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SUPPLEMENT PAPER

Localization of premature ventricular contractions from the papillary muscles using the standard 12-lead electrocardiogram: a feasibility study using a novel cardiac isochrone positioning system

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Aims The precise localization of the site of origin of a premature ventricular contraction (PVC) prior to ablation can facilitate the planning and execution of the electrophysiological procedure. In clinical practice, the targeted ablation site is estimated from the standard 12-lead ECG. The accuracy of this qualitative estimation has limitations, particularly in the localization of PVCs originating from the papillary muscles. Clinical available electrocardiographic imaging (ECGi) techniques that incorporate patient-specific anatomy may improve the localization of these PVCs, but require body surface maps with greater specificity for the epicardium. The purpose of this report is to demonstrate that a novel cardiac isochrone positioning system (CIPS) program can accurately detect the specific location of the PVC on the papillary muscle using only a 12-lead ECG.

Methods and results Cardiac isochrone positioning system uses three components: (i) endocardial and epicardial cardiac anatomy and torso geometry derived from MRI, (ii) the patient-specific electrode positions derived from an MRI model registered 3D image, and (iii) the 12-lead ECG. CIPS localizes the PVC origin by matching the anatomical isochrone vector with the ECG vector. The predicted PVC origin was compared with the site of successful ablation or stimulation. Three patients who underwent electrophysiological mapping and ablation of PVCs originating from the papillary muscles were studied. CIPS localized the PVC origin for all three patients to the correct papillary muscle and specifically to the base, mid, or apical region.

Conclusion A simplified form of ECGi utilizing only 12 standard electrocardiographic leads may facilitate accurate localization of the origin of papillary muscle PVCs.

Keywords Electrocardiographic imaging • Non-invasive • Electrocardiographic imaging • Papillary muscles premature ventricular contraction localization

Introduction

Catheter ablation is an effective therapy for treatment of symptomatic premature ventricular contractions (PVCs). Prior to the ablation procedure, the targeted anatomic ablation site is estimated using qualitative descriptions of the standard 12-lead ECG waveforms.[1,2] These qualitative descriptions often yield poor localization of the PVC origin to the cardiac anatomy.[3] In particular, the localization of the arrhythmic origin in the papillary muscles has limitations.[4] Electrocardiographic imaging (ECGi), using a patient-specific model

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What's new?

- The combination of an ECG-vector based approach and electrocardiographic imaging (ECGi) techniques improves the localization of premature ventricular contractions.
- Premature ventricular contractions originating from the papillary muscles can be localized to different regions of the papillary muscles using the novel ECG-vector approach of the cardiac isochrone positioning system.

of the heart, may enhance the location accuracy of the PVC origin. Recently, ECGi has been successfully applied in clinical research to determine the origin of outflow tract PVCs[3] and complex ventricular activation.[5,6] However, these ECGi methods only localize to the epicardium of the heart. Consequently these programs were not designed to locate PVCs from the papillary muscles. Recently, a cardiac isochrone positioning system (CIPS) has been introduced to localize the PVC origin to any region of the myocardial anatomy.[7] The purpose of this study was to test the hypothesis that CIPS could localize PVCs originating from a papillary muscle. The 12-lead ECG from three patients was used by CIPS to localize the origin of ventricular activation originating from either the base, mid, or apex of the papillary muscle area.

Methods

Patient selection

Two females (57 and 80 years) and one male (32 years), who underwent radiofrequency ablation of symptomatic idiopathic PVCs were included in the study (*Table 1*). Each patient signed an informed consent and the study was approved by the UCLA Institutional Review Board (#14-000837).

Patient-specific model

Cardiac isochrone positioning system uses a patient-specific cardiac and torso model derived from MRI and patient-specific electrode positions derived from a 3D Kinect camera. For all three patients, the morphing software 'CIPS anatomy' was used to reconstruct MRI-based anatomical models of heart, lungs, and thorax,[8] with the posterior and anterior papillary muscles incorporated in the heart model.

