

# Ventricular activation pattern assessment during right ventricular pacing; ultra-high-frequency ECG study

Karol Curila<sup>1</sup>, Pavel Jurak<sup>2</sup>, Josef Halamek<sup>3</sup>, Frits Prinzen<sup>4</sup>, Petr Waldauf<sup>1</sup>, Jakub Karch<sup>1</sup>, Petr Stros<sup>5</sup>, Filip Plesinger<sup>6</sup>, Jan Mizner<sup>1</sup>, Marketa Susankova<sup>1</sup>, Radka Prochazkova<sup>1</sup>, Ondrej Sussenbek<sup>1</sup>, Ivo Viscor<sup>7</sup>, Vlastimil Vondra<sup>7</sup>, Radovan Smisek<sup>8</sup>, Pavel Leinveber<sup>9</sup>, and Pavel Osmancik<sup>1</sup>

<sup>1</sup>Charles University and University Hospital Kralovske Vinohrady

<sup>2</sup>Institute of Scientific Instruments

<sup>3</sup>Institute of Scientific Instruments Czech Academy of Sciences

<sup>4</sup>Maastricht Univeristy

<sup>5</sup>Cardiocenter, Third Faculty of Medicine, Charles University

<sup>6</sup>Institute of Scientific Instruments of the Czech Academy of Sciences

<sup>7</sup>Institute of Scientific Instruments AS CR

<sup>8</sup>Czech Academy of Sciences

<sup>9</sup>St. Anne's University Hospital

November 26, 2020

## Abstract

Background: Right ventricular (RV) pacing causes delayed activation of remote ventricular segments. We used the UHF-ECG to describe ventricular depolarization when pacing different RV locations. Methods: In 51 consecutive patients, temporary pacing was performed at the RV apex, anterior and lateral wall, and at the RV septum with (cSp) and without direct conductive tissue engagement (mSp) (further subclassified as RVIT and RVOT for septal inflow and outflow positions). The timing of UHF-ECG electrical activations were quantified as: left ventricular lateral wall delay (LVLWd; V8 activation delay), RV lateral wall delay (RVLWd; V1 activation delay), and LV lateral wall depolarization duration (V5-8d). Results: The LVLWd was shortest for cSp (11 ms (95% CI; 5;17), followed by the RVIT (19 ms (11;26) and the RVOT (33 ms (27;40), ( $p < 0.01$  between all of them), although the QRSd for the latter two were the same (153 ms (148;158) vs. 153 ms (148; 158);  $p = 0.99$ ). The RVOT caused longer V5-8d (9 ms (3;14) compared to the RVIT (1 ms (-5;8),  $p < 0.05$ ). RV apical capture not only had a worse LVLWd (34 ms (26;43) compared to mSp (27 ms (20;34),  $p < 0.05$ ), but its RVLWd (17 ms (9;25) was also the longest compared to other RV pacing sites (mean values for cSp, mSp, anterior and lateral wall captures being below 6 ms),  $p < 0.001$  compared to each of them. Conclusions: UHF-ECG ventricular dyssynchrony parameters show that cSp offers the best ventricular synchrony followed by RVIT pacing, which should be preferred over RVOT and other RV myocardial pacing locations.

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Karol Curila MD, PhD, MSc (1), Pavel Jurak MSc, PhD (2), Josef Halamek MSc, PhD (2), Frits Prinzen PhD (3), Petr Waldauf MD (4), Jakub Kach MSc (1), Petr Stros MD (1), Filip Plesinger MSc, PhD (2), Jan Mizner MD (1), Marketa Susankova MSc (1), Radka Prochazkova MSc (1), Ondrej Sussenbek MD (1), Ivo Viscor MSc, PhD (2), Vlastimil Vondra, Dr., PhD (2), Radovan Smisek MSc (2,5), Pavel Leinveber MSc (6) and Pavel Osmancik MD, PhD (1)

1. Cardiocenter, Third Faculty of Medicine, Charles University and University Hospital Kralovske Vinohrady, Prague, Czech Republic
2. Institute of Scientific Instruments, the Czech Academy of Sciences, Brno, Czech Republic
3. Department of Physiology, Cardiovascular Research Institute Maastricht, Maastricht University Medical Center, Maastricht, the Netherlands
4. Dept. of Anesthesia and Intensive Care, Charles University and University Hospital Kralovske Vinohrady, Prague, Czech Republic
5. Brno University of Technology, Faculty of Electrical Engineering and Communication, Department of Biomedical Engineering, Technická 12, Brno 61600, Czech Republic
6. International Clinical Research Center, St. Anne's University Hospital, Brno, Czech Republic

#### Address for correspondence:

Karol Curila, MD, PhD., MSc

Cardiocenter, Third Faculty of Medicine, Charles University, Srobarova 50, 100 34 Prague, Czech Republic,  
Phone: + 420 267 162 621

Email: karol.curila@fnkv.cz, ORCID identifier: 0000-0003-3523-6358

**Disclosures:** participating research institutions filed European patent application EP 19212534.2: "Method of electrocardiographic signal processing and apparatus for performing the method."

