ONLINE SUPPLEMENT

- **The Complete Dataset of ECGI-Imaged Human Ventricular Tachycardia**

- **Table S1. Results from EP Studies**

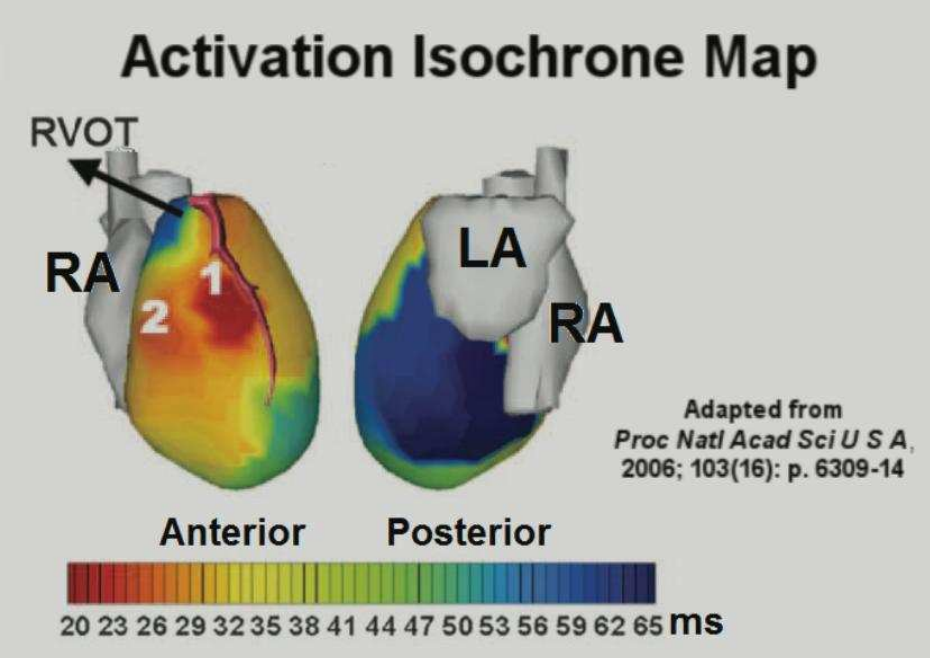
The Complete Dataset of ECGI-Imaged Human Ventricular Tachycardia

Patient number	Movie	EPS-Determined VT Characteristics	Ejection Fraction	Ventricular Substrate
NORMAL	**N1**		70%	Normal
RV1		Focal, Anterior-Left RVOT	60%	Inferior noninschemic scar
RV2		Focal, Midseptal RVOT	70%	Normal
RV3		Focal, Midseptal RVOT	65%	Normal
RV4		Focal, Posterior-Right RVOT	58%	Normal
RV5		(Not inducible during EPS)	35%	Anterior ischemic scar
RV6		Focal, Free Wall RVOT	55%	Normal
RV7	**RV7**	Focal, Midseptal RVOT	60%	Normal
RV8		Focal, Free Wall RVOT	55%	Normal
RV9	**RV9**	Focal, Midseptal RVOT	40%	Nonischemic cardiomyopathy
RV10		Focal, Inferobasal RV septum	50%	Normal, prior WPW ablation
RV11	**RV11**	Focal, Posterior-Right RVOT	60%	Normal
LV1	**LV1**	Focal, Epicardial Apicolateral LV	10%	Nonischemic cardiomyopathy
LV2	**LV2**	Reentrant, Endocardial, Inferoseptal LV	40%	Inferior ischemic scar
LV3	**LV3**	Reentrant, Endocardial, Apicolateral LV	55%	Lateral nonischemic scar (sarcoid)
LV4	**LV4**	Left Posterior Fascicular	70%	Normal
LV5	**LV5**	Left Posterior Fascicular	65%	Normal

LV6		Focal, Epicardial, Anterolateral LV	40%	Anterolateral nonischemic scar (sarcoid)
LV7		Focal, Left coronary cusp	40%	Nonischemic cardiomyopathy
LV8		(EPS not performed)	40%	Valvular cardiomyopathy
LV9		Reentrant, Endocardial, Inferoseptal LV	25%	Inferior ischemic scar
LV10		(EPS not performed)	45%	Nonischemic (Kawasaki Disease)
LV11	**LV11**	Reentrant, Endocardial, Apical LV Aneurysm	25%	Anterior ischemic scar
LV12	**LV12**	(EPS not performed)	30%	Anterior, inferior & lateral ischemic scar
LV13	**LV13**	Focal, Epicardial, Posterolateral LV	30%	Nonischemic cardiomyopathy
LV14	**LV14**	Endocardial, Apical LV Aneurysm	25%	Apical ischemic scar
LV15		Focal, Epicardial, Anterior LV (Great cardiac vein)	45%	Normal

EPS: electrophysiology study; LV: left ventricle; RV: right ventricle; RVOT: right ventricular outflow tract; WPW: Wolff-Parkinson-White Syndrome.
Note that movies are provided for a subset of representative cases.

NORMAL CARDIAC VENTRICULAR ACTIVATION



Normal Ventricular Epicardial Activation. ECGI isochrone maps in the anterior and posterior views are shown. Earliest epicardial activation is in the anterior right ventricle (dark red, locations 1 and 2). Activation continues in the left ventricle, with the area of latest activation near the inferolateral left ventricular base (dark blue). Corresponding ECGI epicardial activation movie is provided (**Movie N1**). LA: left atrium; RA: right atrium; RVOT: right ventricular outflow tract.

RIGHT VENTRICULAR TACHYCARDIAS (RV1-RV11)

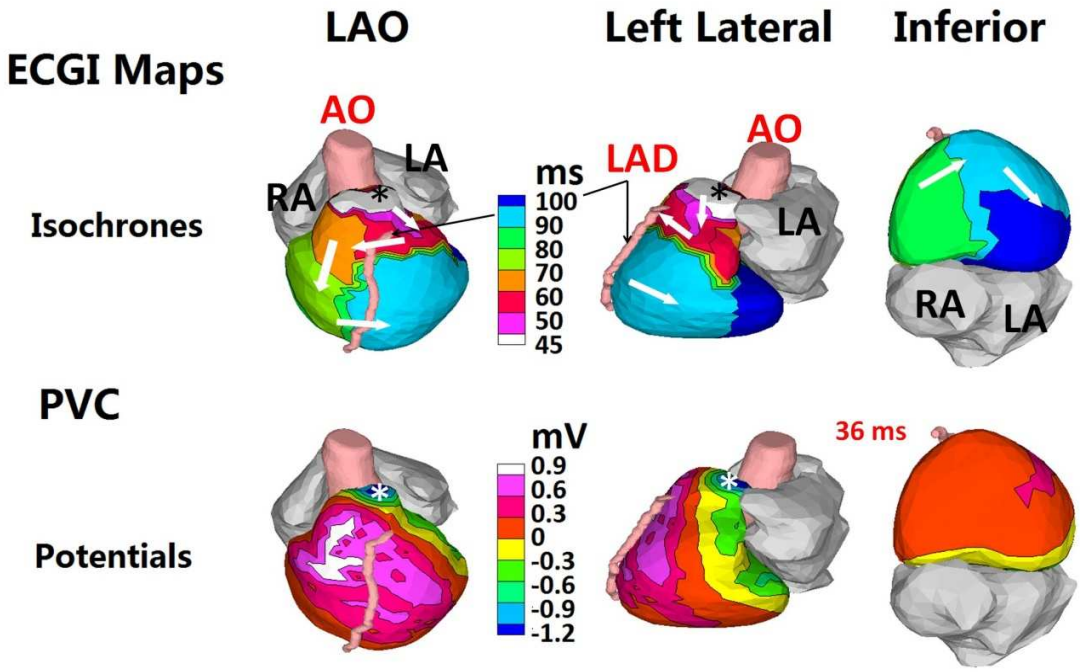


Figure RV1: ECGI of an anterior-left RVOT tachycardia. Isochrone maps (upper row) and potential maps (lower row, 36 ms from the onset of QRS) for a VT (spontaneous PVC) beat in three views. Asterisks indicate the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation. AO = Aorta, LA = Left Atrium, LAD = Left Anterior Descending Coronary Artery, LAO = Left Anterior Oblique, RA = Right Atrium. PVC = Premature Ventricular Contraction beat

Description: ECGI-derived activation sequences show that the earliest activation site of the VT is in the mid-septal RVOT region. The activation wavefront propagates towards the left lateral aspect of the RVOT (white, pink), and encounters a line of block. The wavefront propagates slowly across the inter-ventricular septum, as shown by the crowded isochrones near the left anterior descending artery. Activation of the left ventricle proceeds apex to base, with the basal lateral LV the last area to activate. This pattern of activation can be considered a “signature” of Left Bundle Branch Block (LBBB) ventricular activation. An area of early intense negative potential minimum at the same site as isochronal initiation with a radial activation wavefront spread is consistent with a focal, rather than reentrant, mechanism.

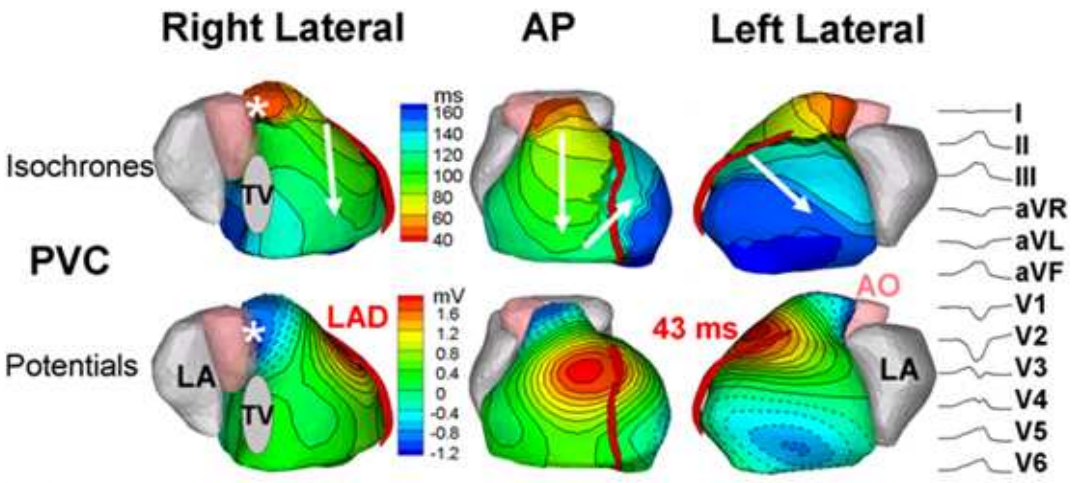


Figure RV2: ECGI of a mid-septal RVOT tachycardia. Isochrone maps (upper row) and potential maps (lower row, 43 ms from the onset of QRS) during a spontaneous PVC beat in three views. White asterisk indicates the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation. The conventional 12-lead ECG for the PVC is shown on the right. AP=Anteroposterior, TV = Tricuspid Valve.

Description: ECGI-derived activation sequence during the PVC begins in the right ventricle and proceeds along the anterior RV from base to apex. The wavefront encounters a line of block at the superior portion of the ventricular septum. The wavefront circumvents the block area ("U-shaped activation"), and activation of the left ventricle proceeds apex to base, with the basal lateral LV the last area to activate.

Compared to RV1, this patient lacks the early activation of the anterior left ventricle, as seen in the left lateral view. This distinguishes a "septal" location from an "anterior-left" location. Compare with LV15, which was mapped to the anterior inter-ventricular vein (an adjacent epicardial structure).

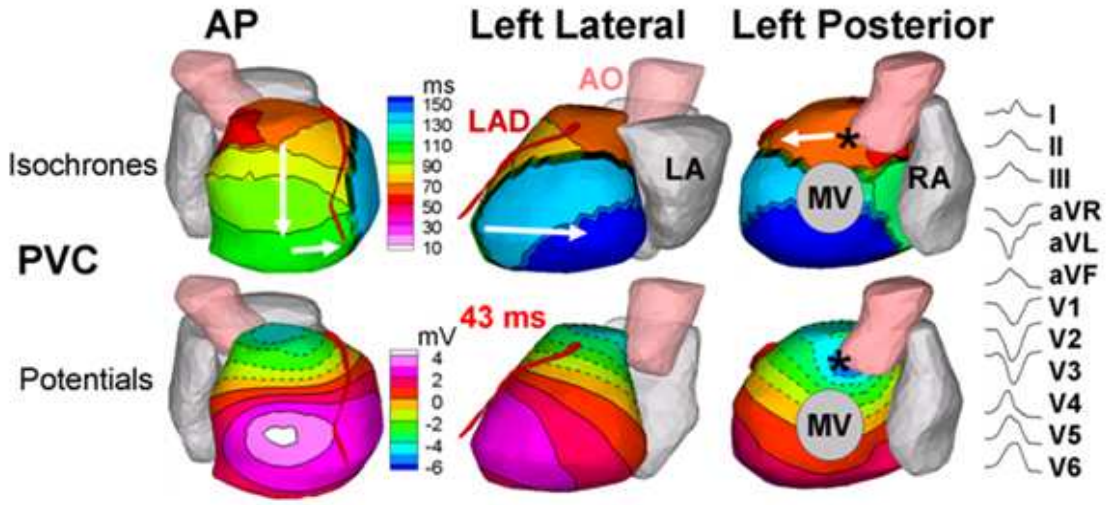


Figure RV3: **ECGI of a mid-septal RVOT tachycardia.** Isochrone map (upper row) and potential map (lower row, 43 ms from the onset of QRS) for a PVC beat in three views. Black asterisk indicates the ECGI determined VT origin. Arrows indicate the activation wavefront propagation direction. The conventional 12-lead ECG during PVC is shown on the right.

Description: Compared to patient RV2, this patient has a markedly positive signal in lead I, suggesting a more leftward activation pattern. The difference between patient RV2 and RV3 in surface ECG morphology can be accounted for by different cardiac geometries relative to the body-surface leads. In this case, the surface ECG suggests different locations for the RV3 and RV2 arrhythmias foci, but ECGI, which takes into account the specific patient anatomy, shows otherwise. This ECGI finding was supported by catheter mapping, with similar “mid-septal” locations in these patients.

