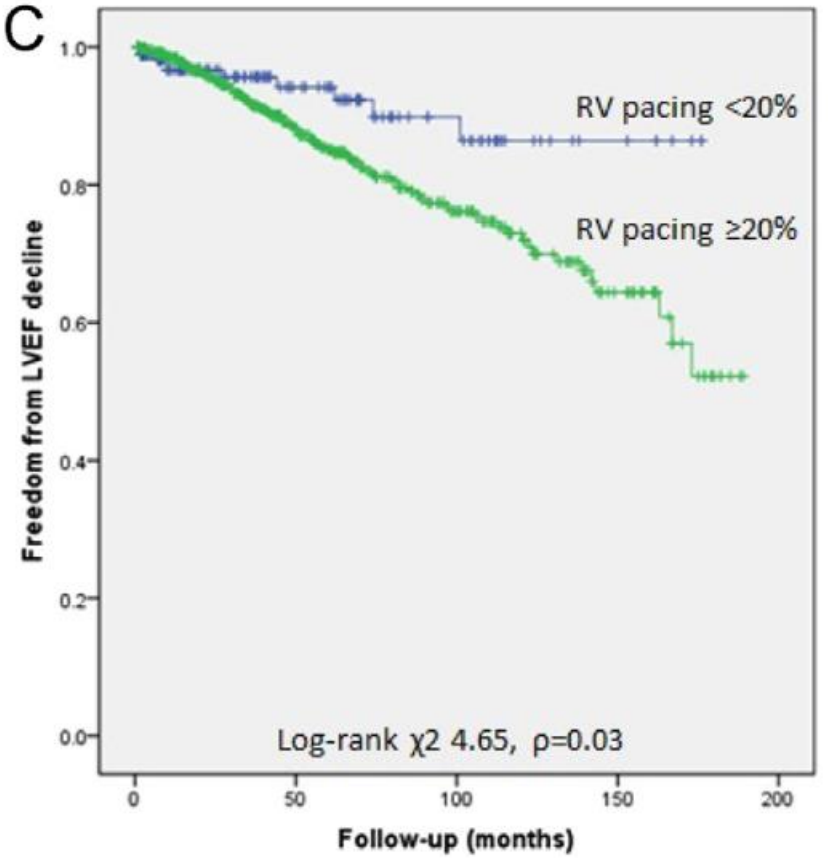
Left Ventricular pacing : an upcoming standard ?

B. Maille

Limitless of Bradycardia pacing: Right ventricular pacing induced cardiomyopathy

- Deleterious effect of chronic (20%) RV pacing which induced LV asynchrony
  - Maximize intrinsic conduction
  - Or cardiac resynchronization therapy

- Incidence: 12%
  - 873 patients with PM implantation and normal LVEF
  - 101 (12%) LVEF < 40%
  - 29 upgrade: 84% of CRT response (increase in LVEF> 10%)



Kiehl, Erich L., Tarek Makki, Rahul Kumar, Divya Gumber, Deborah H. Kwon, John W. Rickard, Mohamed Kanj, et al. « Incidence and Predictors of Right Ventricular Pacing-Induced Cardiomyopathy in Patients with Complete Atrioventricular Block and Preserved Left Ventricular Systolic Function ». *Heart Rhythm*, Focus Issue: Devices, 13, nº 12 (1 décembre 2016): 2272-78. https://doi.org/10.1016/j.hrthm.2016.09.027.

Right ventricular pacing induced cardiomyopathy

-
-

Limitation:
- Increased risk of CIED infection
- Earlier battery depletion
- Increased economical cost

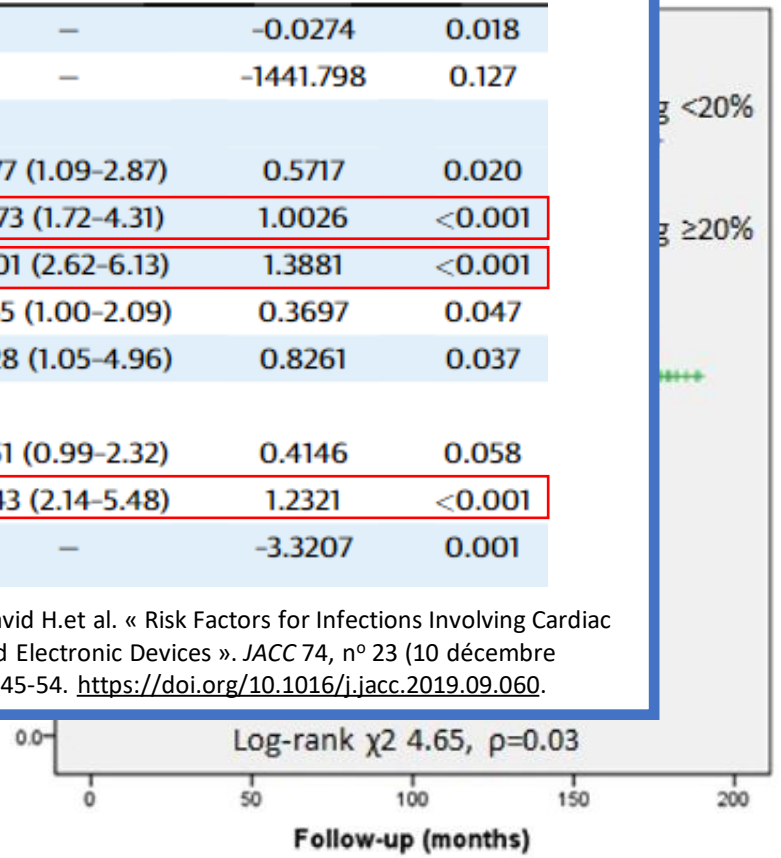
Upgrade CRT

TABLE 3 Full Prediction Model for Hospitalization due to Device Infection

	OR (95% CI)	β Coefficient	p Value
Age*	—	-0.0274	0.018
1/age²*	—	-1441.798	0.127
Procedure type (reference: pacemaker)			
ICD	1.77 (1.09-2.87)	0.5717	0.020
CRT	2.73 (1.72-4.31)	1.0026	<0.001
Revision/upgrade†	4.01 (2.62-6.13)	1.3881	<0.001
Renal insufficiency	1.45 (1.00-2.09)	0.3697	0.047
Immunocompromised	2.28 (1.05-4.96)	0.8261	0.037
Number of previous procedure (reference: 0)			
1	1.51 (0.99-2.32)	0.4146	0.058
≥2	3.43 (2.14-5.48)	1.2321	<0.001
Intercept	—	-3.3207	0.001

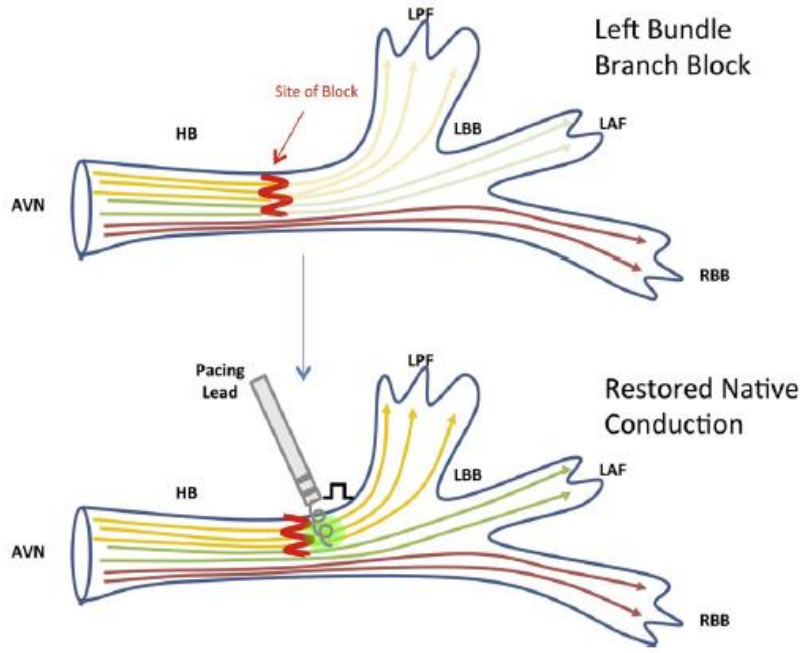
>>> THE GOOD DEVICE, THE FIRST TIME

Birnie, David H.et al. « Risk Factors for Infections Involving Cardiac Implanted Electronic Devices ». *JACC* 74, nº 23 (10 décembre 2019): 2845-54. https://doi.org/10.1016/j.jacc.2019.09.060.



