New insights on post-myocardial infarction ventricular tachycardia ablation: defining patient-tailored endpoints to improve outcome

De Riva Silva, M.

1

General Introduction and Outline of Thesis

GENERAL INTRODUCTION AND OUTLINE OF THE THESIS

Ventricular tachycardia after myocardial infarction

One to two percent of patients surviving an acute myocardial infarction (MI) develop monomorphic ventricular tachycardia (VT) over time, often more than a decade after the acute ischemic event.[1] Of importance, occurrence of VT may not only be a cause of disabling symptoms such as palpitations, dyspnea or syncope but it is also an important cause of sudden cardiac death (SCD) in this population.[2–4]

Implantable cardioverter defibrillators (ICDs) are effective in terminating VT and have demonstrated to increase survival in post-MI patients presenting with a cardiac arrest due to hemodynamically unstable VT or ventricular fibrillation (VF)[5–7]. However, it is important to highlight that ICDs do not prevent VT recurrence. Although the majority of VTs can be terminated by anti-tachycardia pacing (ATP) and therefore, some patients might be asymptomatic even if they suffer from recurrent VT, some VTs only terminate with ICD shocks, which can be a cause of pain and psychological distress and have even been associated with increased mortality[8–12]. In addition, some clinical presentations, such as VTs that do not terminate after multiple ICD interventions, slow VTs that are not recognized by the ICD or highly symptomatic VTs despite termination with ATP may require additional therapy to terminate VT and/or to avoid VT recurrence.

Treatment options in these scenarios are anti-arrhythmic drugs (AAD), catheter ablation and surgical ablation. Use of AAD is, however, often limited by their disappointing efficacy and their frequent side effects leading to drug discontinuation, and, surgical ablation, although potentially very effective, it is an invasive procedure associated with high morbidity.[13–15]

Catheter ablation has evolved into a very important therapy for VT after MI. In the last three decades, important progress in the understanding of the post-MI VT substrate and technological advancements have increased the efficacy and safety of the procedure. However, ablation still acutely fails in approximately 10% of the patients and VT recurs in 10 to 50% depending on baseline patient characteristics and follow-up time.[16–18]

Several crucial aspects which would likely contribute to improve ablation acute and long-term efficacy such us the deep comprehension of the VT substrate, the optimal ablation endpoints and the limitations of the technique remain unclear.

Mechanism and substrates for monomorphic ventricular tachycardia after myocardial infarction: implications for mapping and ablation

The majority of sustained VTs after MI are due to reentry involving areas of myocardial scar. In regions of scar, coupling of surviving myocardial bundles is reduced by interspersed fibrosis, diminished gap junction density and decreased connexin expression resulting in slow conduction and eventually in conduction block. Slow myocardial conduction through an isthmus protected by areas of dense fibrosis and/or valvular annuli acting as fixed conduction barriers or areas of functional conduction block only present at rapid rates, allows for initiation and maintenance of a stable re-entrant VT. [19–21]

Ablation in the setting of post-MI VT relies on the identification of the critical isthmus of the reentry circuit followed by transection of the isthmus, ideally with transmural and durable radiofrequency lesions. In patients presenting with hemodynamically stable VT, this can be best achieved through accurate characterization of the VT circuit by means of activation and entrainment mapping.[22] However, approximately 10% of patients currently referred for ablation are not inducible for any tachycardia during the procedure and up to 70% are inducible for one or more unstable VTs due to hemodynamic compromise requiring immediate interruption, transition to a different morphology or spontaneous termination.[16–18,23,24] In these scenarios, interrogation of multiple sites to define the re-entry circuit by analysis of the intracardiac activation sequence and/or the response to entrainment is not possible. In addition, scars frequently present a complex three-dimensional architecture, with multiple areas of slow conduction that may act as potential isthmuses for future VTs, even if they have not yet occurred spontaneously and are not inducible during the procedure.

