Ventricular Arrhythmias Arising from the Left Ventricular Outflow Tract below the Aortic Sinus Cusps: Mapping and Catheter Ablation via Transseptal Approach and Electrocardiographic Characteristics

Running title: Ouyang et al.; Ablating LVOT-VA via transseptal approach

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Abstract

**Background** - VA originating from the anterosuperior left ventricular outflow tract (LVOT) represents a challenging location for catheter ablation. This study investigates mapping and ablation of ventricular arrhythmias (VA) from anterosuperior LVOT via a transseptal approach.

**Methods and Results** - This study included 27 patients with symptomatic VA, in whom 13 patients had previous failed ablations. LVOT endocardial 3D-mapping via retrograde transaortic and antegrade transseptal approaches were performed. Previous ECG markers for procedure failure were analyzed. In all patients, earliest activation with low-amplitude potentials was identified at the antero-superior LVOT 5.1±2.8mm below the aortic cusp and preceded QRS onset by 39.5±7.7ms only via an antegrade transseptal approach using a ‘reversed S-curve’. In all patients, pace mapping failed to demonstrate perfect QRS morphology match. The anatomical location was below the left coronary cusp (LCC) in 16, below the LCC/right coronary cusp (RCC) junction in 8, and below the RCC in 3 patients. Radiofrequency (RF) energy resulted in rapid disappearance of VAs in all patients. ECG analysis showed aVL/aVR Q-wave amplitude ratios >1.4 in 7, III/II R-wave amplitude ratios >1.1 in 10, and Peak deflection index >0.6 in 11 patients. There were no complications or clinical VA recurrence during a mean follow-up of 8.4±2.5 months.

**Conclusions** - The anterosuperior LVOT can be reached via a transseptal approach with a reversed S-curve of the ablation catheter. The rapid effect from RF energy indicates that the VA is most likely located under the endocardium. Also, previous ECG markers for procedure failure need further investigation.

**Key words:** catheter, ablation, mapping, ventricular arrhythmia
Most ventricular arrhythmias (VA) in patients without structural heart disease originate from the right ventricular outflow tract (RVOT) or left ventricular outflow tract (LVOT)\(^1\). Catheter ablation in these anatomical areas has been established as an effective and curative therapy\(^1\)-\(^8\). In some cases, VA arises from an area in the LVOT located antero-superior to the aortic-mitral continuity (AMC), termed the left ventricular summit (LVS)\(^5\)-\(^6\). Ablation of this type of VA is still challenging. Epicardially, it is bound by the left anterior descending artery (LAD), left circumflex artery (LCX) and the distal part of the great cardiac vein (GCV)\(^9\). The anatomical region superior to the GCV has been previously described as an area inaccessible to catheter ablation, and the area inferolateral to the GCV as more accessible via epicardial ablation\(^9\). We sought to determine mapping, ablation and ECG characteristics of VA originating from the anterosuperior LVOT via an antegrade transseptal approach.

**Methods**

**Study Population**

In 2012-2013, 27 consecutive patients with symptomatic VAs and with ECGs suggestive of VAs arising from the anterosuperior LVOT underwent radiofrequency (RF) ablation at three centers: Thirteen patients at Asklepios Klinik St. Georg, Hamburg, 10 at the 1st Affiliated Hospital of Nanjing Medical University in Nanjing, and 4 at Guangdong Provincial People’s Hospital in Guangzhou.

All patients underwent physical examination, 12-lead ECG, 24-hour Holter monitor, and transthoracic echocardiogram (TTE) to assess left ventricular (LV) function prior to ablation. Transesophageal echocardiography was only performed to exclude left atrial thrombus in older patients due to potential risk of asymptomatic atrial fibrillation.
Electrophysiological Study

The study with both transaortic and transseptal approaches was approved by our institutional review committee and all patients provided written informed consent prior to the procedure. After withdrawal of anti-arrhythmic drugs (AAD) for at least 5 half-lives, all patients underwent electrophysiological evaluation under sedation with intravenous propofol at Asklepios Klinik in Hamburg in 4, and without sedation in the remaining 23 patients. Catheters were placed in the right ventricle via femoral veins and within the distal coronary sinus (CS) via femoral or left subclavian veins. Twelve-lead surface ECGs and intracardiac electrograms were recorded simultaneously by a digital multichannel system (EPMed, SJM), filtered at 30-400Hz for bipolar electrograms and at 0.05-400Hz for unipolar electrograms. If clinical arrhythmias failed to occur spontaneously, programmed stimulation was performed. The standard protocol consisted of ventricular stimulation at two basic drive cycle lengths with up to two extrastimuli, to a minimum coupling interval of 230ms. If VA was not inducible at baseline, intravenous isoproterenol infusion (2–5μg/min) was administered to provoke clinical arrhythmias.

