Role of High-Resolution Image Integration to Visualize Left Phrenic Nerve and Coronary Arteries During Epicardial Ventricular Tachycardia Ablation

Seigo Yamashita, MD, PhD; Frédéric Sacher, MD, PhD; Saagar Mahida, MBChB, PhD; Benjamin Berte, MD; Han S. Lim, MBBS, PhD; Yuki Komatsu, MD; Sana Amraoui, MD; Arnaud Denis, MD; Nicolas Derval, MD; François Laurent, MD; Michel Montaudon, MD, PhD; Mélèze Hocini, MD; Michel Haïssaguerre, MD, PhD; Pierre Jaïs, MD, PhD; Hubert Cochet, MD, PhD

Background—Epicardial ventricular tachycardia (VT) ablation is associated with risks of coronary artery (CA) and phrenic nerve (PN) injury. We investigated the role of multidetector computed tomography in visualizing CA and PN during VT ablation.

Methods and Results—Ninety-five consecutive patients (86 men; age, 57±15) with VT underwent cardiac multidetector computed tomography. The PN detection rate and anatomic variability were analyzed. In 49 patients undergoing epicardial mapping, real-time multidetector computed tomographic integration was used to display CAs/PN locations in 3-dimensional mapping systems. Elimination of local abnormal ventricular activities (LAVAs) was used as ablation end point. The distribution of CAs/PN with respect to LAVA was analyzed and compared between VT etiologies. Multidetector computed tomography detected PN in 81 patients (85%). Epicardial LAVAs were observed in 44 of 49 patients (15 ischemic cardiomyopathy, 15 nonischemic cardiomyopathy, and 14 arrhythmogenic right ventricular cardiomyopathy) with a mean of 35±37 LAVA points/patient. LAVAs were located within 1 cm from CAs and PN in 35 (80%) and 18 (37%) patients, respectively. The prevalence of LAVA adjacent to CAs was higher in nonischemic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy than in ischemic cardiomyopathy (100% versus 86% versus 53%; P<0.01). The prevalence of LAVAs adjacent to PN was higher in nonischemic cardiomyopathy than in ischemic cardiomyopathy (93% versus 27%; P<0.001). Epicardial ablation was performed in 37 patients (76%). Epicardial LAVAs could not be eliminated because of the proximity to CAs or PN in 8 patients (18%).

Conclusions—The epicardial electrophysiological VT substrate is often close to CAs and PN in patients with nonischemic cardiomyopathy. High-resolution image integration is potentially useful to minimize risks of PN and CA injury during epicardial VT ablation. (Circ Arrhythm Electrophysiol. 2015;8:371-380. DOI: 10.1161/CIRCEP.114.002420.)

Key Words: ablation techniques ■ coronary vessels ■ diagnostic imaging ■ epicardial mapping ■ phrenic nerve ■ ventricular tachycardia

Catheter ablation is an effective treatment strategy for recurrent and drug-refractory and scar-related ventricular tachycardia (VT). Potential strategies for VT ablation include targeting of the critical isthmus of the VT circuit during sustained VT1–3 or substrate-based ablation during sinus rhythm (SR), particularly in patients with poorly tolerated or noninducible VT.4,5 Targeting local abnormal ventricular activities (LAVAs) has recently been proposed as an effective approach for scar-related VT ablation.7

In a proportion of VT patients, an epicardial approach is required to fully eliminate the arrhythmogenic substrate. Although epicardial VT ablation has been proven helpful, particularly in nonischemic cardiomyopathy (NICM), which is typically associated with epicardial scar,6 its effectiveness is limited by the risk for damaging vulnerable structures, such as coronary arteries (CAs) and phrenic nerve (PN).6,7 According to current guidelines, coronary angiography is recommended previous and after epicardial radio frequency (RF) deliveries.12 However, it cannot be repeated before every RF application.

Real-time high-resolution image integration of multidetector computed tomography (MDCT) is emerging as an important adjunctive imaging technique for characterization of the arrhythmogenic substrate in patients with scar-related VT.13,14 MDCT has also the advantage of allowing sub millimetric...
WHAT IS KNOWN

- Epicardial ablation is efficient in the management of ventricular tachycardia refractory to endocardial ablation, but exposes to coronary artery and phrenic nerve injury
- Image integration was shown to be useful to provide an accurate localization of scar during catheter ablation procedures
- Multidetector computed tomography can assess cardiac anatomy with high spatial resolution.

