

Update on arrhythmogenic syndromes

Rationale and indication of transcatheter ablation in patients with Brugada Syndrome

Dr. Federico Ferraris

Cardiology Department - University of Turin, Italy

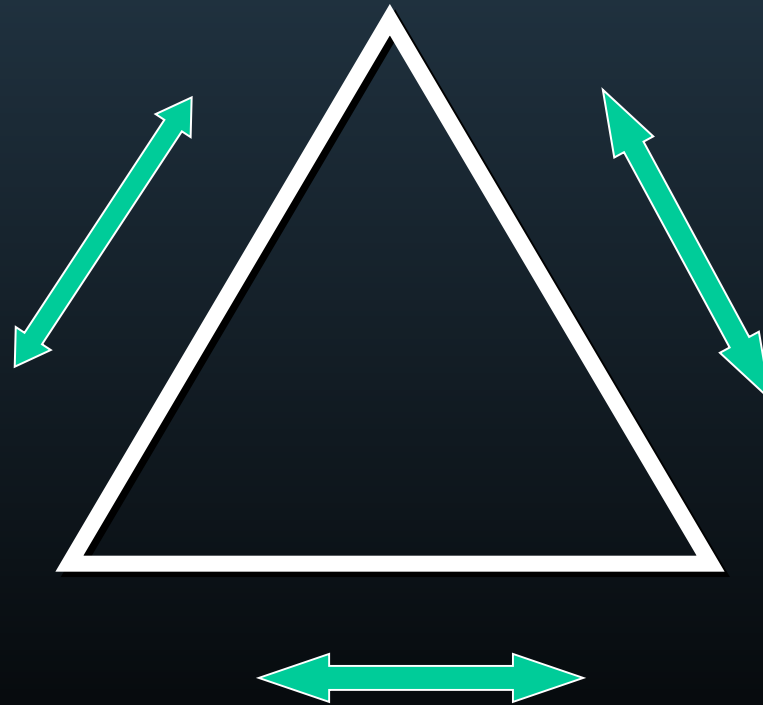


Arrhythmias in Brugada syndrome: interventional treatment target

Coumel Triangle

Trigger

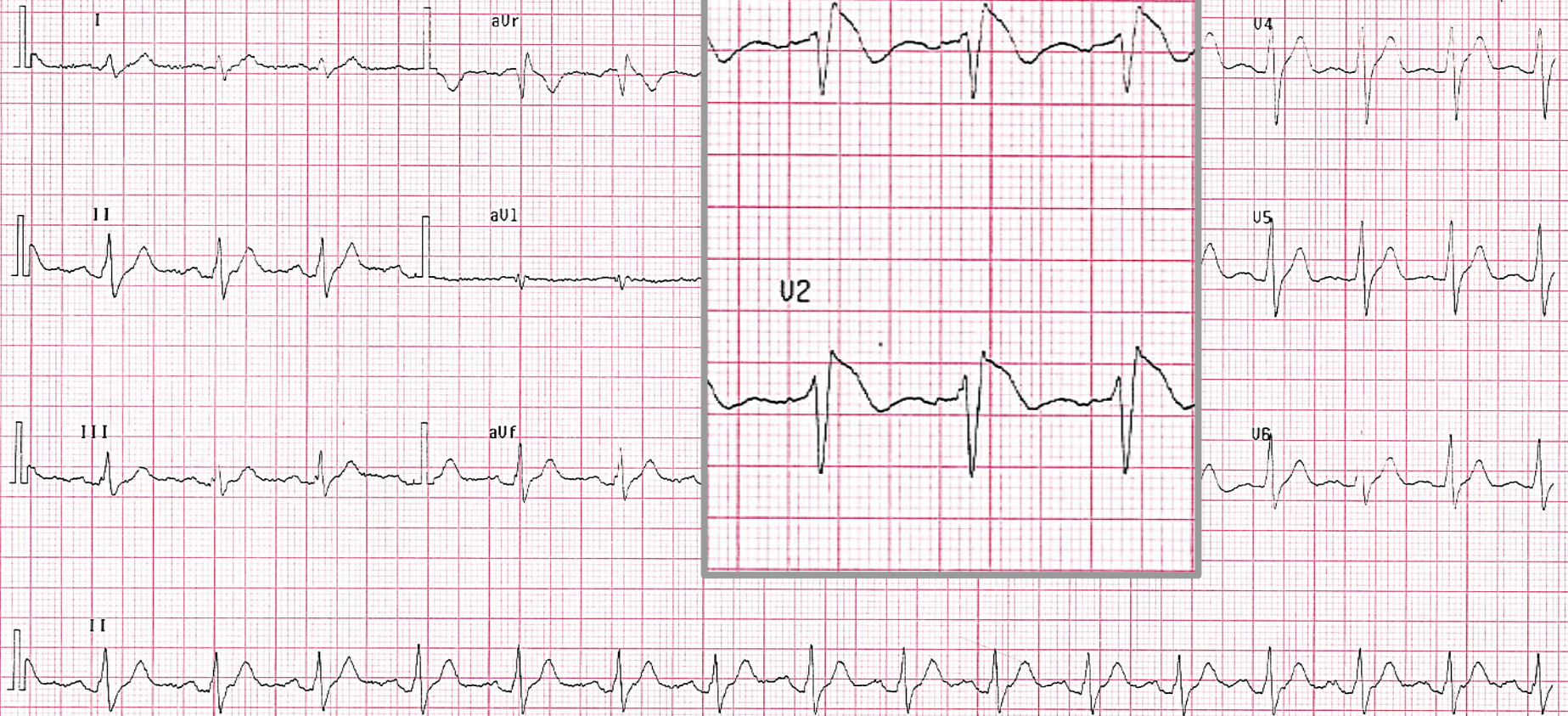
Substrate



~~Autonomic
Nervous
System~~

Clinic case

25/04/2016 ore 23:33



RS FC 100 bpm, QTa 320 msec, QTc 413 msec

I episodio

26/04/2016 ore 14:19:04



RS FC 100 bpm, QTa 340msec, QTc 439 msec



VFIB 20:19:17 26/04/2016

San Giovanni

ECG: 10 mm/mV, 25 mm/s, Sito#0, Letto 222, [0.05 - 150]

II episodio

26/04/2016 ore 18:51.



RS FC 80 bpm, QTa 360 msec, QTc 416 msec

III episodio

26/04/2016 ore 20:19



San Giovanni

ECG: 10 mm/mV, 25 mm/s, Sito#0, Letto 222, [0.05 - 150]

IV episodio



Episodi



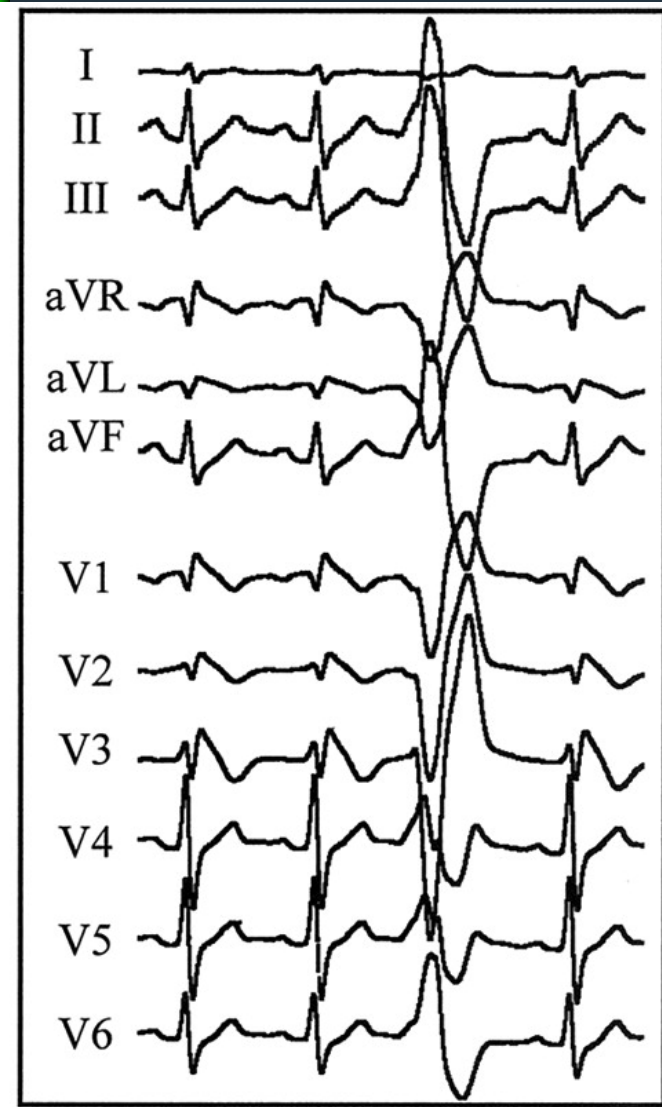
di

**RVOT "benign"
ectopy**

**Trigger, and
potential target
for ablation**

19:11

Trigger ablation in Brugada



Ablation of **RVOT** or **Purkinje network ectopy** initiating ventricular fibrillation

No VF recurrences
17 months followup

3 patients

Arrhythmias in Brugada syndrome:

interventional treatment target

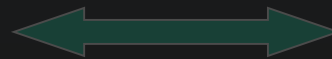
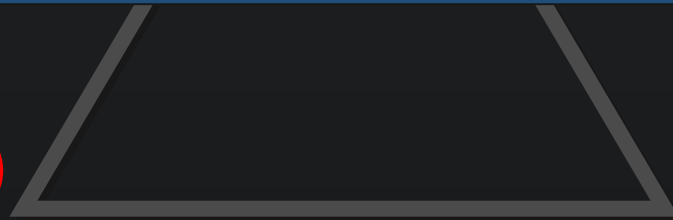
Coumel Triangle

