

Epicardial ablation in Brugada syndrome



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Case 1

- M/52 yrs

- BHx>

Seizure like movement during sleeping, Visit other hospital

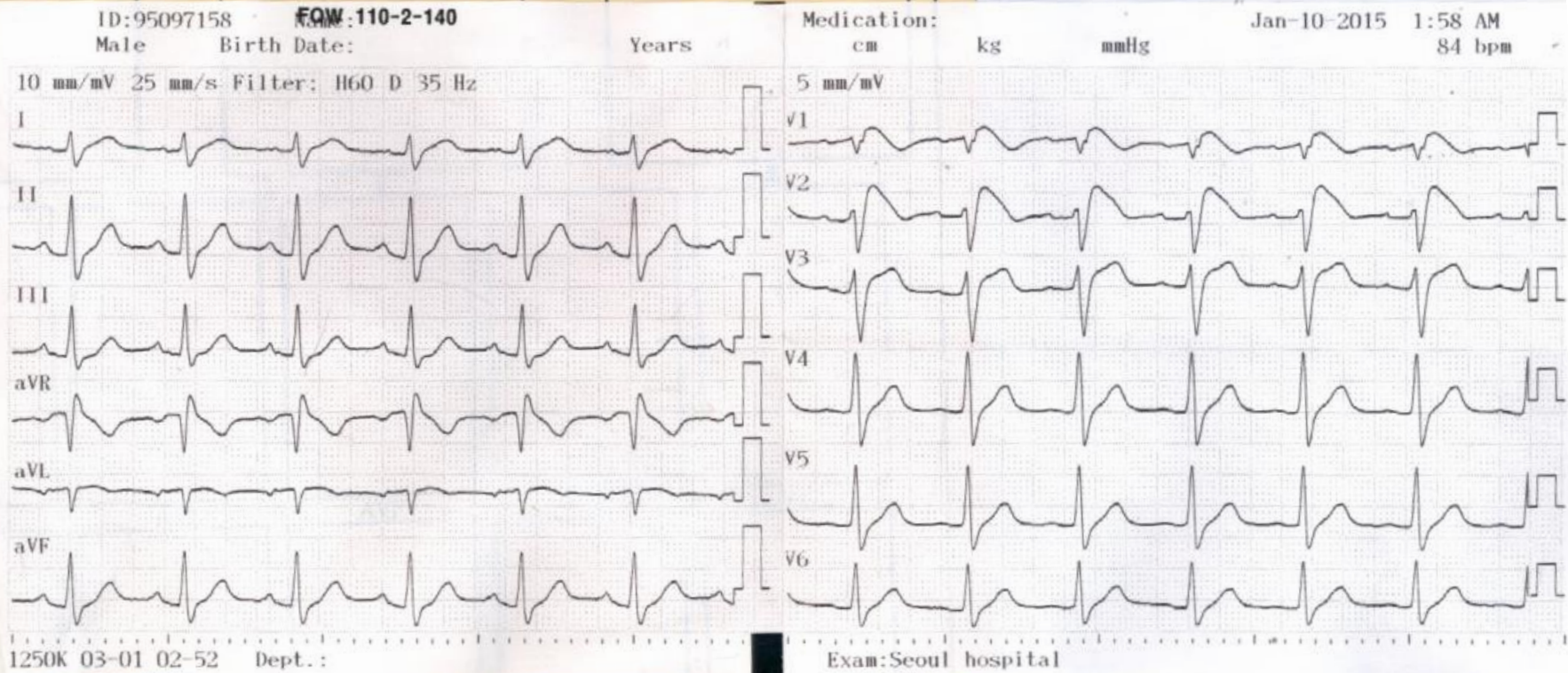
sudden cardiac arrest & VF

Resuscitated after CPR and defibrillation

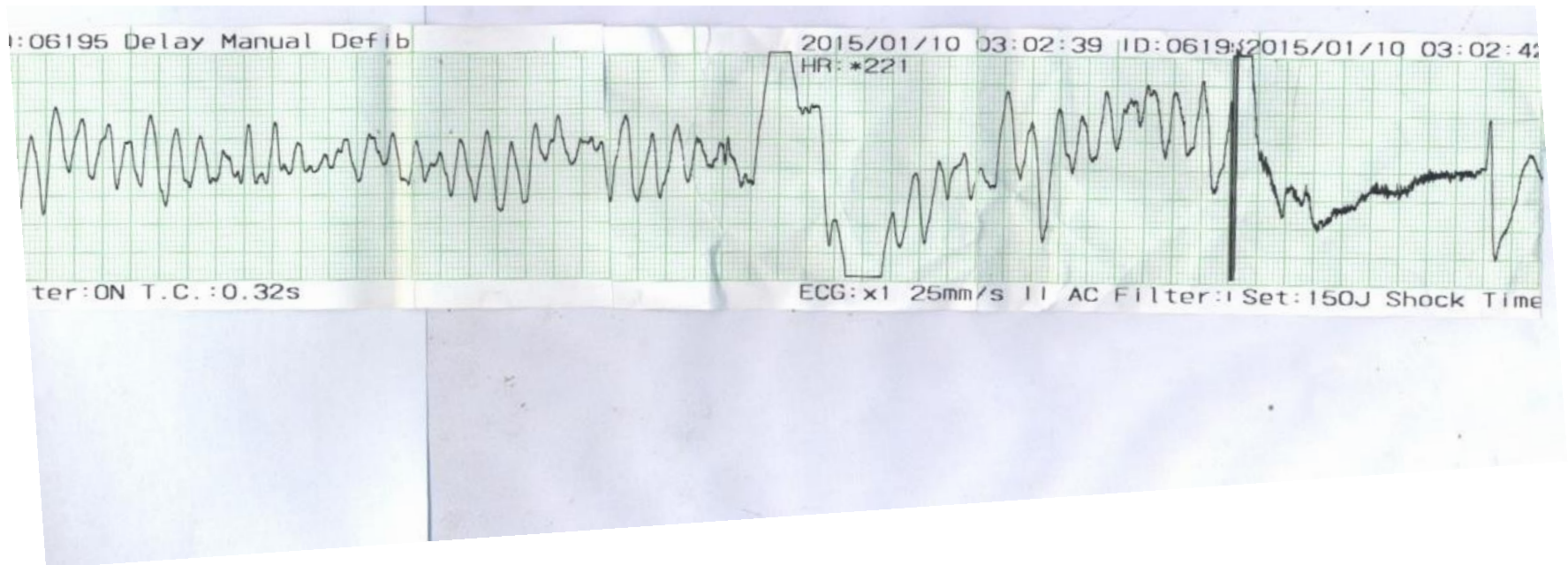
2 years prior to admission; seizure like movement