The electrode positions in the model need to be accurately determined to reduce localization errors of the PVC origin.[9] Just prior to starting the ablation procedure, the Kinect camera and experimental software (Pkinect, Peacs BV, Arnhem, The Netherlands) were used to capture an image of the electrode positions on the chest wall. This experimental software has not been validated, but the Kinect camera has already been used with patients,[10,11] the error made by the camera is <5 mm. The 3D images were then registered to the patient-specific model of the patient (*Figure 1*). The registered image allowed the accurate positioning of the electrode positions on the reconstructed thorax model.

The 12-lead ECG

Standard 12-lead ECGs sampled at 977 Hz were recorded during the ablation procedure using Cardiolab, GE. This system stores the visualized, filtered signal data. The clinical ECGs containing a PVC were exported to a USB and then exported to the CIPS. A representative PVC of the clinical ECG waveforms was selected for each patient. Fiducial points, i.e. onset and end QRS, were determined manually. Subsequently the ECG was baseline corrected between two successive QRS onsets. No additional filtering was applied to any of the used ECG signals, i.e. the

Table 1 Patient characteristics, gender, age, weight, chest circumference, and ejection fraction (EF)

Patient	Gender	Age	Weight kg	Chest circumference (mm)	EF (%)
1	F	57	60	902	50
2	M	32	96	1049	58
3	M	28	64	887	60

None of the patients had a history of myocardial infarction.

Table 2 Comparison between the localization of ablation site from the electro-anatomical maps and the origin of the PVCs based on CIPS on the papillary muscles (PAP)

Patient	Location ablation site		PVC localization by CIPS
1	Posteromedial PAP	PVC 1	Posteromedial PAP (mid)
2[a]	Anterolateral PAP	PVC 1	Anterolateral PAP (apex)
	Anterolateral PAP	PVC 2	Anterolateral PAP (base)
3	Anterolateral PAP	PVC 1	Anterolateral PAP (apex/mid)
	Anterolateral PAP	PVC 2	Anterolateral PAP (mid)
	Anterolateral PAP	PM1	Anterolateral PAP (mid)
	Anterolateral PAP mid	PM2	Anterolateral PAP (mid)

[a]The term anterolateral papillary muscle is used, as mentioned in the EP report, although it would be more correct to call it the posterior papillary muscle.

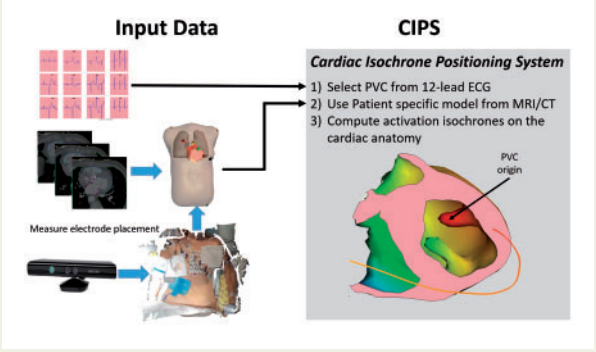

Figure 1 Cardiac isochrone positioning system overview; Input to the system are (1) The 12-lead ECG, (2) the MRI for patient specific model reconstruction, and (3) the 3D image to localize the ECG electrodes. These three inputs are used by CIPS to localize the PVC origin.