WHAT THE STUDY ADDS

- Multidetector computed tomography can localize the left phrenic nerve in most patients, and its course over the left ventricular free wall is highly variable between patients.
- Segmentations of the left phrenic nerve and coronary arteries can be integrated in 3-dimensional mapping systems to assist epicardial ablation.
- The epicardial substrate of ventricular tachycardia is more often close to coronary arteries and left phrenic nerve in nonischemic than in ischemic cardiomyopathy.
- When adjacent to coronary arteries or phrenic nerve, the epicardial substrate of ventricular tachycardia can be ablated from the endocardium, although this strategy is more likely to succeed in ischemic and arrhythmogenic right ventricular cardiomyopathy than in nonischemic cardiomyopathy.

reconstruction of CAs and PN. In this study, we assessed the ability of MDCT to allow safe ablation procedures by displaying high-resolution reconstruction of CAs and PN, and sought to define the anatomic relationship of CAs and PN locations with the electrophysiological substrates (LAVAs) according to the VT pathogenesis in patients undergoing epicardial VT ablation for scar-related VT.

Methods

Study Population

Ninety-five consecutive patients with drug-refractory and scar-related VT were enrolled in this study. VT pathogenesis was categorized as ischemic cardiomyopathy (ICM), NICM, or arrhythmogenic right ventricular cardiomyopathy (ARVC). All patients underwent preprocedural MDCT. The PN detection rate and anatomic variability was assessed by extra stimulation with 2 drive trains (600 and 400 ms) with peak-to-peak amplitudes of 0.5 to 1.5 mV and <0.5 mV were used to define the low voltage and the dense scar zone, respectively. After creating a complete endocardial mapping geometry, including the CS, left atrium (with 4 pulmonary veins and left atrial appendage), (3) persistence of clinical VT after ablation from the endocardial aspect, (4) absence of contraindications to epicardial access such as previous cardiac surgery. After LV access was attained, a 50 U/kg heparin bolus was administered intravenously, aiming for an activated clotting time >250 s during procedure. Endocardial and epicardial electroanatomical mapping was performed during SR using CARTO3 or NavX systems. An irrigated catheter with a 3.5 mm-tip (Navistar Thermocool; Biosense Webster) or a multipolar high-density mapping catheter (PentaRay; Biosense Webster) was used for mapping, and peak-to-peak amplitudes of 0.5 to 1.5 mV and <0.5 mV were used to define the low voltage and the dense scar zone, respectively. After creating the voltage map during SR, inducibility was assessed by extra stimulation with 2 drive trains (600 and 400 ms) with ≤3 extrastimuli decremented to 200 ms from the right ventricular apex.

Image Integration

After creating a complete endocardial mapping geometry, including the CS, left atrium (with 4 pulmonary veins and left atrial appendage), mitral annulus, LV endocardium, and aortic root, point-based registration with the imaging model was initiated using a first set of coupled points on the aforementioned landmarks. Of note, the rhythm during the acquisition of the 3D geometry was the same as the one during preprocedure MDCT acquisition in all patients (1 atrial fibrillation, 11 pacing, and 37 SR). The patient with atrial fibrillation was successfully ablated with a 50 U/kg heparin bolus was administered intravenously, aiming for an activated clotting time >250 s during procedure. Endocardial and epicardial electroanatomical mapping was performed during SR using CARTO3 or NavX systems. An irrigated catheter with a 3.5 mm-tip (Navistar Thermocool; Biosense Webster) or a multipolar high-density mapping catheter (PentaRay; Biosense Webster) was used for mapping, and peak-to-peak amplitudes of 0.5 to 1.5 mV and <0.5 mV were used to define the low voltage and the dense scar zone, respectively. After creating the voltage map during SR, inducibility was assessed by extra stimulation with 2 drive trains (600 and 400 ms) with ≤3 extrastimuli decremented to 200 ms from the right ventricular apex.

Image Processing

Image processing was performed by using a dedicated in-house software solution (MUSIC software; Liryc—Université de Bordeaux/Inria—Sophia Antipolis, France). Myocardial and vascular structures were segmented on the MDCT series. Segmented images were used to generate 3D surface meshes of the endocardium, epicardium, CAs, coronary sinus (CS), and PN. Myocardial structural substrate was also segmented, defined as areas of wall thinning <5 mm in ICM and NICM, or myocardial hypodensity in ARVC. The resulting 3D objects were imported into 3D-mapping systems (EnSite NavX; St. Jude Medical, St. Paul, MN; or CARTO3; Biosense Webster, Diamond Bar, CA). All imaging models were available for real-time integration during the subsequent electrophysiological procedures.

