

ORIGINAL RESEARCH

VENTRICULAR ARRHYTHMIA

Transmural Activation Mapping of Ventricular Arrhythmias With High-Frame Rate Echocardiography and Validation Against Contact Mapping



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ABSTRACT

BACKGROUND The restriction of activation mapping to the ventricular surface of contemporary mapping systems often leads to failure to correctly identify the true sites of origin (SoOs) of intramural and/or subepicardial ventricular arrhythmias (VAs), reducing procedural success.

OBJECTIVES The aim of this study was to evaluate if noninvasive electromechanical wave imaging (EWI) can locate the SoOs of VAs along the endo-epicardial axis in patients with and without structural heart disease.

METHODS Patients with VAs requiring ablation underwent preprocedural transthoracic EWI to identify the SoOs and validate using contact mapping. Local electromechanical activation was defined as time point of the downward zero crossing on the incremental axial strain curve. The site of earliest activation on contact mapping and/or successful ablation was employed as ground truth for VA SoO.

RESULTS Twenty-eight patients underwent EWI, and 25 proceeded to contact mapping (56% men, mean age 53 ± 16 years, mean left ventricular ejection fraction $47\% \pm 28\%$, 52% with late gadolinium enhancement (LGE) on magnetic resonance imaging). Five patients were excluded (insufficient or different ventricular tachycardia or ventricular ectopic activity at the time of EWI vs contact mapping). EWI mapping correctly localized the VA SoOs in 17 of 20 (85%) of the cases and mapped them to the adjacent segments in the remaining ones. In the presence of scar, EWI localized 81.8% of the VA SoOs ($n = 9$ of 11) correctly compared with 88.9% ($n = 8$ of 9) in patients without ($P = \text{NS}$). The transmural SoOs (endocardial, midmyocardial, or epicardial) were successfully identified in 18 of 20 cases (90%; $P = \text{NS}$ for LGE-positive vs LGE-negative patients).

CONCLUSIONS EWI correctly identified the transmural SoOs of focal VAs, including in the presence of scar, in the majority of cases using contact mapping as the gold standard and thus could support preprocedural planning, including requirement for epicardial access and/or ablation techniques. The absence of a true gold standard for clinical transmural mapping remains an important challenge for the validation of novel mapping technologies. (JACC Clin Electrophysiol. 2025;11:667-681) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

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ABBREVIATIONS AND ACRONYMS

2D	= 2-dimensional
3D	= 3-dimensional
AHA	= American Heart Association
EAM	= electroanatomical mapping
ECG	= electrocardiography
EMA	= electromechanical activation
Eat	= electromechanical activation time
EMD	= electromechanical delay
EWI	= electromechanical wave imaging
LGE	= late gadolinium enhancement
LV	= left ventricle/ventricular
MRI	= magnetic resonance imaging
RV	= right ventricle/ventricular
SoO	= site of origin
TTE	= transthoracic echocardiography
VA	= ventricular arrhythmia
VE	= ventricular ectopic activity
VT	= ventricular tachycardia
ZC	= zero crossing

Percutaneous catheter ablation is an established treatment modality for ventricular arrhythmias (VAs).¹ Procedural success relies on the correct identification of functionally critical sites to target. Yet a major shortcoming of current mapping technologies is the restriction to time-consuming, sequential surface measurements and the lack of true transmural mapping to appreciate complex 3-dimensional (3D) activation patterns, even with the most advanced mapping technology.² This is particularly important for intramural and/or subepicardial sites, which are not routinely assessed but are common VA origins in nonischemic substrates.^{3,4}

ELECTROMECHANICAL WAVE IMAGING: A NONINVASIVE TRANSMURAL MAPPING TECHNOLOGY. Electromechanical wave imaging (EWI) is an echocardiography-based mapping modality that could enable noninvasive true transmural activation mapping to preprocedurally identify challenging ablation targets, including intramural and/or subepicardial sites of origins (SoOs) to guide procedural planning, risk stratification and patient counseling.

The concept of EWI has previously been reported⁵ and is illustrated in [Figure 1](#). In brief, at the tissue level, the myocardial de-

polarization triggers after a delay of several milliseconds the electromechanical activation (EMA). Spatially, this EMA forms the electromechanical wave front that follows the propagation pattern of the electrical activation sequence. EWI can transmurally map this deformation using incremental axial strain estimation. In the apical views, the shortening during systole corresponds to a positive-to-negative flip on the incremental axial strain curve. EWI uses this downward “zero crossing” (ZC) (see [Figure 1D](#)) to annotate the local EMA time (EMAt) at each recording site. High frame rates and an accurate strain imaging technique capable of estimating the small regional interframe deformation are required to record precise activation maps. EWI has been validated in preclinical studies against contact mapping with strong correlation in the left ventricle (LV) and right ventricle

(RV)⁶ and has been shown to be reproducible in humans.⁷

Here, we present a proof-of principle study using transthoracic EWI to evaluate if this noninvasive technology allows to correctly distinguish the SoOs of VAs along the endoepicardial axis in patients with and without structural heart disease and validate against electroanatomical mapping (EAM). Secondly, we evaluated the diagnostic accuracy of EWI activation mapping in the presence of myocardial scar as detected on cardiac magnetic resonance imaging (MRI).