**Funding sources:** This paper was supported by the Charles University Research Program Q38, Research Centre program No. UNCE/MED/002, 260530/SVV/2020 and by the CAS project RVO:68081731, and by Ministry of Education, Youth, and Sports of the Czech Republic, project LQ1605

#### Abstract

**Background :** Right ventricular (RV) pacing causes delayed activation of remote ventricular segments. We used the UHF-ECG to describe ventricular depolarization when pacing different RV locations.

**Methods :** In 51 consecutive patients, temporary pacing was performed at the RV apex, anterior and lateral wall, and at the RV septum with (cSp) and without direct conductive tissue engagement (mSp) (further subclassified as RVIT and RVOT for septal inflow and outflow positions). The timing of UHF-ECG electrical activations were quantified as: left ventricular lateral wall delay (LVLWd; V8 activation delay), RV lateral wall delay (RVLWd; V1 activation delay), and LV lateral wall depolarization duration (V5-8d).

**Results:** The LVLWd was shortest for cSp (11 ms (95% CI; 5;17), followed by the RVIT (19 ms (11;26) and the RVOT (33 ms (27;40), ( $p < 0.01$  between all of them), although the QRSd for the latter two were the same (153 ms (148;158) vs. 153 ms (148; 158);  $p = 0.99$ ). The RVOT caused longer V5-8d (9 ms (3;14) compared to the RVIT (1 ms (-5;8),  $p < 0.05$ ). RV apical capture not only had a worse LVLWd (34 ms (26;43) compared to mSp (27 ms (20;34),  $p < 0.05$ ), but its RVLWd (17 ms (9;25) was also the longest compared to other RV pacing sites (mean values for cSp, mSp, anterior and lateral wall captures being below 6 ms),  $p < 0.001$  compared to each of them.

#### Conclusions:

UHF-ECG ventricular dyssynchrony parameters show that cSp offers the best ventricular synchrony followed by RVIT pacing, which should be preferred over RVOT and other RV myocardial pacing locations.

Keywords: pacing, myocardial, conductive system, ventricular dyssynchrony, ultra-high-frequency ECG

#### Introduction

Right ventricular (RV) apical pacing causes ventricular dyssynchrony with an increased risk of heart failure [1]. Despite attempts to reduce it by changing the pacing location (RV septal vs. RV apex), no clinical benefit has been observed. As was shown, the standard fluoroscopic criteria for exact lead placement are insufficient, and many leads that were considered to be in the septum based on fluoroscopy, were, in fact,

anchored in the anterior wall [2, 3]. Furthermore, septal positions might represent a mix of more or less dyssynchronous pacing, which ultimately brings no advantage over RV apical pacing.

In recent years, His bundle pacing (HBP) has shown promising results [4], but its benefits are counterbalanced by an increase in pacing lead reinterventions [5]. These shortcomings could potentially be moderated by placing the lead tip in the ventricular septal para-hisian area, beyond the annulus of the tricuspid valve. This would ensure pure myocardial capture during low output pacing and concomitant myocardial and conductive tissue capture during higher output pacing. In our study, we called the high-output para-hisian capture as conductive system septal pacing (cSp) to differentiate it from myocardial septal (mSp) or pure myocardial para-hisian pacing in which conduction tissue is not captured directly.

UHF-ECG is an imaging method displaying the activation pattern and time differences between the activation of specific ventricular segments. Time-spatial resolution is possible thanks to an analysis of the ultra-high frequency components of ventricular myocyte action potentials in peri-myocardial tissue and the practical use of UHF-ECG was documented in previous reports [6, 7].

The aim of the study was to describe in detail the activation patterns seen during RV pacing with and without direct conduction system engagement.

## Methods

### *Study population*

Consecutive patients with an indication for pacemaker implantation due to bradycardia, under the care of a single physician between 9/2019 to 2/2020, were included. The project was approved by the Ethics Committee of the Faculty Hospital Kralovske Vinohrady, Prague, CZ, and all subjects signed informed consent before enrollment.

### *Pacemaker implantation*

The left subclavian approach was preferred per study protocol. After the venous system was reached, the atrial pacing lead was temporarily placed in the apex of the right ventricle. Then the His bundle region was mapped using a SelectSecure lead (model 3830, 69 cm, Medtronic Inc., Minneapolis, MN), which was delivered through a fixed-curve sheath (C315 HIS, Medtronic, Minneapolis, MN), as previously described [8]. Once the His bundle signal was identified, to ensure the para-hisian ventricular position of the lead tip, it was moved to the right ventricle, behind the hinge of the septal leaflet of the tricuspid valve. An X-ray and an electrogram (EGM) of the atrial, His bundle, and ventricular signals were used to navigate the lead tip to the area of the basal interventricular septum. At this location, atrial signals significantly decreased or disappeared, but His bundle signals were present before lead fixation - Figure 1. In case of uncertainty, an injection of contrast agent through a C315 HIS sheath was performed to verify ventricular lead tip placement. Once the proper ventricular septal position of the lead tip was achieved, it was fixed using 3–5 clockwise rotations to anchor it into the septal ‘para-hisian’ position, which was followed by pacing with outputs between 0–5V at 0.5 ms. cSp was confirmed when a wide, notched, or slurred QRS complexes during low output pacing, which narrowed and had a reduced R wave peak time (RWPT) at V6 (LVAT) during high output pacing were observed. Thereafter the atrial lead with a pre-shaped stylet was moved from the apical position and temporarily placed in pre-specified locations in the right ventricle (RV septum, anterior wall, and lateral wall). For appropriate lead placement in these locations, the SelectSecure lead and C315His sheath, already positioned in the basal septal region, were used as landmarks – Supplementary Figure 1. For all pacing locations, X-ray cine loops in two projections (RAO 20–30deg and LAO 20–30deg) were generated and stored for further analysis. In patients with an indication for a dual-chamber pacemaker, the atrial lead was removed from the ventricular position and was fixed in the right atrium at the end of the procedure. Stored ventricular pacing positions of the atrial lead were later retrospectively reviewed by an experienced physician blinded to the intended position. The exact location of the lead tip was determined to be one of the following: RV myocardial septal – mSp, apical, anterior wall or lateral wall. Moreover, mSp positions were further classified as (a) the septal right ventricular inflow tract (RVIT) or (b) the septal right

