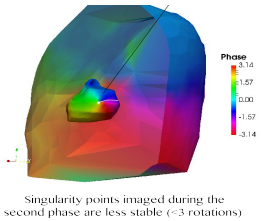
Roma – *PLACE meeting- 1st October 2022*

Arrhythmias originating from Purkinje fibers
Focus on their role in VF/ Sudden Cardiac Death

Pr Michel Haissaguerre

LIRYC : Cardiac Electrophysiology and Modeling **Bordeaux**

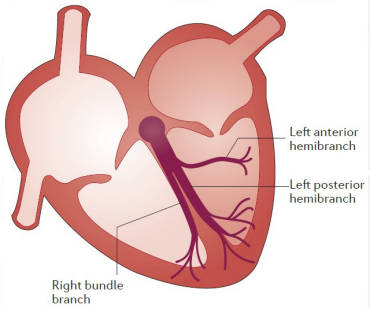


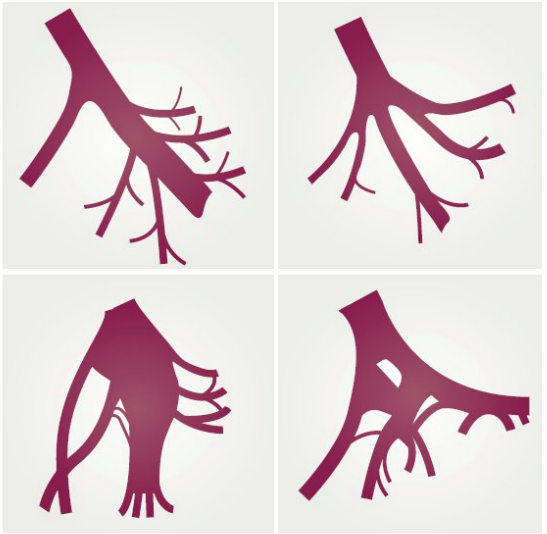
Animal & Human Heart | Structural imaging | Functional mapping | Modeling

université de BORDEAUX

Disclosures : Grants from Biosense Webster-– Medtronic

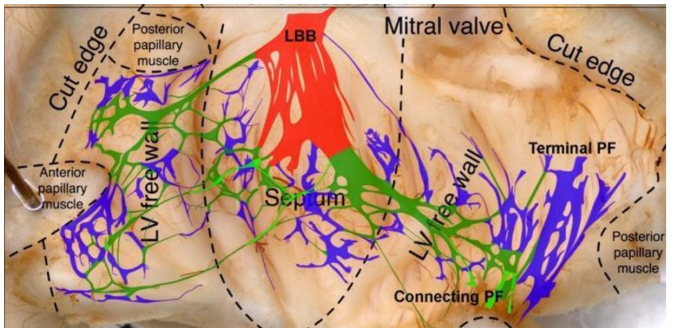
Purkinje fibers and network : Unique cells - Complex architecture- Pleiomorphic presentations



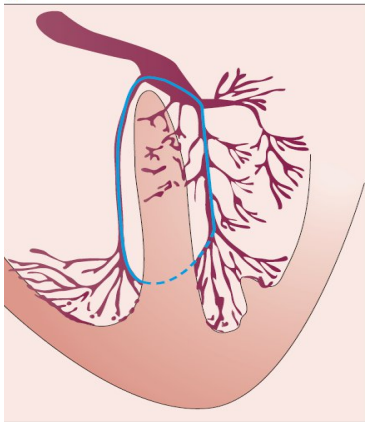


Variability of Purkinje branching in Man

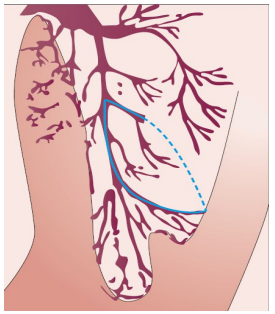
Unique properties within the Heart, in Excitability and in Conduction



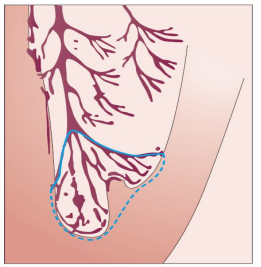
Bundle branch Reentry



Fascicular VT (verapamil-sensitive)



Distal Fascicle-network



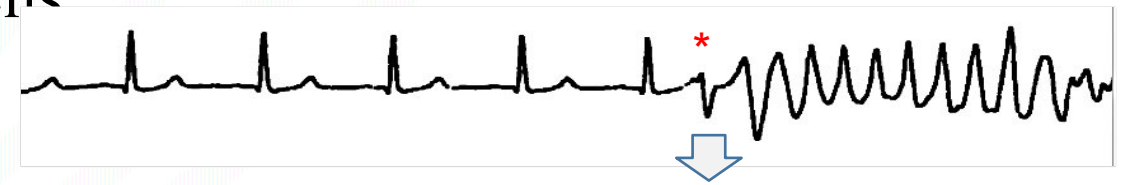
Abnormal Purkinje excitability

Purkinje cells as a Trigger

Specific phenotypes as CPVT, LQT, MEPPC …
will not be addressed

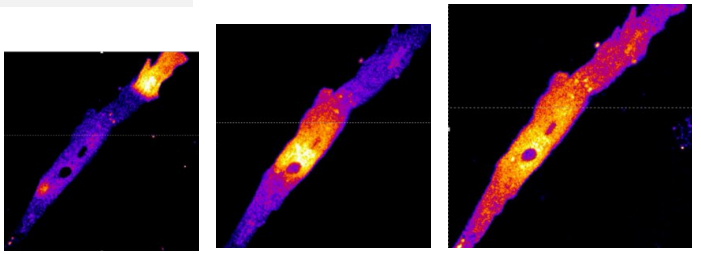
Mapping the initiation of VF

Idiopathic VF : Triggers from the distal Purkinje cells



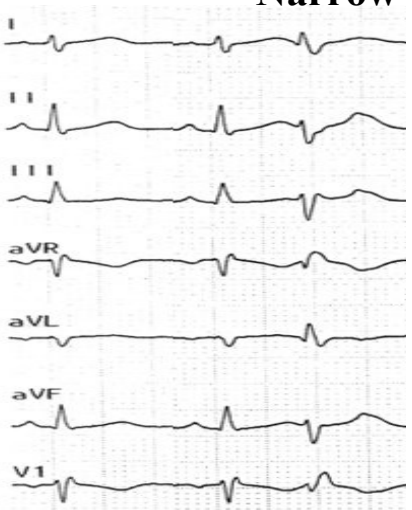
This concerns **7-15% of Idiopathic VF**
(Short Coupled Torsades - Coumel Ph)

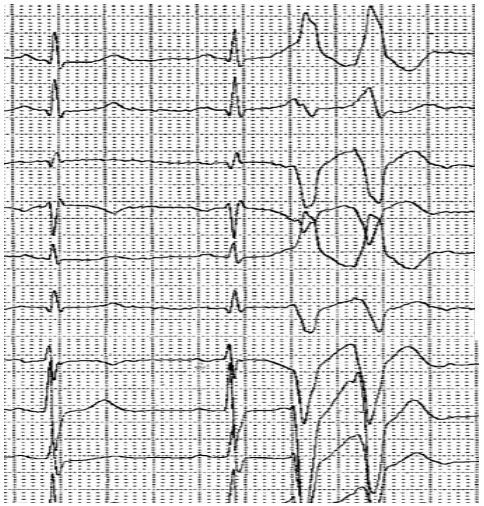
Calcium wave inside the cell

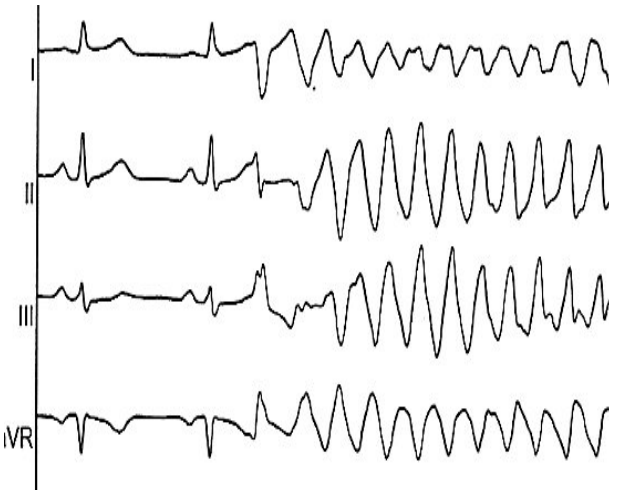


Distinct & complex Ca handling (3 Ca -release channels in the membrane of endoplasmic reticulum)