Trans-axial images were reviewed by 2 observers in consensus to evaluate the detection rate of PN on MDCT data. When detected, the course of the left PN in the mediastinum and along the left ventricular (LV) free wall was analyzed as follows: the minimum distance to the left atrial appendage tip was measured and the location of the PN along the LV free wall was expressed in percentage of base to apex distance, as measured on a 4-chamber reconstruction. The detection and anatomic variability of left PN on MDCT are illustrated in Figure 1.
versus 3D mapping; 65±15 beats per minute versus 64±14 beats per minute; \(P=0.89\). In case the NavX system was used, field scaling was first applied to the geometry (to compensate for variations in impedance between the heart chambers and venous structures), then the acquired geometry was fused to the MDCT model with 4 to 8 landmarks (LV apex, aortic root, mitral valve, CS, and pulmonary veins). Second, fusion points were applied additionally at sites of local mismatch between the 2 superimposed geometries (Figure 2). This process molded the created geometry surface onto the MDCT surface and bended the 3D navigation space within the geometry, thereby improving the accuracy of image registration.16 When using CARTO platform, registration was refined using automatic surface registration. In addition, a 6F-decapolar catheter (Xtrem, Sorin, France; or Dynamic, BARD Electrophysiology) was placed into the CS as distally as possible to partly enter an anterior or lateral vein. This catheter was used as a spatial reference to detect a potential shift of the map, thereby monitoring the accuracy of MDCT registration throughout the procedure (Figure 2).

Ablation

In patients with inducible and hemodynamically tolerated VT, ablation was performed using conventional activation and entrainment mapping techniques. After restoration of SR, substrate-based ablation targeting LAVA was performed. In case of noninducible or poorly tolerated VT, only LAVA-based ablation was performed. LAVAs include all identified poorly coupled signals, and are defined as (1) sharp, high-frequency ventricular potentials distinct from the far-field ventricular electrogram, (2) potentials occurring after the far-field ventricular electrogram in SR, and (3) potentials that may display double or multiple components separated by low-amplitude signals or an isoelectric interval. When LAVAs were buried in the QRS complex and fused with the far-field ventricular electrogram, pacing maneuvers were performed to distinguish LAVA from far-field ventricular electrogram.7 RF power was applied at a maximum of 50 W endocardially and 35 W epicardially with a temperature limit of 42°C for 60 s. Low RF power (25 W) was restricted to sites close to the conduction system or CAs. On the basis of previous reports from Sacher et al17 demonstrating larger lesions because of catheter parallel orientation during epicardial ablation, power delivery during epicardial ablation was limited to 35 W. The end point of the procedure was the elimination of LAVA and noninducibility of clinical VT by extra stimuli with the same protocol as before ablation.

The management of epicardial LAVAs was performed as follows: as a rule, RF energy was always delivered first endocardially, while monitoring LAVAs from the epicardium with a multipolar high-density mapping catheter, to minimize the risk of extracardiac damage. When epicardial LAVAs were within 1 cm from PN on MDCT
segmentation, PN capture was confirmed by pacing with 25 mA/2 ms. In case endocardial ablation failed to eliminate epicardial LAVAs, 100 to 300 mL of saline were infused in the pericardium before endocardial ablation and RF was delivered after confirming the loss of phrenic capture during pacing. When LAVAs were within 5 mm from the CAs on the integrated image, a coronary angiography was performed, and a decision was made whether to deliver RF energy epicardially. The presence or absence of CA and PN injury were assessed by monitoring 12-lead ECG (ST-T change) and diaphragmatic movement.

Statistical Analysis
Quantitative data were expressed as the mean±SD when normally distributed, and median (interquartile range) otherwise. Comparison between groups was analyzed by using unpaired Student t test or Wilcoxon rank-sum test based on the distribution of the values. The χ² test was used to analyze categorical variables, unless the expected values in any cells were <5, in which case Fisher exact test was used. Comparisons of continuous variables about pathogeneses were made using 1-way ANOVA or Kruskal–Wallis test based on the distribution of the values. Logistic regression analysis was used to identify significant predictors of PN detection on MDCT. All tests were 2-tailed, and P<0.05 was considered significant. Statistical analyses were performed using the MedCalc software package, version 11.2 (MedCalc Software, Mariakerke, Belgium).

Results
Patient Characteristics
The clinical characteristics of the patient cohort are summarized in Table 1. The mean age of total population was 57±15 years. The VT pathogenesis was ICM in 54 of 95 (57%), NICM in 23 of 95 (24%), and ARVC in 18 of 95 (19%). Forty-nine patients had an epicardial approach and a PN visible on MDCT (18 ICM, 17 NICM, and 14 ARVC). Image integration was successfully performed in all patients and the mean surface registration error in the CARTO system was 3.9±1 mm. In cases in which the NavX system was used 36±19 points were used for image integration.

