

CARDIOMIOPATIA ARITMOGENA: WHAT'S NEW?

TV nella cardiomiopatia non ischemica: limiti e aspettative dell'approccio ablativo

Massimo Tritto

UOC Elettrofisiologia

IRCCS Humanitas Research Hospital

Rozzano (MI)

Conflitti di interesse

- nulla da dichiarare

- Le tachicardie ventricolari hanno un impatto negativo (qualità di vita e prognosi) nei pazienti con cardiopatia strutturale
- L'ICD prolunga la sopravvivenza ma gli interventi (soprattutto quelli con shock) peggiorano la qualità di vita e aumentano sia le ospedalizzazioni che la mortalità, in misura tanto maggiore quanto più sono frequenti
- L'ablazione è uno strumento fondamentale nella gestione clinica di questi pazienti

Outcomes of catheter ablation for ventricular tachycardia in structural heart disease: a meta-analysis and quality appraisal of trials

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Handling Editor: Frieder Braunschweig

Pazienti quasi sempre con cardiopatia ischemica!

Aims

Methods and results

MEDLINE, PubMed, EMBASE and Cochrane were searched for randomized controlled trials (RCTs) of patients with structural heart disease allocated to receive either CA or standard treatment. Outcomes of interest were: all-cause and cardiovascular (CV) mortality, VT recurrence, incidence of appropriate ICD therapy, CV hospitalizations and VT storm. Evidence was appraised using the risk of bias tool and the grading of recommendations assessment, development and evaluation (GRADE) approach. Trial-level pairwise meta-analyses were conducted for all outcomes. Reconstructed time-to-event data meta-analysis was also performed for all-cause mortality 13 RCTs ($n = 1735$ patients) were included in the meta-analysis with a follow-up duration of 6–52 months. No significant reduction in all-cause mortality was observed at trial level meta-analysis (risk ratio [RR] 0.87, 95% confidence interval [CI] 0.70–1.08, heterogeneity [I^2] = 0%), or reconstructed individual patient data meta-analysis [hazard ratio (HR) 0.79, 95%CI 0.57–1.11 at 3 years]. However, our pooled estimates, observed effect size and GRADE assessments suggest a potential mortality reduction in the ablation group. Patients who underwent CA experienced a significant reduction in CV hospitalizations (RR 0.78, 95%CI 0.65–0.94, $I^2 = 41\%$), VT storm (RR 0.78, 95%CI 0.63–0.97; $I^2 = 5\%$), VT recurrence (RR 0.83, 95%CI 0.72–0.95, $I^2 = 21\%$), and appropriate ICD therapy (RR 0.74, 95%CI 0.61–0.89, $I^2 = 32.5\%$) compared to control groups.

Conclusion

A potential all-cause mortality reduction by catheter ablation requires further confirmation in a properly powered RCT. No reduction in cardiovascular mortality was found. VT recurrence, CV hospitalizations, VT storm and ICD therapy were all significantly reduced by catheter ablation in patients with structural heart disease.

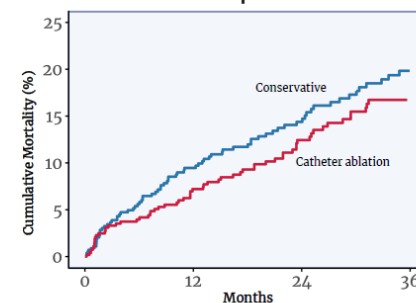
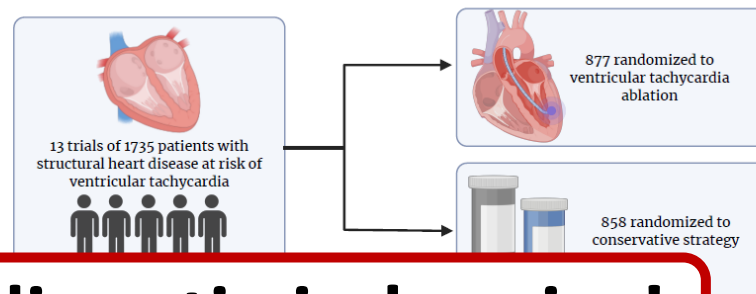
Lay summary

We examined the effectiveness of catheter ablation (CA) for treating ventricular tachycardia (VT) in patients with structural heart disease, particularly those facing recurrent implantable cardioverter defibrillator shocks or unable to tolerate medications by analysing several randomized controlled trials. The findings suggest that while CA may not significantly reduce overall mortality, it can lead to fewer recurrences of VT and hospitalizations related to cardiovascular problems.

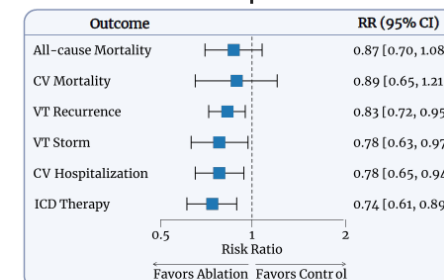
Graphical abstract

DOES CATHETER ABLATION OF VENTRICULAR TACHYCARDIA REDUCE MORTALITY IN PATIENTS WITH STRUCTURAL HEART DISEASE?

PUBMED, MEDLINE, EMBASE and Cochrane for randomized controlled trials
search until December 2024



Reconstructed Time-to-Event
HR: 0.79 (95% CI 0.57–1.11) at 3 years

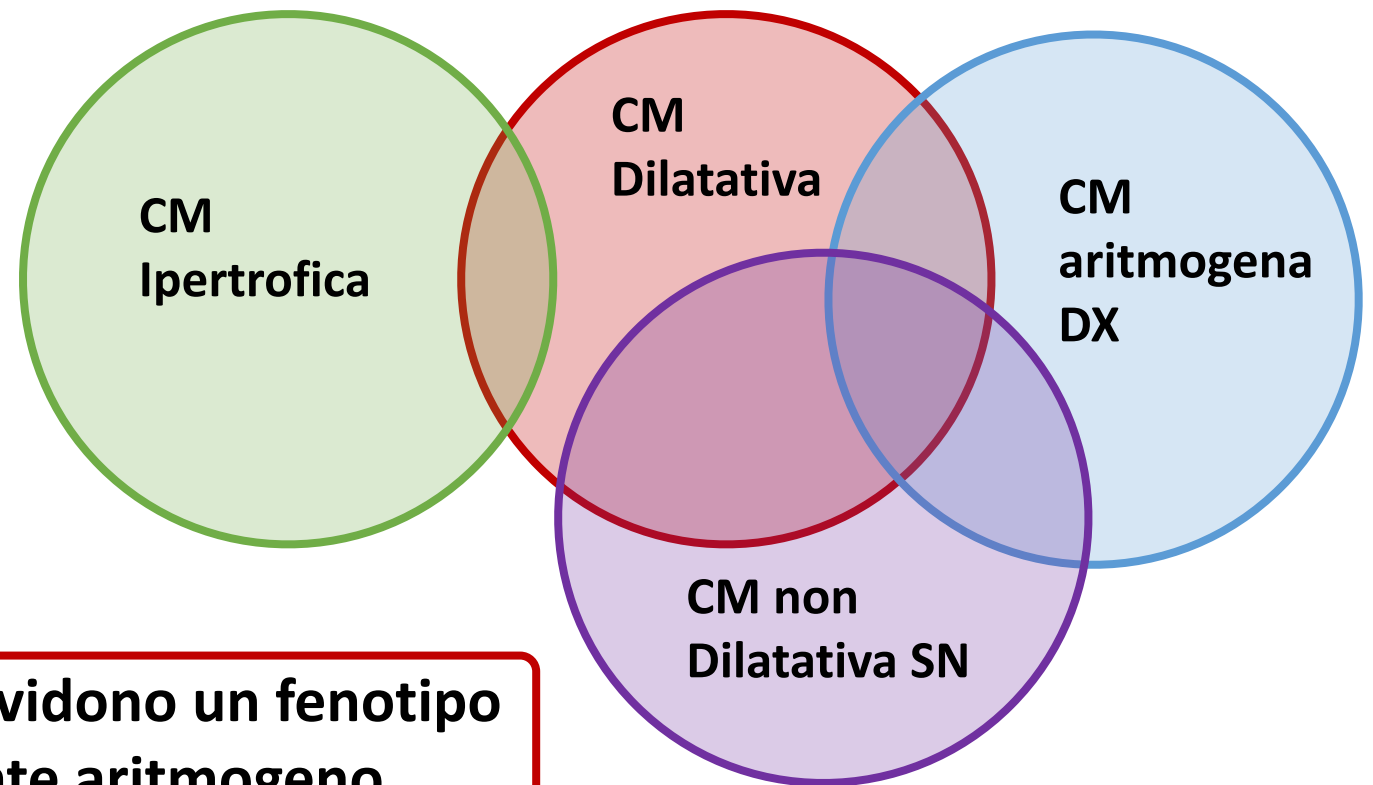


Trial level Meta-Analysis
Mortality RR: 0.89 (95% CI 0.70–1.08)

Malattie del muscolo cardiaco non in relazione a ridotto apporto di sangue (coronaropatia ostruttiva) o sovraccarico emodinamico (valvulopatie, ipertensione arteriosa)

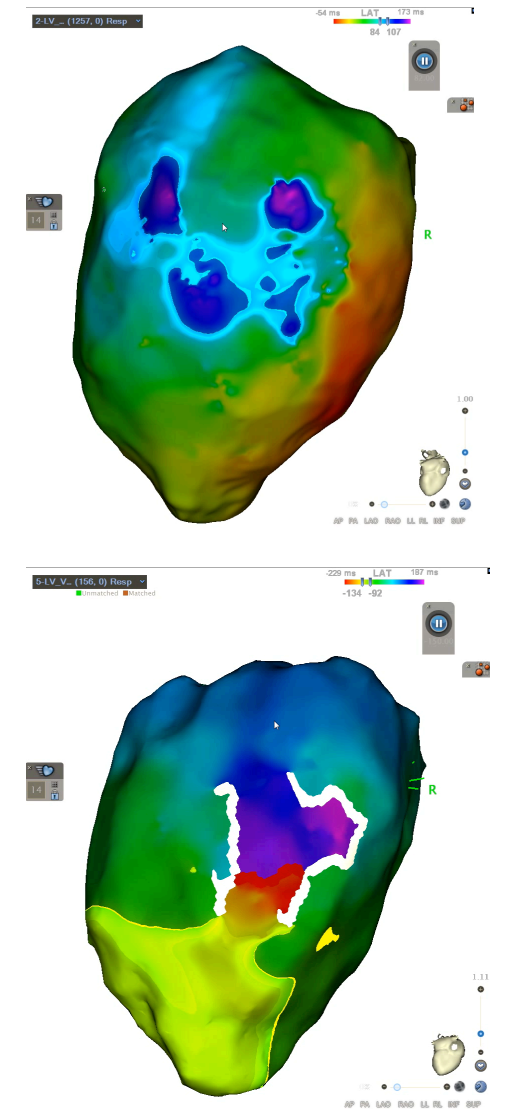
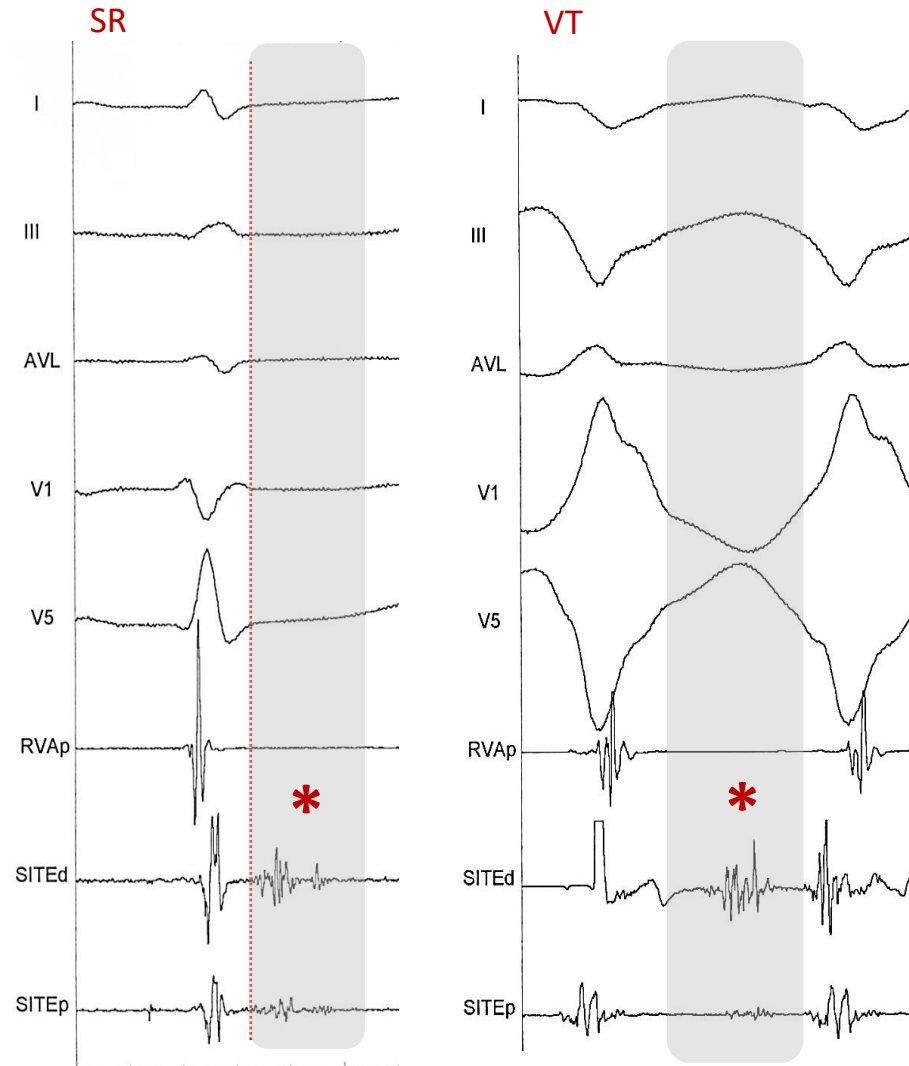
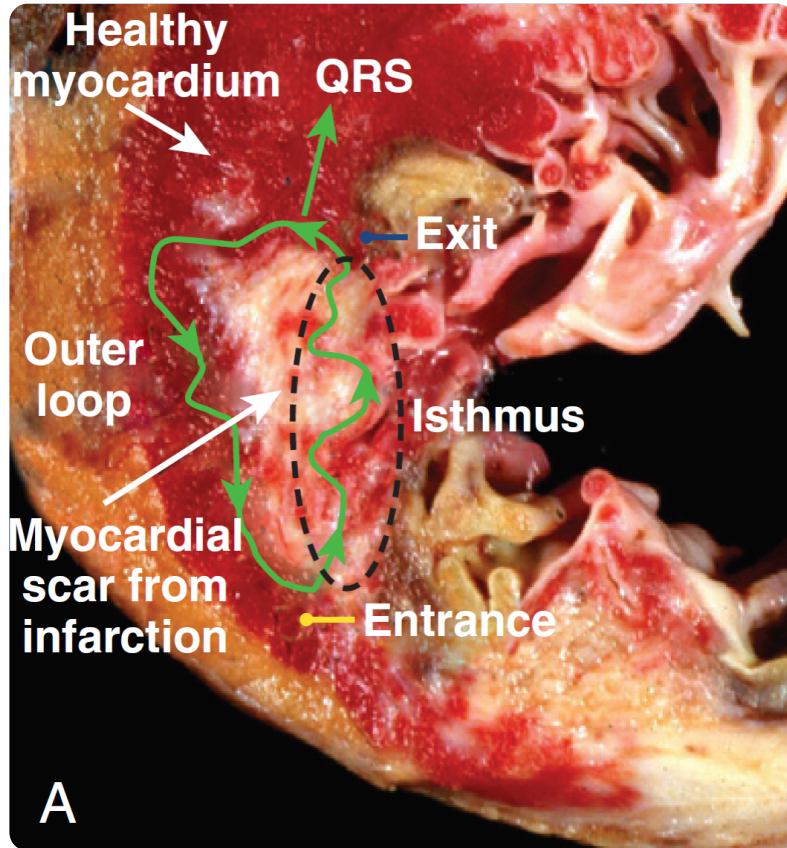
Eziologia