Substrate-based VT ablation techniques have been developed with the main purpose of targeting areas of slow conduction within the scar area during stable sinus or paced rhythm. These sites represent putative surrogates of the VT isthmuses and are therefore critical sites to target when aiming to eliminate present and future VTs.[23,25–28]

The first step of all substrate-based ablation approaches consist on the delineation of the electroanatomical (EA) scar area by bipolar voltage mapping. Accurate identification of the scar area is important since, on one hand, it almost invariably contains at least parts of the VT circuit and, on the other hand, the surviving myocardium beyond the scar should be spared from ablation injury because it may contribute to cardiac function. Up to now, the majority of centers use an uniform cut-off of 1.5mV to discriminate scar from normal myocardium and a cut-off of 0.5mV to discern between dense scar and scar border zone. However, it is important to realize that these cut-off values were only validated by gross histopathology to detect the dense scar core.[23,29,30] Accordingly,

in patients with transmural infarctions, a cut-off of 1.5mV seems to precisely distinguish between the scar and preserved myocardium. However, this is not the case in patients with non-transmural infarctions, in whom high voltage signals generated by large surviving bundles of myocardium located in the sub-epicardium or surrounding the necrotic area may contaminate the local electrical activity leading to an underestimation of the scar area when an uniform cut-off of 1.5mV is applied.[31] In fact, a mismatch between the non-transmural infarct size defined by bipolar voltage mapping and contrast-enhanced magnetic resonance imaging (CE-MRI), the gold standard for fibrosis identification, has been observed.[32] In addition, termination of VT in areas with bipolar voltage larger than 1.5mV has been reported, further emphasizing the limitations of bipolar voltage mapping to detect the entire potential arrhythmogenic substrate in this patient population.[33] This is relevant since small non-transmural scars are currently increasingly encountered in patients who underwent reperfusion of the infarct related artery during the acute MI.[31] Mapping with multipolar catheters with small electrodes and narrow interelectrode spacing and ventricular pacing from multiple sites may help to separate local from far-field signals and to identify additional low-voltage areas not detected during sinus rhythm.[33,34] However, low voltage is not a synonym of arrhythmogenic substrate and ablation based only on electrogram amplitude may lead to damage of viable myocardium not involved in VT.

The second step of substrate mapping is therefore to identify electrograms consistent with slow conduction within the scar area that may be critical for VT circuits.[27,35] Isolated and late potentials have been demonstrated to be specific surrogates of VT isthmuses and, in accordance, late potential elimination has been associated with improved ablation outcomes.[36] However, although endocardial scar is almost invariably found in patients with old infarctions, in up to one third of post-MI patients, late potentials are not present.[26] These patients have typically small, non-dense scars which are associated with the presence of fast VTs.[26] Of note, for fast VTs, slow conduction and block might be functional, only present at fast rates, and hence, not detectable if mapping is performed during sinus rhythm or continuous pacing only.[21] In this setting, additional manoeuvres, such as RV extra-stimulation might be necessary to unmask areas of slow conduction responsible for VT.

Endpoints of post-MI VT ablation: non-inducibility and beyond

Since the advent of post-MI VT ablation, the response to programmed electrical stimulation (PES) at the end of the procedure has been used to assess the acute ablation result and to predict the mid-long term probability of VT recurrence.[37–40] Non-inducibility of VT after ablation has been associated with VT free survival in many studies.[16,41–43] However, using non-inducibility as a single ablation endpoint has limitations. In fact, there is a

significant number of patients who do not experience VT recurrence despite remaining inducible for VT at the end of the procedure and there is also an important number of patients who present VT recurrence despite being categorized as non-inducible after the last RF application. This might be explained by several factors. First, the definition of non-inducibility has not been uniformly applied and while some have used non-inducibility of the clinically documented VT or VTs with a similar CL to the clinical VT, others have used inducibility of any VT for definition.[16,36,37,39,40] This is important, since while persistent inducibility of the clinical VT or slow VTs with a CL similar to the (presumed-) clinical VT has clearly been associated with a high chance of VT recurrence, the impact of inducibility of non-clinical, particularly fast VTs remains unclear. Second, VT induction is a probabilistic phenomenon and, therefore, performing multiple evaluations over time likely increases the chance of induction.[44,45] In addition, the applied PES protocol, which should include the introduction of at least three extra-stimuli with short coupling intervals from multiple ventricular sites also influences the probability of induction, especially of fast VTs.[46–48] However, PES protocols are not uniformly and entirely performed after ablation in all EP laboratories, which affects the interpretation of the data.