- FHx of syncope or SCD> none

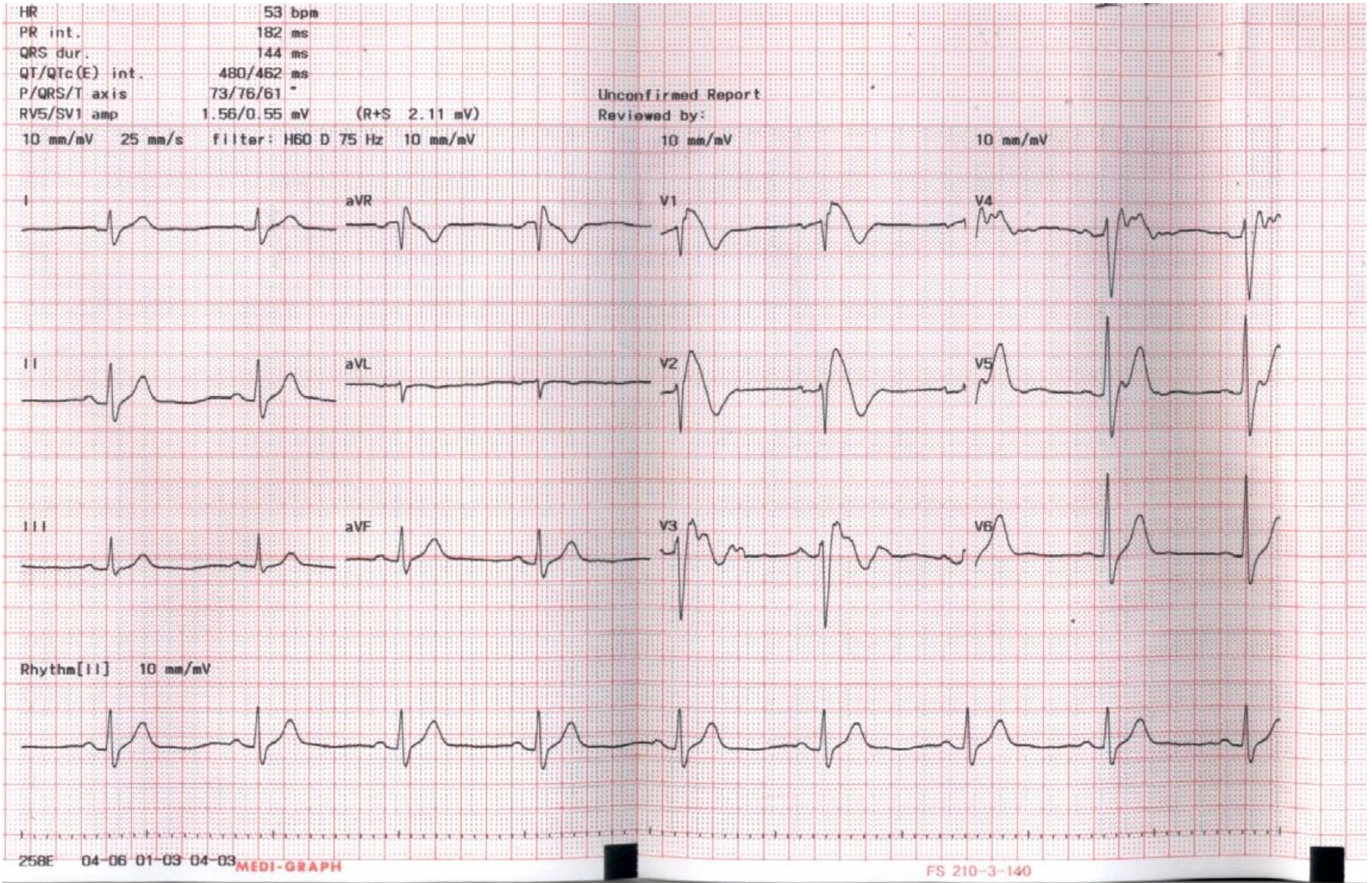
Initial ECG at other hospital



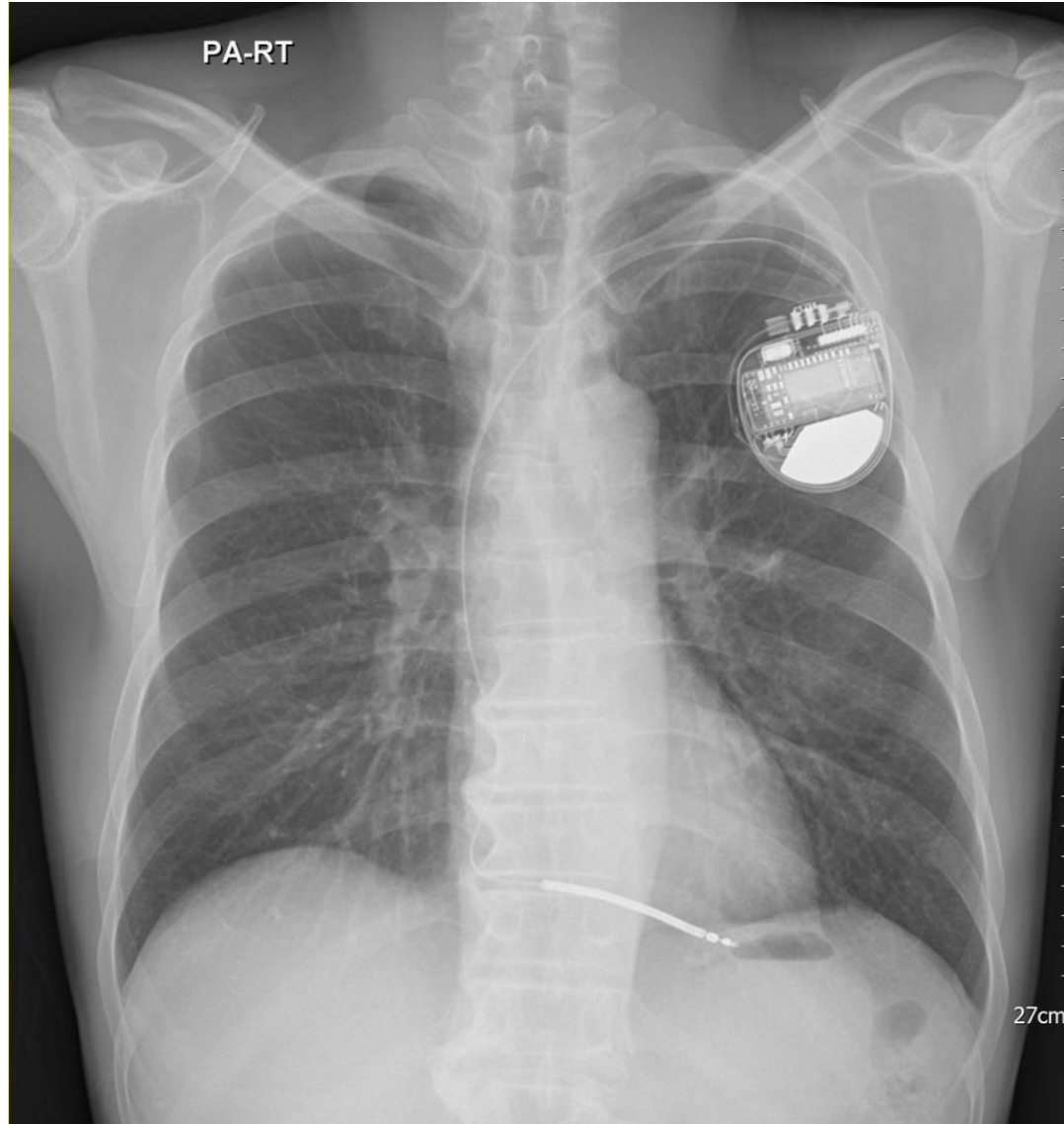
VF at other hospital



ECG at ER



ICD implantation; secondary prevention



Appropriate shock d/t VF

Treated VT/VF Episode #4

Device: Evera XT VR DVBB2D4

Serial Number: BWJ604772S

Date of Visit: 06-Jul-2015 09:21:14

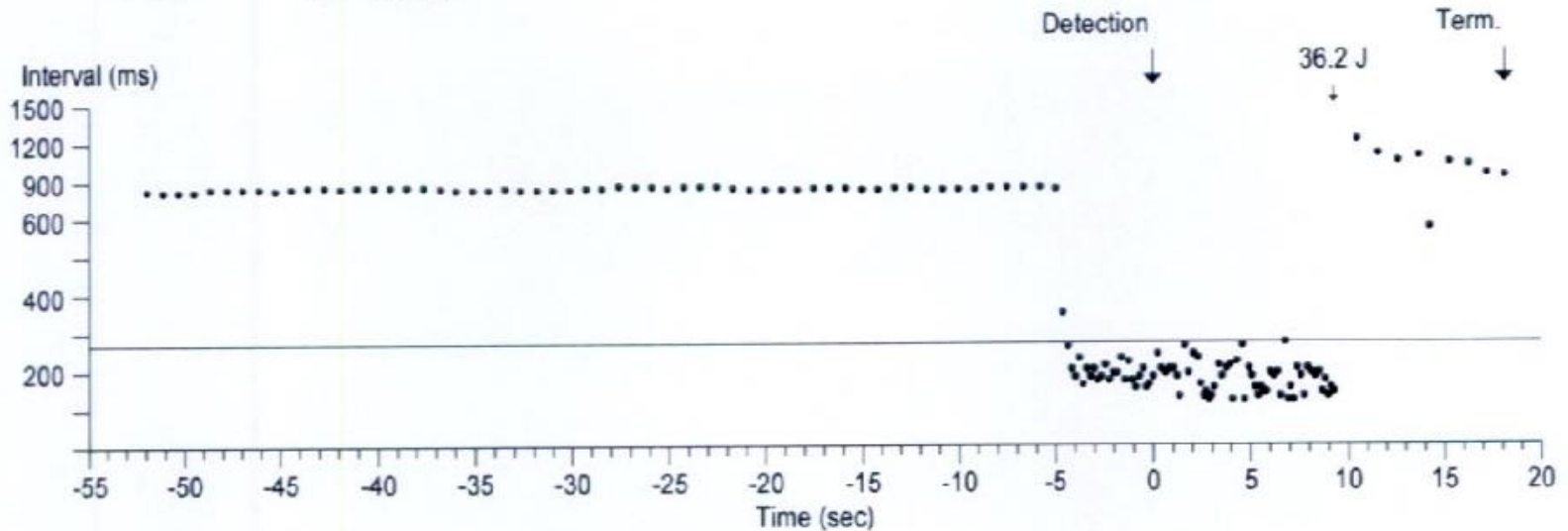
Patient: SUNG JAE, LEE

ID: 32037533

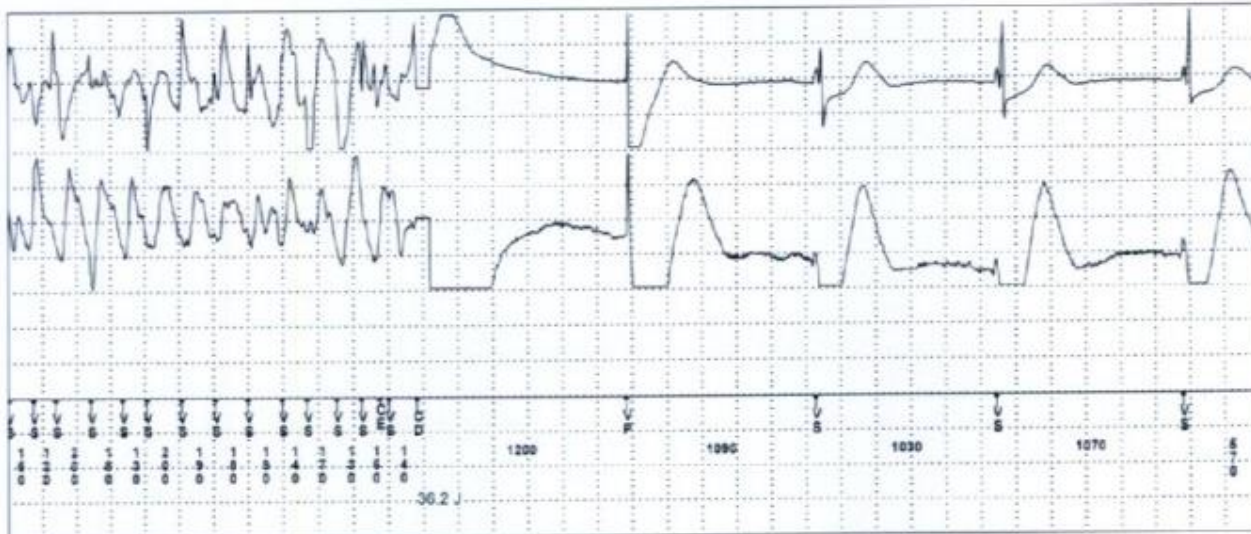
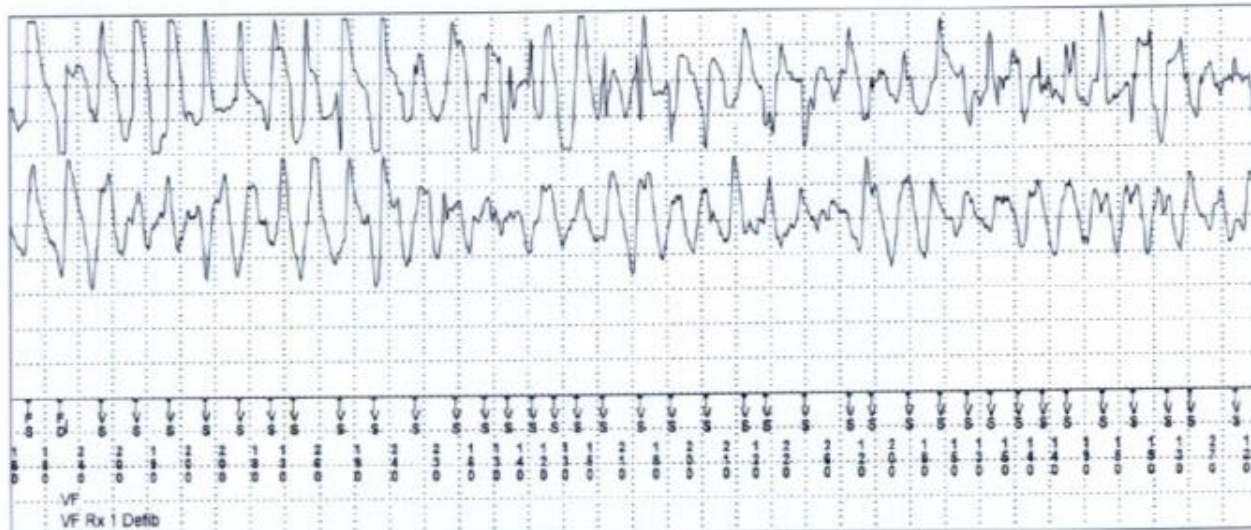
Physician: Ghoj, In-Seok ---

Type	ATP Seq	Shocks	Success	ID#	Date	Time hh:mm	Duration hh:mm:ss	Avg bpm V	Max bpm V	Activity at Onset
VF	0	35J	Yes	4	02-Jul-2015	23:01	:15	353	--	Rest