Trigger

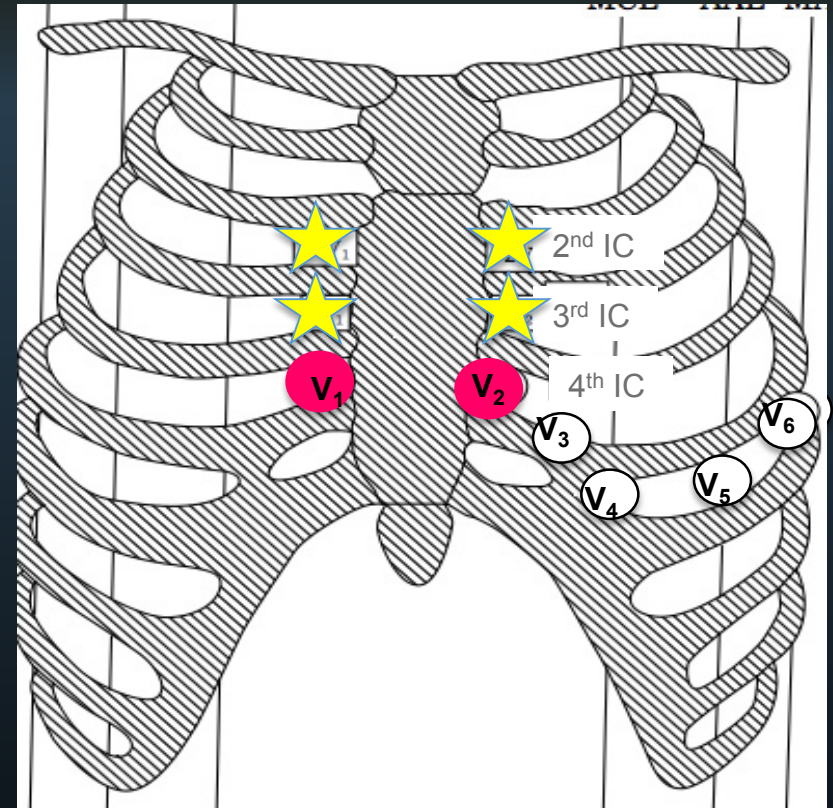
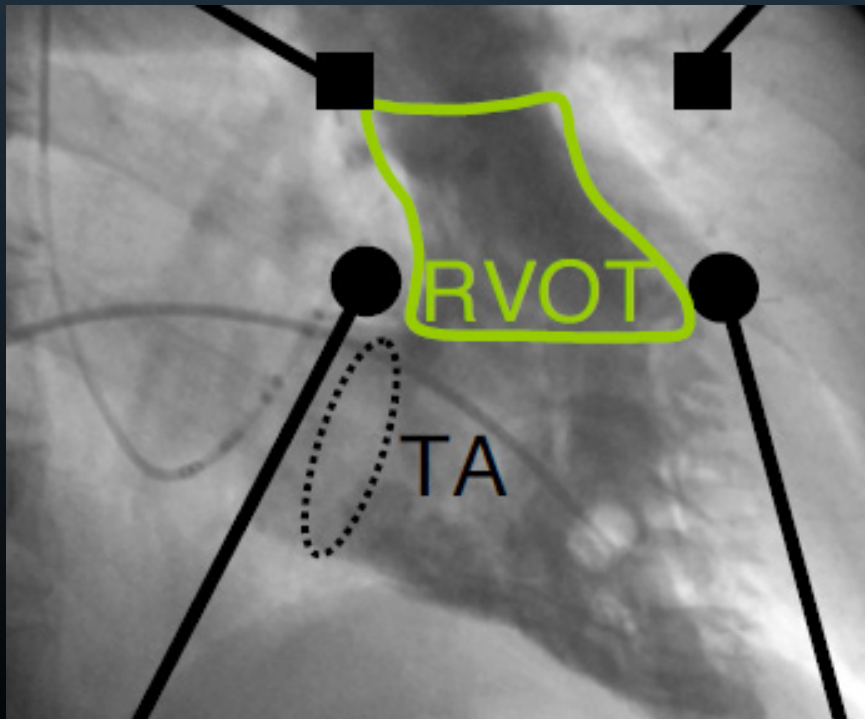
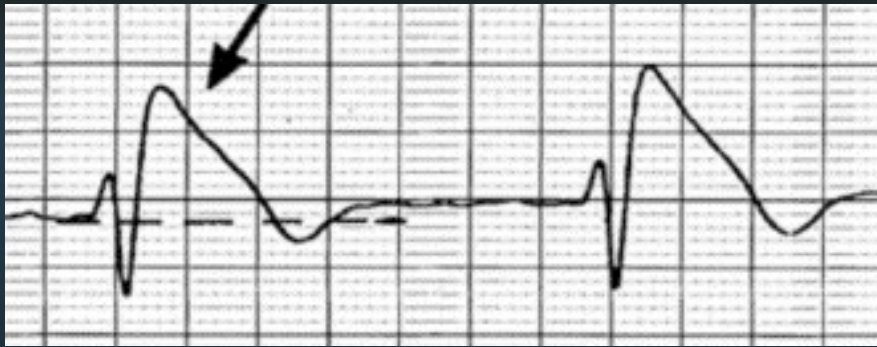
Which is the substrate if Brugada's syndrome hearts are **"structurally normal"**?

Substrate

~~Autonomic Nervous System~~



Brugada syndrome **anatomical** substrate: RVOT



**Right ventricular
outflow tract**

Surface ECG



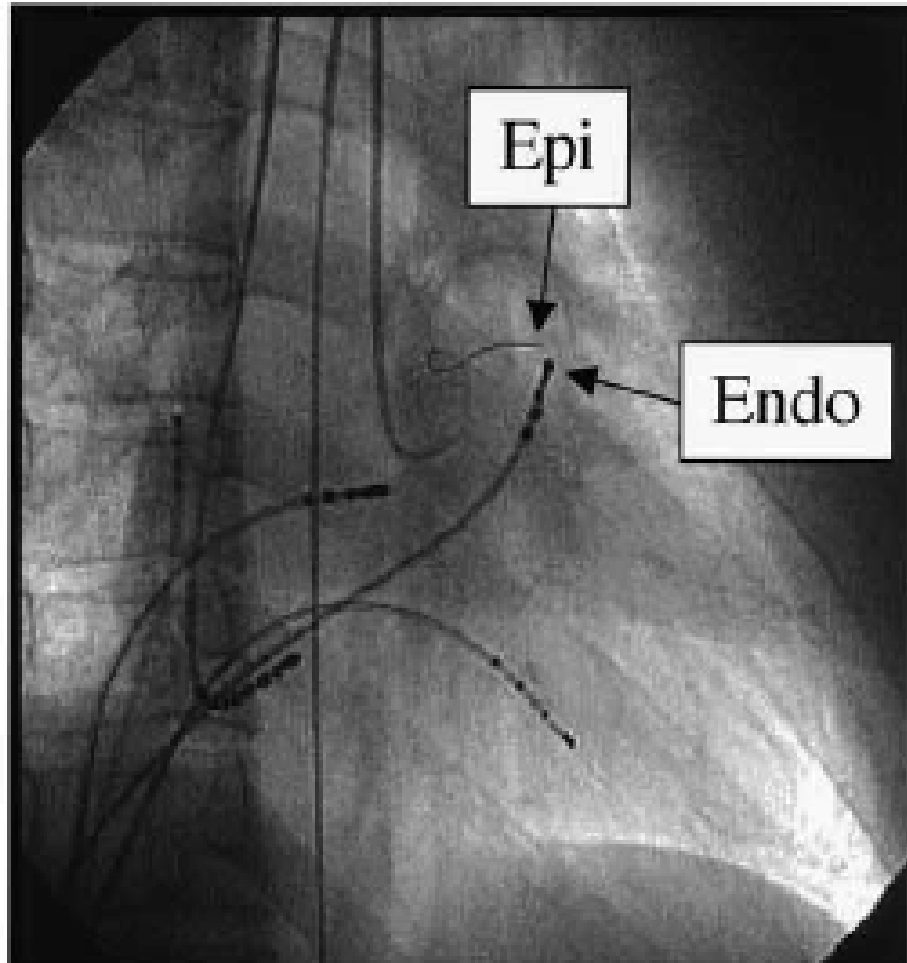
**Local electrical
signals**

Anomalous electrical activity on epicardial RVOT

Electrode in conus branch of right coronary artery and endocardium

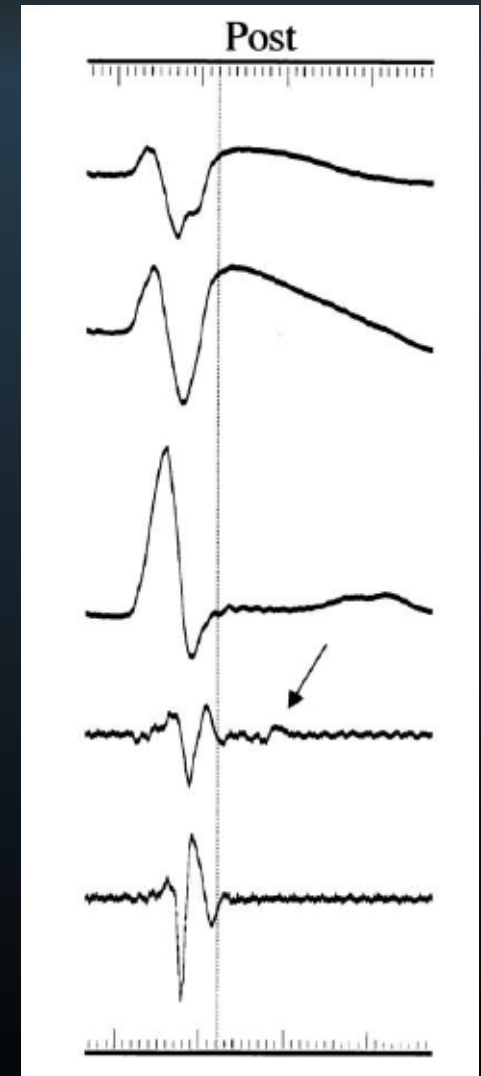
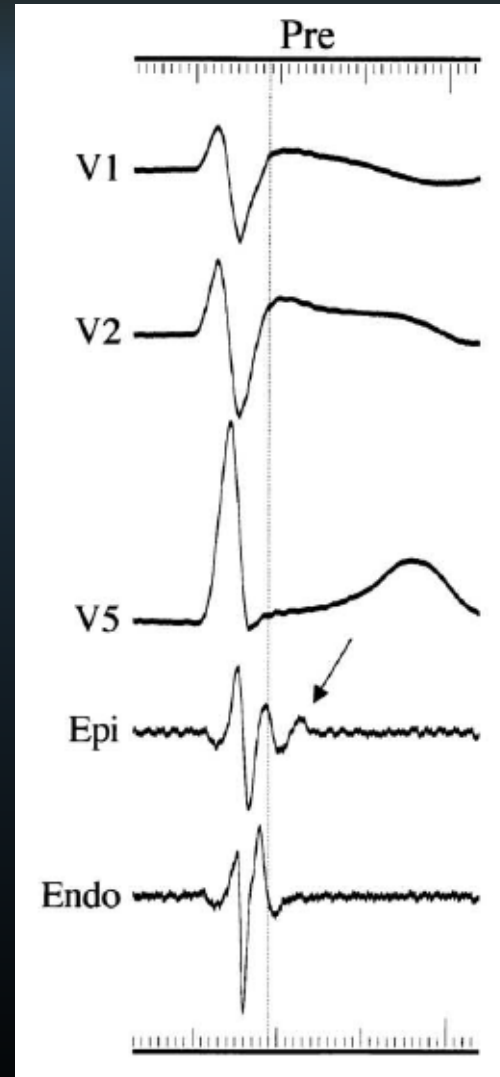
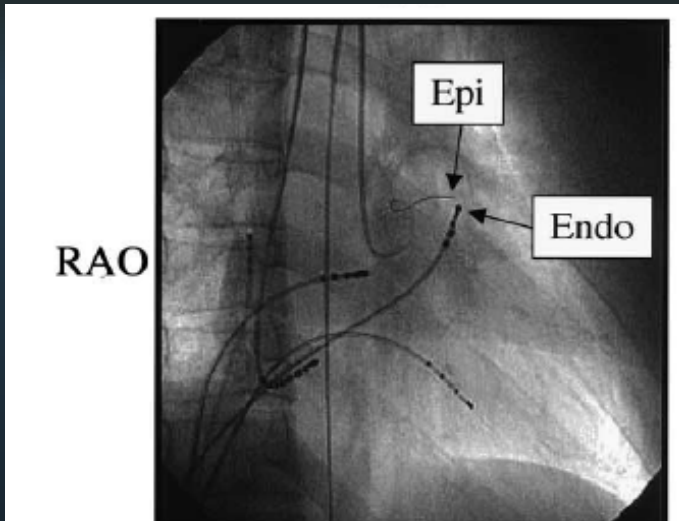
Ic challenge

RAO



Electrode in conus branch of right coronary artery and endocardium

lc challenge



Delayed potential
only on epicardium

More delay with lc

Arrhythmia/Electrophysiology

Prevention of Ventricular Fibrillation Episodes in Brugada Syndrome by Catheter Ablation Over the Anterior Right Ventricular Outflow Tract Epicardium