ventricular outflow tract (RVOT) in the RAO projection – Figure 2.

The distances between cardiac silhouette lines (a+b) and the lead with cSp capture to the lower cardiac silhouette (a) were measured in mm – Figure 2. The location of the para-hisian region with cSp capture, with respect to the diameter of the heart silhouette, was calculated as  $(a/a+b) \times 100$  and reported as percentages. All ECG recordings during pacings of the right ventricular septum were reviewed retrospectively using EP LabSystem software (Boston Scientific, MA, USA) at 25, 100, and 200 mm/s, as needed. HV intervals (calculated as the mean value between 2 consecutive beats), LVAT, the types of ventricular capture, and the ratio between the atrial and ventricular signal amplitudes in mV (A/V amplitude ratio) were measured after lead fixation in the para-hisian area during spontaneous rhythm and pacing at 100 mm/s.

### *UHF-ECG data acquisition and analysis*

A VDI monitor (Ventricular Dyssynchrony Imaging monitor, ISI Brno, Cardion, FNUSA, CZ, 2018) was used to record and analyze the 5 kHz 14-lead ECG signals with a 3 nV resolution and a frequency range of 1.5 kHz. UHF-ECG data were collected during 2–3 minutes of the RV apical, cSp, mSp, anterior wall, and lateral wall pacing at 100–120 beats per minute. Signal processing and UHF-ECG map construction are described in detail elsewhere [6]. To describe the time course of depolarization propagation in the ventricles, the centers of mass (Mxc) under specific leads (i.e., Vx) were determined. Mxc was calculated as the center of mass of UHF-QRS amplitudes above the 50 percent threshold of the baseline to peak magnitude. To quantify LV and RV dyssynchrony, time delays from the earliest center of mass (first activation) to M8c and M1c were measured (LVLWd and RVLWd, respectively). To describe the duration of LV lateral wall depolarization, the time delay between M5-8c (V5-8d) was measured – Figure 3. The onset and the end of the QRS complex were marked manually using custom-made software, providing high-resolution QRS signals. Global QRS durations (QRSd) were measured from the earliest to the latest deflection in any of the 12 leads (V7 and V8 were excluded from QRSd calculations). During ventricular pacing, the beginning of the QRS was measured from the highest amplitude of the pacing artifact.

### **Statistics**

Exploratory data analysis was performed for all parameters. Unpaired measurement comparisons were made using the unpaired t-test. Repeated measurement comparisons of QRSd, and Mxc during different RV captures were made using a linear mixed effect model (LMEM) with the Tukey multiple comparison test. The results of these models are presented as means with 95% confidence intervals and comparisons as mean differences with 95% confidence intervals and p-values. A p-value < 0.05 was considered statistically significant. RStudio version 1.2.1335 with R version 3.6.1 was used to perform statistical analyses. LMEM was done using lme4 version 1.1-21. If not specified, all values are shown as means (95%, CI). All analyses are available as a PDF R markdown document in appendices.

### **Results**

A total of 300 different ventricular activations (51 spontaneous rhythms, 46 c-Sp, 61 m-Sp, 48 RV anterior wall, 48 RV lateral wall, and 46 RV apical captures) were recorded in 51 patients – their characteristics are shown in Table 1. The average procedural time was 98 ± 23 min., and one procedural complication was observed (a pericardial effusion that resolved spontaneously). Other procedural characteristics are shown in Table 1. Of 48 RV anterior wall positions, 9 were found to be septal since they exceeded the 25deg angle to the horizontal plane in the LAO (all of them were classified as RVOT). Of the 60 mSp positions, 30 were classified as RVIT and 30 as RVOT. Two records (one marked as mSp and one as the lateral wall) were not analyzed since the X-ray images were not stored. As a result, definitive analyses were performed on 32 spontaneous rhythms without a bundle branch block (narrow QRS group), 46 cSp, 69 mSp (30 RVIT, 39 RVOT), 39 RV anterior wall, 47 RV lateral wall, and 46 RV apical wall captures.