PN Detection and Anatomic Variability on MDCT
The left PN was detected in 81 of 95 (85%) patients on MDCT. The clinical characteristics associated with PN detection are shown in Table 1. Univariable analysis showed that PN was more likely to be detected when patients were older and when epicardial fat was present over the LV free wall. At multivariable analysis, the presence of epicardial fat was an independent predictor for detecting PN (odds ratio, 10.9; 95% confidence interval, 2.39–50.03; P=0.003). All detected PNs were located close to the tip of the left atrial appendage (9±6 mm; range, 1–29 mm). In contrast, the course of the PN along the LV free wall was highly variable (65±15% of base to apex distance; range, 20% to 88%).

Mapping Results in Patients With Both the Endocardial and Epicardial Approach
In the 49 patients with both the endocardial and epicardial mapping, the mean number of mapping points during endocardial and epicardial electroanatomical mapping were 424±267 and 706±557, respectively. Endocardial and epicardial LAVAs were observed in 30 (61%) and 44 (90%) patients (endocardium/epicardium, 16 [89%/15 [83%] in ICM; 5 [29%/15 [88%] in NICM; and 9 [64%]/14 [100%] in ARVC). The mean number of LAVA points/patient was 22±24 on the endocardium, and 35±37 on the epicardium. Two patients (4%) demonstrated no LAVA in both the endocardium and the epicardium (1 NICM and 1 ICM). On the endocardium, the low-voltage area and the prevalence of LAVA was higher in patients with ICM as compared with NICM and ARVC (71 [50–110] versus 20 [2–36] versus 36 [21–62] cm²; P<0.001; 89% versus 29% versus 64%; P<0.001). On the epicardium, the low-voltage area and the prevalence of LAVA were similar between VT pathogeneses (Table 3; Figures 3 and 4).

Distribution of LAVA With Respect to CAs and PN
Epicardial LAVAs were observed within 1 cm from CAs in 35 of 44 (80%) patients. The prevalence of LAVA adjacent to CAs was higher in patients with NICM and ARVC than in those with ICM (NICM versus ARVC versus ICM, 100% versus 86% versus 53%; P=0.005). The CA involved was predominantly the right CA in patients with ARVC, and the left circumflex artery in patients with NICM. Epicardial LAVAs were observed within 1 cm from PN in 18 of 44 (37%) patients. The prevalence of LAVAs adjacent to PN was higher in NICM than in ICM and ARVC (NICM versus ICM versus ARVC, 93% versus 27% versus 0%; P<0.001) (Table 3; Figures 3 and 4).

Ablation
Of the 49 patients with endocardial and epicardial mapping, 47 exhibited LAVAs, which were located on the epicardium in 44 patients. Epicardial ablation was performed in 37 of 49 (76%) patients. Before epicardial ablation, coronary angiography was performed in 11 of 37 (30%) patients because of the proximity of CAs. In these patients, the distance between coronary and catheter tip was not found to be different on the 3D registered image versus on coronary angiography (3.7±1.9 mm versus 5.1±3.4 mm, respectively; P=0.36). Saline infusion was performed in 6 of 37 (16%) patients because of the proximity of PN. In all the 6 patients, phrenic pacing confirmed the PN location as displayed from MDCT segmentation. Of the 47 patients with LAVA, complete LAVA elimination in both the endocardium and the epicardium was achieved in 31 patients (66%). Of note, complete LAVA elimination was only achievable in 44% (7/16) of patients with NICM (Table 3). Of the 16 patients with incomplete LAVA elimination, the proximity

Table 1. Patients’ Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total Population (n=95)</th>
<th>Endocardium/Epicardium Population (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age, y</td>
<td>57±15</td>
<td>53±15</td>
</tr>
<tr>
<td>Men</td>
<td>86 (91%)</td>
<td>45 (92%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²²</td>
<td>27±4.3</td>
<td>27±4.4</td>
</tr>
<tr>
<td>ICM</td>
<td>54 (57%)</td>
<td>18 (40%)</td>
</tr>
<tr>
<td>NICM</td>
<td>23 (24%)</td>
<td>17 (34%)</td>
</tr>
<tr>
<td>ARVC</td>
<td>18 (19%)</td>
<td>14 (28%)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>37±15</td>
<td>41±15</td>
</tr>
<tr>
<td>Previous VT ablation</td>
<td>15 (16%)</td>
<td>11 (22%)</td>
</tr>
<tr>
<td>ICD/CRTD</td>
<td>76 (80%)</td>
<td>41 (84%)</td>
</tr>
</tbody>
</table>