Koonlawee Nademanee, MD; Gumpanart Veerakul, MD; Pakorn Chandanamatta, MD;
Lertlak Chaothawee, MD; Aekarach Ariyachaipanich, MD; Kriengkrai Jirasirojanakorn, MD;
Khanchit Likittanasombat, MD; Kiertijai Bhuripanyo, MD; Tachapong Ngarmukos, MD

The Role of Ablation in Brugada Syndrome

*Koonlawee Nademanee, M.D.
Pacific Rim Research Institute at White Memorial
Medical Center in Los Angeles & Bangkok
Medical Center in Thailand*

From caliper to catheter, 2012

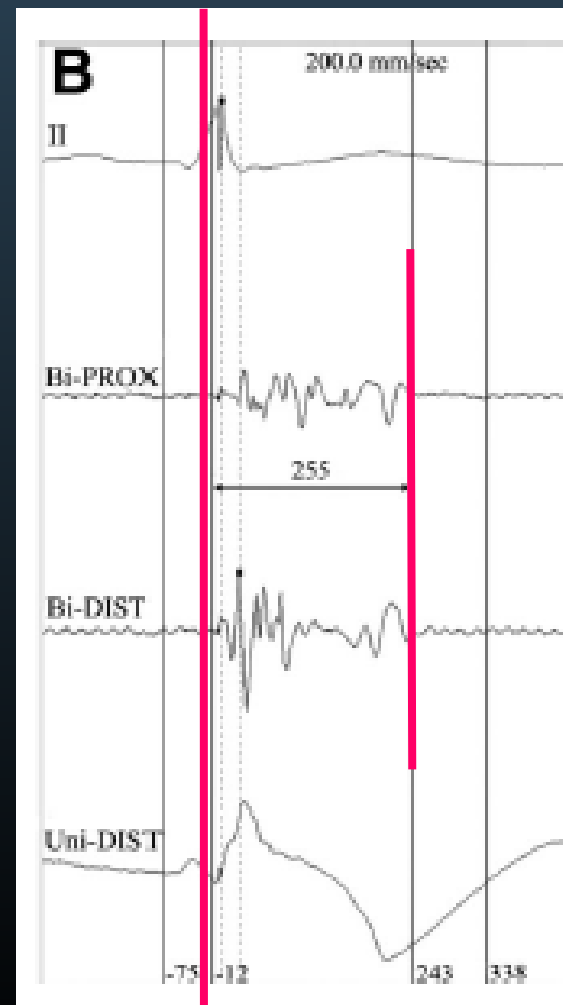
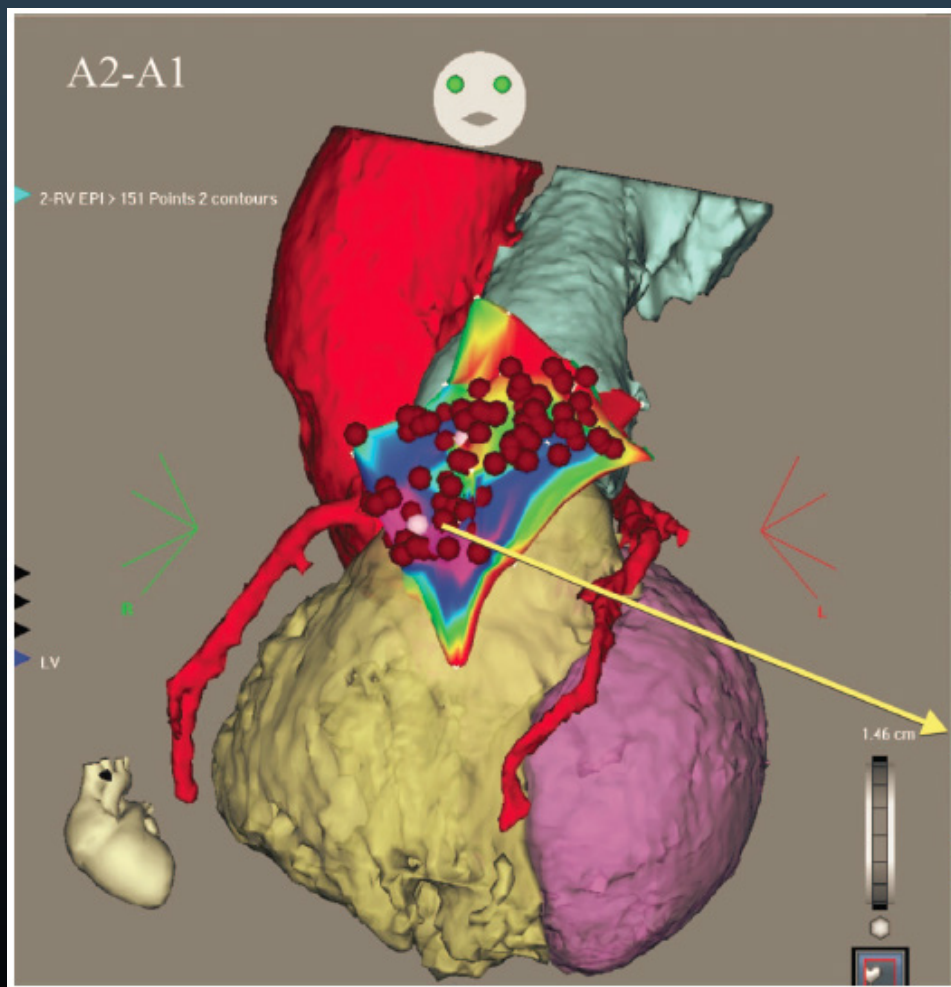


9 Brugada
ICD patients

2-6 shock
previous month

RVOT mapping,
endo and
epicardial

Low and
fractionated
potentials



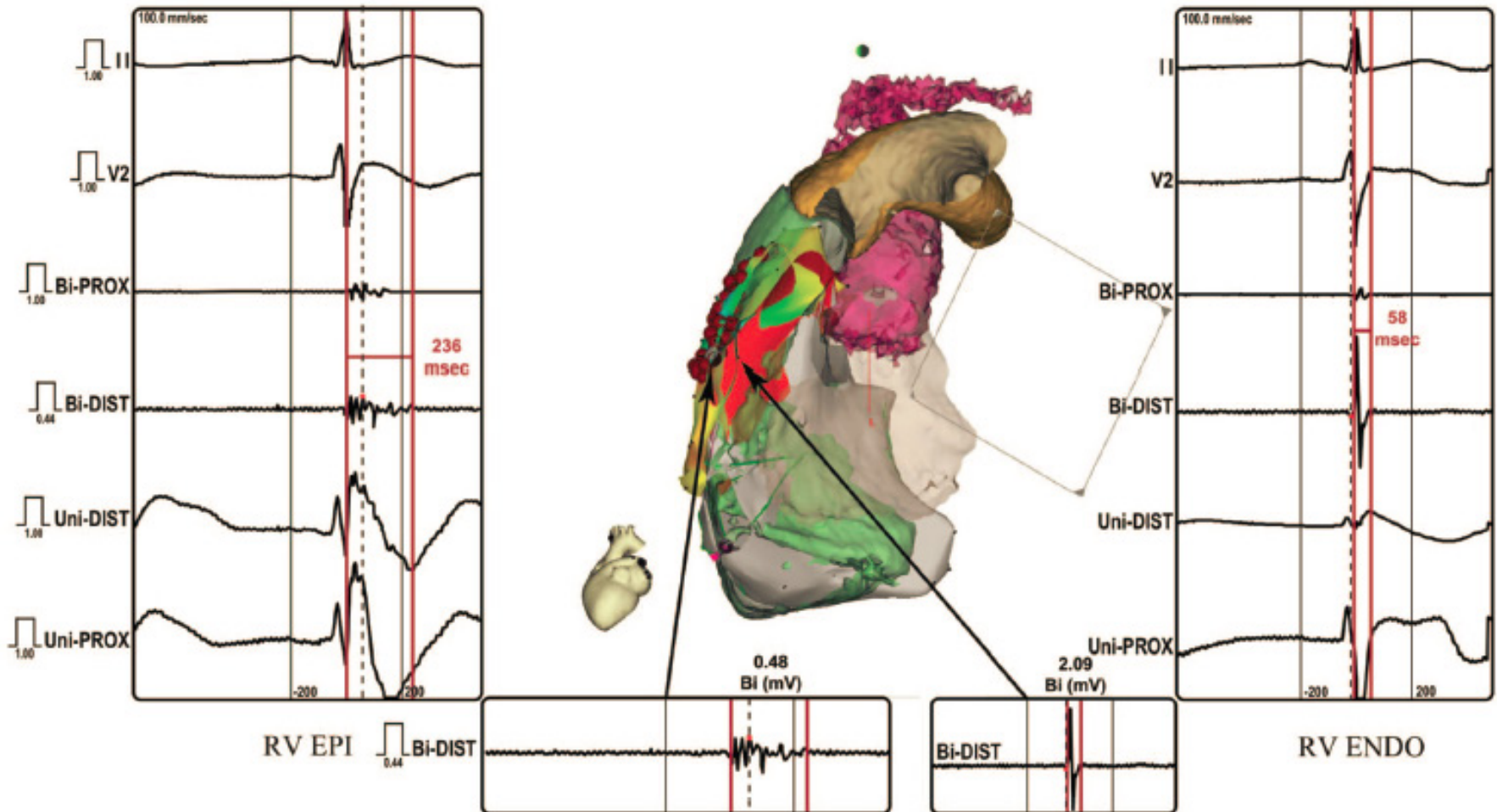
9 Brugada
ICD patients

*2-6 shock
previous month*

RVOT mapping,
endo and
epicardial

Low and
fractionated
potentials

Only on the
epicardial wall



RF epicardial ablation

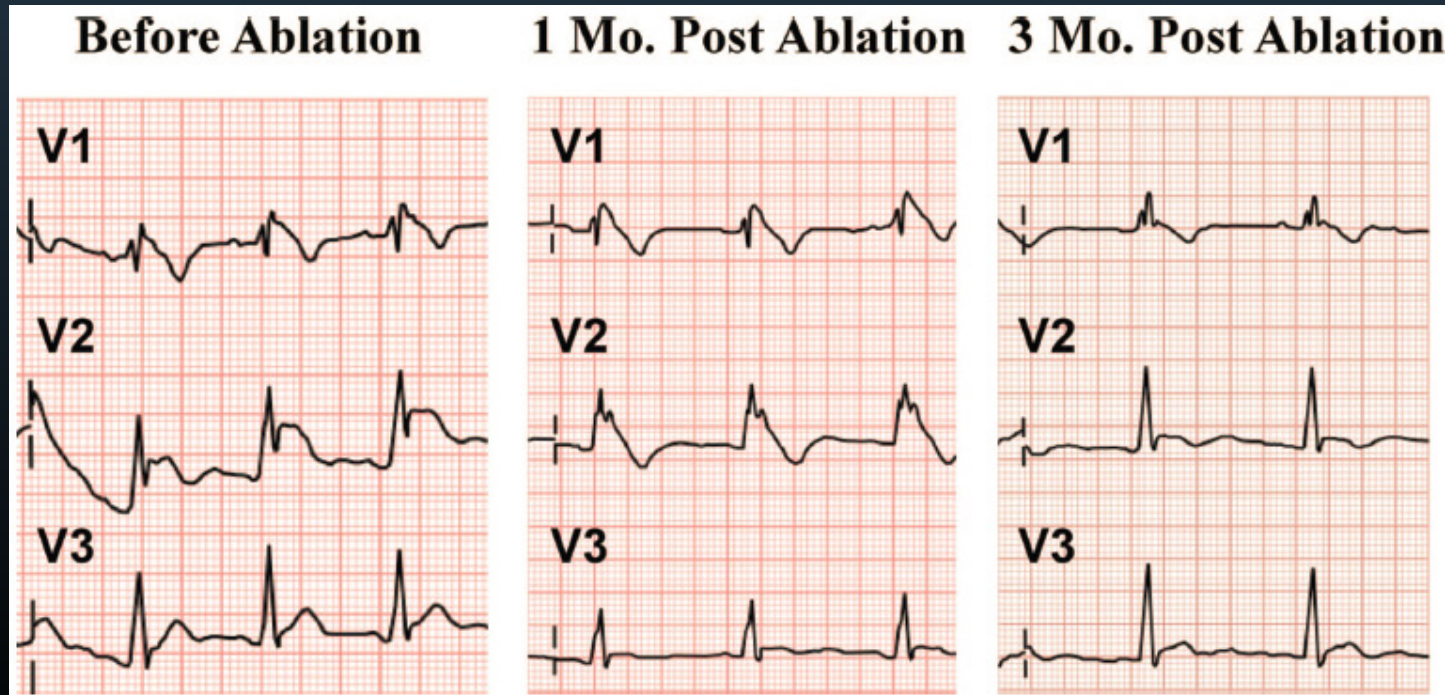
Fragmented
potential
abolition

Complications: 2 pericarditis, resolved spontaneously in 1 week

2 years
followup

1 VF recurrence

Progressive ECG
normalization



Fragmented Potentials

**Delayed
Conduction**

Brugada Syndrome

**Structurally
normal heart**



Just functional?