- Geneticamente determinate
- Acquisite
 - ☑ Infiammatorie
 - ☑ Infettive
 - ☑ Tossiche
 - ☑ Metaboliche



Condizioni eterogenee che condividono un fenotipo prevalentemente o esclusivamente aritmogeno

Scar-related VT





ESC

European Society
of Cardiology

European Heart Journal (2018) 39, 2867–2875
doi:10.1093/eurheartj/ehy168

CLINICAL RESEARCH

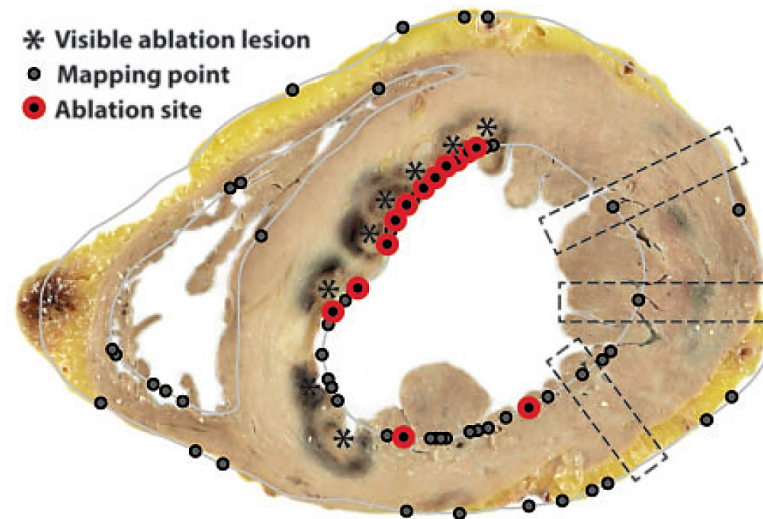
Arrhythmia/electrophysiology

Whole human heart histology to validate electroanatomical voltage mapping in patients with non-ischaemic cardiomyopathy and ventricular tachycardia

Claire A. Glashan¹, Alexander F.A. Androulakis¹, Qian Tao², Ross N. Glashan¹, Lambertus J. Wisse³, Micaela Ebert¹, Marco C. de Ruiter³, Berend J. van Meer³, Charlotte Brouwer¹, Olaf M. Dekkers⁴, Daniel A. Pijnappels¹, Jacques M.T. de Bakker⁵, Marta de Riva¹, Sebastiaan R.D. Piers¹, and Katja Zeppenfeld^{1*}

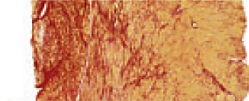
Integration of electroanatomical voltage mapping with gross pathology

- * Visible ablation lesion
- Mapping point
- Ablation site



Highly variable
fibrosis pattern
seen in histology

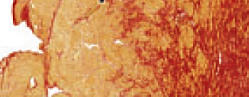
Sub-endocardial: 30%



Mid-wall: 19%



Sub-epicardial: 17%



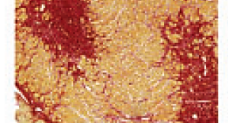
Transmural: 28%



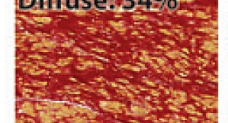
Architecture
distinct from that
seen post-MI

Common:

Patchy: 55%



Diffuse: 34%



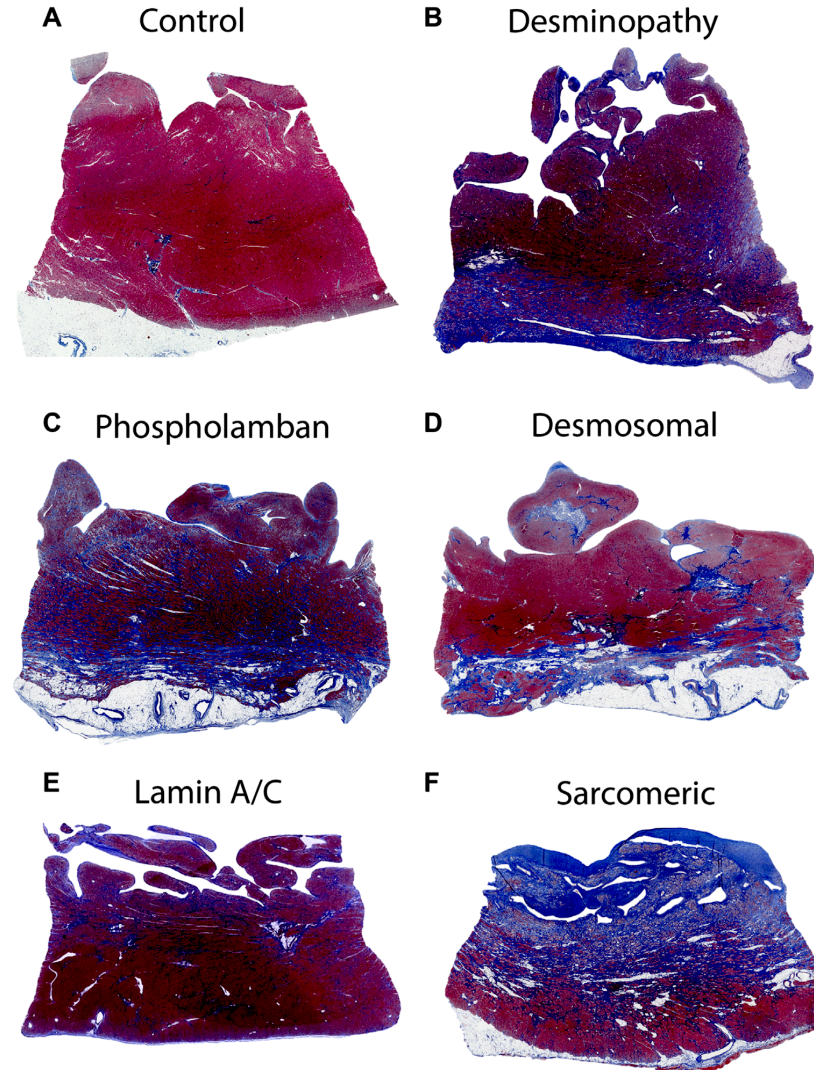
Rare:

Compact: 3%

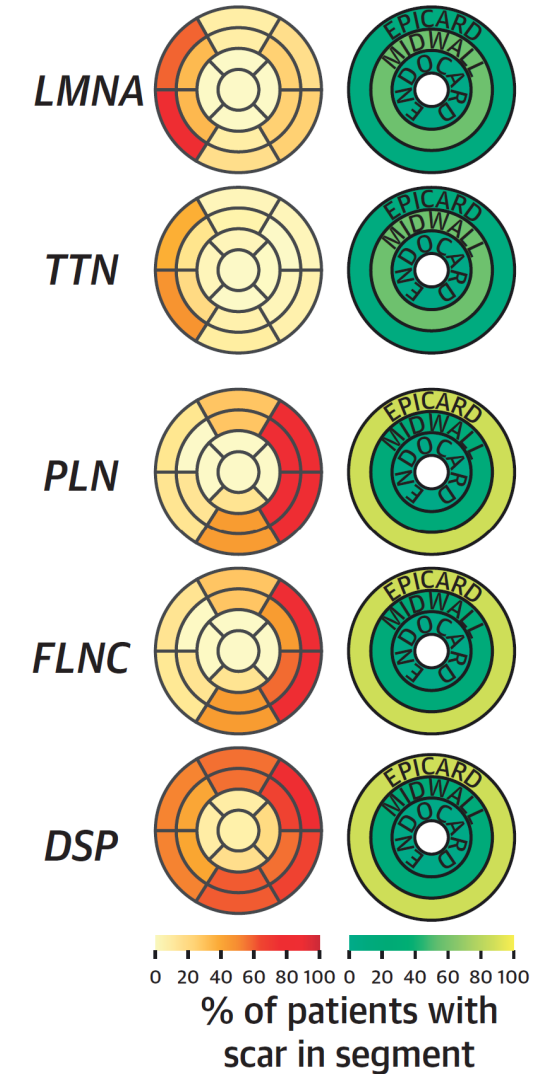


La fibrosi a chiazze o diffusa può generare meccanismi aritmogeni (ad es spiral reentry, automatismo, ecc) e/o target di ablazione differenti rispetto alle aritmie legate a una cicatrice compatta

Genetic variants
are associated
with prevalent
scar distributions



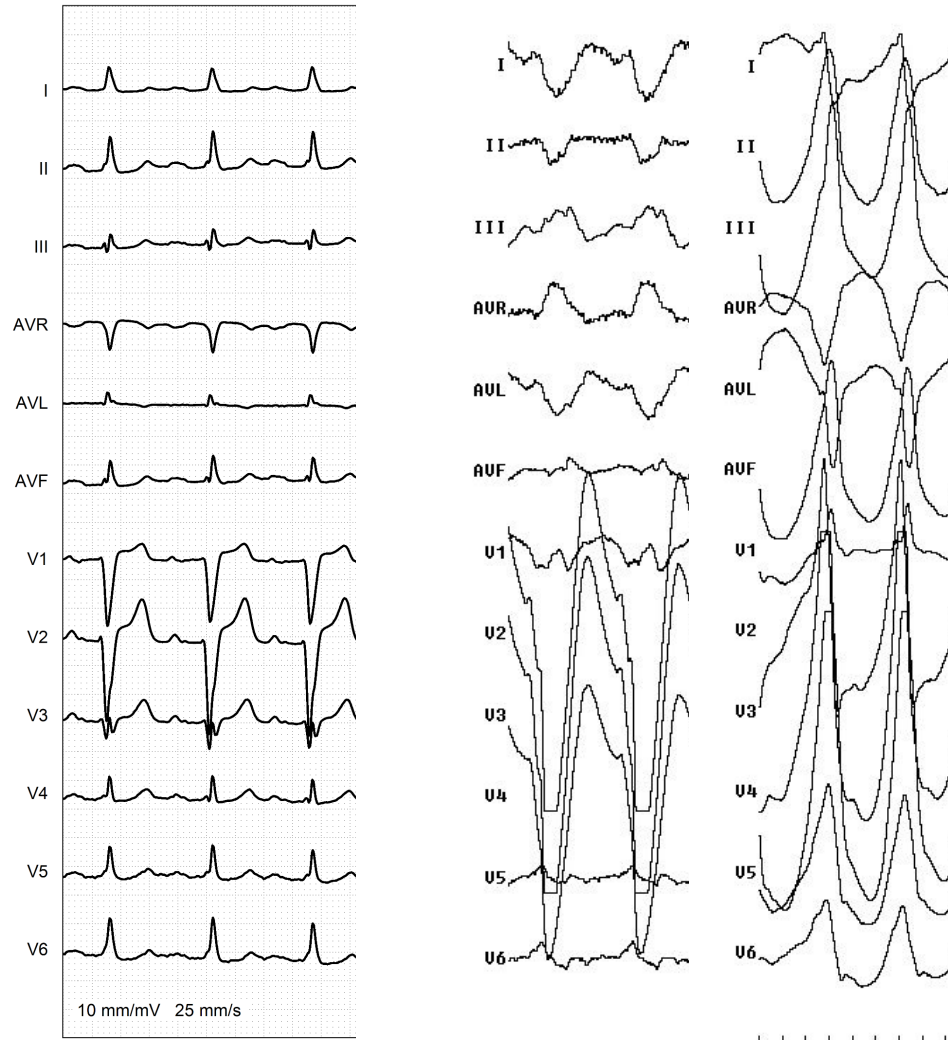
Bhaskaran A et al. Heart Lung and Circulation 2019;28:84-101



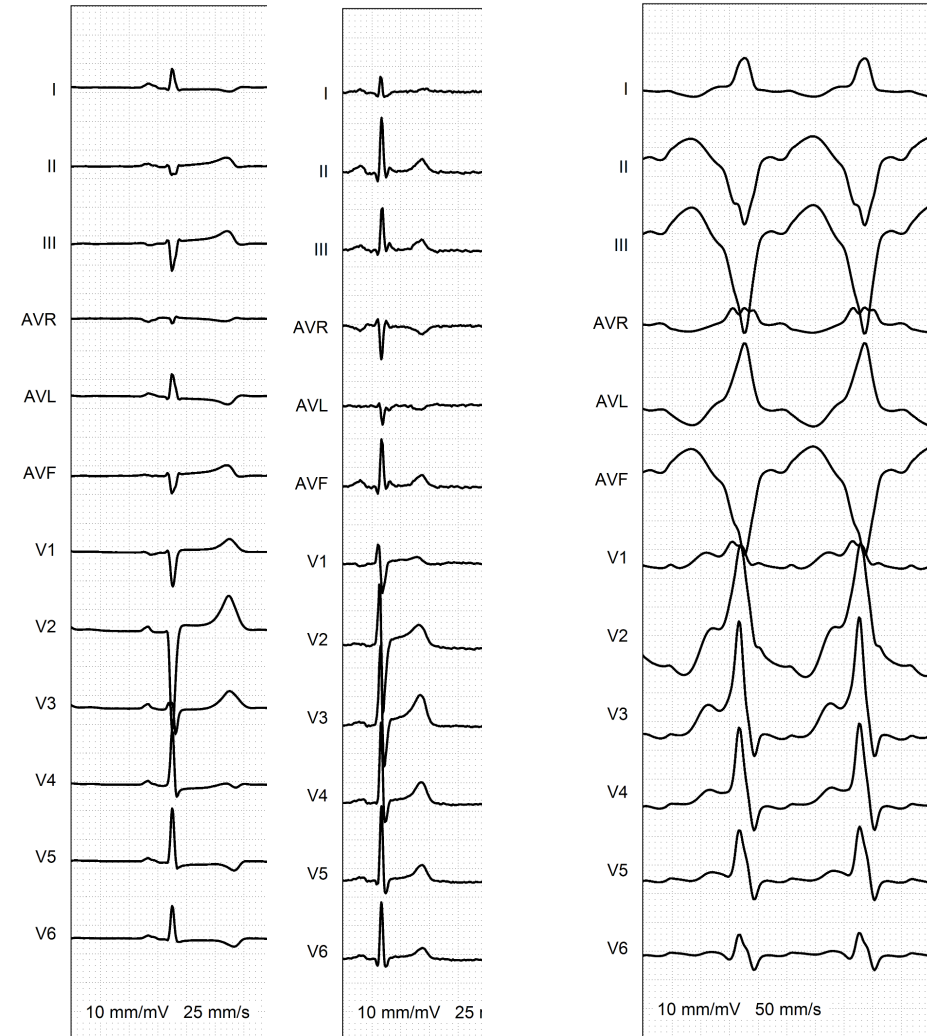
Zeppenfeld K et al. JACC EP. 2024;10:585–603.

