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ORIGINAL ARTICLE

Rotational Activation Pattern During Functional Substrate Mapping: Novel Target for Catheter Ablation of Scar-Related Ventricular Tachycardia

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BACKGROUND: Recent advancements in a 3-dimensional mapping system allow for the assessment of detailed conduction properties during sinus rhythm and thus the establishment of a strategy targeting functionally abnormal regions in scar-related ventricular tachycardia (VT). We hypothesized that a rotational activation pattern (RAP) observed in maps during baseline rhythm was associated with the critical location of VT.

METHODS: We retrospectively examined the pattern of wavefront propagation during sinus rhythm in patients with scar-related VT. The prevalence and features of the RAP on critical VT circuits were analyzed. RAP was defined as >90° of inward curvature directly above or at the edge of the slow conductive areas.

RESULTS: Forty-five VTs in 37 patients (66±15 years old, 89% male, 27% ischemic heart disease) were evaluated. High-density substrate mapping during sinus rhythm (median, 2524 points) was performed using the CARTO3 system before VT induction. Critical sites for reentry were identified by direct termination by radiofrequency catheter ablation in 21 VTs or by pace mapping in 12 VTs. Among them, RAP was present in 70% of the 33 VTs. Four VTs had no RAP at the critical sites during sinus rhythm, but it became visible in the mappings with different wavefront directions. Six VTs, in which intramural or epicardial isthmus was suspected, were rendered noninducible by radiofrequency catheter ablation to the endocardial surface without RAP. RAP had a sensitivity and specificity of 70% and 89%, respectively, for predicting the elements in the critical zone for VT.

CONCLUSIONS: The critical zone of VT appears to correspond to an area characterized by the RAP with slow conduction during sinus rhythm, which facilitates targeting areas specific for reentry. However, this may not be applicable to intramural VT substrates and might be affected by the direction of wavefront propagation to the scar during mapping.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: cardiomyopathies ■ catheter ablation ■ electrophysiology ■ mapping ■ ventricular tachycardia

Radiofrequency catheter ablation plays an important role in the reduction of ventricular tachycardia (VT) burden with structural heart disease, thus improving patient prognosis.[1] The second decade of the 21st century commenced with vigilant assessment of abnormal substrates followed by ablation strategies targeting the presumed reentrant circuit with substrate modification. Abnormal cardiac tissues such as low-voltage areas,

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For Sources of Funding and Disclosures, see page 22.

WHAT IS KNOWN?

- A functional substrate mapping that is performed during sinus rhythm enables the detailed analysis in conduction abnormalities in structural heart disease, thus the improvement of ablation efficacy for ventricular tachycardia has been described.
- The areas of maximal slowing depicted as an isochronal crowding in activation maps correlate a critical site of ventricular tachycardia circuit.

WHAT THE STUDY ADDS

- Rotational activation pattern around a localized line of conduction block can be identified in baseline functional substrate mappings and correlates with sites most specific to ventricular tachycardia critical isthmus.
- Different wavefront propagation produced by right and left ventricular pacing has a potential for unveiling the inapparent rotation activation pattern in mappings during baseline rhythm.
- Arrhythmogenic substrates in deep myocardial layers is not associated with rotation activation pattern in surface mappings.

Nonstandard Abbreviations and Acronyms

ARVC	arrhythmogenic right ventricular cardiomyopathy
CLs	cycle lengths
IC	isochronal crowding
ICM	ischemic cardiomyopathy
IQR	interquartile ranges
LV	left ventricle
NICM	nonischemic cardiomyopathy
RAP	rotational activation pattern
TCL	tachycardia cycle lengths
VT	ventricular tachycardia

local abnormal ventricular activities, activation slowing, and deceleration zones are potentially related to critical reentry circuits.[1–5]

Recent advancements in mapping systems allowed for the assessment of detailed conduction properties during sinus rhythm and thus the establishment of a strategy targeting functionally abnormal regions.[2] Conduction velocity slowing depicted with isochronal crowding (IC) in the baseline sinus rhythm map corresponds to critical sites for VT.[2,5] In real-world settings, however, areas of IC during baseline rhythm may be distributed at multiple sites within a scar and sometimes spread as wide-band lesions, thus requiring additional information to localize the specific site of the VT reentry circuit.

As regions with IC that serve as anchors for VT reentry are often formed around a localized line of conduction block,[2] we hypothesized that the area with a rotational propagation around the wavefront discontinuity with IC during baseline rhythm could be associated with sites most prone to reentry. The aim of this study was to examine the relationship between the critical site of the VT isthmus and the area characterized by the rotational activation pattern (RAP) on baseline maps during intrinsic and ventricular paced rhythm.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. This study was approved by the local Ethics Committee (approval number R03-009).

Study Participants

We performed a retrospective analysis of patients who underwent catheter ablation for scar-related VT and high-density electroanatomical maps of diseased chambers at baseline acquired between January 2016 and April 2021 at the University of Tsukuba Hospital. Baseline structural heart diseases were categorized as ischemic cardiomyopathy (ICM), nonischemic cardiomyopathy (NICM), and arrhythmogenic right ventricular cardiomyopathy (ARVC). A requisite for a high-density substrate map is a mapping point density with a fill threshold of ≤5 mm. We excluded patients without high-density maps for the baseline rhythm or whose VT was noninducible or unsustainable by induction with programmed stimulation. All patients or families provided written informed consent for ablation procedures.

Electroanatomical Mapping and Ablation Strategy

Detailed methods are provided in the Supplemental Material. High-density substrate mapping during basal rhythm (sinus rhythm or atrial paced rhythm) and ventricular paced rhythm was performed using the CARTO system (Biosense Webster, Diamond Bar, CA) with a multielectrode catheter; Pentaray (2-6-2-mm interelectrode spacing; Biosense Webster), or DecaNav (2-8-2-mm interelectrode spacing; Biosense Webster). Electrograms were automatically collected during sinus rhythm and ventricular paced rhythm using a Wavefront Annotation (Biosense Webster), which fixes on the points with maximal unipolar dV/dt only within the window demarcated by the beginning and end of the bipolar electrogram complex.[6] However, at sites with multicomponent or fractionated local electrograms, automated mapping systems typically annotated far-field potentials that often generate a more negative dV/dt value than that of near-field late potentials. We reviewed the annotated local potentials during the procedures and manually moved the annotation to the reproducible latest potentials to mark the maximal discontinuity as necessary. In a diseased porcine model of infarct demonstrated that the conduction velocity decreased ≤25.0 cm/s.[5] Hence, the activation maps were displayed as isochronal maps of 10 ms steps, and the IC was defined as ≥4 isochrones within 10 mm.[7]

Following completion of substrate mapping, VT induction was attempted with programmed ventricular stimulation from the right ventricular apex at 2 base cycle lengths (CLs; 400 and 600 ms), with up to 3 extrastimuli decremented to ventricular refractoriness. When hemodynamically stable VT was induced, electroanatomical activation mapping was performed to depict the tachycardia circuit and superimposed on the anatomic reconstruction of the ventricle. However, in the case of hemodynamically unstable VT, ablation of the VT substrate guided by pace mapping and targeting local abnormal potentials was performed.