ARVC indicates arrhythmogenic right ventricular cardiomyopathy; CRTD, cardiac resynchronization therapy defibrillator; ICD, implanted cardioverter defibrillator; ICM, ischemic cardiomyopathy; LVEF, left ventricular ejection fraction; NICM, nonischemic cardiomyopathy; and VT, ventricular tachycardia.
of CAs and PN was involved in 12 (75%). Of the 44 patients with epicardial LAVAs, incomplete elimination because of the proximity to CAs was observed in 8 patients (18%) (7 NICM and 1 ARVC) (Table 4; Figure 5). This proximity (<5 mm) was confirmed by coronary angiography in all the 8 patients. In 3 patients, a proximity between an LAVA site and a CA was found on the registered 3D image, but coronary angiography demonstrated that the catheter tip was >5 mm away from CA, resulting in possible LAVA elimination from the epicardium. Furthermore, in 4 patients (9%, all NICM), LAVAs close to PN could not be eliminated, despite saline or air insufflation of the pericardium (because of persisting phrenic capture). However, of the 35 patients with epicardial LAVA close to CAs, LAVAs could be eliminated by endocardial ablation in 15 (43%, 6 ICM and 9 ARVC). Of the 18 patients with epicardial LAVA close to PN, LAVAs could be eliminated by endocardial ablation in 3 of 18 patients (17%, 3 ICM) (Table 4; Figure 5). Moreover, LAVA close to CAs in ICM and ARVC could be eliminated from endocardial aspect more frequently than that in NICM (Table 4). Minor complications (200–300 mL of pericardial

Table 2. Patients’ Characteristics in Patients With and Without PN Detection and Predictors for Detecting PN by Multidetected Computed Tomography

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PN Detection (n=81)</th>
<th>No PN Detection (n=14)</th>
<th>Univariable Analysis</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
</tr>
<tr>
<td>Patient age, y</td>
<td>58±14</td>
<td>49±18</td>
<td>1.04 (1.00–1.08)*</td>
<td>0.037*</td>
</tr>
<tr>
<td>Male sex</td>
<td>74 (91%)</td>
<td>12 (86%)</td>
<td>1.76 (0.33–9.51)</td>
<td>0.53</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26±5.8</td>
<td>27±4.0</td>
<td>1.05 (0.90–1.22)</td>
<td>0.54</td>
</tr>
<tr>
<td>ICM</td>
<td>32 (51%)</td>
<td>7 (64%)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>NICM</td>
<td>15 (24%)</td>
<td>2 (18%)</td>
<td>1.64 (0.30–8.86)</td>
<td>0.57</td>
</tr>
<tr>
<td>ARVC</td>
<td>16 (25%)</td>
<td>2 (18%)</td>
<td>1.75 (0.33–9.41)</td>
<td>0.51</td>
</tr>
<tr>
<td>Epicardial fat over LV wall</td>
<td>62 (77%)</td>
<td>3 (21%)</td>
<td>12.0 (3.02–47.39)*</td>
<td>0.001*</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>4 (4.9%)</td>
<td>2 (14%)</td>
<td>0.31 (0.05–1.89)</td>
<td>0.24</td>
</tr>
<tr>
<td>ICD/CRTD</td>
<td>67 (83%)</td>
<td>9 (64%)</td>
<td>2.66 (0.77–9.15)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

ARVC indicates arrhythmogenic right ventricular cardiomyopathy; CI, confidence interval; CRTD, cardiac resynchronization therapy defibrillator; ICD, implanted cardioverter defibrillator; ICM, ischemic cardiomyopathy; LV, left ventricle; NICM, nonischemic cardiomyopathy; OR, odds ratio; and PN, phrenic nerve.
Table 3. Clinical Variables According to Ventricular Tachycardia Pathogenesis

<table>
<thead>
<tr>
<th></th>
<th>ICM (n=18)</th>
<th>NICM (n=17)</th>
<th>ARVC (n=14)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age, y</td>
<td>66±9</td>
<td>48±10</td>
<td>42±15</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Men</td>
<td>17 (94%)</td>
<td>15 (88%)</td>
<td>13 (93%)</td>
<td>0.79</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>30 (23–37)</td>
<td>40 (25–45)</td>
<td>60 (59–65)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Previous ablation</td>
<td>1.2±0.5</td>
<td>1.1±0.3</td>
<td>1.8±1.1</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Endocardium