The average height of the position with cSp capture was 40 ± 5% of the heart silhouette in the RAO. The mean A/V ratio was 4 ± 4%, and in 29 of 46 patients with cSp, the atrial signal amplitude was lower than 0.05 mV on the EGM in the cSp location. A wide range of HV/RBBpoV intervals was observed (30–83 ms),

with an average value of  $50 \pm 13$  ms. There were seven patients with HV intervals shorter than 35 ms. Their LVLWd and RVLWd were similar compared to those with  $HV > 35$  ms; 19 ms (10;27) vs 10 ms (7;14),  $p = 0.14$  for LVLWd and 3 ms (-6;12) vs 1 ms (-3;5),  $p = 0.70$  for RVLWd, but QRSd was significantly shorter (126 ms (112;139) vs 141 ms (135;146);  $p = 0.02$ ). Their UHF-ECG maps with measured parameters are shown in Supplementary Figure 2.

Conductive system septal pacing showed superior depolarization patterns compared to all other pacing locations - Figure 4 and Supplementary Figure 3. QRSd and LVLWd were significantly shorter during cSp than during RVIT ( $p < 0.01$  for both) and RVOT pacing ( $p < 0.001$  for both). Although both RVIT and RVOT had virtually the same QRSd ( $p = 0.99$ ), the LVLWd and V5-8d were significantly longer for RVOT capture ( $p < 0.001$  for LVLWd and  $p < 0.05$  for V5-8d). cSp capture resulted in wider QRS complexes compared to the 'narrow QRS' group, but RVLWd and LVLWd were similar ( $p = 0.2$  and  $p = 0.6$  respectively). cSp and RVIT capture caused the same V5-8d as the spontaneous narrow group ( $p > 0.99$ ) - Figure 5 and table 2.

Regarding RV pacing locations without direct conductive tissue engagement, the shortest LVLWd was observed during mSp, followed by RV apical ( $p = 0.02$  between them), lateral and anterior wall capture being the longest. Compared to each of the others, the longest RVLWd was observed during RV apical capture ( $p < 0.001$ ). The V5-8d was significantly shorter in mSp compared to other RV myocardial captures ( $p < 0.001$  to each of them) - Figure 6 and table 3.

## Discussion

This UHF-ECG study describes in detail the time delays between the activation of ventricular segments during RV pacing and shows: (1) pacing of the basal interventricular septum with conductive system engagement produces the smallest ventricular dyssynchrony compared to other myocardial captures of the right ventricle and (2) pacing of RV septal inflow area results in less LV ventricular dyssynchrony than septal RVOT pacing, although no differences in QRSd were observed between them.

### *UHF-ECG dyssynchrony during septal pacing*

The pacing of the RV septum has been considered to be more physiological than apical pacing [9]. However, its clinical benefit was never shown in a prospective randomized trial [2, 3]. But the right ventricular septum is not a homogenous structure. It consists of an inflow and outflow tract, and also the His bundle and its ramification are localized in its basal part. The pacing in the basal septal area with concomitant myocardial and conduction tissue engagement produced the most physiological UHF-ECG depolarization pattern in our study. In seven patients, proximal RBB capture rather than His bundle capture was seen when this was considered based on the duration of HV intervals. QRSd in these seven patients was significantly shorter but the difference in the LVLWd didn't reach statistical significance compared to other cSp captures due to the proximal position of the pacing lead within the right Tawara bundle in most of them. An example of how the distance of the lead capturing the septal conduction system from the plane of the tricuspid valve can influence the ventricular depolarization pattern and the QRSd is shown in Figure 7.

An important shortcoming of studies comparing the clinical benefit of RV septal and apical pacing involved inadequate definitions of lead placement in the septum. They were often based on ECG or X-ray criteria, both of which have been shown to be inaccurate [10, 11]. This led to incorrect placement of pacing leads on the anterior wall (e.g., in the anteroseptal groove) in a substantial percentage of patients [2, 3]. To overcome this shortcoming, we used the position of the lead in the para-hisian area displayed in the LAO and RAO projections as a landmark. Its position in the RAO projection was used to approximate the position of the crista supraventricularis [12]. Pacing in the RVOT region above this level has been shown to lead to significantly worse UHF-ECG LV dyssynchrony compared to pacing on or below the level. Interestingly the mean QRSd was the same in RVIT and RVOT captures, which corroborates previous studies showing QRSd to be an imperfect marker of ventricular dyssynchrony during ventricular pacing [13]. The difference in the LVLWd between these two pacing locations is highly likely a result of different distances from the left ventricular subendocardial Purkinje system. Since it is located in the lower third of the LV septum

and LV free wall, time to its activation is necessarily shorter during RVIT pacing, which is anatomically directly opposite. Once it is activated, its contribution to left ventricular depolarization is greater during RVIT capture, which was also reflected by a shorter V5-8d compared to RVOT captures.

