How to use intracardiac echocardiography to identify ventricular tachycardia substrate in ischemic cardiomyopathy

David F. Briceño, MD, FHRS,[*] Andres Enriquez, MD, FHRS,[†] Jorge Romero, MD, FHRS,[*] Carlos Tapias, MD, FHRS,[‡] Pasquale Santangeli, MD, PhD, FHRS,[§] Robert Schaller, DO, FHRS,[§] Gregory Supple, MD, FHRS,[§] Diego Rodriguez, MD, FHRS,[‡] Luis C. Saenz, MD, FHRS,[‡] Fermin C. Garcia, MD, FHRS[‡§]

From the [*]Division of Cardiology, Montefiore Medical Center, Albert Einstein College of Medicine, New York, New York, [†]Heart Rhythm Service, Department of Medicine, Queen's University, Kingston, Ontario, Canada, [‡]Fundación Cardioinfantil, Instituto de Cardiología, Bogotá, Colombia, and [§]Electrophysiology Section, Cardiovascular Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

Introduction

Intracardiac echocardiography (ICE) has contributed to the development of invasive electrophysiology by facilitating mapping and ablation based on real-time evaluation of cardiac anatomy during cardiac interventional procedures.[1] In the context of ventricular tachycardia (VT) ablation, routine applications of ICE include guidance of transseptal catheterization, navigation of catheters within the cardiac chambers, monitoring of catheter-tissue contact, assessment of lesion formation, and early detection of complications.[1] ICE is particularly useful for mapping structures that are not visualized by fluoroscopy (ie, cardiac silhouette), such as the valve leaflets, interventricular septum, papillary muscles (PMs), or moderator band. Another key role of ICE is the identification and delineation of arrhythmogenic substrate in scar-related VT. This role has been further refined by the ability to integrate real-time ICE images with electroanatomic maps, providing supplementary anatomical guidance to facilitate substrate-guided ablation. Herein, we describe the utility of ICE to assess and accurately define the arrhythmogenic substrate in patients with ischemic cardiomyopathy undergoing VT ablation.

KEYWORDS Arrhythmia substrate; Coronary artery disease; Intracardiac echocardiography; Ischemic cardiomyopathy; Ventricular tachycardia

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ICE technical aspects

For the anatomic analysis described in this review, the ICE catheter is advanced via femoral approach and deployed to the "home view" position in the mid-right atrium.[1] Once the imaging window is aligned to the right ventricle (RV), the right atrium is visualized, as well as the anterior and posterior leaflets of the tricuspid valve and the RV. With clockwise (posteriorly) and counter-clockwise rotation (anteriorly), the left atrial structures (ie, mitral valve, left atrial appendage, and pulmonary veins) and right atrial structures can be delineated, respectively. Likewise, gentle clockwise rotation relative to the plane of the tricuspid valve allows for initial anatomical evaluation of the left ventricle (LV) with particular visualization of the inferobasal region. To examine this region (also known as the posterior-superior process of the LV), it is often necessary to slightly flex the catheter anteriorly to better image the plane of the noncoronary aortic cusp and membranous septum. Typically, if further rotation is applied, the superior aspect of the coronary sinus ostium is seen. At that point, counter-clockwise rotation is applied. This region is visualized between the most posterior aspect of the noncoronary cusp and coronary sinus ostium and medial to the tricuspid valve.

From the home view, the ICE catheter can be maneuvered into the RV by applying anterior tilt to visualize the tricuspid valve and advancing the catheter through the valve, after which the anterior tilt is released. Gentle posterior tilt can sometimes facilitate LV visualization. Clockwise rotation

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in the RV allows visualization of the LV structures in a posterior-to-anterior sequence, beginning with the interventricular septum, followed by the posteromedial PM and the anterolateral PM. As shown in the examples below, PMs are nicely imaged with ICE from the RV, and most importantly, mid-basal substrates can be visualized and assessed appropriately. From this view, further clockwise rotation allows imaging of the basal aspects of the LV and outflow tracts. With the ICE catheter positioned adjacent to the proximal septum and the base of the RV outflow tract, the aortic and pulmonary valve cusps can be detailed. Likewise, localization of the left main coronary artery can be achieved from this view. Further rotation opens up the proximal ascending aorta, the take-off of the right coronary artery, and finally the lateral RV free wall until reaching back to the initial position (360-degree rotation).