Narrow QRS (LV Purkinje) and **Short Coupling (R-on-T)**

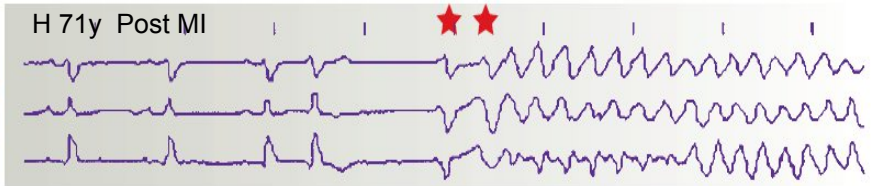






Mapping the initiation of VF

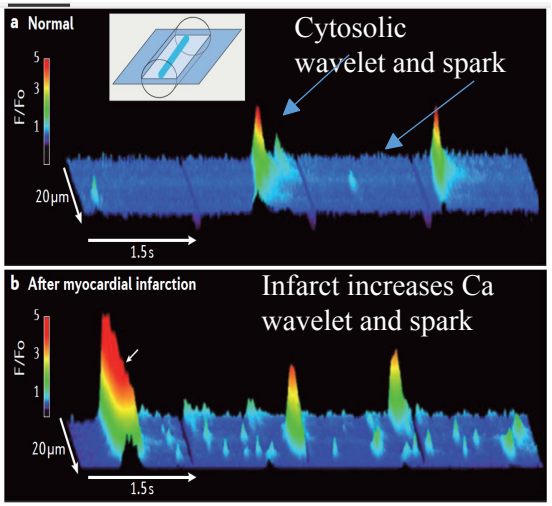
Purkinje provide main triggers in VF storms with Structural heart disease



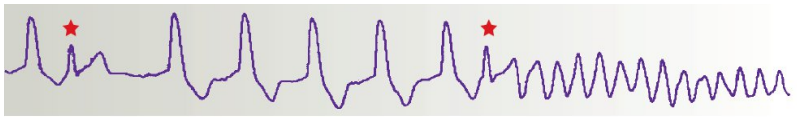
Typical VF storm post MI
On ECMO

Incidence : 90% VF in Isch HD
In other SHD, few reports suggest a significant role

Structural heart disease	77/85
Ischaemic heart disease	90%
Dilated cardiomyopathy	8/15 53%
Hypertrophic cardiomyopathy	5/5 100%
Valvular heart disease	4/4 100%
Myocarditis	2/2
Amyloidosis	2/2



Purkinje implication **may be underestimated** as the VF onset is rarely documented



F42y DCM with LBBB) : unique VF on monitoring shows narrow QRS* indicative of Purkinje origin

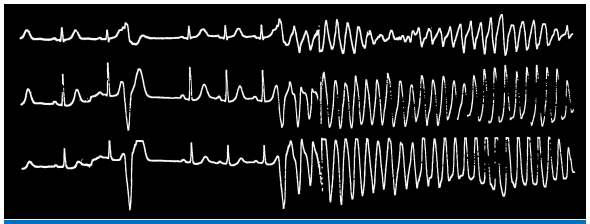
Ventricular arrhythmias and the His–Purkinje system

Michel Haissaguerre[1], Edward Vigmond[2], Bruno Stuyvers[2], Meleze Hocini[1]

Trigger ablation is very effective
(except multifocal PVCs)

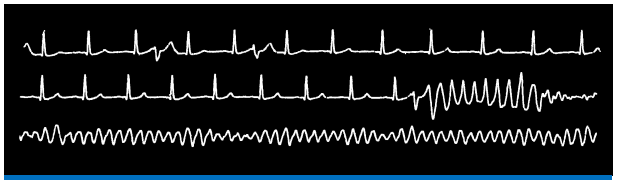
Long-Term Follow-Up of Idiopathic Ventricular Fibrillation Ablation

A Multicenter Study



Man 45 yr >300 ICD shocks
Ablation May 2000: 16 min RF delivery
No VF/ICD intervention in 22 years

End point : elimination of PVCs and local Purkinje potentials

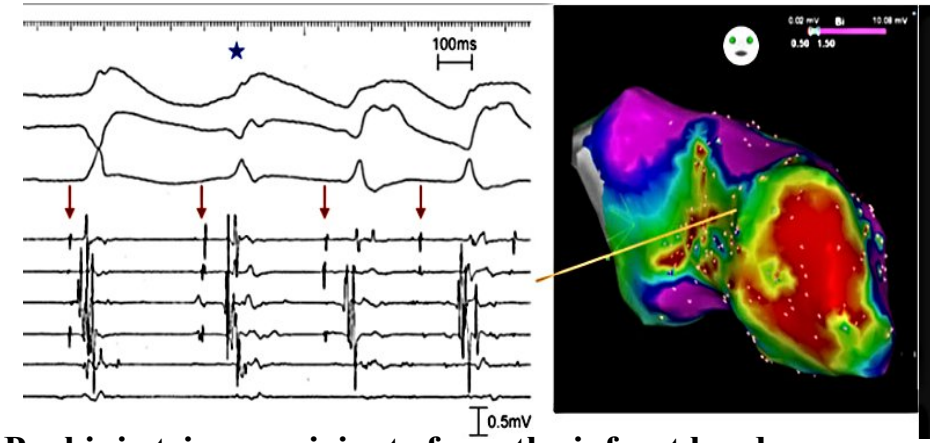


F 37 yr Single ectopy site
Ablation May 2000: 3 min RF delivery
No VF in 22 years

Median Follow-up 5 Years : 31 of 38 (**86%**) **had no recurrence** on ICD monitoring

Catheter Ablation of Refractory Ventricular Fibrillation Storm After Myocardial Infarction

A Multicenter Study



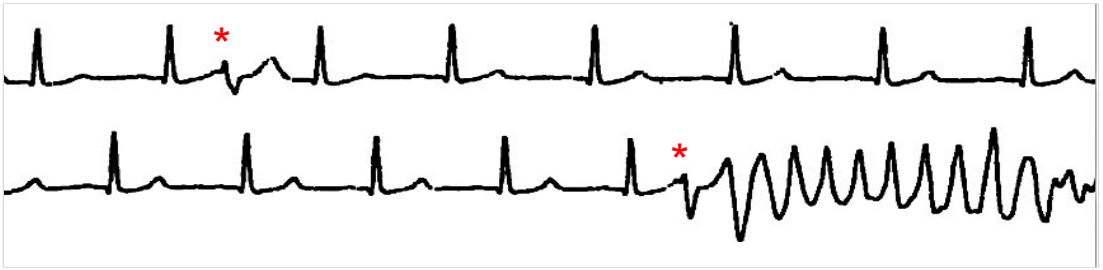
Purkinje trigger originate from the infarct border zone
(0.5-1.5mV LV) **in 80% and from dense scar (<0.5mV) in 14%**

110 patients, 65years , LVEF 31%

VF storm **successfully treated with ablation in 84%** (92 pts). Only 1 recurrence.