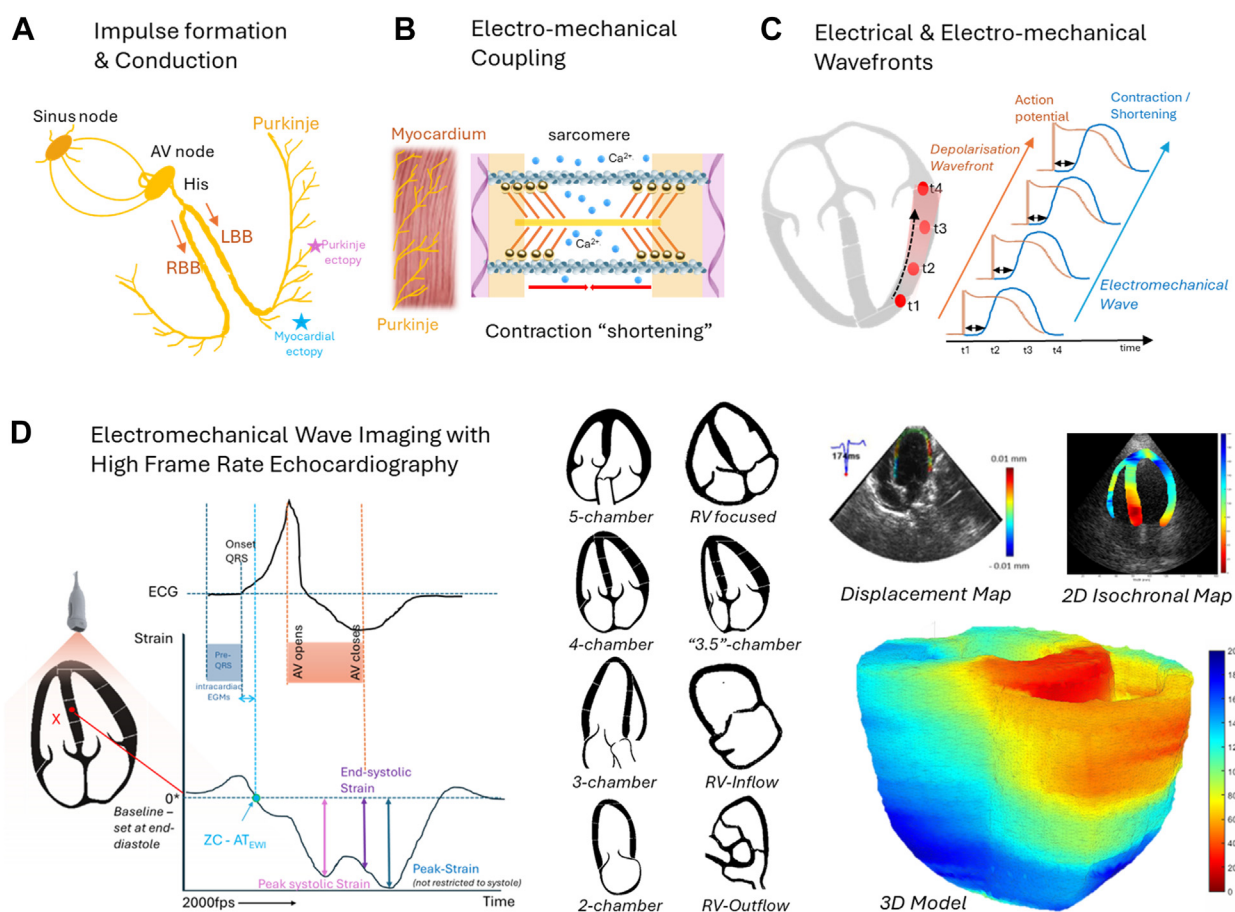
METHODS

Patients awaiting elective clinically indicated catheter ablation procedures for complex, presumed focal ventricular ectopic activity (VE) or ventricular tachycardia (VT) documented on 12-lead electrocardiography (ECG) and cardiac MRI to establish the presence or absence of myocardial scar were prospectively recruited. “Complex” VA was defined as any of the following: 1) VA in association with underlying structural heart disease; 2) non-outflow tract VE or VT configuration on ECG; and 3) suspected epicardial SoO on the basis of ECG (see [Supplemental Appendix Part 1](#) for criteria) and/or previous unsuccessful endocardial procedures. The presence, segmental location, and extent (endocardial, mid-myocardial, subepicardial, or transmural) of myocardial scar was defined per clinical MRI. The study was approved by our local Institutional Review Board (14/LO/0360). All patients provided written informed consent.

Patients underwent elective high-frame rate transthoracic echocardiography (TTE) for EWI with simultaneous ECG and subsequent percutaneous catheter ablation procedures with high-density activation mapping with 3D EAM systems. EWI mapping was performed unblinded to ECG but prior to the ablation procedure. The SoO on EWI maps was defined as earliest activation in any view following coregistration of respective surface electrocardiographic VE or VT beats and located on a modified AHA model to define a segmental SoO and along the transmural axis to define a transmural SoO (for RV segments, endocardial vs epicardial; for LV

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

FIGURE 1 Concept of Electromechanical Wave Imaging

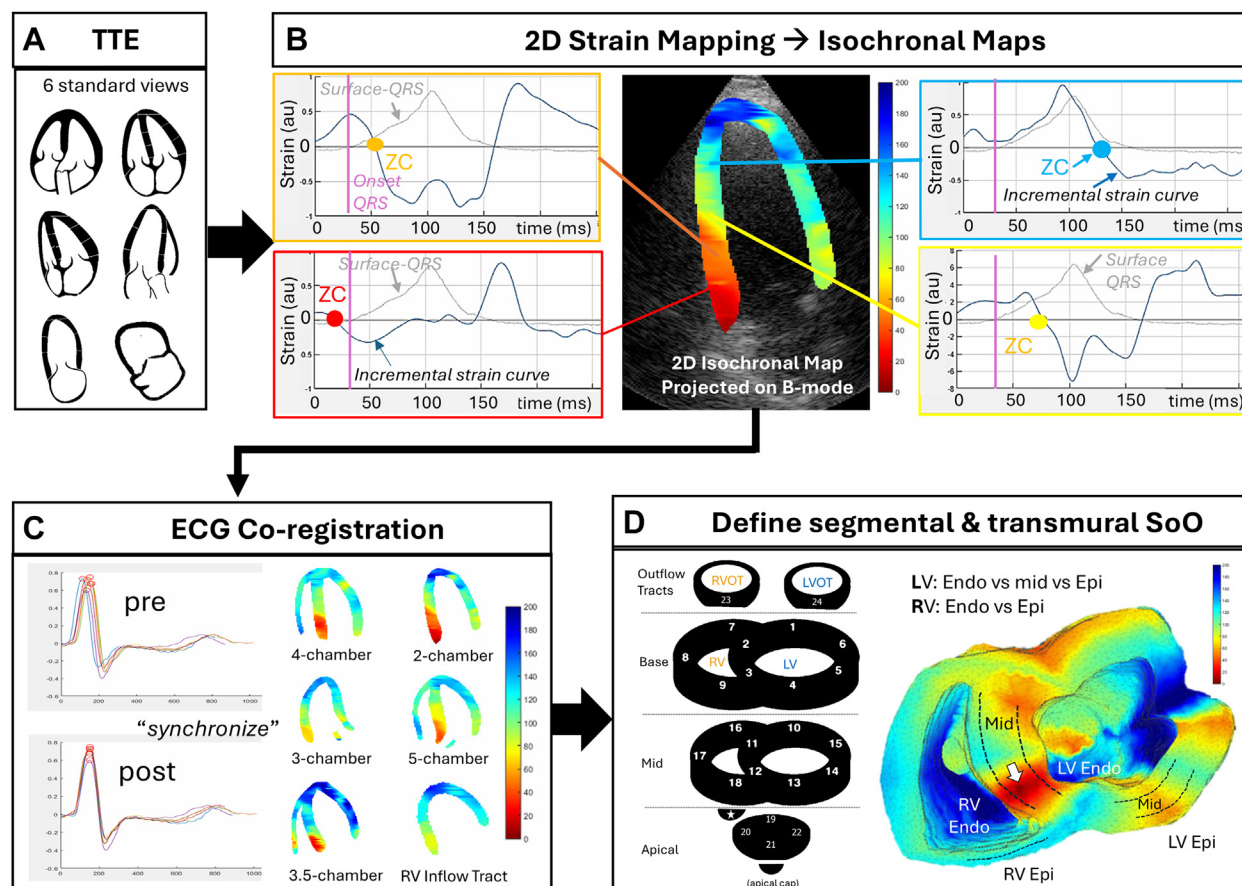


(A) Impulse formation and conduction. (B) Electromechanical coupling. (C) Electrical and electromechanical wave fronts. (D) Electromechanical wave imaging with high-frame rate echocardiography. The onset of the local electromechanical activation can be identified as "zero crossing" (ZC) on the strain curve at each recording site and related to the surface QRS. This concept and derived clinical value differ from traditional strain imaging assessing "peak systolic," "end-systolic" "peak strain" that are reported as global or regional values. With 2-dimensional (2D) transthoracic echocardiography, data acquisition across numerous views is required to reconstruct 3-dimensional (3D) activation patterns. AT_{EWI} = activation time in electromechanical wave imaging; AV = atrioventricular; ECG = electrocardiogram; LBB = left bundle branch; RBB = right bundle branch; RV = right ventricular.

segments, endocardial vs midmyocardial vs epicardial) (Supplemental Figure 1.1). Additionally, electromechanical prematurity (the earliest ZC pre-surface QRS in milliseconds, if any), total EMA time, and dominant propagation pattern (in-plane, transmural, or centrifugal) were assessed.

EAM, diagnosis of the SoO, and ablation were performed per routine clinical care by an electrophysiologist blinded to the results of EWI mapping. The site of earliest activation on contact mapping and successful ablation site as diagnosed by the clinical operator were defined as ground truth for SoO.

Epicardial origin was confirmed by direct epicardial mapping or suspected if no pre-QRS activation and/or broad early area with r wave in unipolar electrograms and/or no suppression with radiofrequency ablation was recorded on endocardial maps. Intramural SoO was suspected on the basis of combined RV and LV, respectively endo-epicardial activation mapping features (including broad area of early activation and/or no pre-QRS on opposing surfaces and/or failure to abolish VA with ablation), or coronary venous wire mapping. Papillary muscle origin was diagnosed on the basis of anatomical location (confirmed by

FIGURE 2 Key Steps for Ventricular Arrhythmia Mapping With Electromechanical Wave Imaging

(A) Following data acquisition on transthoracic echocardiography (TTE), (B) 2D isochronal maps are generated by defining local EMA at uniformly selected local recording sites across the map. For each strain curve on the 2D isochrone map, the ZC is identified, and local activation time is defined by the time from ZC relative to the onset of QRS (the x-axis represents time in milliseconds, and the y-axis represents strain in arbitrary units [au], defined as change in length divided by original length). (C) ECG coregistration is required to ensure synchronized isochrones across all views. (D) The site of origin (SoO) is defined in a modified American Heart Association segment model and along the transmural axis. Endo = endocardial; Epi = epicardial; LV = left ventricular; LVOT = left ventricular outflow tract; Mid = midmyocardial; RVOT = right ventricular outflow tract; other abbreviations as in [Figure 1](#).

intracardiac echocardiography or coregistered computed tomographic model) and supported by the presence of typical pleomorphic VE configuration with subtle changes.