• V-V VF = 270 ms

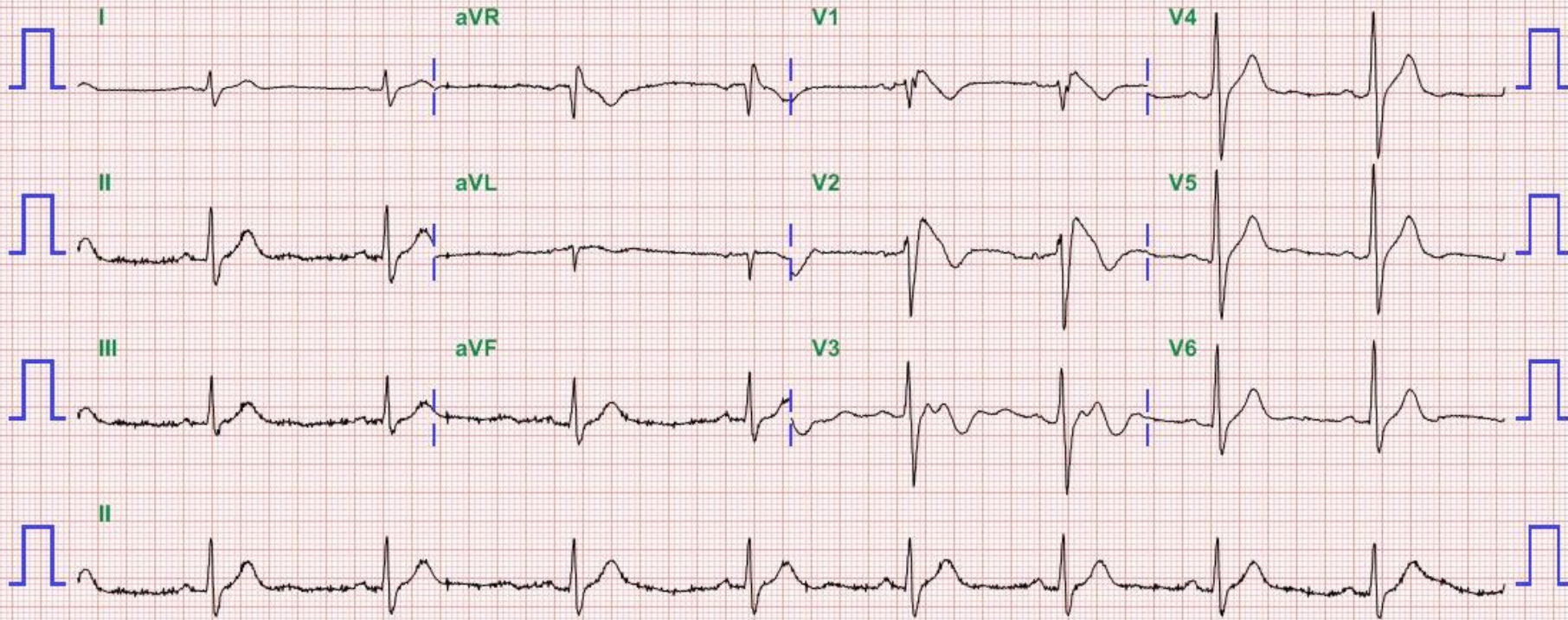


Appropriate shock d/t VF



Quinidine 300mg tid

ECG; consistent Brugada type I



Appropriate shock d/t VF during quinidine

Treated VT/VF Episode #14

Device: Evert XT VR DVBB2D4

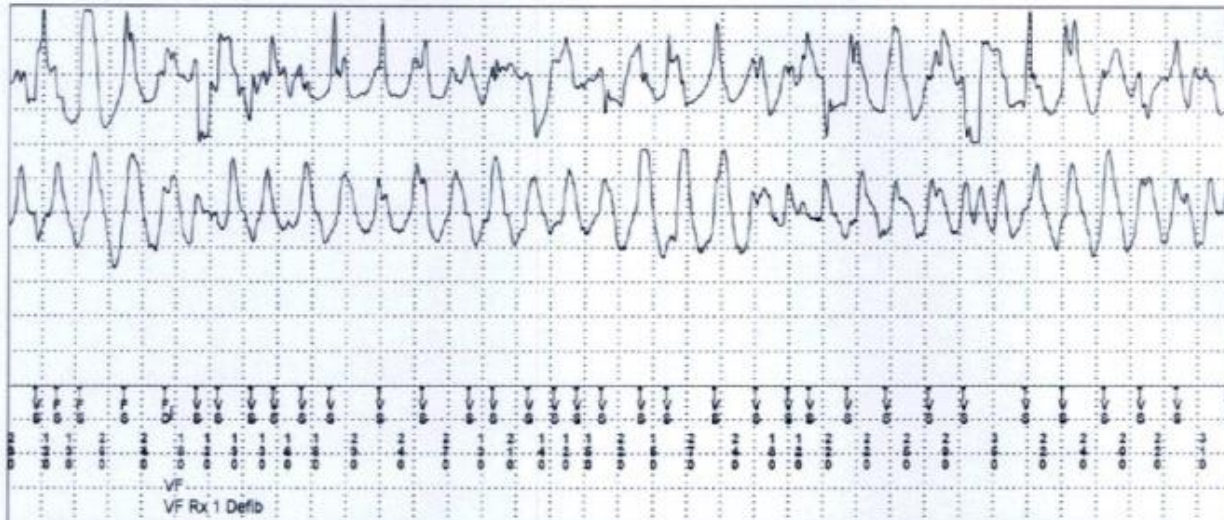
Serial Number: BWJ604772S

Date of Visit: 16-May-2016 12:19:13

Patient: SUNG JAE, LEE

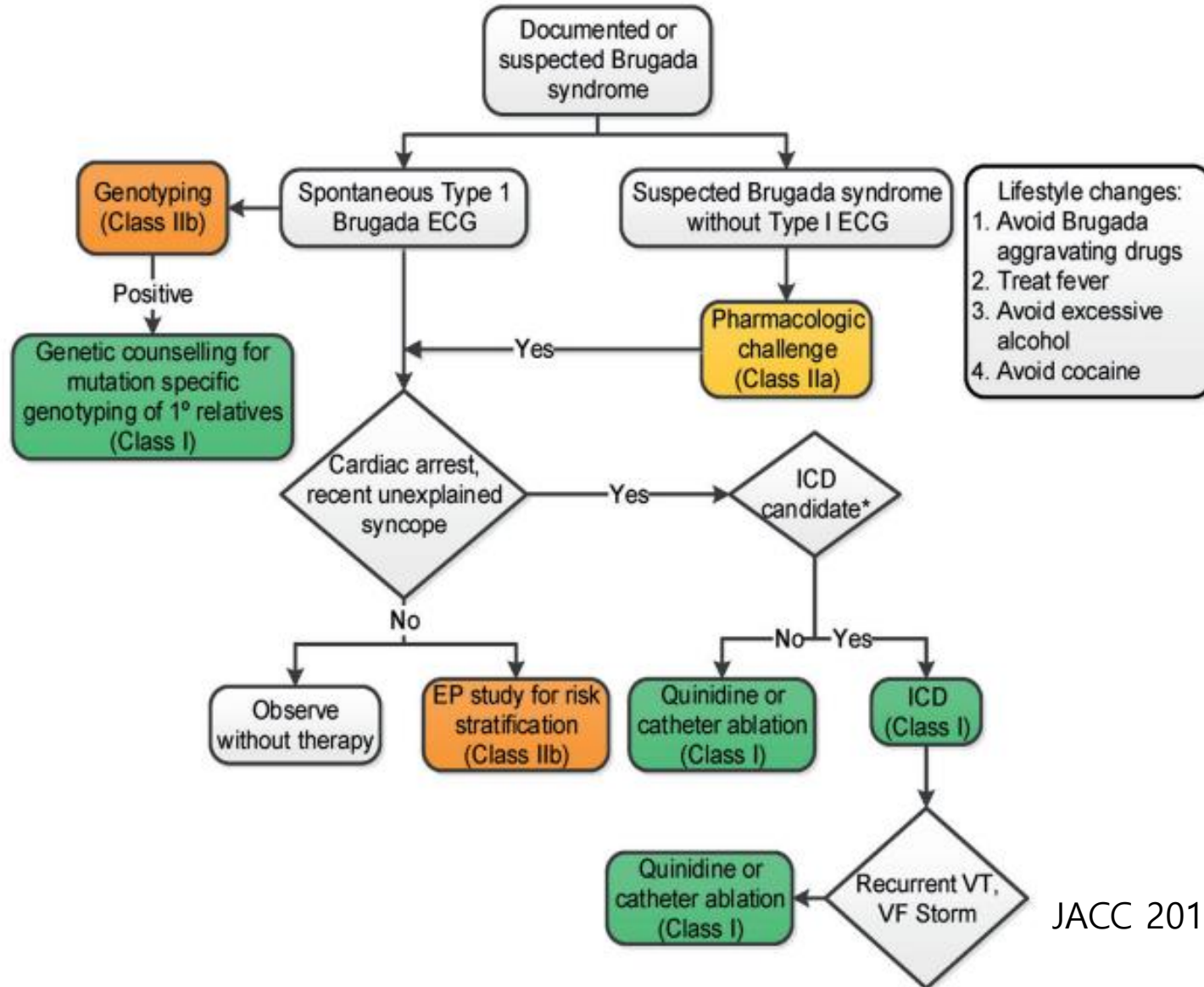
ID: 32037533

Episode #14 - VF Chart speed: 25.0 mm/sec



**What is your next
option?**

Prevention of SCD in BrS



JACC 2017 VA/SCD guideline

Recommendations for BrS

COR	LOE	RECOMMENDATIONS
I	B-NR	1. In asymptomatic patients with only inducible type 1 Brugada electrocardiographic pattern, observation without therapy is recommended.
I	B-NR	2. In patients with Brugada syndrome with spontaneous type 1 Brugada electrocardiographic pattern and cardiac arrest, sustained VA or a recent history of syncope presumed due to VA, an ICD is recommended if meaningful survival of greater than 1 year is expected (S7.9.1.3-4,S7.9.1.3-6).
I	B-NR	3. In patients with Brugada syndrome experiencing recurrent ICD shocks for polymorphic VT, intensification of therapy with quinidine or catheter ablation is recommended (S7.9.1.3-7–S7.9.1.3-11).
I	B-NR	4. In patients with spontaneous type 1 Brugada electrocardiographic pattern and symptomatic VA who either are not candidates for or decline an ICD, quinidine or catheter ablation is recommended (S7.9.1.3-7,S7.9.1.3-9–S7.9.1.3-11).
IIa	B-NR	5. In patients with suspected Brugada syndrome in the absence of a spontaneous type 1 Brugada electrocardiographic pattern, a pharmacological challenge using a sodium channel blocker can be useful for diagnosis (S7.9.1.3-12–S7.9.1.3-14).
IIb	B-NR ^{SR}	6. In patients with asymptomatic Brugada syndrome and a spontaneous type 1 Brugada electrocardiographic pattern, an electrophysiological study with programmed ventricular stimulation using single and double extrastimuli may be considered for further risk stratification (S7.9.1.3-1,S7.9.1.3-6, S7.9.1.3-13,S7.9.1.3-15–S7.9.1.3-17).
IIb	C-EO	7. In patients with suspected or established Brugada syndrome, genetic counseling and genetic testing may be useful to facilitate cascade screening of relatives (S7.9.1.3-18–S7.9.1.3-20).

Recommendations for BrS

Risk stratification, prevention of SCD and treatment of VA

ICD implantation is recommended in patients with BrS who: (a) Are survivors of an aborted CA and/or (b) Have documented spontaneous sustained VT. ^{980,990-992}	I	C
ICD implantation should be considered in patients with type 1 Brugada pattern and an arrhythmic syncope. ^{990,992,996}	IIa	C
Implantation of a loop recorder should be considered in BrS patients with an unexplained syncope. ^{997,999}	IIa	C
Quinidine should be considered in patients with BrS who qualify for an ICD but have a contraindication, decline, or have recurrent ICD shocks. ^{922,1006,1007}	IIa	C

Isoproterenol infusion should be considered in BrS patients suffering electrical storm. ¹⁰⁰⁸	IIa	C
Catheter ablation of triggering PVCs and/or RVOT epicardial substrate should be considered in BrS patients with recurrent appropriate ICD shocks refractory to drug therapy. ¹⁰¹⁰⁻¹⁰¹⁵	IIa	C
PES may be considered in asymptomatic patients with a spontaneous type I BrS ECG. ¹⁵⁵	IIb	B
ICD implantation may be considered in selected asymptomatic BrS patients with inducible VF during PES using up to 2 extra stimuli. ¹⁵⁵	IIb	C
Catheter ablation in asymptomatic BrS patients is not recommended.	III	C

Catheter ablation may be considered in patients with a history of electrical storms or repeated appropriate ICD shocks.	IIb	C	201, 455
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Catheter ablation for BrS

Mapping and Ablation of Ventricular Fibrillation Associated With Long-QT and Brugada Syndromes

Michel Haïssaguerre, MD; Fabrice Extramiana, MD; Mélèze Hocini, MD; Bruno Cauchemez, MD; Pierre Jaïs, MD; Jose Angel Cabrera, MD; Geronimo Farre, MD; Antoine Leenhardt, MD; Prashanthan Sanders, MBBS; Christophe Scavée, MD; Li-Fern Hsu, MBBS; Rukshen Weerasooriya, MBBS; Dipen C. Shah, MD; Robert Frank, MD; Philippe Maury, MD; Marc Delay, MD; Stéphane Garrigue, MD; Jacques Clémenty, MD

Endocardial ablation of ventricular ectopy (RVOT or purkinje) prevented VF.