### *UHF-ECG dyssynchrony during myocardial RV pacing*

The shortest LVLWd was observed with mSp, follow by RV apical capture and was similar during RV lateral and anterior wall captures. Interestingly, the V5-8d, which reflects the speed of depolarization in the LV lateral wall, was similar during RV apical, anterior and lateral wall pacings, but in all of them significantly longer compared to mSp capture. This is likely a reflection of the differences in electrical wavefront propagation in the LV during RV pacing. RV apical wall capture relies mostly on cell-to-cell LV activation, contrary to RV septal capture, which also uses (after trans-septal signal transition) the left ventricular Purkinje system to activate the left ventricular mass [14]. Our results suggest that similar to RV apical capture, during both RV anterior and lateral wall captures, the left ventricular mass under V5-V8 is being activated mainly through slower myocardial conduction. However, the longer distance from the RV lateral wall and anterior wall to the LV lateral wall under V8 is responsible for the significantly longer time delay between the first activation and activation under the V8 compared to RV apical capture. This accented electrical LV dyssynchrony may be the cause of worse outcomes in patients observed in some clinical studies in which the pacing lead was placed in the RV anterior wall or lateral wall [3, 15]. The LVLWd during RV apical capture was only slightly longer compared to all mSp captures, but as was discussed before, significant differences exist between septal locations (RVIT vs RVOT). Noteworthy was that significant RVLWd, during RV apical pacing, was documented. It is a reflection of concomitant RV dyssynchrony during apical pacing; our observation was very similar to the one documented using an ECGi in patients with heart failure [16].

### **Limitations**

This was a UHF-ECG analysis of ventricular depolarization patterns from different types of ventricular pacing during implant procedures. The data acquisition for UHF-ECG analysis was performed immediately after lead fixation in a predefined location and confirmation of ventricular capture. It is possible that during lead fixation in the para-hisian area, damage to the conductive tissue occurred in some patients, which could have influenced the paced ventricular depolarization pattern. Data were not compared to any other invasive or noninvasive electrocardiographic methods, and no hemodynamic or echocardiographic measurement of mechanical dyssynchrony was performed.

### **Summary**

UHF-ECG differentiates ventricular depolarization patterns during RV septal, apical, anterior wall, and lateral wall pacing and between different locations on the RV septum. Of these locations, capture of the basal interventricular septum with conductive tissue engagement proved to offer the best depolarization pattern, with placement in the right ventricular inflow tract being the second best. The latter position should be considered as an alternative for ventricular pacing when pacing the His-Purkinje conduction system is not possible or available. Our results show that UHF-ECG provides detailed and additional information on electrical ventricular dyssynchrony during RV pacing.

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Table 1: Patients and procedural characteristics

Age (years), mean $\pm$ SD	78 $\pm$ 8
Male gender, n (%)	35 (67)

Age (years), mean $\pm$ SD	78 $\pm$ 8
Comorbidities:	
Heart failure, n (%)	11 (22)
Coronary heart disease, n (%)	20 (39)
Diabetes mellitus, n (%)	25 (49)
Hypertension, n (%)	41 (80)
LV ejection fraction (%), mean $\pm$ SD	56 $\pm$ 7
LV wall thickness ((septum + posterior wall)/2) (mm), mean $\pm$ SD	11 $\pm$ 1
Pacing indications:	
AV block, n (%)	29 (57)
SSS, n (%)	10 (20)
Bi-, trifascicular block, n (%)	8 (15)
Atrial tachy-fibrillation with planned AV junctional ablation, n (%)	4 (8)
QRS morphology	
LBBB, n (%)	5 (10)
RBBB, n (%)	14 (27)
Without BBB, n (%)	32 (63)
Procedural characteristics	
A/V amplitude ratio, (%), mean $\pm$ SD	4 $\pm$ 4
HV interval *, (mm), mean $\pm$ SD	50 $\pm$ 13
Procedural duration, (min), mean $\pm$ SD	98 $\pm$ 23
RWPT in V6 during cSp capture of ventricles, (ms), mean $\pm$ SD	96 $\pm$ 9
RWPT in V6 during myocardial basal septal capture of ventricles, (ms), mean $\pm$ SD	118 $\pm$ 11
Height of basal septal region with cSp capture to heart silhouette diameter, %, mean $\pm$ SD	40 $\pm$ 5

SSSy – sick sinus syndrome, AV – atrioventricular, LBBB – left bundle branch block, RBBB – right bundle branch block, BBB – bundle branch block, UHF-ECG – ultra-high frequency ECG, \* HV – His to ventricle (RBB potential-ventricle intervals in patients with HV < 35 ms are included), RWPT – R wave peak time, cSp – conductive system septal pacing

Table 2: Mixed effect model values for LVLWd, RVLWd, V5-8d, during cSp, RVIT, RVOT captures and spontaneous rhythms without bundle branch blocks (for detailed statistics see appendix B).

	spontaneous narrow	cSp	RVIT	RVOT
LVLWd	8 (1;16) ms	11 (5;17) ms	19*+ (11;26) ms	33 (27;40) ms
RVLWd	6 (-1;13) ms	1 (-5;7) ms	6 (-1;14) ms	6 (-1;13) ms
V5-8d	2 (-4;8) ms	2 (-3;7) ms	1 (-5;8) ms	9++§ (3;14) ms

\* p < 0.001 vs RVOT, + p < 0.01 vs cSp

++ p < 0.01 vs cSp, SS p < 0.05 vs RVIT

Table 3: Mixed effect model values for LVLWd, RVLWd, V5-8d, during cSp, mSp, RV anterior, lateral wall, and apical wall captures (for detailed statistics see appendix C).