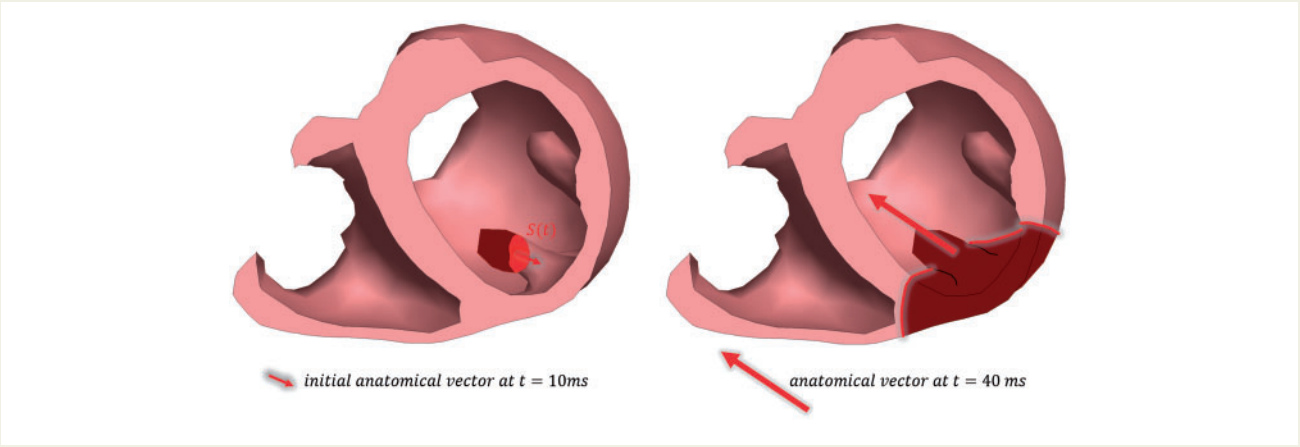

Figure 2 Activation wave front, indicated in light red, originating from the apex of the papillary muscle $S(t)$ at $t = 10$ ms and $t = 40$ ms. At 10 ms the initial anatomical vector points from apex to the base of the papillary muscle, but at 40 ms a significant part of the ventricular apex is already activated. The resulting anatomical vector points now from apex to base of the left ventricle, i.e. in the opposite direction.

un-augmented nine signals V_R, V_L, V_F, V_1–V_6 referenced to the Wilson central terminal.

Premature ventricular contraction localization: the cardiac isochrone positioning system

Cardiac isochrone positioning system is based on the myocardial activation estimation methods developed over the past decade in Nijmegen.[12–14] A major improvement of this ECGi method was the introduction of the myocardial distance function to test many cardiac activation patterns.[15] The fastest route algorithm[16] is an adaptation of the myocardial distance function used to simulate the heterogeneous nature of the ventricular activation. In the previous work the measured ECG was compared with the simulated ECG.[14,17,18] Using this system, the simulated activation originating from a ventricular position that generated the best match between simulated and measured ECG was selected as the PVC origin.[7] In this study the same components are used, but instead of comparing simulated and measured ECGs, the ECG-derived vector direction is compared with the anatomical vector direction. Several methods exist to transfer the 12-lead ECG into a VCG x, y, z signal.[19] None of these methods is able to take the heart orientation—the source—and lead position—the sensors—into account. Within the CIPS frameworks this information is available.

The ECG-derived vector ($\overrightarrow{V_{ecg}(t)}$) at time t of the QRS is determined by

(1) testing the position of vector at any node of the ventricular mesh (v_{pos}); and then
(2) adding the ECG value at time t ($ecg_{lead}(t)$) multiplied by the normalized vector between this position and the lead position of the ECG electrode.

The Wilson central terminal was used for all signals, i.e. only the un-augmented leads VR, VL, VF, and V1–6 were used to compute the ECG-derived vector at time t.

The anatomical vector is derived from the simulated isochrones starting from v_{pos}. Each isochrone represents a 3D surface within the myocardium at the moment of depolarization. The depolarization moves through the myocardium and consequently this moving 3D surface S has a direction. For each time instant this 3D surface can be represented by a single vector; a mean anatomy derived vector at time t (see *Figure 2*). This vector is gives the average direction of the wave front at time t. For the current algorithm only the angle between the anatomical vector, $\overrightarrow{V_{anatomy}(t)}$, and the ECG-vector, $\overrightarrow{V_{ecg}(t)}$, is used. When both vectors at time t are pointing in the same direction, i.e. when the angle $\alpha(t)$ between the two vectors at time t is small, the more likely it is the PVC is originating from the node that produced the $\overrightarrow{V_{anatomy}(t)}$. The angle $\alpha(t)$ between the two vectors at time t can be computed by

$$\alpha(t) = \cos^{-1}\left(\frac{\overrightarrow{V_{anatomy}(t)} \cdot \overrightarrow{V_{ecg}(t)}}{\left|\overrightarrow{V_{anatomy}(t)}\right|\left|\overrightarrow{V_{ecg}(t)}\right|}\right)$$

For the localization of the PVC origin three angles have been computed for each node on the heart geometry (v_{pos}): (i) the initial ($t = 30$ *ms*) after onset QRS, (ii) the mid-QRS vector ($t = 0.5 \times$ *QRS duration*), and (iii) the terminal QRS vector ($t = 0.8 \times$ *QRS duration*). The minimum of the sum of the two angles α, representing the mid-QRS and terminal QRS determine the global region of the PVC or stimulus origin. Within this area the minimal initial difference angle α is used to accurately locate the PVC or stimulation origin position.