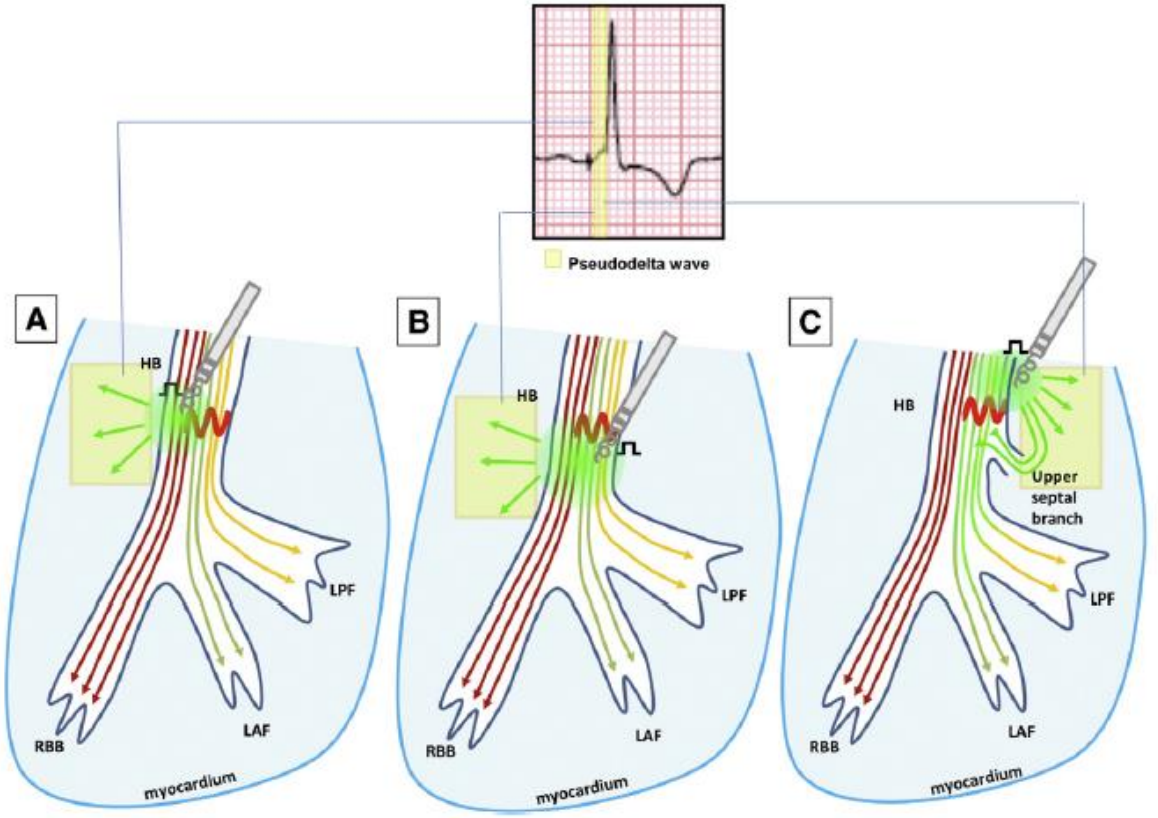
Kiehl, Erich L
« Incidence and Predictors of Right Ventricular Pacing-Induced Cardiomyopathy in Patients with Complete Atrioventricular Block and Preserved Left Ventricular Systolic Function ». *Heart Rhythm*, Focus Issue: Devices, 13, nº 12 (1 décembre 2016): 2272-78. https://doi.org/10.1016/j.hrthm.2016.09.027.

Conduction system pacing: His bundle



Longitudinal dissociation

>>> bypassing bloc



Physiological mechanisms of QRS narrowing in bundle branch block patients undergoing permanent His bundle pacing☆