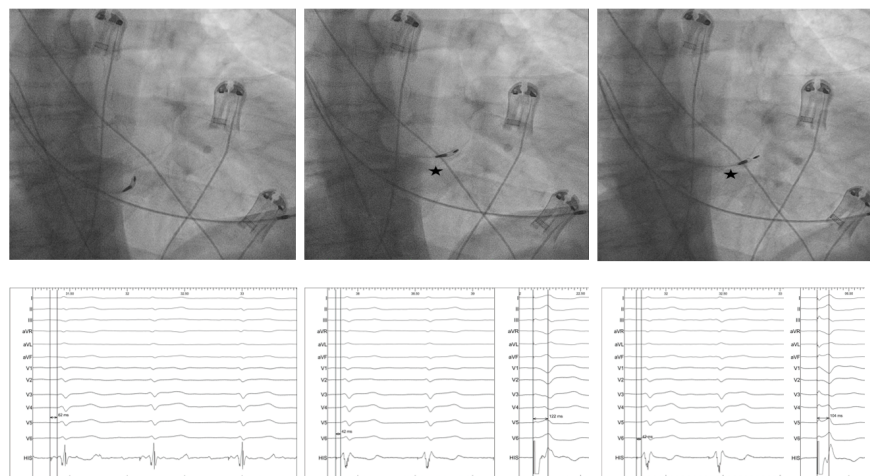
	cSp	mSp	anterior wall	lateral wall	RV apex
LVLWd	11 (3;20) ms	27*+ (20;34) ms	56 (47;65) ms	59 (51;67) ms	34 (26;43) ms
RVLWd	1 (-7;9) ms	6 (-1;13) ms	2 (-7;11) ms	0 (0;0) ms	17++ (9;25) ms
V5-8d	5 (-5;9) ms	5§ (0;11) ms	21 (14;29) ms	17 (10;24) ms	24 (17;31) ms

\*  $p < 0.05$  vs RV apex, +  $p < 0.001$  vs anterior and lateral wall

++  $p < 0.001$  vs each of the others

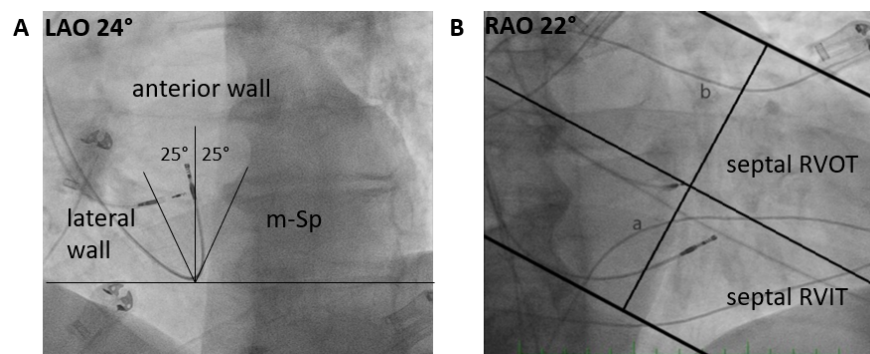
§  $p < 0.001$  vs anterior, lateral wall and RV apex

Figure 1: A description and presentation of the method used to place the pacing lead for conductive system septal pacing (cSp).



In this patient, the His bundle potential with HV interval was 62 ms in the first position – left panel. The QRS amplitude was 1.9 mV and atrial activity could be easily identified on the EGM. Then the lead was moved towards the right ventricle to the para-hisian location – middle panel. The atrial activity was no longer recognizable, the QRS amplitude increased to 2.8 mV, and the HV interval shortened to 42 ms. Pacing with an output between 1.0 V–3.5 V at 0.5 ms led to myocardial capture of the ventricles (cSp capture was present with outputs above 3.5 V at 0.5 ms). The pacing lead was fixed inside the septum with 3 rotations – right panel. The QRS amplitude further increased to 3.5 mV and cSp capture occurred starting as 1.25 V at 0.5 ms (myocardial capture was present between outputs of 0.75–1.25 V at 0.5 ms). Asterisks show the first position of the lead.

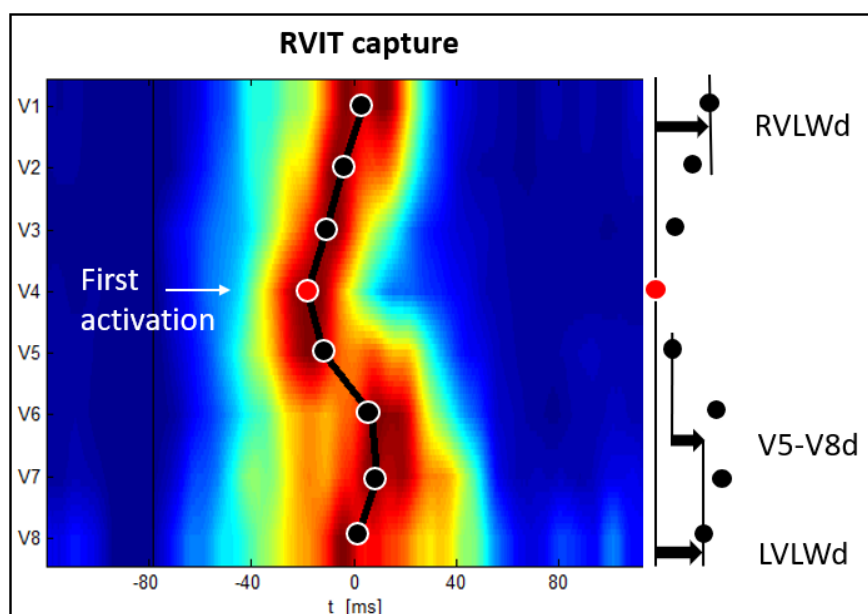
Figure 2: Panel A: The method used to distinguish between RV septal, anterior, and lateral wall positions in the LAO projection. Panel B: the method used to differentiate between RVIT and RVOT lead positions within mSp in the RAO projection.