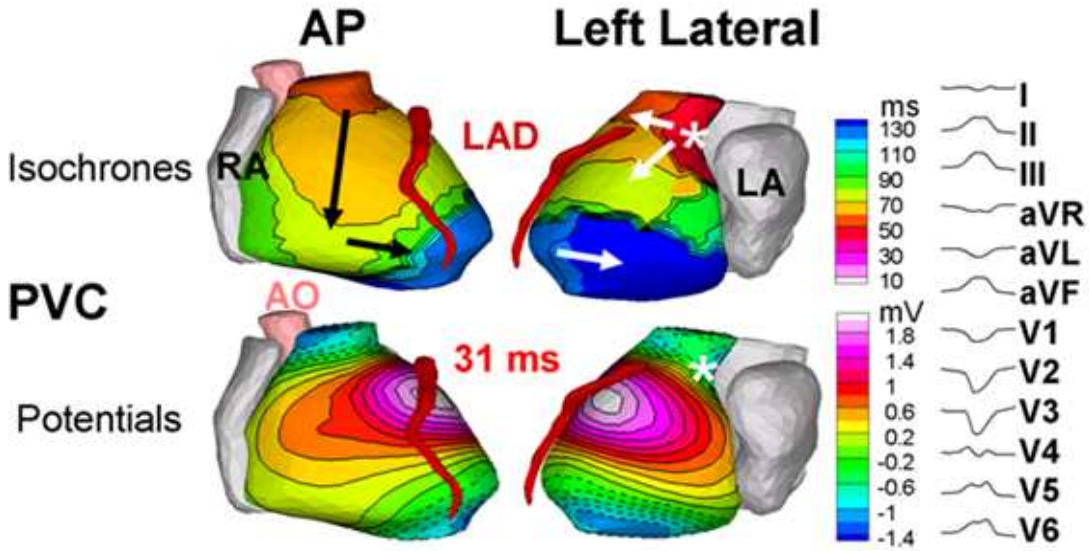


Figure RV4: **ECGI of a posterior-right RVOT tachycardia**. Isochrone map (upper row) and potential map (lower row, 31 ms from the onset of QRS) for a PVC beat in two views. White asterisk indicates the ECGI determined VT origin. Arrows show the activation wavefront propagation direction. The conventional 12-lead ECG during the PVC is shown on the right.

Description: The overall activation pattern for this patient was consistent with the "signature" LBBB pattern. The area of earliest activation on these isochrone maps varied slightly when compared to the mid-septal RVOT location of patient RV2. With a posterior right origin, the earliest isochrone and negative potential minimum were in the most posterior portion of the RVOT. Interestingly, the earliest propagation pattern included a portion of the anterior LV as well as the RV. The area of slowed conduction in this patient was displaced apically and laterally from the septum relative to patient RV3, but the overall LBBB signature pattern was preserved. The early anterior LV activation may account for the decreased terminal leftward forces on the conventional 12-lead ECG.

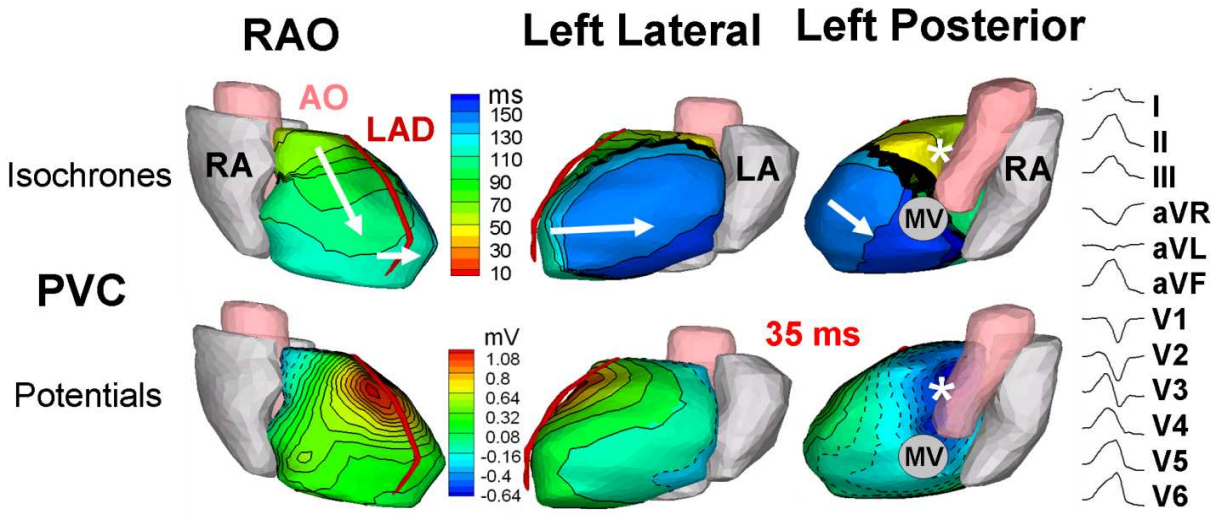


Figure RV5: ECGI of an anterior left RVOT tachycardia (noninducible during EPS). The isochrone map (upper row) and potential map (lower row, 35 ms from the onset of QRS) for a PVC beat in three views. White asterisk indicates the ECGI determined VT origin. The white arrows show the direction of the activation wavefront propagation. The conventional 12-lead ECG during the PVC is shown on the right.

Description: The overall activation pattern for this patient was also consistent with the "signature" LBBB pattern. This case demonstrates an anterior left origin with the earliest isochrone and minimum negative potential occurring anteriorly in the RVOT. The activation pattern advanced quickly and preferentially down the anterior right ventricle, with modest early anterior LV activation.

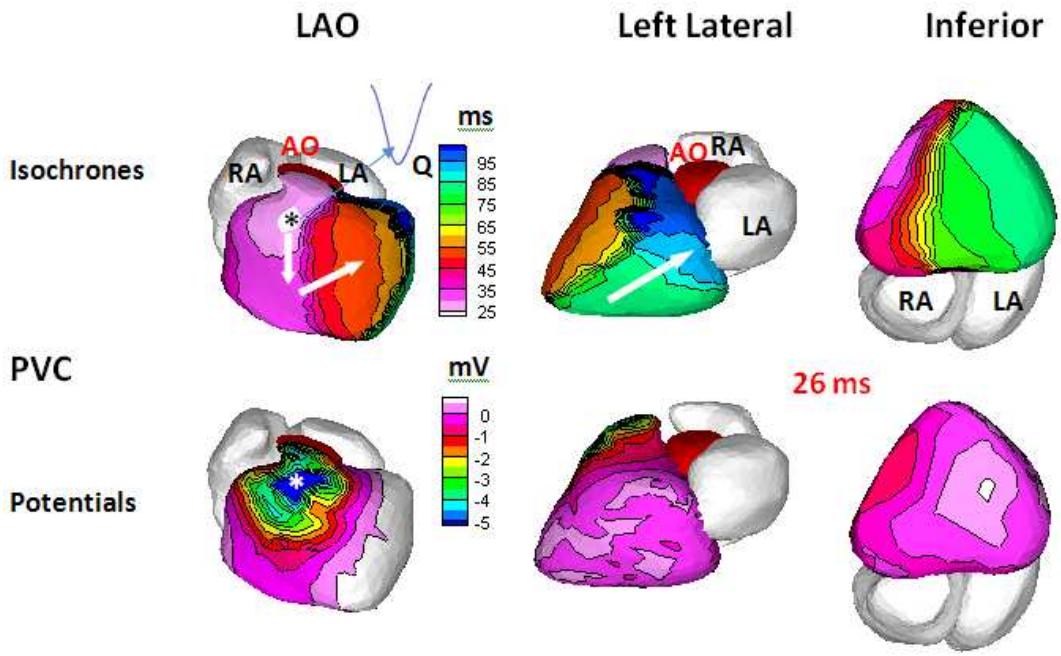


Figure RV6: ECGI of a free wall RVOT tachycardia. Isochrone map (upper row) and potential map (lower row, 26 ms from the onset of QRS) during PVC beat in three views. Asterisk indicates the ECGI determined origin of PVC. White arrows indicate the direction of activation wavefront propagation. The local ECGI electrogram from the VT origin site (blue arrow) is shown**.**

Description: The origin of this tachycardia is dramatically different than prior examples (RV1-RV5). Both the earliest isochrone and location of intense local minimum is in the lateral-free wall location of the RVOT. Propagation occurs rapidly down the right ventricle from base to apex. The wavefront demonstrates some delay across the ventricular septum, prior to activating the left ventricle, ending at the LV base.

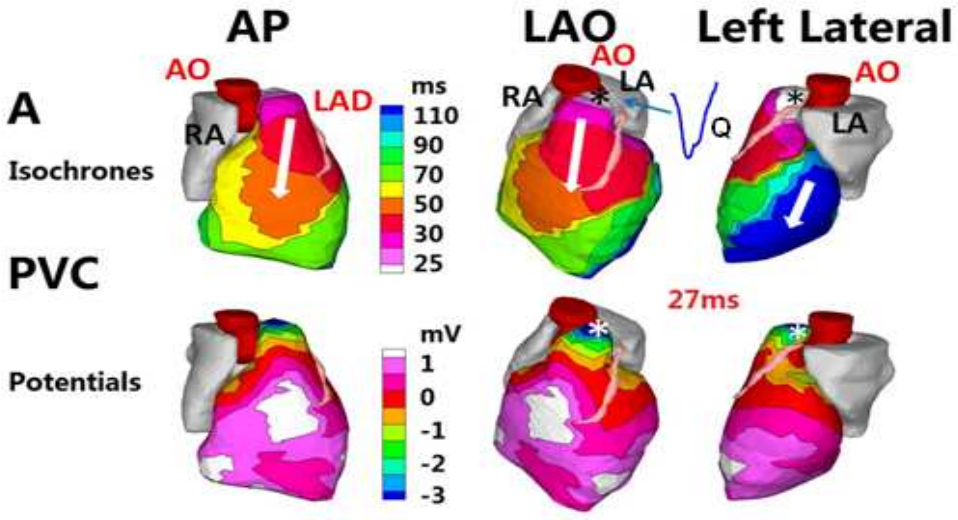


Figure RV7: ECGI of a mid-septal RVOT tachycardia. Panel A: isochrone map (upper row) and potential map (lower row, 27 ms from the onset of QRS) during a spontaneous PVC beat in three views. Asterisks indicate the ECGI determined mid-septal RVOT VT origin. White arrows indicate the direction of activation wavefront propagation. The local ECGI electrogram from the VT origin site (blue arrow) is shown**.** Corresponding ECGI epicardial activation movie is provided (**Movie RV7**).

Description: Similar to RV2 and RV3, the ECGI-derived activation sequence during the PVC begins in the mid-septal RVOT and proceeds along the anterior RV from base to apex, with the posterior-lateral LV activated last. An area of early intense negative potential at the same site as isochronal initiation with a radial activation wavefront suggests a focal mechanism.

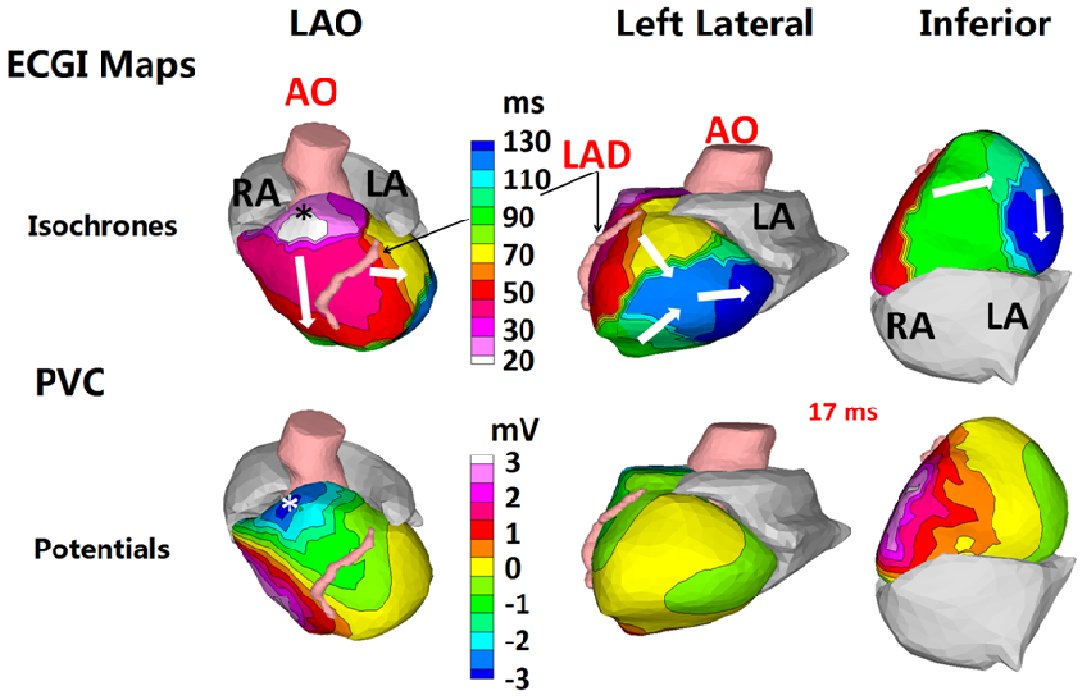


Figure RV8: ECGI of a free wall RVOT tachycardia. Isochrone maps (upper row) and potential maps (lower row, 17 ms from the onset of QRS) for a VT beat in three views. Asterisks indicate the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation.

Description: Similar to RV6, the origin of this arrhythmia is squarely along the posterior aspect of the free wall of the RVOT.