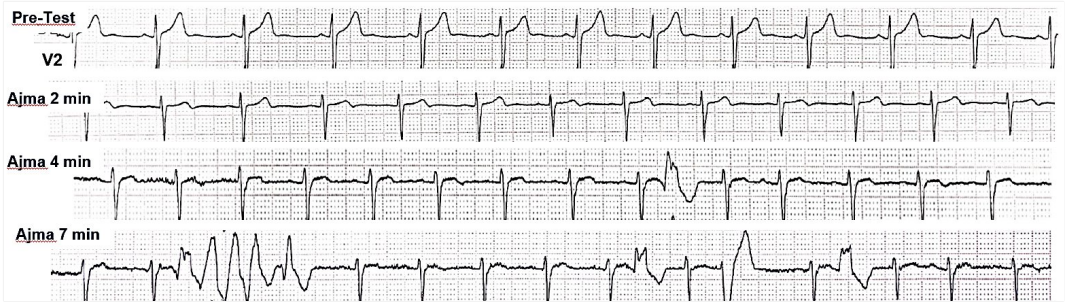
27% in-hospital deaths , notably LVEF < 30%

The Problem : Short Coupled PVCs and VF risk (in normal hearts) are **unpredictable**



Inconsistent induction with Isuprel, Pacing maneuvers , Calcium injection etc is a serious limitation to risk prediction of this malignant arrhythmia

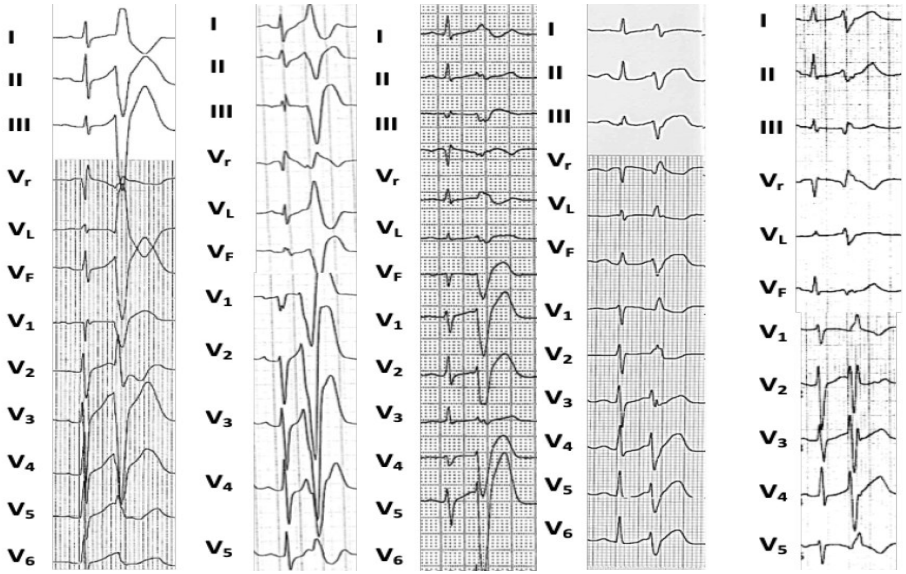
Ajmaline test 1mk/kg with the purpose of unmasking Brugada ECG pattern



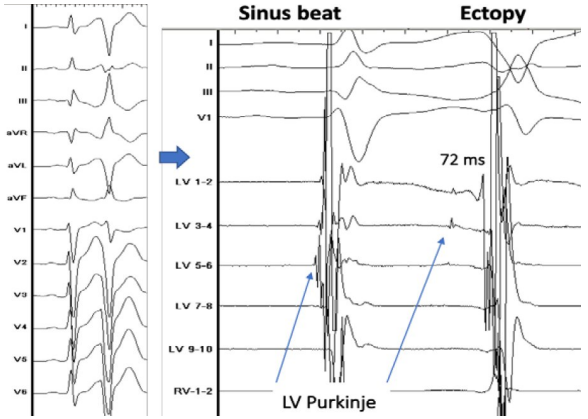
Drug provocation of malignant Purkinje ectopy

16 pts, 8 women, 36yrs : referred for VF or Syncope
(2 pts had VF during propofol anesthesia)

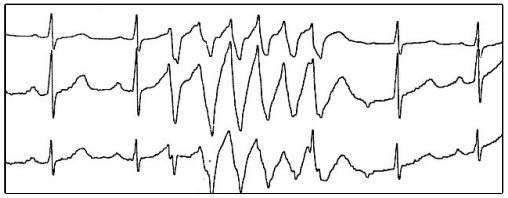
Without any Brugada pattern, **ScPVCs were induced on Ajmaline or Flecainide, (at 234sec = 4^{e} min)**

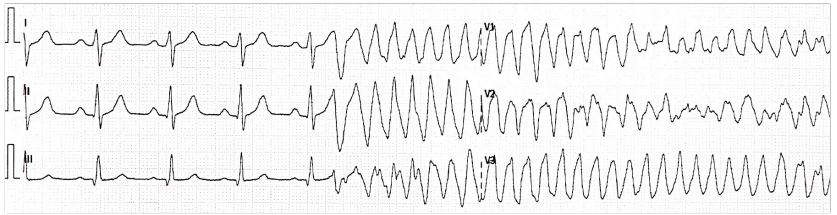


Mapping in 9 : Purkinje origin



Polymorphic VT or VF in 9 (56%)

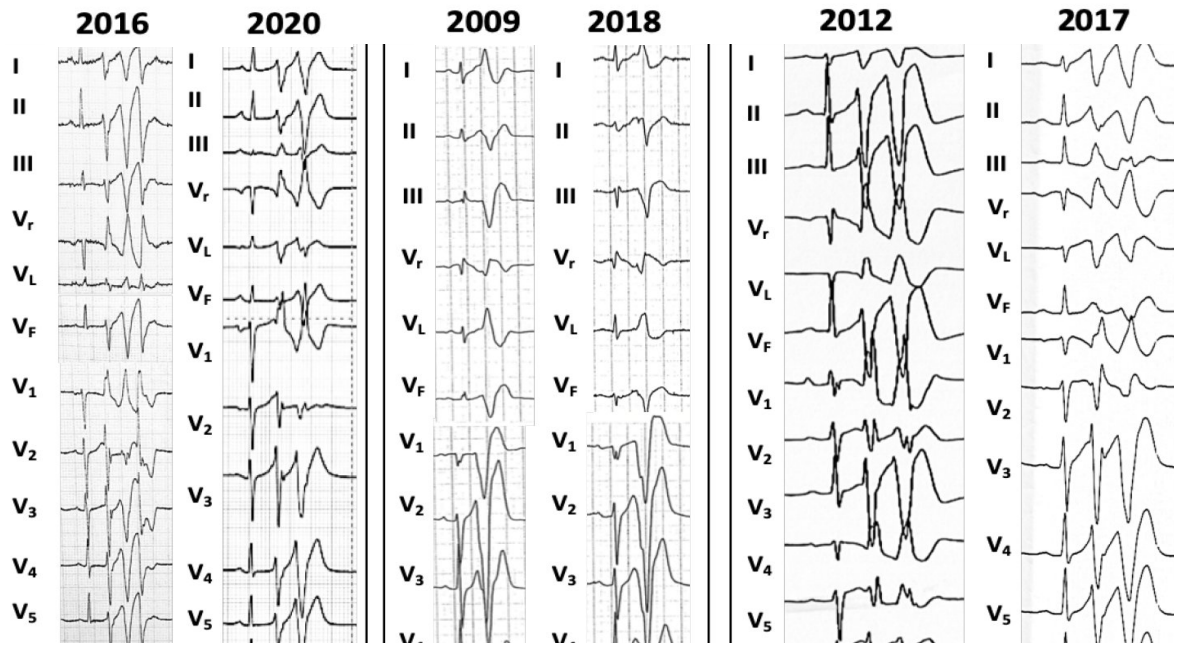




Escande et al HRJ 2022

Reproductibility of a 2nd NaBl test (45mths later) in 7 of 7 patients : indicate a distinct mechanism/subset

No mutation SCN5A, RyR2 and others (one DPP6)



Na blocker test was the only way to reveal malignant PVCs in 6 patients with unexplained VF or syncope