EWI DATA ACQUISITION AND PROCESSING. EWI was performed with a phased-array transducer (64-element aperture, 2.5 MHz, 0.32-mm pitch) connected to a noncommercial research ultrasound system (Vantage Systems of Verasonics) controlled using a custom-made MATLAB (The MathWorks) script.

Image acquisition followed a standardized process. A detailed description is provided in [Supplemental Figure 1.2](#) and is summarized in [Figure 2](#). In brief, 2-dimensional (2D) imaging was acquired at 2,000 frames/s and simultaneous ECG in 6 standard echocardiographic views (4-, 5-, 3.5-, 3-, and 2-chamber and RV inflow tract). Additional views were acquired per suspected SoO on ECG (eg, RV focused views). Axial resolution is estimated at 0.03 mm (20-MHz axial sampling rate); lateral resolution at 0.43 mm at 5 cm, 0.84 mm at 10 cm, and 1.4 mm

at 15 cm imaging depth; and temporal resolution at 0.5 ms (2,000 frames/s). Reproducibility was assessed on the basis of both repeated acquisition of the same echocardiographic view in the same scan and, for patients in VT or bigeminy at the time of scan, for consecutive or bigeminal beats capture within the same prospective 4-second high-frame rate window.

STATISTICAL ANALYSIS. Categorical variables are displayed as frequency counts and percentage and continuous variables as mean $\pm$ SD if normally distributed or as median (IQR) if not normally distributed and were compared using Student's *t*-test or the Mann-Whitney *U* test, respectively, analysis of variance with the post hoc Tukey test for pairwise comparison or the Kruskal-Wallis test as appropriate. To compare differences between the proportion of correct EWI localization of cardiac segments and myocardial layer (endocardial, midmyocardial, or epicardial) for patients with and without late gadolinium enhancement (LGE) on cardiac MRI, independent-samples proportion tests were performed in SPSS (IBM). Correlation analysis used Pearson or Spearman correlation according to normality assumptions. Statistical significance was set at $\alpha = 0.05$. Statistical analysis was performed using SPSS Statistics version 29.

RESULTS

This was a prospective single-center cohort study. Twenty-eight patients were recruited and attended for mapping with EWI. In 3 patients with successful EWI mapping, the subsequent contact mapping procedure was canceled and patients were treated medically. In 4 patients (14.2%), insufficient VAs at the time of TTE prevented EWI mapping. One patient presented with frequent VEs during EWI mapping but re-entrant VT with a different morphology during contact mapping (Supplemental Figure 1.3 for a summary of the recruitment process). Overall, 20 patients underwent successful EWI VA mapping and contact mapping that allowed validation of the EWI data set.

BASELINE DEMOGRAPHICS. Baseline demographics of the 25 patients who underwent (attempted) EWI and subsequent contact mapping are reported in Table 1. Eighteen patients (72%) presented with VE/VT in the context of underlying heart disease (12 dilated, 2 suspected arrhythmogenic, 1 hypertrophic cardiomyopathy; 3 with mitral valve disease) and 7 (28%) with idiopathic VE or VT. The mean left ventricular ejection fraction was $47.5\% \pm 28.7\%$.

In 52% of patients, LGE was identified locating midmyocardially in 5 (38.5%) and subepicardially in

TABLE 1 Baseline and Procedural Characteristics (n = 25^a)

Baseline demographics	
Male	14 (56)
Age, y	53 $\pm$ 16 (22-77)
BMI, kg/m ²	24.8 $\pm$ 4.4 (19-36)
Etiology	
DCM	12 (48)
ARVC	2 (8)
HCM	1 (4)
Mitral valve disease	3 (12)
Idiopathic	7 (28)
LVEF, %	47.5 $\pm$ 28.7
RVEF, %	52.0 $\pm$ 12.0
LGE on cardiac MRI	13 (52)
Midmyocardial	5 (38.4)
Subepicardial	3 (23.1)
Complex pattern ^b	5 (38.4)
Cardiac device	9 (36)
ICD shock	5 (20)
ICD ATP	1 (4)
VE burden, %	29 $\pm$ 12
Multifocal VE on ECG	10 (40)
AARs	
BB or CCB ^c	23 (92)
Class IC AAR	3 (12)
Amiodarone	2 (8)
Previous ablation	10 (40)
Procedural characteristics	
Anesthesia	
Local	16 (64)
General	9 (36)
Mapping approach	
Epicardial access	6 (24)
Coronary venous map	5 (20)
Including coronary wire	2 (8)
Combined RV/LV map	10 (40)
ICE	4 (16)
Activation mapping	24 (96)
With IV isoprenaline	14 (56)
Complementary pace map	18 (72)
EAM SoO	
Epicardial ^d	7 (28)
Including suspected epicardial SoO ^d	4 (16)
Midmyocardial	12 (48)
Including papillary muscle VA	5 (20)
Endocardial	5 (20)
Abandoned	1 (4)

Values are n (%) or mean $\pm$ SD. ^aIncluding 4 patients with attempted EWI but insufficient VE or VT to acquire a complete data set. ^bDifferent scar patterns across segments of either midmyocardial plus subendocardial and/or subepicardial or midmyocardial plus transmural or subepicardial plus transmural. ^cStand-alone or in combination with class IC AAR or amiodarone. ^dEpicardial SoO was suspected on the basis of endocardial with or without coronary venous mapping features.

AAR = antiarrhythmic drug; ARVC = arrhythmogenic right ventricular cardiomyopathy; ATP = antitachycardia pacing; BB = beta-blocker; BMI = body mass index; CCB = calcium-channel blocker; DCM = dilated cardiomyopathy; EAM = electroanatomical mapping; ECG = electrocardiography; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter-defibrillator; ICE = intracardiac echocardiography; IV = intravenous; LGE = late gadolinium enhancement; LV = left ventricular; LVEF = left ventricular ejection fraction; MRI = magnetic resonance imaging; RV = right ventricular; RVEF = right ventricular ejection fraction; SoO = site of origin; VA = ventricular arrhythmia; VE = ventricular ectopy.

TABLE 2 Summary of EWI Ventricular Arrhythmia Localization for 20 Patients With EWI and Contact Mapping Data

	mAHA SoO	P Value	Effect Size ± SE (95% CI)	Transmural SoO	P Value	Effect Size ± SE (95% CI)
Total cohort	17/20 (85.0)			18/20 (90)		
LGE positive	9/11 (81.8)	0.660	0.071 ^a ± 0.157 (−0.278 to 0.380) ^b	10/11 (90.9)	0.881	−0.02 ^a ± 0.136 (−0.353 to 0.280) ^b
LGE negative	8/9 (88.9)			8/9 (88.9)		
	Prematurity		Effect Size (95% CI)	EMA Time		Effect Size (95% CI)
Total cohort	−14.0 ± 12 ms			195 ± 21 ms		
LGE positive	−13.4 ± 8 ms	0.780	Cohen's <i>d</i> = 0.127 (−0.756 to 1.008)	200 ± 25 ms	0.270	Cohen's <i>d</i> = 0.512 (−0.392 to 1.401)
LGE negative	−14.5 ± 9 ms			189 ± 13 ms		

^aReported effect size = difference in proportions. ^bNewcombe's method (SPSS version 29). mAHA SoO reports the proportion of cases in which segmental EWI SoO and EAM SoO collocated to the same anatomical segment of the mAHA, as shown in [Figure 2D](#) and [Supplemental Figure 1](#). Transmural SoO reports the proportion of cases in which EWI SoO along the endoepicardial axis collocated to the same layer as diagnosed on EAM. Prematurity is the earliest electromechanical activation in any view ahead of the onset of surface ECG QRS. EMA time is total EMA time as the absolute time from the earliest ZC to the last ZC in milliseconds.

EMA = electromechanical activation; EWI = electromechanical wave imaging; mAHA = modified American Heart Association model; ZA = zero crossing; other abbreviations as in [Table 1](#).

3 (25%). Complex mixed scar patterns were present in 5 patients (38.4%).