Ablation procedure

Activation mapping was performed with a single-point irrigated mapping catheter (ThermoCool, Biosense Webster, Diamond Bar, CA, USA). Electroanatomic mapping was performed to guide localization (CARTO, Biosense Webster). The earliest site of activation was ablated up to 50 W, with temperature limit of 45°C. Intracardiac echocardiography was used to image the papillary musclesand to confirm contact with the ablation catheter.

Results

Three patients undergoing electrophysiological mapping and ablation of symptomatic PVCs originating from the papillary muscles were

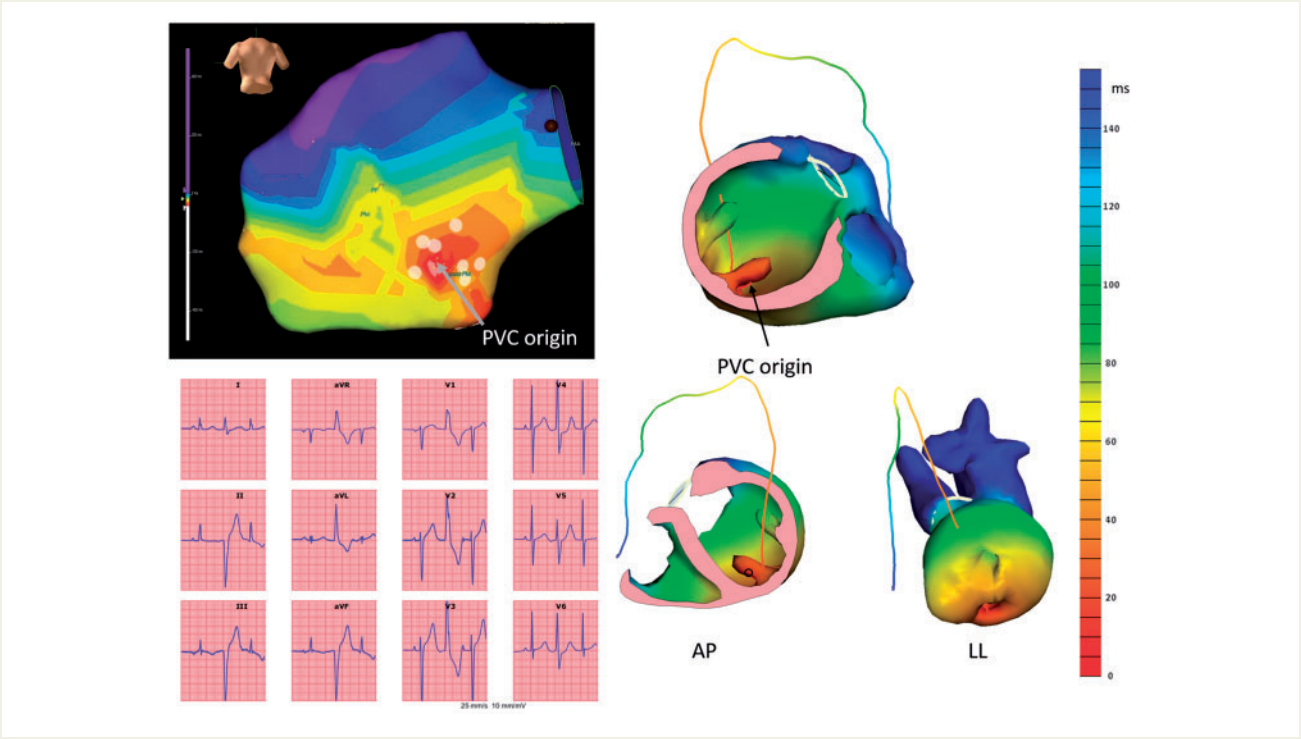

Figure 3 Results for Patient 1. Left panel: The NAVX electro-anatomical map of the PVC. Middle panel: The isochrones and derived PVC origin as localized by the CIPS. The coloured line is the CIPS vector trajectory, starting in the posteromedial papillary muscle, moving towards the apex (pink line) subsequently showing dominant activation going in the superior-anterior direction ending in the right RVOT region. Right panel: the 12-lead ECG as used by CIPS. All CIPS results are shown in AP view. The black circle indicates the CIPS localization of the activation origin.

studied (*Table 1*). Both the electro-anatomical maps and the clinical EP mapping were used as the gold standard for the 12-lead localization. One was identified with non-ischaemic cardiomyopathy, the other two patients had no cardiac pathology; no scar tissue was detected in any of the patients. The electro-anatomical mapping systems have limitations to visualize thepapillary muscles, as shown in *Figures 2–4*.

In each of the CIPS figures the vector trajectory derived from the ECG is shown. The trajectory starts from the localized PVC origin to the position where the activation wave ends. This trajectory is shown as a coloured line, where the line colours are the same as used in drawing the isochrones on the ventricular myocardium.

Patient 1 showed a PVC originating from the basal part of the posteromedial papillary muscle (*Figure 3*). The CIPS localized the PVC close to the posterior basal part of the papillary muscle, visualized as the start of CIPS vector trajectory originating from this area (red line).