Radiofrequency energy was delivered with irrigated tip ablation catheter (ThermoCool Smart Touch; Biosense Webster) at 30 to 50 W and the maximum temperature limit set at 45°C for 60 to 90 s per application. Complete success was defined as noninducibility of any VT, while partial success was defined as the noninducibility of clinical VT. This was evaluated with repeated programmed stimulation in patients with a stable hemodynamic status.

Characterization of the Critical Sites for the VT Circuit

The VT termination site during radiofrequency energy application without an ectopic beat was determined as a critical site for the reentrant circuit. Depending on the time phase in relation to the diastolic interval, the termination site was assigned to one of the 3 main segments of VT: the entrance (inward curvature), common pathway (pathway between both lateral isthmus boundaries or a stimulus-QRS/tachycardia CL [TCL] between 30% and 70%), and exit (outward curvature or stimulus-QRS/TCL ≤30%).[8]

In addition to direct termination with radiofrequency application, we also defined sites with good pacemap scores and either multiple exit sites or pace mapping induction of VT as a part of critical VT circuits.[8–10] A good pacemap score was defined as a correlation value of 89% or more.[11] When pacemap scores of 89% or higher were recorded at 2 or more points, the point with the longest stimulus to QRS was adopted as the critical site.

RAP During Baseline Rhythm

The RAP during sinus rhythm and ventricular paced rhythm was assessed offline. RAP was defined as the site showing wavefront propagation rotating >90° (inward curvature) directly above or at the edge of the IC areas. To delineate the quantitative characteristics of RAP, we adopted the Newton-Raphson method to approximate the angle of the RAP's orbit[12] (methods are provided in Figure S1). The angular velocity was calculated by dividing the angle of the RAP's orbit by the time difference between the earliest and latest sites around the RAP.

At each critical site of the VT reentrant circuit identified by direct termination during radiofrequency application or the pace mapping response, the presence of RAP during sinus rhythm and ventricular paced rhythm was analyzed. If VTs were not terminated by radiofrequency application, those sites were labeled as nonterminated sites and imposed on the sinus rhythm and paced rhythm maps. Since points mapped during arrhythmia could be spatially displaced from their corresponding location during baseline rhythm,[13] the existence of RAP was adjudicated within a 1 cm radius around nonterminated sites. The analysis of RAP existence was interpreted by 2 independent electrophysiologists blinded to the procedural information.

Statistical Analysis

Continuous variables are expressed as the mean±SD or as the median with interquartile ranges (IQR) and were analyzed using a Mann-Whitney *U* test or Wilcoxon signed-rank test according to whether the data were normally distributed or not. The Shapiro-Wilk test was used to test whether the data set was normally distributed. All categorical variables are expressed as raw numbers and percentages and were compared using Fisher exact test. Correlations were examined using Pearson correlation. All analyses were performed using R statistical software (R Foundation for Statistical Computing, Vienna, Austria, version 3.1.1).

RESULTS

Study Participants

During the study period, 205 catheter ablation procedures in 159 patients with structural heart disease were performed. Of these, 167 procedures were excluded due to noninducibility, inadequate baseline maps (no high-density mapping at VT area or ablation catheter used for mapping), and hemodynamical intolerance without determination of critical circuits by pace mapping. Finally, a total of 38 procedures were analyzed in 37 patients. The Table lists the patients' clinical characteristics.

Ablation Outcome

Initial substrate mapping was performed during sinus rhythm or atrial pacing rhythm in 35 procedures and during RV pacing in 3 with atrioventricular block. In 5 procedures, the left ventricular (LV) endocardium was

Table. Baseline Characteristics of the Patients

	n=37
Age, y	66±15
Male (%)	32 (86)
LVEF, %	37±16
Preprocedural ICD/CRT-D implantation (%)	25 (68)
Prior VT ablation (%)	14 (38)
0	23 (62)
1	5 (14)
2	7 (19)
3	2 (5)
Underlying structural heart disease	
Ischemic cardiomyopathy (%)	10 (27)
Nonischemic cardiomyopathy (%)	21 (57)
ARVC (%)	6 (16)
Amiodarone (%)	15 (41)
BNP, pg/mL	206 (87–479)

Values are presented as the mean±SD, median (Q1–Q3), or n (%). ARVC indicates arrhythmogenic right ventricular cardiomyopathy; BNP, B-type natriuretic peptide; CRT-D, cardiac resynchronization defibrillator; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; and VT, ventricular tachycardia.

also mapped with 2 different wavefront directions: sinus rhythm and RV apical pacing in 3 procedures, and sinus rhythm and LV pacing in the other 2. There was a median of 2524 (IQR, 1635–3141) points per baseline map. Of the 43 maps, the median number of RAP identified per map was 1 (IQR, 0–2): Twenty-eight percent did not have RAP, 28% had a single RAP, 35% had 2 RAPs, and the rest of 9% had 3 RAPs. The number of ICs per map was significantly higher than that of RAPs ($P<0.01$): the median number was 2 (IQR, 1–3). Five percent had no IC, 28% had single IC, 26% had 2 ICs, and 42% had ≥3 ICs.

Sustained VT was inducible in all 38 procedures. A total of 111 VTs were induced. Sixty-six VTs were excluded because the VT circuits could not be identified, or no radiofrequency application was attempted during tachycardia. Finally, 45 VTs were analyzed in this study: 21 VTs were terminated by radiofrequency application, 12 VTs whose critical sites were identified by pace mapping, and 12 VTs that were not interrupted by the radiofrequency attempt.

The median procedure time was 5 hours, and the median ablation time was 34 minutes. The procedural end points of complete and partial success were 76% and 21%, respectively. In the remaining one patient, no further induction was performed because of the advanced procedural duration and impaired LV ejection fraction.

Analysis of the VT Termination Site

Of the 45 VTs included in the present study, 21 VTs in 21 patients were terminated by radiofrequency application. The CL of the terminated VTs was 431 ms (350–490 ms). Success sites were located in the LV endocardium in 12 patients (5 in the ICM and 7 in the NICM), in the RV endocardium in 3 with ARVC and one with NICM, and at epicardial sites in 5 patients (3 in the ICM and 2 in the NICM). The median time to termination during radiofrequency application was 11 s (range, 5–20 s).

In 14/21 VTs, the termination sites corresponded to the area of IC observed in the baseline maps. However, IC was distributed in a band-shaped zone with a median length of 55 mm (IQR, 34–65 mm). Among these 14 VTs, the termination site colocalized to the area of the RAP in 13 VTs. The sites showing RAP were localized at very low-voltage areas (<0.5 mV) in 11 (85%) and relatively low-voltage areas (<1.5 mV) in 2 (15%). The median number of isochrone colors surrounding the RAP within a 1 cm radius was 5 (=50 ms; range, 4–14 colors).

Figure 1 and Video S1 present an example of a patient with remote anterior infarction who underwent epicardial ablation. An epicardial bipolar voltage map shows a dense scar at the mid to apical portion of the anterior wall. An activation map during VT demonstrates figure-eight reentry. An entrainment pacing at the isthmus showed concealed fusion and postpacing interval-TCL=4 ms (Figure S2). The application of radiofrequency energy to the isthmus terminated the VT in 1 second. The patient had a long IC lesion (97 mm), and the VT termination site was accompanied by the RAP during sinus rhythm.