The anatomic information provided by ICE can also be incorporated into the electroanatomic mapping system. This is available in the CARTO mapping system with CARTOSOUND module (Biosense Webster, Diamond Bar, CA). It uses a modified ICE catheter (SoundStar) that contains a location sensor that can be visualized in the electroanatomic map. Multiple 2-dimensional slices of the chamber or anatomical structure of interest are obtained and the endocardial border from each image is traced either manually or using edge-detection software. These images can be integrated to build into an online 3-dimensional shell. Voltage and activation mapping information can then be applied to this anatomic reconstruction. Another feature of the system is the catheter green tip overlay feature that enhances catheter navigation. When the ultrasound beam intersects with the ablation catheter tip, a green icon displays in real time in the ultrasound viewer window corresponding to the anatomical localization of the ablation catheter tip. A similar feature is the maps tags intersection in which, when the ultrasound beam intersects, an anatomical area that has been tagged or a lesion tag of the same color will appear in the ultrasound real-time image in the ultrasound viewer window.

Substrate identification

The following case series depicts the utility of ICE for ventricular arrhythmogenic substrate characterization in patients with ischemic cardiomyopathy. Either an 8F phased-array ICE catheter (Siemens, Mountain View, CA) or a 9F phased-array catheter (ViewFlex Xtra; St. Jude Medical, St Paul, MN) was used. When the CARTO mapping system was utilized, the CARTOSOUND module was used to allow integration of the electroanatomic map with an ICE-derived anatomic shell of the heart and valves as described above. Thus, before mapping, a detailed echocardiographic evaluation and anatomic reconstruction was created and substrate characteristics were analyzed. The hallmark of ischemic VT substrate identified by ICE is myocardial wall motion abnormality (hypokinesis or akinesis) associated with thinning and hyperechogenicity that corresponds to a coronary territory and correlates with voltage and electrogram (EGM) abnormalities.[2] Once the ICE-based cardiac analysis was completed, the electroanatomic map was created using a 3.5-mm-tip open irrigated catheter with a 2-mm ring electrode and a 1-mm interelectrode distance (ThermoCool SmartTouch; Biosense Webster, Diamond Bar, CA) or a 3.5-mm-tip open irrigated catheter with a 2-mm ring electrode and a 2-mm interelectrode distance (TactiCath Ablation Catheter; St. Jude Medical). Bipolar EGMs were filtered at 30–500 Hz, displayed at 100 mm/s sweep speed, and stored for off-line analysis. Activation and voltage maps were created with point-by-point mapping with the ablation catheter during intrinsic atrioventricular conduction or paced rhythm. A multipolar mapping catheter was used to complement the voltage map for case 3 and case 5 (PentaRay, Biosense Webster; Advisor HD Grid, St. Jude Medical, respectively). Acquired EGMs were reconstructed into 3-dimensional voltage maps and area measurements made with the incorporated CARTO or the Ensite Precision mapping systems (St. Jude Medical). Mapping density was sufficient to allow complete surface representation with a fill threshold of up to 15 mm. Normal bipolar endocardial and epicardial EGM voltage were defined as a peak-to-peak amplitude $\geq$1.5 mV and $\geq$1.0 mV, respectively; "dense scar" was defined as $\leq$0.5 mV.[3]

Case 1: Characterization of intracavitary structures and relation to substrate

A 77-year-old man with a history of coronary artery disease and remote percutaneous coronary intervention to the right coronary artery underwent electrophysiology study for recurrent VT. ICE revealed severely decreased LV function with an akinetic inferior wall and mid to apical inferolateral hyperechogenicity (Figure 1). ICE was useful to understand the endocardial-to-epicardial substrate distribution, suggesting a predominantly epicardial substrate component toward the base with a preserved subendocardium protected by the posteromedial PM, while the mid and apical portions of the ventricle had a more transmural appearance with the presence of a subendocardial component (Figure 1). Importantly, this pattern of scar distribution was confirmed by the electroanatomic voltage map with preserved basal subendocardial voltage and predominantly epicardial abnormalities basally compared to endo-epicardial transmural abnormalities towards the apical region. VTs were induced and isthmus sites were identified in the endocardial and epicardial aspects of the scar, requiring extensive endo-epicardial substrate modification. These isthmus sites correlated with the initial ICE survey where endocardial isthmuses were located in the apical region of the scar, while epicardially these were more basal. In this case ICE was important to expedite substrate characterization by focusing mapping efforts to areas previously identified as abnormal during the initial ICE evaluation and it was also helpful to the timely decision to obtain epicardial access. We have previously demonstrated that in patients with inferior ischemic scar, VT may arise from the area underneath the posteromedial PM, limiting endocardial