Epicardial catheter ablation for BrS ; epicardial substrate modification

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Association®



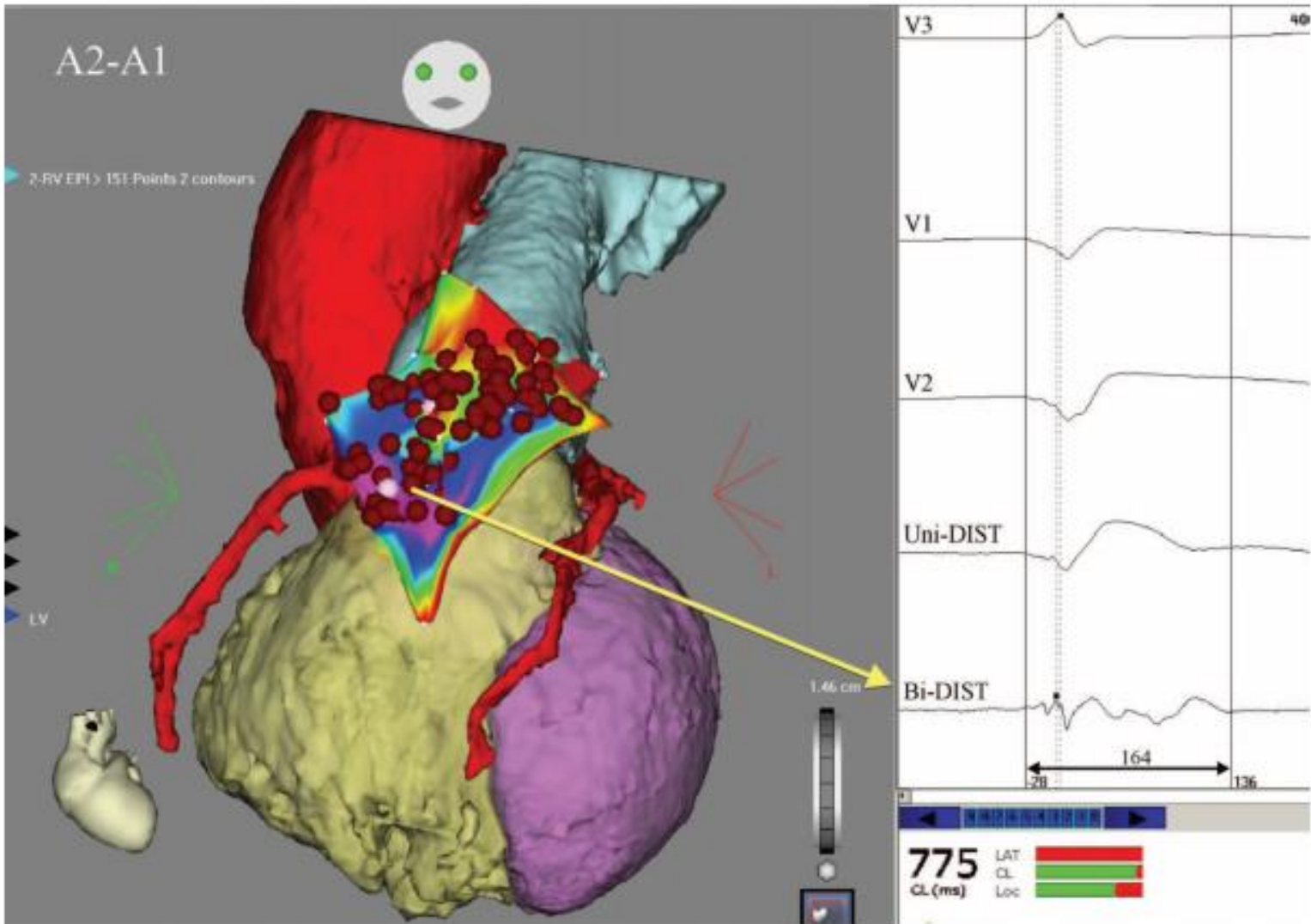
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Prevention of Ventricular Fibrillation Episodes in Brugada Syndrome by Catheter Ablation Over the Anterior Right Ventricular Outflow Tract Epicardium

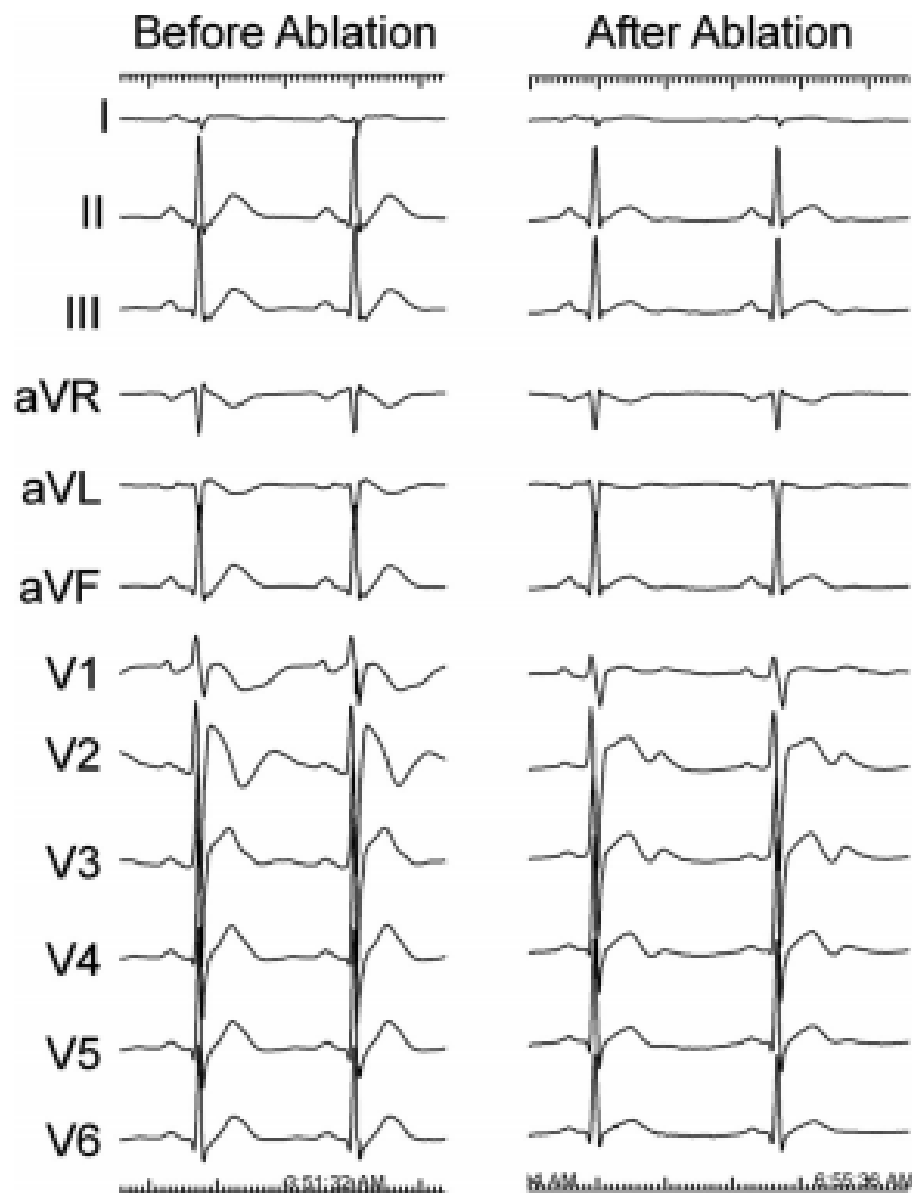
Koonlawee Nademanee, Gumpanart Veerakul, Pakorn Chandanamatta, Lertlak
Chaothawee, Aekarach Ariyachaipanich, Kriengkrai Jirasirojanakorn, Khanchit
Likittanasombat, Kiertijai Bhuripanyo and Tachapong Ngarmukos

Circulation published online Mar 14, 2011;

Low voltage, prolonged duration of the fractionated electrogram > 150ms



Normalization of Brugada ECG pattern after the end of successful procedure



Circulation 2011;123:1270

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

Background—Whether Brugada syndrome (BrS) depends on functional epicardial substrates, which may be definitively eliminated by radiofrequency ablation, remains unknown.

Methods and Results—Patients with BrS underwent epicardial mapping to identify areas of abnormal electrograms as target for radiofrequency ablation. Substrate identification consisted in mapping right ventricle epicardial surface before and after flecainide (2 mg/kg per 10 minutes). After radiofrequency ablation, flecainide and remap confirmed elimination of abnormal substrate, BrS ECG pattern, and ventricular tachycardia/ventricular fibrillation inducibility. Flecainide testing was performed at each follow-up visits ≤ 6 months. Fourteen patients with BrS, median age 39 years (30.3–42.3) with implantable cardioverter–defibrillator were enrolled. Low-voltage areas (<1.5 mV) were commonly identified on the anterior right free wall and right ventricular outflow tract, which increased after flecainide from 17.6 cm² (12.1–24.2) to 28.5 cm² (21.6–30.2; $P=0.001$). Similarly, areas with abnormal electrograms increased after flecainide from 19.0 (17.5–23.6) to 27.3 cm² (24.0–31.2; $P=0.001$). After 23.8 minutes (18.1–28.5) of radiofrequency ablation, abnormal electrograms disappeared, whereas low-voltage areas were replaced by scar areas (<0.5 mV) of 25.9 cm² (19.6–31.0). Substrate elimination resulted in BrS ECG pattern disappearance and no ventricular tachycardia/ventricular fibrillation inducibility without complications. After a median follow-up of 5 months (3.8–5.3), ECG remained normal despite flecainide.

Conclusions—In patients with BrS, there is a relationship between abnormal ECG pattern, the extent of abnormal epicardial substrate, and ventricular tachycardia/ventricular fibrillation inducibility. Ablation of the substrate identified in the presence of flecainide can eliminate the BrS phenotype and warrants further study. (*Circ Arrhythm Electrophysiol.* 2015;8:1373-1381. DOI: 10.1161/CIRCEP.115.003220.)

Key Words: Brugada syndrome ■ flecainide ■ heart ■ phenotype ■ sudden cardiac death

Electrical Substrate Elimination in 135 Consecutive Patients With Brugada Syndrome

Carlo Pappone, MD, PhD*; Josep Brugada, MD, PhD*; Gabriele Vicedomini, MD; Giuseppe Ciconte, MD; Francesco Manguso, MD, PhD; Massimo Saviano, MD; Raffaele Vitale, MD; Amarild Cuko, MD; Luigi Giannelli, MD; Zarko Calovic, MD; Manuel Conti, MD; Paolo Pozzi, Eng; Andrea Natalizia, PhD, Eng; Simonetta Crisà, Eng; Valeria Borrelli, PhD; Ramon Brugada, MD, PhD; Georgia Sarquella-Brugada, MD, PhD; Marco Guazzi, MD; Alessandro Frigiola, MD; Lorenzo Menicanti, MD; Vincenzo Santinelli, MD

Background—There is emerging evidence that localization and elimination of abnormal electric activity in the epicardial right ventricular outflow tract may be beneficial in patients with Brugada syndrome.