Alexandra E. Teng, MD, Louis Massoud, Olujimi A. Ajijola, MD, PhD*

UCLA Cardiac Arrhythmia Center, Los Angeles, CA

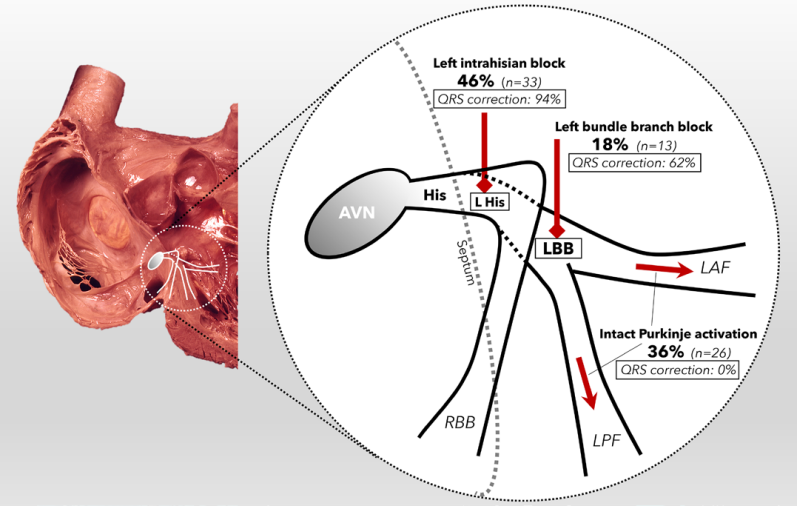
→ Bradycardia and heart failure pacing

HBP Limitation

1. Located in the central fibrous septum

- successful implanted rate 70-90% / high pacing threshold / leads dislodgment

2. Risk of Progressive disease of the conduction tissue resulting in RV conventional pacing



3. Based on longitudinal dissociation of the His bundle

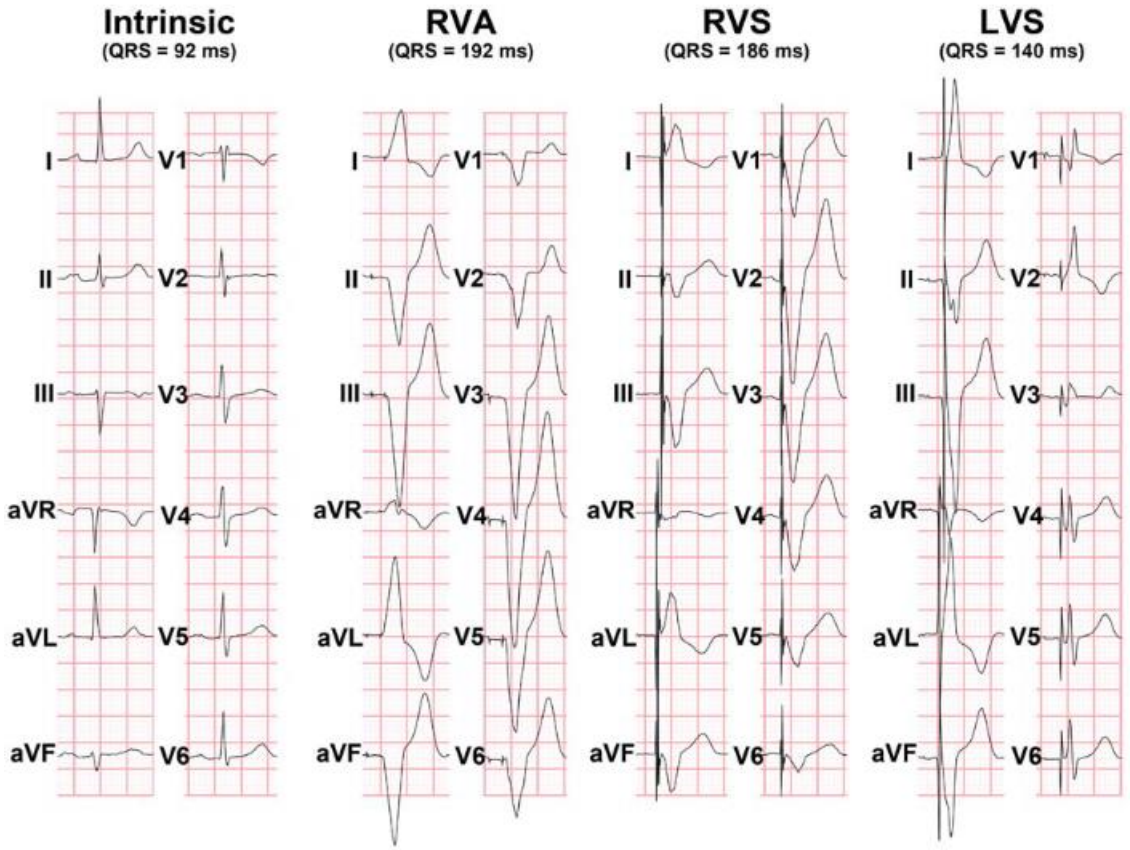
→ **Not always true**

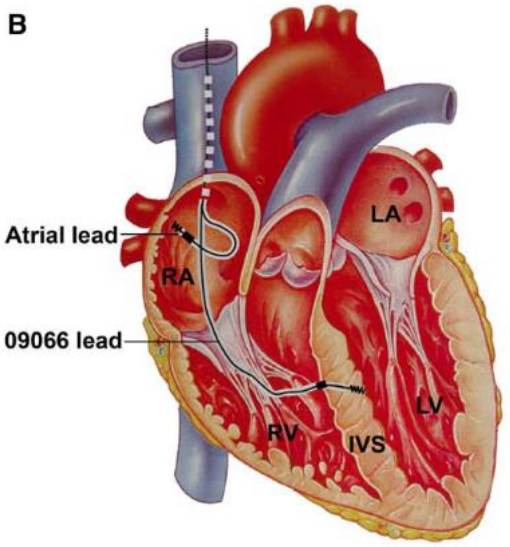
Upadhyay Gaurav A., et al.. « **Intracardiac Delineation of Septal Conduction in Left Bundle-Branch Block Patterns** ». *Circulation* 139, nº 16 (16 avril 2019): 1876-88. https://doi.org/10.1161/CIRCULATIONAHA.118.038648.

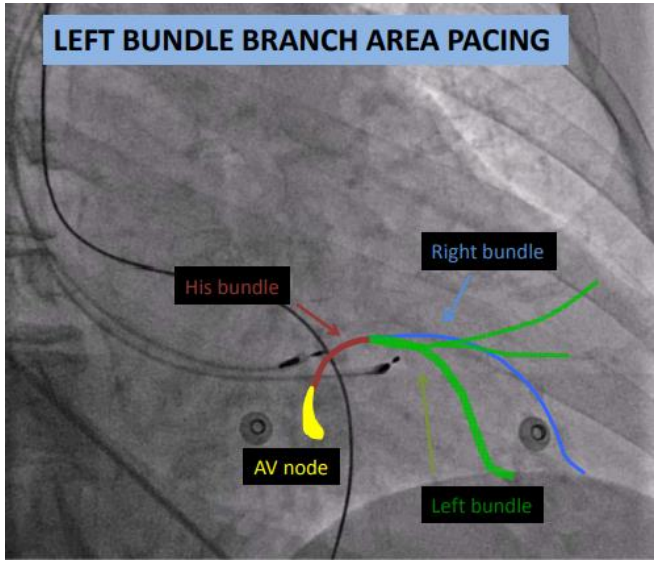
LV physiological pacing:

- Expected benefits?

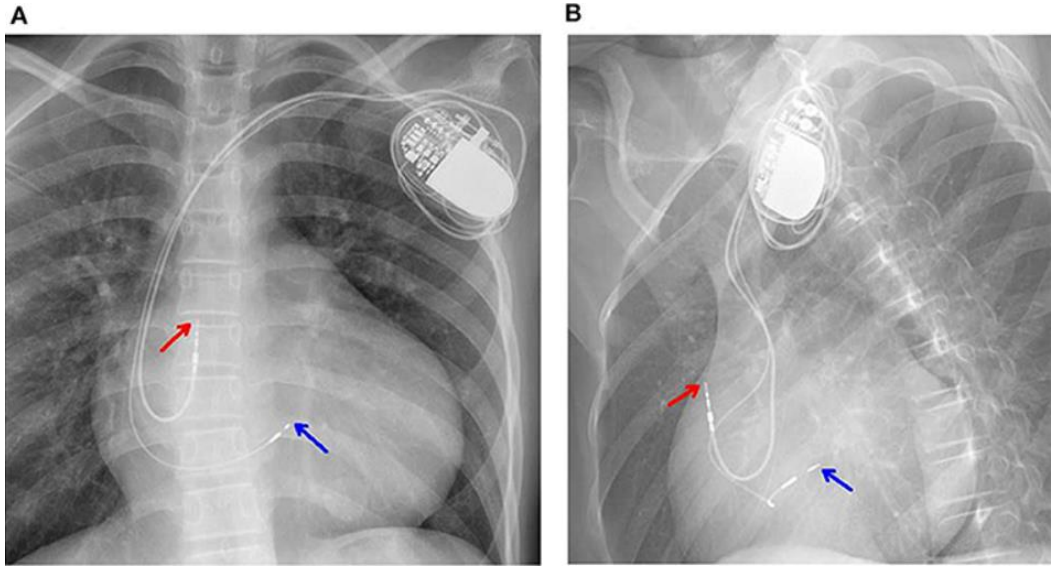
→ Bradycardia and heart failure pacing





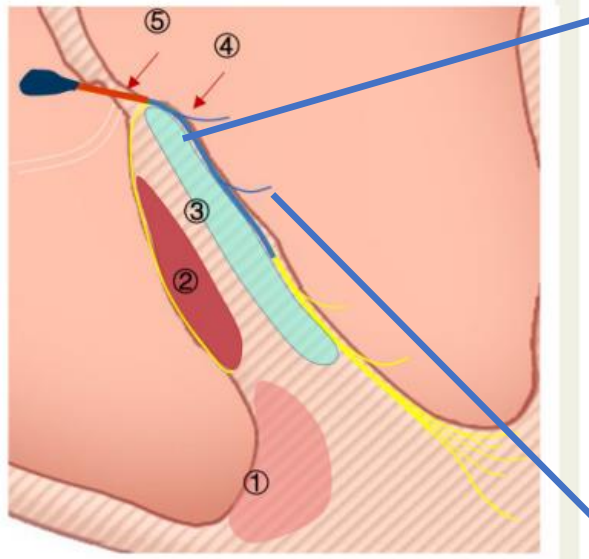


Mafi-Rad, Masih et al.« Feasibility and Acute Hemodynamic Effect of Left Ventricular Septal Pacing by Transvenous Approach Through the Interventricular Septum ». *Circulation: Arrhythmia and Electrophysiology* 9, nº 3 (mars 2016): e003344. https://doi.org/10.1161/CIRCEP.115.003344.