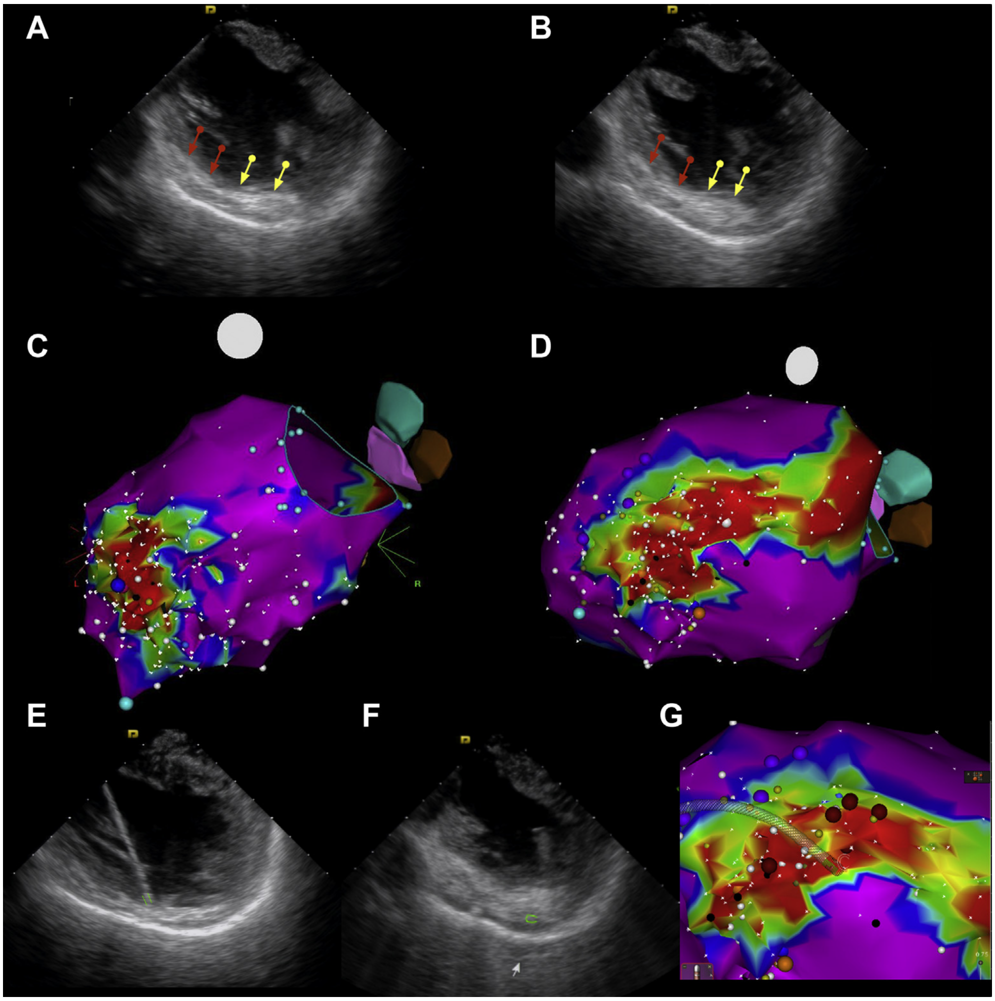

Figure 1 **A, B:** Intracardiac echocardiography (ICE) showing mid-apical large inferolateral echodensity (*arrows*) suggestive of transmural scar. This area of scar can be seen below the posteromedial papillary muscle. Scar area has a predominantly epicardial substrate component toward the mid ventricle protected by the posteromedial papillary muscle compared to the more apical substrate, where an endocardial pattern is seen (*red arrows*: more epicardial; *yellow arrows*: more endocardial); **C, D:** Endocardial (**C**) and epicardial (**D**) moderate-sized inferior-inferolateral mid-apical scar was identified with detailed voltage map, which was consistent with echodensity noted in ICE. **E:** ICE imaging showing ablation catheter in an endocardial isthmus site. **F, G:** ICE and electroanatomic map illustrating catheter in the epicardial space just opposite to outer edge of the scar identified on ICE (*green tip*) in a an epicardial isthmus site (**G** is a magnification of **D** focused on the voltage map).

ablation.[4] In these cases, the critical isthmus typically is localized to an area underlying the posteromedial PM and, thus, is inaccessible to mapping and ablation from the endocardium. Intraprocedural ICE may be useful to define the arrhythmogenic substrate, with good correlation between the imaging-defined scar and the electroanatomic map. Additionally, identification of the catheter tip during mapping and ablation provides reassuring information regarding catheter location and proximity to the tissue combined with force sensing to warrant catheter tip contact endocardially (as shown in Figure 1E) and epicardially (as shown in Figure 1F) to facilitate mapping and ablation and avoid complications.