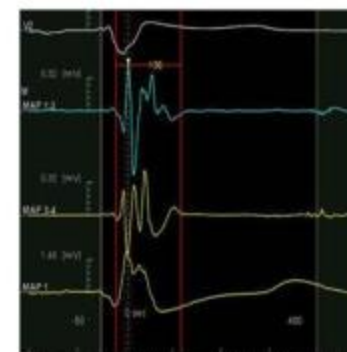
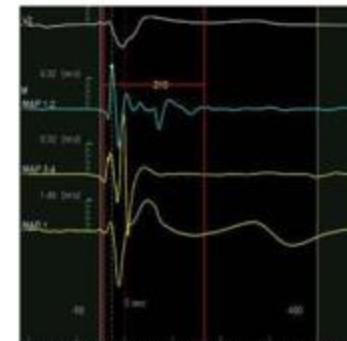
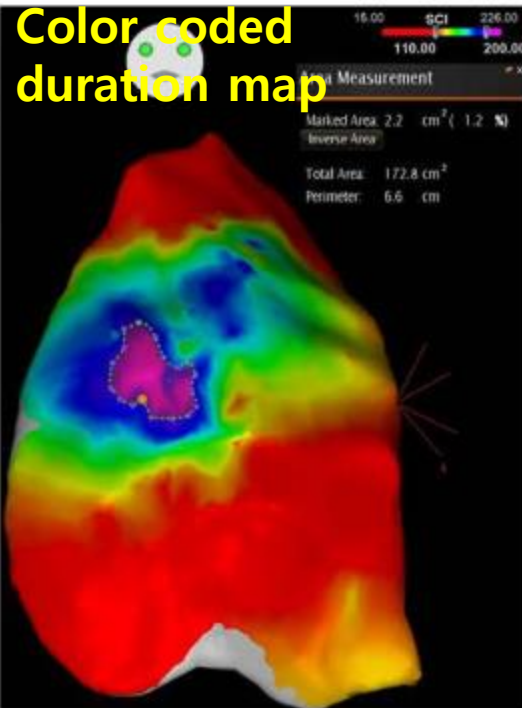
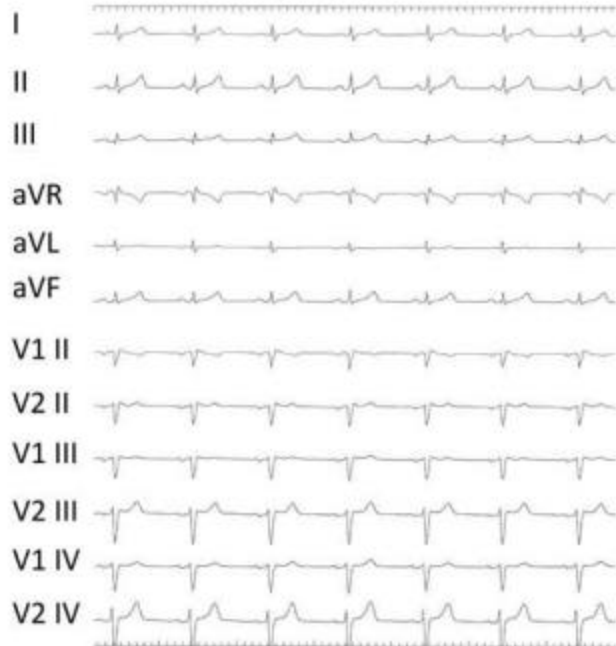
Methods and Results—A total of 135 symptomatic Brugada syndrome patients having implantable cardiac defibrillator were enrolled: 63 (group 1) having documented ventricular tachycardia (VT)/ventricular fibrillation (VF) and Brugada syndrome–related symptoms, and 72 (group 2) having inducible VT/VF without ECG documentation at the time of symptoms. About 27 patients of group 1 experienced multiple implantable cardiac defibrillator shocks for recurrent VT/VF episodes. Three-dimensional maps before and after ajmaline determined the arrhythmogenic electrophysiological substrate (AES) as characterized by prolonged fragmented ventricular potentials. Primary end point was identification and elimination of AES leading to ECG pattern normalization and VT/VF noninducibility. Extensive areas of AES were found in the right ventricle epicardium, which were wider in group 1 ($P=0.007$). AES increased after ajmaline in both groups ($P<0.001$) and was larger in men ($P=0.008$). The increase of type-1 ST-segment elevation correlated with AES expansion ($r=0.682$, $P<0.001$). Radiofrequency ablation eliminated AES leading to ECG normalization and VT/VF noninducibility in all patients. During a median follow-up of 10 months, the ECG remained normal even after ajmaline in all except 2 patients who underwent a repeated effective procedure for recurrent VF.

Conclusions—In Brugada syndrome, AES is commonly located in the right ventricle epicardium and ajmaline exposes its extent and distribution, which is correlated with the degree of coved ST-elevation. AES elimination by radiofrequency ablation results in ECG normalization and VT/VF noninducibility. Substrate-based ablation is effective in potentially eliminating the arrhythmic consequences of this genetic disease.

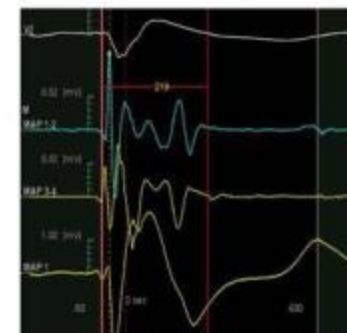
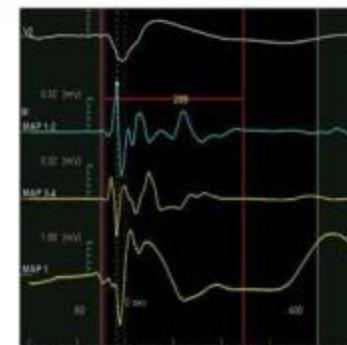
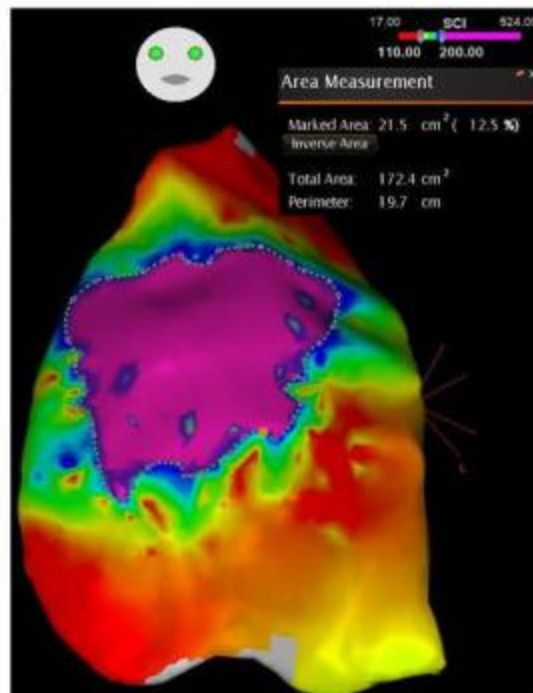
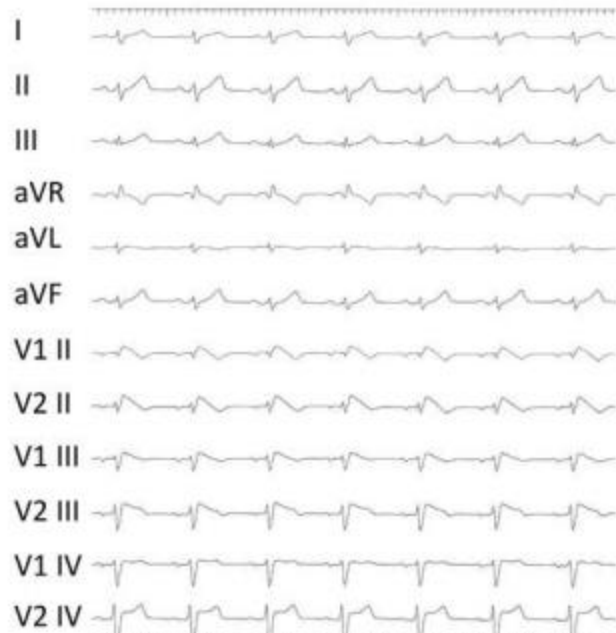
Clinical Trial Registration—URL: <https://clinicaltrials.gov>. Unique identifier: NCT02641431.

(*Circ Arrhythm Electrophysiol.* 2017;10:e005053. DOI: 10.1161/CIRCEP.117.005053.)

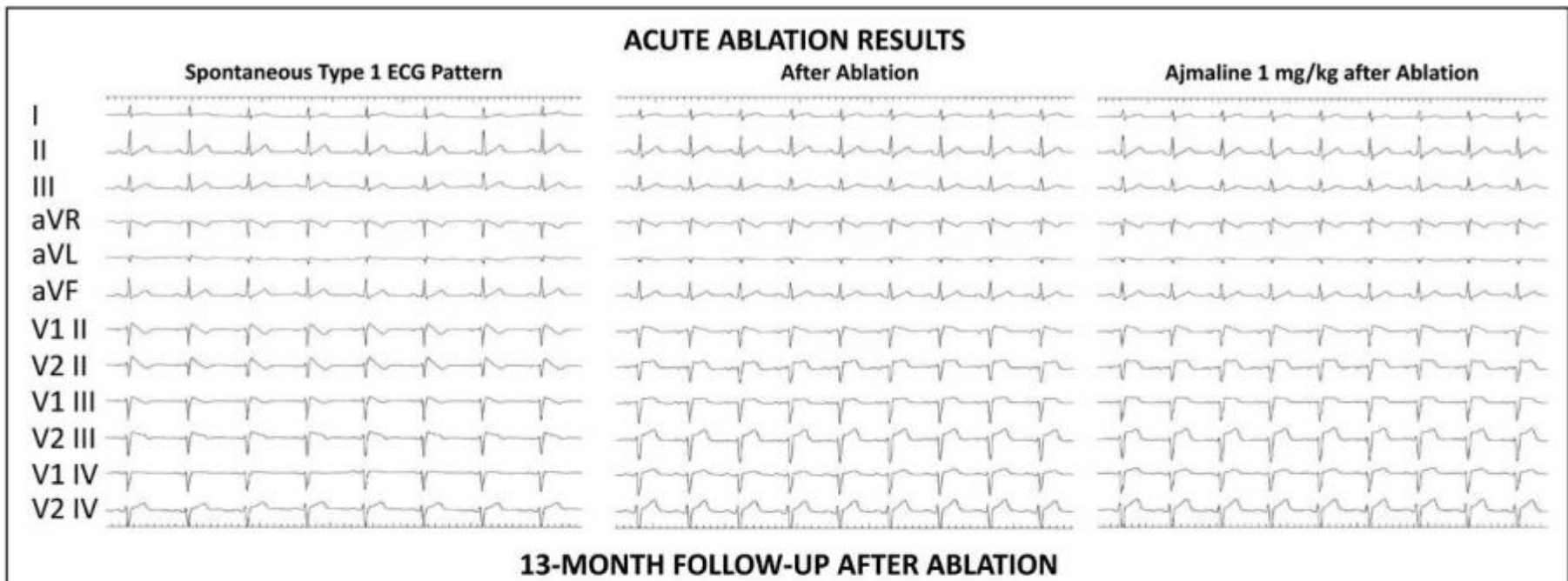
BASELINE



AJMALINE CHALLENGE



ECG changes after ablation




1. AES is commonly located in the right ventricle epicardium and ajmaline exposes its extent and distribution, which is correlated with the degree of coved ST-elevation.
2. AES elimination by ablation results in ECG normalization & VT/VF noninducibility.
3. Substrate-based ablation is effective in potentially eliminating the arrhythmic consequences of this genetic disease.



Case

Case Report

Early Response after Catheter Ablation of the Epicardial Substrate in a Patient with Brugada Syndrome Can Be Predicted by High Precordial Leads