Patient 2 showed two different PVC morphologies as shown as blue and red lines in the 12-lead ECG (*Figure 4*). Differences in QRS morphologies were predominantly found in the precordial leads V1, V5, and V6. PVC 1 was localized by CIPS to the apex of the anterior papillary muscle as also shown by the Carto electro-anatomical map. PVC 2 was localized to the base of the same papillary muscle. The deeper Q-wave in V1 of PVC 1 compared with PVC 2 may support the distinction between apical and basal parts of the papillary muscle by CIPS.

Patient 3 showed two different PVC morphologies, and two different pace maps were recorded, one from the mid-part of the papillary muscle and one from the mid-position of the papillary muscle (*Figure 5*). For Patient 3 the position of the ablation lesions and for the mid-superior pacing position were confirmed with an intracavitary echo (ICE) image,[20] see *Figure 6*, Pace map 2. The lesions, indicated as the white areas in the ICE image, are located in the mid-portion of the papillary muscle, the same region where CIPS localized the PVC origin from the 12 lead.

Discussion

Our pilot study suggests that the CIPS was able to localize PVCs to different parts of bothpapillary muscles. The CIPS localizes the PVC origin to any of the nodes of the patient-specific ventricular model. Thus, CIPS is able to localize the PVC to any position on the papillary muscle (see *Table 2* and *Figures 3–6*). The improved vector-based CIPS method compares the direction of the ECG-derived vector, the vector cardiogram (VCG), and the anatomical-based vector derived from computed activation sequences. The method does not take into account the amplitude of this ECG-derived VCG. This approach eliminates several modelling errors involved in the previously described equivalent dipole layer-based method, where the simulated ECG was correlated to the measured ECG.[7,14] The simulated ECG used the same fastest route-based activation sequences,[16] but the simulation of