3-D Mapping strategy of the cardiac chambers

In patients with frequent premature ventricular contractions (PVC) or ventricular tachycardia (VT), 3-D electroanatomical mapping was initially performed of the RVOT and GCV via the CS. LV access was achieved via a retrograde transaortic and antegrade transseptal approach in all patients. Transseptal puncture was performed through the antero-inferior fossa ovalis guided by fluoroscopy, slightly posterior to the mapping catheter placed in the non-coronary sinus cusp (NCC) (Figure 1A-B). In our experience, this approach facilitates access into the LV, in particular to the anterosuperior LVOT. Transseptal sheaths were continuously flushed with heparinized saline at 20ml/hour. During the procedure, unfractionated heparin was administered
to maintain activated clotting times between 250-300 seconds.

Electroanatomic mapping methodology has been previously described\textsuperscript{10}. In brief, mapping was performed using a steerable 7.5F, D-curve catheter with a 3.5mm irrigated-tip electrode (Navi-Star ThermoCool, Biosense Webster, Diamond Bar, CA, USA). Point-by-point mapping was performed to create anatomical maps of the RVOT and GCV via the CS. Earliest ventricular activation was annotated in each chamber. When GCV access was difficult, contrast medium was injected through the irrigated catheter tip to define the course of the CS and facilitate advancement into the GCV.

Complete anatomical mapping of the aortic root annotating the earliest ventricular activation in the RCC (right coronary sinus cusp) or LCC (left coronary sinus cusp) always preceded earliest ventricular activation obtained during LV mapping. Two important clinical reasons led to this strategy: 1) Anatomical distance between the aortic sinus cusp (ASC) and endocardial LVOT should theoretically be <12mm, unless myocardial hypertrophy is present on echocardiography before ablation. This value was arbitrarily chosen as myocardial thickness >12mm is considered hypertrophic. If the distance is >12mm, this indicates the anterosuperior LVOT was inadequately mapped; 2) During aortic root mapping, site of earliest ventricular activation in the RCC or LCC helps to locate the anatomical origin below the ASC during LV mapping.

LV mapping was performed initially via the transaortic approach. With this approach, LVOT access was generally difficult, particularly the anatomical area just below the right and left ASC. This was also demonstrated on 3-D mapping, with a large distance between the aortic root and LV. In contrast, LVS access below the ASCs can be achieved via the transseptal approach, using a reversed S-curve of the ablation catheter (Figure 2). Once the mapping catheter
was below the ASCs, clockwise and counter-clockwise rotation manipulates it toward the RCC and LCC, respectively (Figure 2 A-D). During the procedure, the time from the onset of the surface QRS morphology to the peak sharp deflection in a pre-defined lead was measured. Subsequently, all measurements of activation timing throughout the procedure was then measured from the onset of the ventricular activation to this peak sharp deflection of the surface ECG to identify the site of earliest activation. The timing from the onset of the ventricular activation to the onset of the QRS is then calculated. Earliest ventricular activation in the LVS was again annotated on 3-D electroanatomical mapping. If the overall site of earliest ventricular activation was found below the ASC, angiography was performed to identify the exact anatomical location. Thus, anatomical sites of VA origins were defined by a combination of aortic root/coronary angiography and 3-D mapping. In addition, distance between the site of successful ablation within the LVOT identified by the earliest activation during PVC/VA mapping and the closest portion of the ASCs was measured offline.

To visualize the local ventricular electrogram potentials, intracardiac electrograms were amplified, and sites of VA origins were identified by earliest ventricular activation on bipolar recordings during clinical VAs. In addition, pacemapping from bipolar electrodes was performed at sites of earliest ventricular activation. During pacemapping, the lowest pacing output (2-20mA) and pulse width (0.5-10ms) were used to capture the ventricular myocardium.

**Irrigated radiofrequency ablation**

Irrigated RF current was delivered in temperature-controlled mode, with maximum power of 40 Watts, temperature limit of 43°C and flush rate of 20ml/min\textsuperscript{11}. RF application was immediately stopped if catheter dislodgement occurred or if clinical PVC/VAs were still present 20 seconds after start of ablation. Time until maximum power and disappearance of clinical VAs were
recorded. A safety RF application, applying the same RF settings used during the initial
successful energy delivery was deployed in all patients. After successful ablation, intravenous
administration of isoprenolol and programmed stimulation were performed to re-provoke clinical
VAs.

**QRS Morphology on surface ECG during Clinical VAs**

Detailed analysis of clinical PVC/VAs was performed offline using either the EPMed System
(SJM) with a recording speed of 50-100mm/s, or 12-lead ECG with a recording speed of 25-
50mm/s.

The following parameters were analyzed during clinical PVCs or the first beat of VT: 1) QRS duration; 2) R-wave amplitudes of inferior leads (II, III, aVF) and R-wave amplitude ratio of lead III/II; 3) QS-wave amplitudes in leads aVL and aVR and the ratio of aVL/aVR; 4) Peak
deflection index (PDI) in inferior leads, defined as duration from QRS onset on surface ECG to
latest peak in the inferior leads/total QRS duration\(^\text{12}\). 5) Number and percentage of patients with
QS wave ratio of aVL/aVR >1.4\(^\text{13}\), with R-wave ratio of III/II >1.1\(^\text{9}\), and with PDI >0.6\(^\text{12}\). All
measurements were independently performed by three physicians.