Further investigations to understand mechanism: Pathological study

6 heart of patients died suddenly, with Brugada syndrome in relatives

6 normal hearts matched

6 biopsies in fragmented zones in Brugada patients during toracotomy (ablation/ICD lead extraction)

Fibrosis

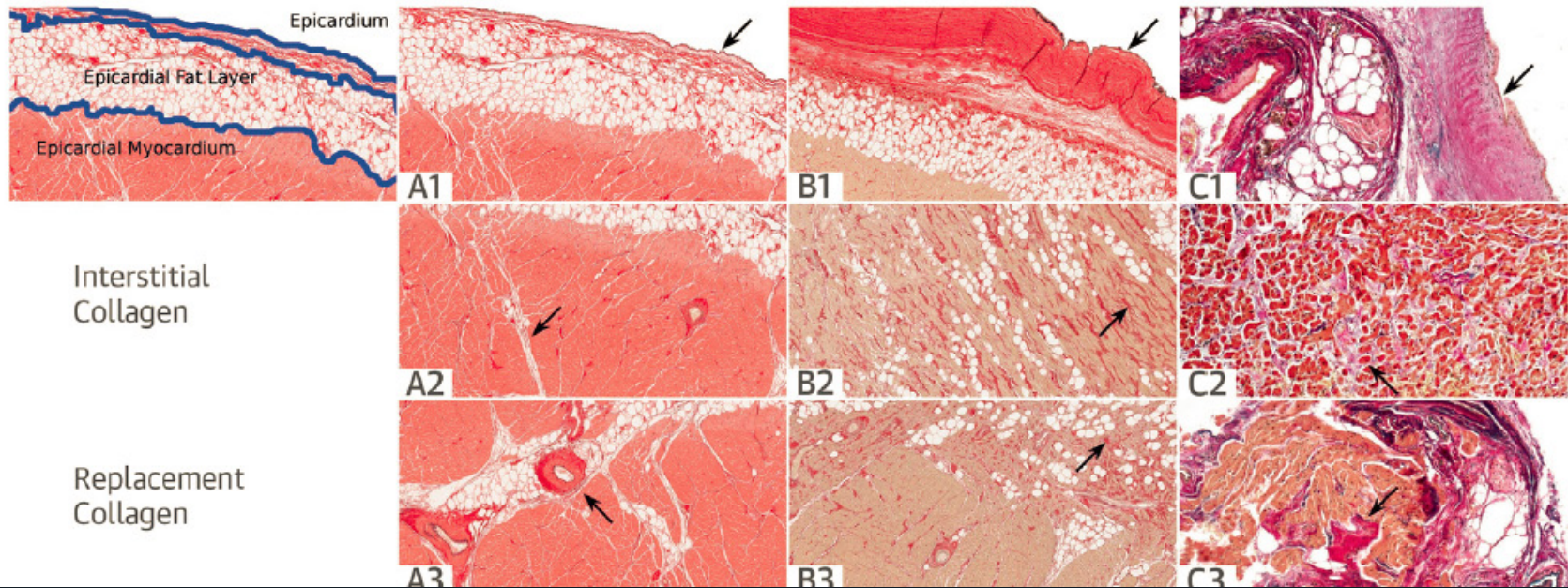
**Connexin
(gap junctions)**

**Fat
infiltration**

Post mortem
Brugada

Post mortem
normal

In vivo Brugada

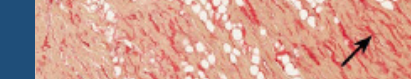
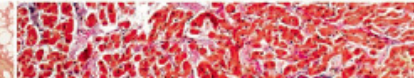
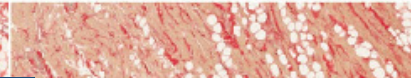
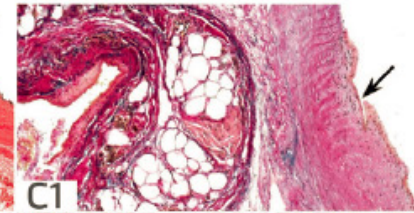
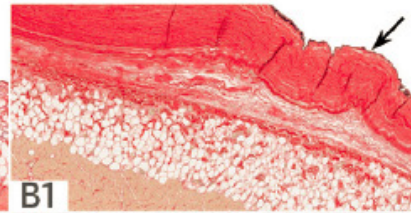
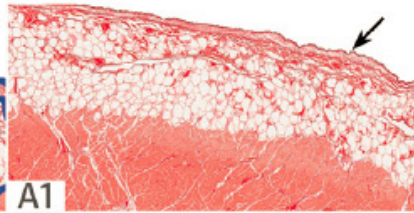
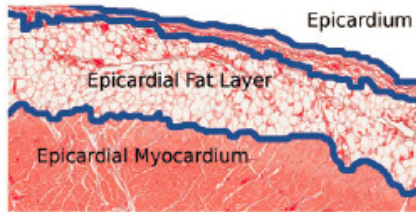


More collagen:
Fibrosis
(not detected by MRI)

Post mortem
brugada

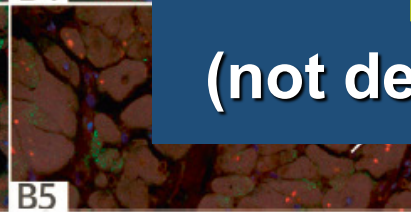
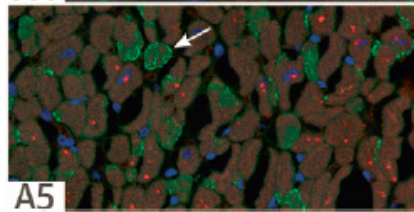
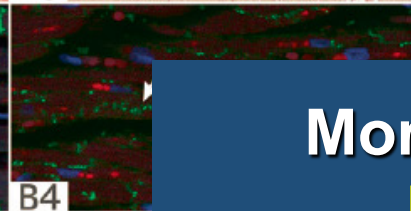
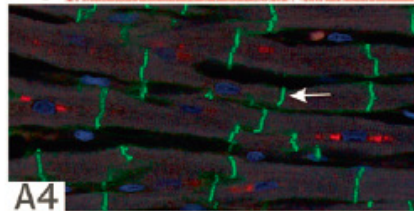
Post mortem
normal