Panel A: Using the LAO projection, a horizontal line at the level of the lowest part of the pacing lead was drawn. Then 2 lines with angles of 25° to the perpendicular line delineated the anterior wall in the LAO projection.

Panel B: Parallel lines on the upper and on the lower heart silhouette were drawn in the RAO projection. Then a third line parallel to the other two was drawn through the lead tip in the para-hisian region, which divided the right ventricular septum into the RVIT (on or below the line) and the RVOT (above the line).

Figure 3: Schematic representation of the calculated parameters from the UHF-ECG maps.



The dark line connects the center of masses (solid points) under the specific lead, which are displayed on the y-axis. Time (ms) is displayed on the x-axis. During RVIT capture shown, the first activation occurred under V4 (M4c) and RVLWd = M4c to M1c, LVLWd = M4c to M8c, and V5-V8d = M5c to M8c in ms.

Figure 4: Impact of lead placement on the pattern of ventricular depolarization in different RV locations in one patient. The plane of the tricuspid valve is highlighted using a contrast agent or a dashed white line. Please note the distance of the cSp lead from the tricuspid annulus, which was approximately 15 mm.

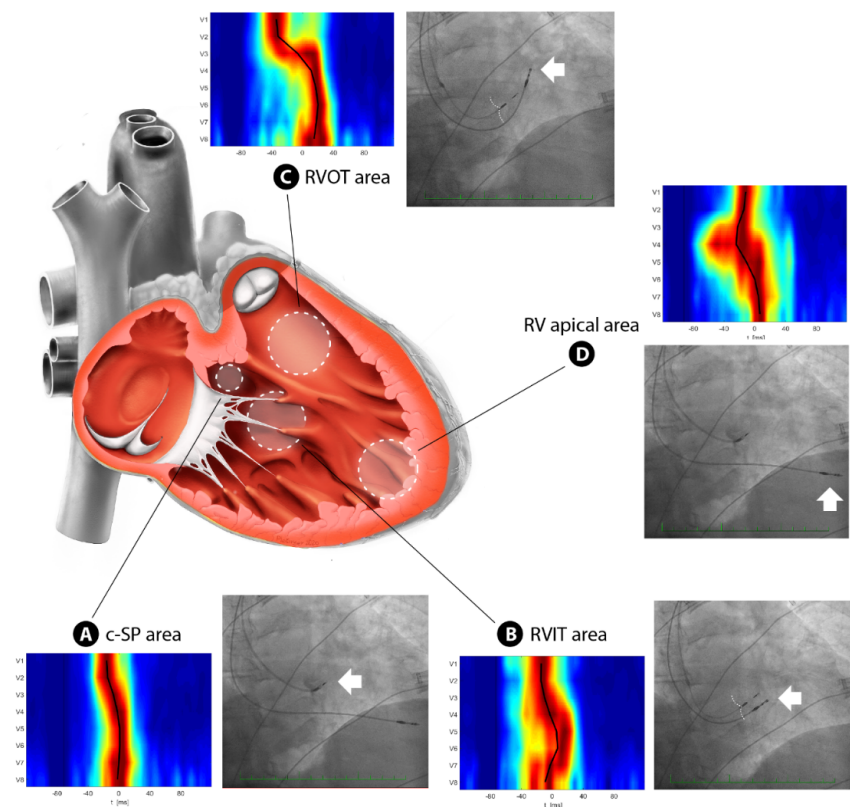
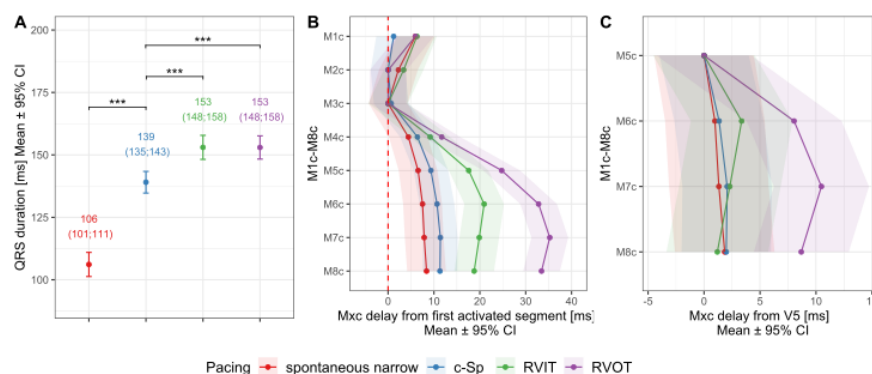
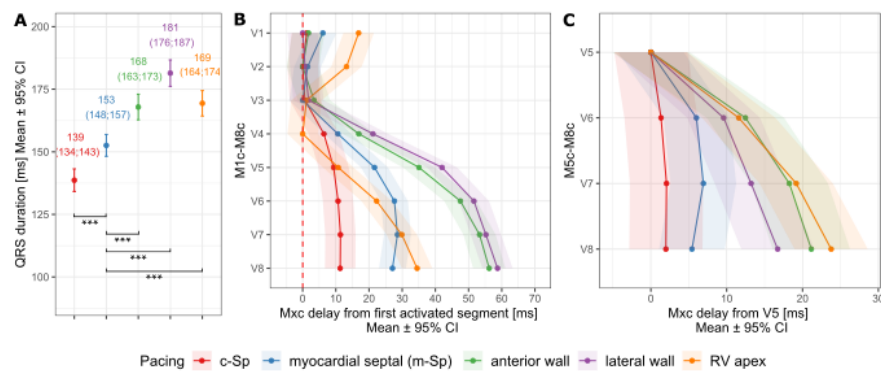