**Procedure success and follow-up**

Ablation success was defined as; 1) absence of spontaneous or provoked clinical VAs at end of
procedure, and 2) absence of the latter on 48-hour ECG monitoring post-ablation off AADs. VA
burden was documented on 24-hour holter monitoring before and after ablation. TTE was
performed immediately before discharge, 3 and 6 months after ablation in all patients. Follow-up
was performed either by referring physicians or in outpatient clinics.

**Statistical analysis**

Continuous variables are expressed as mean ± standard deviation.
Results

Study population

Patient and clinical data are shown in Table 1. No structural heart disease was found except in 2 patients (7.4%), who had a history of coronary artery disease with no disease progression before ablation. No patient had LV hypertrophy on echocardiography. All patients were refractory to at least one AAD prior to ablation. A history of amiodarone therapy was documented in 2 (7.4%) patients, which was ineffective and stopped 6 months before ablation. Prior to the index procedure, 13/27 (48.1%) patients had failed ablation procedures (1 ablation attempt in 8, 2 attempts in 3, 3 attempts in 1, 4 attempts in 1 patient). Previously failed targets are shown in Table 1. In these 13 patients with failed ablation, only 3 patients had previously failed ablation attempts at AK St. Georg. Also, the failed ablations in the LVOT were performed with only the transaortic approach.

Mapping and Ablation

In 27 patients, frequent PVCs or short runs of VT were present during the entire procedure. Although there was a slight reduction in the frequency of PVCs in the 4 patients ablated with sedation, PVCs still occurred frequently. Therefore, intravenous isoprenolol was not administered before LV mapping.

In the retrograde transaortic maps, closest anatomical distance between the ASCs and LVOT was >12mm in all 27 patients (Figure 3 A-B). Complete LVS mapping was only achieved via transseptal approach (Figure 3 C-D). No area with pathological potentials and low amplitudes was found below the ASCs during sinus rhythm. On bipolar recording, earliest ventricular activation was identified in the LVOT, antero-superior to the AMC, preceding the QRS onset by 39.5±7.7ms during clinical VAs (Figures 4-5, table 2); whereas ventricular activation on unipolar
recordings demonstrated QS morphology with delayed activation compared to bipolar recordings (Figure 4). During sinus rhythm, a small atrial potential was always seen before the ventricular activation (Figure 5). Furthermore, prior to ablation, pacemapping was performed at the site of earliest ventricular activation, demonstrating mismatch of the QRS morphology compared to the clinical VA in all 27 patients (Supplemental figure).

3-D mapping and aortic angiography demonstrated the anatomical location of VAs were below the LCC in 16/27 (59.3%) (Figure 4 B), below the RCC/LCC junction in 8/27 (29.6%) (Figure 5) and below the RCC in 3/27 (11.1%) patients. Mean distance from the site of earliest ventricular activation in the LVOT identified via transseptal approach, to the closest portion of the ASC was 5.1±2.8mm. VA originating below the LCC had a mean distance to the LCC of 7.4±3.5mm, below the LCC/RCC junction and below the RCC of 3.8±0.9mm and 3.7±1.8mm, respectively (Table 2).

**Irrigated radiofrequency ablation**

RF energy utilized and clinical effects during RF ablation are shown in table 2. RF energy was applied only via transseptal approach in these 27 patients. No patient had RF-induced VA or vagal reaction during ablation. Mean time to clinical VA disappearance was 5.5±3 seconds, with mean maximum power of 38.5±5.8W (table 2). Time to maximum power at the site of VA origin was 12.1±7.5 seconds in temperature-controlled mode (table 2). The VAs were successfully abolished with a mean of 2.3±1.4 RF applications. No ST segment or T wave change was observed during ablation in any of the 27 patients. Procedure time was 127±57min with fluoroscopy time of 12.3±6.4 min.

During the ablation procedure, PVCs with a completely different morphology was rarely observed and were only seen in 2/27 patients, and were not targeted for ablation.
ECG Analysis

During clinical VA, RBBB morphology was present in 3/27 patients (11.1%), and in these patients VA origin was below the LCC (Figure 6 A). LBBB morphology with an early transition at V2-3 was seen in the remaining 24/27 patients (88.9%) (Figure 6 B-C). During clinical VA, no S-wave on V5 and V6 leads was seen in any patient. All patients presented with inferior axis and high R-waves in leads II, III and aVF, and deep Q-waves in aVL and aVR. Mean QRS duration was 157±24ms with PDI of 0.58±0.06.

Detailed analysis of inferior lead R-wave amplitudes and Q-waves in aVR and aVL, as well as III/II R-wave amplitude ratio >1.1, aVL/aVR Q-wave amplitude ratios >1.4 and PDI >0.6 are shown in table 3.