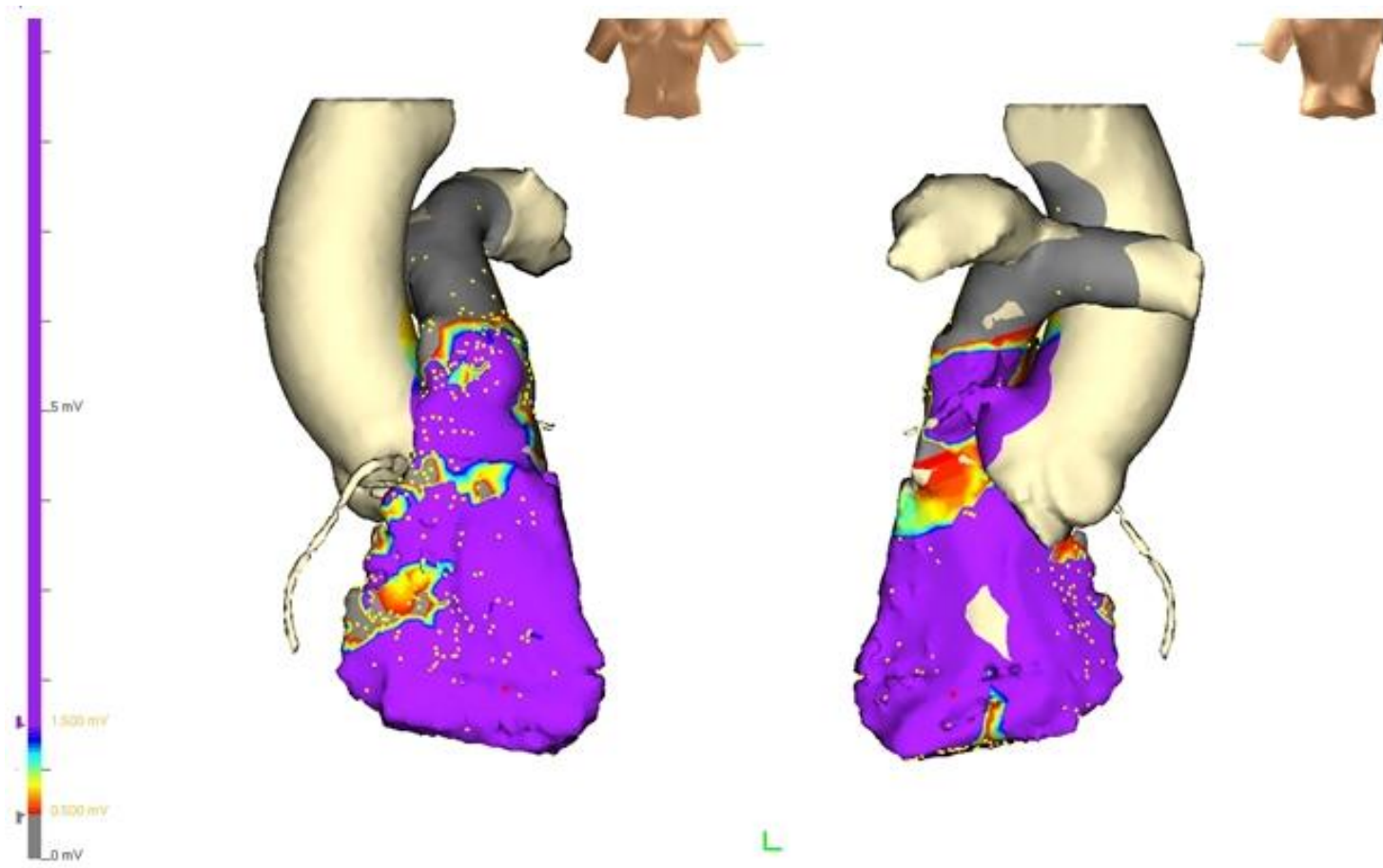
**Yae Min Park,¹ Mi Sook Cha,¹ Hanul Choi,¹ Woong Chol Kang,¹ Seung Hwan Han,¹
In Suck Choi,¹ Eak Kyun Shin,¹ and Young-Hoon Kim ²**

¹Cardiology Division, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, Republic of Korea

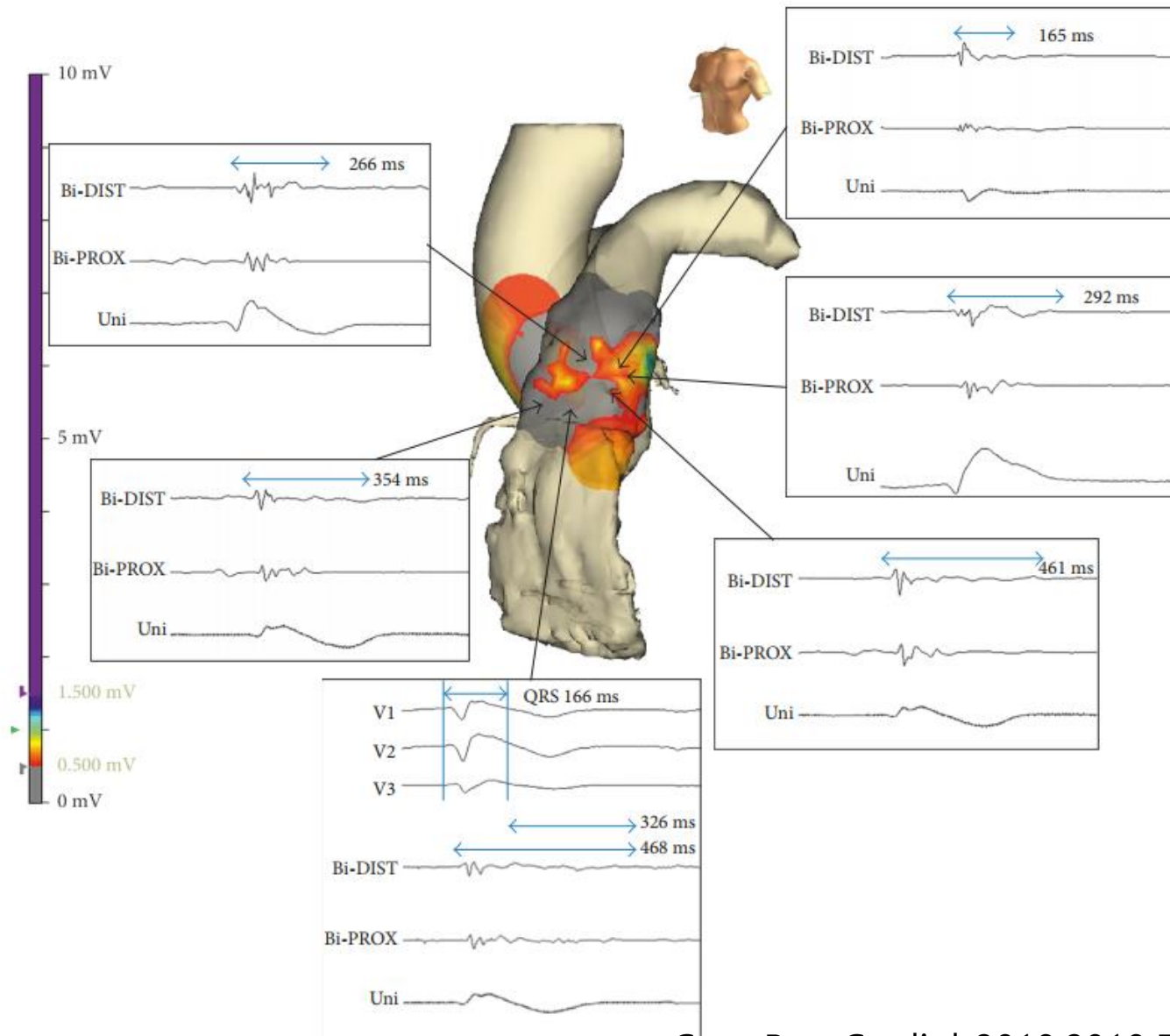
²Cardiology Division, Department of Internal Medicine, Korea University Anam Hospital, Seoul, Republic of Korea

Correspondence should be addressed to Young-Hoon Kim; yhkmd@unitel.co.kr

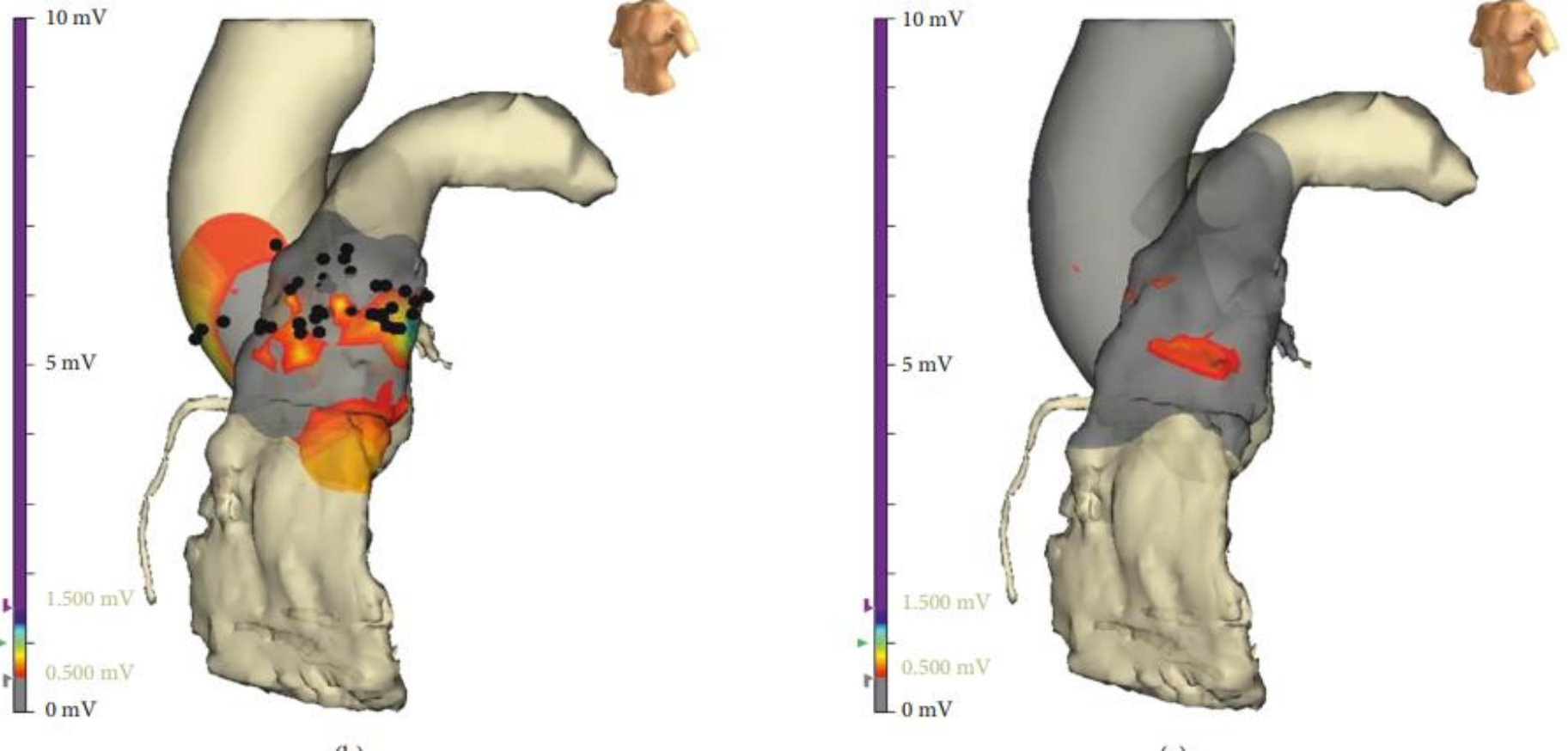
Endocardial voltage mapping



Epicardial substrate mapping



Scar change after ablation



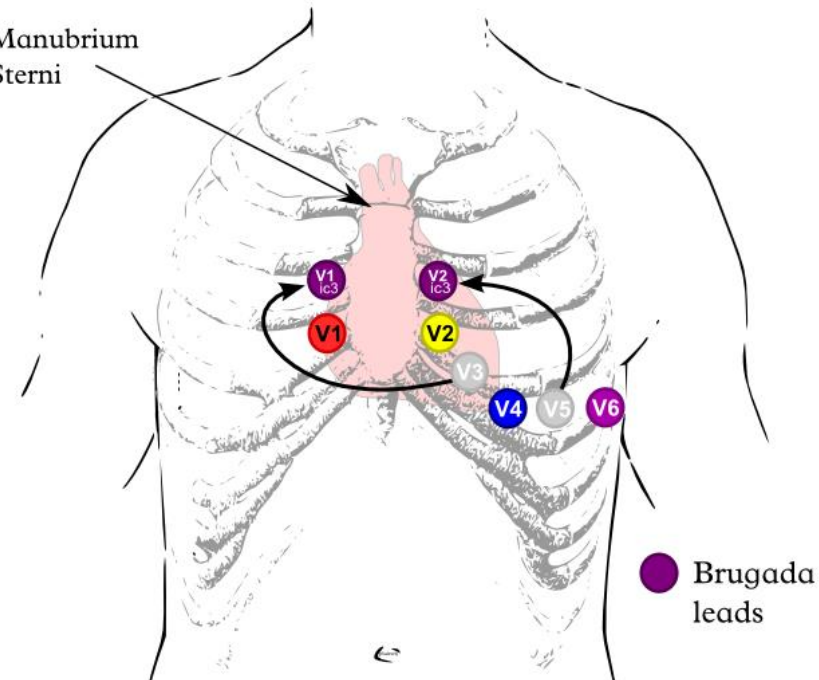
**No significant change after flecainide infusion (2mg/kg)
No inducibility of VF**