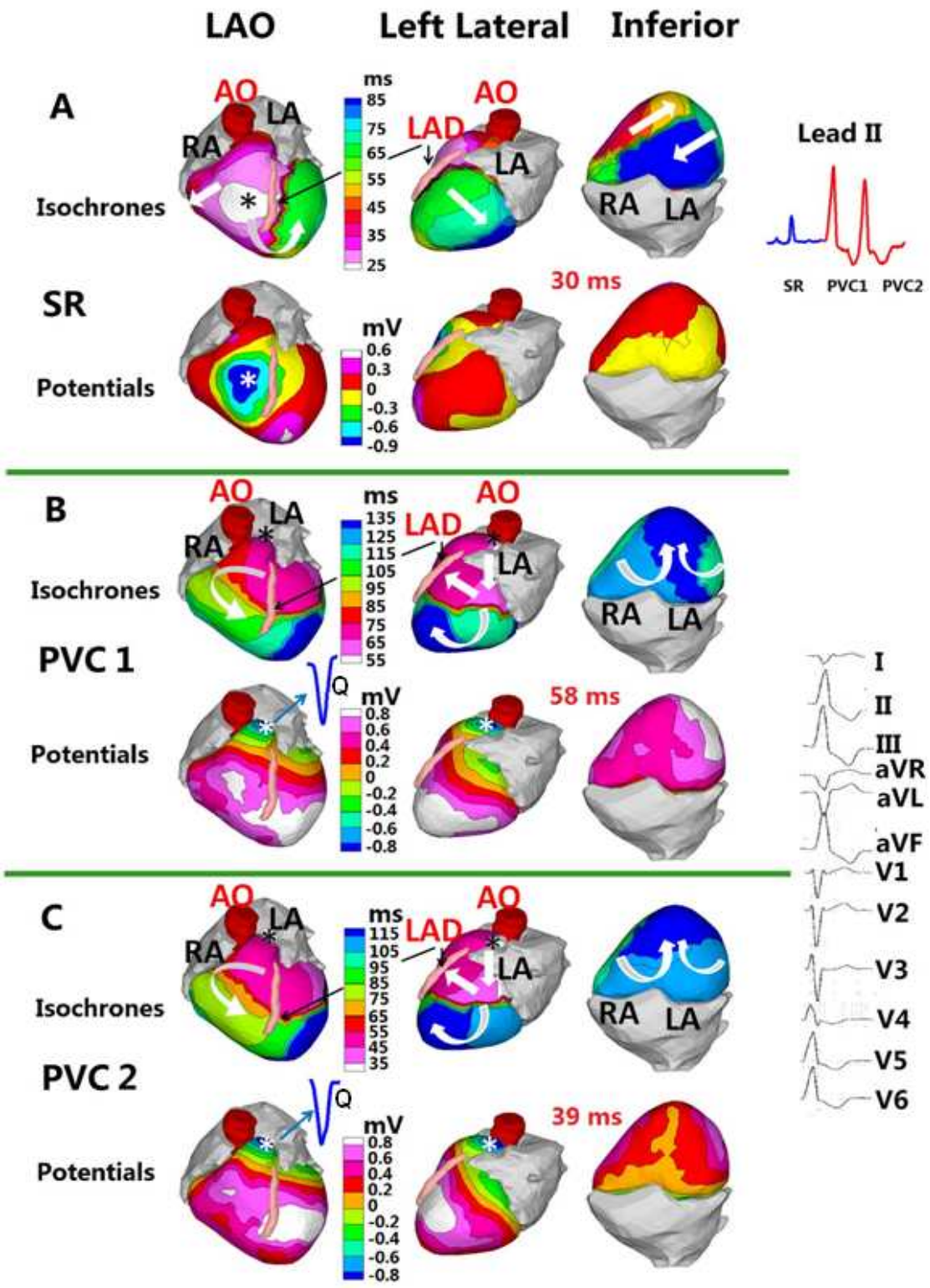


Figure RV9: ECGI of a midseptal RVOT tachycardia. A sinus beat (SR) was followed by two PVCs (see Lead II at the upper right corner). Panel A:

isochrone map (upper row) and potential map (lower row, 30 ms from the onset of QRS) for a sinus beat. Asterisks indicate RV epicardial breakthrough. White arrows show the sinus activation propagation sequence. Panel B and Panel C: isochrone maps and potential maps (58 ms and 39 ms from the onset of QRS) for PVC1 and PVC2, respectively, in three views. Asterisks indicate the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation. The conventional 12-lead ECG for the PVC is shown on the lower right. Corresponding ECGI epicardial activation movie is provided (**Movie RV9**).

Description: During EP study, attempts of catheter ablation in the posterior septal RVOT were only transiently successful (recurrence within two minutes). ECGI-derived activation sequences show that the earliest activation site of PVCs is in the mid-septal RVOT region. However, interestingly, the major activation wavefront starts from the posterior-lateral basal LV, and encounters a line of block perpendicular to the LAD, similar to the anterior-left origin of RV1 and coronary cusp origin of LV7.

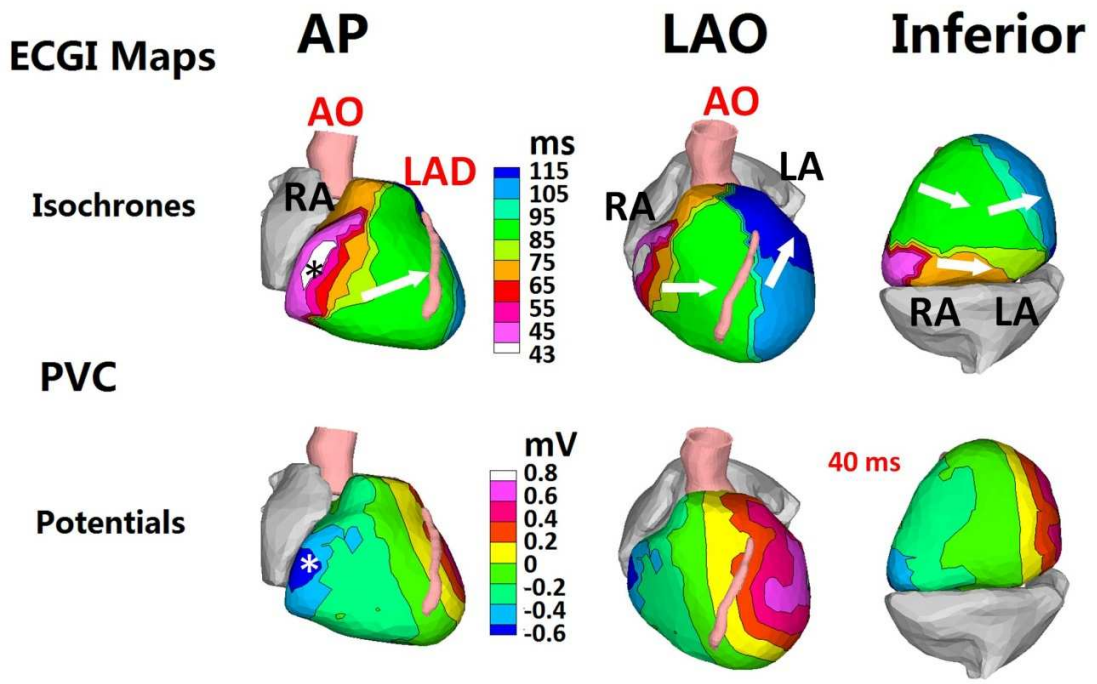


Figure RV10: ECGI of an RV base tachycardia. Isochrone maps (upper row) and potential maps (lower row, 40 ms from the onset of QRS) for a VT beat in three views. Asterisks indicate the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation.

Description: ECGI-derived activation sequences show that the earliest activation site of PVC is in the anterior basal RV region, an atypical RV location. The lateral basal LV region is the latest to activate. The activation sequence has an LBBB pattern with left superior axis.

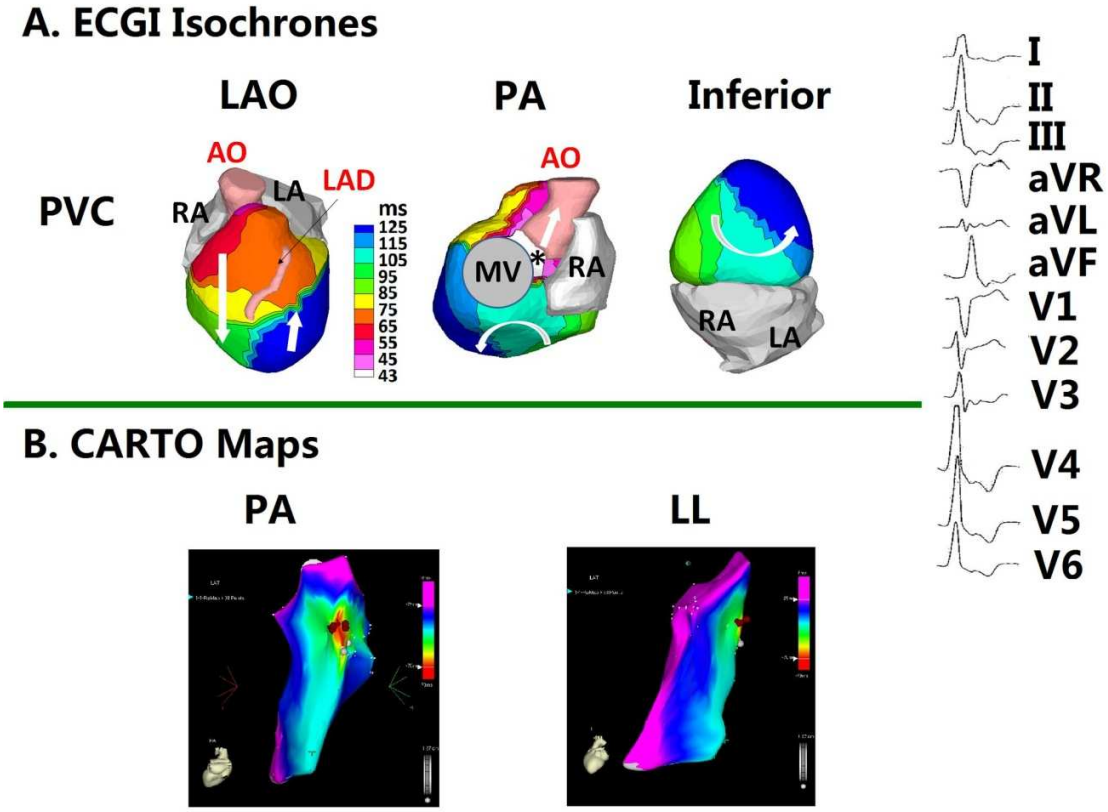


Figure RV11: ECGI of a posterior-right RVOT tachycardia. Panel A: isochrone maps for a PVC in three views. Asterisk indicates the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation. The conventional 12-lead ECG for the PVC is shown on the right. Panel B: Invasive catheter (CARTO) activation maps are shown in posterior (PA) and left lateral (LL) projections, with early activation at the posterior RVOT (red region). The red dots are ablation sites. Corresponding ECGI epicardial activation movie is provided (**Movie RV11**).

Description: The isochrone map from ECGI reconstruction shows the earliest activation in the posterior RVOT, which is consistent with the EP study findings (Panel B, red region in CARTO maps). The wavefront appears on RV epicardium about 20 ms after the RVOT septal initiation and proceeds inferiorly along the anterior RV wall. The wavefront encounters a line of block near the LAD. It slowly activates the LV from base to apex, leaving the apical LV the last to activate. This activation sequence has a

LBBB-VT pattern. Ablation at the posterior RVOT site (Panel B, red dots) successfully terminated the arrhythmia.

LEFT VENTRICULAR TACHYCARDIAS (LV1-LV15)

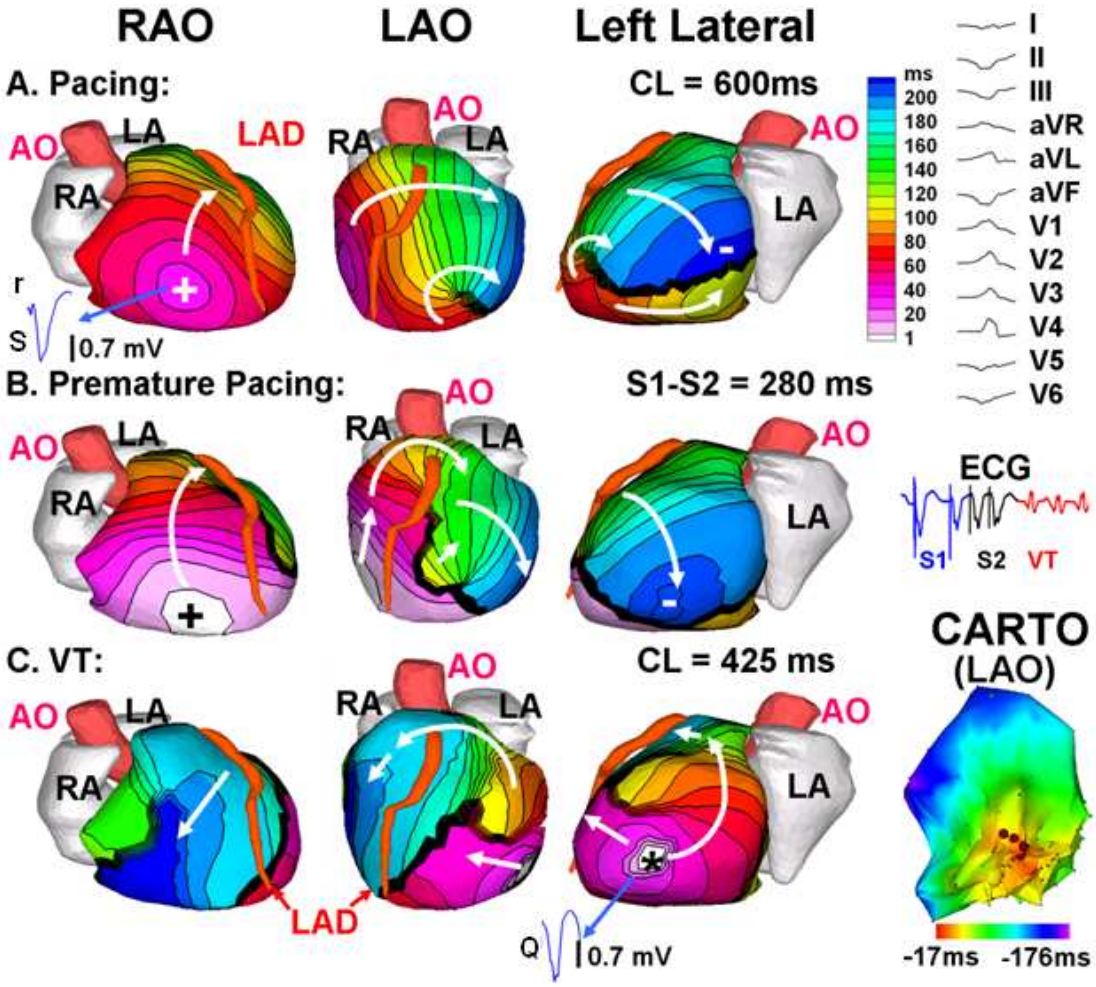


Figure LV1: ECGI of a focal ventricular tachycardia induced by programmed electrical stimulation. Panel A: Epicardial activation sequence during drive train (S1) pacing at cycle length of 600ms. (RAO = right anterior oblique, LAO=left anterior oblique). White arrows show direction of wavefront propagation. Thick black line indicates conduction block. Earliest epicardial activation site is marked by + and corresponds to the underlying endocardial pacing site. ECGI epicardial electrogram from this site is shown (blue arrow) with rS complex, consistent with endocardial activation. The conventional 12-lead ECG during VT is shown on the right. Panel B: Premature (S2) pacing at 280ms coupling interval from the same pacing site. The major wave front is forced to pivot around the extended line of block. There is some fusion with an intramural trans-septal front (small

white arrow). Panel C: VT; earliest epicardial activation site is marked by asterisk. ECGI electrogram from the VT origin site is shown (blue arrow). A body surface ECG is shown on the right of Panel B. All S1 beats (blue) are similar, as are the two S2 beats (black) and all VT beats (red). Invasive LV endocardial activation map of the VT in LAO projection is in Panel C, right (red is early).