In summary, all patients had an inferior axis with high R-waves in leads II, III and aVF, and deep Q-waves in aVL and aVR. 19/27 patients (70.4%) had greater R-wave deflections in lead III compared to II, and of these 19 patients, 18 had VA origins below the LCC or LCC/RCC junction. A lead III/II R-wave amplitude ratio >1.1 was observed in 10/27 (37.0%) and aVL/aVR Q-wave amplitude ratio >1.4 was noted in 7/27 (25.9%) patients. A higher amplitude ratio was found in patients with VA origins below the LCC and LCC/RCC junction, and the lowest amplitude ratio was noted if the site of origin was below the RCC. In addition, PDI >0.6 was found in 11 (40.7%) patients, in whom VAs were located below the LCC in 8, below the LCC-RCC junction in 2 and below the RCC in 1 patient.

Follow up

No complications occurred during or after ablation procedures. During a mean follow-up of 8.4±2.5 months, no patients received AAD therapy. No clinical PVC/VA recurrence was seen on 48-hour holter monitor following ablation, while the mean PVC burden was 78±148/24h three
months after ablation. Furthermore, in patients with LVEF <50% before ablation, LVEF on TTE normalized 3 months post ablation in 4/5 patients, except in the patient with coronary artery disease.

**Discussion**

**Anatomical Consideration of LVOT**

A thorough understanding of LVOT anatomy is important for proper localization of the VA origin and facilitates catheter ablation. Spatially, the aortic root occupies a central location within the heart, with the LVS antero-superior to the aortic root. The anteriorly situated RVOT passes slightly superiorly and leftward relative to the aortic root. The conical-shaped RVOT is superior to the aortic valve (Figure 7). The LVOT consists of both muscular and fibrous portions\(^1,5\). This is in contrast to the RVOT, which is comprised entirely of myocardium. The septal portion of the LVOT, although primarily muscular, includes the membranous portion of the ventricular septum. The posterior quadrant of the LVOT consists of an extensive fibrous curtain that extends from the fibrous skeleton of the heart across the anterior leaflet of the mitral valve, and supports the aortic valve leaflets at the AMC. The lateral and anterior LVOT are again muscular structures\(^14\). Also, the aortic root is connected to the muscular ventricular septum, with the remaining one-third in fibrous continuity with the mitral valve anterior leaflet\(^2,14-16\). The RCC and anterior part of the LCC are connected with the ventricular musculature at their bases because the semilunar leaflets are hinged superiorly to the aortic wall but inferiorly to muscle\(^2,14-16\). The entire NCC does not come in contact with the LV myocardium. Therefore, the NCC is exclusively composed of fibrous walls, located between the right and left atria, immediately anterior to the interatrial septum, and is the most posterior of the 3 sinuses (Figure 3-5)\(^17\).
Epicardially, the LAD and LCX lie superior to the aortic portion of the LVOT and occupy the most superior portion of the LV (Figure 8 B-C, F), termed the LV summit by McAlpine. This region near the GCV and the anterior interventricular vein (AIV) is a major source of idiopathic VAs from the LV. Yamada et al describes that the LVS is bisected by the GCV into an area lateral to this structure and is accessible to epicardial ablation, and a superior region that is very difficult to ablate due to the location of the coronary arteries and the thick layer of epicardial fat that overlies the proximal portion of these vessels.

**Previous studies of catheter ablation of LVOT**

One third of all idiopathic VAs and ~70% of idiopathic VAs originating from the LV originate from the LVOT in previous studies. LVOT-VA predominantly occurs in men and usually presents with PVCs, which is in line with our data. Mapping demonstrates that VAs frequently occur from the aortic root and LV endocardial and epicardial myocardium adjacent to the GCV and LAD, near the MA. In VAs from the aortic root, the LCC is the most common location, followed by the RCC and L-RCC junction. Rarely, VA origins can be located in the NCC, based on successful ablation. Also, catheter ablation is very effective in abolishing these VAs from the aortic root. However, VAs from the myocardium just below the coronary sinus cusps have been generally difficult to ablate with a published ablation failure rate of 5-10%. Several parameters have been previously defined to predict ablation failure.

In previous studies using mapping and ablation from the CS and transaortic approaches, ECG parameters such as aVL/aVR Q-wave amplitude ratios >1.4, III/II R-wave amplitude ratios >1.1 and PDI >0.6 were used as criteria to identify ablation failure. In these cases, the epicardial LVOT was proposed as the VA origin. Recently, Abularach et al performed ablation at the LCC and adjacent regions to abolish LVOT VAs below the ASC in 16 patients, of whom 4
had previous failed ablation attempts. The authors found that the anatomical distances between sites of the epicardial veins and the closest ASC was greater in those 7 patients with failed ablation compared to the 9 patients who were successfully ablated (20.4±12.1mm VS 11±6.5mm; P<0.01). Based on these findings, they proposed that an anatomical distance >15mm was associated with failed ablation and may indicate an epicardial site of origin.