As stated before, substrate-based ablation approaches were developed to allow targeting non-inducible and poorly tolerated VTs with the general aim of eliminating all potential arrhythmogenic areas during stable rhythm. Multiple endpoints for substrate ablation of scar-related VT have been proposed which could be divided into two groups; anatomical-based and EGM-based approaches. Anatomical approaches include performance of linear lesions, scar homogenization and core isolation.[23,25,49] EGM-based approaches target late and isolated potentials, all local abnormal ventricular activities or EGMS displaying slow-conduction characteristics during the applications of extra-stimuli (functional substrate ablation).[28,36,50] Although several of these approaches have shown to increase VT-free survival compared to ablation based on inducible VTs, to date no prospective comparison between the different techniques has been performed and therefore, the optimal substrate-based ablation endpoint for a given patient remains unknown.

AIM AND OUTLINE OF THE THESIS

The present thesis aims to provide new insights on catheter ablation of post-MI VT. Improved understanding of the underlying VT substrate in different types of MI, re-assessment of old and development of new physiologically meaningful ablation endpoints and recognition of the limitations of the technique will likely contribute to optimize procedural outcomes in the future.

In **chapter 2**, the value and limitations of the oldest and easiest-available mapping tool for VT, the 12-lead ECG, are extensively reviewed. The chapter is illustrated with several paradigmatic cases. **Chapter 3** analyzes the influence of individual patient characteristics and, in particular, of the left ventricular (LV) function, on the predictive value of non-inducibility after ablation for VT recurrence and cardiac mortality in the population currently referred for post-MI VT ablation. The objectives of **chapter 4** are to propose a new definition for fast VT based on the individual ventricular refractory period (VRP) and to assess the prognostic value of persistent inducibility after ablation of non-clinical VTs with a CL close to VRP in a mixed cohort of patients with ischemic and non-ischemic cardiomyopathy. In **chapter 5**, a systematic approach for post-MI VT substrate identification based on the analysis of electrograms within the scar area with RV extra-stimulation is proposed. In addition, the outcome of the procedure for the different infarct subtypes when using elimination of electrograms displaying functional slow conduction characteristics as ablation endpoint is analyzed. The prevalence of myocardial calcification and its impact in the acute and long-term outcome of endocardial ablation for post-MI VT is evaluated in **chapter 6**. Finally, a summary of the thesis, conclusions and future perspectives are provided in **chapter 7**.

REFERENCE LIST

1. Henkel DM, Witt BJ, Gersh BJ, Jacobsen SJ, Weston SA, Meverden RA, Roger VL. Ventricular arrhythmias after acute myocardial infarction: A 20-year community study. *Am Heart J* 2006;**151**:806–812.
2. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML, Multicenter Automatic D. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N. Engl. J. Med. 2002. p. 877–883.
3. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, Davidson-Ray LD, Fraulo ES, Fishbein DP, Luceri RM, Ip JH, Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med* 2005;**352**:225–237.
4. Buxton AE, Lee KL, DiCarlo L, Gold MR, Greer GS, Prystowsky EN, O'Toole MF, Tang A, Fisher JD, Coromilas J, Talajic M, Hafley G, Multicenter Unsustained T. Electrophysiologic testing to identify patients with coronary artery disease who are at risk for sudden death. N. Engl. J. Med. 2000. p. 1937–1945.
5. Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997;**337**:1576–1583.
6. Kuck KH, Cappato R, Siebels J, Ruppel R, Investigators C. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest - The Cardiac Arrest Study Hamburg (CASH). Circulation. 2000. p. 748–754.
7. Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, Mitchell LB, Green MS, Klein GJ, O'Brien B, Investigators C. Canadian implantable defibrillator study (CIDS) - A randomized trial of the implantable cardioverter defibrillator against amiodarone. Circulation. 2000. p. 1297–1302.
8. Andersen A, Damj T, Jb J, Ss P. Anxiety, depression, ventricular arrhythmias and mortality in patients with an implantable cardioverter defibrillator: 7 years' follow-up of the MIDAS cohort. Gen. Hosp. Psychiatry. Gen Hosp Psychiatry; 2020. https://pubmed.ncbi.nlm.nih.gov/32866884/ (10 January 2021)
9. Magyar-Russell M-R, Bd T, Jx C, T B, Ea K, Pp S, M MBB, E A, M R, N A, Je M, Rc Z. The prevalence of anxiety and depression in adults with implantable cardioverter defibrillators: a systematic review. J. Psychosom. Res. J Psychosom Res; 2011. https://pubmed.ncbi.nlm.nih.gov/21911099/ (10 January 2021)
10. Broek K van den, Fb T, M H, M A, Ph van der V, J D. Emotional distress, positive affect, and mortality in patients with an implantable cardioverter defibrillator. Int. J. Cardiol. Int J Cardiol; 2013. https://pubmed.ncbi.nlm.nih.gov/21963213/ (11 October 2020)
11. Wilkoff B, Bd W, Rs S, Sl M, F L, Sw L, Um B-G, Ms W, Ic VG, Bm H, Ml B, Kk H. Strategic programming of detection and therapy parameters in implantable cardioverter-defibrillators reduces shocks in primary prevention patients: results from the PREPARE (Primary Prevention Parameters Evaluation) study. J. Am. Coll. Cardiol. J Am Coll Cardiol; 2008. https://pubmed.ncbi.nlm.nih.gov/18687248/ (11 October 2020)
12. Wilkoff BL, Ousdigian KT, Sterns LD, Wang ZJ, Wilson RD, Morgan JM, EMPIRIC Trial Investigators. A comparison of empiric to physician-tailored programming of implantable cardioverter-defibrillators: results from the prospective randomized multicenter EMPIRIC trial. *J Am Coll Cardiol* 2006;**48**:330–339.