Description: This patient had a nonischemic cardiomyopathy and at the end of her EP study, she was deemed to have a nonendocardial focal VT at the apical-lateral LV. Double ventricular extrastimuli induced hemodynamically tolerated VT at a cycle length of 390ms. With drive train pacing (S1, Panel A), the earliest epicardial activation starts from the pacing site (white +) near the RV apex and propagates both superiorly and inferiorly towards the left ventricle. ECGI epicardial electrogram from the site of earliest epicardial activation shows rS morphology, consistent with endocardial initiation of the paced beats. The epicardial activation sequence during premature ventricular extrastimuli (S2) from the same site is shown in Panel B. The premature beat retains a similar overall activation pattern to drive train pacing, with two distinct differences. First, the line of block is elongated over the anterior septum towards the base of the heart (LAO view), demonstrating its functional nature. Second, in the LV the line of block shifts inferiorly and the latest activation region (white -) is delayed and shifted apically (left lateral view). Panel C shows epicardial activation during the first beat of induced VT. The earliest epicardial activation (black star in left lateral view) occurs at the latest activation region of the previous S2 paced beat, suggesting triggered activity as the mechanism. The activation wavefronts propagate towards both the apex and the base (white arrows). The activation wavefront that propagates towards the apex encounters a line of block. The activation wavefront that propagates towards the base turns around the line of block and propagates toward the RV. The electrogram from the earliest epicardial site is a pure Q wave, indicating an epicardial origin of the VT. A three-dimensional endocardial map was created during the procedure, showing the earliest activation in a large area in the anterolateral apex. At the conclusion of the procedure, it was deemed that the likely mechanism was focal, and that the endocardium was not the site of origin. These conclusions are consistent with the ECGI images and electrograms. Corresponding ECGI epicardial activation movie is provided (**Movie LV1**).

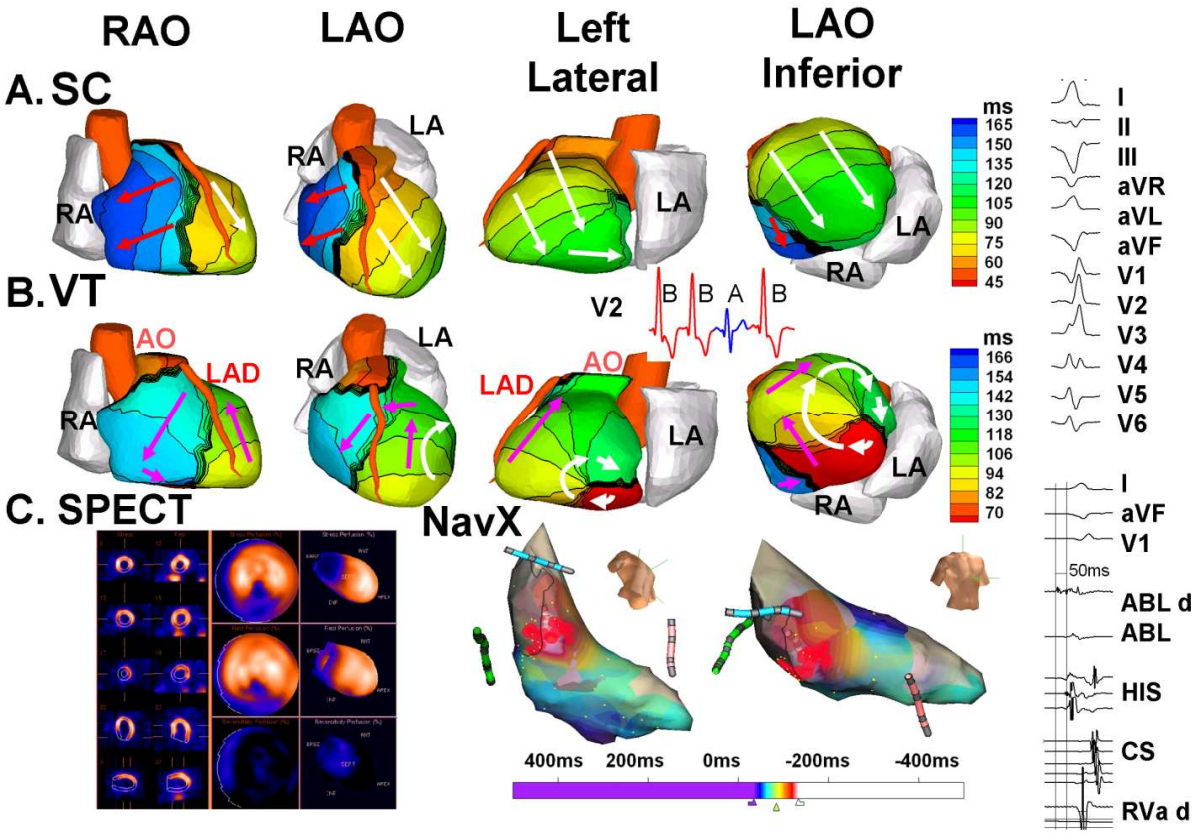


Figure LV2: ECGI of reentrant VT from inferobasal scar. Panel A: Four views of activation sequence during a sinus capture (SC) beat (labeled A, blue on the V2 ECG). Arrows indicate direction of the activation wavefronts. Panel B: Activation sequence during VT beats (labeled B, red on the V2 ECG). White arrows indicate a clockwise lateral loop (left lateral and LAO inferior views); Pink arrows show propagation into the RV in a counter-clockwise fashion. Panel C: Left: SPECT images showing a scar at the inferobasal LV region (blue). Right: NavX invasive endocardial map of VT activation (red early, blue late). The conventional 12-lead ECG during VT and the ablation-catheter signals are shown on the right side of the figure.

Description: This patient had an extensive inferoseptal scar from a prior inferior wall myocardial infarction (SPECT image in Panel C) and presented with slow hemodynamically tolerated VT. As shown by ECG lead V2 (inset), sinus capture (SC) beats occasionally interrupted the VT rhythm. ECGI images of an SC beat and a VT beat are shown in panels A and B, respectively. The origin of each ECGI-imaged VT beat was the inferior base

of the heart (red, LAO and left lateral views). The propagation pattern of the VT consisted of two wave fronts. One (white arrows) propagated clockwise, with a high degree of curvature, toward the base of lateral LV, where it encountered an inferior line of block. The other (pink arrows) propagated superiorly toward the base where it made a slow counter-clockwise turn around a line of block near the septum to RV. The latest activation during VT was at the lateral base of the RV. This second wavefront connected with the first wavefront at the inferior base, where the next activation wavefront begins. In this region of the inferobasal septum, ECGI reconstructs low-amplitude, highly fractionated electrograms, consistent with a scar (data not shown). Corresponding ECGI epicardial activation movie is provided (**Movie LV2**), showing a short period of earliest pre-systolic activation near the inferior border zone of the scar. The subsequent VT beat begins near this border zone exit site. During the ablation procedure, a voltage map confirmed the inferobasal septal scar (Panel C). A limited invasive activation map during the slow VT showed the earliest activation in the scar border zone in the inferobasal septum, with the earliest electrogram signal >50 ms before the surface QRS (shown in right lower corner).

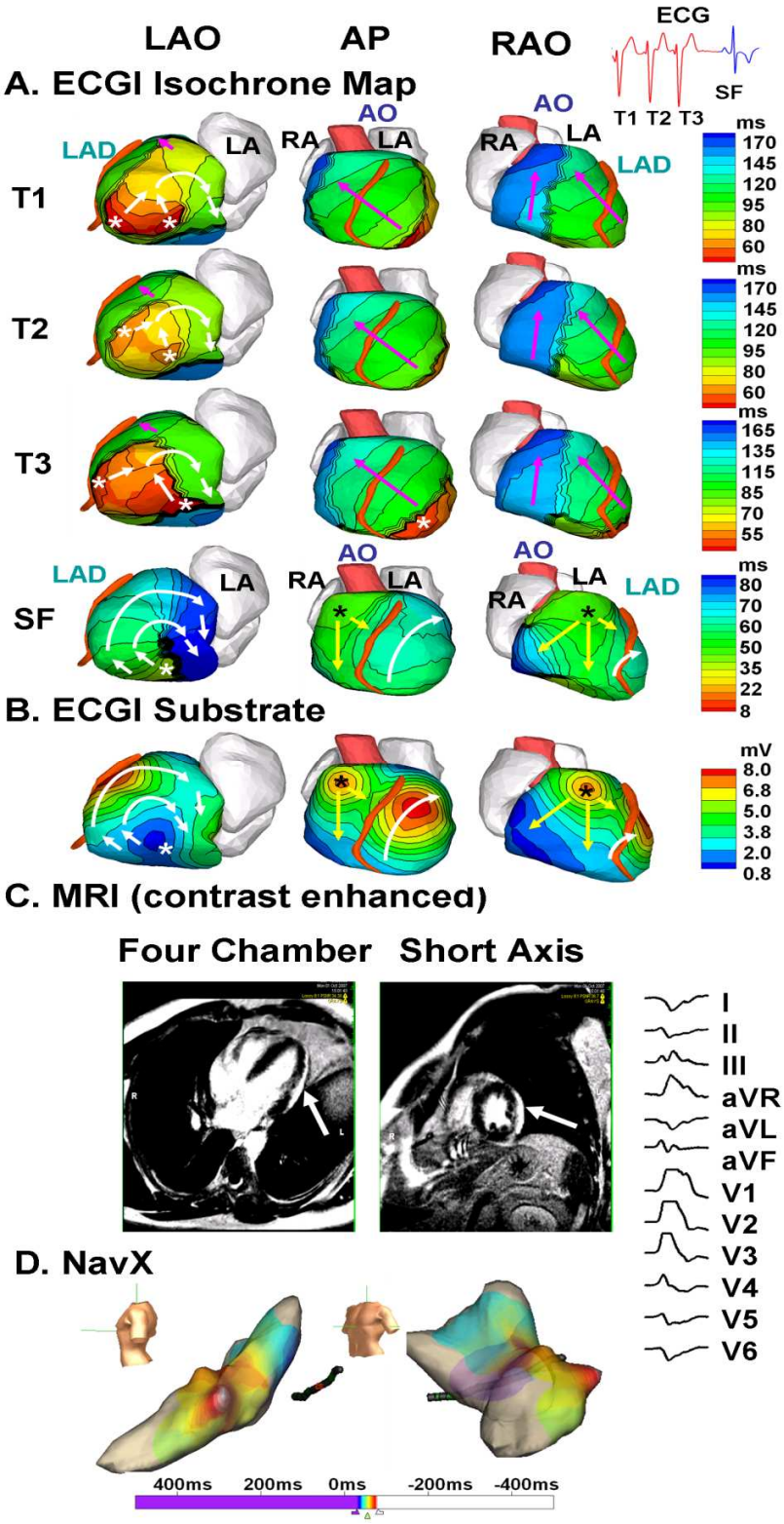

LAO
AP
RAO
ECG
SF
T1 T2 T3
A. ECGI Isochrone Map
T1
T2
T3
SF
LAD
LA
RA
AO
ms
170
145
120
95
80
60
165
135
115
85
70
55
50
35
22
8
B. ECGI Substrate
mV
8.0
6.8
5.0
3.8
2.0
0.8
C. MRI (contrast enhanced)
Four Chamber
Short Axis
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
D. NavX
400ms
200ms
0ms
-200ms
-400ms

Figure LV3: ECGI of a reentrant VT from mid-lateral LV (lateral wall infiltrative cardiomyopathy). Panel A. Activation patterns for three consecutive VT beats (T1, T2, T3) and one fusion beat of sinus and VT activation (SF) in three views. The displayed beats are marked by T1, T2, T3 and SF on one surface ECG. Asterisks mark earliest epicardial activation sites and arrows the propagation direction of the activation wave front. For the VT beats, white arrows show the clockwise rotating wave fronts and pink arrows show a second wavefront that activates the RV. The black asterisk and yellow arrows in SF map show normal RV breakthrough site and activation, which fuses with VT activation (white asterisk and arrows). Panel B. Substrate map during a sinus beat, created using peak-to-peak magnitude of ECGI epicardial electrograms (low potentials indicating scar are blue; scale in mV). Arrows indicating the activation pattern are superimposed, demonstrating how the wavefront relates to the underlying scar substrate. Panel C. Contrast-enhanced (gadolinium) MRI images in two views. The LV mid-lateral scar appears bright (arrows). Panel D. NavX map of endocardial activation during VT; regions of earliest activation are red. The conventional 12-lead ECG of the VT is shown on the right.

Description: This patient presented with syncope and sustained VT on ambulatory monitoring. A gadolinium-enhanced MRI revealed patchy myocardial and subepicardial enhancement in the lateral LV, consistent with a focal myocarditis or cardiac sarcoid. ECGI during VT identified two distinct areas of early epicardial activation (white asterisks, Panel A), which differed locally from beat to beat (T1, T2, T3). The propagation pattern varied somewhat based on the relative contribution of the two sources, but the images in the figure show that for all beats the wavefront turns clockwise and propagates to the LV lateral base with a high degree of curvature, where it reaches a line of block in the inferolateral base. A fusion beat is also shown (SF) with a combination of normal anterior RV activation and abnormal inferolateral VT activation. Electrogram analysis showed both pure Q wave and rS pattern during VT, consistent with both epicardial and endocardial involvement. Panel B shows a peak-to-peak amplitude "substrate map" of ECGI epicardial electrograms obtained during the SF beat. The mid-lateral LV has a region of low amplitude (blue), which corresponds closely to the MRI scar images. The activation sequence is superimposed on the substrate map, demonstrating its relationship to the scar substrate (blue). During the ablation procedure, pre-ablation activation mapping detected an earliest endocardial activation site in the inferolateral

LV, which corresponds to the earliest region of epicardial activation mapped by ECGI. ECGI epicardial activation movie is provided (**Movie LV3**).

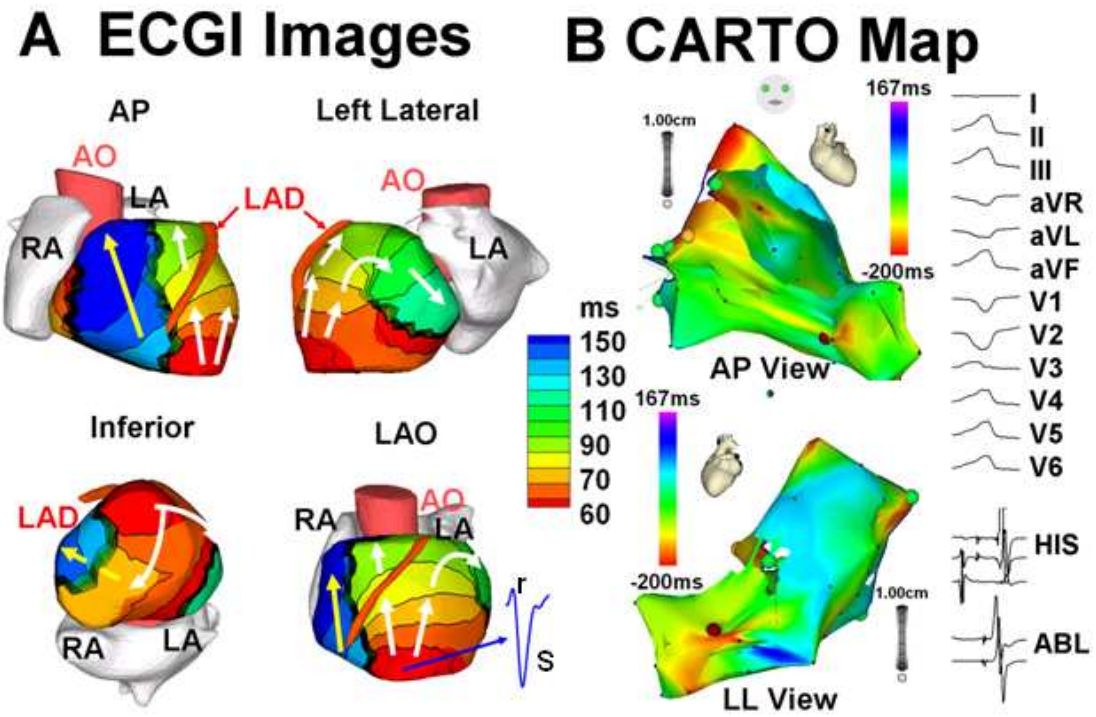


Figure LV4: ECGI of left posterior fascicular VT. Panel A: Four views of the activation sequence during VT. White arrows indicate the activation pathways during the first 120 ms. Yellow arrows indicate the activation sequence of anterior-lateral RV after a long conduction delay. Epicardial electrogram with rS morphology at apex (blue arrow) indicates endocardial or deep intramural origin of the VT. Panel B: Endocardial CARTO activation maps in AP and left-lateral views demonstrate successful ablation at an endocardial site (red sphere) that corresponds to the ECGI-imaged site of earliest epicardial activation. The conventional 12-lead ECG and catheter recordings during the induced VT are shown on the right.