EAM. Procedural details are reported in [Table 1](#). Antiarrhythmic drugs were stopped 5 days before the procedure, with 2 patients continued on amiodarone.

EAM SoOs were endocardial in 5 patients (16%) and midmyocardial in 12 (48%). Five of 12 midmyocardial sites were associated with a papillary muscle. An epicardial focus was diagnosed and/or suspected in 7 patients (28%), with 3 patients undergoing epicardial mapping, and in 4 patients suspected on the basis of indirect endocardial mapping features. One procedure was abandoned because of insufficient VE, and no SoO was defined (see [Table 1](#)).

Of the 13 MRI cases with LGE, in 7 (53.8%) the modified AHA model VA SoOs correlated with the LGE-positive MRI segment. In 5 (38.4%), VA SoOs were mapped to segments adjacent to scar. In 1 patient, VA SoO was not associated with scar. Twenty-three of 25 patients underwent radiofrequency ablation, and 2 underwent complementary coronary venous ethanol ablation. Acute and mid-term procedural outcomes are reported in [Supplemental Appendix Part 2](#).

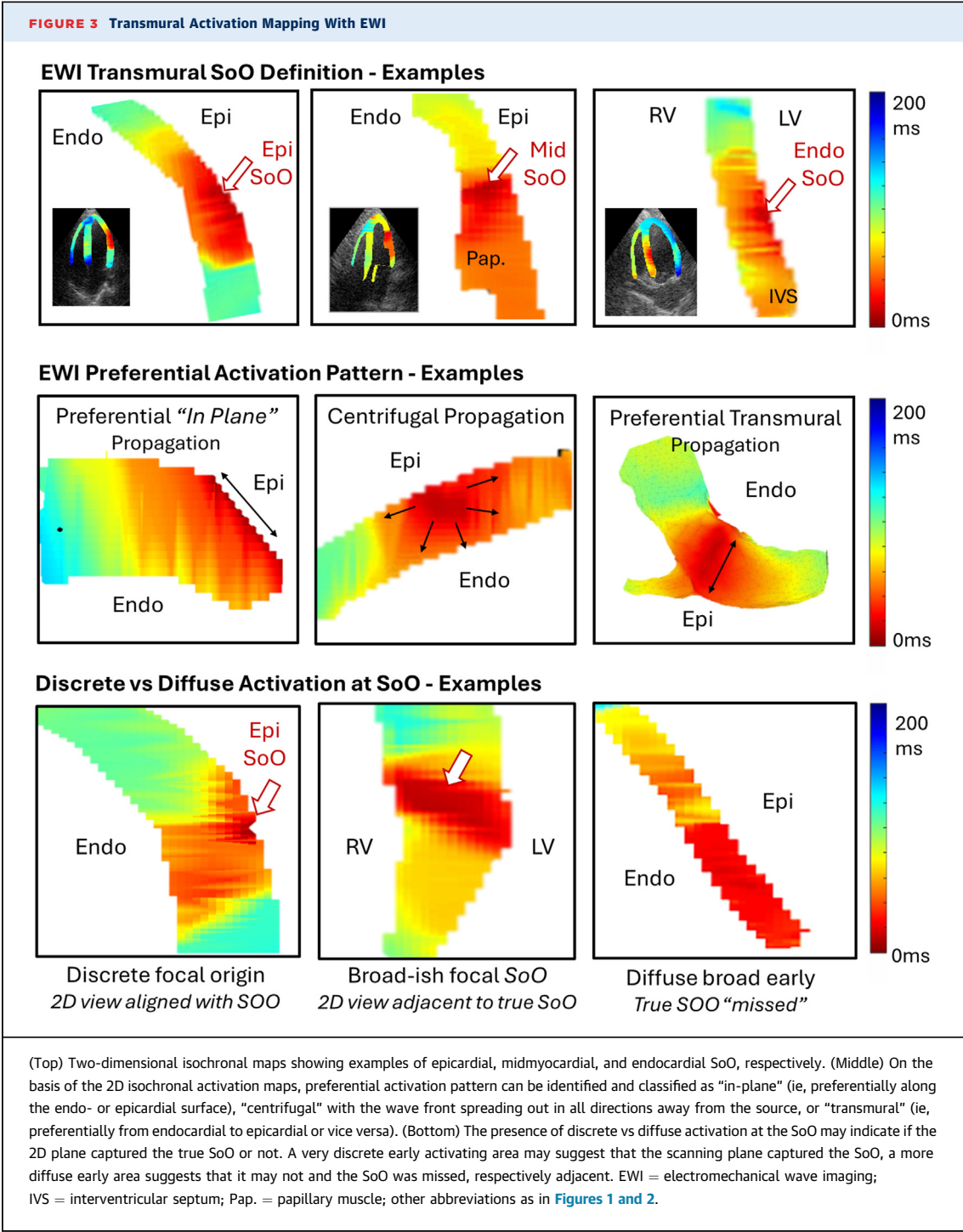
EWI LOCALIZATION OF VA SoO. A complete EWI data set with a corresponding same-rhythm contact map for validation was successfully acquired in 20 patients for the dominant VE or VT. Five additional patients were excluded: 4 because of the absence of inducible arrhythmia at the time of the EWI (ie, no EWI VA maps were available for comparison) and 1 because of different arrhythmias at the time of EWI and EAM (ie, no map of the same VA was available for comparison).

Anatomical "segmental" SoO. EWI localized the VA SoOs to the correct modified AHA model segment in 17 of 20 cases (85%) and mapped the residual 3 to

adjacent segments. The failed modified AHA model allocations related to RV VE, lateral papillary muscle VE, and inferoseptal VE. Both misannotated left-sided VAs were in patients with LGE on MRI, and the papillary muscle was described as poorly formed with suspected congenital malformation. The patient with inferoseptal VE had pectus excavatum with suboptimal echocardiographic quality. In the remaining 9 of 11 patients (81.8%) with LGE on MRI, EWI correctly localized the VA SoOs. Two cases of RV VE/VT required additional atypical echocardiographic views for correct localization and would have been missed in standard views. There was no statistically significant difference in the correctly identified segmental SoOs in patients with (9 of 11 [81.8%]) or without (8 of 9 [88.9%]) evidence of LGE in cardiac MRI (*P* = 0.66).

In 5 patients, more than 1 VE configuration was repeatedly recorded during EWI, but only in 3 patients was the second configuration captured in at least 4 of the 6 main views that allowed an estimate of the SoOs. All second configurations were mapped to a different segment (2 adjacent, 1 remote). In 1 patient with suspected papillary muscle origin, very discrete changes in configuration were noted but were processed as 1 configuration.

Transmural SoO. EWI successfully identified transmural (endocardial vs midmyocardial vs epicardial) SoOs in 18 of 20 patients (90%). In 3 of these 18, the area of earliest activation on EWI encompassed both the midmyocardium and subepicardium (in 2 cases with midmyocardial SoOs) or midmyocardium and subendocardium (in 1 case with an endocardial SoO). One "failed" ablation case was mapped to an endocardial segment whereas EAM suggested an intramural focus. In the second "failed" case, the segmental SoO was in agreement with EAM, but activation was too diffuse, preventing definition of a