<table>
<thead>
<tr>
<th></th>
<th>Mapping points, n/pt</th>
<th>Low-voltage area, cm²</th>
<th>Presence of LAVA</th>
<th>LAVA points, n/pt</th>
<th>LAVA &lt;1 cm from CAs</th>
<th>LAVA &lt;1 cm from PN</th>
<th>Epicardial ablation</th>
<th>Coronary angiography</th>
<th>RF time (endocardium), min</th>
<th>RF time (epicardium), min</th>
<th>Total procedure time, min</th>
<th>Complete LAVA elimination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>392 (247–523)</td>
<td>71 (50–110)</td>
<td>16 (89%)</td>
<td>21 (15–34)</td>
<td>8/15 (53%)</td>
<td>4/15 (27%)</td>
<td>12 (67%)</td>
<td>0 (0%)</td>
<td>23 (17–32)</td>
<td>5 (2–12)</td>
<td>295 (240–320)</td>
<td>12/17 (71%)</td>
</tr>
<tr>
<td></td>
<td>230 (187–449)</td>
<td>20 (2–36)</td>
<td>5 (29%)</td>
<td>13 (7–19)</td>
<td>15/15 (100%)</td>
<td>14/15 (93%)</td>
<td>15 (88%)</td>
<td>9 (53%)</td>
<td>9 (5–24)</td>
<td>22 (13–29)</td>
<td>310 (250–375)</td>
<td>7/16 (44%)</td>
</tr>
<tr>
<td></td>
<td>486 (301–845)</td>
<td>36 (21–62)</td>
<td>9 (64%)</td>
<td>12 (10–15)</td>
<td>12/14 (86%)</td>
<td>0/14 (0%)</td>
<td>10 (71%)</td>
<td>2 (14%)</td>
<td>29 (14–42)</td>
<td>13 (8–15)</td>
<td>300 (280–300)</td>
<td>12/14 (86%)</td>
</tr>
</tbody>
</table>

Endocardium

|                        | 16 (89%)            | 5 (29%)              | 21 (15–34)     | 12 (10–15)       | 5 (2–12)         | 295 (240–320)    | 12/17 (71%)       |

Discussion

Main Findings

This study demonstrates the feasibility of using MDCT to detect CAs/PN and reports on the distribution of PN/CAs with respect to the electrophysiological VT substrate (LAVA) in the most common VT pathogenesis. Specifically, we demonstrate that (1) MDCT accurately delineates the PN in a high proportion of patients, (2) the prevalence of epicardial LAVA sites close to PN and CAs is higher in patients with NICM as compared with those with ICM, and (3) high-resolution integrated imaging is valuable in minimizing risk of PN and CA damage during epicardial VT ablation, regardless of the underlying cause of VT.

Visualization of the Left PN on MDCT

In this study, MDCT could detect the PN and describe its course in 85% of patients. The patients in whom the PN could be detected were likely to be older and to exhibit epicardial fat over the LV free wall. A previous study had reported that the PN could be identified in 74% of patients, and that the patients in whom PN was not detected were older and more commonly women. The discrepancy between our results and those from this previous study may be explained by the differences between the studied populations, and particularly by the limited number of women included in this study (9/74). The relationship with epicardial fat has not been previously studied, and could be explained by the increased contrast between PN and surrounding tissues in the presence of fat. Indeed, the visualization of the PN is easier when low-fat densities surround it as opposed to when no fat is present over the LV wall, because in the latter the PN can be confounded with the adjacent myocardium. To our knowledge, this study first report on the anatomic variability of left PN course along the LV. Our results show that the PN is consistently close to the tip of the left atrial appendage, and therefore, this location is of value to detect the proximal part of its course along the heart. In contrast, the course of the PN along the LV free wall was found to be highly variable, with some patients exhibiting a basal course, and others exhibiting an apical course. This interpatient variability substantiates the use of noninvasive imaging to characterize the course of the left PN and its relationship with the structural substrate of VT before epicardial ablation.

Relationship Between LAVA and CAs/PN

This study demonstrates a clustering of epicardial LAVAs in the vicinity of CAs in NICM and ARVC, and in the vicinity of the PN in NICM, which is consistent with several previous reports. Garcia et al. reported that the critical isthmuses of VT circuits in ARVC are more commonly found in a triangle at the basal lateral aspect of the right ventricle, adjacent to the right CA. In nonischemic DCM, abnormal electrograms are known to be more frequent on the basal lateral aspect of the LV, and therefore, often close to the left circumflex artery. As for PN location, Fan et al. reported that 7 of 10 (70%) patients with NICM exhibited phrenic capture within the low-voltage area, and stressed out the importance PN identification and protection before epicardial ablation. These results indicate that epicardial ablation in patients with NICM and ARVC is at higher risk of CAs and PN injury.