Of the 8/21 VTs where the RAP was not observed in the maps during sinus rhythm, 2 cases manifested the RAP at the termination sites in maps acquired during the different activation wavefronts (one was paced at the RV apex and the other was at the anterolateral branching vein of the coronary sinus). Figure 2 and Video S2 present an example that functional substrate mapping acquired during a different wavefront direction unveiled the RAP.

The segments on VT circuits were identified in a total of 20 VTs, and complete activation mappings were created in 8 VTs and entrainment pacing-based determination occurred in the other 12 patients. The median electrogram-QRS and electrogram-QRS/TCL were 62 ms (42–111 ms) and 19% (9%–27%), respectively. At the VT termination site where RAP was present during the baseline and paced rhythm, the VT circuits were located at the exit in 10/14 (71%) and central proximal in 4/14 (29%). In the remaining case, VT was terminated by ablation while slowly moving the catheter, and either the analysis of local electrogram or entrainment pacing had not been performed; thus, the elements on the circuit were unevaluable.

Characteristics of VT Termination Sites Without RAP

Of a total of 21 VTs that were terminated during ablation, the aforementioned 15 VTs (71%) had successful termination sites colocalizing to the RAP in the maps at the intrinsic and paced rhythm. In the all remaining 6 VTs without the RAP, an intramural or epicardial substrate was suspected: 2 cases had a 2F electrode catheter placed inside the branching of the coronary sinus and entrainment pacing from that 2F catheter demonstrated concealed fusion with a postpacing interval within 30 ms of the TCL together with the stimulus-QRS not exceeding the electrogram-QRS interval. Figure 3 shows a representative case without RAP at the successful VT termination site. While there was no RAP on the LV endocardium, the epicardial electrogram from coronary sinus branch was proved to be at the central isthmus of the circuit. Radiofrequency energy application to the opposite endocardial site interrupted VT in 18 s.

In the other 4 cases, 2 had an ARVC cause, one was ICM, and the other was in the dilated phase of hypertrophic cardiomyopathy; endocardial activation mapping during VT showed a centrifugal spread pattern, and the radiofrequency energy application to the earliest site resulted in termination of VT, suggestive of 3-dimensional VT circuits and the endocardium serving as an exit

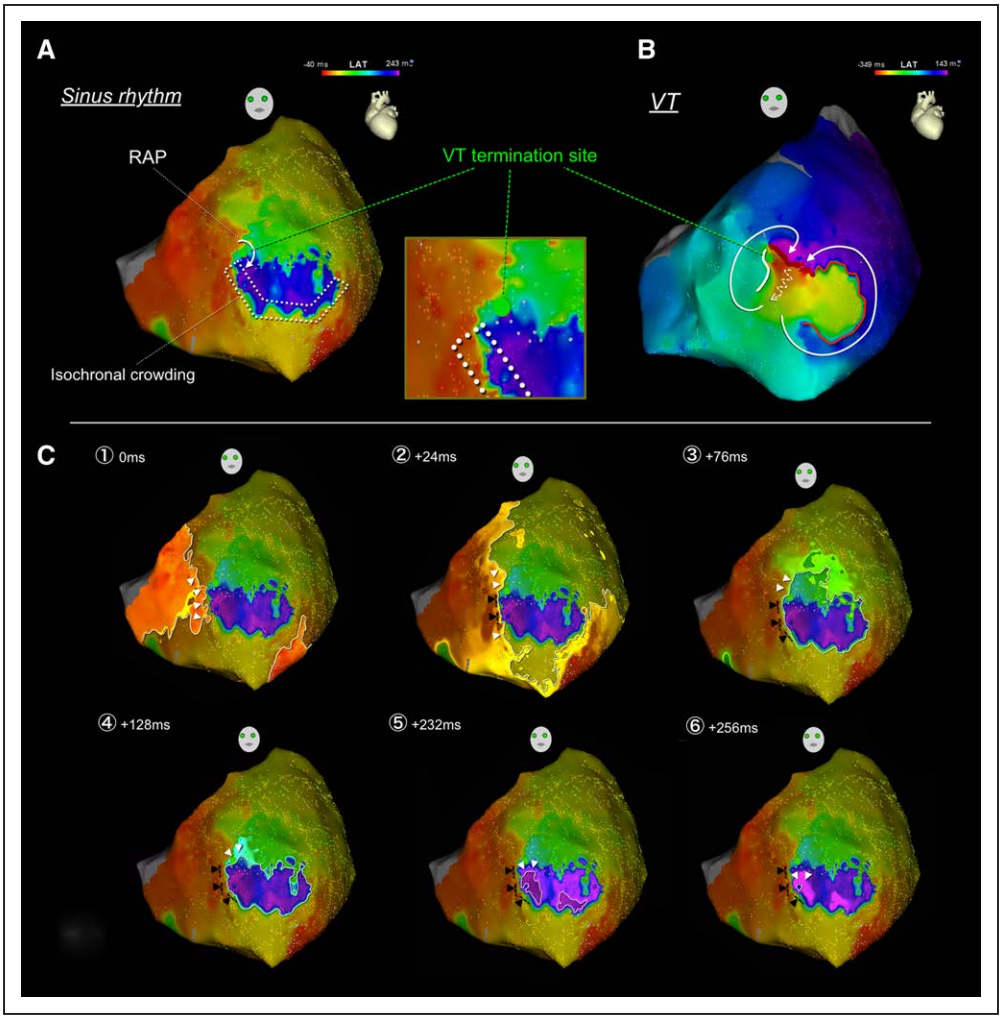

Figure 1. Rotational activation pattern in mapping during sinus rhythm.
A, Activation map of the ventricular epicardium (left anterior oblique view) with ischemic heart disease during sinus rhythm. The earliest activation sites arising from the mid anteroseptal and posterolateral wall are colored red, and the latest centripetally propagated into the mid-anterior wall are colored purple. The slow conduction area, showing 4 or more concentrations of isochrones, is delineated as a band-like lesion extending 90 mm in a line (encircled by a dotted polygon). The green tag represents the location where clinical ventricular tachycardia (VT) was terminated by radiofrequency catheter ablation. This tag is reflected from the activation map of the VT in **B** with the same coordinates. A rotation activation pattern (RAP) was observed at the site of VT termination. **B**, Activation map during VT shows the entire diastolic pathway sandwiched by the lateral boundary of the block (white line) and adjacent bystander region (red). VT was terminated 1 s after energy application. **C**, Serial change in wavefront propagation. The local activation time depicted on upper left panel is set as 0 ms. White arrowheads indicate the sites with spared conduction velocity near the area of isochronal crowding, while black arrowheads indicate the sites where conduction velocity was markedly decreased (Video S1).

site or an outer loop. Figure 4 shows an example of a patient with ICM. The earliest activated site on the endocardial map during VT served as the outer loop, and VT was terminated by radiofrequency application to this site. In this case, the RAP was not observed at the successful ablation site on either the baseline activation map or the paced rhythm activation map.