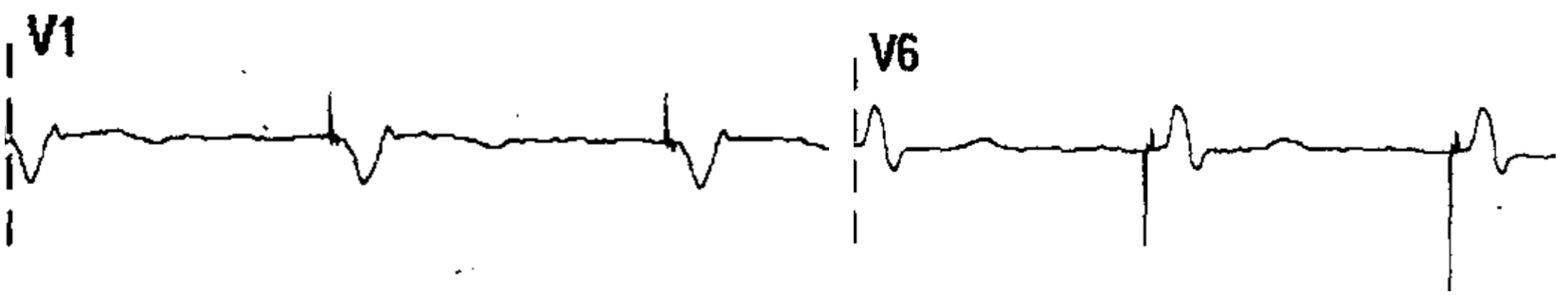
Frontiers

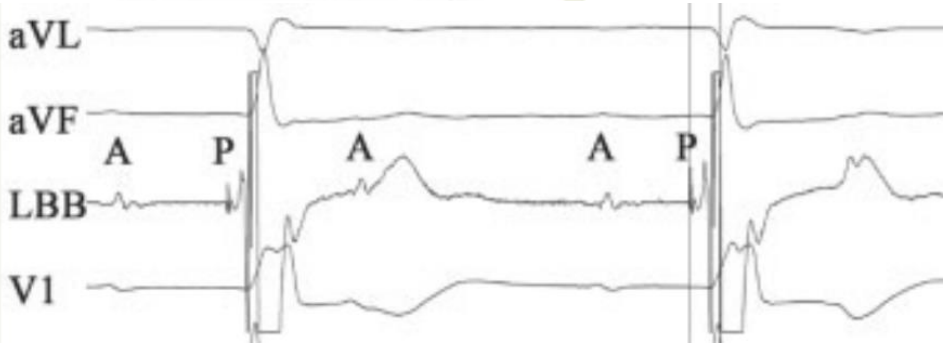
Area of pacing

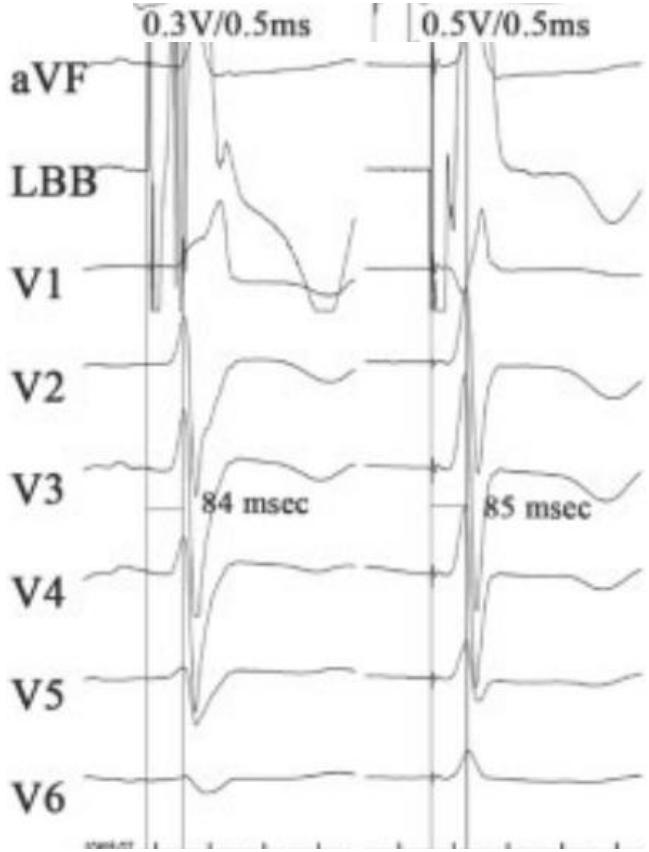


①: RV apex
②: RV septum
③: Deep LV septum
④: proximal LBB
⑤: His bundle

Left ventricular septum (12 leads ECG criteria):
- Final R wave in V1 (Incomplete RBBB pattern)
- Short Stim to R wave in V6 (LVAT)





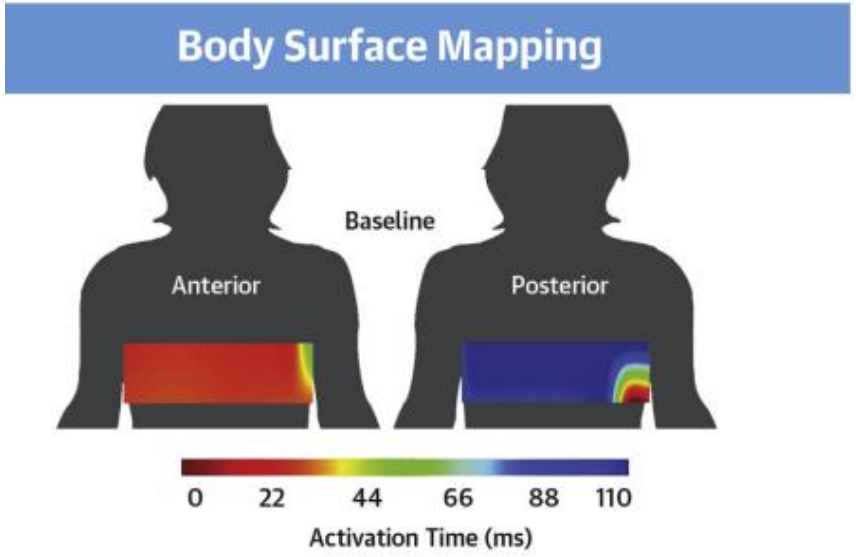


Left bundle /Fascicular Branch pacing (Purkinje system capture):

- LBB potential
- Typical RBBB morphology
- Stim to LVAT (V6) (LVAT):
  - Short and stable< 80ms
  - Abrupt shortening > 10ms