13. Connolly S, P D, Rs R, M G, S B, Es F, K T, J C, M T, B C, Gc G, Sh H. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: the OPTIC Study: a randomized trial. JAMA. JAMA; 2006. https://pubmed.ncbi.nlm.nih.gov/16403928/ (12 October 2020)
14. Kuhlkamp V, Mewis C, Mermi J, Bosch RF, Seipel L. Suppression of sustained ventricular tachyarrhythmias: A comparison of d,l-sotalol with no antiarrhythmic drug treatment. J. Am. Coll. Cardiol. 1999. p. 46–52.
15. Kienzle MG, Miller J, Falcone RA, Harken A, Josephson ME. Intraoperative endocardial mapping during sinus rhythm: relationship to site of origin of ventricular tachycardia. *Circulation* 1984;**70**:957–965.
16. Stevenson WG, Wilber DJ, Natale A, Jackman WM, Marchlinski FE, Talbert T, Gonzalez MD, Worley SJ, Daoud EG, Hwang C, Schuger C, Bump TE, Jazayeri M, Tomassoni GF, Kopelman HA, Soejima K, Nakagawa H, Multictr Thermocool VTAT. Irrigated Radiofrequency Catheter Ablation Guided by Electroanatomic Mapping for Recurrent Ventricular Tachycardia After Myocardial Infarction The Multicenter Thermocool Ventricular Tachycardia Ablation Trial. Circulation. 2008. p. 2773–2782.
17. Sapp JL, Wells GA, Parkash R, Stevenson WG, Blier L, Sarrazin J-F, Thibault B, Rivard L, Gula L, Leong-Sit P, Essebag V, Nery PB, Tung SK, Raymond J-M, Sterns LD, Veenhuyzen GD, Healey JS, Redfearn D, Roux J-F, Tang ASL. Ventricular Tachycardia Ablation versus Escalation of Antiarrhythmic Drugs. *N Engl J Med* 2016;**375**:111–121.
18. Marchlinski FE, Haffajee CI, Beshai JF, Dickfeld T-ML, Gonzalez MD, Hsia HH, Schuger CD, Beckman KJ, Bogun FM, Pollak SJ, Bhandari AK. Long-Term Success of Irrigated Radiofrequency Catheter Ablation of Sustained Ventricular Tachycardia. *J Am Coll Cardiol* 2016;**67**:674–683.
19. Debakker JMT, Vancapelle FJL, Janse MJ, Tasseron S, Vermeulen JT, Dejonge N, Lahpor JR. SLOW CONDUCTION IN THE INFARCTED HUMAN HEART - ZIGZAG COURSE OF ACTIVATION. Circulation. 1993. p. 915–926.
20. Wit AL, Peters NS. The role of gap junctions in the arrhythmias of ischemia and infarction. *Heart Rhythm* 2012;**9**:308–311.
21. Anter E, Tschabrunn CM, Buxton AE, Josephson ME. High-Resolution Mapping of Postinfarction Reentrant Ventricular Tachycardia: Electrophysiological Characterization of the Circuit. *Circulation* 2016;**134**:314–327.
22. Stevenson WG, Khan H, Sager P, Saxon LA, Middlekauff HR, Natterson PD, Wiener I. Identification of reentry circuit sites during catheter mapping and radiofrequency ablation of ventricular tachycardia late after myocardial infarction. *Circulation* 1993;**88**:1647–1670.
23. Marchlinski FE, Callans DJ, Gottlieb CD, Zado E. Linear ablation lesions for control of unmappable ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. Circulation. 2000. p. 1288–1296.
24. Di Biase L, Burkhardt JD, Lakkireddy D, Carbucicchio C, Mohanty S, Mohanty P, Trivedi C, Santangeli P, Bai R, Forleo G, Horton R, Bailey S, Sanchez J, Al-Ahmad A, Hranitzky P, Gallinghouse GJ, Pelargonio G, Hongo RH, Beheiry S, Hao SC, Reddy M, Rossillo A, Themistoclakis S, Dello Russo A, Casella M, Tondo C, Natale A. Ablation of Stable VTs Versus Substrate Ablation in Ischemic Cardiomyopathy. *J Am Coll Cardiol* 2015;**66**:2872–2882.
25. Di Biase L, Santangeli P, Burkhardt DJ, Bai R, Mohanty P, Carbucicchio C, Dello Russo A, Casella M, Mohanty S, Pump A, Hongo R, Beheiry S, Pelargonio G, Santarelli P, Zucchetti M, Horton R, Sanchez JE, Elayi CS, Lakkireddy D, Tondo C, Natale A. Endo-Epicardial Homogenization of the Scar Versus Limited Substrate Ablation for the Treatment of Electrical Storms in Patients With Ischemic Cardiomyopathy. J. Am. Coll. Cardiol. 2012. p. 132–141.