Determination of Critical Circuits By Pace Mapping and Association With RAP

Of the VTs that were not ablated during tachycardia due to hemodynamic intolerance, we analyzed 12 VTs in 11 patients in whom the isthmuses were identified by pace mapping. The cause was ICM in 9% (n=1), NICM in 55% (n=6), and ARVC in 36% (n=4). The median number of points acquired during pace mapping was 34 (IQR, 30–46). After radiofrequency ablation by the guidance of pace mapping, the target VT became noninducible. Compared with the VTs terminated by radiofrequency application, VTs whose critical isthmuses were defined by pace mapping had a shorter TCL (431 ms [350–490 ms] versus 319 ms [278–395 ms], P=0.01).

The median percentage morphology match between the 12-lead ECG obtained during VT and pace mapping was 94% (91%–98%), and the median stimulus-QRS interval was 60 ms (48–89 ms). RAP was present in 6 sites with the best correlation with a decent conduction

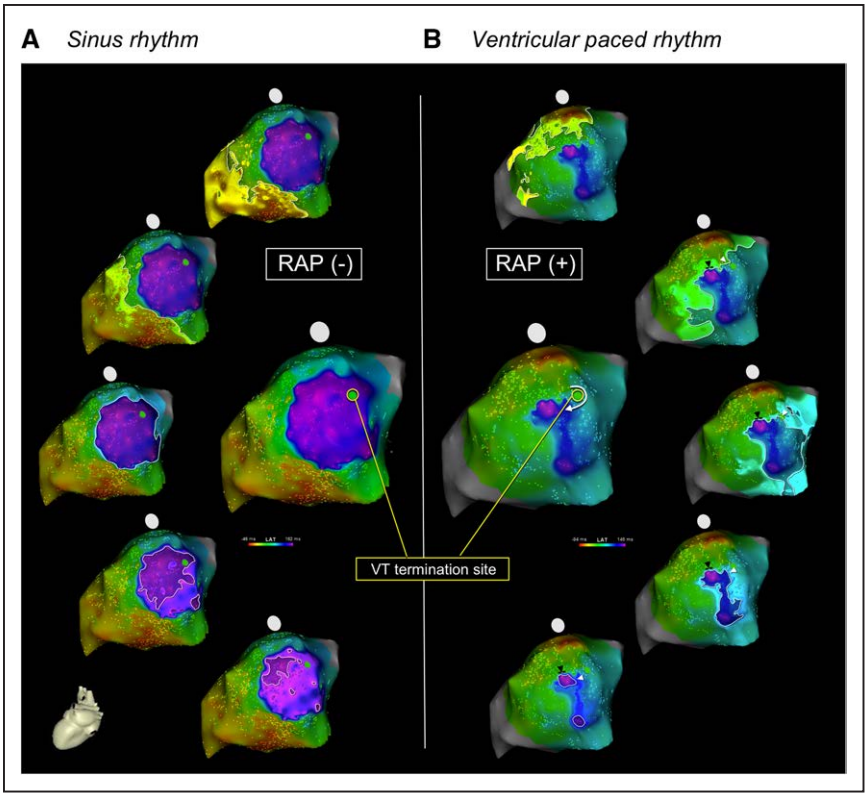

Figure 2. Example of the endocardial maps with different wavefront propagation.
A, Activation map created during sinus rhythm. The wavefront of the activation centripetally propagated into the latest activation zone (purple region). At the basal lateral wall of the left ventricle, the green tag highlighted by the yellow circle indicates the site where the ventricular tachycardia (VT) was terminated by radiofrequency catheter ablation (RFCA). This site is located with a wavefront collision and is not accompanied by isochronal crowding (IC) or the rotation activation pattern (RAP). **B**, Activation map created during ventricular paced rhythm from the anterior interventricular vein. RAP became visible at the site of VT termination (green tag; Video S2).

delay in maps acquired during intrinsic rhythm. At the 2 sites, RAP was not present in the baseline maps but appeared during remapping during LV pacing rhythm (pacing from the lateral branch of the coronary vein). Finally, 8 of 12 sites (67%) were accompanied by RAP in maps acquired during the intrinsic and paced rhythm.

Electrophysiological Characteristics of RAP Associated With the VT Critical Sites

Among the 33 VTs whose critical sites were determined by direct termination (n=21) or pace mapping guidance (n=12), RAP was observed in 19 (58%) during baseline rhythm and in additional 4 (13%) during paced ventricular rhythm. Out of 23 maps where critical VT sites corresponded to the RAP, 11 maps (48%) required manual re-annotations after the auto-annotations for the visualization of RAP. In all cases whose RAP was inapparent in the maps with the initial auto-annotations, late potentials with bipolar amplitudes raging 0.07 and 0.43 mV were overlooked. All these late potentials were located at the later activated regions in the total activation duration rather than the center of the RAP.

Although not significant, RAP was more prevalent in the setting of ICM than in NICM, including ARVC (88% versus 64%, *P*=0.38). The angle and angular velocity of the orbit of the RAP were 182±52 degree and 4417±2492 degree/s, respectively. There was no correlation between the angular velocity and heart rate of the clinical VT (*r*=0.11 [95% CI, −0.38 to 0.55], *P*=0.66, Figure S3). The earliest and latest local activation timings within a 1 cm diameter around the RAP were recorded at 42±15% and 82±13% of the entire activation duration in the mapped chamber, respectively (Figure 5). Local activation duration within a 1 cm diameter accounted for a mean of 41±15% of the entire activation duration.

Among 23 VTs where the RAP was observed in the initial maps, remapping after the radiofrequency energy applications to and around the RAP sites was attempted in 9 procedures. In all 9 maps, the RAP disappeared at the original sites. Of them, 3 maps showed new RAPs distant from the original RAP site (10, 12, and 15 mm, respectively). Although RAPs were observed in all 3 maps, no VTs were inducible at the time of remapping. Additional ablations were performed for the substrate modification in 2 these 3 procedures and the RAPs completely disappeared in the final functional substrate mappings.

Comparison of RAP Among Critical Sites and Nontermination Sites

The RAP prevalence was analyzed at 60 sites, including 33 critical sites in 33 VTs that were determined by direct termination (n=21) or pace mapping (n=12) and 27 sites in 20 VTs that were not interrupted by ablation.