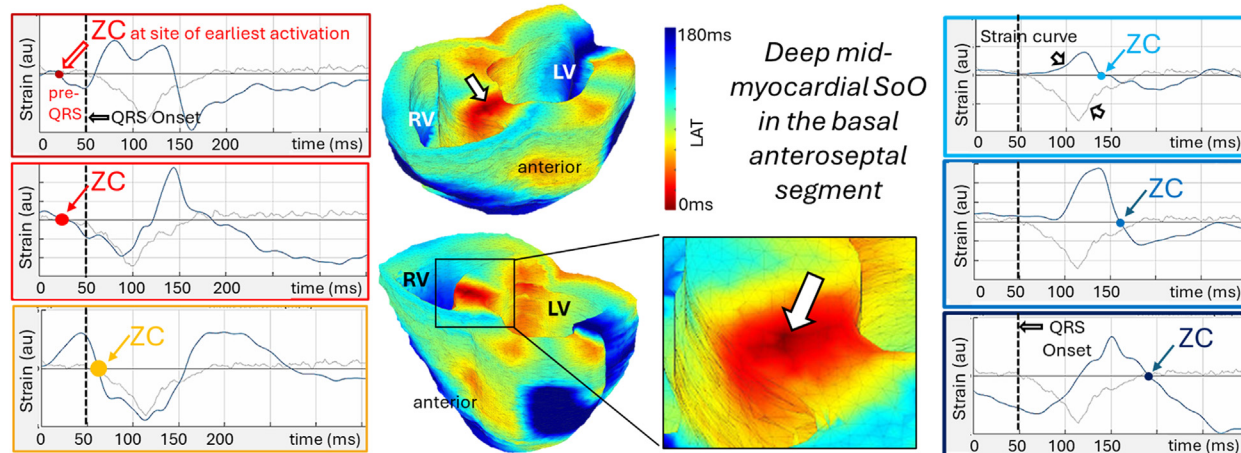


transmural SoO ([Table 2](#), [Supplemental Table 1.1](#)). There was no statistically significant difference between patients with (10 of 11 [90.9%]) and those without (8 of 9 [88.9%]) scar ($P = 0.881$). [Figure 3](#) illustrates examples of transmural mapping with EWI detecting the earliest site of origin on the endo-

epicardial axis. [Figures 4 to 7](#) demonstrate examples of EWI mapping with corresponding electro-anatomical maps and electrocardiograms. Results of reproducibility analysis and Bland Altman plots, for EWI VA mapping are reported in [Supplemental Appendix Part 3](#).

FIGURE 4 Example of Intramural Basal Septal Focus

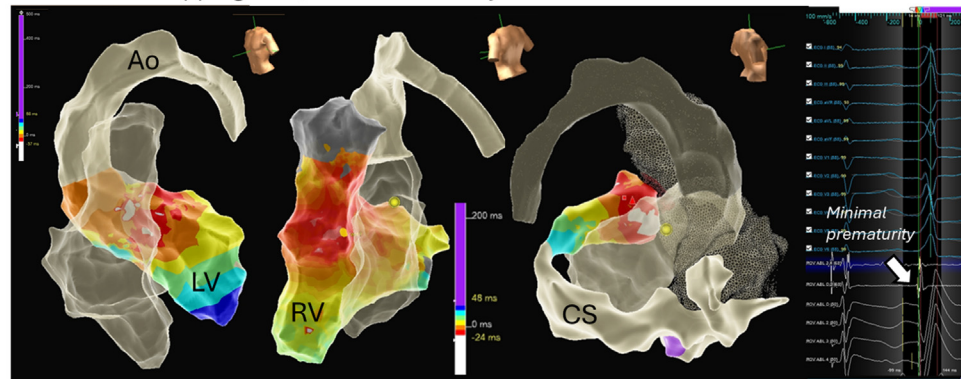
A 3D EWI models and exemplary strain curves



B 12-lead ECG



C Contact mapping of LV, RV and Coronary sinus and intracardiac EGM



(A) Three-dimensional EWI model with representative strain curves of selected isochrones in relation to QRS onset (black vertical line). In the strain curve panel, the x-axis represents time (milliseconds), and the y-axis represents strain in arbitrary units, defined as change in length divided by original length. The magnified portion of the 3D EWI model illustrates a SoO (dark red) in the midmyocardial basal antero-septal segment (white arrow). (B) Twelve-lead ECG of ventricular ectopy (VE). (C) Electroanatomical maps of the LV, RV, and coronary sinus (CS) demonstrating broad early activation from all sites and <20 ms ahead of QRS. Radiofrequency energy was delivered from the RV, LV, and CS, leading to a reduction but not elimination of VE. Ao = aorta; EGM = electrogram; other abbreviations as in [Figures 1 and 2](#).

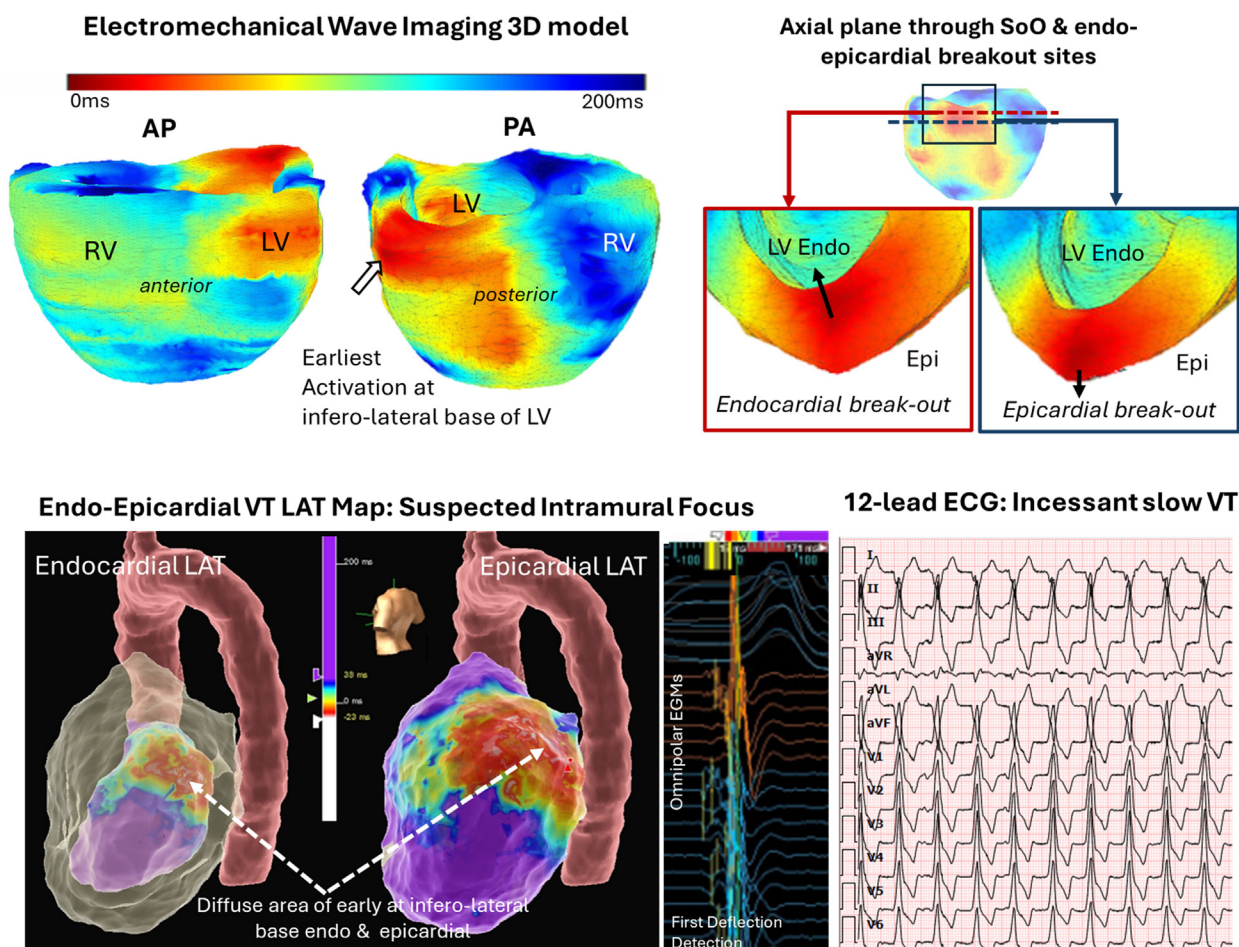
Secondary features. Prematurity of EMA was -14 ± 12 ms (presurface QRS) for the total cohort. There was no statistically significant difference in measured prematurity of the EMA in LGE-positive vs LGE-negative cases or on the basis of transmural SoO.

Global EMAt was 195 ± 21 ms, shortest in VAs with endocardial origin (median 183 ± 8 ms) followed by midmyocardial (191 ± 15 ms), and longest in epicardial SoOs (207 ± 30 ms), but no statistical significance was observed across different groups. In LGE-positive cases, EMAt was longer (200 ± 25 ms) compared

with LGE-negative cases (189 ± 13 ms) ([Table 2](#)). There was a statistically significant moderate negative correlation between EMAt and left ventricular ejection fraction ($r_s = -0.549$; $P < 0.05$) and a moderate positive correlation between EMAt and QRS duration ($r_s = 0.48$; $P = 0.032$).