Description: This patient had fascicular VT, thought to be a microreentrant circuit involving the distal Purkinje network. . In Panel A, the VT earliest epicardial activation is over a large area at the apex. A broad wavefront propagates towards the LV base. One segment rotates clockwise to the lateral base. A second segment propagates inferiorly toward the posterior base (inferior view) and after a long conduction delay activates the RV and propagates superiorly towards the base of the heart. This is consistent with the RBBB pattern seen on the conventional 12-lead ECG. The ECGI local electrogram at the apex (blue arrow) clearly shows rS morphology,

identifying an endocardial or intramural origin of VT. ECGI epicardial activation movie is provided (**Movie LV4**).

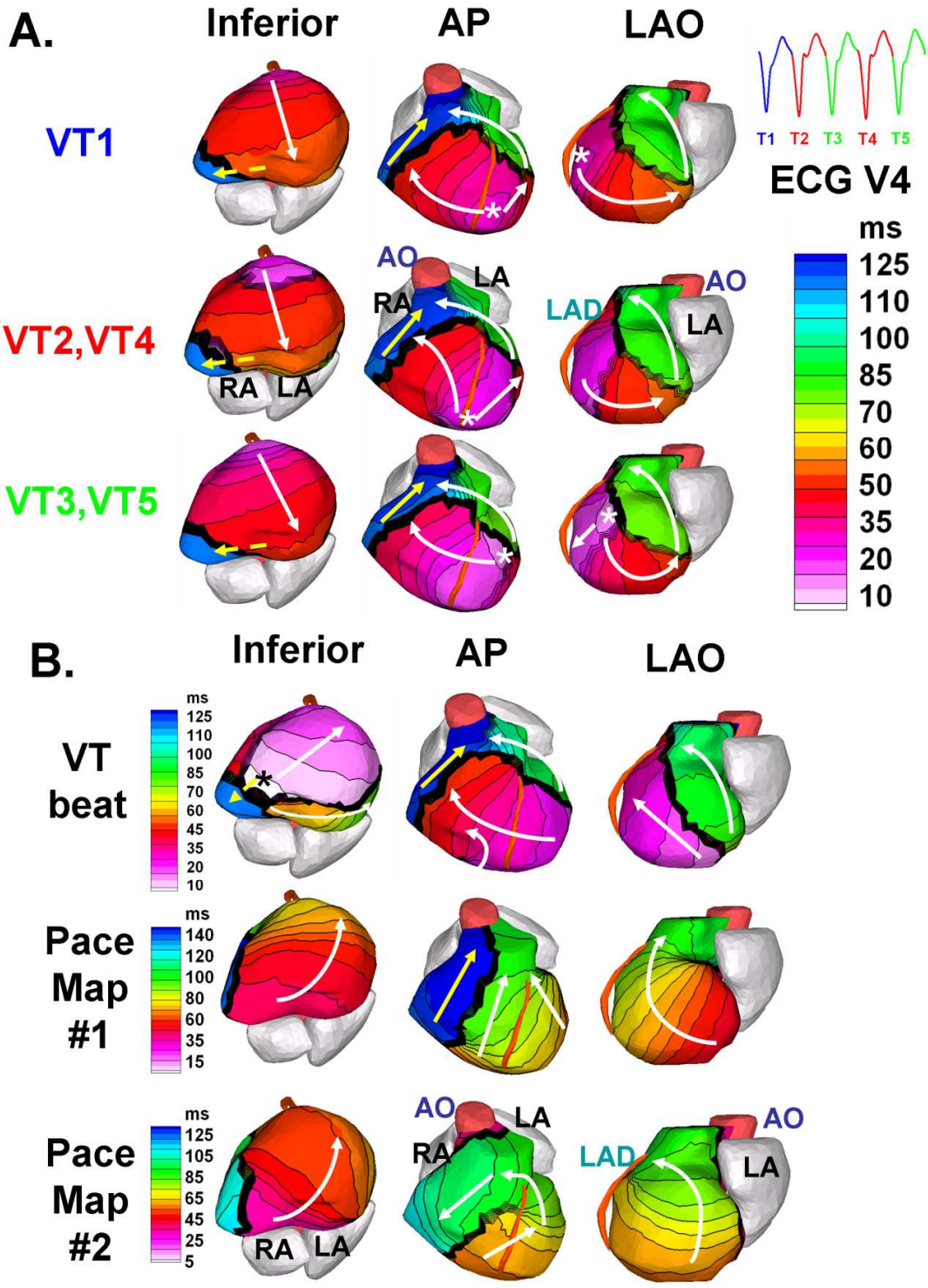


Figure LV5: ECGI of a Left Fascicular VT. Panel A: Three morphologies of VT within five consecutive beats. Each row shows the ECGI activation map for one VT morphology. The five consecutive VT beats in lead V4 are color coded based on the morphology (VT1=blue, VT2 and VT4=red, VT3 and VT5=green). White arrows indicate the direction of the activation wavefronts. Yellow arrows indicate slow conduction and late RV activation. Asterisk marks the earliest epicardial activation site for the beat. Panel B: ECGI maps of epicardial activation during the VT beat chosen as the "target" for a 12-lead pacemap ablation approach (top row). The pacemapping technique implies that pacing from the site of origin of the VT would produce an identical QRS morphology on the conventional 12-lead ECG. In the middle and bottom rows, two examples of ECGI maps are shown of epicardial activation during endocardial pacing from sites near the left posterior fascicle. For these activation patterns, the 12-lead features did not match those of the VT.

Description: The conventional 12-lead ECG showed monomorphic VT and clinically, despite extensive mapping, the procedure was ultimately abandoned due to the inability to obtain a reasonable pacemap match. Interestingly, in contrast to 12-lead ECG, ECGI demonstrated considerable differences in the epicardial activation of the VT beats. The first pattern (VT1) has the earliest activation at the LV apex, with an apex-to-base activation pattern. The second pattern (VT2, VT4) shows the earliest activation closer to the RV apex, with a slightly different apex-to-base activation pattern. The third pattern (VT3, VT5) shows the earliest activation on the mid-anterolateral LV, with a very different base-to-apex initial activation. Noninvasive ECGI was able to accurately identify the spontaneous, dynamic transitions of VT activation patterns which were not recognized on the standard 12-lead ECG.

During the EPS, the VT beat chosen for pacemapping was never replicated, and ultimately the procedure was unsuccessful. In retrospect, ECGI of the VT beat chosen for pacemapping was considerably different than the other imaged VT beats, which may explain the inability to successfully map and ablate the VT. ECGI epicardial activation movie is provided (**Movie LV5**).

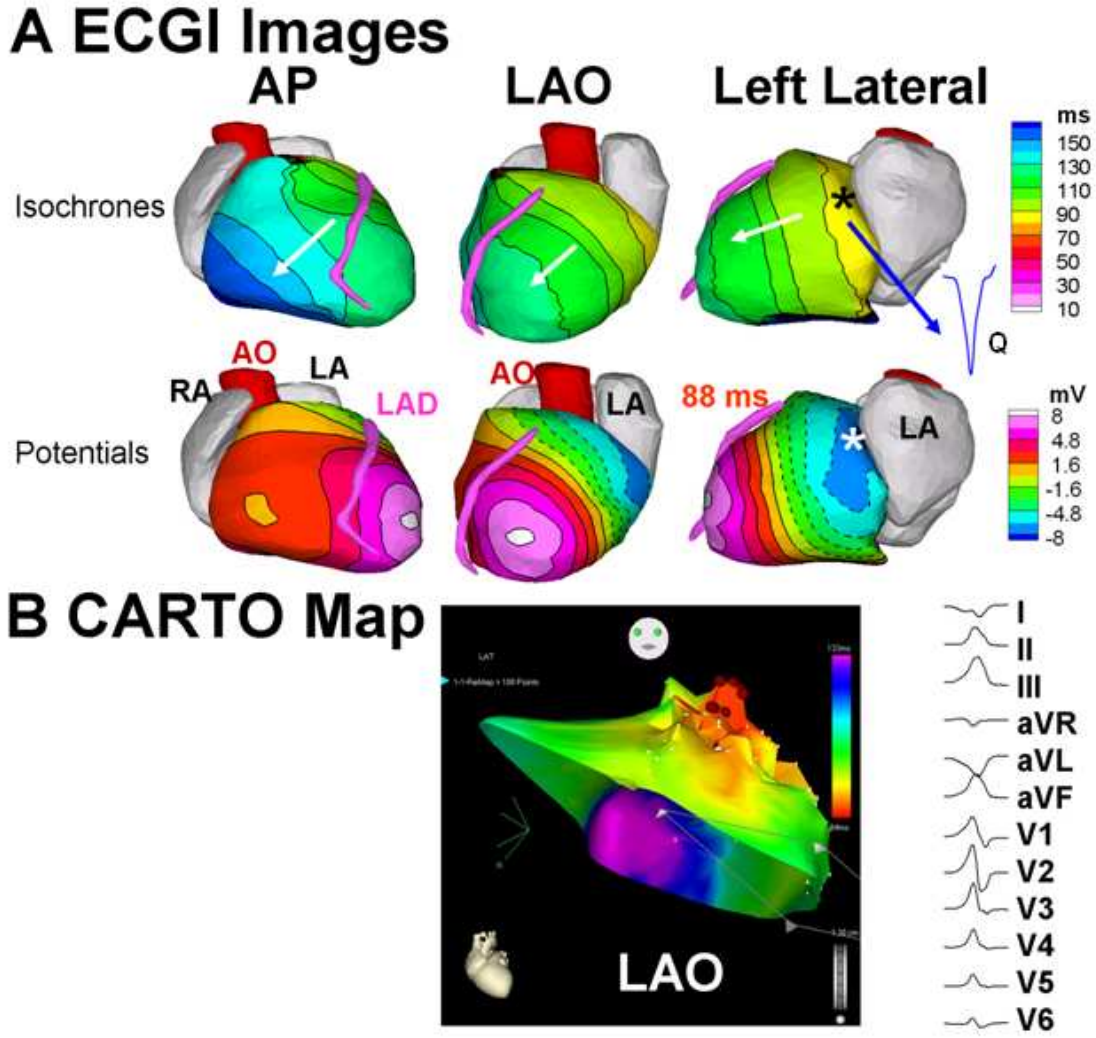


Figure LV6: ECGI of an epicardial anterior basal focal VT. Panel A. Isochrone map (upper row) and potential map (lower row, 88 ms from the onset of QRS) during VT beat in three views. Asterisk indicates the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation. Epicardial electrogram with Q wave at the earliest activation region is shown in blue. Panel B. Epicardial electroanatomical map (CARTO) is shown in LAO projection, with early activation at the anterolateral base (red). The conventional 12-lead ECG during a VT beat is shown on the right.

Description: This patient (also included as patient LV3 in this study) presented eight months after his first endocardial ablation with frequent

nonsustained VT and worsening heart failure symptoms. His cardiac function had deteriorated over time. On conventional 12-lead ECG, he had three distinct morphologies of VT. His predominant arrhythmia had characteristics consistent with an epicardial location, and an epicardial ablation was performed. ECGI images are shown here. Isochrone map and potential map show earliest activation during VT in the anterolateral base (Panel A). The propagation pattern is radial from a central focus, and the local electrogram is pure Q wave, consistent with an epicardial source. Electroanatomic mapping of the epicardial surface during VT (Figure 8B) was entirely consistent with the noninvasive ECGI findings.

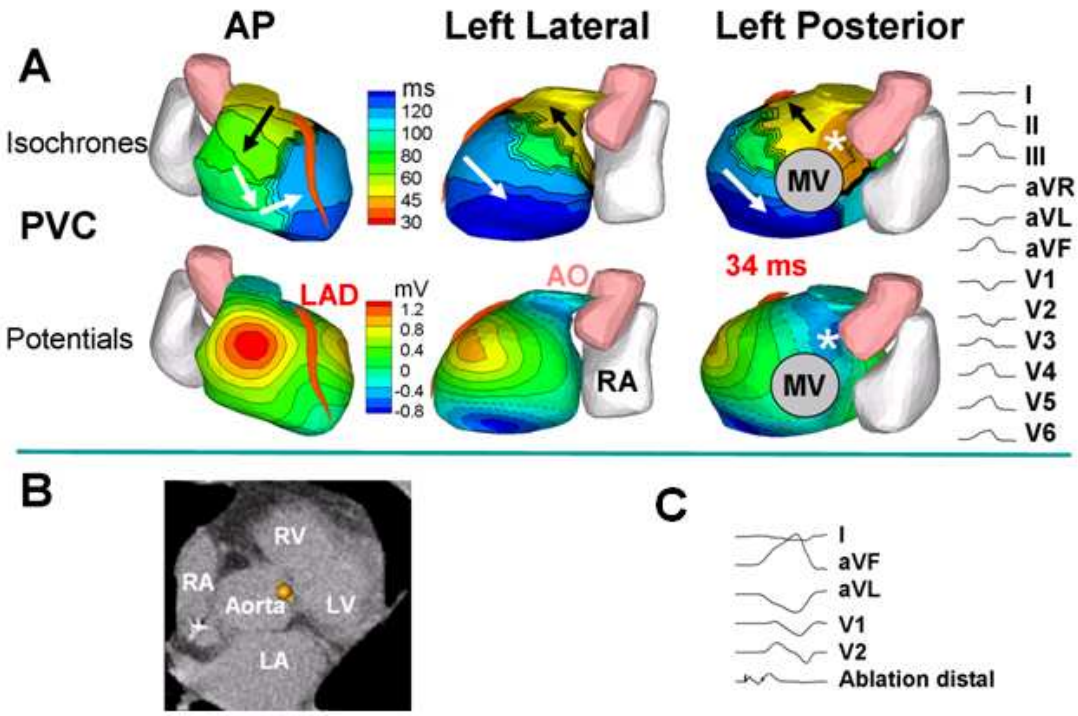


Figure LV7: ECGI of tachycardia originating in the left coronary cusp of the aorta. Panel A: Isochrone map (upper row) and potential map, (lower row, 34 ms from the onset of QRS) for a PVC beat in three views. White asterisk indicates the ECGI determined RVOT VT origin. Arrows indicate the activation wavefront propagation direction. The conventional 12-lead ECG from a PVC is shown on the right. Panel B shows a CT cross section image; yellow dot indicates the ECGI determined VT origin. Panel C shows the surface ECG of a PVC during the EP study and (bottom) the electrogram recorded with ablation catheter at the site of the left coronary aortic cusp.