Scar localization in non ischemic CMs: role of 12-lead ECG

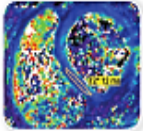
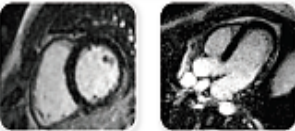
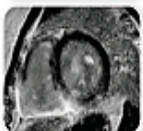
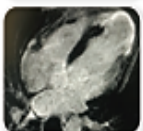
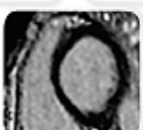
Septal substrate



LV free wall substrate

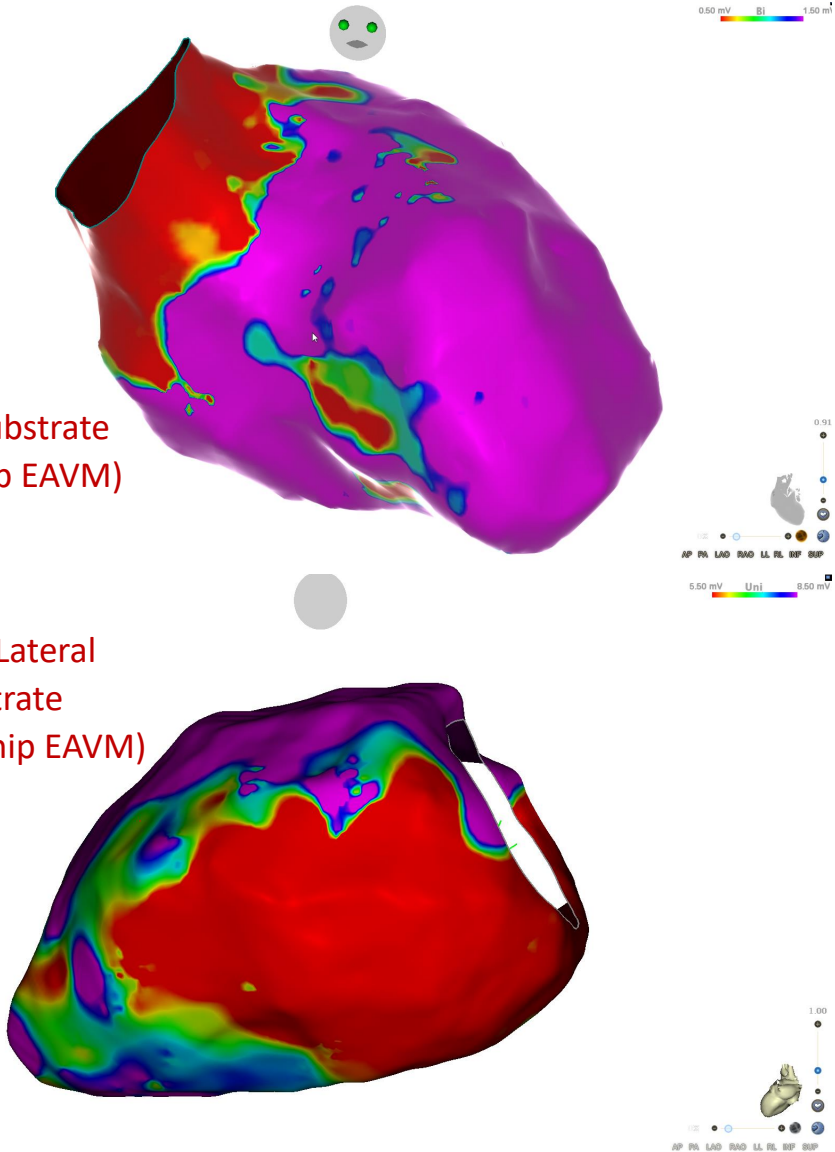


Scar localization in non ischemic CMs: role of MRI and EAM

DCM	Short T2*		Haemochromatosis
	Subepicardial LGE		Post-myocarditis
	Lateral wall epicardial LGE		Dystrophinopathy
	Subepicardial and midwall LGE at basal septum +/- extension into inferolateral wall and RV insertion points		Sarcoidosis
	Apical transmural LGE		Chagas disease
NDLVC	Ring-like and/or subepicardial LGE pattern		DSP variants FLNC variants DES variants
	Septal mid-wall LGE		Laminopathy
ARVC	Fat and LGE (transmural RV plus sub-epicardial-midmural LV free wall)		Desmosomal variants

Septal substrate
(Endo Bip EAVM)

Postero-Lateral
EPI substrate
(Endo Unip EAVM)



Non ischemic CMs: results of VT catheter ablation

Study	# Pts	Procedural strategy	Acute success (VT nonind)	Follow-up duration	Long-term VT-free survival
Tokuda et al. (2012) ¹⁵	226	Combined (Endo + Epi)	55%	52.8 months	77%
Oloriz et al. (2014) ²⁹	87	Combined (Endo + Epi)	81%	18 months (median)	49%
Dinov et al. (2015) ⁸⁷	102	Combined (Endo + Epi)	61%	24 months	47%
Muser et al. (2016) ⁴	282	Combined (Endo + Epi)	82%	48 months (median)	69%
Gökoğlan et al. (2016) ⁶³	93	Combined (Endo + Epi)	53%	14 ± 2 months	48%
Muser et al. (2017) ⁸⁶	71	Combined (Endo + Epi)	68%	45 months (median)	48%
Siontis et al. (2017) ⁹⁸	96	Combined (Endo + Epi)	41%	7.6 months (median)	54%
Vaseghi et al. (2018) ⁹⁹	780	Combined (Endo + Epi)	65%	12.8 months (median)	69%
Tzou et al. (2018) ¹⁰⁰	88	Combined (Endo + Epi)	NA	12 months	82%
Okubo et al. (2020) ¹⁰¹	403	Combined (Endo + Epi)	80%	32 months (median)	57%
Zeppenfeld et al. (2022) ⁵	281	Combined (Endo + Epi)	60%	21 months (median)	51%

Non ischemic CMs: results of VT catheter ablation

REVIEW



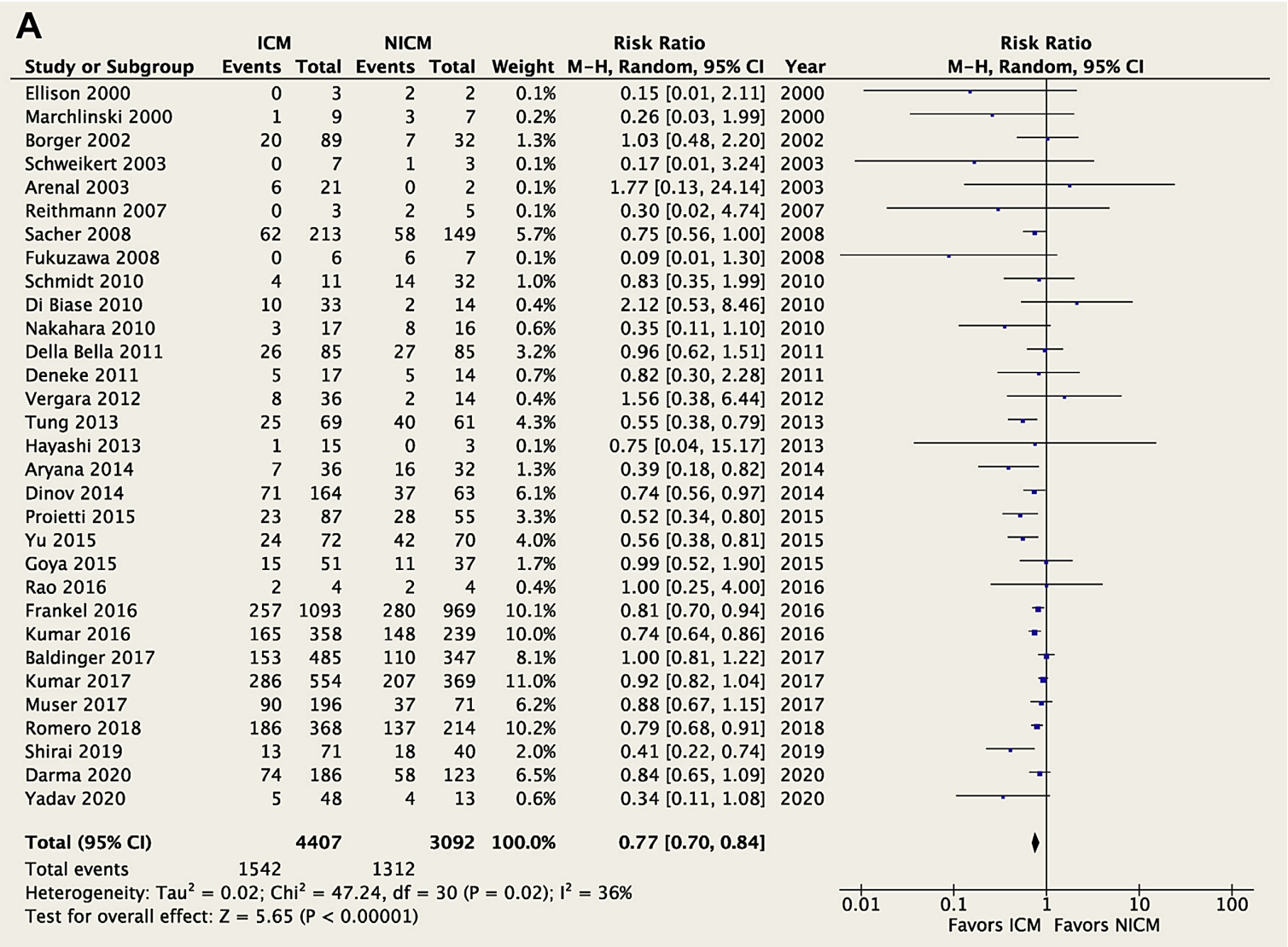
Catheter Ablation for Ventricular Tachycardia in Ischaemic Versus Non-Ischaemic Cardiomyopathy: A Systematic Review and Meta-Analysis

Aran Kanagaratnam, MD ^{a,1}, Sohaib A. Virk, MD ^{a,1},
Timmy Pham, BMedSci ^{a,b}, Robert D. Anderson, MBBS ^{a,b,c},
Samual Turnbull, BSc ^{a,b}, Timothy Campbell, BSc ^{a,b},
Richard Bennett, MBChB ^{a,b}, Stuart P. Thomas, PhD ^{a,b},
Geoffrey Lee, MBChB, PhD ^c, Saurabh Kumar, MBBS, PhD ^{a,b,d,e}

^aDepartment of Cardiology, Westmead Hospital, Sydney, NSW, Australia
^bWestmead Applied Research Centre, University of Sydney, Sydney, NSW, Australia
^cDepartment of Cardiology, Royal Melbourne Hospital, Melbourne, Vic, Australia; Faculty of Medicine, Dentistry, and Health Science, University of Melbourne, Melbourne, Vic, Australia

Received 23 January 2022; accepted 28 February 2022; online published ahead-of-print 25 May 2022