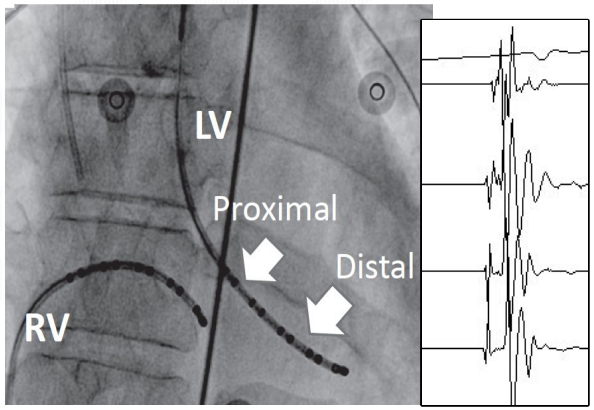
Last 6 months: > 10 cases observed

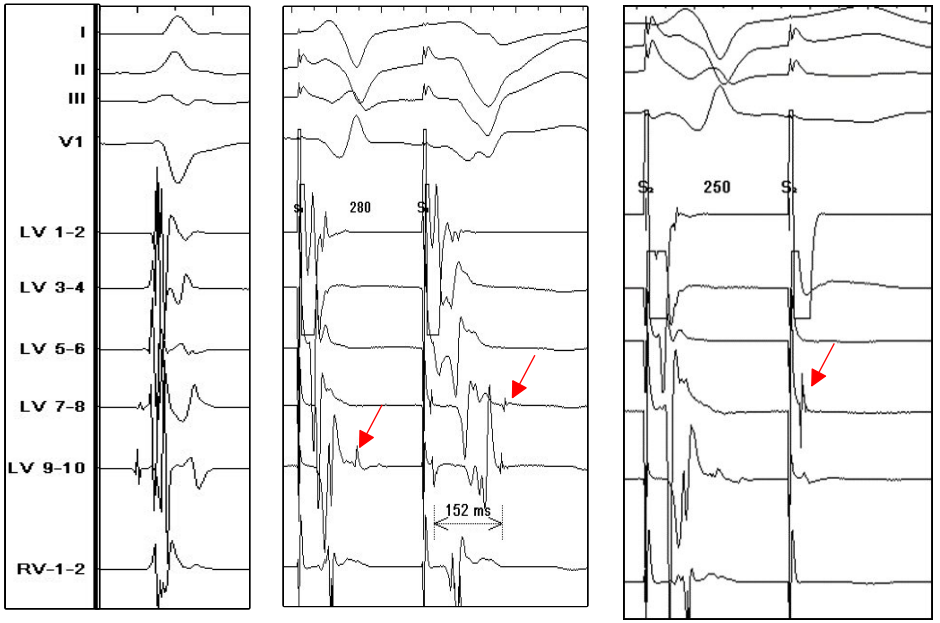
We anticipate a significant part of ScPVC susceptibility may be revealed by Na blocker , and **be used to identify subjects at risk**

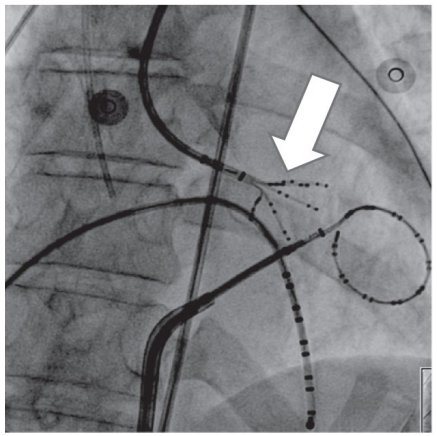
Abnormal Purkinje conduction

Purkinje system as a driver

LV Purkinje is mapped during programmed stimulation and VF induction

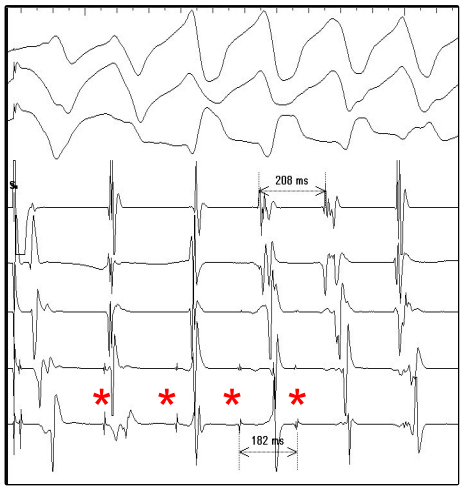






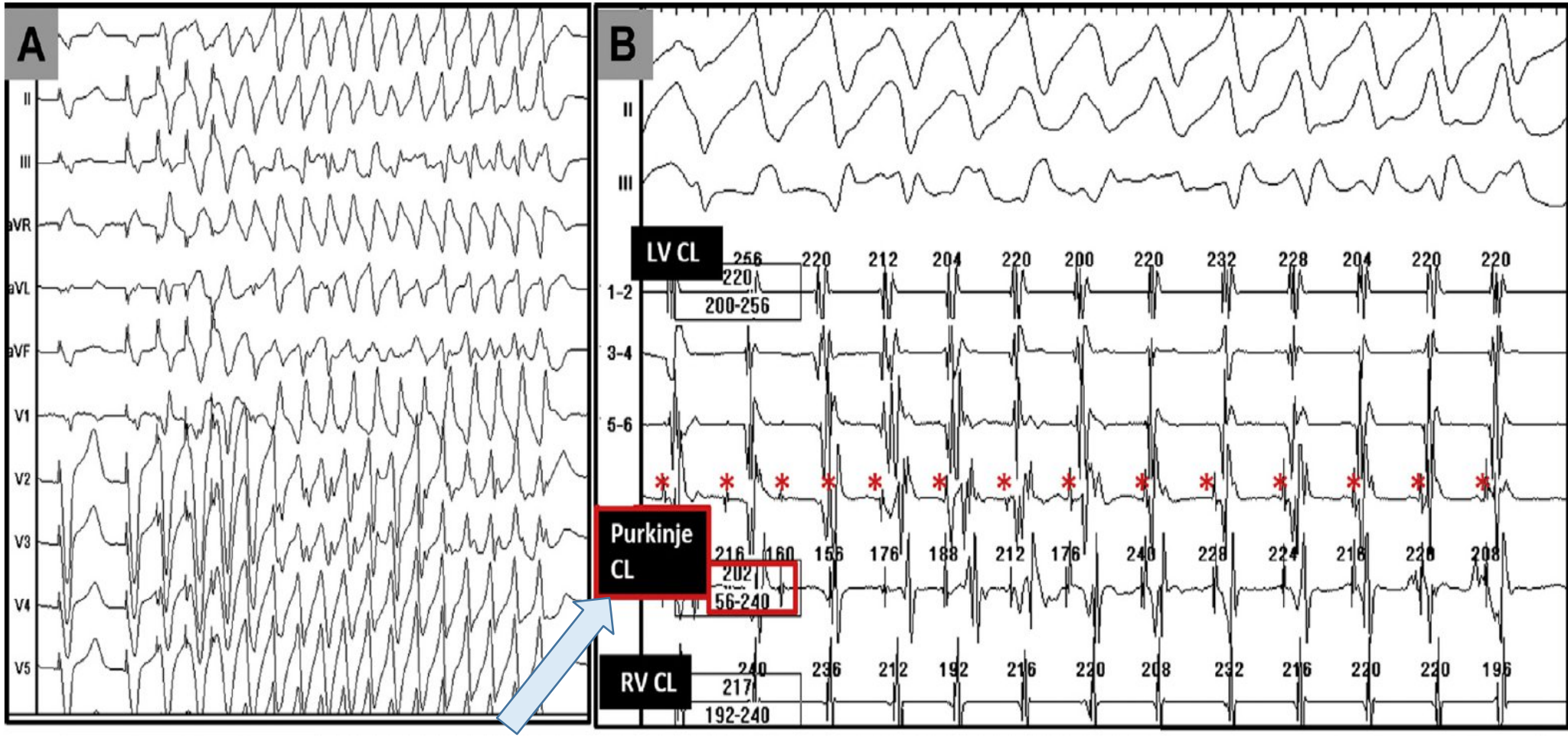
Aim : Look for repetitive Purkinje activity associated 1:1 with myocardium

Normal < 3 beats



Unexplained/Idiopathic VF in a 15y girl (family SCD)