Description: Spontaneous PVCs from Patient LV7 had the most leftward position of earliest isochrone and potential minimum of all outflow tract PVCs studied. The area of focal initiation (white asterisks in panel A) begins at the base of the left side of the aorta, near the left coronary cusp. The propagation pattern includes part of the anterior LV but continues superiorly and rightward towards the anterior RV (white arrows) and then across the septum in a typical LBBB pattern. When superimposed onto the CT scan

obtained during ECGI, the origin of the VT is found to be in the left coronary cusp of the aorta, which concurs with the findings of the EP study.

Of note, despite published data for interpreting the ECG for left-sided outflow VT, [references 43, 44 in main text] the conventional 12-lead ECG in this case does not readily identify the correct location of the VT. Because there is significant variability in patient size, heart-torso relationships and 12-lead ECG lead placement, the standard ECG criteria can sometimes be misleading. ECGI takes into account these patient-specific factors, and may be a more accurate imaging tool for this difficult region of the heart. In this case, some of the 12-lead features are consistent with established criteria for left coronary cusp PVC (small R wave in V2, R/S ratio >30% in V2), but some are not (R wave duration index > 50%, W-shaped QRS in V1, QS or rS in lead I). The role of ECGI in determining aortic cusp SOO and a comparison to the standard 12-lead ECG criteria should be explored with larger cohorts of outflow tract tachycardias and is a subject of ongoing investigation.

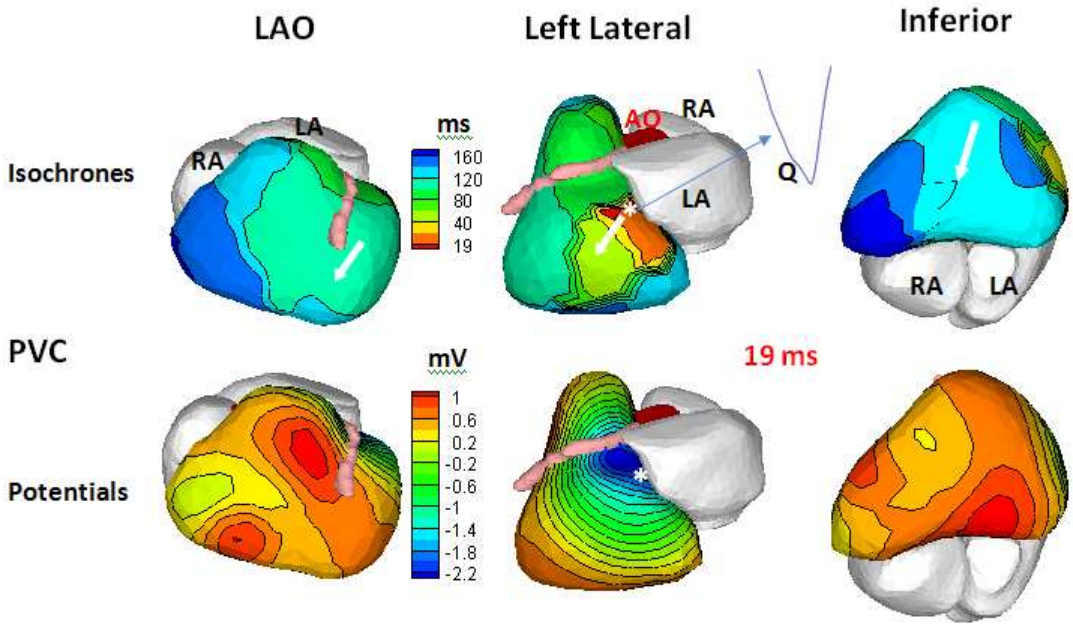


Figure LV8: ECGI of a basal mitral annular PVC. Isochrone map (upper row) and potential map (lower row, 19 ms from the onset of QRS) during PVC beat in three views. Asterisk indicates the ECGI determined origin of PVC as the basolateral mitral annulus region. White arrows indicate the direction of activation wavefront propagation. Epicardial electrogram with Q wave at the earliest activation region is shown in blue.

Description: Spontaneous PVC's from Patient LV8 had a unique initiation and propagation pattern compared to other examples. The initiation occurred near the superior basal mitral annulus and the wavefront propagated down the antero-lateral LV before encountering areas of slow conduction. The ECGI-derived local electrogram (blue arrow) demonstrates a pure Q-wave, indicative of an epicardial origin. An EP study was not performed for this patient.

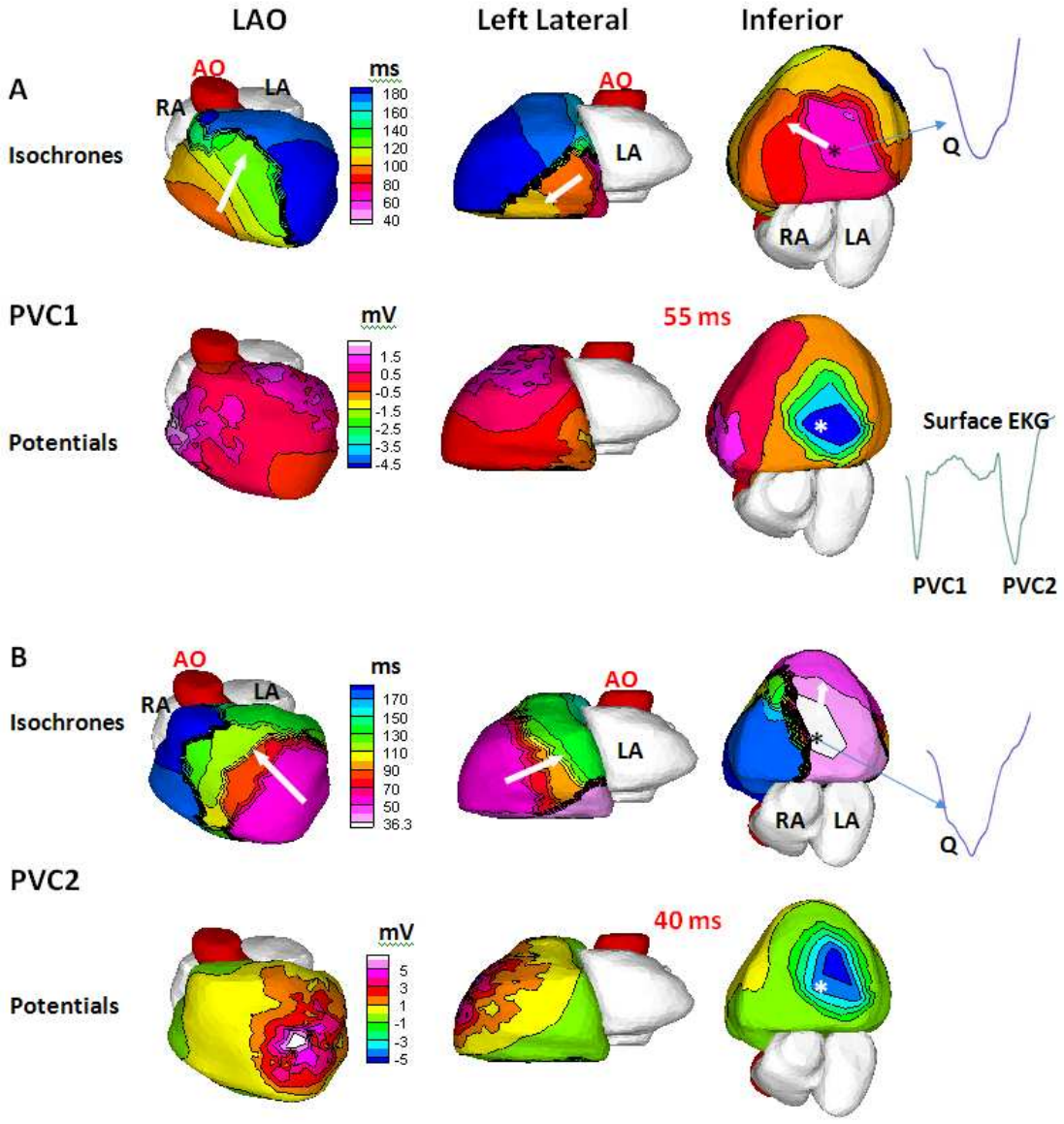


Figure LV9: ECGI of an inferior septal VT. Two PVC morphologies are shown. Panel A: isochrone map (upper row) and potential map (lower row, 55 ms from the onset of QRS) for PVC1. Panel B: isochrone map (upper row) and potential map (lower row, 40 ms from the onset of QRS) for PVC2. In both cases, asterisks indicate the ECGI determined VT origin as the inferior basal septum. White arrows indicate the direction of activation wavefront propagation.

Description: Spontaneous nonsustained VT demonstrates the role of functional conduction changes of diseased myocardium. Although the location of origin is similar in both PVC beats (asterisk at the inferior septum), there is a line of block (thick black line) present in the inferior view only during the second, PVC2 beat. This change in activation sequence is the cause of the markedly different PVC morphologies on the ECG. ECGI-derived local electrogram demonstrates a Q wave (blue arrow) consistent with an epicardial origin.

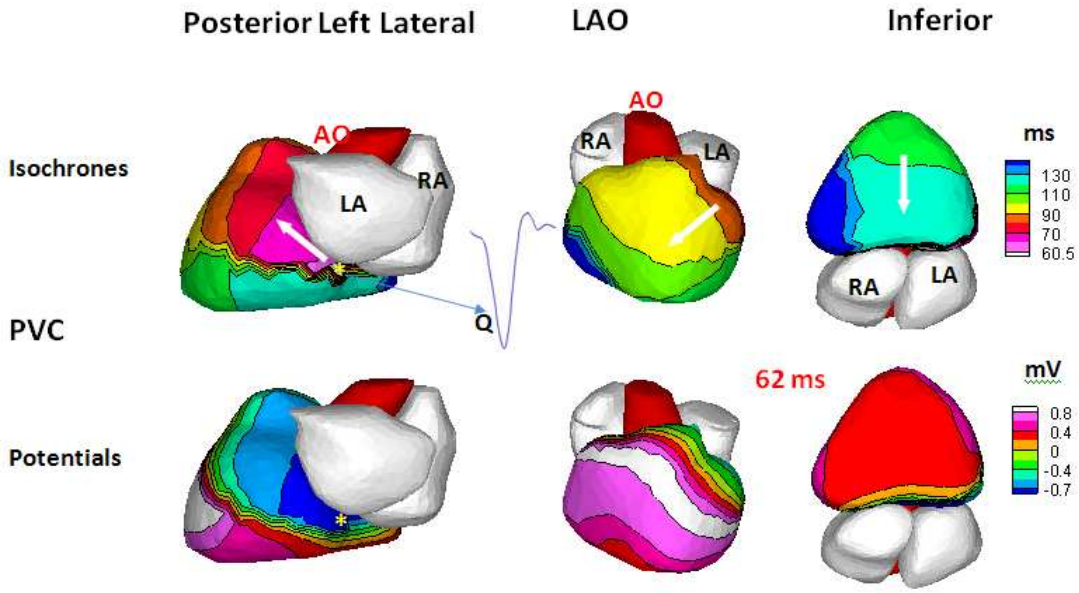


Figure LV10: ECGI of an inferior lateral mitral annular PVC. Isochrone map (upper row) and potential map (lower row, 62 ms from the onset of QRS) during PVC beat in three views. Asterisk indicates the ECGI determined origin of PVC as inferolateral mitral valve region. White arrows indicate the direction of activation wavefront propagation. Epicardial electrogram with Q wave at the earliest activation region is shown in blue. An EP study was not performed for this patient.

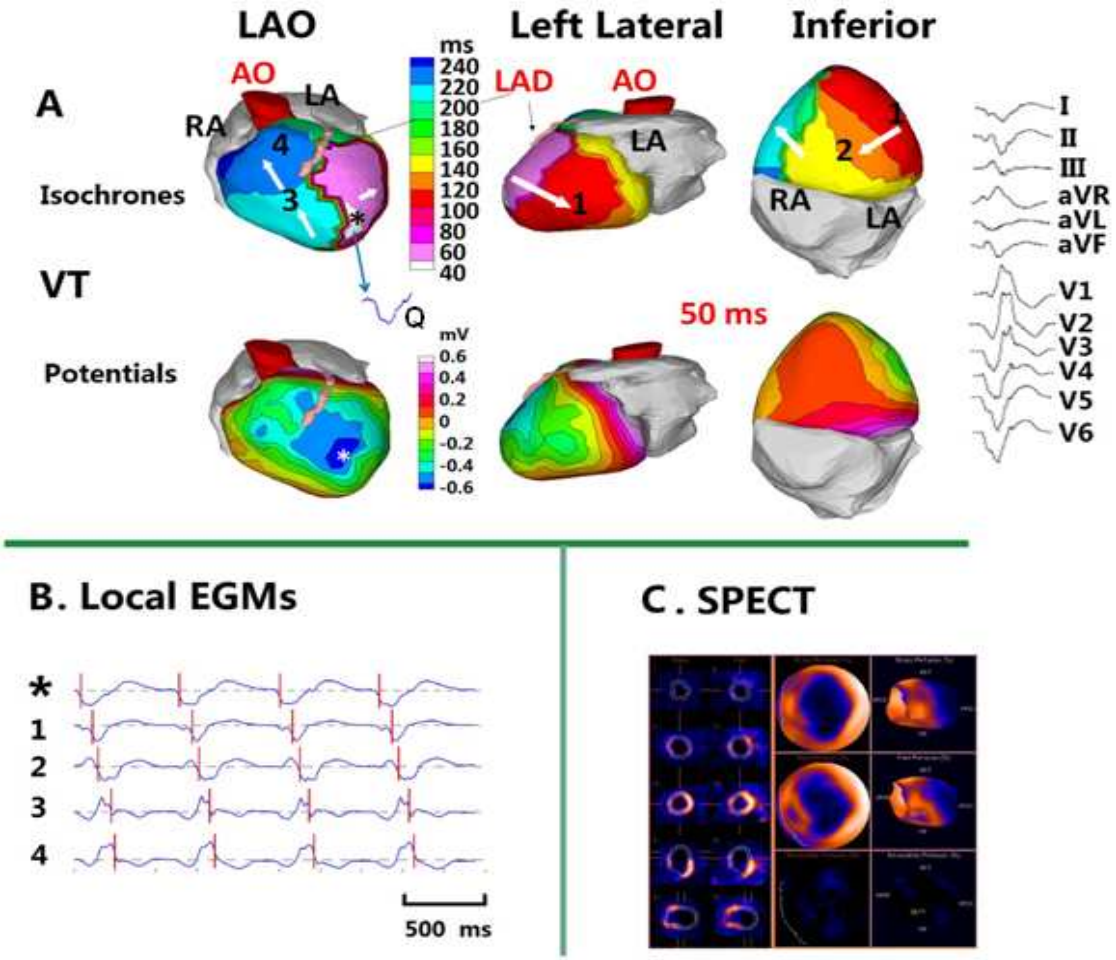


Figure LV11: ECGI of apical scar related reentrant VT. Panel A: isochrone maps and potential maps (50 ms from the onset of QRS) for a VT beat in three views. Asterisks indicate the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation. The conventional 12-lead ECG for one VT beat is shown on the right. Panel B: local unipolar electrograms from five points on the epicardial surface, showing the reentrant mechanism. Numbers corresponds to the locations as marked in Panel A. Vertical red lines indicate the local activation time (maximum negative dV/dt). Panel C: SPECT images showing a large scar at apical LV region (blue).