26. Tsiachris D, Silberbauer J, Maccabelli G, Oloriz T, Baratto F, Mizuno H, Bisceglia C, Vergara P, Marzi A, Sora N, Guarracini F, Radinovic A, Cireddu M, Sala S, Gulletta S, Paglino G, Mazzone P, Trevisi N, Della Bella P. Electroanatomical Voltage and Morphology Characteristics in Postinfarction Patients Undergoing Ventricular Tachycardia Ablation: Pragmatic Approach Favoring Late Potentials Abolition. *Circ Arrhythm Electrophysiol* 2015;**8**:863–873.
27. Bogun F, Good E, Reich S, Elmouchi D, Igic P, Lemola K, Tschopp D, Jongnarangsin K, Oral H, Chugh A, Pelosi F, Morady F. Isolated Potentials During Sinus Rhythm and Pace-Mapping Within Scars as Guides for Ablation of Post-Infarction Ventricular Tachycardia. *J Am Coll Cardiol* 2006;**47**:2013–2019.
28. Jaïs P, Maury P, Khairy P, Sacher F, Nault I, Komatsu Y, Hocini M, Forclaz A, Jadidi AS, Weerasooryia R, Shah A, Derval N, Cochet H, Knecht S, Miyazaki S, Linton N, Rivard L, Wright M, Wilton SB, Scherr D, Pascale P, Roten L, Pederson M, Bordachar P, Laurent F, Kim SJ, Ritter P, Clementy J, Haïssaguerre M. Elimination of Local Abnormal Ventricular Activities: A New End Point for Substrate Modification in Patients With Scar-Related Ventricular Tachycardia. *Circulation* 2012;**125**:2184–2196.
29. Callans DJ, Ren J-F, Michele J, Marchlinski FE, Dillon SM. Electroanatomic Left Ventricular Mapping in the Porcine Model of Healed Anterior Myocardial Infarction: Correlation With Intracardiac Echocardiography and Pathological Analysis. *Circulation* 1999;**100**:1744–1750.
30. Wrobleski D, Houghtaling C, Josephson ME, Ruskin JN, Reddy VY. Use of Electrogram Characteristics During Sinus Rhythm to Delineate the Endocardial Scar in a Porcine Model of Healed Myocardial Infarction. *J Cardiovasc Electrophysiol* 2003;**14**:524–529.
31. Wijnmaalen AP, Schalij MJ, Thüsen JH von der, Klautz RJM, Zeppenfeld K. Early Reperfusion During Acute Myocardial Infarction Affects Ventricular Tachycardia Characteristics and the Chronic Electroanatomic and Histological Substrate. *Circulation* 2010;**121**:1887–1895.
32. Wijnmaalen AP, Geest RJ van der, Huls van Taxis CFB van, Siebelink H-MJ, Kroft LJM, Bax JJ, Reiber JHC, Schalij MJ, Zeppenfeld K. Head-to-head comparison of contrast-enhanced magnetic resonance imaging and electroanatomical voltage mapping to assess post-infarct scar characteristics in patients with ventricular tachycardias: real-time image integration and reversed registration. *Eur Heart J* 2011;**32**:104–114.
33. Tung R, Josephson ME, Bradfield JS, Shivkumar K. Directional Influences of Ventricular Activation on Myocardial Scar Characterization: Voltage Mapping With Multiple Wavefronts During Ventricular Tachycardia Ablation. *Circ Arrhythm Electrophysiol* 2016;**9**.
34. Berte B, Relan J, Sacher F, Pillois X, Appetiti A, Yamashita S, Mahida S, Casassus F, Hooks D, Sellal J-M, Amraoui S, Denis A, Derval N, Cochet H, Hocini M, Haïssaguerre M, Weerasooriya R, Jaïs P. Impact of Electrode Type on Mapping of Scar-Related VT: Mapping of Scar-Related VT. *J Cardiovasc Electrophysiol* 2015;**26**:1213–1223.
35. Jais P, Maury P, Khairy P, Sacher F, Nault I, Komatsu Y, Hocini M, Forclaz A, Jadidi AS, Weerasooryia R, Shah A, Derval N, Cochet H, Knecht S, Miyazaki S, Linton N, Rivard L, Wright M, Wilton SB, Scherr D, Pascale P, Roten L, Pederson M, Bordachar P, Laurent F, Kim SJ, Ritter P, Clementy J, Haissaguerre M. Elimination of Local Abnormal Ventricular Activities A New End Point for Substrate Modification in Patients With Scar-Related Ventricular Tachycardia. Circulation. 2012. p. 2184–2196.
36. Silberbauer J, Oloriz T, Maccabelli G, Tsiachris D, Baratto F, Vergara P, Mizuno H, Bisceglia C, Marzi A, Sora N, Guarracini F, Radinovic A, Cireddu M, Sala S, Gulletta S, Paglino G, Mazzone P, Trevisi N, Bella PD. Noninducibility and Late Potential Abolition: A Novel Combined Prognostic Procedural

