormality – Early repolarization LV endocardial

2 siblings 15 & 10 yrs Died after VF storm or heart transplantation





Early repolarization

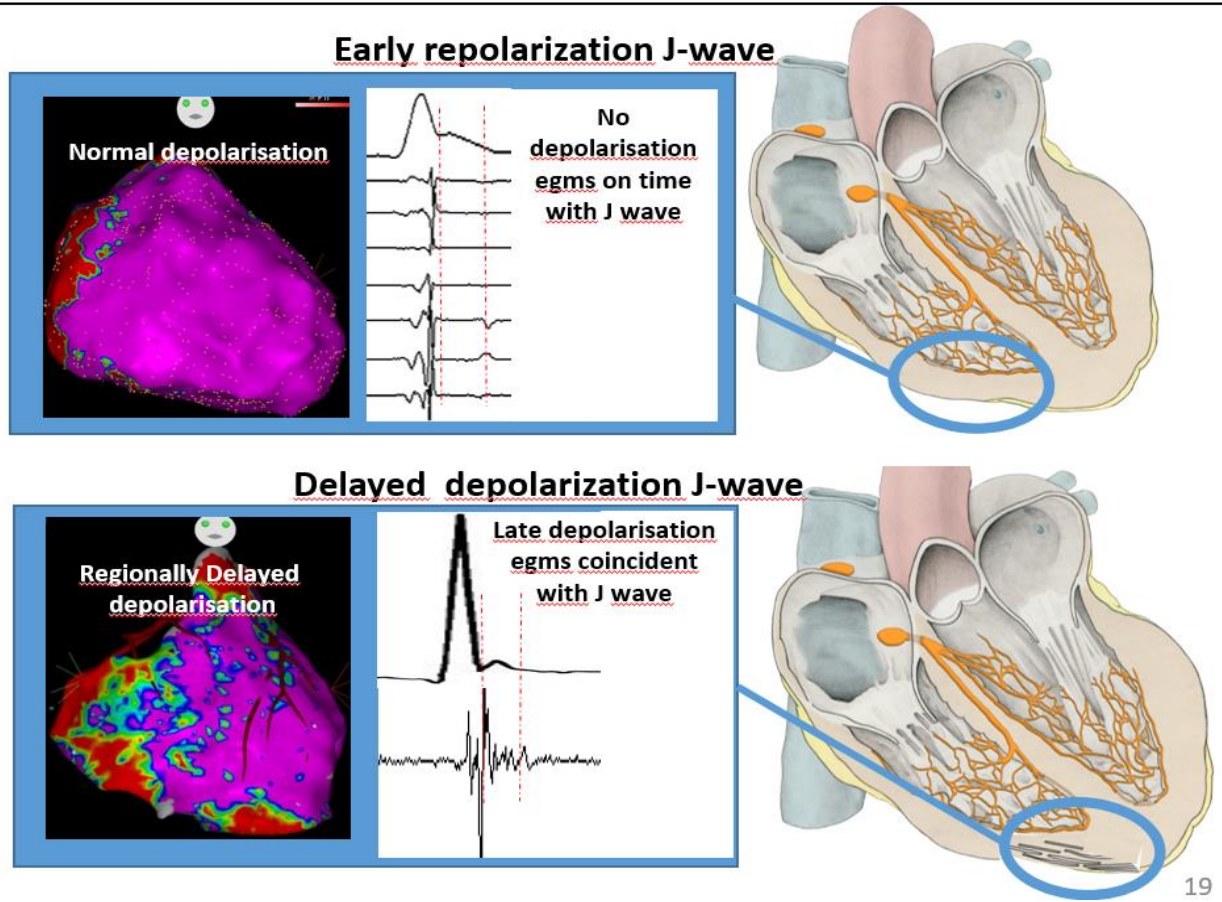


Microelectrode Endo-LV

Optical action potentials or microelectrodes shows repolarization disparities and pronounced upstroke notch after pause in specific regions.

Bernus et al HRS 2019

A spectrum of Substrates underlie J-wave syndromes in Man



REPOLARIZATION GRADIENT

EPICARDIUM (Yan-Antzelevitch)

ENDOCARDIUM (Bernus)

DELAYED ACTIVATION

RV or LV EPICARDIUM

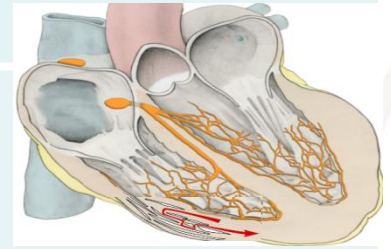
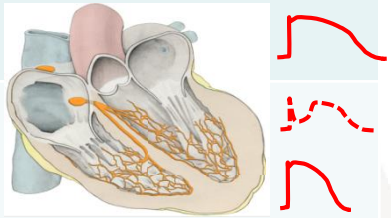
ENDO-EPICARDIUM

Role of PURKINJE topology
(Boineau-Coronel)

IMPLICATIONS FOR GENETIC INTERPRETATION, THERAPY, AND RISK STRATIFICATION

Heart Rhythm J 2018 - Circulation ,in press

SIMPLIFIED CLASSIFICATION OF VF WITHOUT APPARENT SHD

Main arrhythmogenic mechanism	Sudden Cardiac Death with no apparent SHD	Schematic
Conduction Abnormality	**Brugada** **Inferolateral J wave** **IVF with localized conduction abnormality**	
Repolarization Abnormality	**Long QT** **Early Repolarization J wave** **Short QT**	
Abnormal Excitation	**IVF from Purkinje-myocardial sources** **Catecholaminergic Polymorphic VT** **Accidental : Commotio cordis, electrocution,drugs ...**