Fifteen of 20 cases (75%) demonstrated a preferential conduction pattern, with the majority of these (73%) planar within the same ventricular layer. In the other 25%, a centrifugal propagation pattern was observed.

FIGURE 5 EWI Mapping in Incessant Slow VT in Dilated Cardiomyopathy



Case example of a patient with incessant slow ventricular tachycardia (VT) with progressive LV deterioration to an ejection fraction of 15% and 2 previously failed endocardial ablation attempts. (Top) Three-dimensional EWI models and zoom on the SoO. EWI suggested an intramural inferolateral basal LV origin with distinct breakout sites to the LV epicardial and slightly more basal to the LV endocardium (top right). (Bottom) Combined endoepicardial local activation time (LAT) maps during incessant monomorphic VT showed broad early areas on both surfaces with no termination with radiofrequency energy from either site, suggesting a deep intramural focus. The patient underwent coronary venous ethanol ablation with suppression of VT and only isolated VE. AP = anteroposterior; PA = posteroanterior; other abbreviations as in [Figures 1 to 3](#).

DISCUSSION

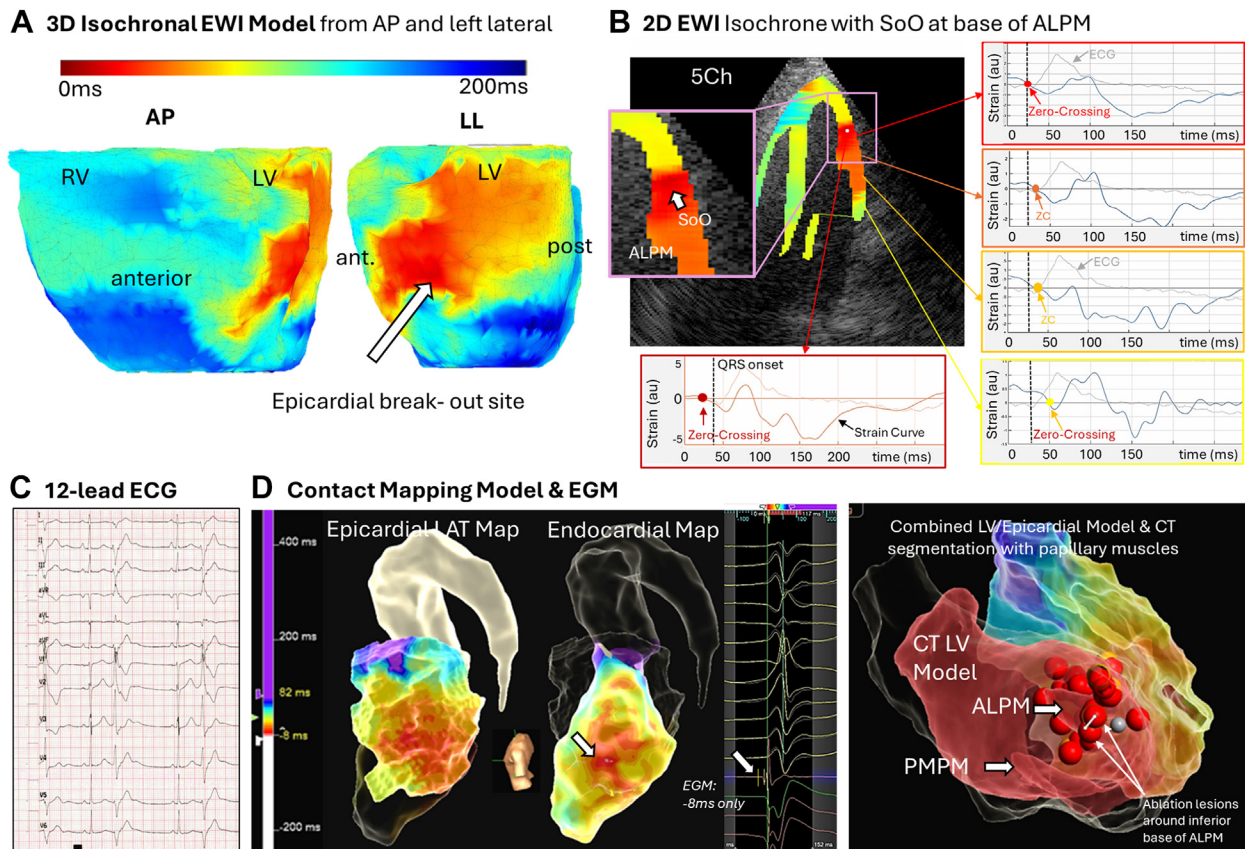
In this study we used an innovative echocardiographic mapping technology to noninvasively locate VA SoOs anatomically and along the transmural axis, with validation against contact mapping. The main results are as follows:

- In a cohort of patients with complex focal VAs, EWI successfully identified the SoOs along the endo-epicardial axis in 90% and correctly localized the anatomical segment in 85% of cases.
- The high spatiotemporal resolution of EWI can correctly differentiate endocardial and epicardial

VA origin, including in the thin-walled RV, but the more complex anatomical shape of the RV poses a greater challenge for precise segmental localization than the ellipsoid LV and requires acquisition of additional (atypical) views.

- The majority of focal VAs in patients with non-ischemic myocardial scar are in close vicinity to scar. Erroneous SoO localization was more common in these patients, but segmental localization with EWI remained good at 81.8%, with the residual cases annotated to adjacent segments.
- Low and/or fluctuating burden or multifocal VAs pose challenges for the current 2D EWI approach

FIGURE 6 Example of Anterolateral Papillary Muscle VE and VT



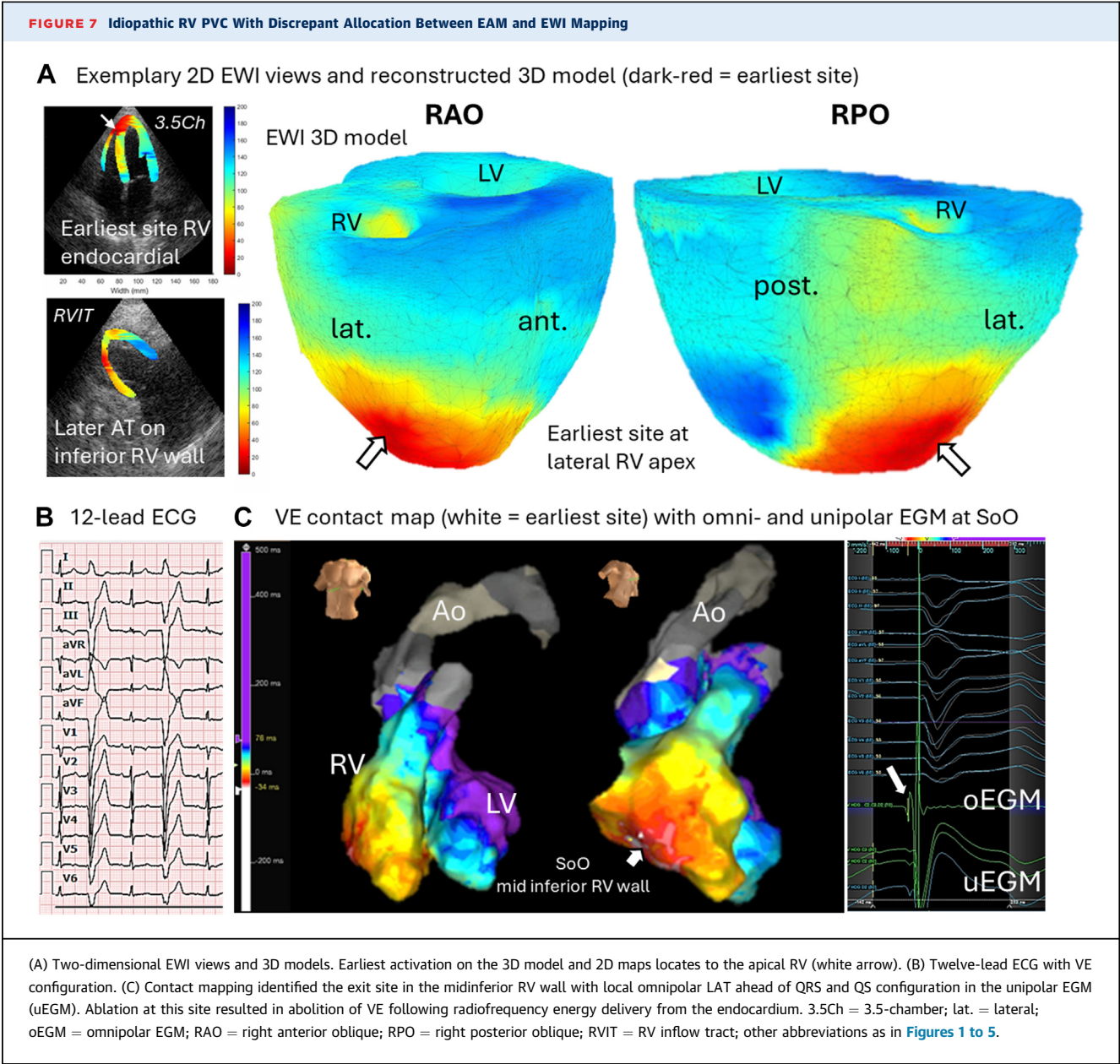
(A) Three-dimensional EWI model with earliest epicardial breakout in the mid anterolateral segment. (B) Two-dimensional isochronal map of the 5-chamber (5Ch) view with anterolateral papillary muscle (ALPM) shows earliest activation originating intramurally at the inferior base of the ALPM. Representative strain curves are shown, with the vertical black line indicating QRS onset, with ZC of strain curve as a surrogate of local electromechanical activation time (the x-axis represents time in milliseconds, and the y-axis represents strain in arbitrary units, defined as change in length divided by original length). (C) Twelve-lead ECG with dominant VE configuration. (D) Epicardial and endocardial LAT map of dominant VE with EGM at earliest site only –8 ms ahead of surface QRS. EAM with computed tomographic (CT) integration and delivered ablation lesions around the papillary muscle: ablation at the inferior base of the anterolateral papillary muscle suppressed the VE. ant. = anterior; AT = activation time; LL = left lateral; M. = magnitude; PMPM = posteromedial papillary muscle; post = posterior; other abbreviations as in [Figures 1 to 5](#).