Case 2: Identification of endocardial substrate

A 64-year-old man with ischemic cardiomyopathy (LV ejection fraction 30%) and multiple percutaneous coronary interventions underwent ablation of recurrent VT. ICE revealed a moderately impaired LV function with inferior wall hypokinesis and subendocardial hyperechoic band in the basal inferolateral wall (Figure 2). The layered 3-dimensional nature of the substrate can be easily identified. In Figure 2A, corresponding to the inferior aspect of the scar, we identified a very basal component of thin akinetic myocardium predominantly subendocardial basal to the posteromedial PM becoming predominantly subepicardial in the apical portion as it dives below the posteromedial PM that also becomes an anatomical obstacle to delivering endocardial radiofrequency to this region of the scar if it were necessary (similar to case 1). Further clockwise rotation in Figure 2B shows the mid lateral LV substrate with thinning and akinesia, and the hyperechoic band basal to the anterolateral PM mostly subendocardially. Finally, in Figure 2C, further clockwise rotation shows a higher lateral LV with the substrate predominantly subendocardial and close to the mitral valve

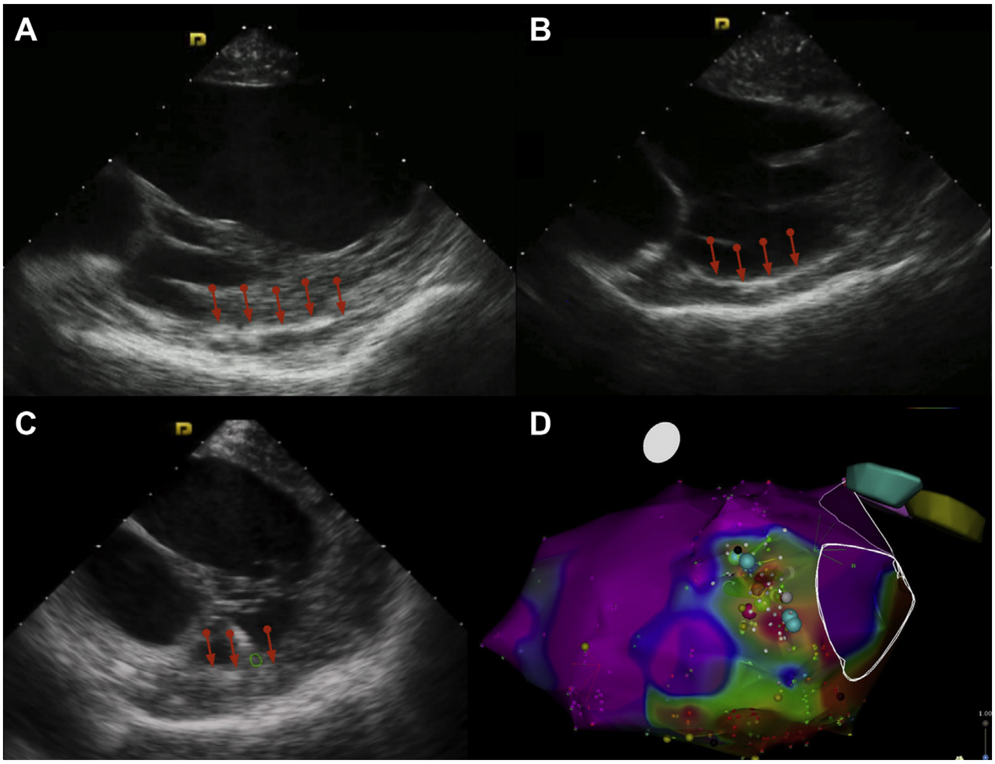

Figure 2 **A–C:** Intracardiac echocardiography (ICE) revealing dense echodensities suggestive of scar in the mid-basal inferolateral left ventricle (*arrows*). This illustration details the extensive layered endocardial scar ranging from the mid inferior left ventricle protected by the posteromedial papillary muscle (**A**) followed by the mid lateral left ventricle protected by the anterolateral papillary muscle (**B**) and finally at the base where the isthmus of the clinical ventricular tachycardia (VT) was identified (**C**). **D:** Voltage mapping revealed basal inferior and inferolateral scar consistent with ICE findings. There was dense scar in the inferior region and border zone regions more basal where the critical VT circuit was ultimately identified (**C**, catheter green tip in ICE at this site).

annulus. Bipolar LV voltage map revealed basal inferior and inferolateral voltage abnormalities that matched ICE findings (Figure 2). Ventricular programmed stimulation easily induced the clinical VT, characterized by right bundle branch block morphology with a right inferior axis and positive concordance across the precordium. The VT isthmus was identified in the basal aspect of the scar where limited ablation successfully eliminated the VT and rendered the patient noninducible. In this case, ICE demonstrated a clearly layered endocardial substrate with the mid portion of the scar protected by the posteromedial PM (similar to case 1) while the basal aspect was readily accessible from the endocardium, allowing mapping efforts to be focused in this area and ultimately locate an isthmus site in an endocardial aspect of this moderate-sized scar. Epicardial mapping would likely have been required if the patient remained inducible, considering that a large portion of the scar is protected by the posteromedial PM (Figure 2A) and, as such, is not accessible from the endocardium.