At 27 sites during 20 VTs, radiofrequency application did not interrupt the tachycardia. Of these 27 sites, RAP was observed in 3 sites (11%). RAP had a sensitivity

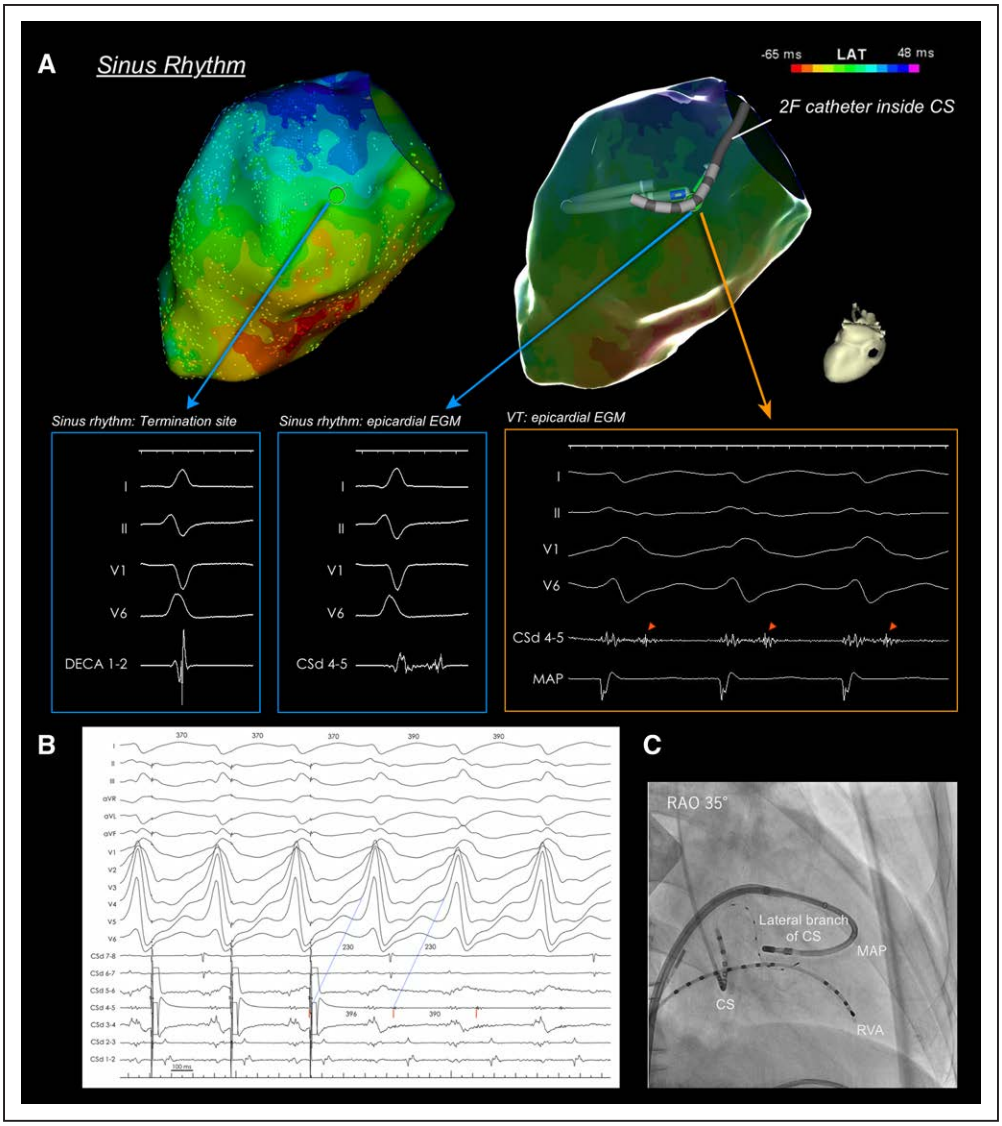

Figure 3. Example of no rotation activation pattern (RAP) at the termination site: endocardium opposite to the epicardial site of central isthmus.

A, Baseline activation map during sinus rhythm in a patient with nonischemic cardiomyopathy (NICM). Endocardial map shows no apparent conduction or electrogram (EGM) abnormality, but a multielectrode catheter inserted into the branch of the coronary sinus (CS) shows fragmented late potential at the basal lateral epicardium. The green tag indicates the endocardial site where ventricular tachycardia (VT) is terminated by radiofrequency catheter ablation (RFCA). During VT, late mid-diastolic potential (red arrow) is recorded on the catheter inside CS, while the ablation catheter (MAP) recorded only an early systolic potential. **B**, Entrainment pacing (overdrive pacing at 370 ms) from the catheter located inside the branch of the CS demonstrated concealed fusion with a postpacing interval (PPI) that is 6 ms longer (396 ms) than the tachycardia cycle length (390 ms). **C**, Fluoroscopic image in the right anterior oblique view (**upper**) and left anterior oblique view (**lower**). An ablation catheter (MAP) is placed at the success site. LAT indicates local activation time; MAP, maping catheter; RAO, right anterior oblique; and RVA, right ventricular apex.

of 70%, specificity of 89%, positive predictive value of 89%, and a negative predictive value of 71% for predicting the element in the critical zone for VT.

DISCUSSION

Main Findings

The present study analyzed in vivo data to delineate the electrophysiological findings responsible for scar-related VT. The major findings of this study are as follows:

1. The critical sites for the reentrant circuit corresponded to areas with activation slowing in maps acquired during the baseline rhythm. In particular, they were more localized at the sites hosting RAP.
2. Some critical regions were invisible in the baseline maps because the direction of the wavefront propagation masks the RAP. Mapping with RV and LV pacing could unveil the RAP.
3. When isthmuses exist in intramural or opposing epicardial tissues, RAP cannot be observed in endocardial maps.