ECG changes after ablation

VF free for 30 months



Manubrium
Sterni



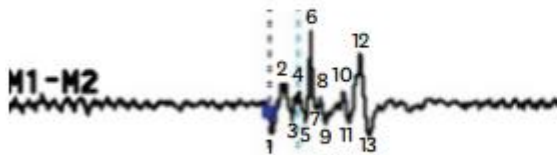
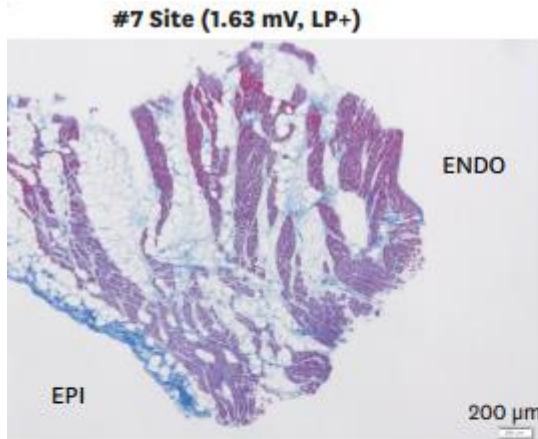
Brugada leads

High precordial leads; 3rd intercostal space

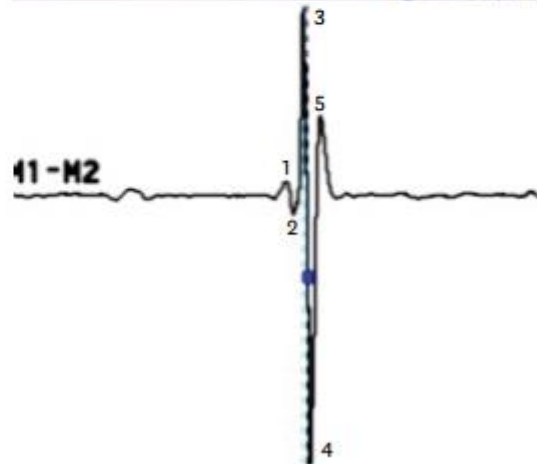
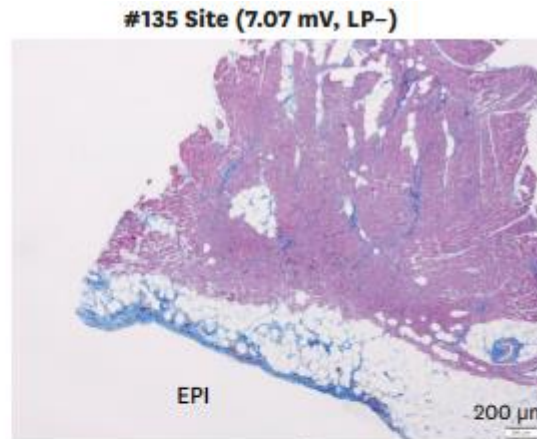
Case Rep Cardiol
2018;2018:5980380

Epicardial biopsy and histology

Late potential+



Late potential-



Methods to enhance epicardial functional substrate

- **Flecainide 2mg/kg 10 minutes**
- **Ajmaline 1mg/kg 5 minutes**
- **Pilsicainide 1mg/kg**
- **Epicardial warm water instillation**

Irrigation catheter, contact-force based catheter, high density mapping

Endpoint of epicardial ablation

- **VT/VF non-inducibility or normalization of the Brugada ECG pattern during the ablation procedure was the initial epicardial ablation endpoint.**



To eliminate all substrate areas with low voltage fractionated signals/late potentials that can be detected by sodium channel blockade.

Outcome after catheter ablation

Study ID	VF Inducibility Preablation	VF Inducibility Postablation	Drug Challenge Postablation	Mean Follow-up Duration (mo)	Freedom from Type Brugada Pattern Relapse	VF free rate	Need of AADs After Ablation	Complications
Nademanee et al, ²¹ 2011	100%	22%	None	20	89%	100%	11%	Mild pericarditis (n = 2)
Brugada et al, ²² 2015	100%	0%	Flecainide	10	100%	100%	NS	Pericarditis (n = 1)
Zhang et al, ²⁵ 2016	100% (n = 9)	0%	Propafenone (n = 9)	25	100%	73% ^a	0%	Pericarditis (n = 2)
Chung et al, ²⁶ 2017	100% (n = 11)	0%	Warm water instillation	3–6	63.6% (n = 11)	93%	0%	None
Pappone et al, ²³ 2017	100%	0%	Ajmaline	10	98.5%	99.3%	0%	Pericardial effusion (n = 5)
Shelke et al, ²⁷ 2018	40%	0%	NS	46	100%	80%	NS	Pericarditis (n = 1)
Haanschoten et al, ²⁸ 2019	Not performed	0% (attempted in 4)	Ajmaline	43	67%	83%	33%	Electromechanical dissociation and hemodynamic collapse after ajmaline (n = 1)
Nademanee et al, ²⁹ 2019	73%	15%	NS	27	3%	91%	0%	Hemopericardium (n = 1)
Providencia et al, ³⁰ 2019	Not performed	Not performed	Ajmaline in 50%	22	87.5%	87.5%	0%	Hemopericardium (n = 1)

Catheter ablation without ICD??

Circulation
Arrhythmia and Electrophysiology



Epicardial Substrate Ablation in Brugada Syndrome: Time for a Randomized Trial!
Arthur A.M. Wilde and Koonlawee Nademanee

Circ Arrhythm Electrophysiol. 2015;8:1306-1308
doi: 10.1161/CIRCEP.115.003500

Should be performed in symptomatic patients with ICD back up

Long-Term Outcomes of Brugada Substrate Ablation: A Report from BRAVO (Brugada Ablation of VF Substrate Ongoing Multicenter Registry)

Koonlawee Nademanee^{ID}, MD; Fa-Po Chung, MD; Frederic Sacher^{ID}, MD, PhD; Akihiko Nogami, MD, PhD; Hiroshi Nakagawa^{ID}, MD, PhD; Chenyang Jiang, MD; Meleze Hocini^{ID}, MD; Elijah Behr^{ID}, MA, MBBS; Gumpanart Veerakul, MD; Jaap Jan Smits, MD; Kohei Yamashiro, MD; Yuichiro Sakamoto, MD; Apichai Khongphatthanayothin^{ID}, MD;

Ablation end points; elimination of PVC-VF triggers, elimination of all abnormal late fractionated electrograms with sodium channel blockers

BACKGROUND: Treatment options for high-risk Brugada syndrome (BrS) with recurrent ventricular fibrillation (VF) are limited. Catheter ablation is increasingly performed but a large study with long-term outcome data is lacking. We report the results of the multicenter, international BRAVO (Brugada Ablation of VF Substrate Ongoing Registry) for treatment of high-risk symptomatic BrS.

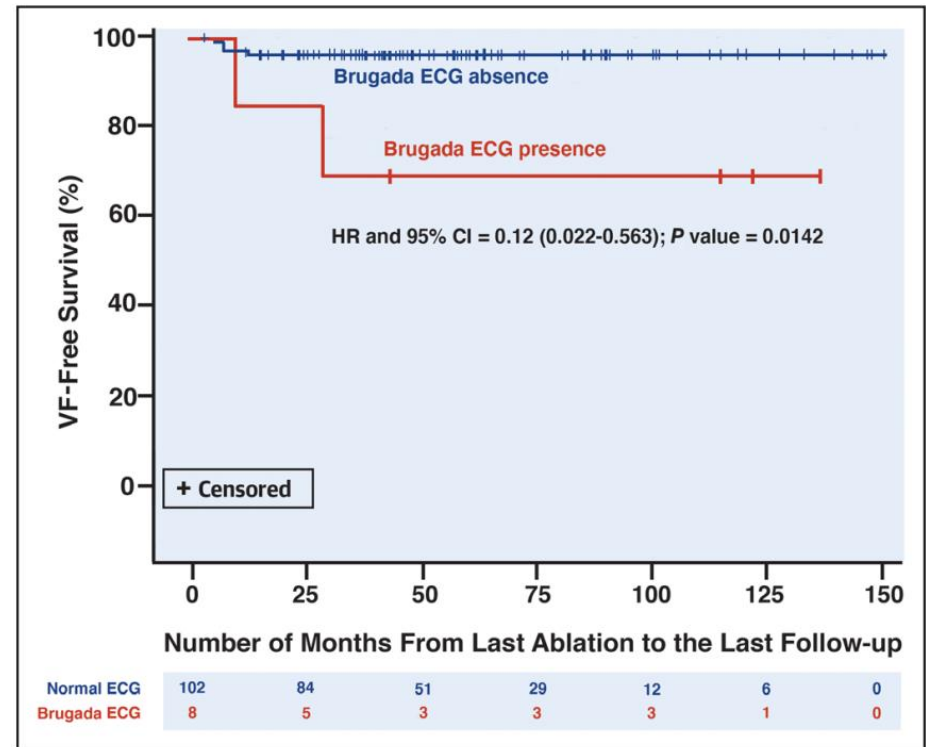
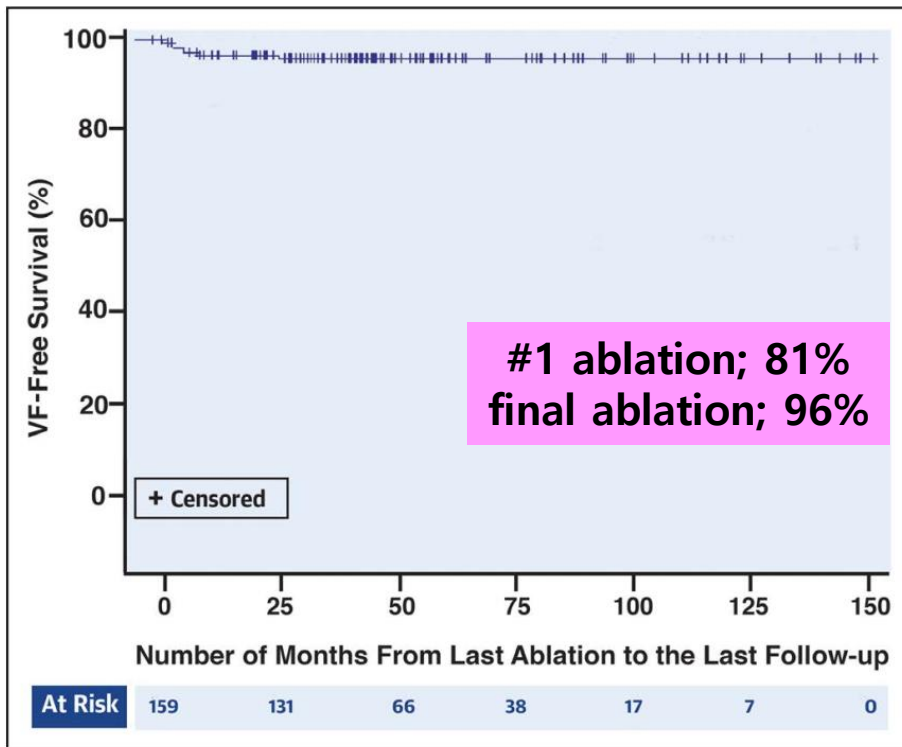
METHODS: We enrolled 159 patients (median age 42 years; 156 male) with BrS and spontaneous VF in BRAVO; 43 (27%) of them had BrS and early repolarization pattern. All but 5 had an implantable cardioverter-defibrillator for cardiac arrest ($n=125$) or syncope ($n=34$). A total of 140 (88%) had experienced numerous implantable cardioverter-defibrillator shocks for spontaneous VF before ablation. All patients underwent a percutaneous epicardial substrate ablation with electroanatomical mapping except for 8 who underwent open-thoracotomy ablation.