Case 3: Identification of anatomic abnormalities and relation to substrate

VT ablation was performed in a 62-year-old man with ischemic cardiomyopathy (LV ejection fraction 20%), multiple percutaneous coronary interventions, and coronary artery bypass graft surgery. ICE ruled out LV thrombus and demonstrated moderately reduced RV function and severely decreased LV function with a large transmural anterior apical and inferior scar with an anteroapical aneurysm (Figure 3). A bipolar voltage map of the LV revealed extensive voltage abnormalities involving the inferior septal, basal, and apical anterior and lateral walls, which were consistent with ICE findings (Figure 3). Late potentials were present in large portions of the scar and at least 7 VT morphologies were induced spontaneously or with catheter manipulation, requiring extensive substrate modification. ICE allowed for enhanced anatomical characterization, particularly aneurysm extension, areas of potential scar, and regions of myocardial thinning. Although transthoracic echocardiogram is a useful noninvasive method for diagnosis of LV aneurysms, further noninvasive studies, such as cardiac magnetic resonance, are often necessary for improved detection and characterization, particularly in patients with equivocal echocardiographic findings. ICE, on the other hand, provides very detailed, direct, and real-time anatomic evaluation in such cases to facilitate mapping and ablation. ICE can detail specific reference points within the neck of the aneurysm by characterizing the inflexion point between the aneurysm and normal tissue. Constant catheter monitoring during mapping and ablation is critical in these cases to avoid myocardial perforation, as extensive areas of myocardial thinning within the aneurysm are typically seen. Furthermore, these patients are

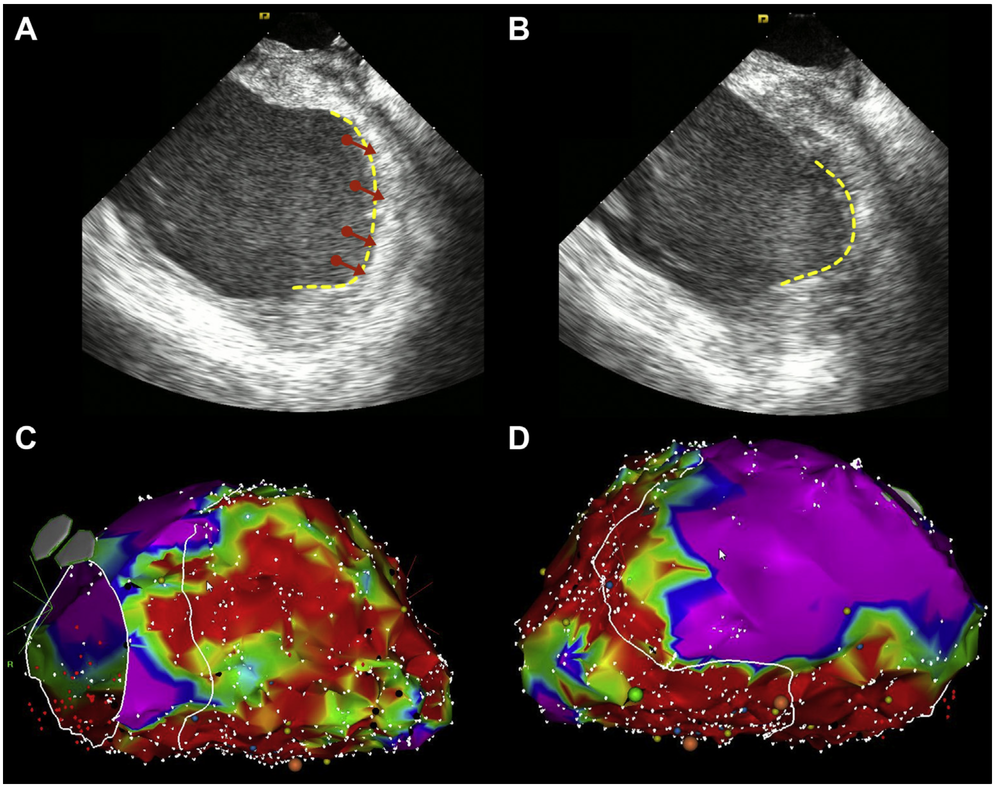

Figure 3 **A, B:** Intracardiac echocardiography (ICE) illustrating a large anterior apical (*arrows*) and inferior scar with an anteroapical aneurysm (*yellow lines*); **C, D:** Voltage mapping revealed extensive inferior septal, basal and apical anterior and lateral scar, with low voltage and diffuse late potentials consistent with ICE findings (**C:** right superolateral view [septal]; **D:** left inferolateral view).