In ICM, the lower prevalence of LAVA adjacent to PN and CAs can be explained by the lower number of epicardial LAVA in this condition as compared with NICM and ARVC.
Indeed, the wavefront of necrosis during ischemia spreads from the endocardium to the epicardium, which results in more scar border zones and VT electrophysiological substrate on the endocardium. In addition, a relationship between LAVA location and PN is obviously mostly encountered when myocardial infarction is in the circumflex territory. Moreover, from a pathophysiological point of view, the coronary damage caused in the substrate vicinity should have less effect on cardiac function in patients with ICM because the territory is often already nonviable. For these reasons, the issue of CAs and PN damage during epicardial VT ablation may be less critical in ICM than in ARVC and NICM.

### Role of Real-Time CAs and PN Integration During Epicardial Ablation

The role of epicardial ablation for VT is expanding. Previous studies have reported acute CA injury, CA spasms, and CA occlusions during epicardial procedures. The use of coronary angiography and a safety distance of >5 mm between the CA and the ablation catheter tip are recommended. However, the introduction of substrate-based strategies has increased the amount of ablation during VT procedures, and it is simply not possible to perform coronary angiography before each epicardial RF delivery. Moreover, coronary angiography is associated with additional procedural risk and exposure to iodinated contrast. In this study, coronary angiography was performed before RF application only in case of a close proximity (<5 mm) with CAs as displayed by MDCT. Among patients who underwent angiography, we demonstrated a good correlation between coronary anatomy on angiography and on registered imaging. However, it is important to note that in 27% of cases who underwent angiography, image integration underestimated the distance between the ablation site and CAs. Furthermore, image integration is associated with substantial registration errors (3.9±1.1 mm in the CARTO system). Therefore, in patients with a proximity (<5 mm) to CAs on registered imaging, angiography remains desirable. Overall, MDCT imaging limited the use

### Table 4. Results of Ablation for LAVAs Close to CAs and PN

<table>
<thead>
<tr>
<th>Pathogenesis</th>
<th>ICM</th>
<th>NICM</th>
<th>ARVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>From CAs</td>
<td>From PN</td>
<td>From CAs</td>
<td>From PN</td>
</tr>
<tr>
<td>Elimination</td>
<td>&lt;1 cm</td>
<td>&lt;1 cm</td>
<td>&lt;1 cm</td>
</tr>
<tr>
<td>(6/8)</td>
<td>(3/4)</td>
<td>(0/15)</td>
<td>(0/14)</td>
</tr>
<tr>
<td>from endocardium</td>
<td>(75)*</td>
<td>(75)†</td>
<td>(0)*‡</td>
</tr>
<tr>
<td>Elimination</td>
<td>2/8</td>
<td>1/4</td>
<td>8/15</td>
</tr>
<tr>
<td>from epicardium</td>
<td>(25)</td>
<td>(25)</td>
<td>(53)</td>
</tr>
<tr>
<td>Incomplete elimination</td>
<td>0/8</td>
<td>0/4</td>
<td>7/15</td>
</tr>
<tr>
<td>from epicardium</td>
<td>(0)</td>
<td>(0)</td>
<td>(47)§</td>
</tr>
<tr>
<td>Minor/major complication</td>
<td>2/0</td>
<td>0/0</td>
<td>0/0</td>
</tr>
</tbody>
</table>

*P<0.001; †P=0.05; ‡P=0.001; §P=0.04.

In this study, the rate of elimination from endocardium/epicardium and incomplete elimination was compared between each pathogenesis. ARVC indicates arrhythmogenic right ventricular cardiomyopathy; CAs, coronary arteries; ICM, ischemic cardiomyopathy; LAVA, local abnormal ventricular activity; NICM, nonischemic cardiomyopathy; and PN, phrenic nerve.
of coronary angiography to only 22% (11/49) of epicardial procedures without complications related to CAs injury in this study. It is also important to note that in this study, 80% of patients had putative epicardial targets within 1 cm of CAs. This observation further highlights the importance of accurate delineation of coronary anatomy in patients undergoing epicardial ablation.