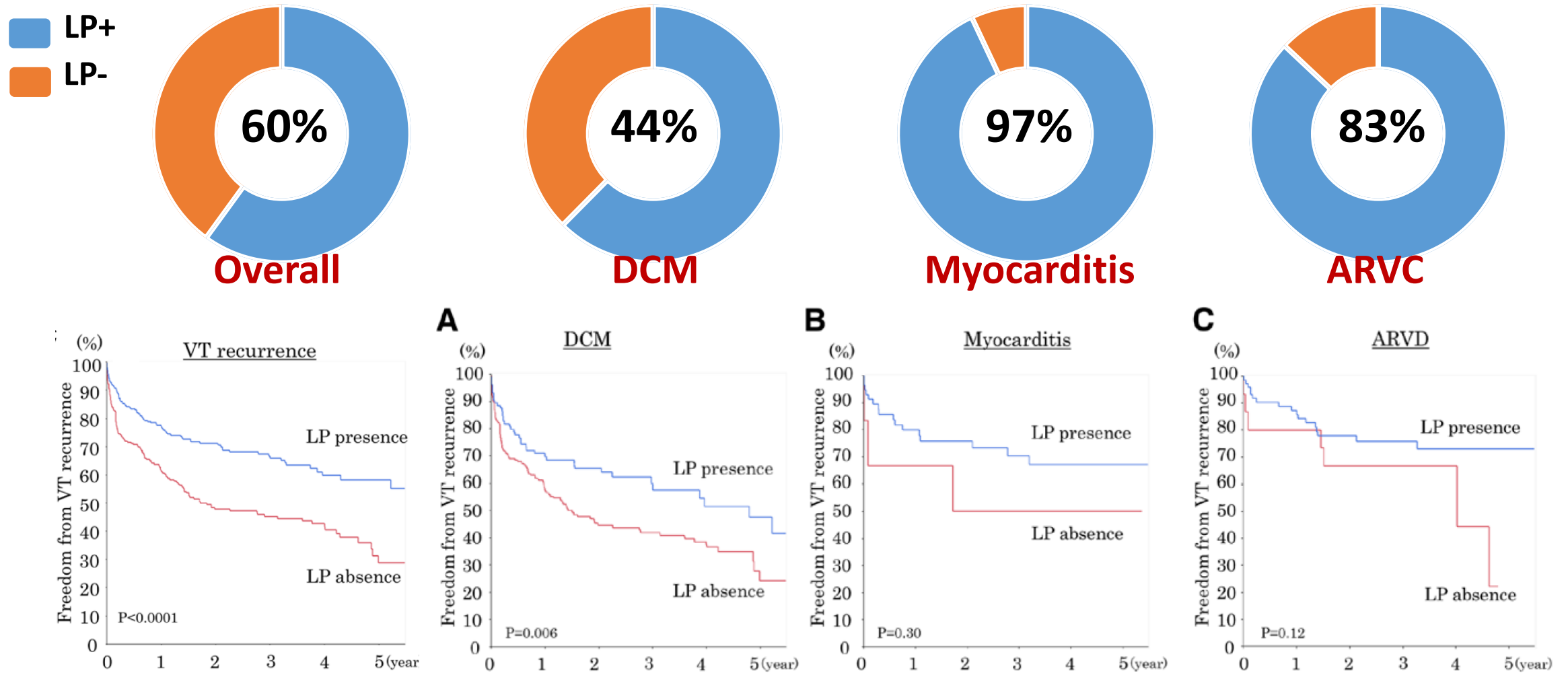
Background	There are differences in substrate and ablation approaches for ventricular tachycardia (VT) in ischaemic (ICM) and non-ischaemic cardiomyopathy (NICM).
Objective	To perform a systematic review and meta-analysis comparing clinical and procedural characteristics/ outcomes of VT ablation in ICM versus NICM.
Methods	Electronic databases were searched for comparative studies reporting outcomes of VT ablation in patients with ICM and NICM. Primary outcomes were acute procedural success, VT recurrence and long-term mortality. Meta-analyses were performed using random-effects modelling.
Results	Thirty-one (31) studies (7,473 patients; 4,418 ICM and 3,055 NICM) were included. Patients with ICM were significantly older (67.0 vs 55.3 yrs), more commonly male (89% vs 79%), had lower left ventricular ejection fraction (29% vs 38%) were less likely to undergo epicardial access (11% vs 36%) and were more likely to require haemodynamic support during ablation (relative risk [RR] 1.30; 95% CI 1.01–1.69). Acute procedural success (i.e. non-inducibility of VT) was higher in the ICM cohort (RR 1.10; 95% CI 1.05–1.15). Recurrence of VT at follow-up was significantly lower in the ICM cohort (RR 0.77; 95% CI 0.70–0.84). Peri-procedural mortality, incidence of procedural complications and long-term mortality were not significantly different between the cohorts.
Conclusions	NICM and ICM patients undergoing VT ablation are fundamentally different in their clinical characteristics, ablation approaches, acute procedural outcomes and likelihood of VA recurrence. VT ablation in NICM has a lower likelihood of procedural success with increased risk of VA recurrence, consistent with known challenging arrhythmia substrate.



Come si spiegano questi risultati apparentemente modesti e inferiori a quelli ottenuti nei pazienti con cardiopatia ischemica?

- Popolazioni eterogenee con substrati differenti per architettura e localizzazione - in relazione alle molteplici eziologie che li hanno determinati - e che pertanto rispondono diversamente all'ablazione
- Target dell'ablazione meno rappresentati/assenti (potenziali ventricolari tardivi) o non utilizzabili (TV non tollerate o elettricamente instabili) in una quota rilevante di casi
- Substrato non raggiungibile per localizzazione anatomica (scar intramiocardica) o non passibile di ablazione per il rischio di danneggiamento delle strutture adiacenti (sistema di conduzione, a. coronarie, n. frenico)

LPs in non ischemic CMs: prevalence



Okubo K et al. *Circ Arrhythm Electrophysiol.* 2020;13:e008307. DOI: 10.1161/CIRCEP.119.008307

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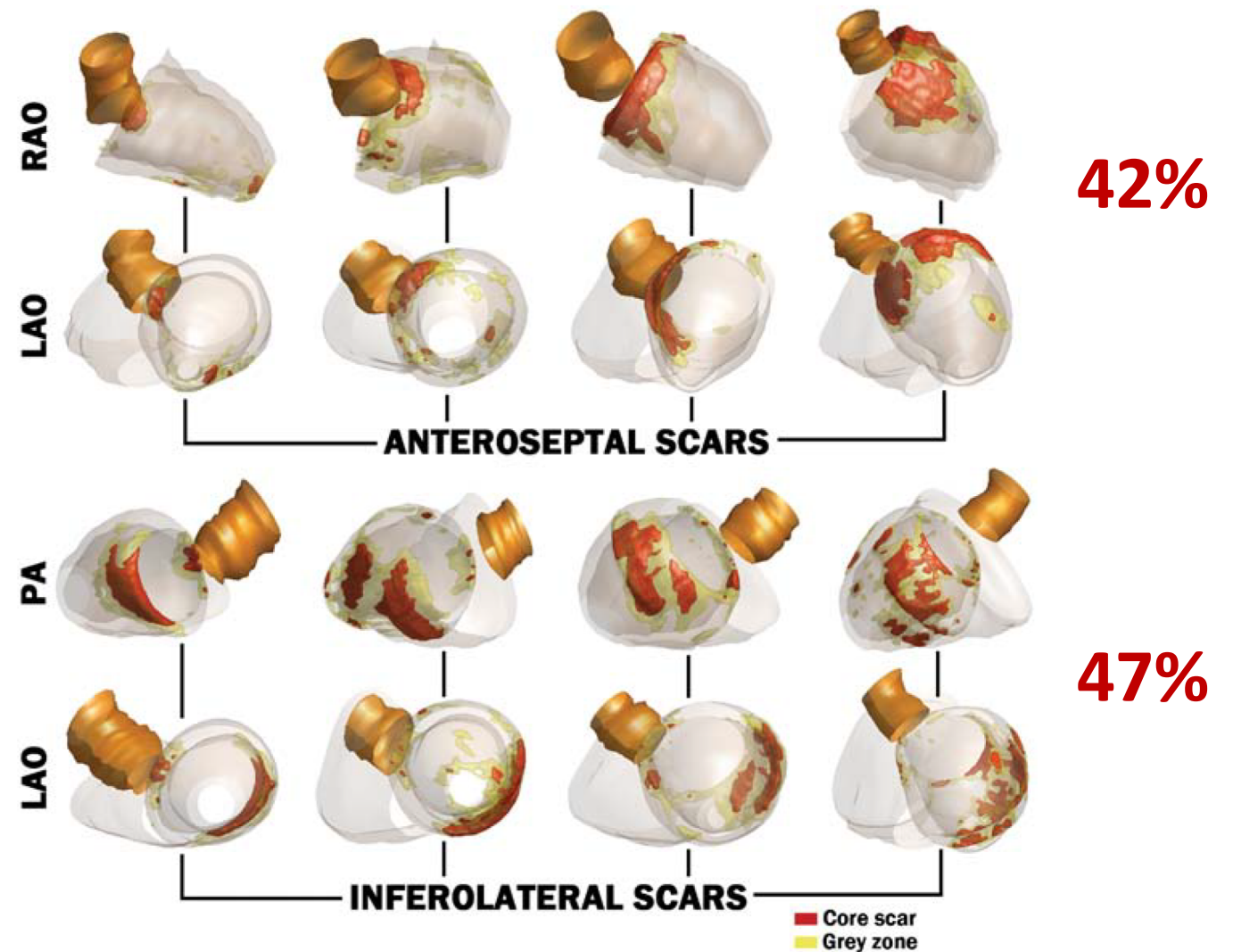
VT ablation in non ischemic CMs: prognostic role of different scar distribution

Contrast-Enhanced MRI-Derived Scar Patterns and Associated Ventricular Tachycardias in Nonischemic Cardiomyopathy Implications for the Ablation Strategy

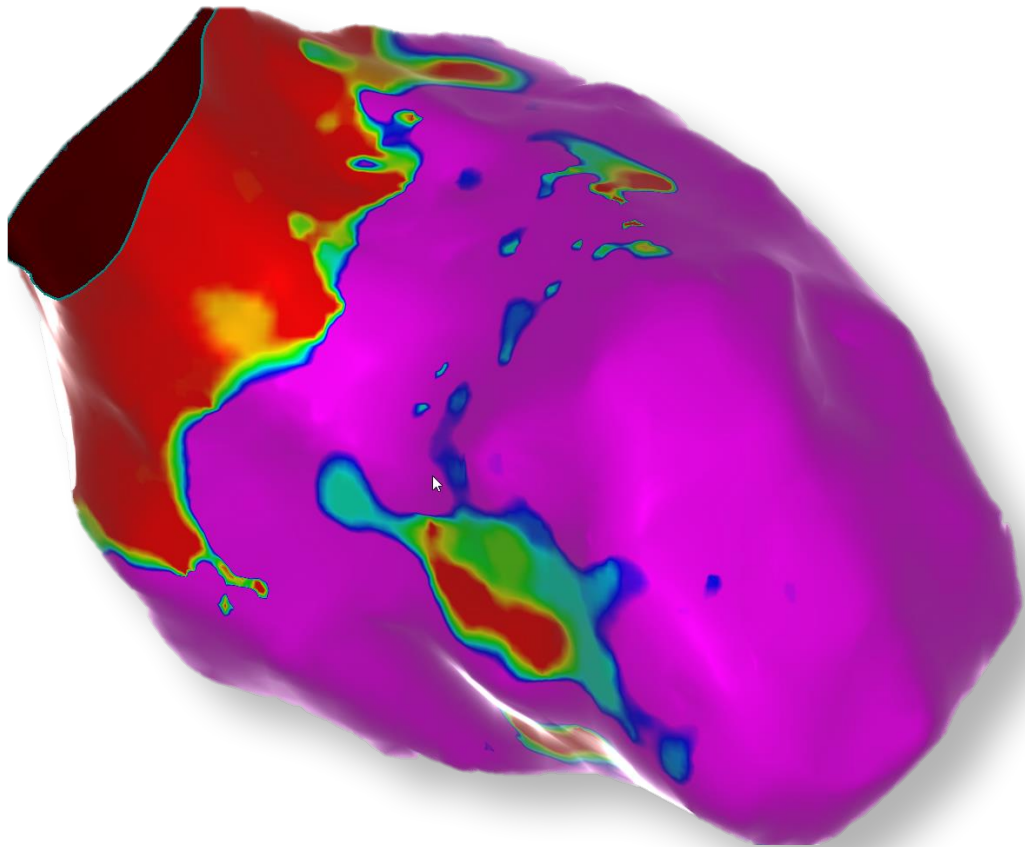
Sebastiaan R.D. Piers, MD; Qian Tao, PhD; Carine F.B. van Huls van Taxis, MD;
Martin J. Schalij, MD, PhD; Rob J. van der Geest, PhD; Katja Zeppenfeld, MD, PhD

VT rec: 50-74%

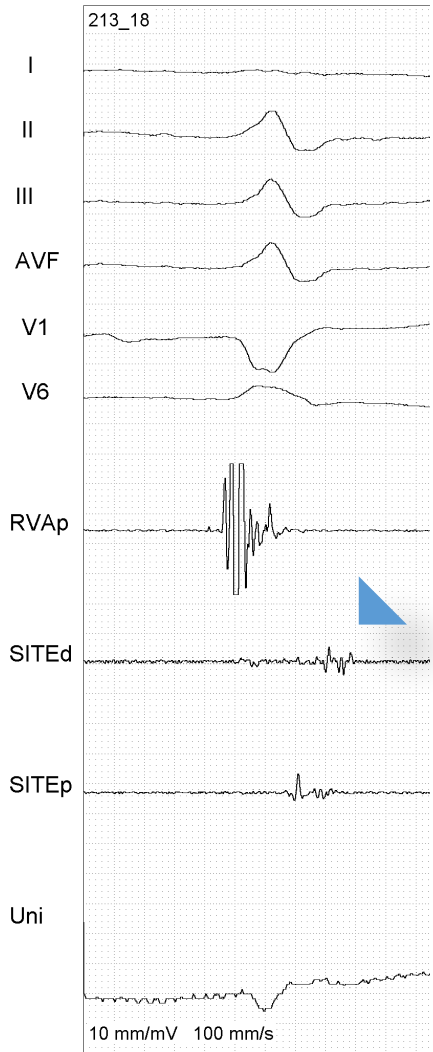
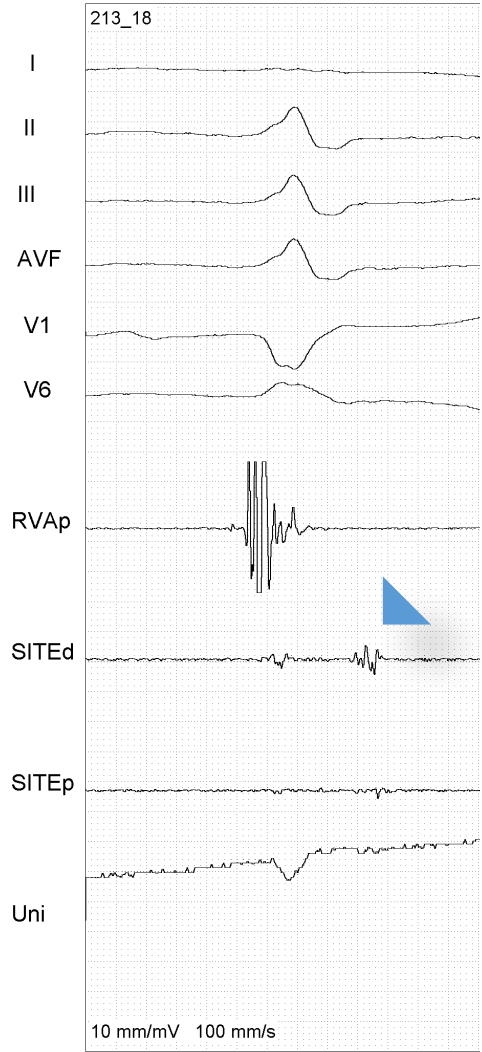
VT rec: 22-25%