at increased risk of LV apical thrombus and ICE can provide a detailed evaluation of this region, considering the anatomical proximity obtained when positioned in the RV, which is directly across from the apex.

Case 4: Scar integration

A 49-year-old man with prior inferior myocardial infarction and preserved LV function recurred with sustained VT after a previous ablation. ICE showed preserved LV function with basal inferolateral hypokinesis corresponding to a large echodense area that involved the mid-myocardium and epicardium. This area of suspected scar was reconstructed using the mapping system software for ICE integration (CARTOSOUND; Biosense Webster) (Figure 4). Endocardial voltage mapping revealed a moderate area of abnormal bipolar voltage with larger unipolar abnormalities in the basal inferolateral region. VT was induced and detailed mapping (activation and pace map) suggested an epicardial circuit. Epicardial access was subsequently obtained and high-density voltage mapping demonstrated abnormal basal inferolateral voltage underlying the region previously identified by ICE. Activation and pace-mapping identified critical components of the VT circuit and extensive ablation in this area rendered the patient noninducible. The use of ICE in this case had a major role in defining substrate location and provided a visual aid for strategic mapping and ablation that ultimately resulted in a successful outcome.

Case 5: Localization of epicardial substrate and catheter guidance

A 76-year-old man with a history of coronary artery disease was referred for ablation of recurrent VT. ICE revealed a basal inferolateral LV scar at the level of the anterolateral PM with a predominant epicardial component (Figure 5). Voltage mapping revealed abnormal endocardial bipolar and extensive unipolar abnormalities in this region. The patient remained inducible after endocardial ablation; therefore, epicardial access was performed revealing extensive voltage abnormalities opposite to the endocardial area of interest where the VT isthmus was identified. Ablation in this site eliminated the clinical VT. This case highlights several important uses of ICE, including location of the VT substrate including site of the heart involved (basal and predominant epicardial), as well as accurate and real-time visualization of the ablation catheter, specifically in the epicardial space where feedback is not always optimal by the usual indirect data currently available—particularly important to visualize the catheter tip against the epicardial surface.

Discussion

The 5 cases presented here illustrate the adjuvant role of ICE for characterization of ischemic VT substrate, a role that is