LV pacing: hemodynamic effects

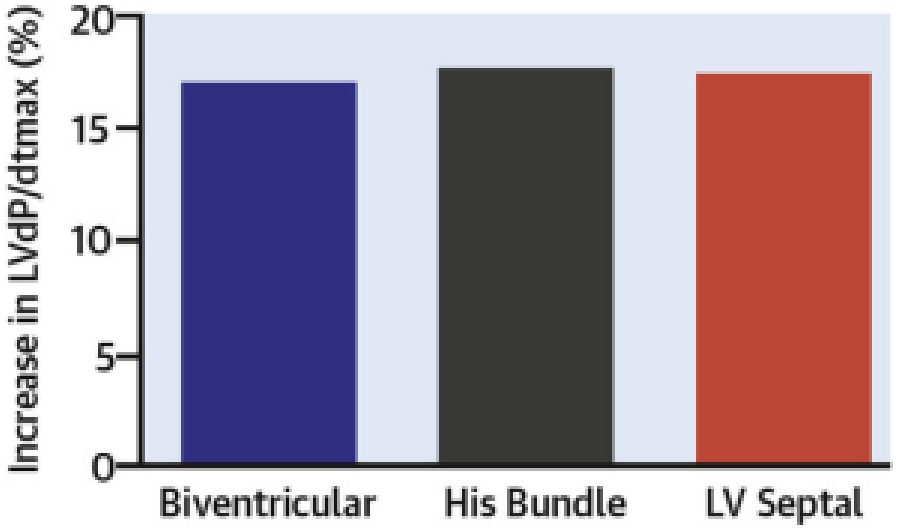
27 patients
CRT implantation
Temporary LV endocardial septal pacing with EP catheter via arterial transfemoral access
Acute body surface mapping and hemodynamics effects

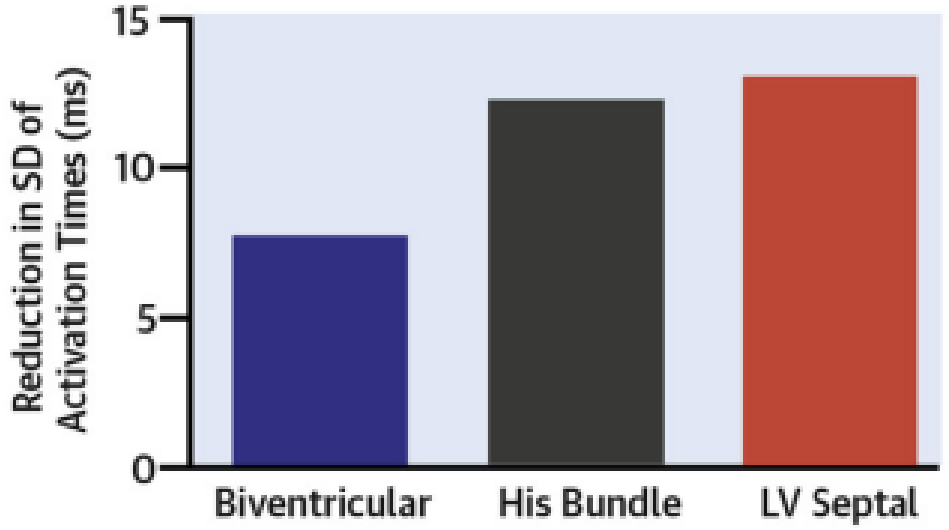


Hemodynamic Effects

Electrophysiological Effects

Salden, Floor C. *JACC* 75, nº 4 (4 février 2020): 347-59. https://doi.org/10.1016/j.jacc.2019.11.040.





< 80 ms

LV pacing feasability, what is currently known?

Prospective Evaluation of Feasibility, Electrophysiologic and Echocardiographic Characteristics of Left Bundle Branch Area Pacing

Vijayaraman et al. Heart rhythm 2019

- 100 patients with pacing indication (11 CRT with failure of LV or His lead placement)
- Follow up: 5.2+/- 3,3 month
- **LBBP successful in 93%**

- LBBP criteria:
  - 63 LBB potentials
  - RBBB in 91 patients
  - QRS duration 136+/-17ms
  - Non selective to selective LBBP in 41 patients / non selective to LVS pacing in 25 patients
  - 10 patients with septal capture only
  - LVAT in V6 75+/-16ms

MELOS

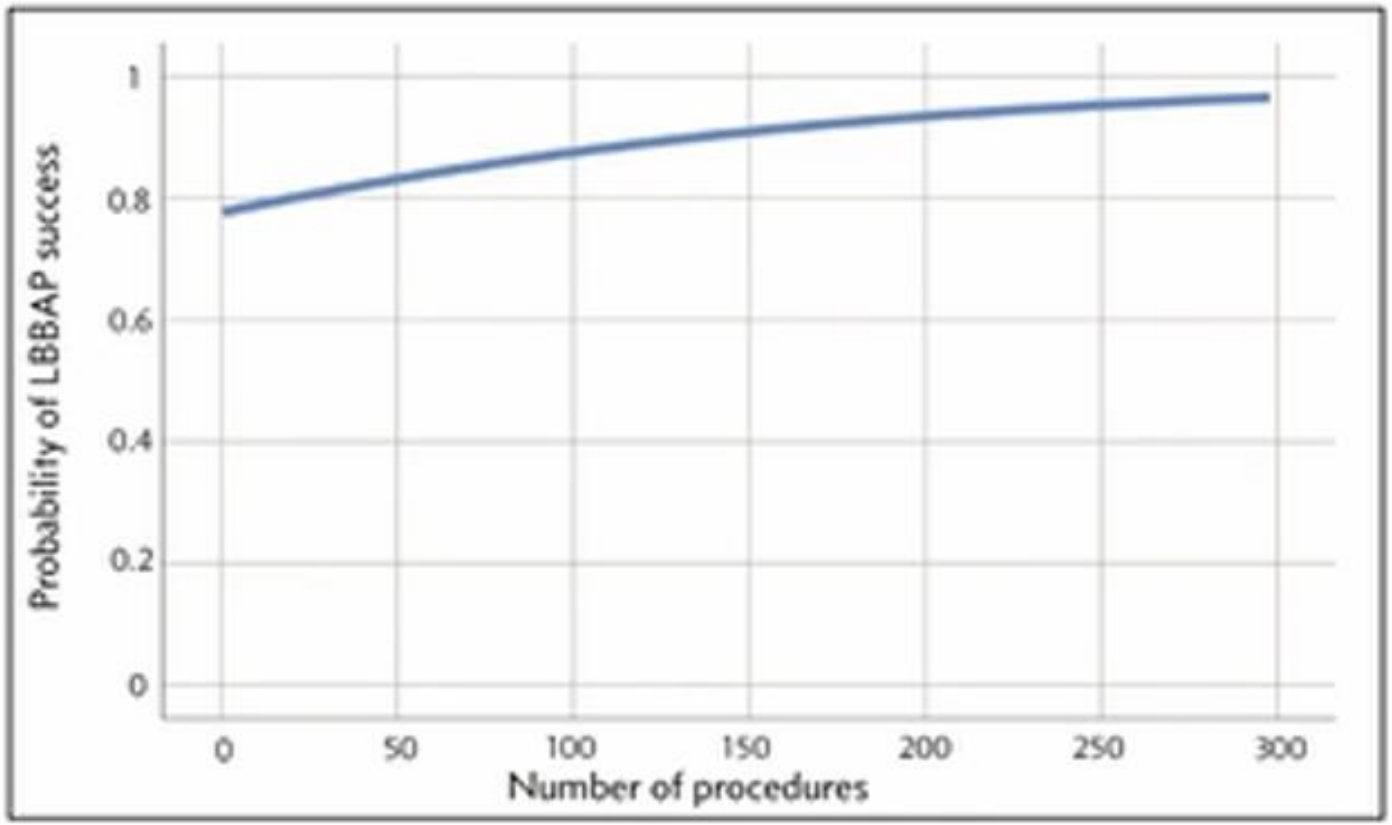
Multicentre European Left Bundle Branch Area Pacing Outcomes Study

Marek Jastrzębski, Grzegorz Kiełbasa, Oscar Cano, Karol Curila, Luuk Heckman, Jan De Pooter, Milan Chovanec, Nard Rademakers, Wim Huybrechts, Domenico Grieco, Zachary I. Whinnett, Stefan A.J. Timmer, Arif Elvan, Petr Stros, Pawel Moskal, Haran Burri, Francesco Zanon, Kevin Vernooy.