VT ablation in non ischemic CMs: antero-septal scar

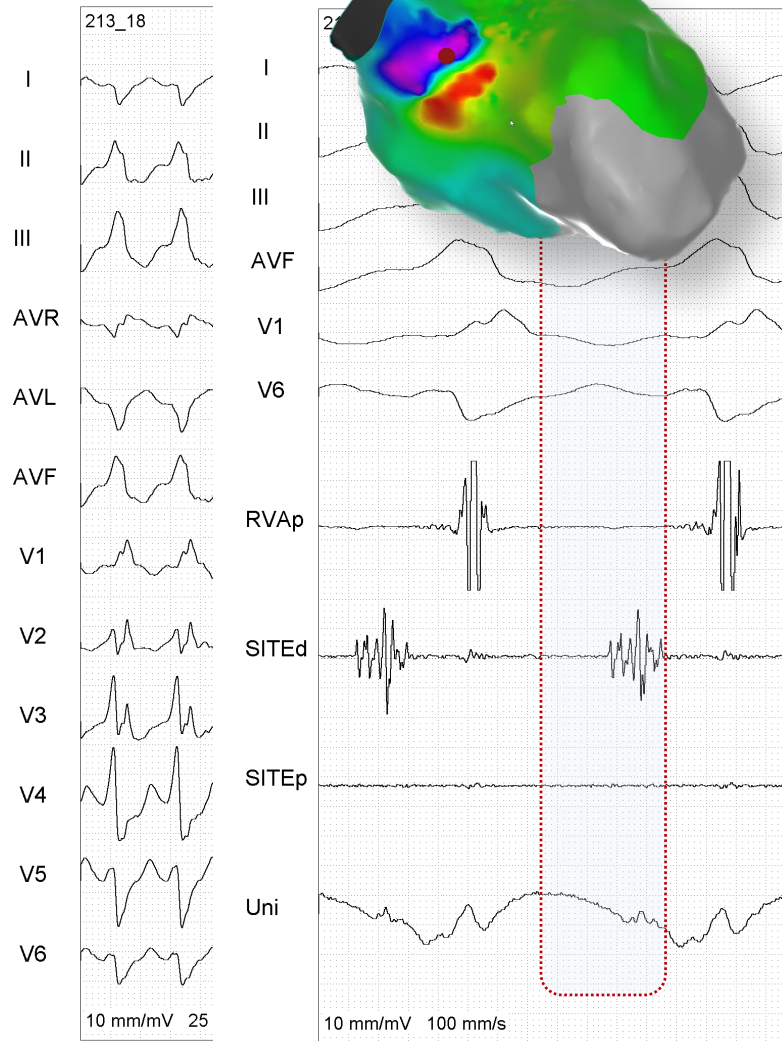


FA, NI DCM

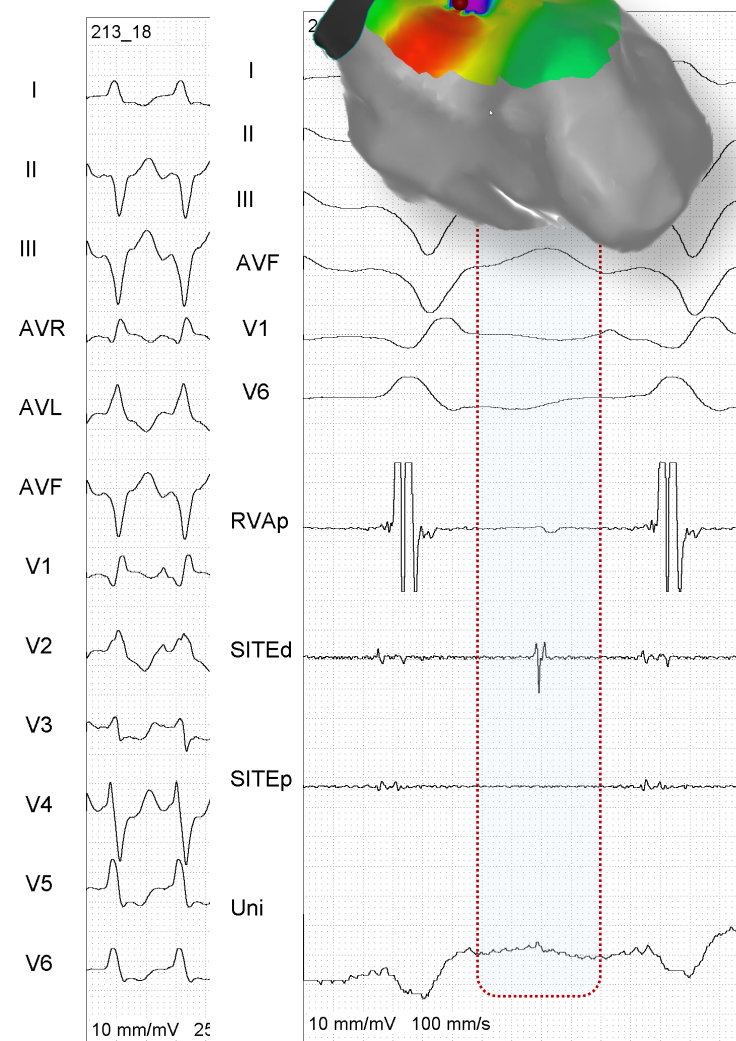


VT ablation in non ischemic CMs: antero-septal scar

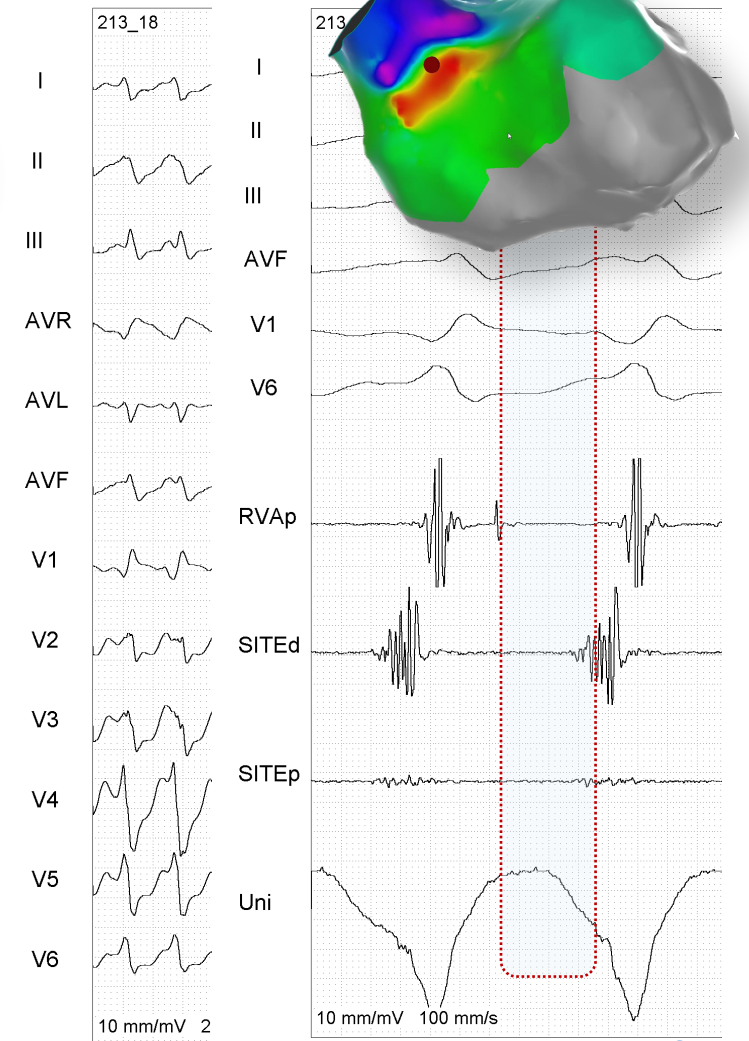
VT #1



VT #2



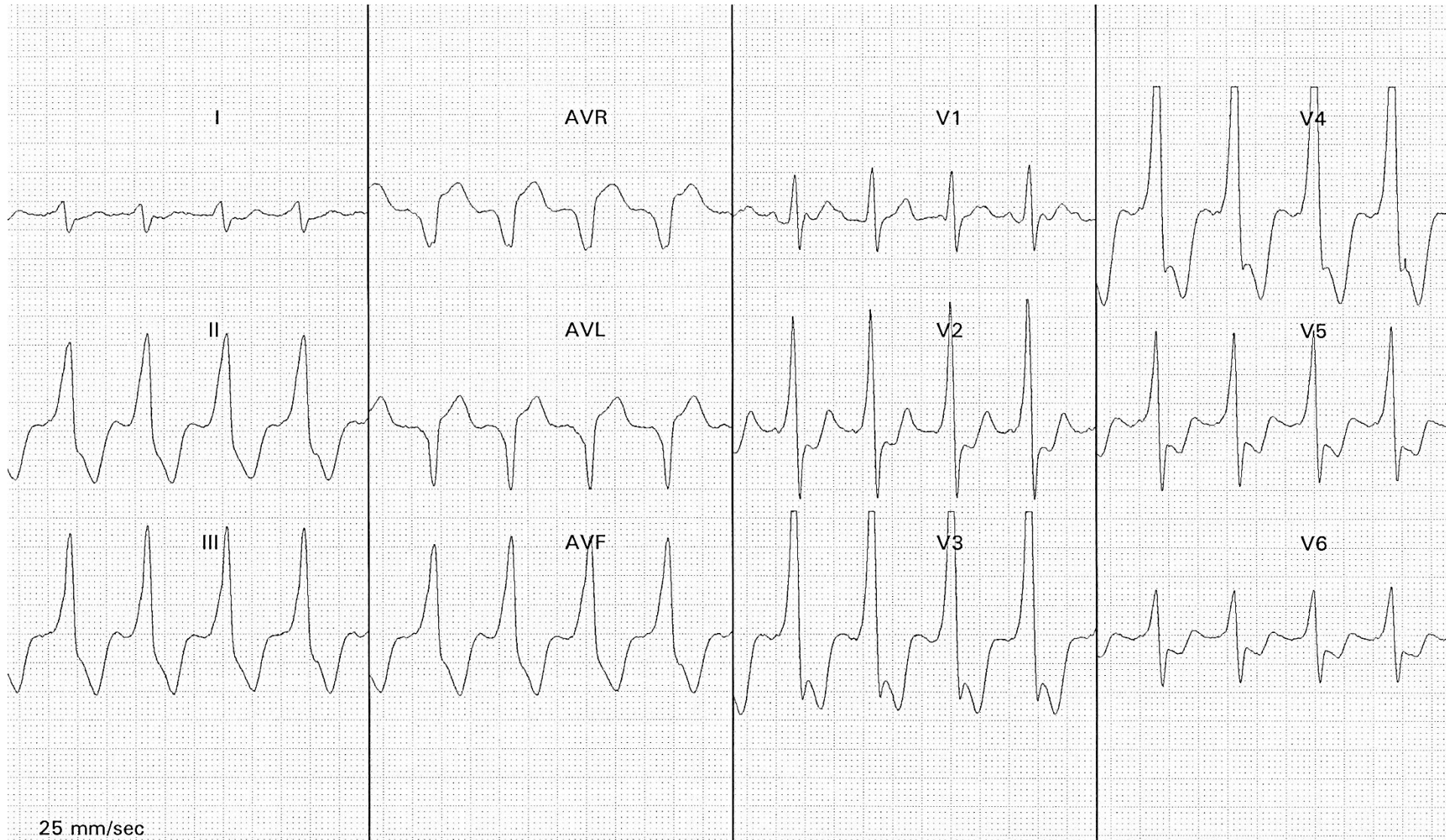
VT #3



FA, NI DCM

VT ablation in non ischemic CMs: antero-septal scar

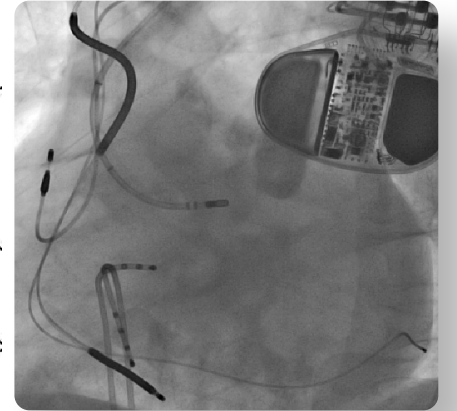
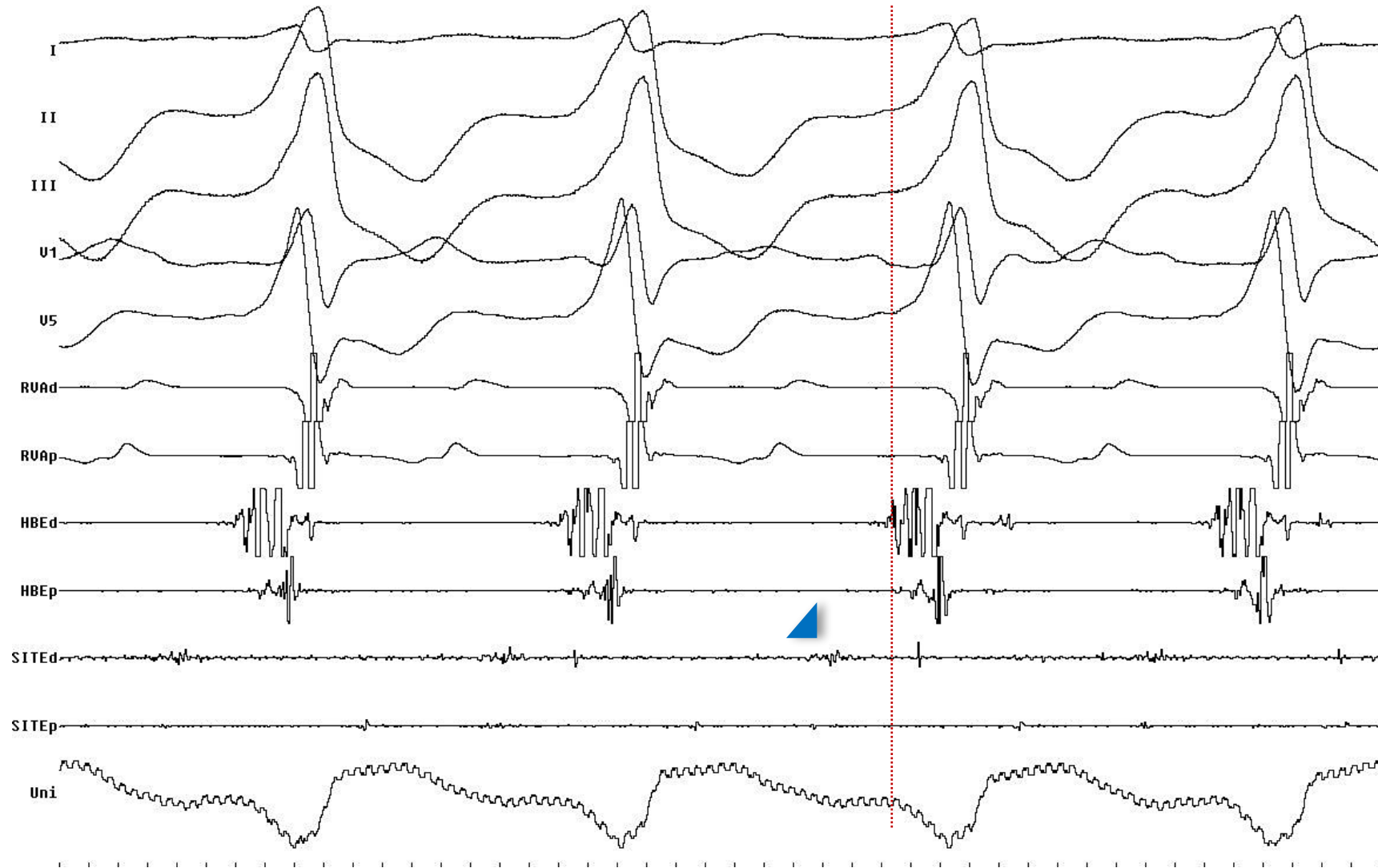
12-lead ECG (incessant VT @110 bpm)