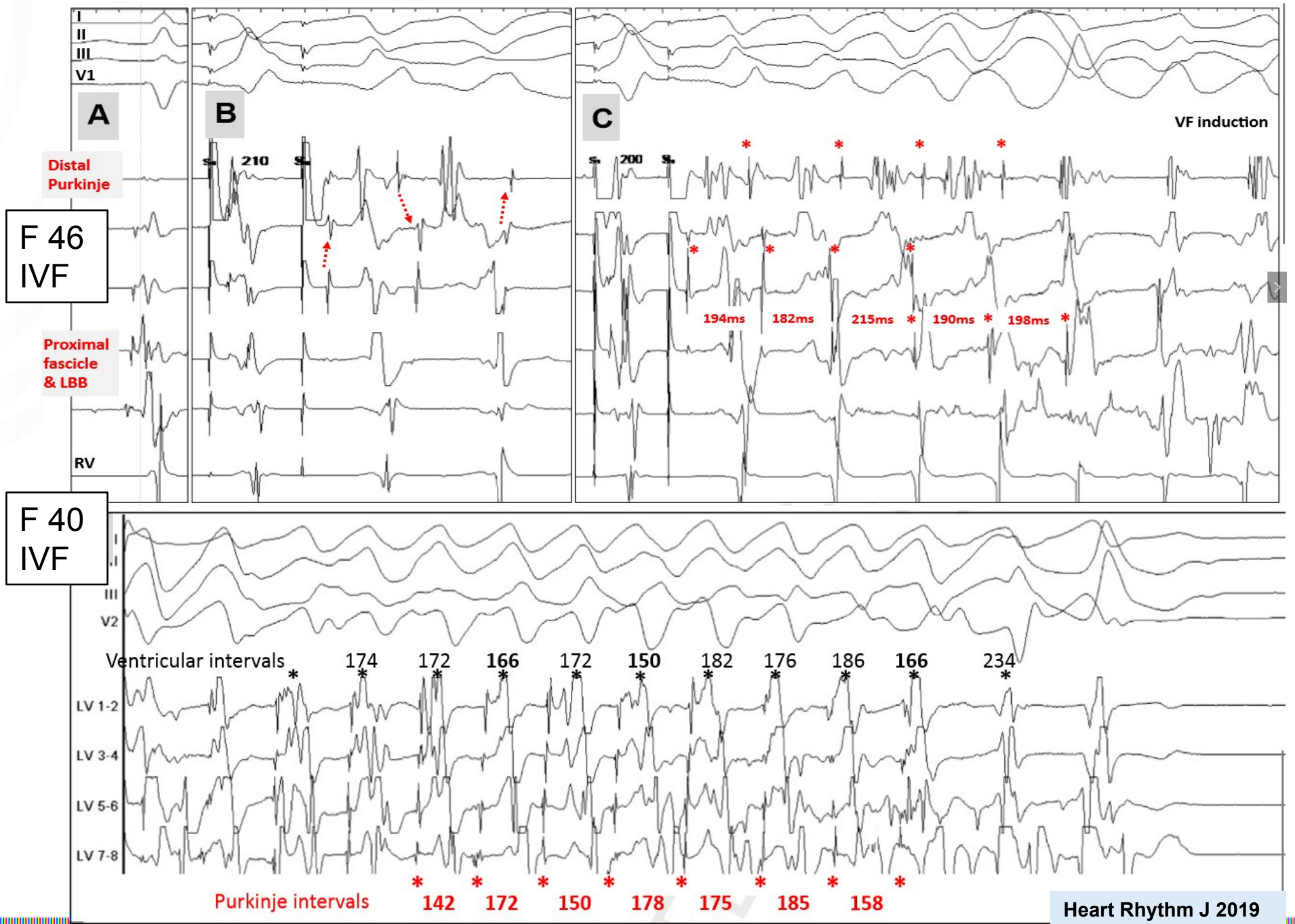
Inducible Purkinje-related polymorphic VT as the only abnormality



Purkinje cycle lengths more rapid than LV and RV cycle lengths

J Am Coll Cardiol EP. 2020;6(6):591-608.

Unexplained/Idiopathic VF in two women -Inducible Purkinje reentry



Heart Rhythm J 2019

Purkinje system in VF associated with Cardiomyopathies (DCM, HCM)

In addition to Purkinje as a potential Trigger

Purkinje as a Driver

Purkinje activities are provoked at the VF induction in 37 % of pts with HCM or DCM)

LV induction usually required (close to distal network**)**

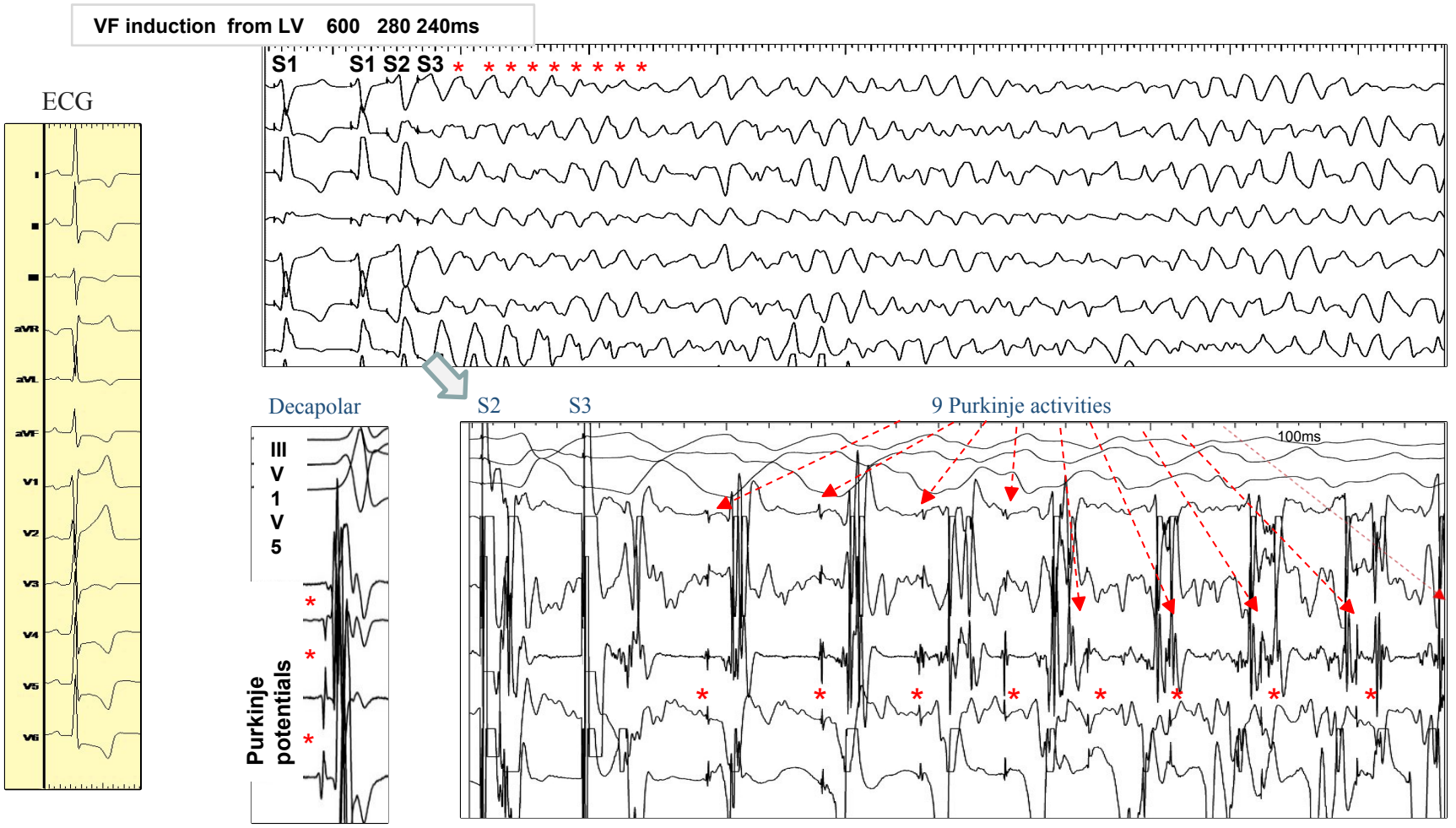
Purkinje present for 14 initial VF beats= 3.1±0.4 sec