End Point for Catheter Ablation of Postinfarction Ventricular Tachycardia. *Circ Arrhythm Electrophysiol* 2014;**7**:424–435.

37. Rothman SA, Hsia HH, Cossú SF, Chmielewski IL, Buxton AE, Miller JM. Radiofrequency Catheter Ablation of Postinfarction Ventricular Tachycardia: Long-term Success and the Significance of Inducible Nonclinical Arrhythmias. *Circulation* 1997;**96**:3499–3508.
38. Tung R, Josephson ME, Reddy V, Reynolds MR, on behalf of the SMASH-VT Investigators. Influence of Clinical and Procedural Predictors on Ventricular Tachycardia Ablation Outcomes: An Analysis from The Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia Trial (SMASH-VT). *J Cardiovasc Electrophysiol* 2010;
39. Kim YH, Sosa-Suarez G, Trouton TG, O'Nunain SS, Osswald S, McGovern BA, Ruskin JN, Garan H. Treatment of ventricular tachycardia by transcatheter radiofrequency ablation in patients with ischemic heart disease. *Circulation* 1994;**89**:1094–1102.
40. Segal OR, Chow AWC, Markides V, Schilling RJ, Peters NS, Davies DW. Long-term results after ablation of infarct-related ventricular tachycardia. *Heart Rhythm* 2005;**2**:474–482.
41. Ghanbari H, Baser K, Yokokawa M, Stevenson W, Della Bella P, Vergara P, Deneke T, Kuck K-H, Kottkamp H, Fei S, Morady F, Bogun F. Noninducibility in Postinfarction Ventricular Tachycardia as an End Point for Ventricular Tachycardia Ablation and Its Effects on Outcomes: A Meta-Analysis. *Circ Arrhythm Electrophysiol* 2014;**7**:677–683.
42. Yokokawa M, Kim HM, Baser K, Stevenson W, Nagashima K, Della Bella P, Vergara P, Hindricks G, Arya A, Zeppenfeld K, Riva Silva M de, Daoud EG, Kumar S, Kuck K-H, Tilz R, Mathew S, Ghanbari H, Latchamsetty R, Morady F, Bogun FM. Predictive Value of Programmed Ventricular Stimulation After Catheter Ablation of Post-Infarction Ventricular Tachycardia. *J Am Coll Cardiol* 2015;**65**:1954–1959.
43. Della Bella P. Catheter ablation and antiarrhythmic drugs for haemodynamically tolerated postinfarction ventricular tachycardia. Long-term outcome in relation to acute electrophysiological findings. *Eur Heart J* 2002;**23**:414–424.
44. Kudenchuk PJ, Kron J, Walance CG, Cutler JE, Griffith KK, McAnulty JH. Day-to-day reproducibility of antiarrhythmic drug trials using programmed extrastimulus techniques for ventricular tachyarrhythmias associated with coronary artery disease. *Am J Cardiol* 1990;**66**:725–730.