It is reported that ablation within the GCV and AIV and in the epicradial space via subxyphoid approach can abolish VA in some patients. There are several limitations in epicardial ablation targeting LVOT-VAs. Firstly, mapping in the GCV and AIV is generally associated with higher impedances, which can prevent RF ablation or limit RF energy. Secondly, due to the close proximity of the coronary arteries and the thick layer of epicardial fat that overlies these vessels, epicardial LVOT ablation is often not feasible. Finally, RF ablation may result in inadvertent injury to the coronary arteries if the ablation target is <5mm away.

**Catheter ablation of VA just below the ASC via transseptal approach**

A previous case report described successful VA ablation emanating from the LVOT in a patient with failed retrograde transaortic approach. In the present study, retrograde anatomical mapping during sinus rhythm was initially performed, following by antegrade transseptal mapping. The anterosuperior LVOT could be reached in all 27 patients via an antegrade transseptal approach using a reversed S-curve on the ablation catheter. Importantly, in order to facilitate the latter approach, the transseptal puncture should target the antero-inferior Fossa ovalis. We observed significant differences in the LVOT anatomical map depending on the approach used, indicating that the superoanterior LVOT cannot be reached via retrograde transaortic access. In contrast to previous studies, none of our patients demonstrated a distance...
between the ablation target and the closest ASC >12mm\textsuperscript{20}. A large distance may be due to non-accessibility using a retrograde approach resulting in failed ablation attempts in some patients\textsuperscript{20}. To overcome this limitation, it was important to perform a complete aortic root map prior to LV mapping. In the present study, an average distance between site of earliest activation and closest ASC was 5.1±2.8mm. Below the LCC, mean distance to the ablation target was slightly greater at 7.4±3.5mm, which may explain why in some patients VAs can be ablated with irrigated RF energy from the LCC\textsuperscript{20}. Also, due to the close anatomical relation with the LCC (Figure 4 B), our ablation strategy may be used as an alternative approach for ablating VAs from the LCC to avoid potential injury to the left main coronary artery if the distance to the artery is <5mm or if the ablation catheter is unstable in the LCC\textsuperscript{9,20}.

In the present study, the ablation target was only identified by earliest ventricular activation, which preceded the QRS onset by 39.5±7.7ms and was not consistent with unipolar electrograms. Additionally, pacemapping at the successful ablation site showed mismatch of QRS morphology to clinical VAs (supplemental figure), suggesting that ablation should be performed whilst the patient is awake, as sedation may result in suppression of clinical VAs. The above unipolar recording and pacemapping findings were similar to that described in previous studies\textsuperscript{5-6,9,20}. Another important finding was that irrigated RF resulted in rapid disappearance of VAs within 10 seconds. The rapid abolishment of VAs by irrigated RF energy strongly suggests that this type of VA may be located subendocardially. On the other hand, complete epicardial mapping via subxyphoid approach was not performed in any of our patients, therefore it is still unknown whether the earliest activation was located subepicardially. Nevertheless, the rapid effect during RF ablation demonstrated that this type of VAs can be successfully abolished via the transseptal approach, whether this is due to an endocardial origin or an epicardial origin in a
region with thin myocardium. More importantly, no RF-related complications occurred via the transseptal approach due to the lack of coronary arteries in the endocardium in these 27 patients. Therefore, we strongly recommend that endocardial mapping at the anterosuperior LVOT via both retrograde and transseptal approaches should be performed initially to avoid potential risks of a suboxiphoid epicardial approach and/or ablation within the GCV and AIV in patients with this type of VA\textsuperscript{22-27}, because recent criteria suggest that it can be difficult to distinguish between an endocardial or epicardial origin\textsuperscript{9,12-13}.

**ECG characteristics of VA below the ASC**

Previous studies attempted to describe ECG criteria to identify the successful ablation site in the LVS\textsuperscript{6-9}. As the LVS is located most superior in the LV (Figure 8), VAs originating from this region exhibit high inferior lead R-wave amplitudes and no S wave in V5/V6\textsuperscript{2-6,9}, RBBB pattern has been described as a rare phenomenon\textsuperscript{5-6,9}. In our study, all patients had high inferior lead R-wave amplitudes of 2.0±0.4mV, and 24/27 (88.9%) had LBBB morphology, which is consistent with previous reports\textsuperscript{5-6,9}.