Purkinje has shorter cycle length (than myocardium 218 vs 230 ms**)**

No such repetitive Purkinje activity was induced in patients with BrS

Eur Heart J 2022

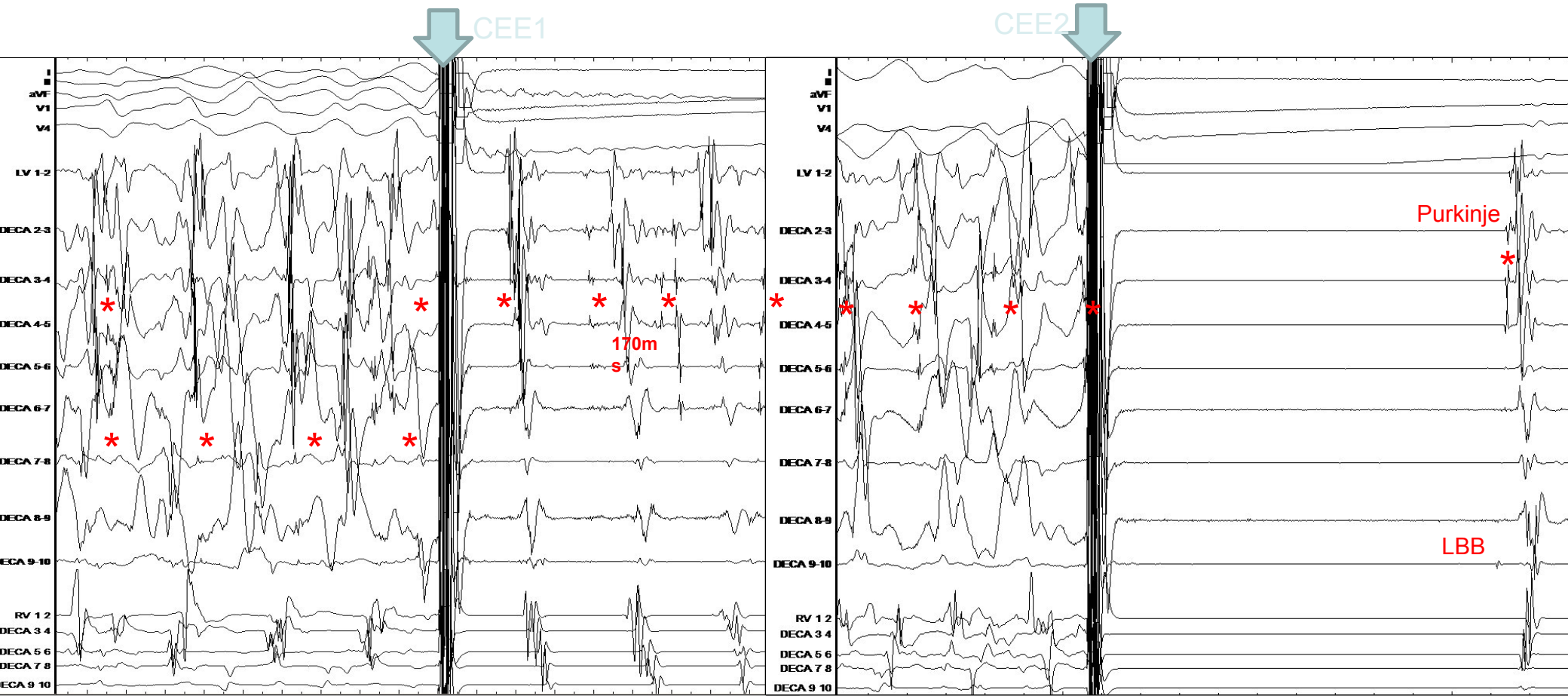
CASE 1 - M 29yrs HCM (septum 27mm) 7 VF on ICD No ectopic PVC/trigger



Importance of multielectrode Purkinje recordings for Purkinje recognition within fractionated myocardial electrograms

Bundle branch reentry is excluded

1st Cardioversion for VF - VF continuation with Purkinje 1:1



CASE - M 63yrs HCM 5 VF on ICD No ectopic trigger

Induction from the LV

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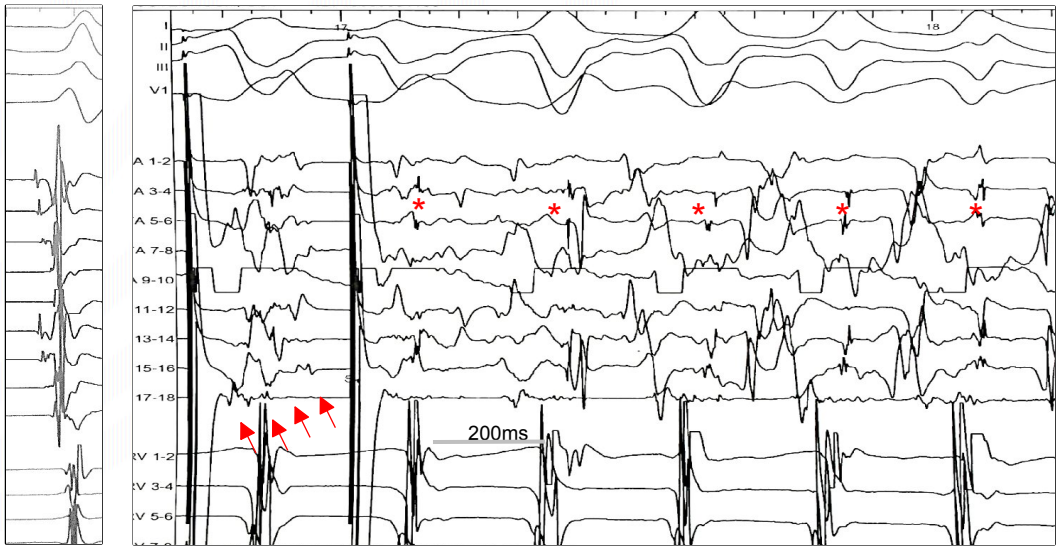
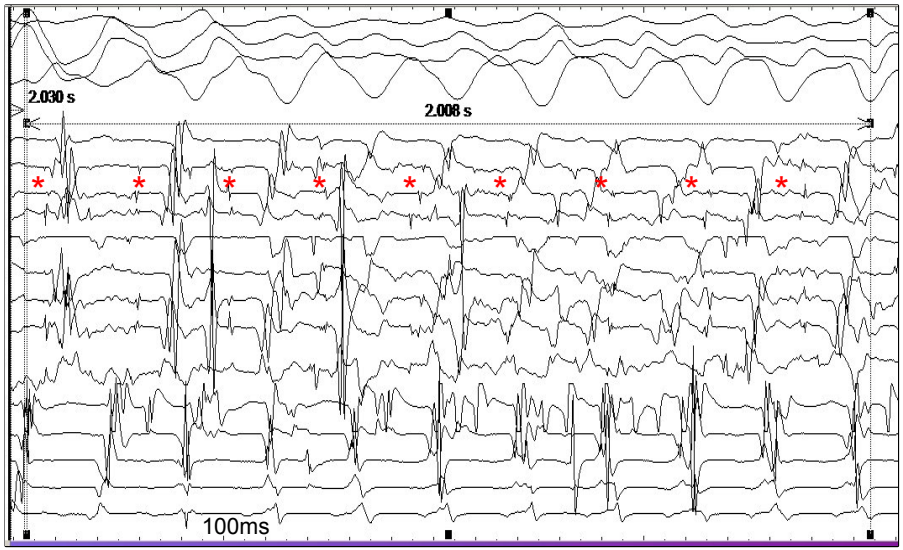
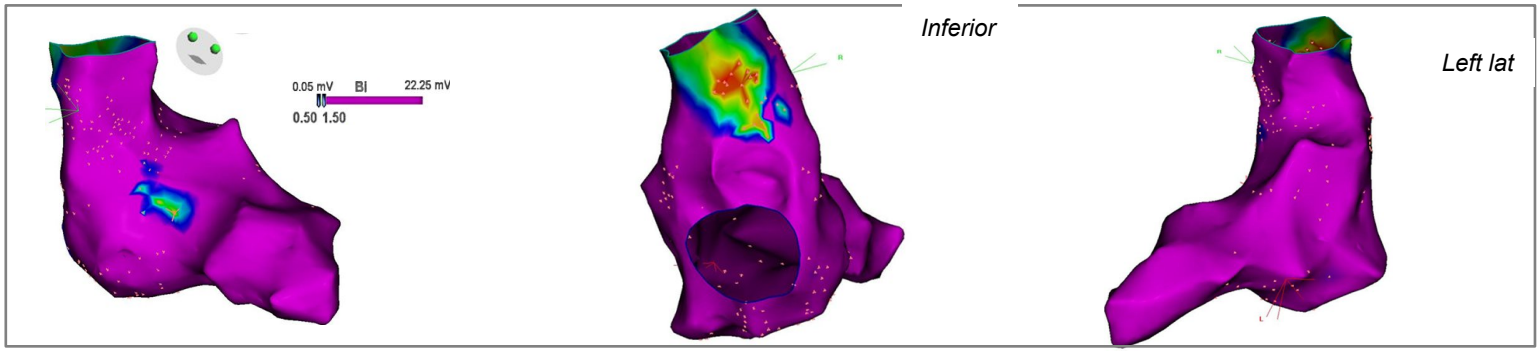
S3-270ms