CENTER	Country	First implant	N of patients	N of operators	Registry type
Amsterdam	Netherlands	02 Dec 2019	61	3	mixed
Antwerp	Belgium	04 Feb 2020	89	1	prospective
Eindhoven	Netherlands	08 Jan 2020	100	2	prospective
Geneva	Switzerland	25 Feb 2020	121	2	ctive
Gent	Belgium	27 Nov 2019	150		
Kraków	Poland	12 Jun 2018	607		prospective
London	United Kingdom	23 Nov 2020	67	4	ive
Maastricht	Netherlands	25 Nov 2019	120	2	mixed
Prague 1	Czechia	21 Nov 2019	358	2	prospective
Prague 2	Czechia	28 Apr 2020	114	1	mixed
Rome	Italy	15 Jan 2020	125	1	prospective
Rovigo	Italy	20 May 2019	202	4	mixed
Valencia	Spain	16 Jun 2019	292	1	prospective
Zwolle	Netherlands	12 Dec 2019	127	2	prospective
SUMMARY	14	12 Jun 2018	n = 2533	31	87% prospective

- Mean age: 73.9 y.
- Female: 57.6%
- Heart failure: 27.5%
- LBBB: 22.4%

Feasibility, Success Rate, Learning Curves



- Capture threshold (0.77 V)
- Sensing (10.6 mV)
- Paced QRS 137 - 145 ms
- Paced V_6 RWPT 77 – 83 ms

success rate:

- bradyarrhythmia: **91.6%**
- for heart failure: **76.8%** (n = 383/499)

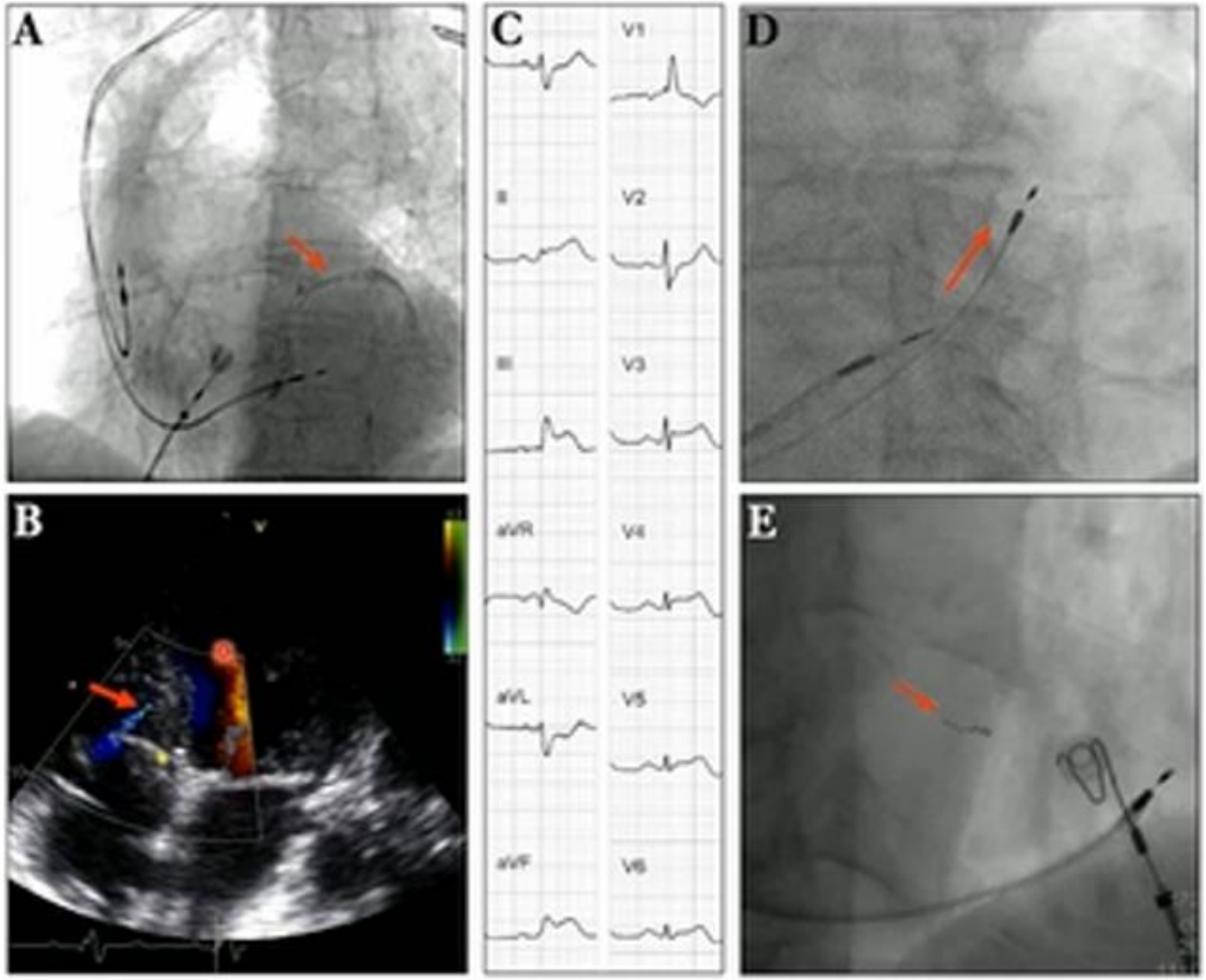
predictors of failure:

- broad baseline QRS
- depressed LVEF
- heart failure

Complications

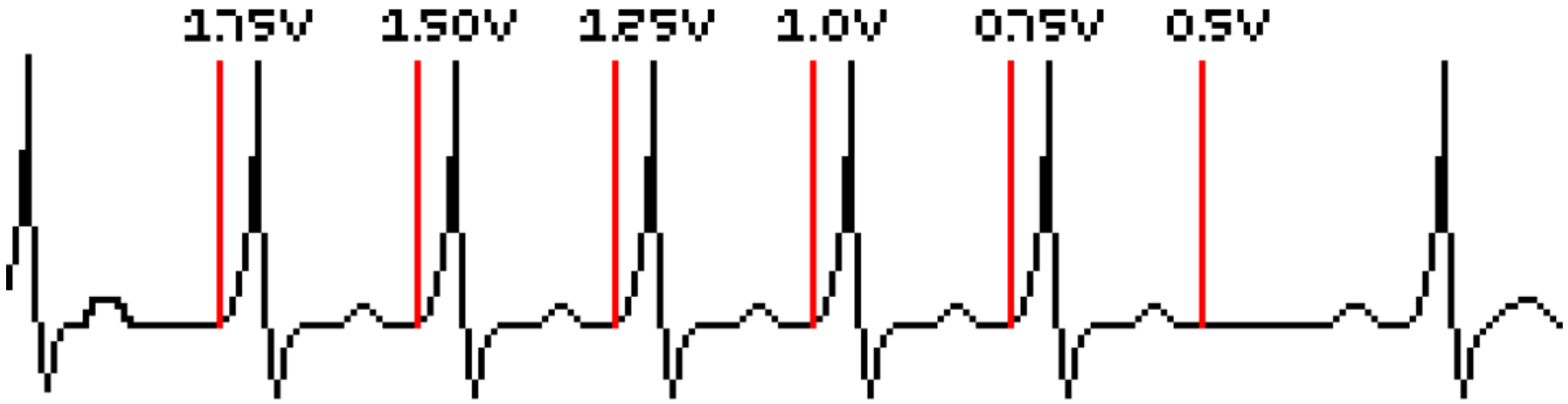
- Intraprocedural IVS perforation - 3.7%
- Delayed IVS perforation - 0.08%
- Acute chest pain - 1%
- ST elevation in multiple leads - 0.24%
- Acute coronary syndrome - 0.43%
- Coronary artery fistula - 0.28%
- LBBAP lead dislodgement - 1.5%
- Threshold > 2 V - 0.67%
- LBBAP lead non-screwable - 0.43%
- Stroke - 0%

TOTAL LBBAP lead related: 8.2%



In review

LV pacing characteristics and long term safety?