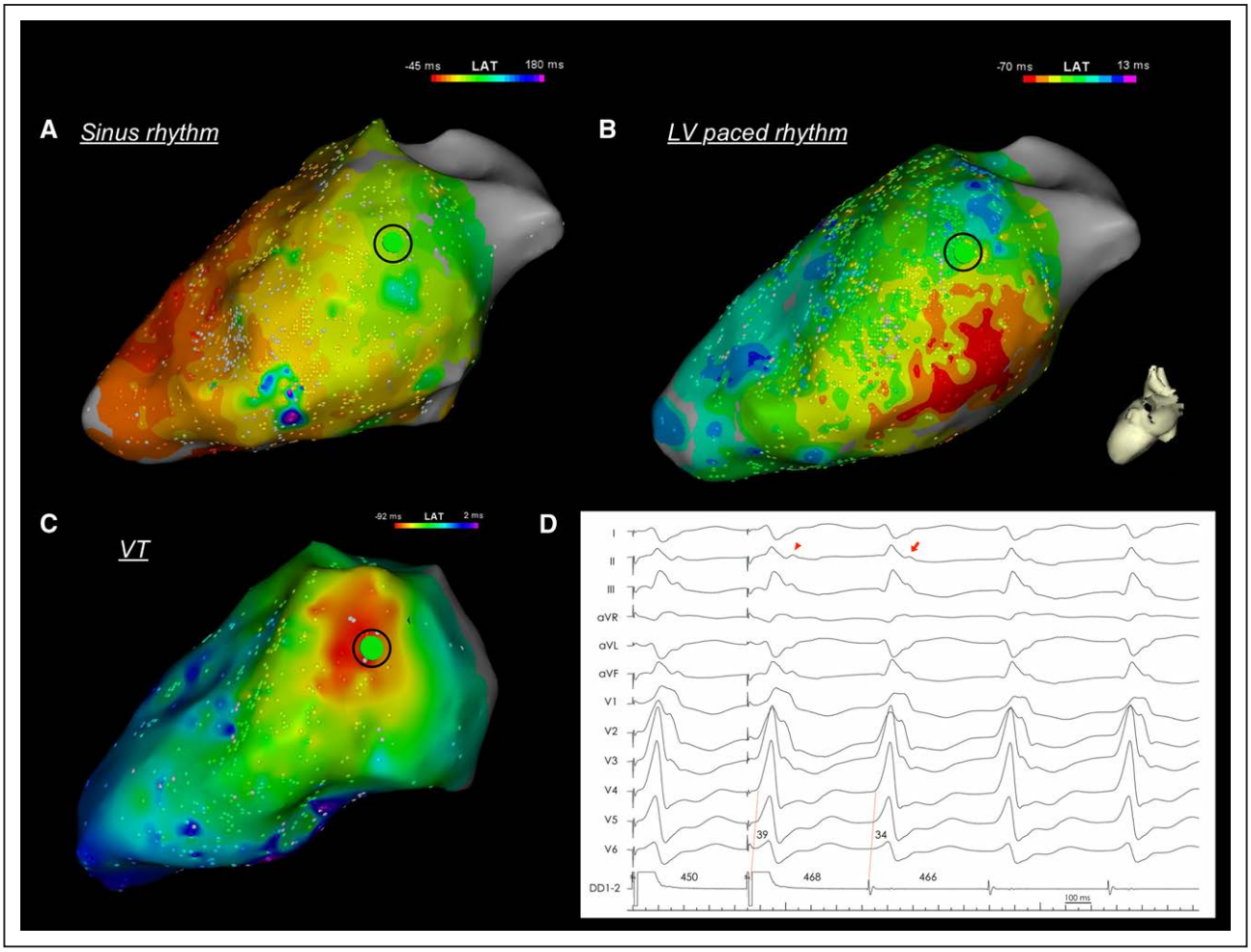

Figure 4. Example of no rotation activation pattern (RAP) at the termination site: outer loop.
Both endocardial activation mapping during sinus rhythm (**A**) and during paced rhythm from the posterolateral branch of the coronary sinus (**B**) do not present with the RAP at the termination site of the ventricular tachycardia (VT), which originated from the basal lateral wall of the left ventricle. A successful ablation site is encircled by a black line. **C**, Endocardial activation mapping during VT shows a centrifugally propagating pattern at the termination site. **D**, Entrainment pacing from the earliest activation site in the endocardial by a duodecapolar catheter (DD 1-2) showed constant fusion. QRS morphologies were similar, but small differences between the entrained beat and VT were observed (highlighted by red arrowheads and red arrows, respectively). Postpacing interval (PPI)-tachycardia cycle length (TCL) was 2 ms and the stimulus (S)-QRS duration was <30% of the VT cycle length, indicating the site at the outer loop of the VT. VT was terminated 4.9 s after RF application. LAT indicates local activation time.

The rapid and precise visualization of the abnormal substrate is required for patients with scar-related VT, especially when the induction of VT causes hemodynamic instability. Given the recent advancements in mapping and ablation techniques, the high-density mapping provides incremental benefit for meeting this growing need. This study describes a new landmark for a critical part of the VT circuit found during functional substrate mappings. The critical sites of VT had a higher prevalence of the RAP in 70% of patients compared with sites without VT termination (Figure 6).

Possible Mechanism of the Involvement of RAP in the VT Circuit

Traditionally, fixed areas of unexcitable tissue serve as anatomic barriers and have been thought to play a critical role in VT maintenance.[14] However, this classic interpretation was not valid in all cases. In recent studies, several mechanisms for VT initiation and maintenance, such as wavefront curvature,[15] source-sink mismatch,[16] and gap junction remodeling[17] have been proposed. Although there is no general acceptance of a model that completely describes the mechanism of VT, formation of a functional block line and subsequent establishment of the diastolic pathway are prerequisites for VT initiation, consistent with both human and canine models.[18] Even if we cannot directly deduce the exact location or width of the function block from baseline maps, the RAP is a substantial landmark that possesses a relatively faster conductive velocity in addition to the functional block.

The previous reports have been suggested that the conduction velocity recorded at the isthmus sites during VT is 2 to 3 times faster than that at exit and entrance

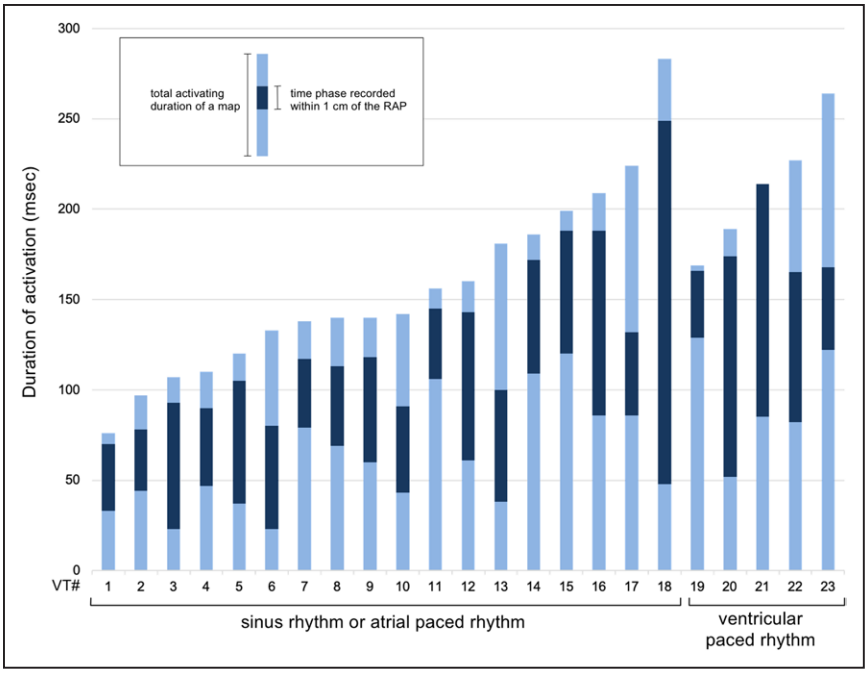

Figure 5. Time and duration of potentials constituting the rotation activation pattern (RAP).
Each bar represents a total activation duration of a map that showed the RAP. The onset of the intrinsic and paced rhythm maps is set as 0. The dark blue bar represents the time phase recorded within 1 cm of the RAP. All of the latest activated sites around the RAP were recorded at 50% or later phase of the total ventricular activation time. Local activation duration within a 1 cm diameter accounted for 41±15% of the entire activation duration. VT indicates ventricular tachycardia.

sites.[19,20] These data support our findings: that is, the RAP is a location of the tissue with relatively preserved conduction properties compared with the surrounding more impaired layers. However, the conduction property at the RAP site represented by the angular velocity did not correlate with the TCL. Based on the present study and a recent study showing that the conduction velocity of the outer loop is the principal determinant of TCL,[21] the RAP seems to occur often in the VT circuit, but it is not the major determinant of TCL.