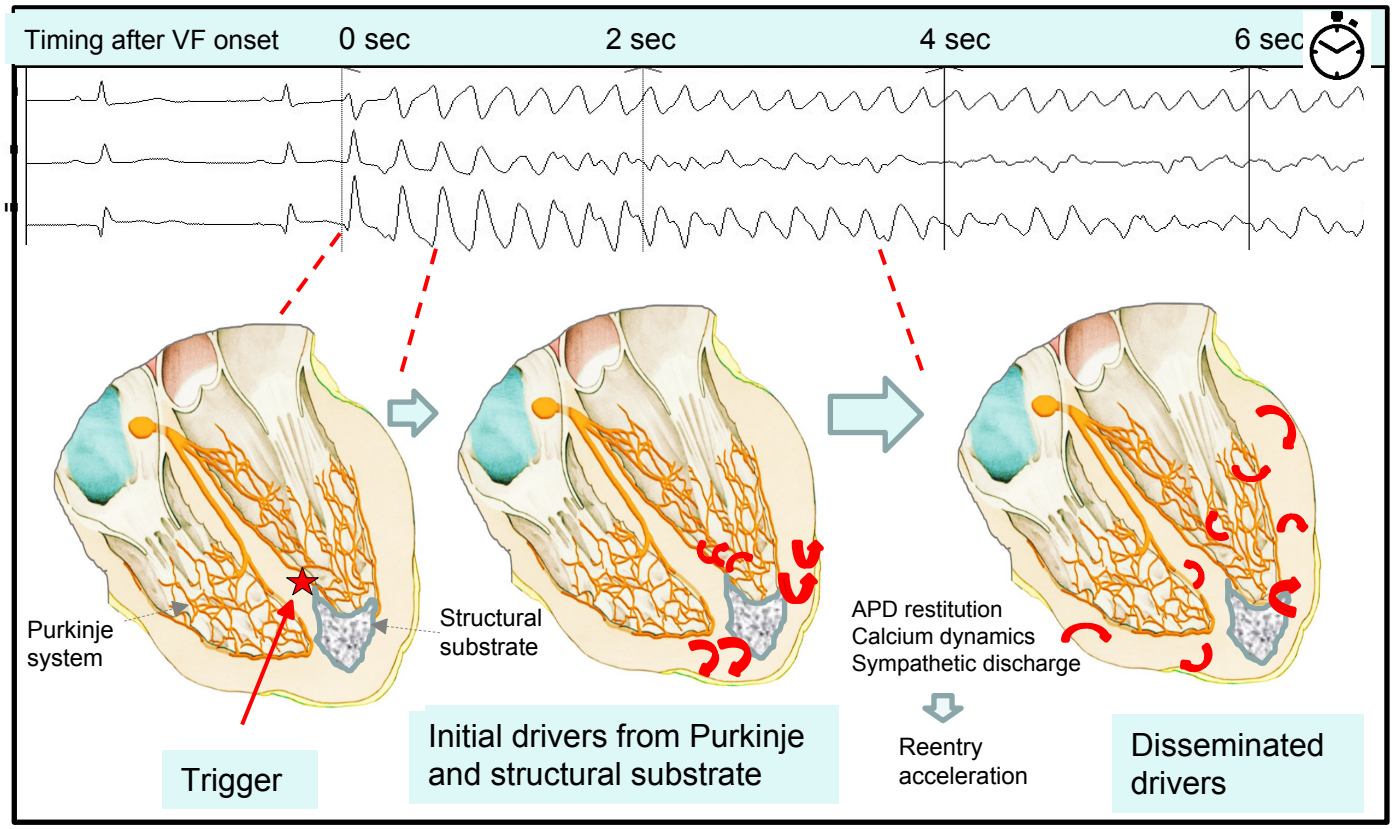




Small low voltage (7cm2) areas And no significant fragmented egms

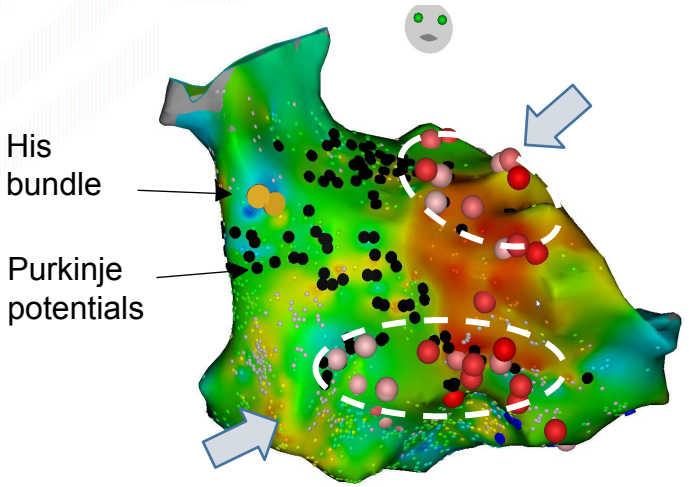


Purkinje network is likely an essential link to VF initial launching and continuity to desorganized VF



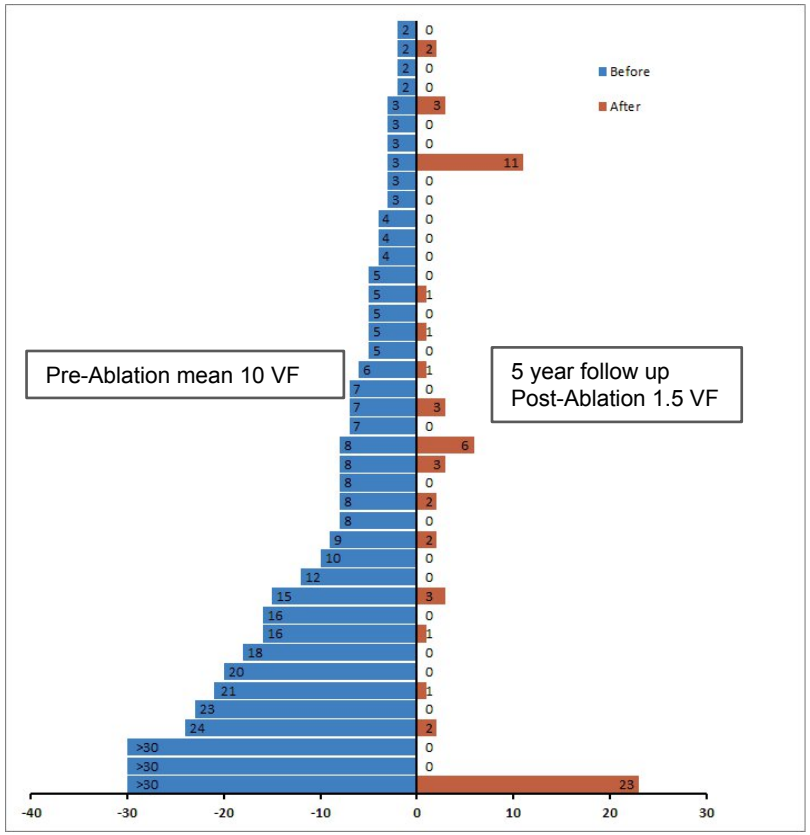
Purkinje ablation alone or added to the myocardial substrate is effective

20 min RF renders VF non inducible



no VF since 24 months (on betablockers)

58 % (14/24) of VF associated with ICM and NICM had Purkinje involvement



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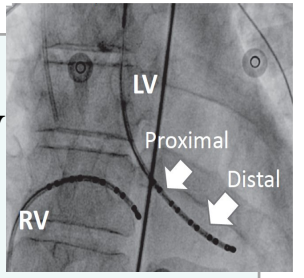
Purkinje mapping is an indispensable part of SCD phenotyping

VF triggers originate from Purkinje :

In a significant part of idiopathic VF
In most ischemic VF
In unknown part of LV structural diseases

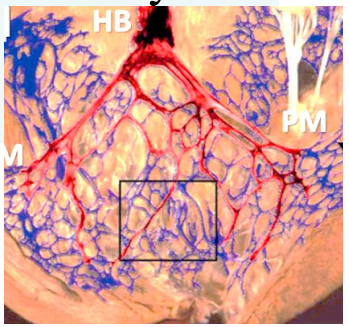
An emerging role as drivers,
Purkinje 'reentries' are inducible by LV



In distinct part of idiopathic VF
In significant part of VF in cardiomyopathies,
lasting for ~ 3 seconds of VF onset

Purkinje activities are **short-lasting but likely an essential link** to VF continuity

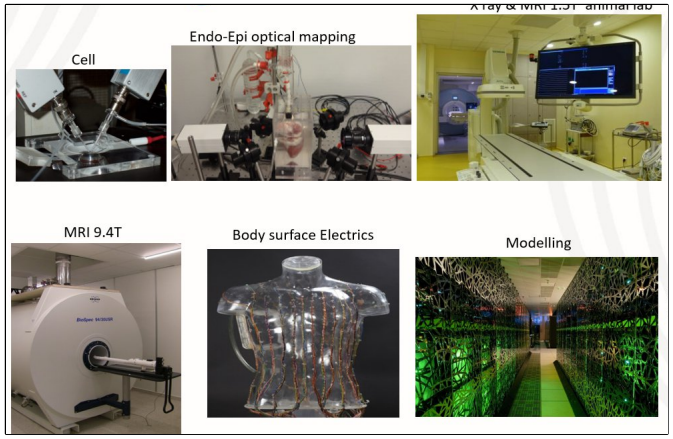
Identification of **individual patients** allows specific treatment



Mapping complexity limit the improvement in knowledge

Members from 18 countries : Cardiac electrophysiology-Imaging-Signal processing-Modeling ...