RESULTS: In all patients, VF/BrS substrates were recorded in the epicardial surface of the right ventricular outflow tract; 45 (29%) patients also had an arrhythmic substrate in the inferior right ventricular epicardium and 3 in the posterior left ventricular epicardium. After a single ablation procedure, 128 of 159 (81%) patients remained free of VF recurrence; this number increased to 153 (96%) after a repeated procedure (mean 1.2 ± 0.5 procedures; median=1), with a mean follow-up period of 48 ± 29 months from the last ablation. VF burden and frequency of shocks decreased significantly from 1.1 ± 2.1 per month before ablation to 0.003 ± 0.14 per month after the last ablation ($P < 0.0001$). The Kaplan-Meier VF-free survival beyond 5 years after the last ablation was 95%. The only variable associated with a VF-free outcome in multivariable analysis was normalization of the type 1 Brugada ECG, both with and without sodium-channel blockade, after the ablation (hazard ratio, 0.078 [95% CI, 0.008 to 0.753]; $P=0.0274$). There were no arrhythmic or cardiac deaths. Complications included hemopericardium in 4 (2.5%) patients.

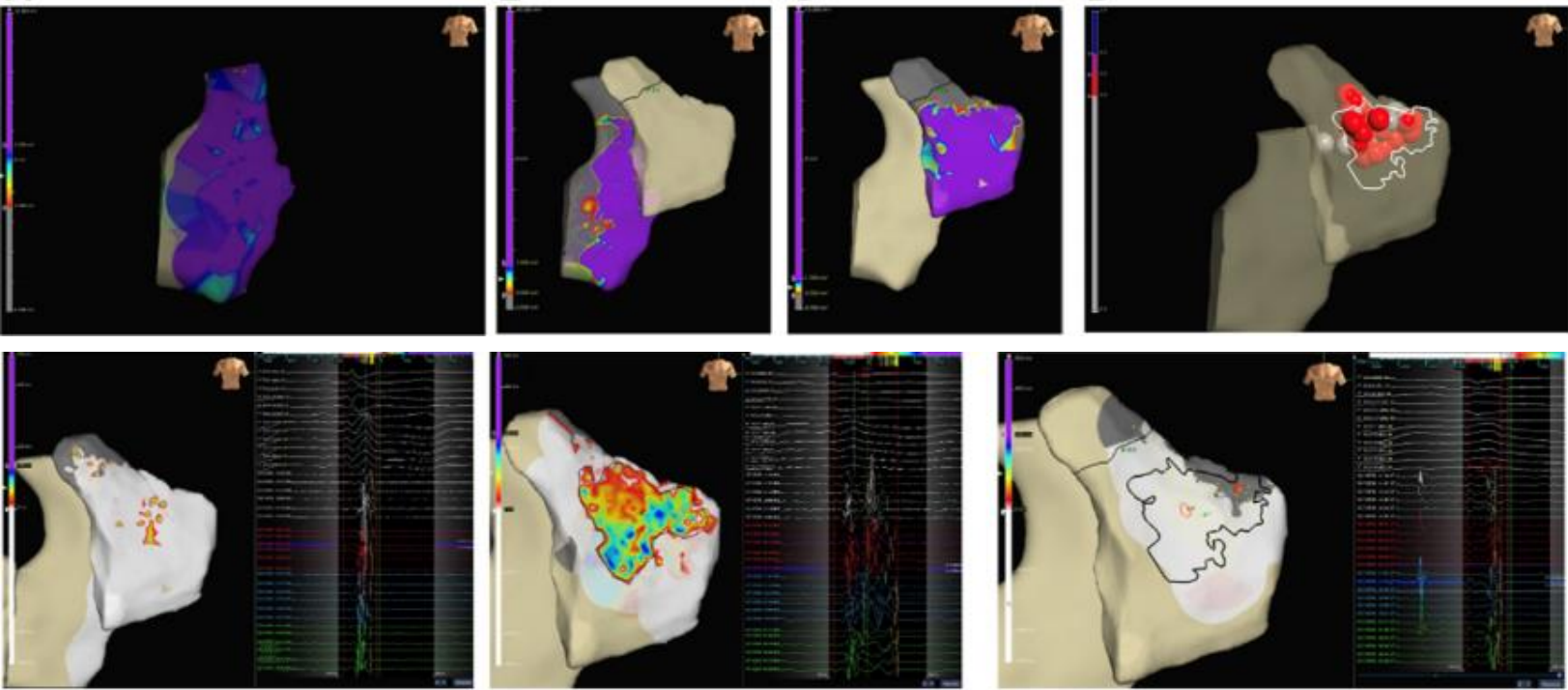
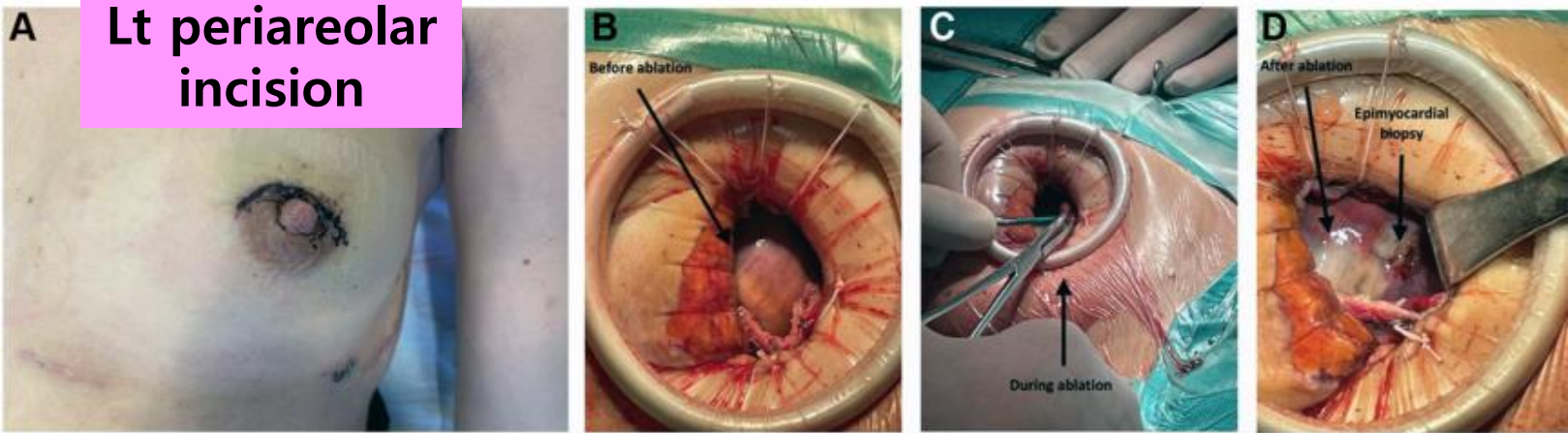
CONCLUSIONS: Ablation treatment is safe and highly effective in preventing VF recurrence in high-risk BrS. Prospective studies are needed to determine whether it can be an alternative treatment to implantable cardioverter-defibrillator implantation for selected patients with BrS.

VF free survival

The only variable associated with a VF-free outcome in multivariable analysis was normalization of the type 1 Brugada ECG.

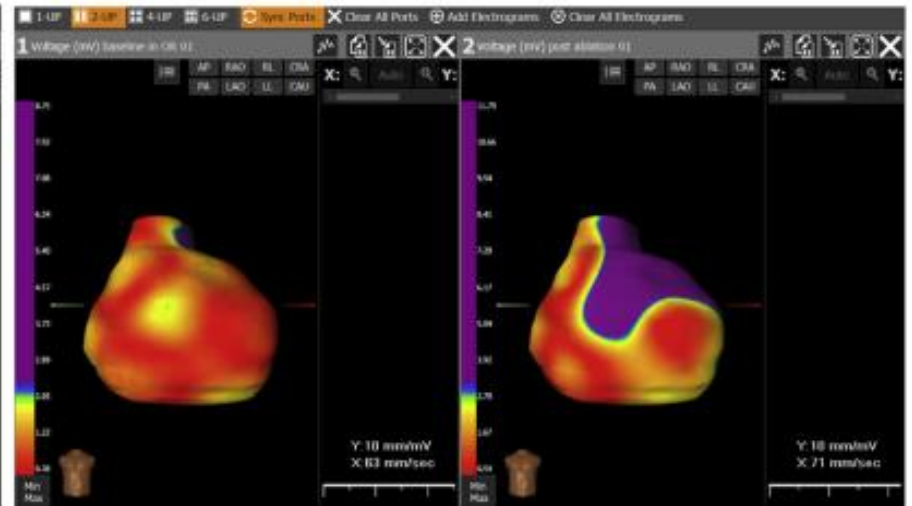
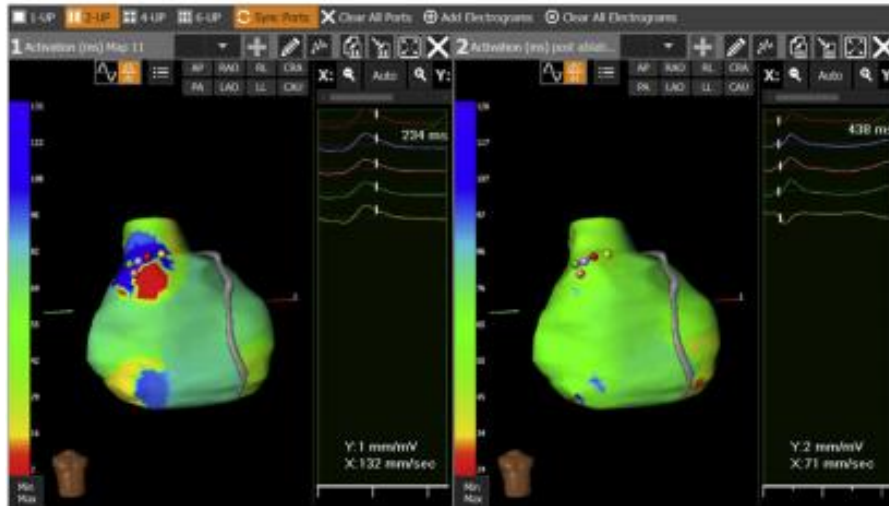
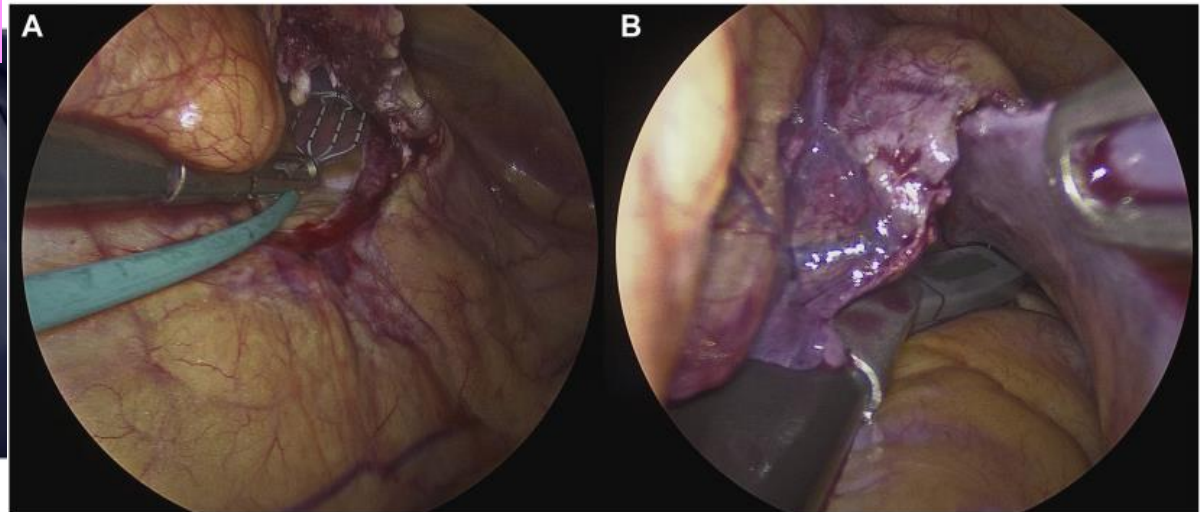


Hybrid minithoracotomy for zero-fluoroscopy



Hybrid surgical ablation, recurrent VT

Left-sided thoracoscopy



Summary

- In patients with BrS experiencing recurrent ICD shocks for polymorphic VT, intensification of therapy with quinidine or catheter ablation is recommended
- BrS patients have a well-defined arrhythmic substrate at epicardial RVOT.
- Catheter ablation with endpoints of elimination of all abnormal potentials before and after sodium channel blocker

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