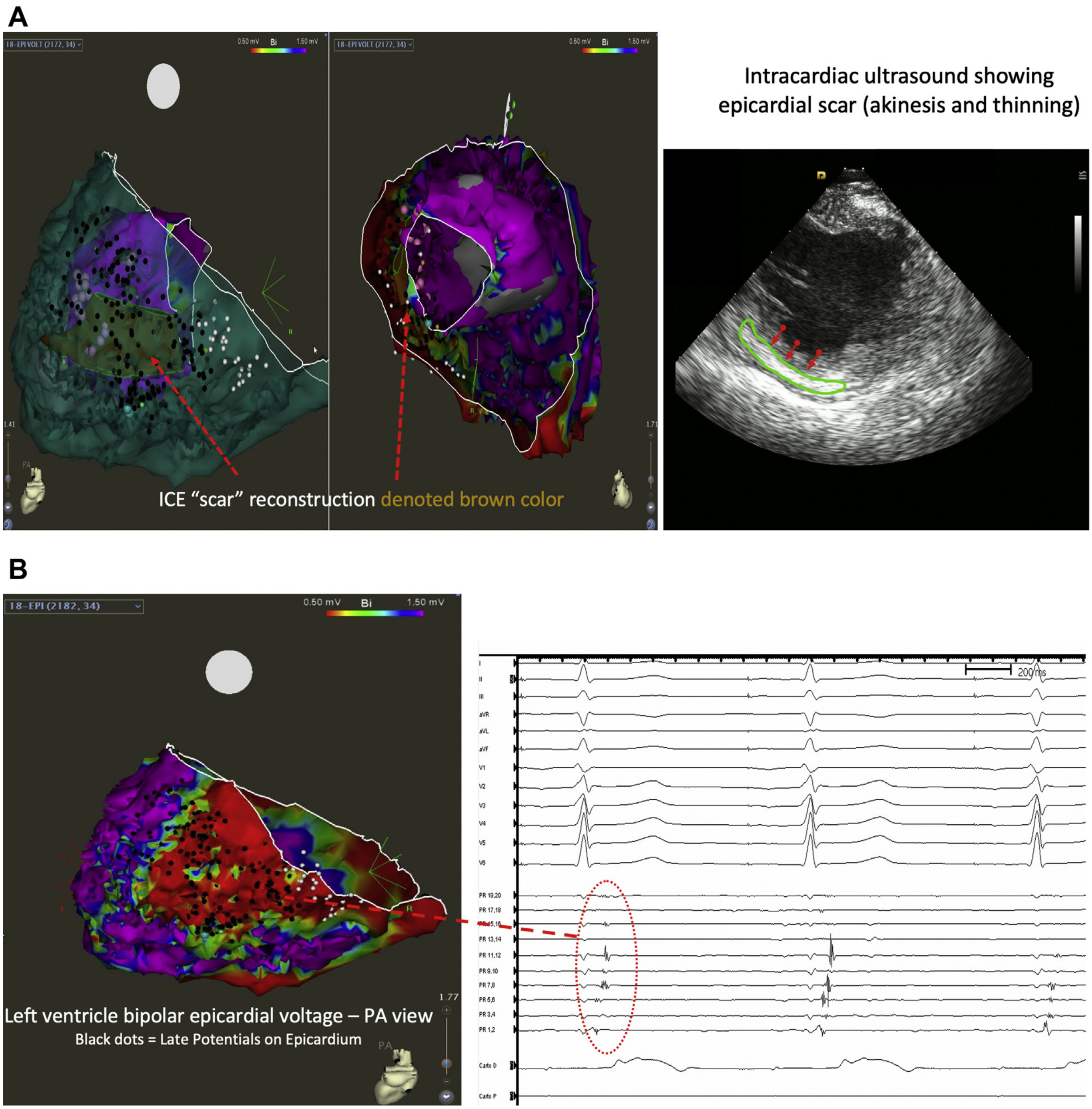

Figure 4 **A:** Intracardiac echocardiography (ICE) demonstrated basal inferolateral hypokinesis corresponding to a large echodense area (*red arrows, green demarcation*). This area of suspected scar was reconstructed using the mapping system software for ICE integration within the voltage map (*brown region*). **B:** High-density epicardial voltage map demonstrated basal inferolateral scar with late potentials underline the region previously identified by ICE.

likely to become more relevant as the resolution of the imaging systems continue to improve.

A recent Heart Rhythm Society consensus document stated that ICE may be useful for assessment of substrate during VT ablation (class IIb),[4] and previous studies have supported this recommendation.[2,5-7] For instance, Bunch and colleagues[6] studied the correlation between ICE imaging and voltage-defined scar in 18 patients with structural heart disease (83% ischemic), with a total of 248 wall segments analyzed. ICE showed good correlation with electroanatomic mapping in 86% of the segments and was more accurate than transthoracic echocardiography. Most importantly, ICE accuracy was higher in the basal segments and ischemic etiology. Hussein and colleagues[2] conducted a similar study in 22 patients with scar-related VT (45% ischemic) using quantitative measures of tissue signal intensity and distribution of signal, as a measure of tissue heterogeneity. The study showed that voltage-defined scar zones had increased signal intensity compared to border zones and normal myocardium, and border zones were more likely to have heterogeneous densities compared to normal myocardium. Software-based color enhancement of areas with signal intensity $\geq$137 SIU (signal intensity units) allowed identification of the VT substrate in all 15 patients with voltage-defined scars. Bala and