In the present study, we also analyzed the location of the RAP in activation maps during VT or by entrainment pacing at the termination sites. Among the VTs that were directly terminated by radiofrequency application, 71% of

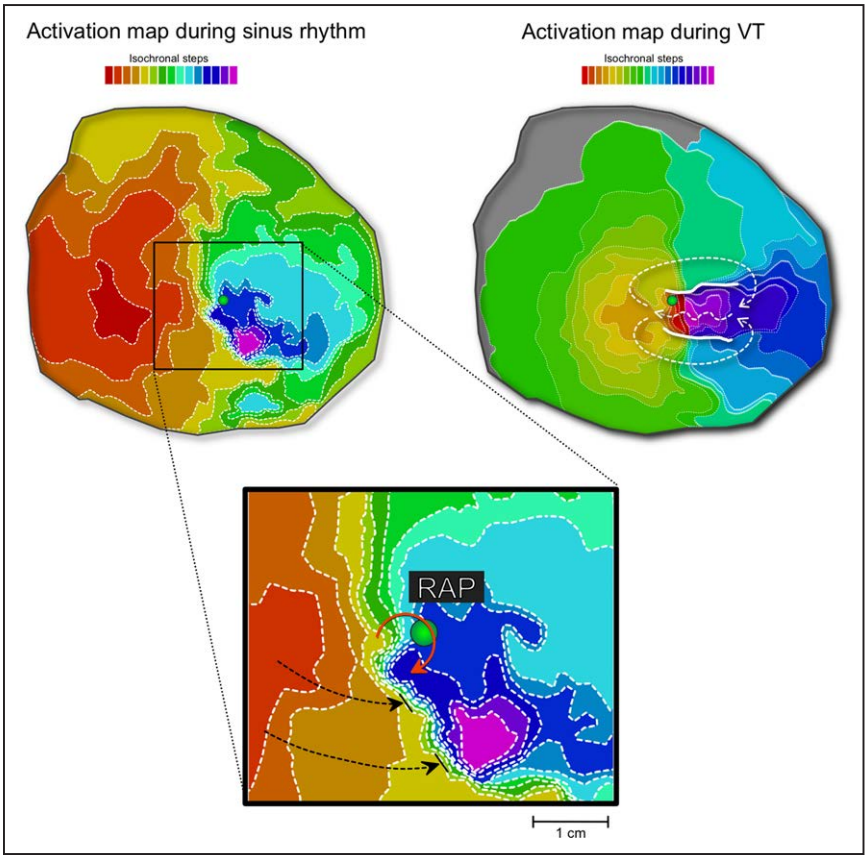

Figure 6. Schema of rotational activation pattern in scar-related ventricular tachycardia (VT).
Schematic of the rotation activation pattern (RAP) in the activation map during sinus rhythm, which appeared beside the wavefront discontinuity depicted with condensed isochronal colors. The site of RAP in sinus rhythm was located at the exit site of critical circuit during VT, where RF energy application interrupted the clinical VT (green tag).

the RAP sites coincided with the exit site. Meanwhile, the critical sites determined by the guidance of pace mapping (cutoff value >89%) showed the presence of RAP in 73% of cases. In a previous clinical study, de Chillou et al[11] reported that pacing at the exit zones and the isthmus exit parts gave better matching scores with a QRS morphology of VT (89% and 84%, respectively) than the entrance part of the isthmus (39%). Although pace mapping guided determination of the VT circuit was a surrogate definition, this fact also implies that the RAP might reflect the exit site in the VT circuit.

Prior Studies on Baseline Activation Mappings

The cumulative evidence from prior studies evaluating the benefit of creating high-density baseline maps suggests that analyzing the conduction property in detail is important to visualize the target of ablation.[2,7,22] An isochronal late activation map is an activation map that is equally divided into eight colors, and the critical sites for reentry were harbored in regions with dense concentrations of 3 or more colors.[22] Anter et al[7] displayed the activation maps with isochronal colors of 10 ms step, identified the impaired conduction site as 4 or more isochrones within 10 mm, and defined it as Reentry-Vulnerable Zones. The RAP, a newly named pattern of propagation in this study, was not defined by a single potential feature, but by the pattern of excitation propagation in this circumstance. This observation is in agreement with these previous reports suggesting that baseline activation mapping has the potential to infer the critical zone for the VT circuit. However, we focused on the dynamic change in the activation wavefront rather than the static indicators described as condensed colors which often appear as wide-band lesions and make it difficult to pinpoint the target for energy application. The observation in the present study may serve as a road map for ablation to target the culprit in scar-related VT during sinus rhythm.

Pitfall of RAP in Clinical Instances

The influence of the wavefront direction cannot be neglected in determining the RAP. In the induction of VT, the direction of activation following stimulation plays an important role in the formation of functional blocks.[18] This observation is in line with the finding of depiction of the impaired conduction property in sinus rhythm by Anter et al[7] who found that mapping during different activation from RV and LV stimulation unmasked an additional slow conduction zone by 33% and 25%, respectively. The spatial distribution of activation slowing can be alternated by the wavefront direction, so that an analysis from single maps can miss the RAP and true foci of VT.

The other factor that affects the invisibility of RAP was the existence of critical isthmuses lying at the intramural tissue or opposing surface from the mapping chamber. As in the general consideration met in identifying abnormal substrates by voltage mapping, bipolar signals have a limited field of view and local signals might be swamped even by catheters with small interelectrode spacing. Throughout the procedures included in our study, electroanatomical points were automatically annotated to maximal dV/dt, and some of them were manually corrected to the latest potentials if needed. Nevertheless, this study showed that RAP was not present at VT termination sites in 30% of patients. Extensive ablation of the endocardium can modify the intramural and even the epicardial substrate to some extent,[23] but if the preprocedural imaging depicts clues of epicardial or subepicardial scars and the subsequent procedure fails to find RAP at the endocardial surface, an epicardial approach might have to be considered.

Study Limitations

Our retrospective, single-center study included a limited number of patients. The decision to attempt entrained mapping, additional mapping during different activation directions, and intense effort for high-density mapping was solely at the operators' discretion. Forty-eight percent of the cases did not show RAP at critical sites in the auto-annotated initial maps, and manual re-annotations to the overlooked late potentials were required. Furthermore, the RAP defined in this study is based on qualitative rather than quantitative analysis. The video of the propagation during the baseline rhythm is mechanically complemented with activation between acquired points by the mapping system; it is impossible to assume that IC reflects a true line of block as it could be a slow conductive area.

Critical sites for VT were determined in only 30% of the induced VTs, thus the true specificity and sensitivity of the RAP for any VT were difficult to estimate. In this retrospective study, a detailed pace mapping around RAP sites to identify the isthmus of unmappable VT was not systematically performed. In fact, 46% of patients had multiple RAP. In this regard, there is a possibility that specificity of RAP may be higher for any VTs.

Finally, this study is a hypothesis-generating research study. We did not analyze the prognosis of patients after catheter ablation due to heterogeneity of the cohort. The involvement of the RAP in VT seems to be obvious, but the ideal ablation strategy around sites of RAP is also unknown. Further prospective studies are needed to identify the impact of RAP and to develop a therapeutic strategy.

Conclusions

The critical zones of VT isthmus appear to correspond to an area characterized by conduction velocity slowing in sinus rhythm map or paced ventricular rhythm map, and

the RAP around the wavefront discontinuity can provide additive functional information to further facilitate targeting most specific sites. However, different wavefront directions influence the appearance of the RAP. Isthmuses in the intramural tissue are the major cause of the inapparent RAP.