LG, NI DCM

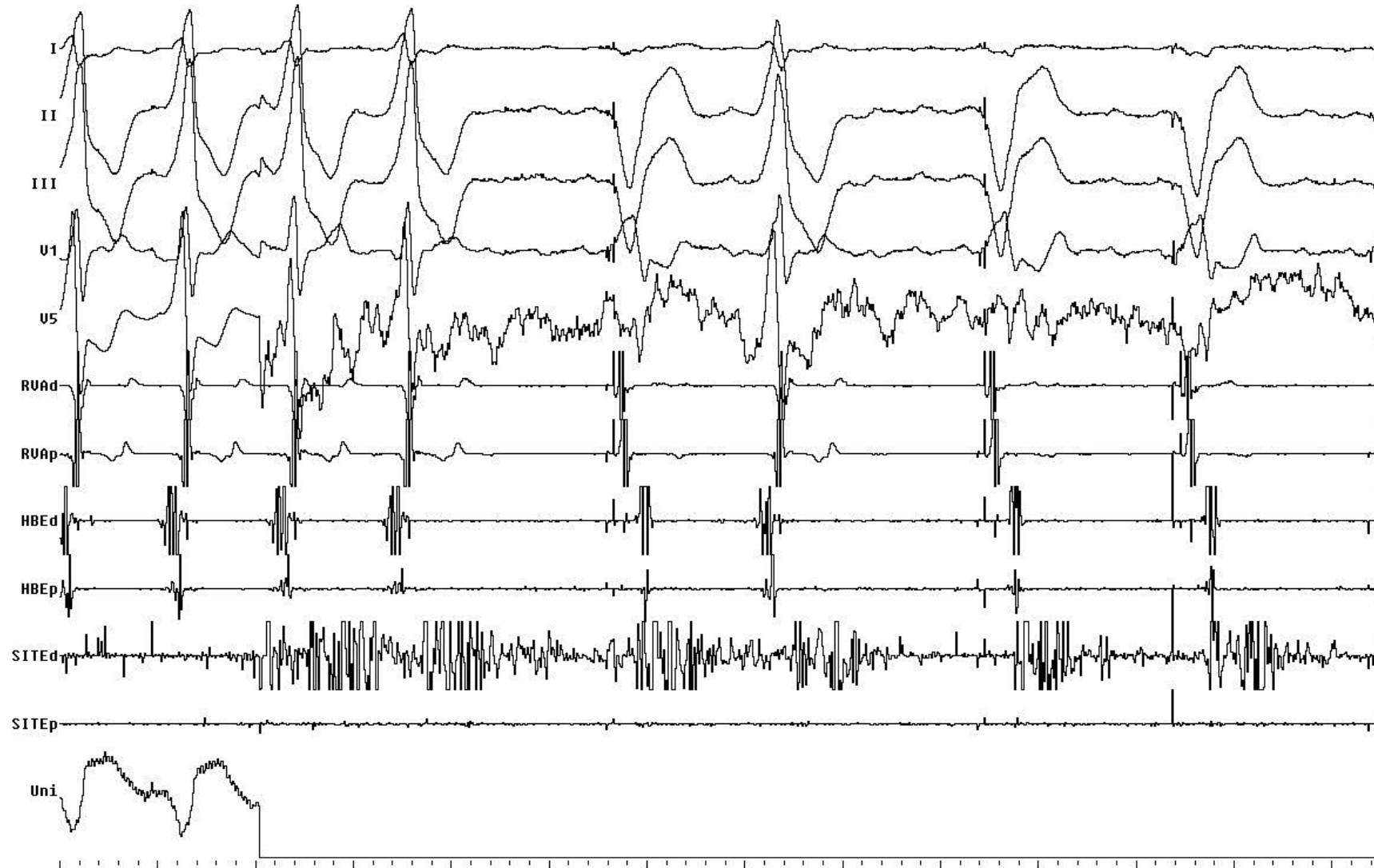
VT ablation in non ischemic CMs: antero-septal scar

Activation mapping (left AOC)