In vivo Brugada



Less Connexin:
reduced **gap junction**
expression

Longitudinal
Connexin43



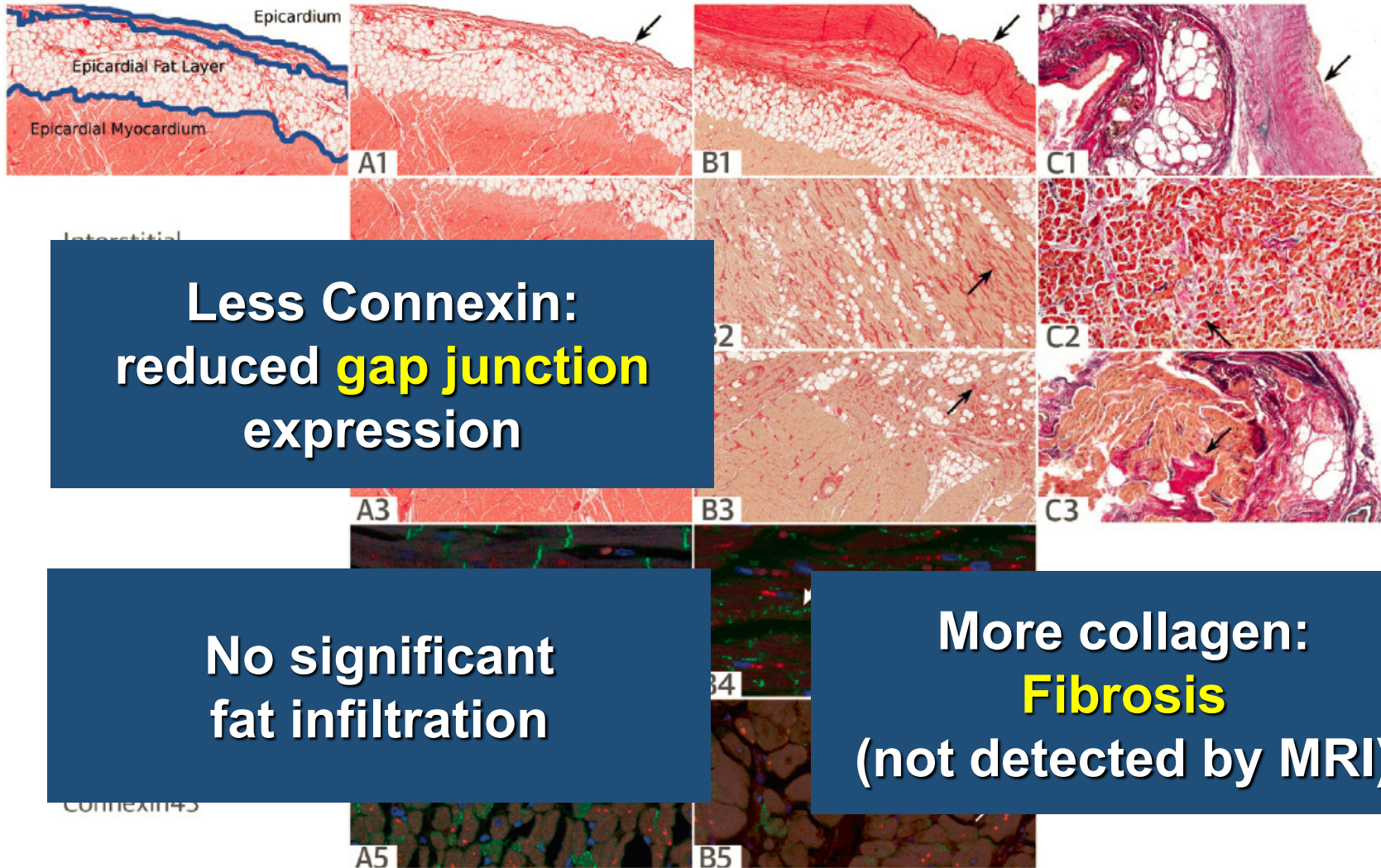
Enface
Connexin43

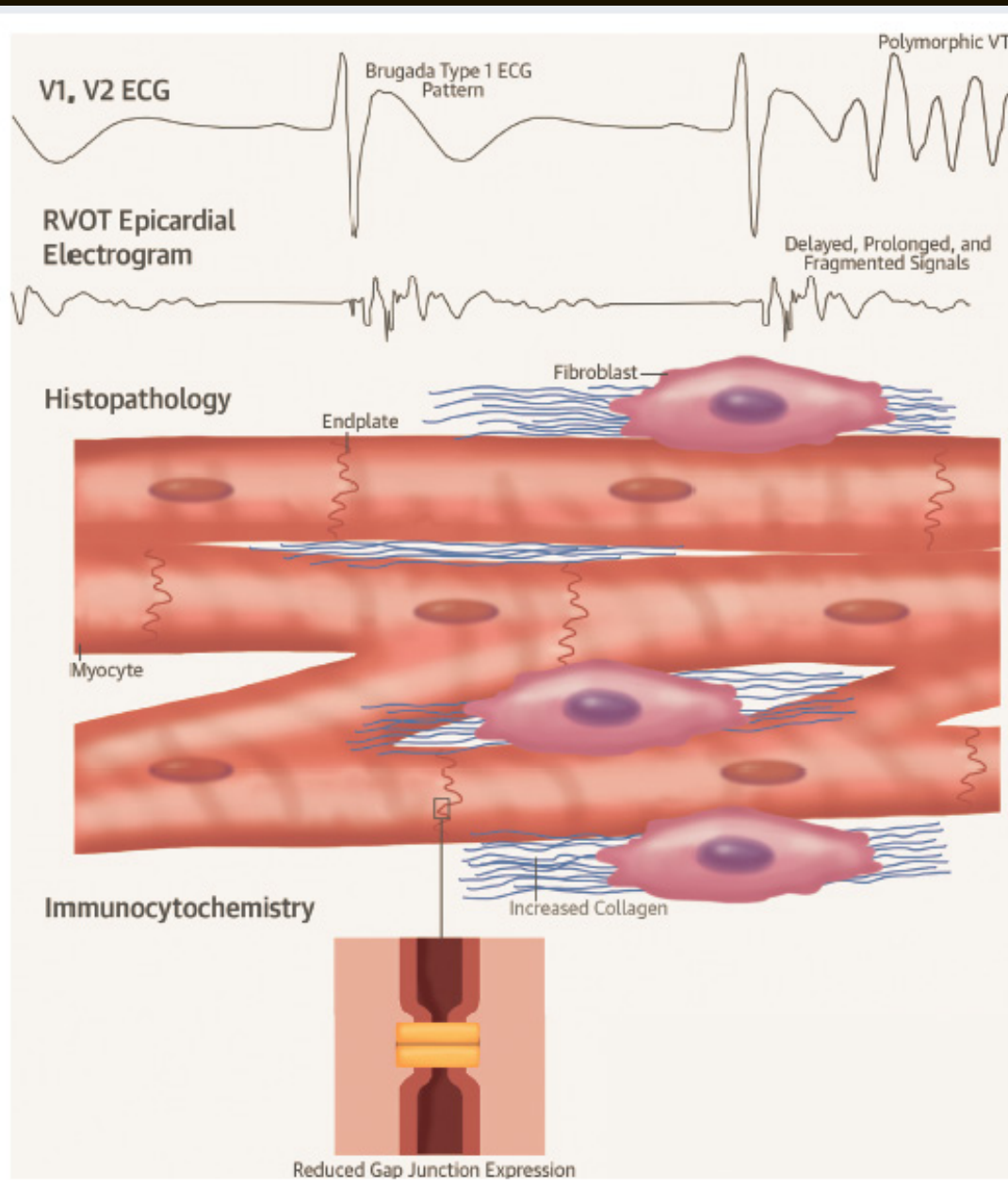
More collagen:
Fibrosis
(not detected by MRI)

Post mortem
brugada

Post mortem
normal

In vivo Brugada





Pathogenetic hypothesis

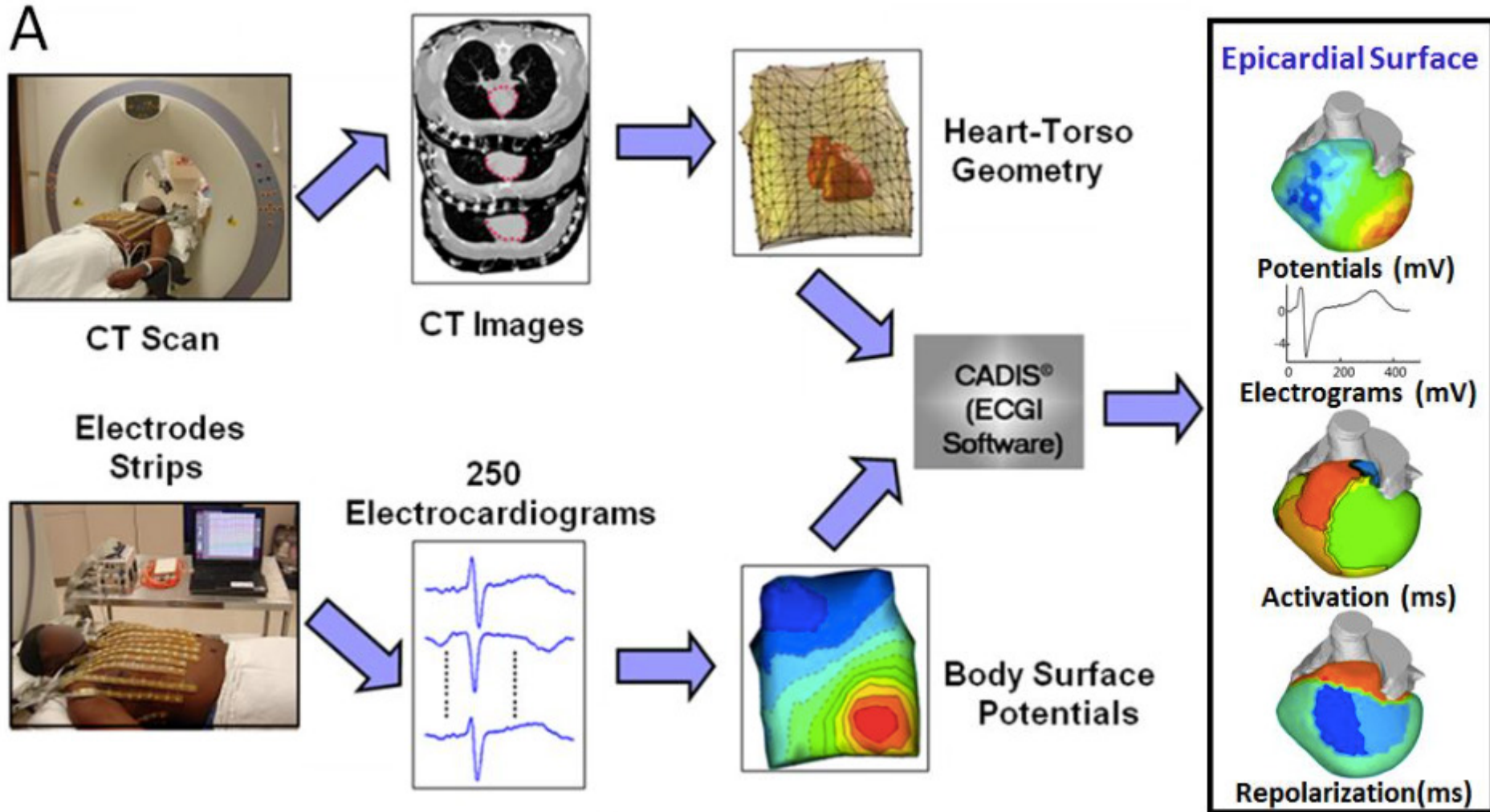
Fibrosis and reduced gap junction in RVOT