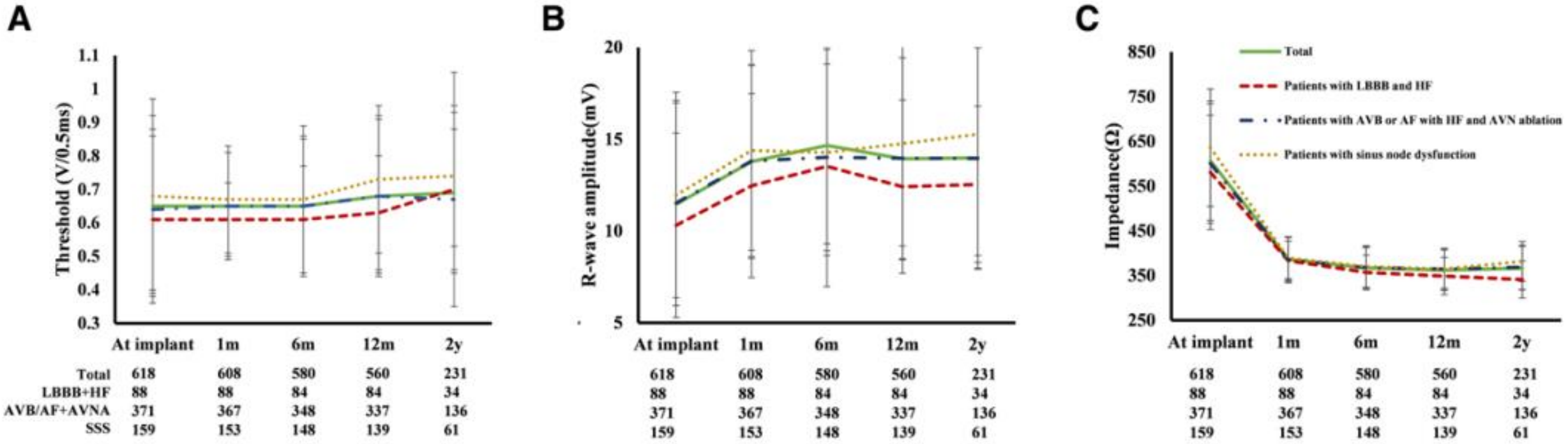


Long-Term Safety and Feasibility of Left Bundle Branch Pacing

Lan Su et al.CIRC AE 2021

- **Successful in 618/632 (97,8%) patients**
- Follow-up 18,6+/-6,7 months
- 88(14.2%) indication of CRT

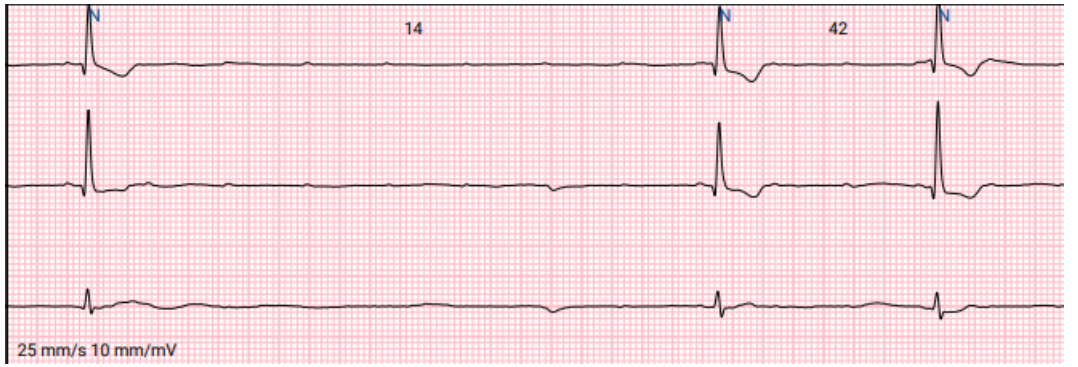
	All patients	LBBB
N	618	88
Preimplant QRS, ms	114.20±32.40	167.22±18.99
Post-LBBP QRS, ms	112.94±16.81	124.02±24.15
Sti-LVAT, ms	73.87±11.36	79.40±11.34
Preimplant mean QRS axis	20.50 (−16.00 to 56.00)	−9.00 (−39.00 to 42.25)
Post-LBBP mean QRS axis	20.00 (−17.00 to 54.00)	35.50 (−3.00 to 54.75)
Preimplant QRS transition zone	3.50 (1.50 to 3.50)	4.50 (3.50 to 4.50)
Post-LBBP QRS transition zone	1.50 (1.50 to 2.50)	1.50 (1.50 to 3.50)
LBB capture characteristic		
RBBB pattern, n (%)	618 (100%)	88 (100%)
LBB potential, n (%)	476 (77.0%)	48 (54.5%)*
Selective LBBP at implant, n (%)	460 (74.4%)	81 (92.0%)
Selective during follow-up, n (%)	191 (30.9%)	43 (48.9%)
Sti-LVAT shortens abruptly,† n (%)	533 (86.2%)	80 (90.9%)



- No serious complication
- 3.3% of any complication

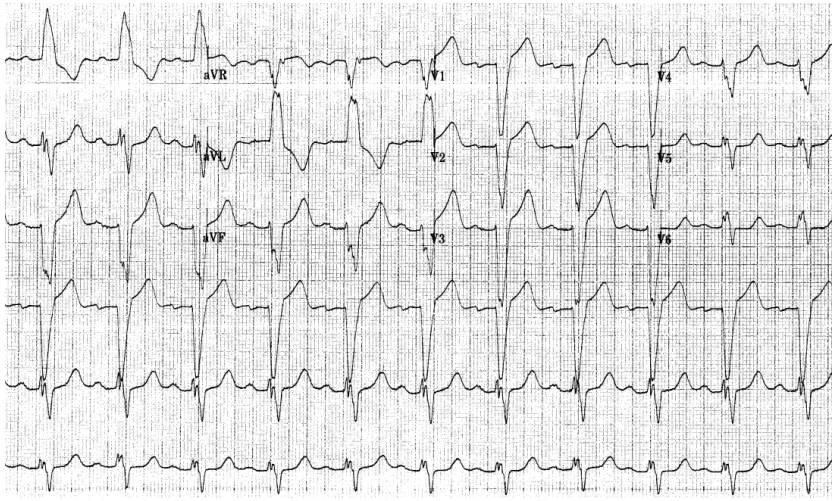
Complications	Patients (n)
Complications during procedure	
Septal perforation	2
Intravenous puncture-related arterial injury	2
Coronary artery injury	0
Complications during follow-up	
Increase of capture threshold >2 V/0.5 ms	6
Loss of conduction system capture	2
Lead revision	2
Pocket infection	2
Hematoma	1
Septal perforation	1

Standard of care…?