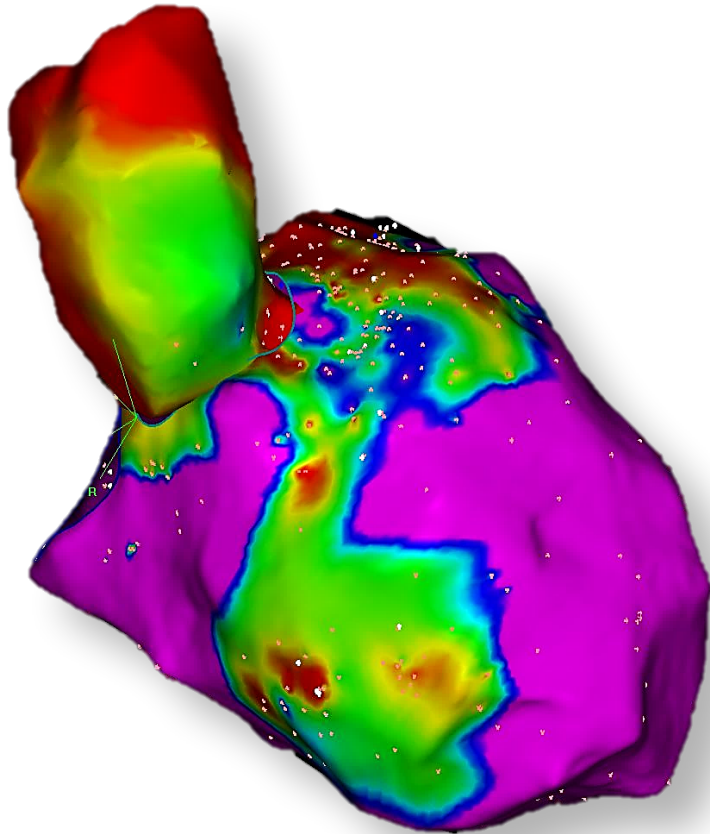
LG, NI DCM

VT ablation in non ischemic CMs: antero-septal scar

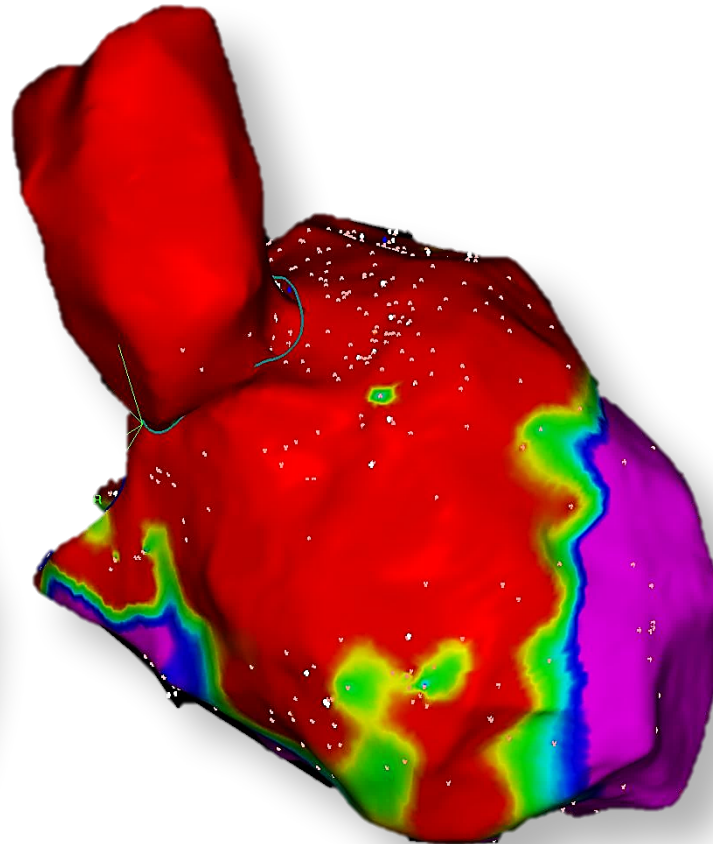


LG, NI DCM

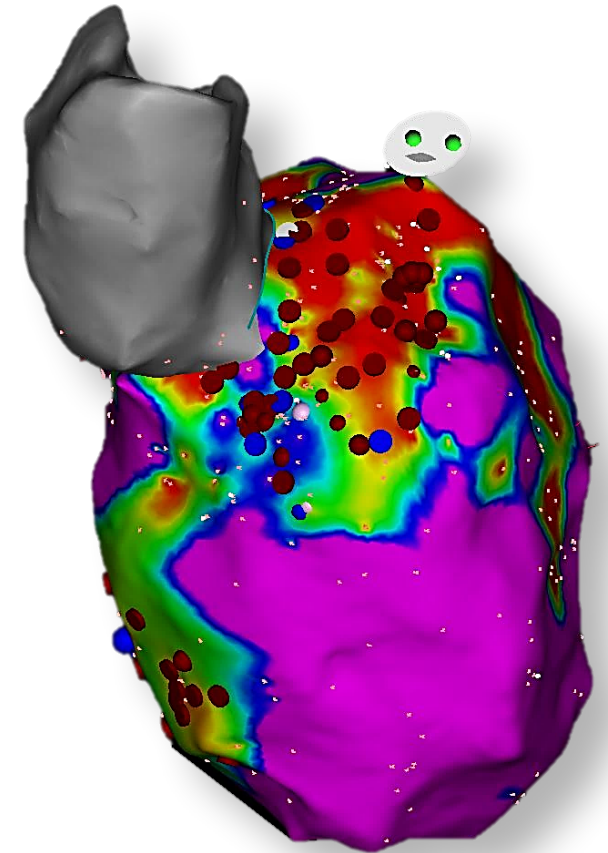
Bipolar EAVM



Unipolar EAVM



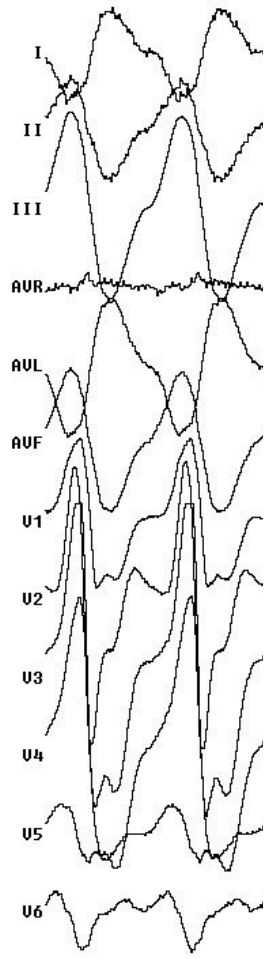
RF Ablation



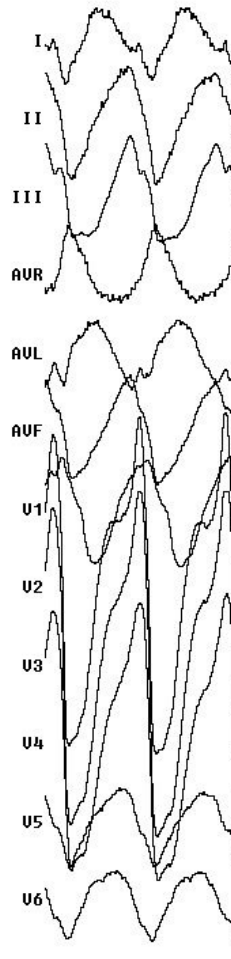
LG, NI DCM

VT ablation in non ischemic CMs: antero-septal scar

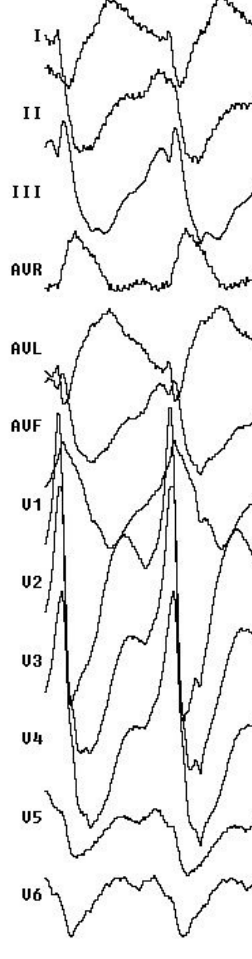
#1, CL 500 ms



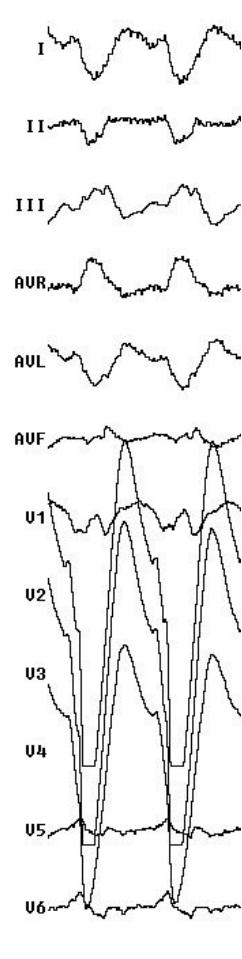
#2, CL 385 ms



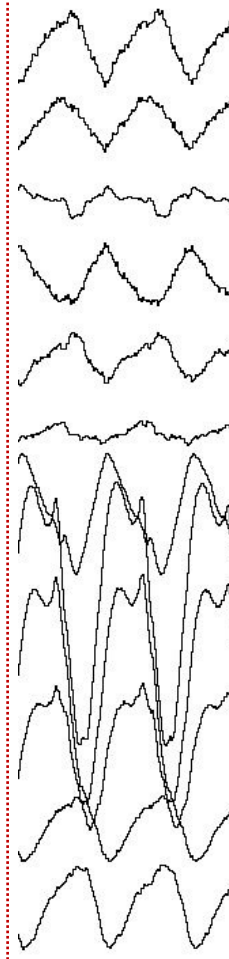
#3, CL 470 ms



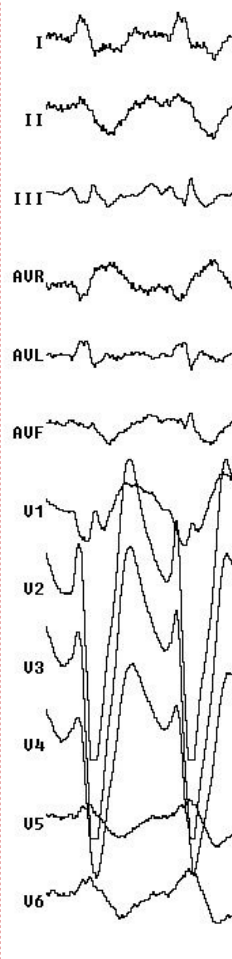
#4, CL 390 ms



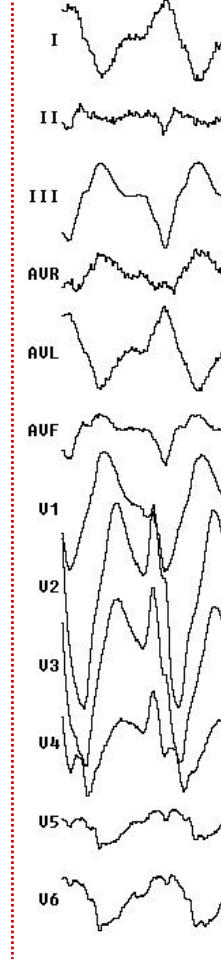
#5, CL 385 ms



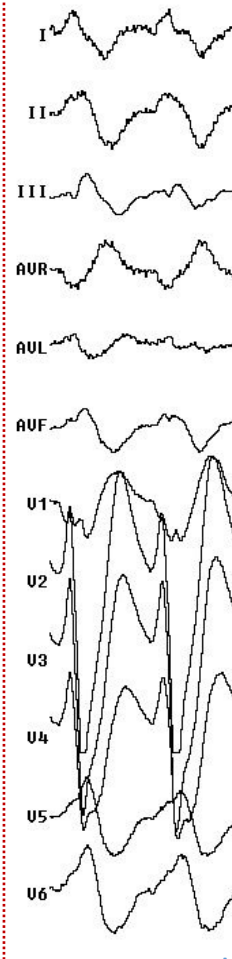
#6, CL 420 ms



#7, CL 365 ms

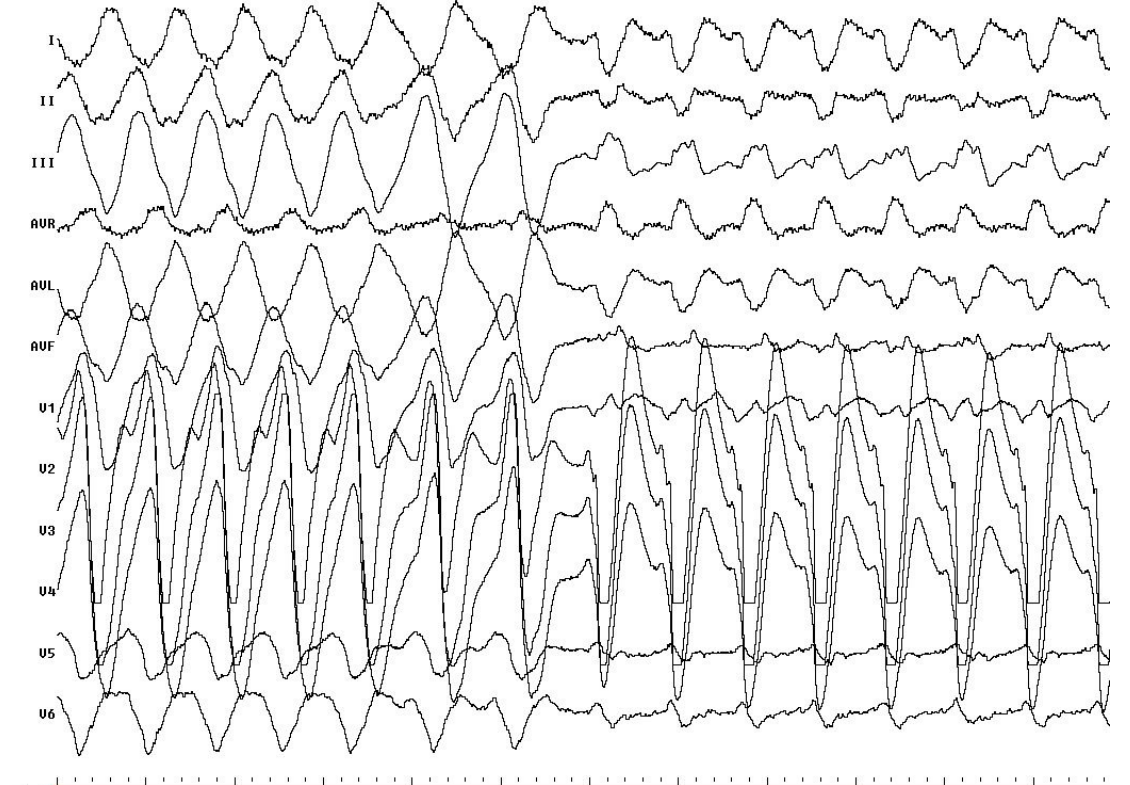
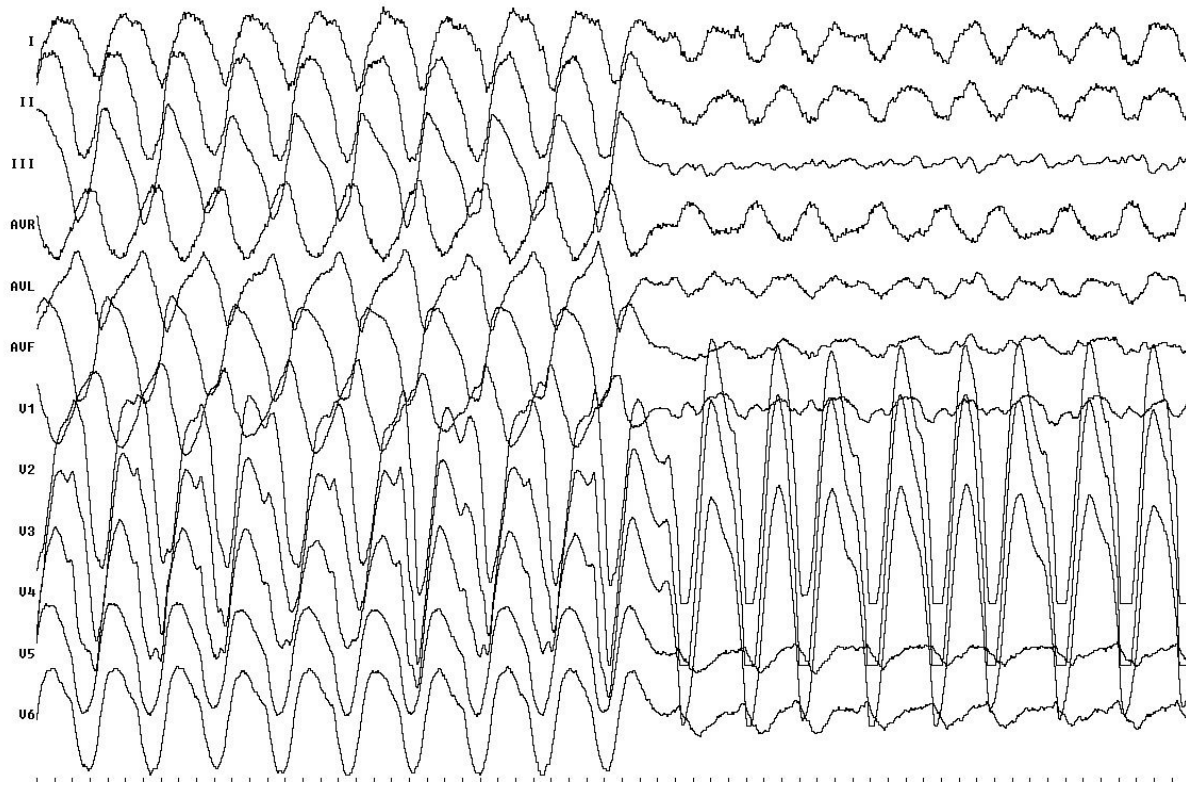


#8, CL 395 ms



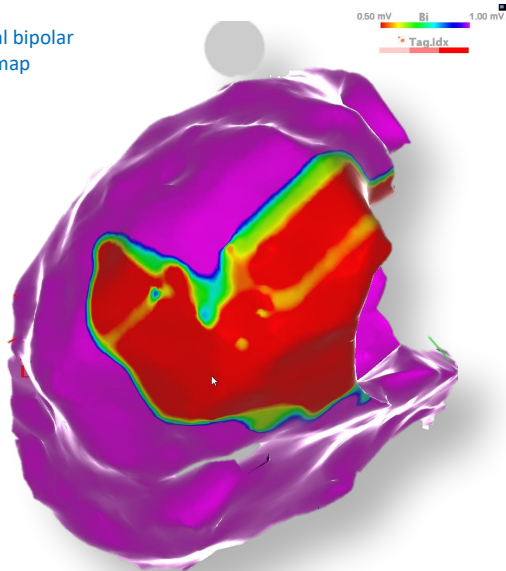
LG, NI DCM

VT ablation in non ischemic CMs: antero-septal scar

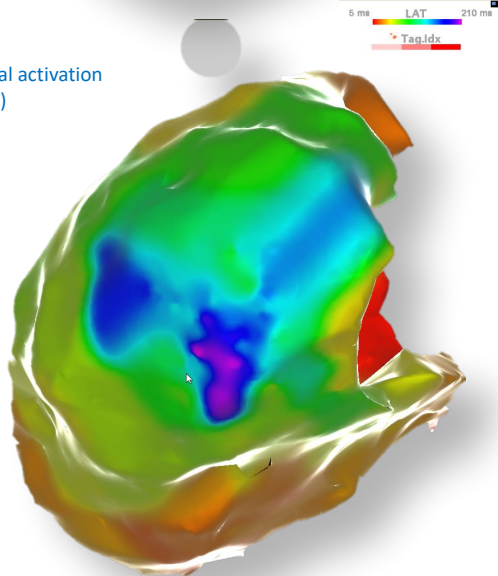


LG, NI DCM

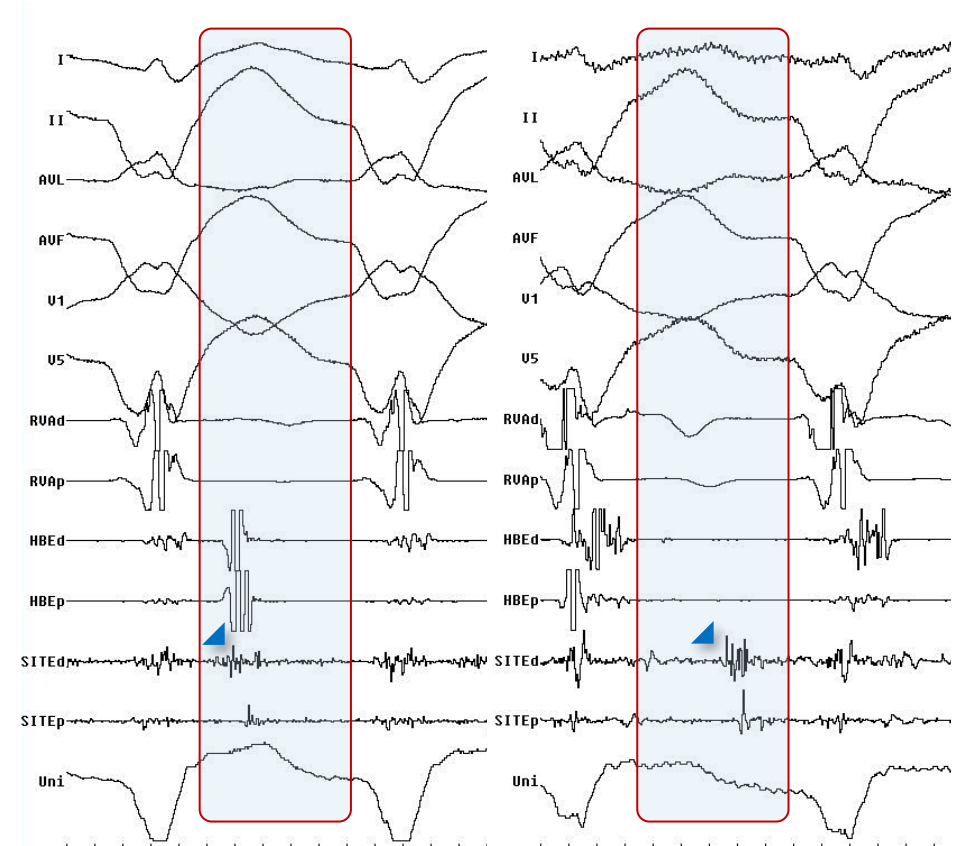
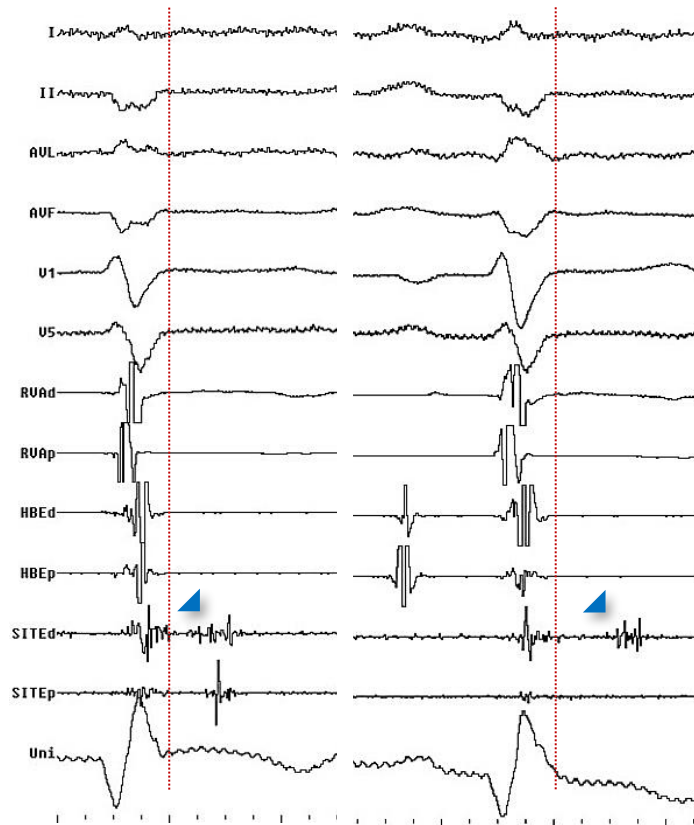
Epicardial bipolar
voltage map