Importantly, previous studies proposed a aVL/aVR Q-wave amplitude ratio >1.4\textsuperscript{13}, III/II R wave amplitude ratio >1.1\textsuperscript{9} and PDI >0.6\textsuperscript{12} as criteria to identify VA not amendable to catheter ablation. The site of origin was most likely located in the presumed inaccessible epicardial LVOT. The present study identified a aVL/aVR Q-wave amplitude ratio >1.4 in 7/27 (25.9%) and III/II R-wave amplitude ratio >1.1 in 11/27 (40.7%) patients. In patients with deep Q-waves in aVL and larger R-waves in III, VA almost always originated below the LCC or LCC/RCC junction, which is consistent with our anatomical finding that the origins are more leftwards and produce large vectors in lead III and against lead aVL (Figure 8). Also, PDI >0.6 was found in 11/27 (40.7%) patients. All patients with previously described ECG marker criteria for ablation...
failure had successful ablation with rapid clinical VA disappearance during RF application using the transseptal approach. In our opinion, further studies are required to answer the question whether previous ECG criteria can be used to identify VA origins that are presumed inaccessible.

**Conclusion**

VAs from the antero-superior LVOT present with LBBB morphology, inferior axis and early transition in the precordial leads on surface ECG in the majority of patients. This region is accessible with an antegrade approach via a anteroinferior transseptal puncture site using a reversed S-curve on the ablation catheter. Clinically, only activation mapping is feasible since VA morphologies do not match QRS morphologies during pacemapping. The earliest activation demonstrating a low-amplitude potential was located 5.1±2.8mm below the ASC. Irrigated RF energy resulted in rapid disappearance of clinical VAs. Therefore, in these patients we strongly recommend that the anterosuperior LVOT should initially be mapped using a combined retrograde and antegrade approach in order to minimize potential risks of subxiphoid epicardial approach and/or ablation within the GCV and AIV. Furthermore, amongst the 27 patients who underwent successful ablation, 7 (25.9%) had aVL/aVR Q-wave amplitude ratios >1.4, 10 (37.0%) had III/II R-wave amplitude ratios >1.1, and 11 (40.7%) had PDI >0.6, which indicates that previous reported ECG criteria predicting ablation failure should be reinvestigated.

**Acknowledgment:** We wish to thank Detlef Hennig for his assistance.

**Conflict of Interest Disclosures:** None.
Reference:


### Table 1: Patient data and basic characteristics

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<td>Age (year)</td>
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<td>Sex (male)</td>
<td>16/27 (59.3%)</td>
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<td>Palpitations</td>
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PVC = premature ventricular contractions; VT = ventricular tachycardia; EF=ejection fraction; RVOT = right ventricular outflow tract; LCC = left coronary sinus cusp; GCV = great cardiac vein; LVOT = left ventricular outflow tract; RCC = right coronary sinus cusp
**Table 2:** Mapping and ablation data.

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</tr>
<tr>
<td>Earliest ventricular activation (ms)</td>
<td>39.5±7.7 (30-57)</td>
<td>37.6±8.1(30-57)</td>
<td>43±8.5 (35-55)</td>
<td>41.3±4.0 (37-45)</td>
</tr>
<tr>
<td>Shortest distance to ASC (mm)</td>
<td>5.1±2.8 (1.6-11.3)</td>
<td>7.4±3.5 (4-11.3)</td>
<td>3.8±0.9 (2.8-5)</td>
<td>3.7±1.8 (1.6-4.7)</td>
</tr>
<tr>
<td>Timing to VA disappearance (sec)</td>
<td>5.5±3.0 (1-19)</td>
<td>7.2±5.4 (2-19)</td>
<td>6.9±3.9 (1-9.2)</td>
<td>5.9±4.3 (1-9)</td>
</tr>
</tbody>
</table>

RF parameter at successful ablation:

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Below LCC</th>
<th>Below Junction of LCC/RCC</th>
<th>Below RCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of RF applications</td>
<td>2.6±1.4 (1-5)</td>
<td>2.3±1.7 (1-5)</td>
<td>2.7±1.2 (2-4)</td>
<td>1.7±1.2 (1-3)</td>
</tr>
<tr>
<td>Maximal power (Watts)</td>
<td>38.5±5.8</td>
<td>38.1±6.3</td>
<td>40.3±6.8</td>
<td>37.7±3.2</td>
</tr>
<tr>
<td>Timing to maximal power (sec)</td>
<td>12.5±7.5</td>
<td>8.4±8.1</td>
<td>12.3±8.7</td>
<td>17±2.6</td>
</tr>
<tr>
<td>Maximal temperature (°C)</td>
<td>39.3±3.4</td>
<td>39.3±4.2</td>
<td>39.0±2.9</td>
<td>39.7±2.3</td>
</tr>
</tbody>
</table>

LCC = left coronary sinus cusp; RCC = right coronary sinus cusp; ASC = aortic sinus cusp; VA = ventricular arrhythmias; RF = radiofrequency
**Table 3:** QRS morphology during ventricular arrhythmias on surface ECG