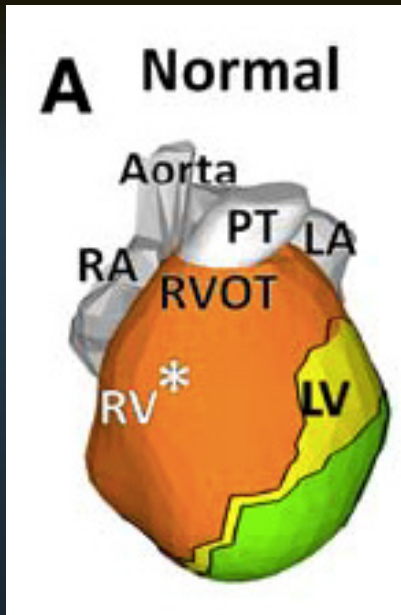
Conduction slowing

Fragmented potential

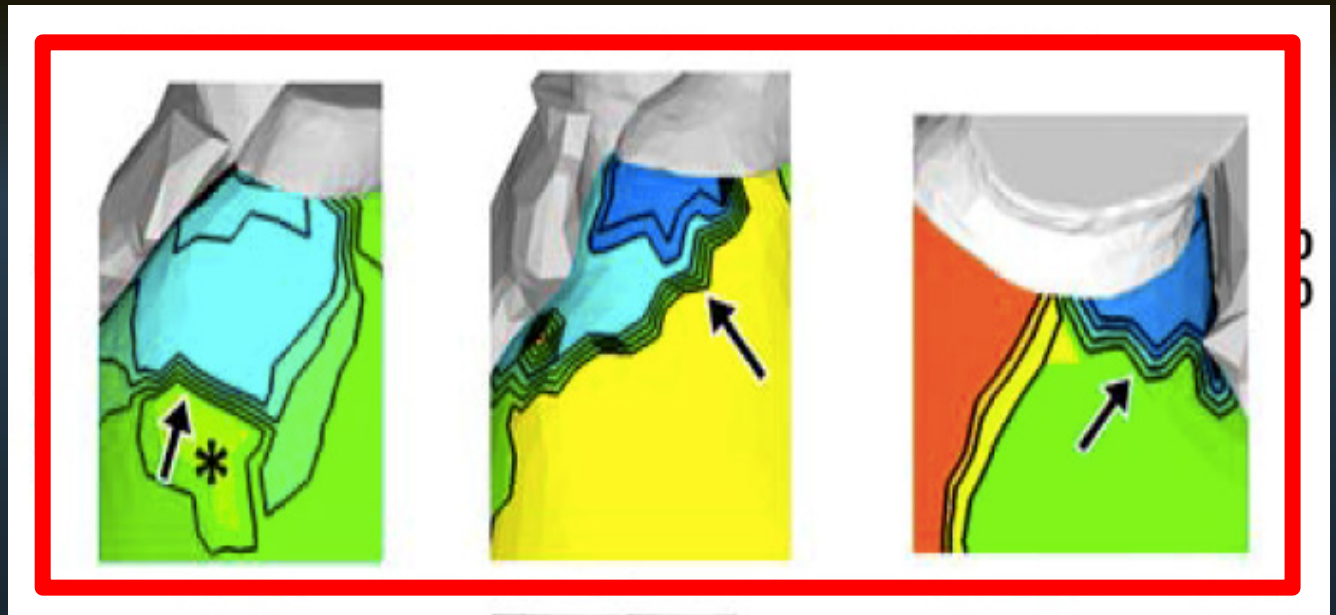
Arrhythmias

Conduction slowing





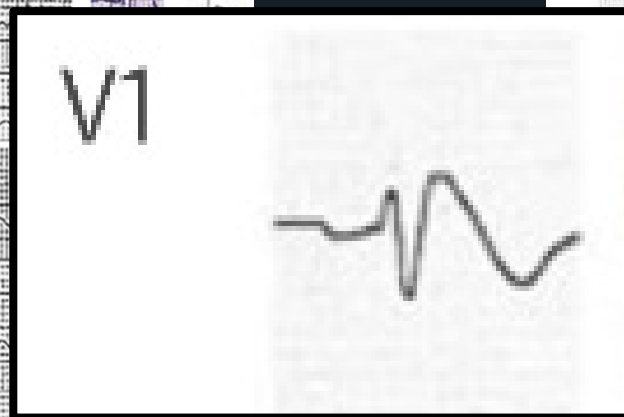
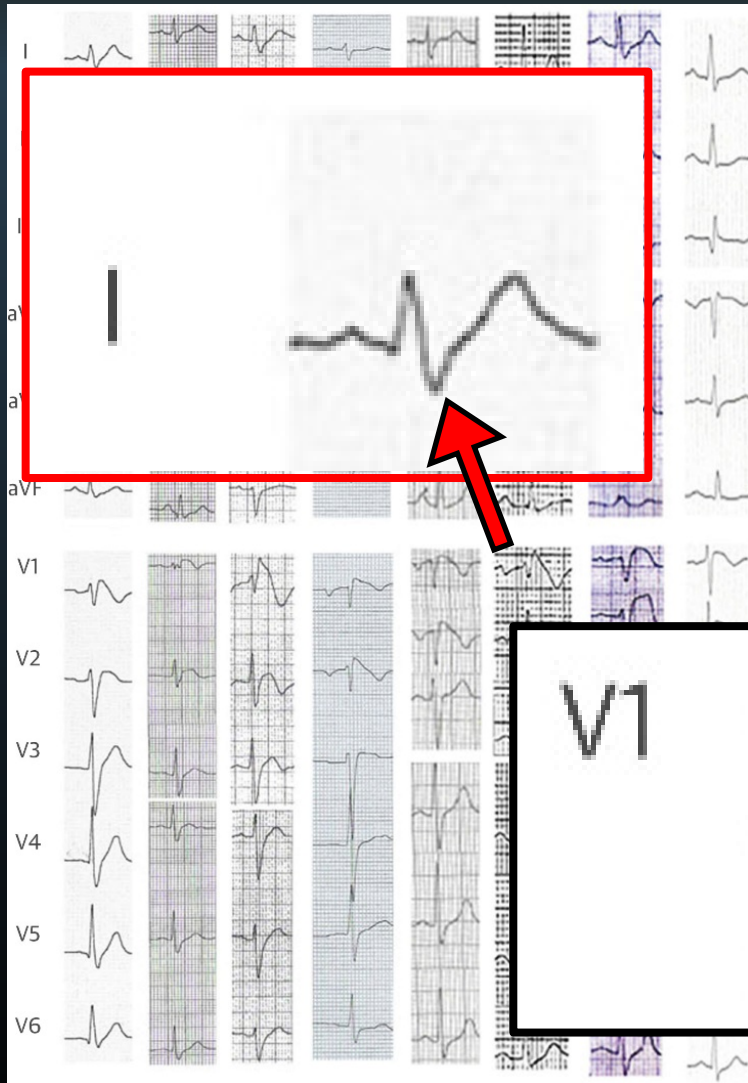
Normal



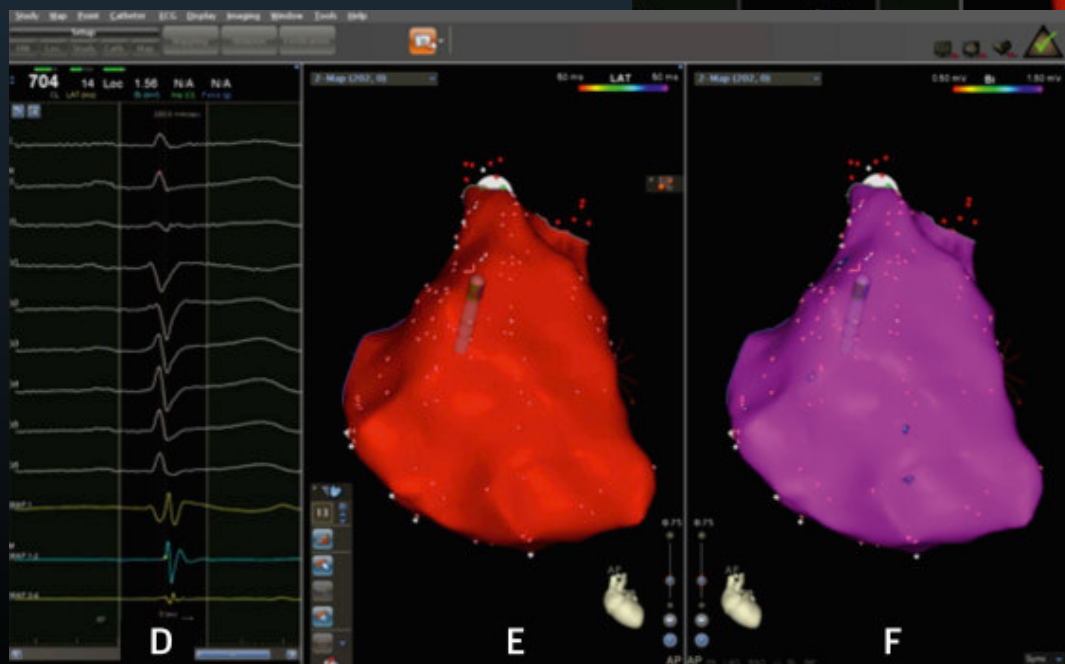
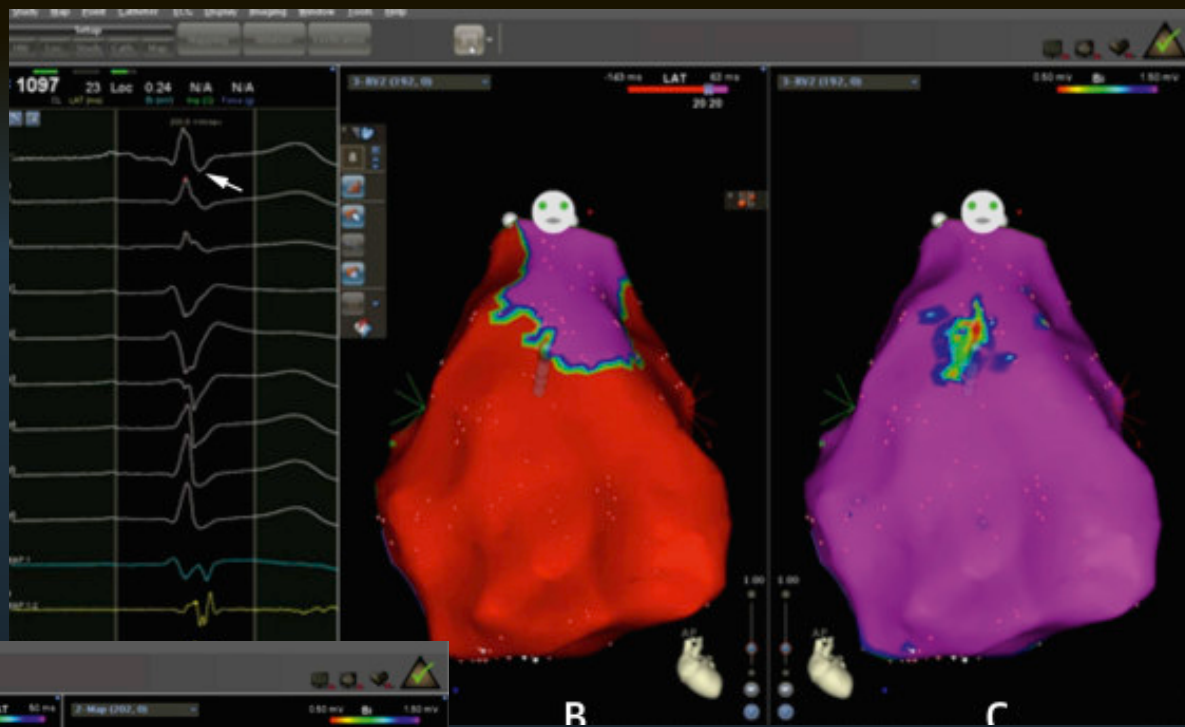
Brugada Syndrome

Delay RVOT activation

RVOT delay and **prognosis**: ECG S wave

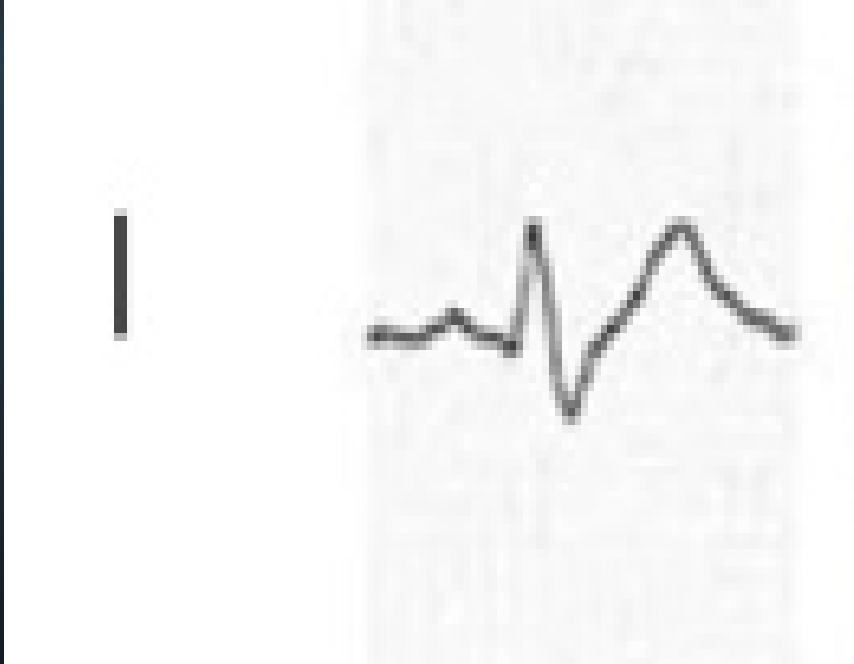


Conduction slowing



RVOT has a
delayed activation

ECG S wave



S wave in D1:

≥ 0.1 mV

≥ 40 ms

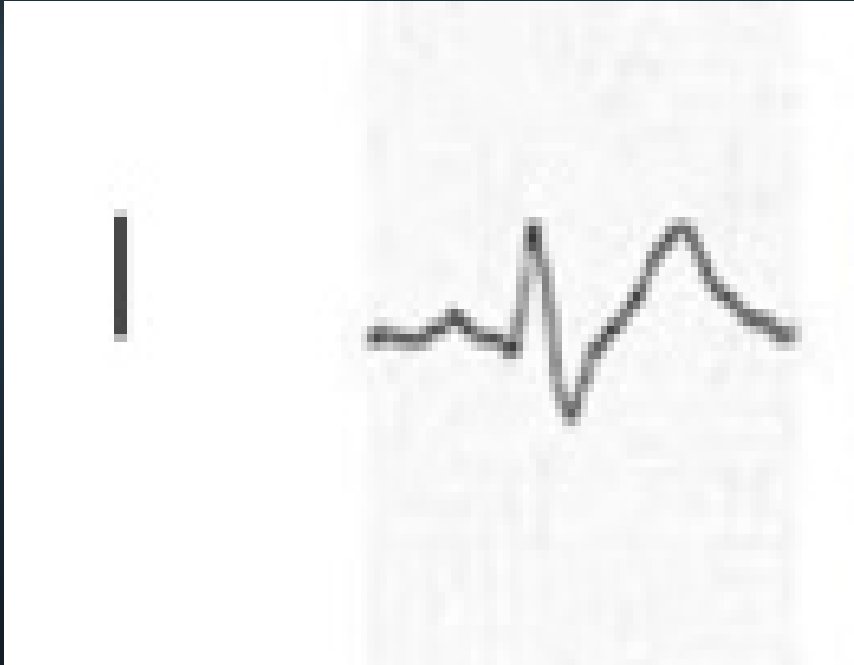
**Ventricular
arrhythmias
recurrence correlation**

sensitivity 96%, specificity 62%

negative predictive value 98%

positive predictive value 20%

ECG S wave



S wave in D1:

≥ 0.1 mV

≥ 40 ms

**Ventricular
arrhythmias
recurrence correlation**

sensitivity 96%, specificity 62%

negative predictive value 98%

positive predictive value 20%

Brugada Syndrome

**RVOT conduction
slowing seems
related to
arrhythmias**

Arrhythmia/Electrophysiology

Prevention of Ventricular Fibrillation Episodes in Brugada Syndrome by Catheter Ablation Over the Anterior Right Ventricular Outflow Tract Epicardium

Koonlawee Nademanee, MD; Gumpanart Veerakul, MD; Pakorn Chandanamattha, MD; Lertlak Chaothawee, MD; Aekarach Ariyachaipanich, MD; Kriengkrai Jirasirojanakorn, MD; Khanchit Likittanasombat, MD; Kiertijai Bhuripanyo, MD; Tachapong Ngarmukos, MD

Original Article

Brugada Syndrome Phenotype Elimination by Epicardial Substrate Ablation

Josep Brugada, MD*; Carlo Pappone, MD, PhD*; Antonio Berruezo, MD, PhD; Gabriele Vicedomini, MD; Francesco Manguso, MD, PhD; Giuseppe Ciconte, MD; Luigi Giannelli, MD; Vincenzo Santinelli, MD

14 Brugada patients

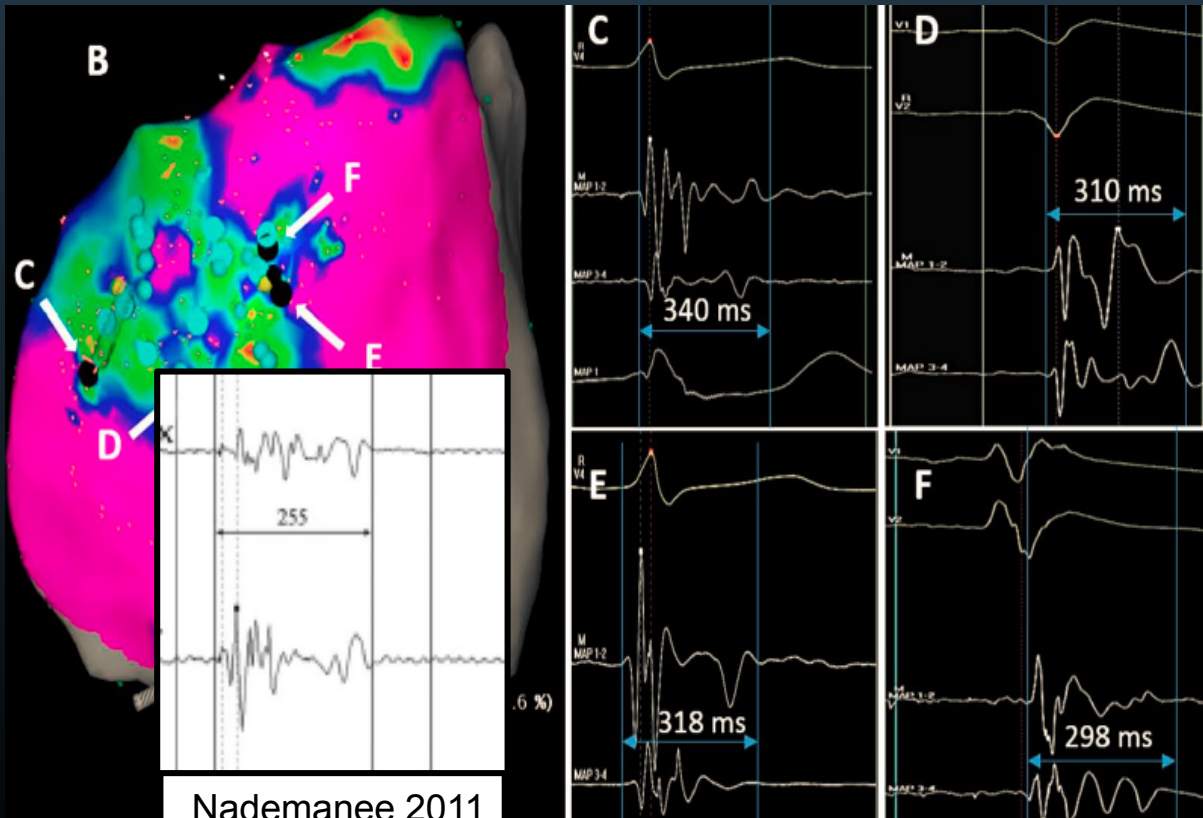
Pattern
spontaneous or
inducible

Positive
EP study

ICD carriers

Endocardial and epicardial mapping

Repeated after **flecainide infusion**



Nademanee 2011

RVOT areas of
low and
fractionated
potentials

Area dimension
**increased after
flecainide**

17.6 cm² → 28.5 cm²

RF ablation

**Complete abolition
fragmentes/delayed
signals in all patients**

**Brugada
pattern
elimination**

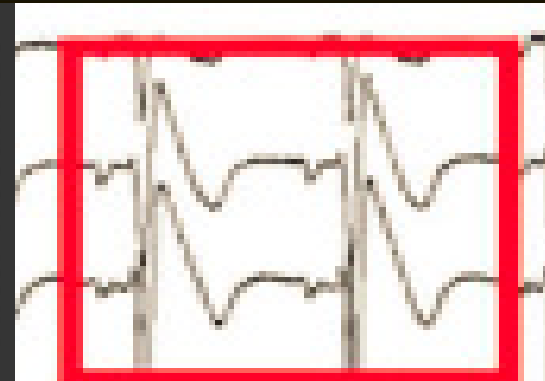
Brugada pattern

Before Ablation

Basal

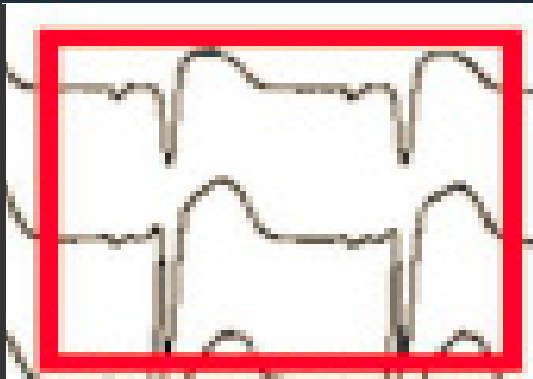


After flecainide

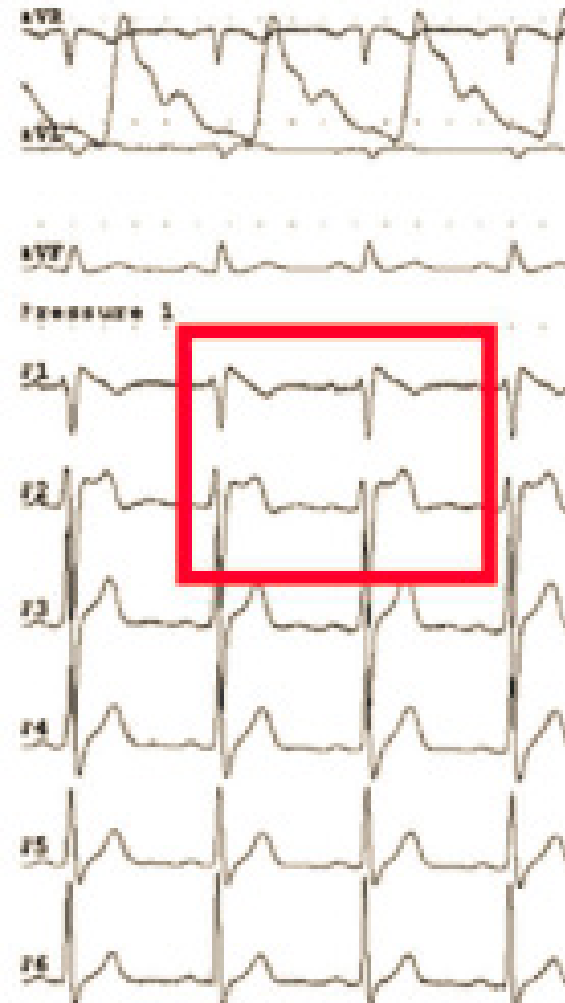
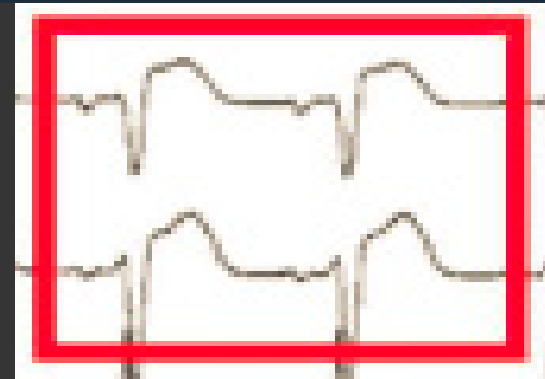