Epicardial activation
map (SR)

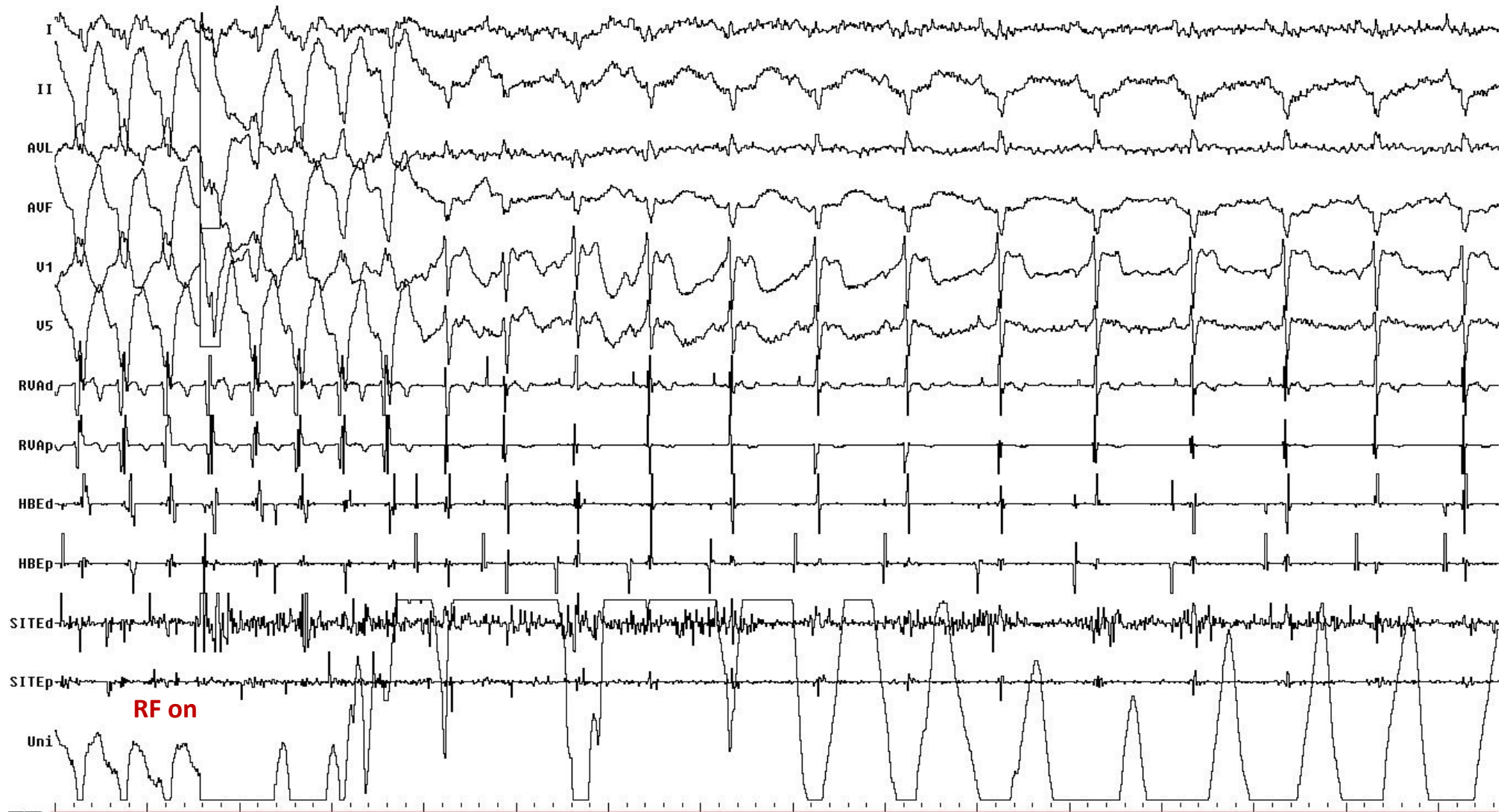


Epicardial mapping

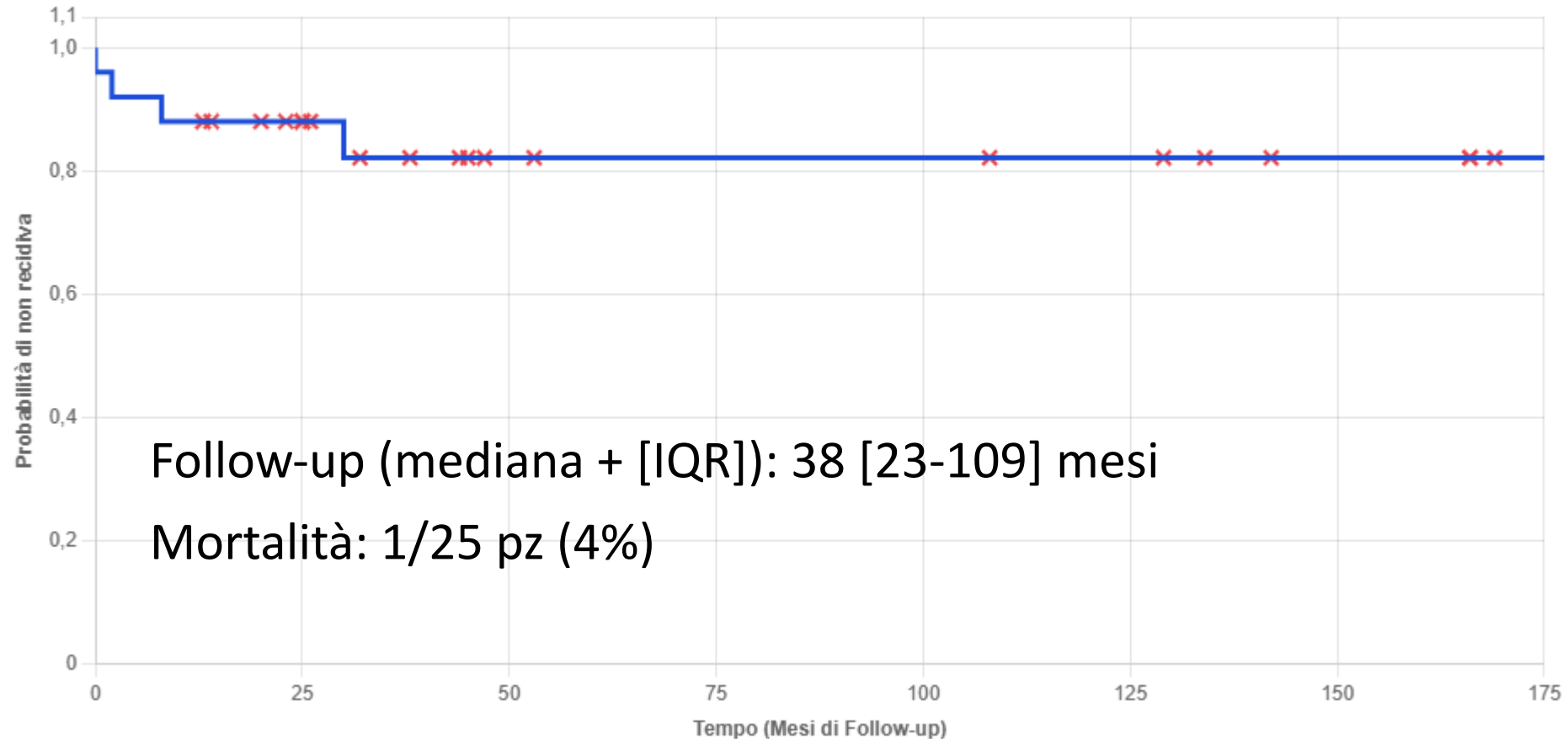


- ✓ M, 48 yrs
- ✓ NI DCM
- ✓ LV EF: 35%
- ✓ Arrhythmic storm

VT ablation in non ischemic CMs: infero-lateral scar



Ablazione transcatetere nella CM aritmogena sn – esperienza in Humanitas



Clinical Outcomes in Patients With Dilated Cardiomyopathy and Ventricular Tachycardia



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ABSTRACT

BACKGROUND Recurrent ventricular tachycardia (VT) due to dilated cardiomyopathy (DCM) is difficult to treat, and long-term outcome data are limited.

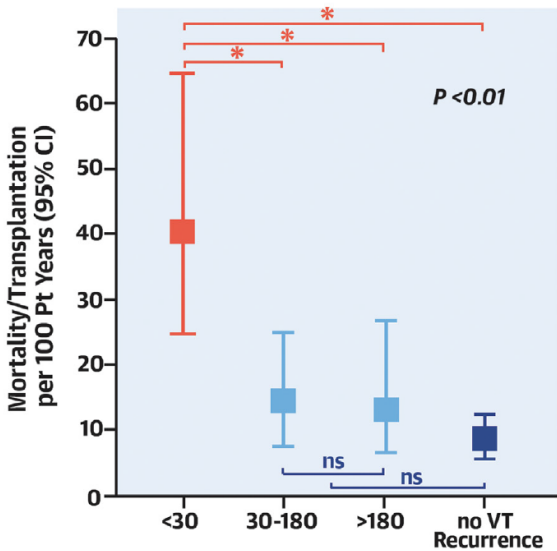
OBJECTIVES The aim of this study was to identify predictors of mortality or heart transplantation (HTx) and VT recurrence.

METHODS Consecutive patients with DCM accepted for radiofrequency catheter ablation (RFCA) of VT at 9 centers were prospectively enrolled and followed.

RESULTS Of 281 consecutive patients (mean age 60 ± 13 years, 85% men, mean left ventricular ejection fraction [LVEF] $36\% \pm 12\%$), 35% had VT storm, 20% had incessant VT, and amiodarone was unsuccessful in 68%. During follow-up of 21 months (IQR: 6-30 months), 67 patients (24%) died or underwent HTx, and 138 (49%) had VT recurrence (45 within 30 days, defined as early); the 4-year rate of VT recurrence or mortality or HTx was 70%. Independent predictors of mortality or HTx were early VT recurrence (HR: 2.92; 95% CI: 1.37-6.21; $P < 0.01$), amiodarone at discharge (HR: 3.23; 95% CI: 1.43-7.33; $P < 0.01$), renal dysfunction (HR: 1.92; 95% CI: 1.01-3.64; $P = 0.046$), and LVEF (HR: 1.36; 95% CI: 1.0-1.84; $P = 0.052$). LVEF $\leq 32\%$ identified patients at risk for mortality or HTx (area under the curve: 0.75). Mortality or HTx per 100 person-years was 40.4 events after early, compared with 14.2 events after later VT recurrence and 8.5 events with no VT recurrence after RFCA ($P < 0.01$ for both). Patients with early recurrence and LVEFs $\leq 32\%$ had a 1-year rate of mortality or HTx of 55%. VT recurrence was predicted by prior implantable cardioverter-defibrillator shocks, basal anteroseptal VT origin, and procedural failure but not LVEF.

CONCLUSIONS Patients with DCM needing RFCA for VT are a high-risk group. Following RFCA, approximately one-half remain free of VT recurrence. Early VT recurrence with LVEF $\leq 32\%$ identifies those at very high risk for mortality or HTx, and screening for mechanical support or HTx should be considered. Late VT recurrence after RFCA does not predict worse outcome. (J Am Coll Cardiol 2022;80:1045-1056) © 2022 by the American College of Cardiology Foundation.

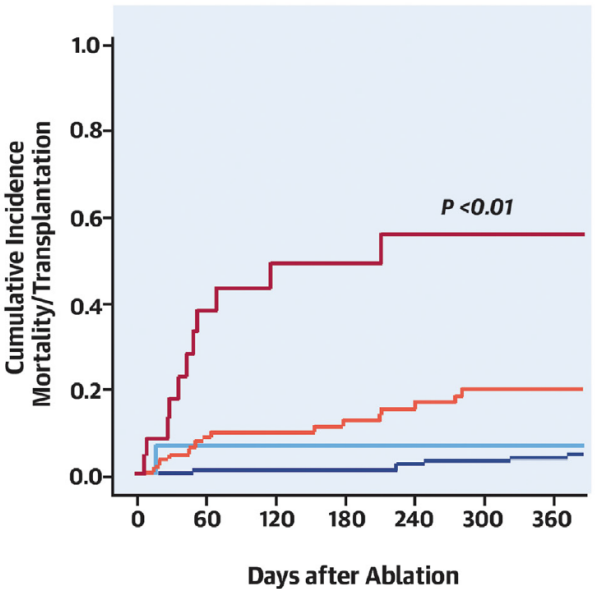
Early VT Recurrence Predicts High Mortality



Days to Recurrent VT after Ablation

After early VT recurrence:
40.4 deaths/tranplants per 100 pt years

Survival <50% for Low LVEF + Early VT Recurrence



Days after Ablation

LVEF $\leq 32\%$ + ER 55% at 1 year
LVEF $\leq 32\%$ no ER 19% at 1 year
LVEF $> 32\%$ + ER 6% at 1 year
LVEF $> 32\%$ no ER 3% at 1 year

Low LVEF and Early VT Recurrence Warrants Early Consideration for Heart Transplantation or LVAD

Strategie / strumenti che potrebbero aiutare a superare gli ostacoli

- Metodiche di imaging (pre-procedura, integrati con sistema di mappaggio EA) con elevato potere di risoluzione (RMN, TAC)
- Mappaggio ad alta densità e definizione per caratterizzare correttamente i substrati possibilmente aritmogeni e il loro coinvolgimento nella TV
- Modalità di erogazione della RF
 - ☑ durata prolungata
 - ☑ soluzione ipotonica
 - ☑ controllo di temperatura
 - ☑ bipolare
 - ☑ diversa conformazione dell'elettrodo distale
- Energie alternative
 - ☑ pulsed field ablation (elettroporazione)
 - ☑ crioterapia a temperatura ultra bassa (-196°C)
 - ☑ alcolizzazione
 - ☑ radioablazione

- Le cardiomiopatie non ischemiche includono un gruppo eterogeneo di substrati aritmogeni, sicuramente più complessi rispetto alla cardiopatia ischemica.
- L'efficacia dell'ablazione appare moderata, ma comunque in grado di migliorare la qualità di vita e ridurre il burden aritmico di questi pazienti
- Un attento inquadramento clinico-strumentale prima della procedura permette di identificare i candidati con maggiore probabilità di risposta e di programmare correttamente la procedura
- La complessità dei pazienti trattati e delle procedure eseguite richiede adeguata esperienza e approccio multidisciplinare
- Progressi nella capacità di identificare il substrato aritmogeno e nella possibilità di raggiungerlo e inattivarlo efficacemente con l'ablazione potranno migliorare ulteriormente l'outcome di questi pazienti