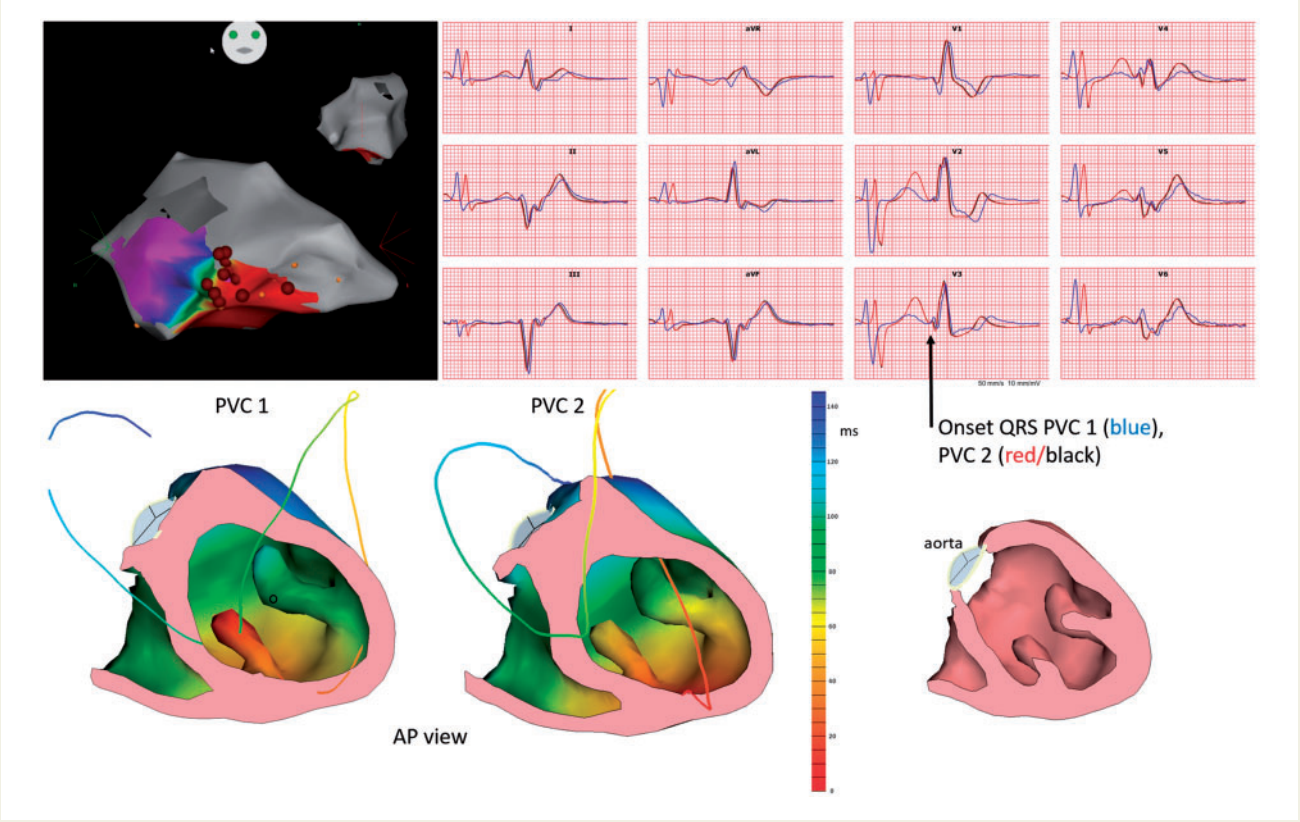

Figure 4 Results for Patient 2. Top-left panel: the CARTO electro-anatomical map of the PVC. Top-right panel: the 12-lead ECG of PVC 1 and 2 as used by CIPS. Bottom-left panels: the isochrones and derived origin of two PVCs as localized by CIPS. The coloured line is the CIPS vector trajectory, starting at the tip of the anterior papillary muscle (PVC 1) or the base of the same papillary muscle (PVC 2), and subsequently showing dominant activation going in the superior-posterior direction ending at the base of the RVOT for the first PVC, and left lateral for the second PVC. Bottom-right panel: AP view of a cross-section of the ventricles. Notice that both papillary muscles are in the same plane. Anterior or posterior papillary muscle classification does apply to both papillary muscles as both papillary muscles are in the same AP plane. All CIPS results are shown in AP view. The black circle indicates the CIPS localization of the activation origin.

the ECG inherently has additional modelling errors, e.g. volume conductor errors that transform the activation waves into ECG signals.