Immediately After Ablation

Basal



After flecainide



RF ablation

**Complete abolition
fragmentes/delayed
signals in all patients**

**Brugada
pattern
elimination**

**Negative
EPS**

Complications: 1 pericarditis, resolved spontaneously in 2 days

**Follow-up:
5 months**

**no arrhythmic
recurrence
(low risk pts)**

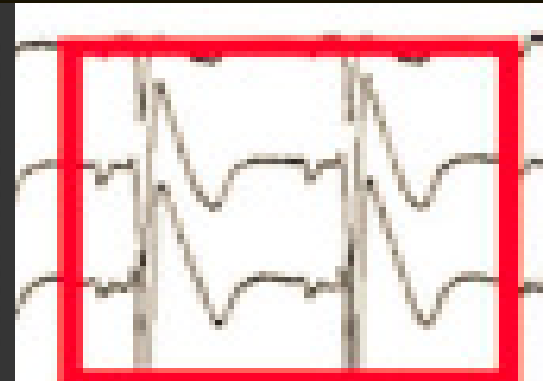
Brugada pattern

Before Ablation

Basal

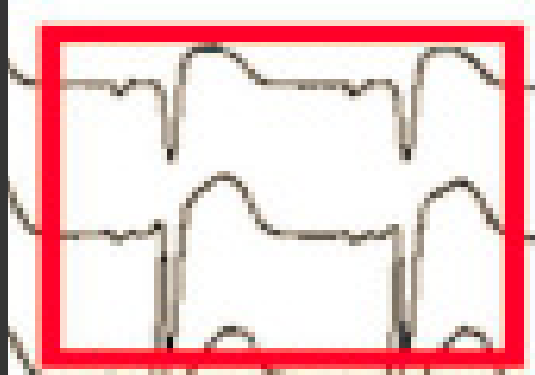


After flecainide

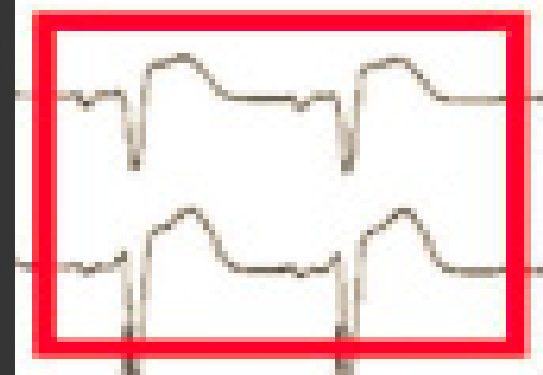


Immediately After Ablation

Basal

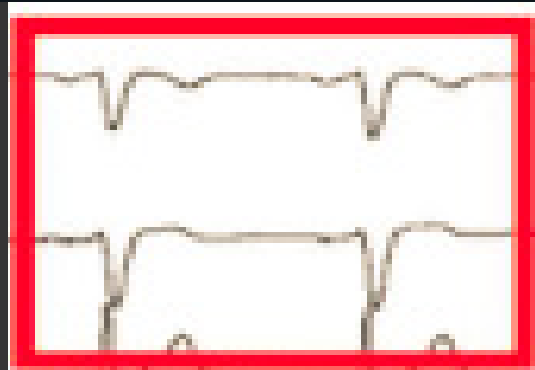


After flecainide

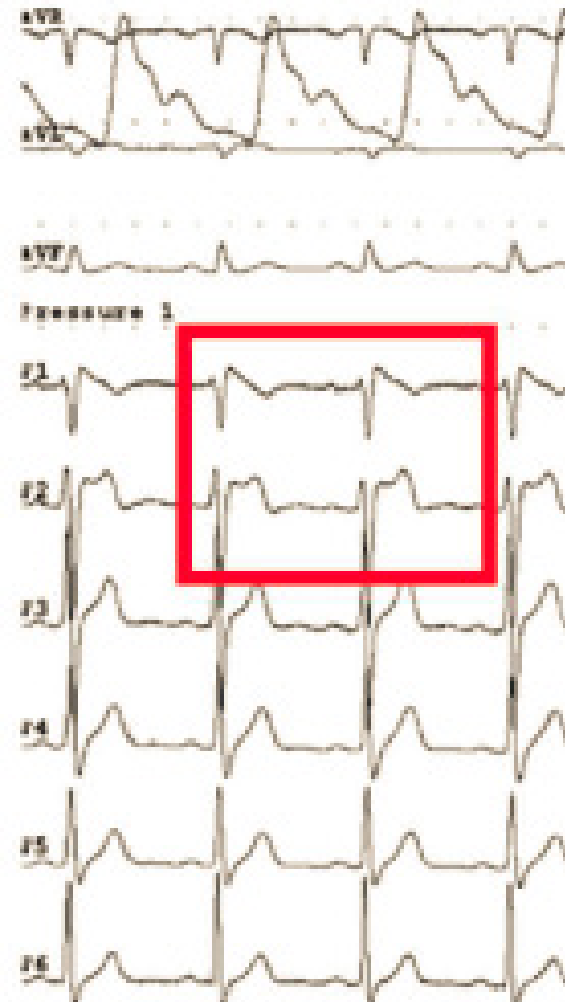


During Followup

Basal



After flecainide



RF ablation

**Complete abolition
fragmentes/delayed
signals in all patients**

**Brugada
pattern
elimination**

**Negative
EPS**

Complications: 1 pericarditis, resolved spontaneously in 2 days

**Follow-up:
5 months**

**no arrhythmic
recurrence
(low risk pts)**

**no Brugada
pattern**

Pappone-Brugada registry update

14→75 patients

2 pericarditis
2 delayed effusion drained

9 (12%) arrhythmic
storm at baseline

Followup 3-20 months

17 (22%)
spontaneous type 1

**No
arrhythmic
event**

2/75 - 2.6%
reablated
for type 1
relapse

34 (45%)
asymptomatic

Arrhythmia/Electrophysiology

ARTICLE IN PRESS

Characterization of the epicardial substrate for catheter ablation of Brugada syndrome

Pei Zhang, MS,^{*} Roderick Tung, MD, FHRS,[†] Zuwen Zhang, BS,^{*} Xia Sheng, MD,^{*} Qiang Liu, MS,^{*} Ruhong Jiang, MS,^{*} Yaxun Sun, PhD,^{*} Shiquan Chen, MS,^{*} Lu Yu, PhD,^{*} Yang Ye, PhD,^{*} Guosheng Fu, MD,^{*} Kalyanam Shivkumar, MD, PhD, FHRS,[†] Chenyang Jiang, MD^{*}

From the ^{}Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China and [†]UCLA Cardiac Arrhythmia Center, UCLA Health System, Los Angeles, California.*

by **Epicardial Substrate Ablation**

Josep Brugada, MD^{*}; Carlo Pappone, MD, PhD^{*}; Antonio Berruezo, MD, PhD;
Gabriele Vicedomini, MD; Francesco Manguso, MD, PhD; Giuseppe Ciconte, MD;
Luigi Giannelli, MD; Vincenzo Santinelli, MD

11 Brugada patients

9 with spontaneous Type 1 pattern

9 previous VF
2 prev syncope

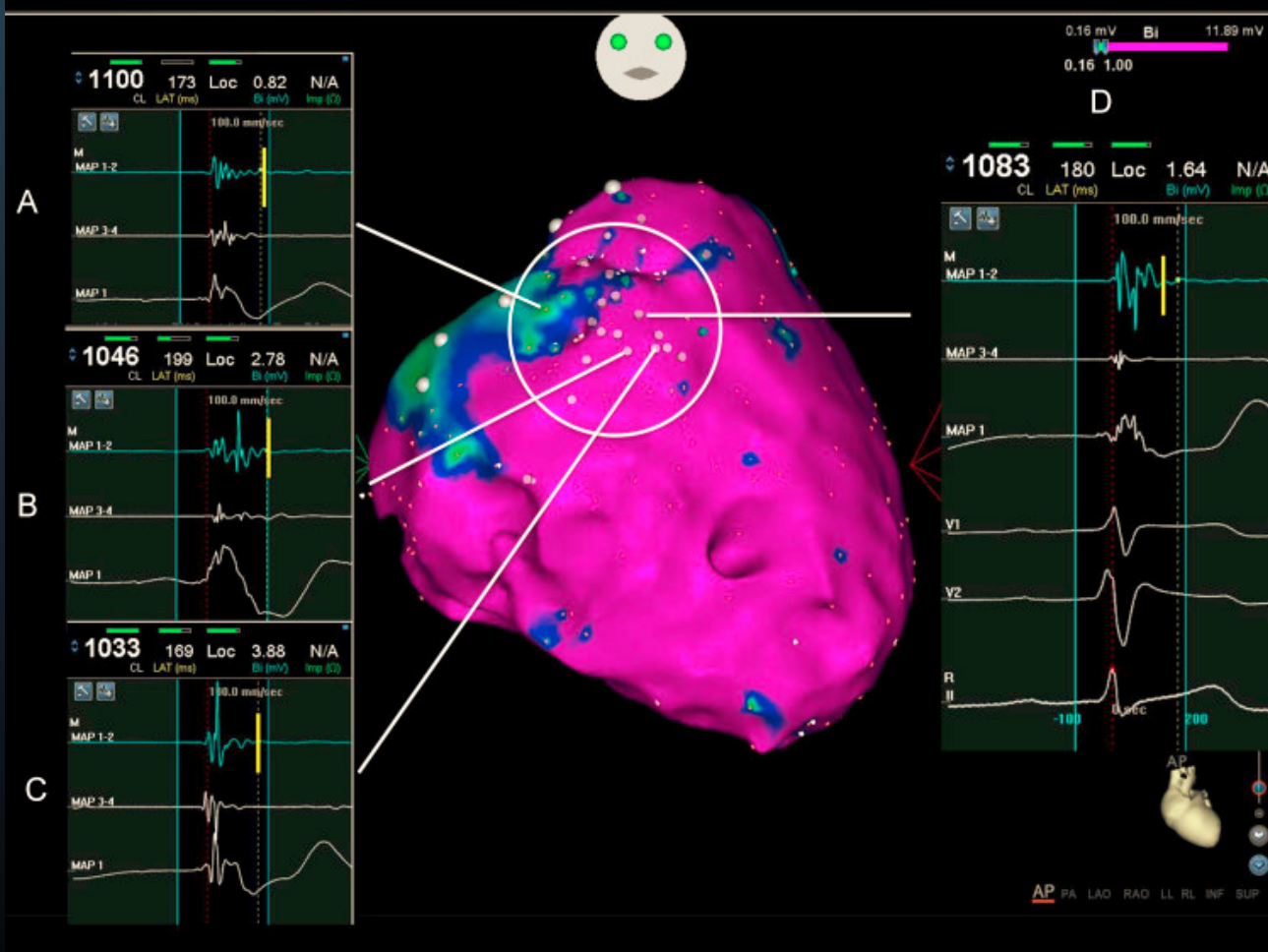
Basal and pharmacologic provocation

RF fragmented signals abolition or reduction

Disappearance type 1

EPS
Negativztation (9 pts tested)

2 pericarditis



Followup 25 +/- 11 months (11 patients)

**1 sudden
cardiac death**

**2 recurrent
VT/VF**

ECG followup

No type 1

**Type 2 or ST
elevation during
followup**

RF epicardial ablation

**Controls
arrhythmic
storms**

**Reverts
ECG Pattern**

**Doesn't protect
completely
from VF/VT**

Low rate of complications in experienced centers

Long term results?

durability?

arrhythmogenic scar?

Indication?

Pei Zhang, MS,* Roderick Tung, MD, FHRS,† Zuwen Zhang, BS,* Xia Sheng, MD,*

Qi Li, MS,* Rui Zhang, MD,* Y. G. Chen, PhD,* Chi Zhang, MD,* J. Y. Chen, PhD,*

Y. Chen, MD,*

C. Chen, MD,*

F. Chen, MD,*

of

Josep Brugada, MD*; Carlo Pappone, MD, PhD*; Antonio Berruezo, MD, PhD;
Gabriele Vicedomini, MD; Francesco Manguso, MD, PhD; Giuseppe Ciconte, MD;

RF ablation in Brugada syndrome indications, our opinion:

We *consider* RF ablation

**Patients with
ICD intervention**

Registro Brugada Piemonte 2001-2016

970 pz, 76% ♂
(età media 43 anni \pm 15)
134 portatori di ICD



Eventi al Follow-up (970 pazienti, 134 ICD)

Follow-up medio: 113 ± 50 mesi

Giugno 2001 – Aprile 2016

25 eventi aritmici

2 decessi



eventi: 2.6% dei pazienti arruolati

0.2% Morte improvvisa

RF ablation in Brugada syndrome indications, our opinion:

We *consider* RF ablation

**Patients with
ICD intervention**

**ICD carriers with no shock
but **previous cardiac arrest****

We *may consider* RF ablation

**ICD carriers with no shock
previous arrhythmic syncope**

**RF epicardial
ablation
is Not
an alternative
to ICD**

Giustetto registro brugada 2016, Sacher Circ 2013

Giustetto, Europace 2009, Sacher Circ 2013, Probst Circualtion 2010

Giustetto registro brugada 2016, Sacher Circ 2013