using prospective 4-second acquisition windows and prevented EWI mapping in 14.2% of the cases.

CLINICAL VALUE OF EWI FOR TRANSMURAL MAPPING OF CARDIAC ARRHYTHMIAS. The accurate identification of the VA SoO to target with ablation is fundamental to any catheter ablation procedure. Preprocedural knowledge about the target is vital for operative planning (eg, epicardial access), procedural risk assessment, and maximizing the efficiency of high-density mapping. Also, the inaccessible intramural space is a major limitation for conventional contact mapping. Although novel ablation

approaches, including ethanol, bipolar radio-frequency, ultralow cryoablation, and pulsed field ablation, may generate deep lesions, optimal targeting is critical.

Current noninvasive diagnostic tools have at best moderate accuracy for endoepicardial differentiation of SoOs, particularly in structural heart disease. Conventional electrocardiographic criteria for this purpose have been proposed⁸ and presume that an epicardial activation source presents with an initial slowed conduction reflected as a prolonged or notched initial part of the QRS until the Purkinje network is engaged.^{9,10} Site-specific values for these criteria have been reported¹¹ but are affected by body



habitus, cardiac rotation, and myocardial scar. Therefore, more precise personalized localization with EWI is needed.

As we demonstrate in this study, the major advantage of EWI is the direct measurement of activation on a tissue level with high spatiotemporal resolution rather than estimation from body surface potentials. This allows mapping with submillimeter precision of endocardial, midmyocardial, and epicardial layers to identify the origin of the electro-anatomical wave. Our study demonstrates its clinical

value by correctly identifying the transmural SoOs in 90% of cases but also highlights the pitfalls of 2D EWI with interplanar gaps. Additional markers, including EMA prematurity and pattern at the earliest site (discrete vs diffuse), should be taken into consideration to judge whether the true SoO has been “captured” and/or is in close proximity to the acquired view ([Figure 3](#)). In cases of very diffuse early activation, additional unconventional views are required to ensure more precise localization. Yet the comparatively high rate of correctly identified

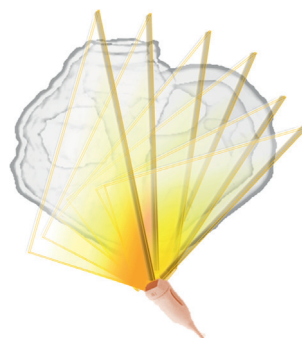
CENTRAL ILLUSTRATION EWI for Transmural Ventricular Activation Mapping

Transthoracic High-Frame Rate Echocardiography:

Unfocused beam with diverging waves
Temporal resolution: 0.5 ms (2,000 fps)

Axial resolution: 0.0385 mm
(20 MHz sampling rate)

Lateral resolution: 0.43 mm
at 5 cm - 1.3 mm at 15 cm



20 Complex VA Cases Undergoing EWI and Electroanatomical Contact Mapping

85% correct anatomical localization

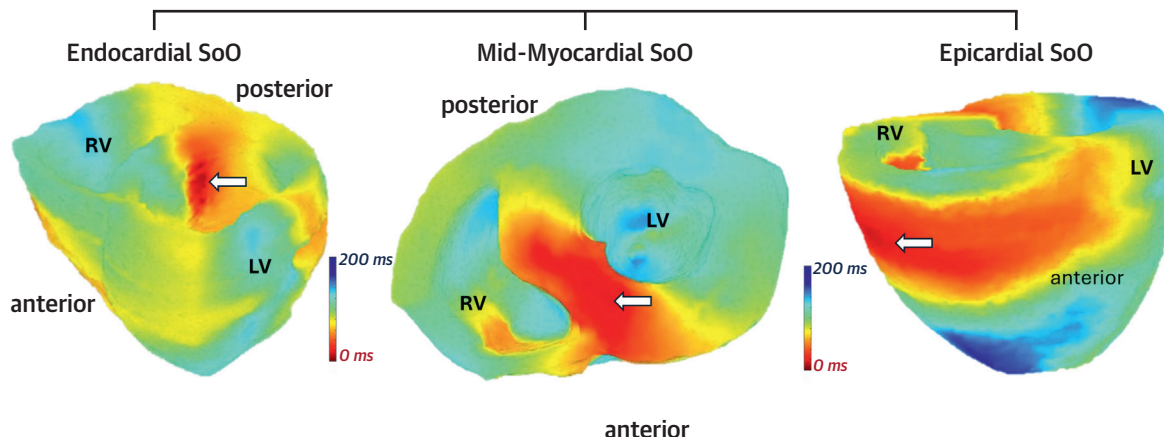
88.8% correct in LGE -ve vs 81.8% LGE +ve MRI

90% correct transmural localization as endocardial, midcardial, epicardial SoO

2D Acquisition



3D Rendering



← = indicating earliest site of activation on 3D model

Support Procedural Planning and Setup (eg, epicardial access)

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ANT = anterior; EWI = electromechanical wave imaging; LGE = late gadolinium enhancement; LV = left ventricle; MRI = magnetic resonance imaging; Post = posterior; RV = right ventricle; SoO = site of origin.

transmural SoOs in our study despite these limitations is encouraging and likely facilitated by the frequent preferential “in-plane” conduction pattern (Central Illustration).