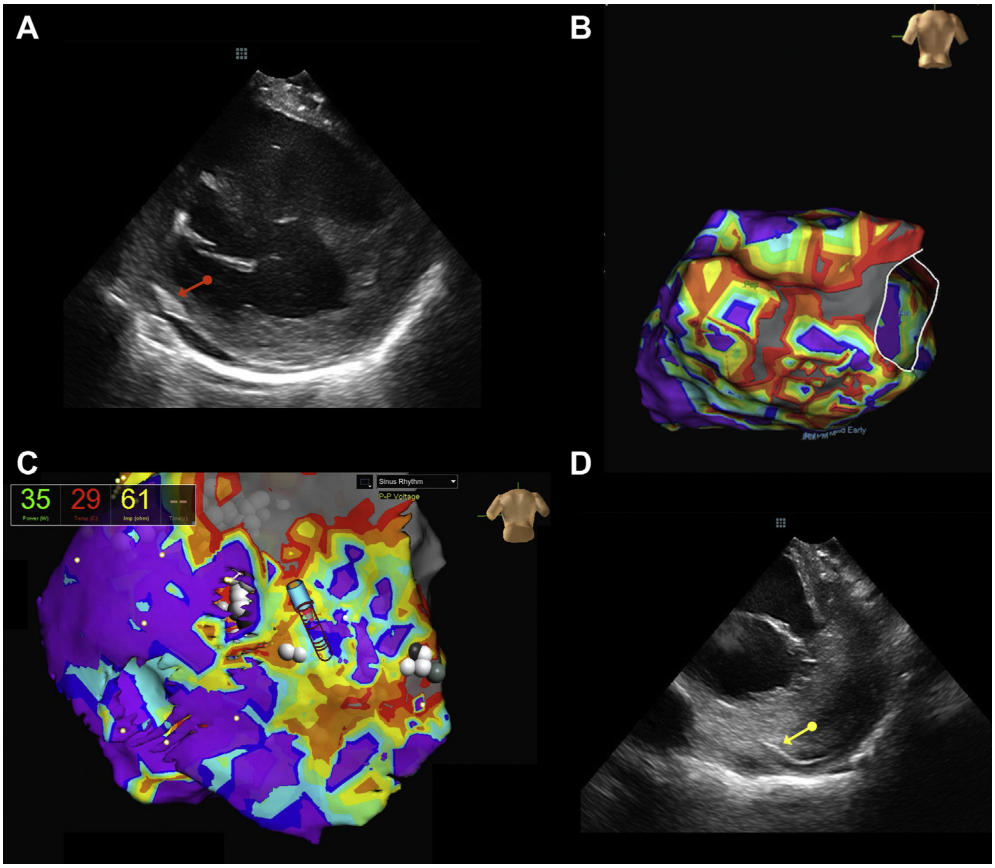

Figure 5 **A:** Intracardiac echocardiography (ICE) illustrating a basal inferolateral left ventricular scar at the level of the anterolateral papillary muscle with a predominant epicardial component (*red arrow*). **B:** Voltage map revealed abnormal endocardial bipolar and extensive unipolar abnormalities in this region. **C, D:** Epicardial voltage map revealing extensive voltage abnormalities opposite to the endocardial area of interest where the ventricular tachycardia (VT) isthmus was identified. Ablation in this site eliminated the clinical VT (**D** shows position of the ablation catheter in the epicardial space, *yellow arrow*).

colleagues[7] also demonstrated that ICE imaging was useful in identifying abnormal epicardial substrate in patients with nonischemic cardiomyopathy who underwent endo-epicardial mapping. In more than half of these patients ICE was also able to identify mid-myocardial echogenicity that correlated with areas of intramural delayed enhancement on magnetic resonance imaging.

Whether the routine use of ICE in the context of VT ablation may translate into improved efficacy and safety outcomes is more difficult to answer. No randomized studies are available. However, a propensity-matched study using MarketScan and Medicare databases analyzed the outcomes of 1324 patients with structural heart disease who underwent VT ablation with and without ICE (662 patients in each group; more than 400 patients with ischemic cardiomyopathy after propensity match).[8] The authors found that the risk of VT-related readmission after 12 months was 24% lower (18.13% vs 22.51%; $P < .05$) and the risk of repeat VT ablation was 30% lower (14.35% vs 19.34%; $P = .02$) among patients in the ICE group compared with the non-ICE group. The rates of complications in this dataset were low overall and did not differ significantly between the 2 groups.

In our view, the main highlights regarding the role of ICE in assessment of ischemic VT substrate, as detailed in each of the presented cases, can be summarized in the next points:

(1) Myocardial hyperechogenicity associated with hypokinesis/akinesis and thinning that corresponds to a coronary territory is the hallmark of ischemic VT substrate identified by ICE and shows good correlation with voltage and electrogram abnormalities on electroanatomic mapping.
(2) ICE can accurately visualize the 3-dimensional distribution of layered endocardial, mid-myocardial, and epicardial substrates.
(3) ICE can facilitate the identification of scar "protected" by endocavitary structures (ie, PMs), requiring an epicardial approach for successful ablation.

(4) ICE-based substrate identification and characterization (location, transmurality, etc) are useful to formulate a mapping and ablation strategy.
(5) ICE provides valuable real-time feedback on catheter-tissue contact to guide accurate signal processing that would reflect on enhanced voltage maps and information regarding lesion formation; it not only shows that we are delivering appropriate and transmural lesions but also gives the operator crucial information to avoid steam pops and myocardial perforation.

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