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Below LCC</th>
<th>Below the junction of LCC/RCC</th>
<th>Below RCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>R wave amplitude in II (mV)</td>
<td>1.8±0.4 (1.1-2.6)</td>
<td>1.8±0.4 (1.1-2.4)</td>
<td>1.7±0.3 (1.3-2.2)</td>
<td>2.1±0.4 (1.8-2.6)</td>
</tr>
<tr>
<td>R wave amplitude in III (mV)</td>
<td>2.0±0.4 (1.3-3.0)</td>
<td>2.0±0.5 (1.3-3.0)</td>
<td>2.0±0.4 (1.6-2.5)</td>
<td>2.1±0.4 (1.7-2.5)</td>
</tr>
<tr>
<td>R wave amplitude III&gt;II</td>
<td>19/27 (70.4%)</td>
<td>11/16 (68.8%)</td>
<td>7/8 (87.5%)</td>
<td>1/3 (33.3%)</td>
</tr>
<tr>
<td>III/II R-wave amplitude ratio &gt;1.1</td>
<td>10/27 (37.0%)</td>
<td>5/16 (31.3%)</td>
<td>5/8 (62.5%)</td>
<td>0/3 (0%)</td>
</tr>
<tr>
<td>Q wave amplitude in aVL (mV)</td>
<td>1.1±0.2 (0.7-1.4)</td>
<td>1.0±0.2 (0.7-1.4)</td>
<td>1.1±0.2 (0.7-1.4)</td>
<td>1.1±0.3 (0.8-1.3)</td>
</tr>
<tr>
<td>Q wave amplitude aVR (mV)</td>
<td>0.9±0.3 (0.4-1.5)</td>
<td>0.8±0.3 (0.4-1.3)</td>
<td>0.9±0.4 (0.4-1.5)</td>
<td>0.9±0.2 (0.7-1.1)</td>
</tr>
<tr>
<td>Q wave amplitude, aVL &gt; aVR</td>
<td>20/27 (74.1%)</td>
<td>12/16 (75%)</td>
<td>5/8 (62.5%)</td>
<td>3/3 (100%)</td>
</tr>
<tr>
<td>aVL/aVR Q-wave amplitude ratio &gt;1.4</td>
<td>7/27 (25.9%)</td>
<td>4/16 (25%)</td>
<td>3/8(37.5%)</td>
<td>0/3 (0%)</td>
</tr>
<tr>
<td>PDI</td>
<td>0.58±0.06 (0.46-0.7)</td>
<td>0.59±0.05 (0.53-0.67)</td>
<td>0.57±0.05 (0.5-062)</td>
<td>0.57±0.12 (0.46-0.7)</td>
</tr>
<tr>
<td>No of PDI &gt;0.6</td>
<td>11/27 (40.7%)</td>
<td>8/16 (50%)</td>
<td>2/8 (25%)</td>
<td>1/3(33.3%)</td>
</tr>
</tbody>
</table>

LCC = left coronary sinus cusp; RCC = right coronary sinus cusp; PDI = Peak deflection index in inferior leads
Figure Legends:

Figure 1: Fluoroscopic views (RAO and LAO) demonstrating transseptal puncture through the anteroinferior Fossa Ovalis in a patient with LVOT-VAs. Note that the transseptal pucture is performed at the anterior third between the aorta and lateral shadow of the right atrium (yellow line) and is slightly posterior to the mapping catheter (Map) in the NCC. The black line outlines the heart shadow. Red lines mark the aortic sinus cusps. CS = coronary sinus catheter; NCC; non-coronary sinus cusp; TP = transseptal puncture.

Figure 2: Fluoroscopic views (RAO and LAO) showing the mapping catheter in the LVOT below the LCC (A+B) and RCC (C+D). Note that the end of the SL1 sheath was kept close to the Fossa Ovalis to allow the mapping catheter to form a reverse S-curve to reach the LVOT and to allow rotation of the mapping catheter clockwise or counter-clockwise to the LCC or RCC. Map = mapping catheter; CS = coronary sinus catheter, LCC = left coronary sinus cusp, RCC = right coronary sinus cusp.

Figure 3: Electroanatomical mapping of the aortic root and LV via only transaortic approach (A-B), and a combination of transaortic and transseptal approaches (C-D). Note that (1) there is wide separation between the LV and aortic root maps when only transaortic approach is used (A-B); (2) there is no space between the LV and aortic root when transseptal mapping is added to the transaortic approach (C-D); (3) the LV volume increases slightly after a combined approach is used; (4) the superior His is located just under and very near to the RCC after complete mapping of His bundle.
L = left coronary sinus cusp (blue tags); R = right coronary sinus cusp (brown tags); N = non-coronary sinus cusp; LV = left ventricle; Yellow tags = sites of His-Purkinje system.

Figure 4: Activation mapping, fluoroscopy and 3-D mapping in a 42-year-old male with 2 previous failed ablation attempts in the RVOT and AMC.

A: Surface ECG leads I, III, V1, and V2, and intracardiac recordings from a catheter within the distal CS and mapping catheter at site of earliest ventricular activation in 6 different sites. From the posteroseptal RVOT, the 3 aortic sinus cusps, GCV and successful ablation site below the LCC. Note that (1) earliest ventricular activation relative to the stable reference taken from the peak R-wave of lead III during clinical PVC; (2) the earliest ventricular activation is located at the LVOT below the LCC; (3) unipolar timing is delayed compared to bipolar recordings at the successful ablation site below the LCC; (4) local unipolar potentials at all 6 sites demonstrate QS-morphology during VAs.