VARIABILITY IN ELECTROMECHANICAL DELAY AND ASSOCIATION IN STRUCTURALLY NORMAL AND ABNORMAL HEARTS. EWI maps should not be confused as electrical activation maps, and accurate

interpretation needs to take into account the complex relationship of electrical and electromechanical wave fronts, particularly in the presence of structural alterations. Previous studies have reported differences in electromechanical delay (EMD) over several tens of milliseconds between apex and base (longer EMD at base),¹² endocardium and epicardium (longer EMD in the epicardium),¹³ as well as dynamic changes depending on the activation sequence (eg, sinus

rhythm vs ventricular pacing vs VT, EMD shorter in VT¹⁴) and rate,¹⁵ distance to impulse origin, and loading conditions (greater EMD at late activating areas,¹⁴ supposedly due to myofiber prestretch caused by contraction of the early depolarization regions¹⁶). This raises the question of how these changes may affect accuracy of VA mapping at different sites and/or setting (pre- vs intraprocedural) or in patients with, for example, VE- or VT-induced heart failure. For the latter, heart failure induced remodeling may further affect EMD. In heart failure, alterations in Ca²⁺ handling have been described as a dominant cause for prolonged EMD due to slowing of myofiber shortening.¹⁷

Lastly, at sites of scar, dissociation between electrical activation assessed by contact mapping and EWI may be observed. Using high-density mapping catheters, low-amplitude fractionation and late potentials may be detected, whereas EWI may not record a measurable deformation at these sites, because of insufficient contractile myocardial mass. Yet in our cohort, there was no statistically significant difference in recorded EMA prematurity between subjects with and those without scar. One could have expected the EMA in the scar cohort to occur later once a critical myocardial mass within in the border zone and adjacent healthy myocardium is activated to cause a measurable deformation. The lack of difference may be explained by the more dominant impact of 2D acquisition, which may have a greater effect on measured prematurity (eg the true SoO may not have been precisely captured by the scanning plan, affecting LGE+ve and LGE–ve patients alike) as well as the fact that focal arrhythmias occurred in the border zone of scar rather than at its center.

Overall, although EMD may be affected by a number of physiological and pathophysiological factors, for mapping of VA in pre-procedural planning, in which the aim is to identify the area and myocardial layer of interest, these mechanistic considerations may be less relevant. In turn, the heterogeneity of EMD is important if the objective of electromechanical mapping is substrate characterization.

EWI FOR ARRHYTHMIA MAPPING: CHALLENGES FOR TRANSLATION INTO CLINICAL PRACTICE. This is the first clinical study to evaluate the diagnostic accuracy of EWI for transmural ventricular mapping in a cohort of patients with complex VAs including patients with myocardial scar. For this purpose, EWI is a promising technology that could in theory conveniently be integrated into routine echocardiography. Yet important practical and technical challenges remain. The current workflow involving prospective

sequential 2D acquisition requires sufficiently frequent and reliable presence of VAs for mapping, which hampered EWI mapping in 14.2% of our patients and makes it an unsuitable modality for patients with infrequent but highly proarrhythmogenic arrhythmias (eg, VE-triggered ventricular fibrillation). Retrospective acquisition may overcome this but would require prolonged continuous scanning with high-frame rate sequences until the VE/VT event. Also, EMA was estimated in sequential 2D planes with comparatively “coarse” probe movement, with standardized views defined by anatomical landmarks (ie, “4”- and “5”-chamber views). Thus, interplanar gaps exist that may harbor the true SoO. Full 3D single-beat acquisition would be preferable to obviate the need for interpolation, improve spatial accuracy, and facilitate mapping of low burden VE/VTs. Such improved spatial localization may allow to accurately measure the exact depth of an intramural focus that may then make it possible to predict the failure (or success) of ablation from a given surface to abolish that source. The use of high-volume rate 3D TTE in humans has been reported^{16,18} and awaits adaptation to EWI for mapping cardiac arrhythmias.

Alternatively, some limitations of TTE may be overcome by expanding the use of EWI to intracardiac echocardiography as well as transesophageal echocardiography as a global intraprocedural mapping modality complementing existing electroanatomical maps.

Lastly, the need for special ultrasound equipment and custom-made postprocessing software remains a barrier to the widespread use of this technology. Time requirements and manual input for generating complete EWI models remain high, and EWI would in its current form not be feasible as part of routine TTEs. Machine learning projects to automate EWI mapping have been reported¹⁹ and are in progress. An important challenge for EWI automation lies in the frequently ambiguous nature of the strain curves. In an optimal case, a single negative peak exists during systole with straight forward selection of the ZC location. Yet incremental strain curves may at times exhibit no ZC or, the opposite, multiple ZCs requiring combined assessment of the wider activation patterns to define EMAt (see [Supplemental Figure 1.5](#) for examples). “No ZC” may be secondary to poor imaging quality and/or challenges in identifying the “baseline” in diastole. “Multiple ZCs” may occur for various reasons, including >1 electromechanical wave reaching the area from different locations and of different amplitudes, strain signal aliasing due to signal noise or more dominant waves that interfere and change the strain pattern (eg, in proximity to valves, which

cause multiple mechanical and natural shear waves that might interfere with the electromechanical strain map). The impact of ambiguous strain curves on EWI mapping is discussed in more detail in [Supplemental Appendix Part 3](#).

STUDY LIMITATIONS. Sample size in this prospective study was limited by the necessary inclusion criteria to select complex focal VAs and perform activation mapping, requiring a high burden of VA at the time of the scan, as well as the logistics of undertaking the research scan requiring specialized equipment and setup. The small number of patients limits the generalizability of our results, and post hoc power analysis suggested that it was underpowered to detect significant differences among the subgroups. No formal power calculation could be performed a priori, because of the absence of any clinical data about diagnostic accuracy of transmural mapping methods in this patient cohort. Yet our pilot data for clinical transmural mapping should inform future prospective studies.

Although our results suggest that EWI can successfully identify the SoOs of VAs noninvasively in the majority of cases, this was limited to patients who had frequent enough VAs at the time of the scan to allow prospective high-frame rate acquisitions. In a subset of patients with noninducibility, EWI VA mapping was not possible, and these patients were excluded from further analysis.

Also, EAM is an imperfect ground truth and delineation of the precise SoO, particularly if intramural, is challenging. Our study highlights the difficulties in validating a true transmural mapping technology in a clinical cohort. Yet despite this, EAM remains the currently accepted gold standard for defining SoOs. Detailed coronary venous mapping with small multielectrode catheters would have been preferred over wire mapping but was not available and in any case is restricted by vascular anatomy. Suspected intramural sites thus had to be indirectly validated by surrogate markers. Yet it is precisely this lack of clinically available intramural mapping technology that EWI may be able to address.

Spatial correlation was performed on segmental basis only because of the numerous inherent challenges of coregistration of pseudo-3D EWI models with intracardiac contact models, as well as the additional difficulty of evaluating the spatial relationship from surface contact map SoO to intramural sites in EWI, preventing a reliable quantitative comparison (ie, distance of the SoO in millimeters). In

turn, the segmental approach has equally been critically viewed as artificially discretizing the anatomical continuity,²⁰ as the correct location may be misassigned because of imposed segmental assignments.

Although technically feasible, 3D EWI models currently cannot be integrated into available mapping systems, because of contractual restrictions preventing loading the data of this patented technology into any commercial mapping system. Formalized agreements are awaited to overcome this administrative barrier.

Last, although we included subjects with myocardial scar, this was limited to nonischemic partial thickness patterns. If the myocardial fibrosis is too extensive, this may limit EWI because of a lack of contractile tissue to delineate the wave front. Equally, in some patients, echocardiographic quality can be prohibitive and EWI mapping therefore not feasible.

CONCLUSIONS

EWI identified the segmental and transmural SoOs of focal VAs, including in the presence of scar, in the majority of patients using EAM as the gold standard. EWI could support preprocedural planning, including the need for epicardial access and/or more complex ablation setup and technology. Prospective studies using EWI to guide intracardiac mapping and ablation are in progress. Automation of EWI analysis, visualization, and integration in clinical echocardiography machines with 3D single-beat EWI to improve spatial accuracy will enable future clinical application.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: EWI is an echocardiography-based mapping modality that noninvasively tracks the electromechanical wave in high temporal and spatial resolution. EWI offers true transmural mapping along the endoepicardial axis, addressing an important gap in current mapping technology. In this study we demonstrate that EWI can be used for complex focal VAs with good diagnostic accuracy to define the segmental and transmural SoOs in patients with and those without nonischemic myocardial scar.

TRANSLATIONAL OUTLOOK: Three-dimensional single-beat EWI and automation of EWI analysis and visualization to improve spatial accuracy and optimize mapping efficiency, respectively, are required to facilitate translation into clinical practice. Integration of EWI into clinical echocardiographic systems and integration of 3D EWI models in EAM systems will further enable future clinical application.

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KEY WORDS electromechanical wave imaging, radiofrequency ablation, transmural mapping, ventricular arrhythmias

APPENDIX For supplemental figures and tables, procedural outcomes, reproducibility and robustness, and supplemental references, please see the online version of this paper.