As in other studies,[21–23] a limitation of our study is the inability to determine the exact location of the PVC focus on the papillary muscle. Consequently, the exact location of the origin of the PVC on the papillary muscle could not be determined from the electro-anatomical activation maps obtained for Patients 1 and 2. For Patient 3, however, an ICE image was obtained. This image shows the location of the scar tissue caused by the ablation, and can thus provide confirmation of the localization of the PVC origin and pacing site by CIPS (see *Figure 6*). For future studies, ICE may be used as a gold standard to localize the PVC origin to the papillary muscles.[24] Intracavitary echo will be able to localize the ablation region and might also be used to localize the position of the catheter on the papillary muscle. However, the current state of the technology will not permit a quantitative comparison between the CIPS results and the catheter position or ablation area, because the distance on the echo images requires calibration to enable measurements in millimetres.

The vector-based CIPS algorithms rely on two components: (i) the anatomical vector, derived from the cardiac anatomy and the assumption of a homogeneous propagation activation wave using the fastest route algorithm,[16] and (ii) the computation of the initial vector of the 12-lead ECG, which can be difficult to detect due to noise or the characteristics of the applied filters in the case the raw ECG signals are not available. In this study the raw ECG signals were not available, because the ECGs stored by the Cardiolab system (GE) were filtered and sometimes even clipped. Such filters can make it difficult to localize stimulation sites as the filters can create large pacing artefacts (often >0.1 mV) in the ECG, interfering with the initial part of the QRS. The papillary muscle cases demonstrate this, as the amplitude of the initial QRS is often <0.1 mV, as shown in the ECGs in *Figures 3–5*. This needs to be taken into consideration when recording the ECG, because most clinical algorithms to localize PVCs use the complete QRS waveform, whereas the localization of the PVC origin in the CIPS algorithm is determined by the comparison of the initial ECG and the anatomical vector direction. For the initial part of the ventricular activation the single vector is an accurate model. Once a significant part of the myocardium is activated both the assumption underlying fastest route algorithm as well as the single vector representation of the complex 3D activation front might not