45. McPherson CA, Rosenfeld LE, Batsford WP. Day-to-day reproducibility of responses to right ventricular programmed electrical stimulation: Implications for serial drug testing. *Am J Cardiol* 1985;**55**:689–695.
46. Mann DE, Luck JC, Griffin JC, Herre JM, Limacher MC, Magro SA, Robertson NW, Wyndham CRC. Induction of clinical ventricular tachycardia using programmed stimulation: Value of third and fourth extrastimuli. *Am J Cardiol* 1983;**52**:501–506.
47. Lin H-T, Mann DE, Luck JC, Krafchek J, Magro SA, Sakun V, Wyndham CRC. Prospective comparison of right and left ventricular stimulation for induction of sustained ventricular tachycardia. *Am J Cardiol* 1987;**59**:559–563.
48. Morady F, DiCarlo L, Winston S, Davis JC, Scheinman MM. A prospective comparison of triple extrastimuli and left ventricular stimulation in studies of ventricular tachycardia induction. *Circulation* 1984;**70**:52–57.
49. Tzou WS, Frankel DS, Hegeman T, Supple GE, Garcia FC, Santangeli P, Katz DF, Sauer WH, Marchlinski FE. Core Isolation of Critical Arrhythmia Elements for Treatment of Multiple Scar-Based Ventricular Tachycardias. *Circ Arrhythm Electrophysiol* 2015;**8**:353–361.
50. Porta-Sánchez A, Jackson N, Lukac P, Kristiansen SB, Nielsen JM, Gizurarson S, Massé S, Labos C, Viswanathan K, King B, Ha ACT, Downar E, Nanthakumar K. Multicenter Study of Ischemic

Ventricular Tachycardia Ablation With Decrement-Evoked Potential (DEEP) Mapping With Extra Stimulus. *JACC Clin Electrophysiol* 2018;**4**:307–315.

51. Sarkozy A, Tokuda M, Tedrow UB, Sieria J, Michaud GF, Couper GS, John R, Stevenson WG. Epicardial Ablation of Ventricular Tachycardia in Ischemic Heart Disease. *Circ Arrhythm Electrophysiol* 2013;**6**:1115–1122.
52. Piers SRD, Everaerts K, Geest RJ van der, Hazebroek MR, Siebelink H-M, Pison LAFG, Schalij MJ, Bekkers SCAM, Heymans S, Zeppenfeld K. Myocardial scar predicts monomorphic ventricular tachycardia but not polymorphic ventricular tachycardia or ventricular fibrillation in nonischemic dilated cardiomyopathy. *Heart Rhythm* 2015;**12**:2106–2114.
53. Piers SRD, Tao Q, Huls van Taxis CFB van, Schalij MJ, Geest RJ van der, Zeppenfeld K. Contrast-Enhanced MRI–Derived Scar Patterns and Associated Ventricular Tachycardias in Nonischemic Cardiomyopathy: Implications for the Ablation Strategy. *Circ Arrhythm Electrophysiol* 2013;**6**:875–883.