B: Left panels (B1-B2) show right (30°) and left (45°) oblique radiographic views of the mapping catheter (Map) at the successful ablation site just below the LCC during left coronary angiography via a 5-F Judkins catheter. Right panels (B3-B4) show electroanatomical maps of the same male patient and demonstrate the successful ablation point (red tag) just below the LCC.

L = left coronary sinus cusp; R = right coronary sinus cusp; LAD = left anterior descending artery; LCX = left circumflex artery, CS = coronary sinus catheter; Map = mapping catheter; GCV = great cardiac vein
**Figure 5:** Fluoroscopy, activation and 3-D mapping in a 34-year-old male with previous failed ablation attempts.

Left panels show right (30°) and left (45°) oblique radiographic views of the mapping catheter (Map) at the successful ablation site just below the LCC/RCC junction during aortic root angiography using a 6-F pigtail catheter. R = right coronary sinus cusp, N = non-coronary sinus cusp; LMCA = left main coronary artery; CS = coronary sinus catheter; Map = mapping catheter. Middle panel shows surface ECG and intracardiac recordings from mapping catheter at the site of earliest ventricular activation below the LCC/RCC junction. Note the local potential precede the QRS by 35ms during ventricular extrasystoles.

Right panels show electroanatomical mapping of the same patient. Light blue tag = earliest activation site in the aortic root; Dark blue tag = earliest activation site in the LV. Red tags = successful ablation points. R = right coronary sinus cusp, N = non-coronary sinus cusp; LMCA = left main coronary artery; CS = coronary sinus catheter; Map = mapping catheter; LV = left ventricle.

**Figure 6:** Typical ECGs from 3 patients with VAs originating from the LVOT below the LCC, LCC/RCC junction and the RCC. (A) ECG recording from a 15-year-old female, in whom the VA origin was located below the LCC, with 2 previous failed ablation attempts in the GCV, LVOT and LCC; (B) ECG recording from a 60-year-old female with VAs originating from below the RCC/LCC junction; (C) ECG recording from a 47-year-old female with VAs originating below the RCC. Note that (1) II, III and aVF have high amplitudes and there is QS-morphology in aVR and aVL during clinical arrhythmias; (2) absolute values of the R-wave amplitudes in II, III and aVF, and the Q-wave amplitude in aVR and aVL are marked on the
surface ECG; (3) there is no S-wave in V5 and V6, with early transition in the precordial leads before V3.

LVOT = left ventricular outflow tract; LCC = left coronary sinus cusp; RCC = right coronary sinus cusp; GCV = great cardiac vein

**Figure 7:** A-F Complete anatomical mapping of the RV, LV, aorta root and distal part of the CS in various views in patients with LVS VAs. Note that (1) the LAD, LCX and AIV have been graphically added as the AIV was inaccessible with the 7-F mapping catheter and coronary artery mapping is not performed; (2) the LVS marked with black arrows, and is close to the aortic cusps bordered by the vessels.

AIV = anterior interventricular vein; CS = coronary sinus, GCV = great cardiac vein; L = left coronary sinus cusp; LAD = left anterior descending artery; LCX = left circumflex artery, LV = left ventricle; LVS = left ventricular summit; N = non-coronary sinus cusp; RV = right ventricle; RVOT = right ventricular outflow tract
Ventricular Arrhythmias Arising from the Left Ventricular Outflow Tract below the Aortic Sinus Cusps: Mapping and Catheter Ablation via Transseptal Approach and Electrocardiographic Characteristics

Feifan Ouyang, Shibu Mathew, Shulin Wu, Masashi Kamioka, Andreas Metzner, Yumei Xue, Weizhu Ju, Bing Yang, Xianzhang Zhan, Andreas Rillig, Tina Lin, Peter Rausch, Sebastian Deiß, Christine Lemes, Tobias Tönnis, Erik Wissner, Roland Richard Tilz, Karl-Heinz Kuck and Minglong Chen

Circ Arrhythm Electrophysiol. published online May 2, 2014;
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3149. Online ISSN: 1941-3084

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Supplemental Material
Figure Legend

Pacemapping in a 49-year-old male with previous failed ablation attempt and VA origin below the LCC/RCC junction (A), and in a 42-year-old male with 2 previous failed ablation attempts and VA origin below the LCC. Note that (1) the left panel shows clinical VES following a sinus beat; (2) the QRS morphology was narrower in duration and lower in amplitude in the inferior leads compared to that during clinical VES when pacing at the VA origins below the LCC/RCC junction (A) and the LCC (B); (3) the QRS morphology in V1 continuously oscillates during pacing (cycle length 570ms). PVC = premature ventricular contraction; LCC = left coronary sinus cusp; RCC = right coronary sinus cusp