PN injury and subsequent diaphragmatic palsy is also a well-recognized complication during epicardial ablation. Although preprocedure MDCT is associated with additional radiation exposure, it is associated with many advantages compared with conventional techniques for delineating PN and CA and alternative imaging techniques, such as MRI. High output pacing was shown to accurately detect the left PN.9 However, epicardial pacing before each ablation is time-consuming, and the registration of PN course as identified on MDCT could help reducing the need for pacing in areas sufficiently far from MDCT-derived PN segmentation. In this study, the use of MDCT resulted in a limited number of pacing maneuvers (only performed in 24% of epicardial procedures). When proximity to PN is identified, the use of saline27 or air28 injection within the pericardium has been proposed to prevent PN damage. In this study, this strategy was not always successful and LAVAs close to PN could not be eliminated in 4 patients (8%, all NICM).

Finally, although MRI is an effective imaging technique, MDCT provides images with higher spatial resolution (<0.5 mm) than MRI, and is more suitable for detecting CAs and PN.

### Figure 5. Epicardial local abnormal ventricular activity (LAVA) close to a coronary artery in a 41-year-old man with postmyocarditis ventricular tachycardia (A)–(C) and epicardial LAVA elimination from endocardial ablation in arrhythmogenic right ventricular cardiomyopathy (ARVC) patient (same patient as in Figure 4B; D and E). Fluoroscopic image (A) and image integration in 3-dimensional mapping system (B) both show a close contact (red arrow) between the catheter tip demonstrating LAVA (C) and the left circumflex artery, preventing epicardial ablation in patient with postmyocarditis. D, Endocardial ablation is performed while monitoring LAVA elimination from the epicardium (red arrows in E) in patient with ARVC. AP indicates anterior–posterior; CS, coronary sinus; HDM, high-density mapping catheter; LCx, left circumflex artery; RAO, right anterior oblique; RF, radiofrequency; and RV, right ventricle.

### Strategy to Eliminate Epicardial LAVAs
In this study, the first strategy applied for the elimination of epicardial LAVAs was to attempt endocardial ablation while monitoring LAVA elimination from the epicardium. This strategy proved successful in most patients with ICM and ARVC, whereas it failed in all patients with NICM. This can be explained by the lower wall thickness encountered in ischemic scars and dysplastic right ventricular walls, as compared with the relatively preserved wall thickness in NICM.11,29 These findings support the use of endocardial ablation as a first line strategy in ICM and ARVC, epicardial ablation being required for resistant sites only, with the use of image integration to minimize the risk of CAs and PN injury. In patients with NICM, our results suggest that a combined endocardial and epicardial ablation approach may be required in most cases.

### Study Limitations
The main limitation of this study is related to its observational design. The effect of CAs/PN integration on patient outcome should be evaluated in a prospective and randomized fashion. Another potential limitation is the heterogeneity of VT pathogeneses in the group with NICM, which can include primitive and secondary dilated cardiomyopathies, granulomatosis, and myocarditis. However, we used NICM as a category because each of these pathogeneses would have been too rare to produce substantial results. Second, the 3D reconstruction of CAs from coronary angiography was not obtained in this study,
thus the accuracy of CA localization on integrated imaging could not be accurately assessed. We used the longest distance on 2D view among several views (left and right anterior oblique, cranial and caudal view) between the catheter tip and CA. To clarify this, accuracy animal studies should be conducted to analyze the localization of ablation lesions close to CA versus holosty

Conclusions

Real-time integration of PN and CAs during VT ablation is feasible with the use of MDCT. The epicardial substrate of VT is frequently adjacent to CAs and PN, particularly in patients with NICM. MDCT registration is useful to select the optimal strategy for VT ablation, minimizing the risk of CAs and PN injury.

Sources of Funding

This research was supported by Leducq Foundation (grant number: 09 CVD 03).

Disclosures

None.

References


Role of High-Resolution Image Integration to Visualize Left Phrenic Nerve and Coronary Arteries During Epicardial Ventricular Tachycardia Ablation

Seigo Yamashita, Frédéric Sacher, Saagar Mahida, Benjamin Berte, Han S. Lim, Yuki Komatsu, Sana Amraoui, Arnaud Denis, Nicolas Derval, François Laurent, Michel Montaudon, Mélèze Hocini, Michel Haïssaguerre, Pierre Jaïs and Hubert Cochet

_Circ Arrhythm Electrophysiol._ 2015;8:371-380; originally published online February 21, 2015; doi: 10.1161/CIRCEP.114.002420

_Circulation: Arrhythmia and Electrophysiology_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/8/2/371

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Arrhythmia and Electrophysiology_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Arrhythmia and Electrophysiology_ is online at: http://circep.ahajournals.org/subscriptions/