Description: In EP study, an activation map of the LV was performed during VT. An early presystolic potential which preceded the surface QRS by 118 ms was noted in the apical lateral region. ECGI identifies the apical lateral LV region as the earliest epicardial activation site, which is consistent with the EP study findings. The isochrones and local electrograms show that the VT has RBBB pattern, and the wavefront propagates clockwise around the apical scar. The antero-lateral basal RV (#4 in Panel A) is activated 200 ms after the initiation of VT (* in Panel A), suggesting extremely slow conduction, which favors reentry. ECGI epicardial activation movie is provided (**Movie LV11**).

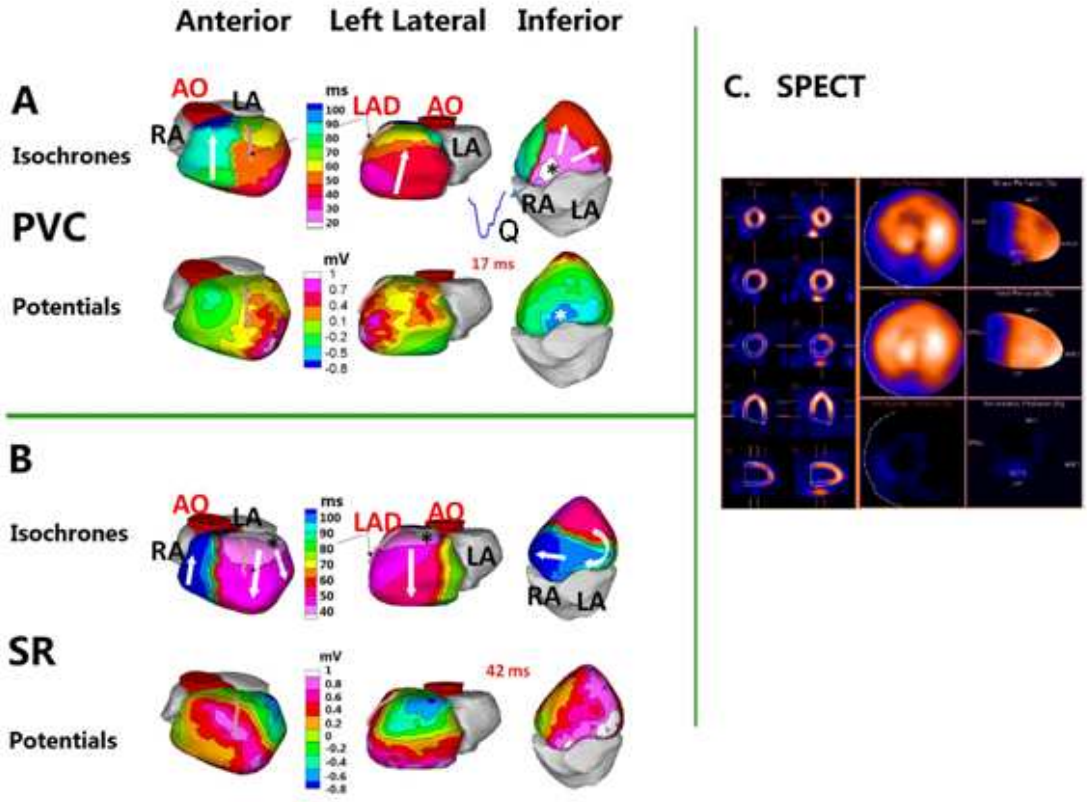


Figure LV12: ECGI of an inferior basal LV PVC. Panel A: isochrone map (upper row) and potential map (lower row, 17 ms from the onset of QRS) during a PVC in three views. Asterisks indicate the inferior basal VT origin. White arrows indicate the direction of activation wavefront propagation. Panel B: isochrone map (upper row) and potential map (lower row, 42 ms from the onset of QRS) for a sinus beat (SR). Asterisks indicate epicardial breakthrough. White arrows show the activation sequence. Panel C: SPECT images showing an inferior myocardial infarction.

Description: This patient has an RBBB activation pattern in sinus rhythm. Slow conduction is present in the inferior wall due to his inferior myocardial infarction. In the PVC beat, ECGI identifies the earliest activation in inferior basal LV near the inferior scar border zone. Low-amplitude and fractionated Q wave electrogram at the earliest site suggests epicardial scar involvement. The activation wavefront activates the inferior LV first, then the anterior and lateral LV wall. The anterior RV is activated after a 50 ms delay at inferior RV wall caused by the scar. ECGI epicardial activation movie is provided (**Movie LV12**).

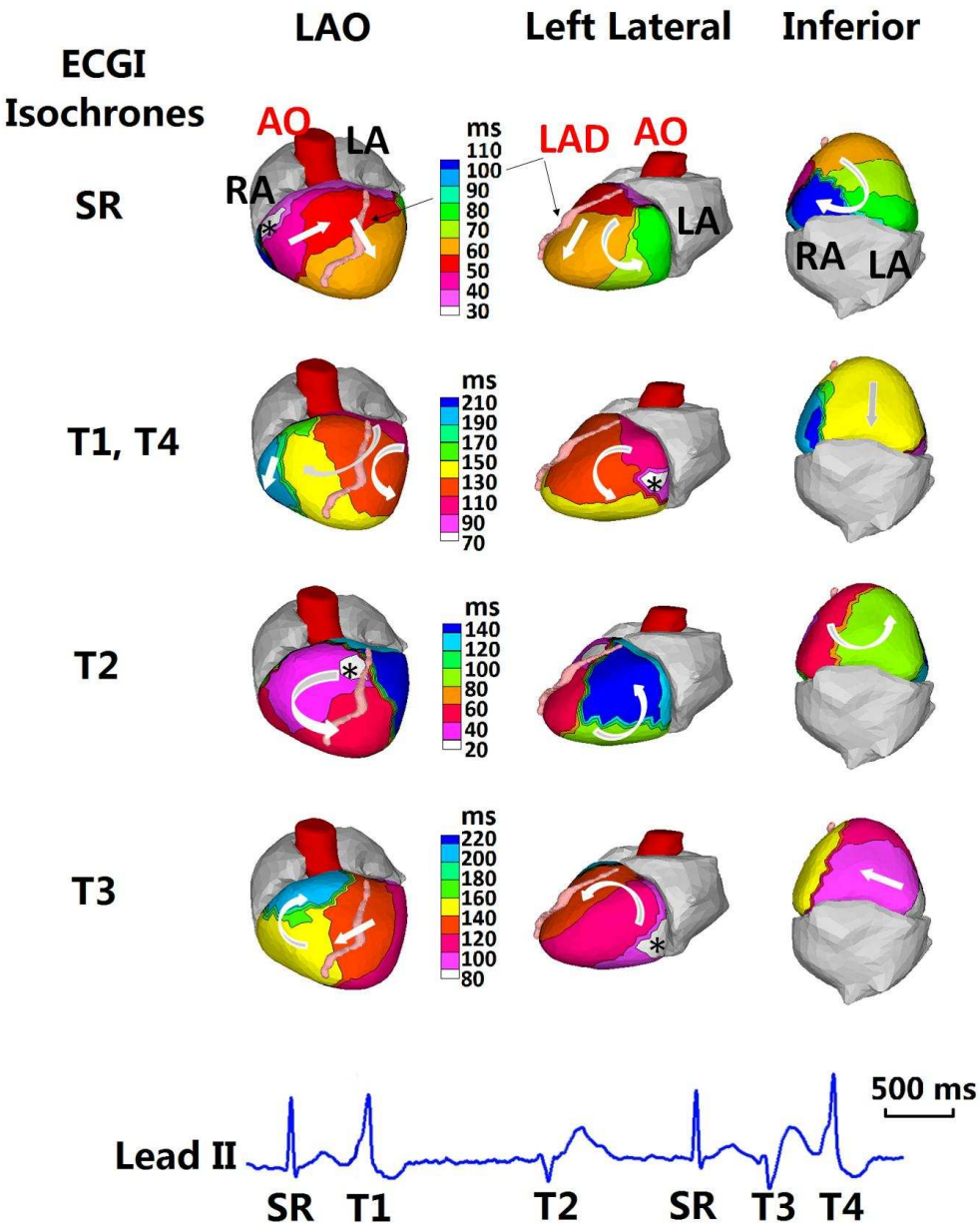

LAO
Left Lateral
Inferior
ECGI
Isochrones
SR
T1, T4
T2
T3
AO
LA
RA
LAD
AO
LA
RA
LA
ms
110
100
90
80
70
60
50
40
30
ms
210
190
170
150
130
110
90
70
ms
140
120
100
80
60
40
20
ms
220
200
180
160
140
120
100
80
Lead II
500 ms
SR
T1
T2
SR
T3
T4

Figure LV13: ECGI of pleomorphic PVCs from the posterolateral LV. Isochrone maps for a run of PVCs (T1- T4) intermingled with sinus beats (SR) in three views. Asterisks indicate the earliest epicardial activation sites determined by ECGI. White arrows indicate the direction of activation wavefront propagation. Lead II is shown on the bottom.

Description: The ECGI-reconstructed propagation patterns of activation wavefronts for most of the PVCs are similar to T1 and T4. This predominant activation sequence starts from the postero-lateral basal LV and proceeds toward the anterior LV and anterior RV, then the inferior walls. Inferior basal RV is activated last. There is a long pause before T2. The T2 PVC origin is located at mid-anterior RV over the septum. It activates the anterior RV, then curves down to the inferior walls, and arrives at the lateral LV last. The QRS duration (120 ms) is slightly shorter than T1 (140 ms). The second sinus beat is followed by T3, which starts from the postero-lateral basal LV, the same initiation site as the predominant PVCs. However, the wavefront first activates the inferior wall, and a second wavefront proceeds from lateral LV to anterior RV, with the RVOT the last to activate. T4, another predominant PVC similar to T1, immediately follows T3. ECGI epicardial activation movie is provided (**Movie LV13**).

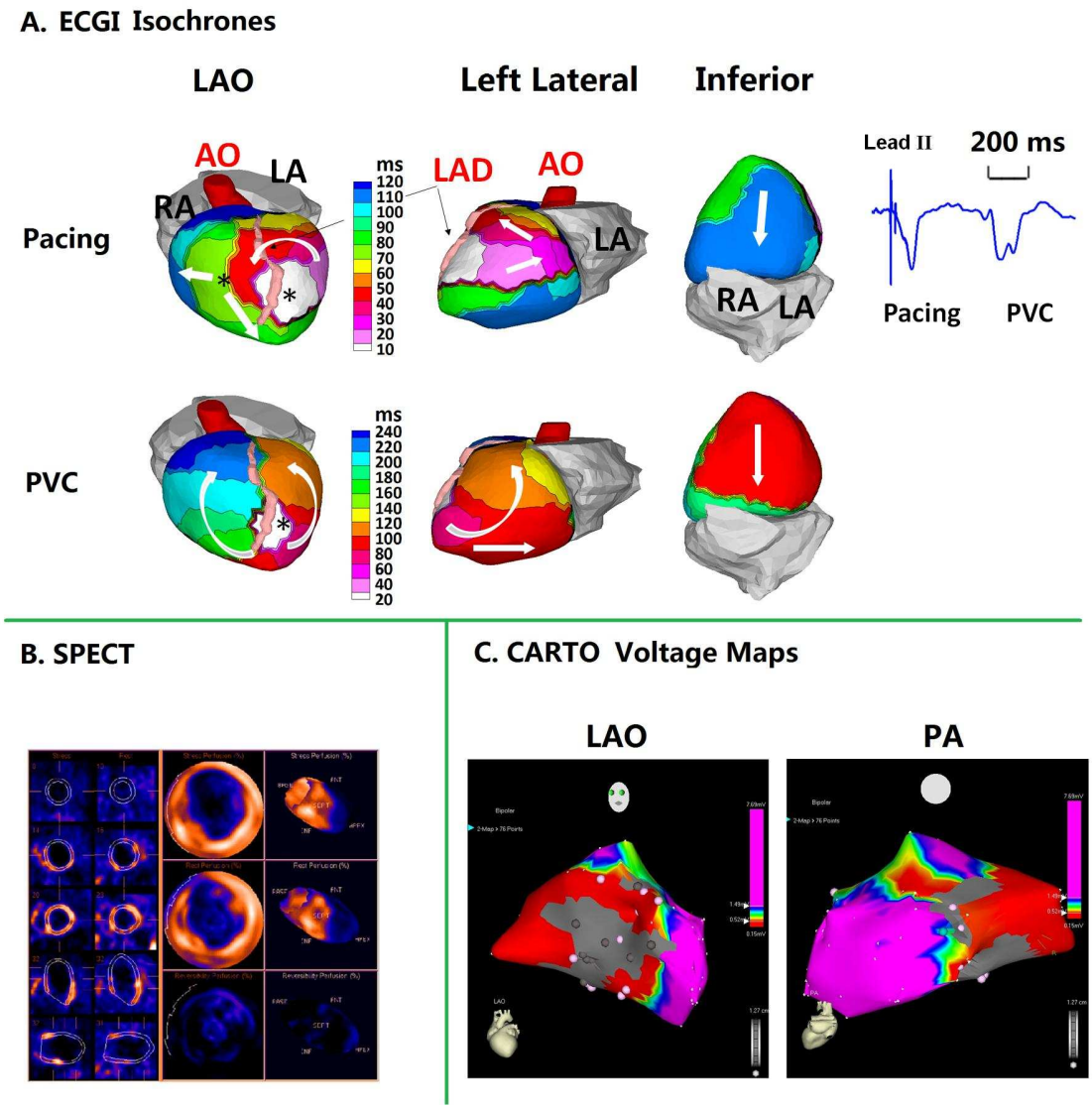


Figure LV14: ECGI of a VT from the anterior-apical LV in a patient with an apical aneurysm. Panel A: isochrone maps for a biventricular pacing beat followed by a PVC in three views. Asterisks indicate the earliest epicardial activation sites determined by ECGI. White arrows indicate the direction of activation wavefront propagation. Lead II is shown on the right. Panel B: SPECT images showing a very large apical infarction extending into the antero-apical and infero-apical wall. Panel C: CARTO voltage maps in LAO and PA projections show a large apical scar consistent with an aneurysm as well as an anterior basal scar.