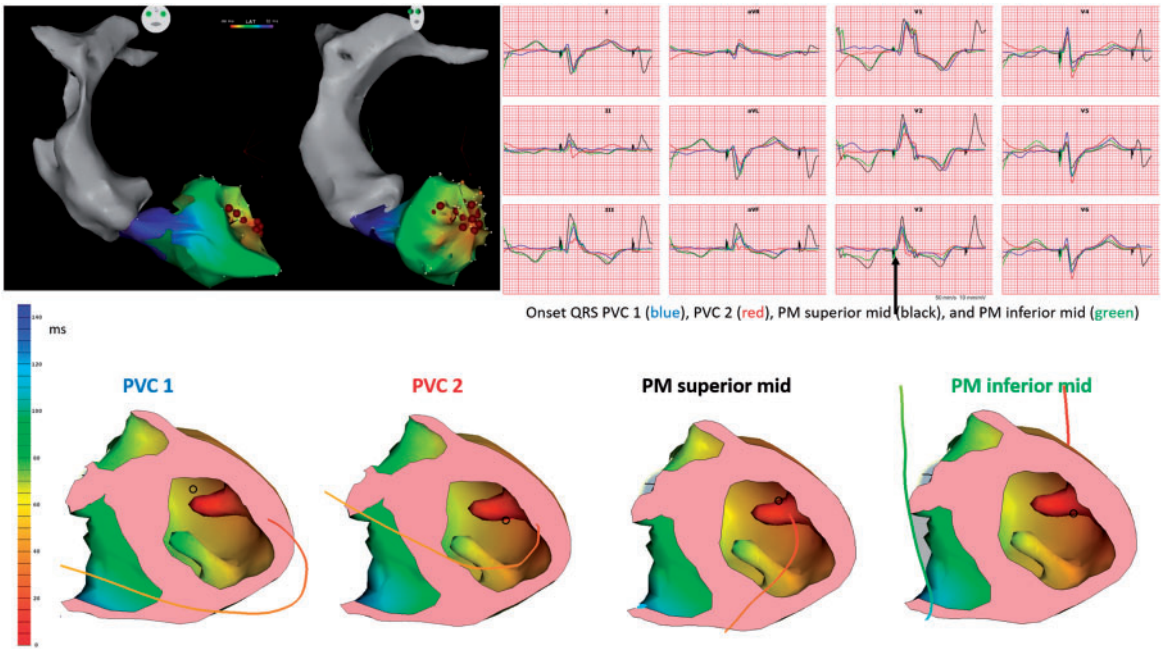

Figure 5 Results for Patient 3. Top-left panel: the CARTO electro-anatomical map of the PVC. Top-right panel: the 12-lead ECG of PVC 1 and 2 as well as two pace maps (PM), one at the mid/apex of the papillary muscle and one from the mid-papillary muscle. Bottom-left panels: the isochrones and derived origin of two PVCs and two PM as localized by CIPS. The coloured line is the CIPS vector trajectory, starting at the superior mid of the anterior papillary muscle (PM1), respectively the inferior mid-papillary muscle. For PVC 2 this is inferior mid, PM1 superior mid, and for PM2 posterior mid. All CIPS results are shown in AP view. The black circle indicates the CIPS localization of the activation origin.

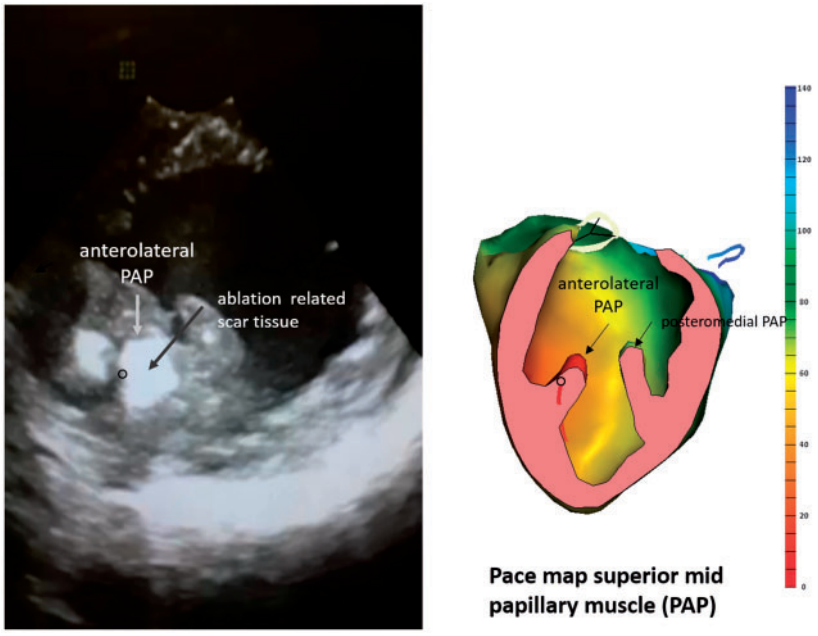

Figure 6 Intra-cavitary echo image (left) with the patient-specific ventricular model with the CIPS-estimated isochrones (right). The black circle indicates the CIPS localization of the activation origin, the mid-segment of the anterolateral papillary muscle. The heart model has been rotated such that it agrees with the orientation of the ICE image.

adequately represent the full complexity of the ventricular activation. This is most probably the case for patients with scar-related VTs whereas in the current approach no scar area was modelled. Further modelling and clinical studies are needed to improve accuracy of this vector-based method for patients with scar involvement.

Limitations

The number of patients in this study is limited, only for one situation the PVC origin was located on the anterolateral papillary muscle, all other cases were related to the posteromedial papillary muscle. Nonetheless, this study demonstrates the feasibility of the fundamental principles on which the system operates, in which the anatomical positions of the papillary muscles in the patient-specific heart model play an important role. The exact location on the papillary muscles was very difficult to determine accurately, as putting a catheters against this cardiac structure already moved the muscle. We have relied on the description of the physician executing the ablation procedure for two of the three cases. Using ICE, however, the localization of the PVC origin was feasible because it allows the visualization of scar tissue in combination with the muscle anatomy.

Conclusions

This study of this novel vector-based ECGi method using only the standard 12-lead ECG may improve the localization of the PVC origin the apical, mid, or basal part of thepapillary muscles.

Conflict of interest: Peter M van Dam is the co-owner of Peacs BV, Arnhem, the Netherlands.

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