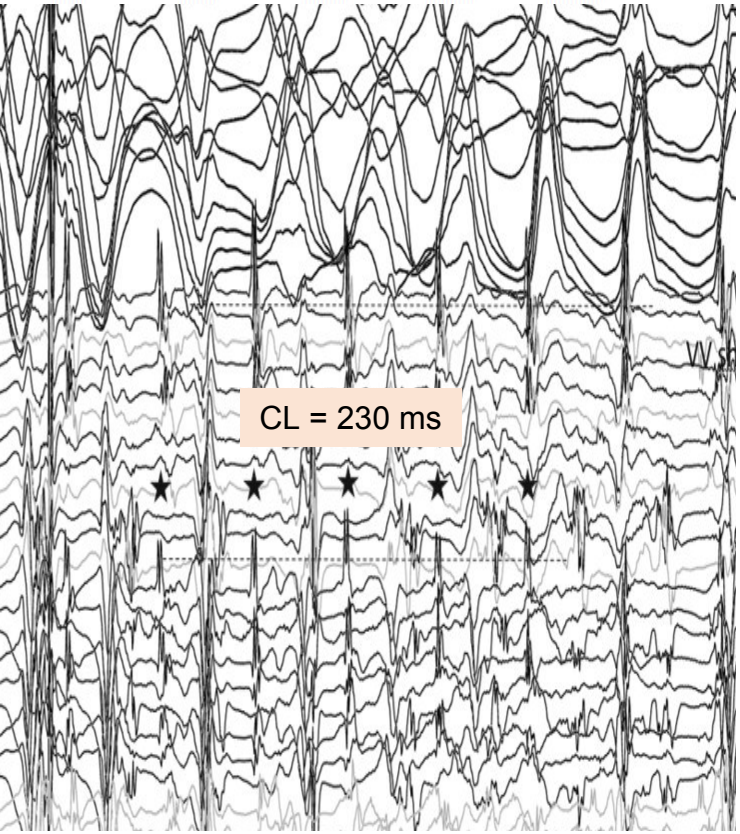
LIRYC : Cardiac Electrophysiology & Modeling Institute



OPEN Positions for SIGNAL processing engineering in sudden cardiac death

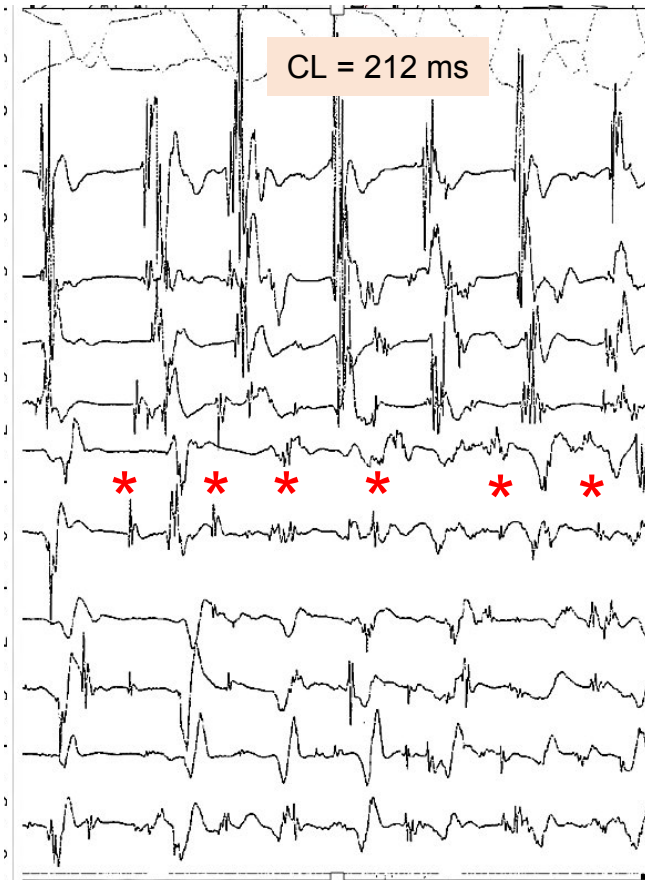
Recent cases of Purkinje-related VF

M 62 DCM



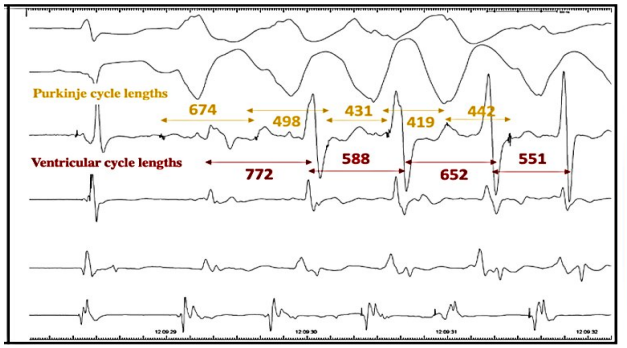
P Santangelli UPenn

M 42 DCM

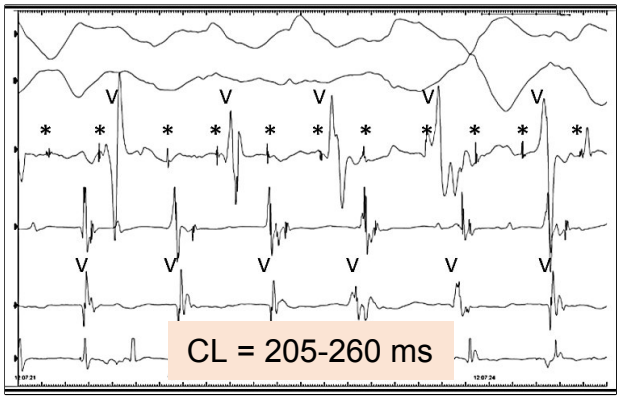


X Waintraub Pitié

F 9 HCM



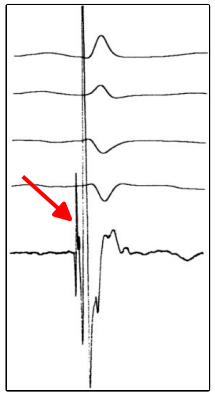
2:1 Purkinje-Myocardium activation



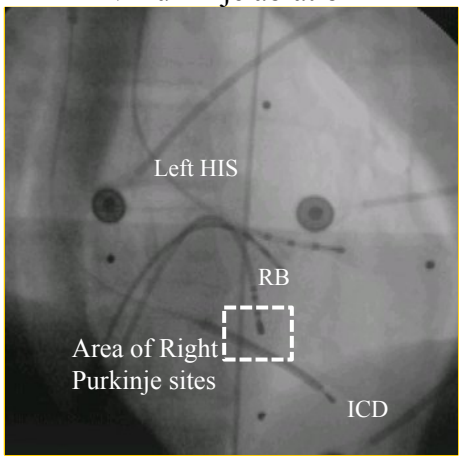
V Waldmann HEGP

Trigger ablation is very effective
(except multifocal PVCs)

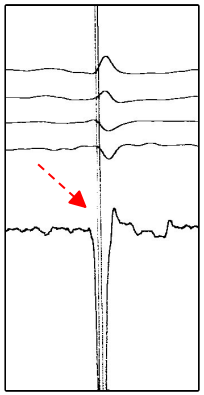
Purkinje site pre ablation



RV Purkinje ablation



Purkinje elimination



Our experience (81 pts)

PURKINJE	**71 pts**
RVOT-LVOT	**8 pts**
MYOCARDIUM	**2 pts**

Mean RF duration
9 ± 5 min/patient

Additional RF applications in surrounding Purkinje to ‘’prune the tree’’

LANCET 2002, Circulation 2002