Figure 5: Mixed effect model for QRSd (panel A), mean Mxc delay from the first activated segment (placed on 0 ms) (panel B) and mean M6-8c delays (panel C) from the M5c (placed on 0 ms) during cSp, RVIT, RVOT captures and spontaneous rhythms without bundle branch blocks.



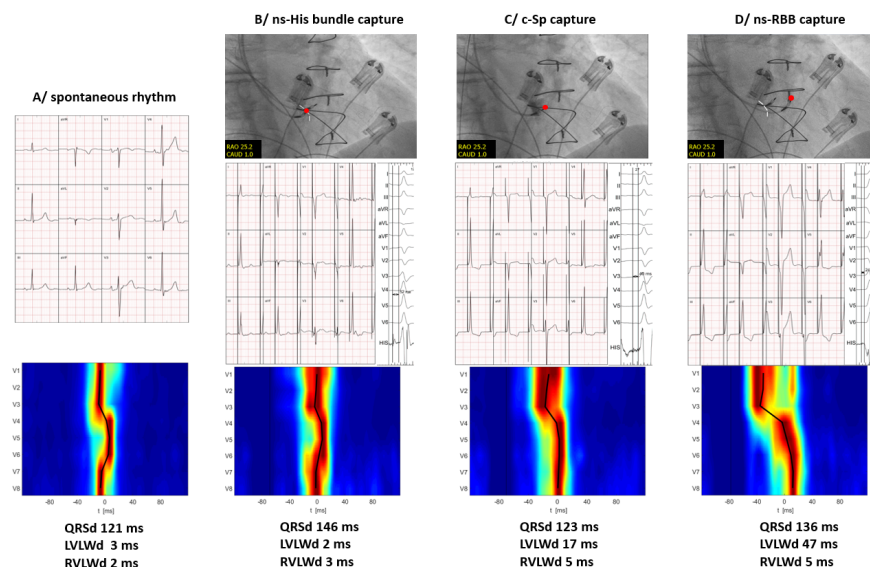
\*\*\* for  $p < 0.001$

Figure 6: Mixed effect model for QRSd (Panel A), mean Mxc delay from the first activated segment (placed at 0 ms) (Panel B) and mean M6-8c delays (Panel C) from the M5c (placed at 0 ms) during cSp, mSp, RV anterior, lateral wall, and apical wall captures.



\*\*\* for  $p < 0.001$

Figure 7: UHF-ECG ventricular depolarization patterns change based on specific pacing locations in the right ventricular septum with conduction system engagement. Please note the minimal difference in QRS morphology between cSp and nsHB capture, despite the UHF-ECG depolarization pattern being significantly different and the fact that the HV interval in the c-Sp location was 40 ms indicating the lead tip being positioned still on the His bundle.



Panel A: During spontaneous rhythm, a specific depolarization pattern of ventricles can be seen with the latest activation under leads V4-V6 and QRSd of 121 ms.

Panel B: During ns-HB capture on the annulus of the tricuspid valve with an HV interval of 52 ms, the pattern of ventricular depolarization was very similar to a spontaneous rhythm, with the latest activation under V4-V6. QRSd prolonged to 146 ms.

Panel C: During cSp, the tip of the pacing lead was placed approximately 14 mm below the plane of the tricuspid valve. Pacing in this location led to a minimal change in QRSd compared to a spontaneous rhythm, but the pattern of ventricular activation changed considerably. The first activated myocardial segments were under leads V1-V3, and the latest activation occurred simultaneously under leads V4-V8. The HV interval in this location was 40 ms.

Panel D: Placement of the pacing lead in the right ventricle following the signals of the right Tawara branch, with nonselective capture, led to prolongation of the LVLWd to 47 ms. The pattern of ventricular activation in this location was similar to cSp capture, but the delay between V1-V3 and V4-V8 was greater, and the activation under V4-V8 was less simultaneous. The HV interval was 28 ms.

Red dots show pacing lead positions. In panel C, the plane of the tricuspid valve is highlighted using a contrast agent; a white dashed line is used in panel B and D.