Description: In the pacing rhythm, the apical lateral LV is stimulated by the LV pacing lead. Due to the large apical scar, the propagation of the wavefront is slow, indicated by the crowded isochrones around the pacing site. In comparison, the RV activation wavefront quickly spreads out to the entire RV, and activates the inferior LV wall last. In the PVC beat, the epicardial initiation site in the apical region is very close to the LV pacing site. The wavefront quickly activates the inferior wall, then swings upward from inferior LV to anterior LV, and stops right next to the LAD. After about 50 ms silence on the epicardium, a second wavefront appears on apical RV, and propagates toward the RVOT. This second wavefront inscribes the notch on Lead II. ECGI epicardial activation movie is provided (**Movie LV14**).

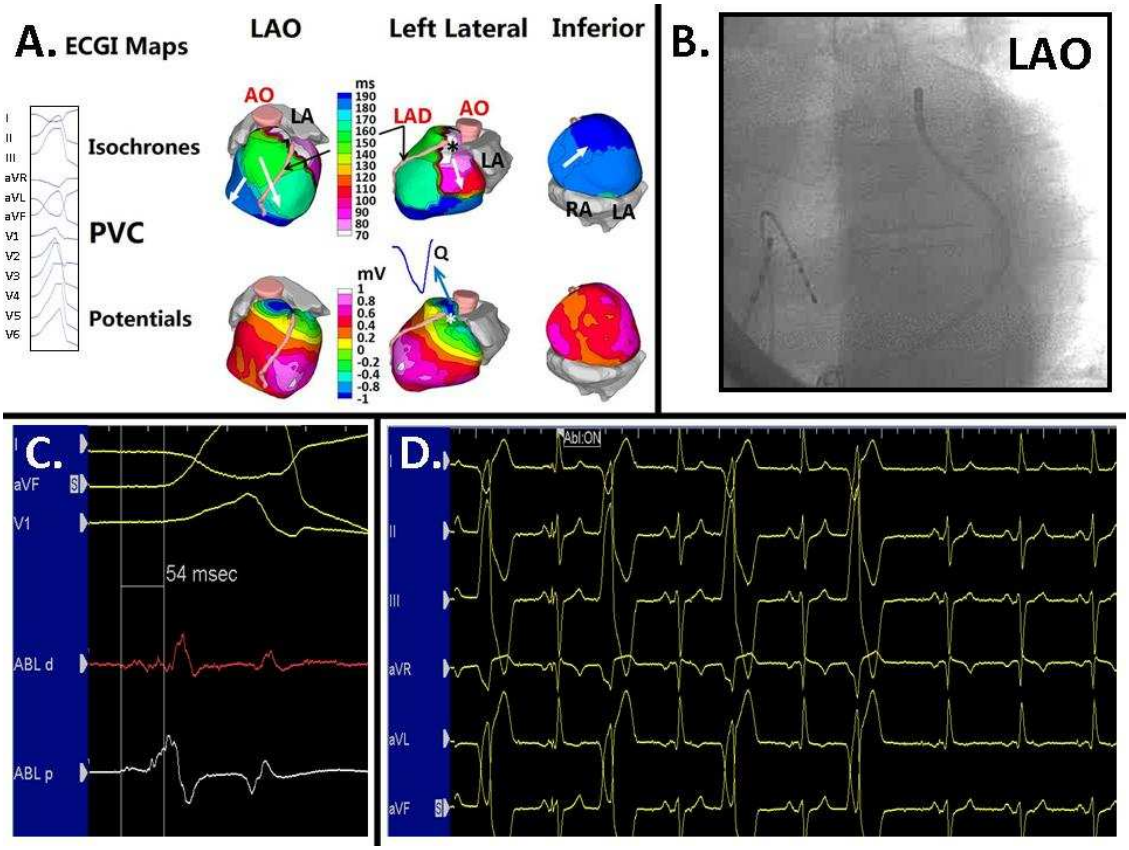


Figure LV 15: ECGI of a VT from the anterior interventricular vein/distal coronary sinus. Panel A: Isochrone maps (upper row) and potential maps (lower row, 60 ms from the onset of QRS) for a PVC beat in three views. Asterisks indicate the ECGI determined VT origin. White arrows indicate the direction of activation wavefront propagation. Panel B: left anterior oblique view of the ablation catheter advanced through the coronary sinus, and the distal tip at the site of successful ablation. Panel C: Bipolar electrogram from the ablation catheter at this site (54 ms pre-QRS). Panel D: Elimination of ventricular ectopy within the first three seconds of radiofrequency ablation at this site.

Discussion: ECGI-derived activation sequence during the PVC begins in the epicardial aspect of the anterior basal ventricle and proceeds first along the lateral LV. The wavefront encounters a line of block at inferolateral LV (crowded isochrones). About 50 ms later, a second wavefront appears on the anterior RV and quickly activates the RV, apical and inferior LV. The pure Q wave morphology of ECGI electrogram from the VT origin site (blue arrow) indicates an epicardial source. Ablation in the anterior interventricular vein successfully terminates the arrhythmia.

Table S1. Results from EP studies

	Timing of ECGI	VT Morphology	VT Induction	Primary VT Cycle Length	Diagnostic Maneuvers	Procedural Endpoint	Conclusion of EPS	Follow Up
RV1	Before EPS	LBBB pattern Inferior	Spontaneous and isoproterenol induced PVC's	N/A	**Activation Map**: anterior septal RVOT, 25 ms preQRS **Pace Map**: 12/12 match, anterior septal RVOT	Noninducible at conclusion	**Anterior-left RVOT**	No recurrence
RV2	Before EPS	LBBB pattern Inferior	Spontaneous and isoproterenol induced PVC's	N/A	**Activation Map**: midseptal RVOT, 19 ms preQRS **Pace Map**: 12/12 match, midseptal RVOT	Noninducible at conclusion	**Mid-septal RVOT**	No recurrence
RV3	Before EPS	LBBB pattern Right Inferior	Spontaneous and isoproterenol induced PVC's	N/A	**Activation Map**: midseptal RVOT, 30 ms preQRS. **Pace Map**: 12/12 match, midseptal RVOT	Noninducible at conclusion	**Mid-septal RVOT**	No recurrence
RV4	Before EPS	LBBB pattern Inferior	Spontaneous and isoproterenol induced PVC's	N/A	**Pace Map**: 12/12 match, posterior septal RVOT	Noninducible at conclusion	**Posterior-right RVOT**	No recurrence
RV5	Before EPS	LBBB pattern Left Inferior	No inducible arrhythmia	N/A	N/A	N/A	**N/A**	Received ICD
RV6	Before EPS	1) LBBB pattern Inferior (initiating PVC's) 2) LBBB pattern Left Superior (clinical VT)	Rapid pacing from RV apex induced sustained clinical VT	290 ms	Clinical VT: **Entrainment:** VT termination **Activation Map:** basal inferior RV, 20ms preQRS Initiating PVC's **Pace Map**: 12/12 match, lateral free wall RVOT	Clinical VT inducible Initiating PVC's noninducible at conclusion	**Initiating PVC's from RVOT free wall** **VT likely from basal inferior RV scar**	VT recurred 6 months later.
RV7	Before EPS	LBBB pattern Inferior	Spontaneous PVC's and isoproterenol induced VT	370 ms	**Activation Map**: midseptal RVOT, 40 ms preQRS	RF terminated the tachycardia. Noninducible at conclusion	**Mid-septal RVOT**	No recurrence
RV8	Before EPS	LBBB pattern Inferior	Spontaneous PVC's and isoproterenol induced VT	390 ms	**Activation Map**: posterior free wall RVOT, 54 ms preQRS	RF terminated the tachycardia. Noninducible at conclusion	**Free wall RVOT**	No recurrence
RV9	Before EPS	LBBB pattern Inferior	Spontaneous PVC's	N/A	**Activation Map:** posterior septal RVOT, 30 ms preQRS **Pace Map:** 11/12 match,	Transient elimination of ectopy, reduction	**Mid-septal RVOT**	Continued high burden of ventricular ectopy

					midseptal RVOT	of ectopy frequency		
RV10	Before EPS	LBBB pattern Left Superior	Spontaneous PVC's	N/A	**Activation Map:** basal inferior septal RV, 22 ms preQRS **Pace Map:** 12/12 match, basal inferior septal RV	Noninducible at conclusion	**Inferobasal RV septum**	No recurrence
RV11	Before EPS	LBBB pattern Inferior	Spontaneous PVC's	N/A	**Activation Map**: posterior right RVOT, 20 ms preQRS **Pace Map:** 12/12 match, posterior right RVOT	Noninducible at conclusion	**Posterior-right RVOT**	No recurrence
LV1	During EPS	RBBB pattern, Right Superior	Double ventricular extrastimuli yielded sustained, tolerated VT	390ms	**Activation Map:** apical lateral LV, 21 ms preQRS **Pace Map:** 12/12 match apical lateral LV **Entrainment:** manifest, PPI-TCL = 74ms	Endocardial RF applications failed to alter the tachycardia.	**Focal.** **Epicardial or midmyocardial origin, near lateral apical LV.**	Underwent heart transplant for refractory heart failure and intractable VT.
LV2	Before EPS	VT1 & 2: RBBB pattern, Left Superior	Spontaneous, sustained tolerated accelerated idioventricular rhythm	VT1: 627ms VT2: 641ms	**Activation Map:** inferobasal septum, borderzone, 67ms preQRS. Highly fractionated signal. **Entrainment**: concealed, PPI-TCL = 13 ms **Voltage Map**: inferobasal septal scar	RF applications terminated the tachycardia. Noninducible at conclusion.	**Reentrant.** **Inferobasal septal scar borderzone.**	ICD implant No recurrence
LV3	Before EPS	VT1: RBBB pattern, Right Superior VT2: RBBB pattern, Right Inferior	Spontaneous, tolerated nonsustained VT	VT1: 463ms VT2: 500ms	**Activation Map:** inferolateral apical LV. Two distinct exit sites corresponding to two VT morphologies. 0-10ms pre QRS.	RF applications eliminated the tachycardia. Noninducible at conclusion.	**Likely reentrant** **Two exit sites from an inferolateral apical scar.**	ICD implant. 8 months later, VT recurred (see LV6)
LV4	During EPS	RBBB pattern, Left Superior	Single LV ventricular extrastimuli induced sustained tolerated VT	317 ms	**Activation Map:** midinferior septum, 30ms pre-QRS, fascicular potential.	RF applications eliminated the tachycardia. Noninducible at conclusion.	**Left posterior fascicular VT**	No recurrence
LV5	During EPS	RBBB pattern, Left Superior	With isoproterenol,	344 ms	**Pace Map:** 10-11/12 match mid-apical septum	No ablation performed due to	**Likely left posterior**	Treated with CCB

			nonsustained VT			patient anxiety and adverse reaction to isoproterenol.	**fascicular VT**	
LV6	Before EPS	RBBB pattern, Right Inferior	Spontaneous VT	1177 ms	**Activation Map:** basal anterior lateral epicardial LV, 80 ms preQRS **Pace Map:** 12/12 match basal anterior lateral epicardium	RF applications eliminated the tachycardia. Noninducible at conclusion.	**Epicardial focal VT from the basal anterior lateral LV**	Underwent heart transplant for refractory heart failure. Explant confirmed cardiac sarcoid.
LV7	Before EPS	LBBB pattern Right Inferior	Spontaneous and isoproterenol induced PVC's	N/A	**Activation Map:** left coronary cusp, 15 ms preQRS.	RF application eliminated ventricular ectopy. Noninducible at conclusion.	**Left coronary cusp origin**	No recurrence
LV8	No EPS	RBBB pattern Left Superior						
LV9	Before EPS	RBBB pattern Right Superior	Spontaneous VT	470 ms	**Entrainment:** inferior Septal LV, concealed, PPI-TCL = 8 ms **Activation Map:** inferior septal LV, 22 ms preQRS, fractionated signal. **Voltage Map:** Large inferior septal scar	RF application terminated the clinical tachycardia. Three additional VTs were inducible at conclusion	**Reentrant VT from the inferior LV septum**	Recurrence of different VT, epicardial access limited by pericardial adhesions.
LV10	No EPS	RBBB pattern Right Inferior						
LV11	Before EPS	RBBB pattern Superior	Spontaneous VT	620 ms	**Activation Map:** apical lateral LV, 118 ms preQRS **Voltage Map:** large anterior apical scar/aneurysm	Catheter trauma terminated the clinical tachycardia. One additional VT was inducible at conclusion	**Reentrant VT originating near the apical lateral LV, likely involving an apical aneurysm**	Recurrence of different VT. Underwent LV aneurysm resection, CAB surgery, modified maze procedure. Ultimately died two weeks later.
LV12	No EPS	RBBB pattern Superior						

LV13	Before EPS	RBBB pattern Right Superior	Spontaneous PVC's	N/A	**Activation Map:** posterolateral mitral annulus, 0 ms preQRS **Pace Map**: 10/12 match at posterolateral mitral annulus **Voltage Map**: Basilar scar around mitral annulus	RF application reduced the ventricular ectopy. Noninducible at conclusion	**Focal PVC's from the basal posterolateral LV** **Likely epicardial.**	Decreased ventricular ectopy
LV14	Before EPS	RBBB pattern Inferior	Ventricular burst pacing yielded hemodynamically unstable VT	303 ms	**Voltage Map:** extensive anteroseptal scar. Fractionated diastolic signal in scar region.	Empiric RF applications in the anterobasal LV. Noninducible at conclusion.	**Reentrant VT, likely involving an isthmus between anteroseptal scar and mitral annulus**	No recurrence
LV15	Before EPS	RBBB pattern Inferior	Spontaneous PVC's, nonsustained VT	320ms	**Activation Map:** distal coronary sinus/great cardiac vein, 54 ms preQRS **Pace Map:** 12/12 match distal coronary sinus/great cardiac vein	RF application eliminated ventricular ectopy. Noninducible at conclusion.	**Focal VT from the great cardiac vein**	No recurrence