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Supplemental Material

Supplemental Methods
Figures S1–S3
Videos S1–S2

REFERENCES

1. Cronin EM, Bogun FM, Maury P, Peichl P, Chen M, Namboodiri N, Aguinaga L, Leite LR, Al-Khatib SM, Anter E, et al; ESC Scientific Document Group. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias. *Europace.* 2019;21:1143–1144. doi: 10.1093/europace/euz132
2. Aziz Z, Shatz D, Raiman M, Upadhyay GA, Beaser AD, Besser SA, Shatz NA, Fu Z, Jiang R, Nishimura T, et al. Targeted ablation of ventricular tachycardia guided by wavefront discontinuities during sinus rhythm: a new functional substrate mapping strategy. *Circulation.* 2019;140:1383–1397. doi: 10.1161/CIRCULATIONAHA.119.042423
3. Jaïs P, Maury P, Khairy P, Sacher F, Nault I, Komatsu Y, Hocini M, Forclaz A, Jadidi AS, Weerasooryia R, et al. 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. doi: 10.1161/CIRCULATIONAHA.111.043216
4. John RM, Stevenson WG. Catheter-based ablation for ventricular arrhythmias. *Curr Cardiol Rep.* 2011;13:399–406. doi: 10.1007/s11886-011-0201-6
5. Anter E, Kleber AG, Rottmann M, Leshem E, Barkagan M, Tschabrunn CM, Contreras-Valdes FM, Buxton AE. Infarct-related ventricular tachycardia: redefining the electrophysiological substrate of the isthmus during sinus rhythm. *JACC Clin Electrophysiol.* 2018;4:1033–1048. doi: 10.1016/j.jacep.2018.04.007
6. El Haddad M, Houben R, Stroobandt R, Van Heuverswyn F, Tavernier R, Duytschaever M. Novel algorithmic methods in mapping of atrial and ventricular tachycardia. *Circ Arrhythm Electrophysiol.* 2014;7:463–472. doi: 10.1161/CIRCEP.113.000833
7. Anter E, Neuzil P, Reddy VY, Petru J, Park KM, Sroubek J, Leshem E, Zimetbaum PJ, Buxton AE, Kleber AG, et al. Ablation of reentry-vulnerable zones determined by left ventricular activation from multiple directions: a novel approach for ventricular tachycardia ablation: A Multicenter Study (PHYSIO-VT). *Circ Arrhythm Electrophysiol.* 2020;13:e008625. doi: 10.1161/CIRCEP.120.008625
8. 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(4 Pt 1):1647–1670. doi: 10.1161/01.cir.88.4.1647
9. Stevenson WG, Friedman PL, Sager PT, Saxon LA, Kocovic D, Harada T, Wiener I, Khan H. Exploring postinfarction reentrant ventricular tachycardia with entrainment mapping. *J Am Coll Cardiol.* 1997;29:1180–1189. doi: 10.1016/s0735-1097(97)00065-x
10. Tung R, Mathuria N, Michowitz Y, Yu R, Buch E, Bradfield J, Mandapati R, Wiener I, Boyle N, Shivkumar K. Functional pace-mapping responses for identification of targets for catheter ablation of scar-mediated ventricular tachycardia. *Circ Arrhythm Electrophysiol.* 2012;5:264–272. doi: 10.1161/CIRCEP.111.967976
11. de Chillou C, Groben L, Magnin-Poull I, Andronache M, MagdiAbbas M, Zhang N, Abdelaal A, Ammar S, Sellal JM, Schwartz J, et al. Localizing the critical isthmus of postinfarct ventricular tachycardia: the value of pace-mapping during sinus rhythm. *Heart Rhythm.* 2014;11:175–181. doi: 10.1016/j.hrthm.2013.10.042
12. Akram S, Ann QU. Newton raphson method. *Int J Sci Eng Res.* 2015;6:1748-1752.
13. Steyers CM III, Sodhi S, Faddis MN, Cooper DH, Cuculich PS, Noheria A. Ablation using 3D maps adjusted for spatial displacement of premature ventricular complexes relative to sinus beats: Improving precision by correcting for the shift. *J Cardiovasc Electrophysiol.* 2019;30:2319–2325. doi: 10.1111/jce.14120
14. de Bakker JM, van Capelle FJ, Janse MJ, Wilde AA, Coronel R, Becker AE, Dingemans KP, van Hemel NM, Hauer RN. Reentry as a cause of ventricular tachycardia in patients with chronic ischemic heart disease: electrophysiologic and anatomic correlation. *Circulation.* 1988;77:589–606. doi: 10.1161/01.cir.77.3.589
15. Kléber AG, Rudy Y. Basic mechanisms of cardiac impulse propagation and associated arrhythmias. *Physiol Rev.* 2004;84:431–488. doi: 10.1152/physrev.00025.2003
16. Ciaccio EJ, Coromilas J, Wit AL, Peters NS, Garan H. Source-sink mismatch causing functional conduction block in re-entrant ventricular tachycardia. *JACC Clin Electrophysiol.* 2018;4:1–16. doi: 10.1016/j.jacep.2017.08.019
17. Cabo C, Yao J, Boyden PA, Chen S, Hussain W, Duffy HS, Ciaccio EJ, Peters NS, Wit AL. Heterogeneous gap junction remodeling in reentrant circuits in the epicardial border zone of the healing canine infarct. *Cardiovasc Res.* 2006;72:241–249. doi: 10.1016/j.cardiores.2006.07.005
18. Segal OR, Chow AW, Peters NS, Davies DW. Mechanisms that initiate ventricular tachycardia in the infarcted human heart. *Heart Rhythm.* 2010;7:57–64. doi: 10.1016/j.hrthm.2009.09.025
19. Frontera A, Melillo F, Baldetti L, Radinovic A, Bisceglia C, D'Angelo G, Foppoli L, Gigli L, Peretto G, Cireddu M, et al. High-density characterization of the ventricular electrical substrate during sinus rhythm in post-myocardial infarction patients. *JACC Clin Electrophysiol.* 2020;6:799–811. doi: 10.1016/j.jacep.2020.04.008
20. 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. doi: 10.1161/CIRCULATIONAHA.116.021955
21. Nishimura T, Upadhyay GA, Aziz ZA, Beaser AD, Shatz DY, Nayak HM, Tung R. Circuit determinants of ventricular tachycardia cycle length: characterization of fast and unstable human ventricular tachycardia. *Circulation.* 2021;143:212–226. doi: 10.1161/CIRCULATIONAHA.120.050363
22. Irie T, Yu R, Bradfield JS, Vaseghi M, Buch EF, Ajijola O, Macias C, Fujimura O, Mandapati R, Boyle NG, et al. Relationship between sinus rhythm late activation zones and critical sites for scar-related ventricular tachycardia: systematic analysis of isochronal late activation mapping. *Circ Arrhythm Electrophysiol.* 2015;8:390–399. doi: 10.1161/CIRCEP.114.002637
23. Komatsu Y, Daly M, Sacher F, Cochet H, Denis A, Derval N, Jesel L, Zellerhoff S, Lim HS, Jadidi A, et al. Endocardial ablation to eliminate epicardial arrhythmia substrate in scar-related ventricular tachycardia. *J Am Coll Cardiol.* 2014;63:1416–1426. doi: 10.1016/j.jacc.2013.10.087