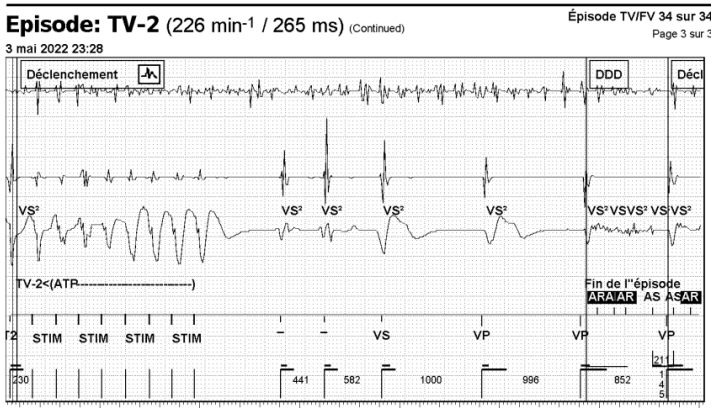


- **Bradycardia pacing?**
  - Compare to RV conventional pacing
    - No LV asynchrony and Pacing induce cardiomyopathy
    - Comparable successful implanted rate and slightly higher rate of related complication
- **Heart failure pacing?**

  (Compare to CRT)
  - Patient not responding to CRT (because of epicardial LV pacing which reverses physiologic activation of the ventricular wall (increase transmural dispersion of repolarization and QT prolongation)
  - Only one lead for LV synchrony / correction of LBBB
  - Comparable hemodynamic aspect



  (Compare to His bundle pacing)
  - HBP limitation: HBP remains challenging / located in the central fibrous septum / based on longitudinal dissociation of the His
  - Stable and optimal myocardial pacing characteristics
  - LV septal pacing in case of loss of LBB pacing because of progression disease of the conduction system



Not yet….

- **Defibrillation?**

Future

Long-term safety and efficacy of the procedure?

Improving definition criteria of LVS, LBB or Left fascicular branch pacing

Improving the design and structure of the lead as well as the delivery tools that will allow easier implantation and stabilization of the lead

Need for randomized controlled studies

- LBBP versus left septal pacing
- LBBP vs CRT
- LBBP vs HBP

Ongoing randomized studies

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Impact of Left Bundle Branch Area Pacing vs. Right Ventricular Pacing in Atrioventricular Block (LEAP-Block) (LEAP-Block)

Current Primary Outcome Measures ICMJE **(submitted: February 2, 2021)**

The primary endpoint is the time to a first event of composite outcomes, including all-cause death, hospitalization for heart failure, and an upgrade to cardiac resynchronization therapy due to pacing induced heart failure. [Time Frame: Within two years after device implantation]

All-cause death: including cardiovascular and non-cardiovascular deaths. Hospitalization for heart failure: an unplanned outpatient or emergency department visit or inpatient hospitalization in which the patient presented with signs and symptoms consistent with heart failure and required medication therapy. Upgrade to cardiac resynchronization therapy (CRT): Upgrade from dual-chamber pacemaker to CRT-Pacemaker/CRT-Defibrillator due to impaired LV function (LVEF decrease to 40% or less).

ClinicalTrials.gov Identifier: NCT04730921

Recruitment Status : Recruiting
First Posted : January 29, 2021
Last Update Posted : March 22, 2022

Estimated enrollment: 500 patients
Multicentric study in China

Conduction System Pacing With Left Bundle Branch Pacing as Compared to Standard Right Ventricular Pacing

Current Primary Outcome Measures ICMJE **(submitted: August 16, 2021)**

- Left ventricular end systolic volume index [Time Frame: 24 months]
  Echo parameter
- Successful implant [Time Frame: 30 days]
  Implant success after 4 attempts at left bundle pacing
- Feasibility of recruitment [Time Frame: 18 months]
  100 patients over 7 centers over 18 months recruitment

ClinicalTrials.gov Identifier: NCT05015660

Recruitment Status : Not yet recruiting
First Posted : August 20, 2021
Last Update Posted : August 20, 2021

Estimated enrollment: 100 patients
McGill university in Montreal,Canada

Left Bundle Area Versus Selective His Bundle Pacing (LEFTBASH)

Current Primary Outcome Measures ICMJE **(submitted: February 21, 2020)**

Ventricular Capture Threshold, 3 months unipolar or Bipolar [Time Frame: 3 months]

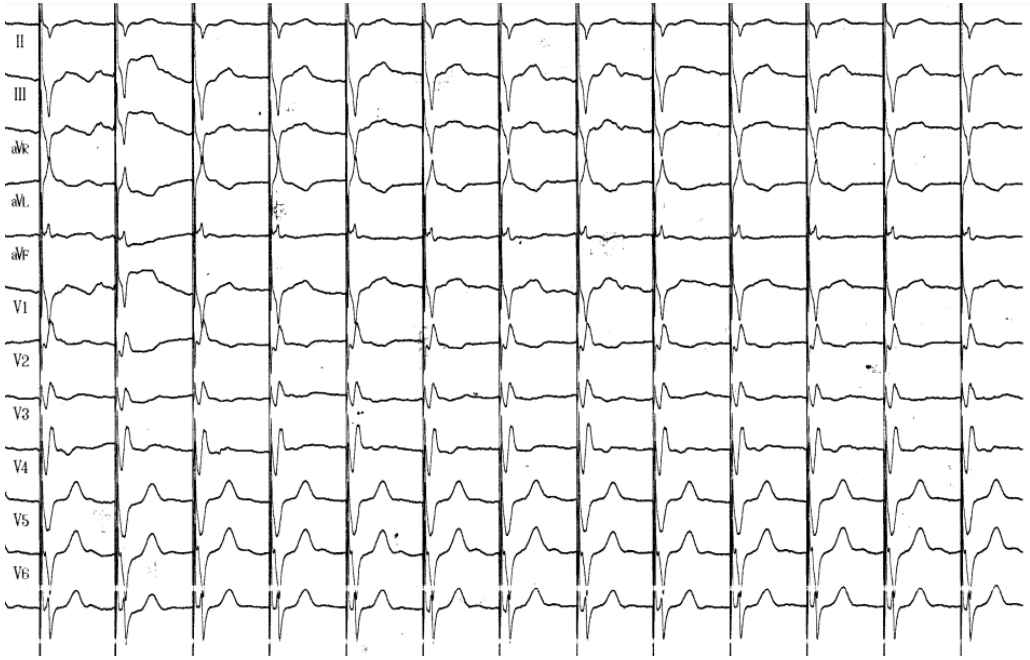
Ventricular capture threshold is the minimum amplitude that consistently results in capture of the ventricular myocardium with a 1.0 millisecond pulse width setting in unipolar or Bipolar output, measured in volts. The measurement is automatically captured and will be interrogated from the pacemaker device at 3 months post implantation.

ClinicalTrials.gov Identifier: NCT04093414

Recruitment Status : Recruiting
First Posted : September 18, 2019
Last Update Posted : November 10, 2021

Beaumont hospital, Michigan, USA

Conclusion: LV pacing appears to be an upcoming standard



- New strategy of conduction system pacing
- High-rate successful implantation
- Using only 1 ventricular lead
- With Consistent pacing characteristics

- Limited but growing evidence for safety and efficacy

- **Large prospective comparative data are still missing to modify guidelines**

Thank you for your attention

Comparison of first performed conduction system pacing feasilibity and safety at short, mid and long term in a monocentric universitary hospital

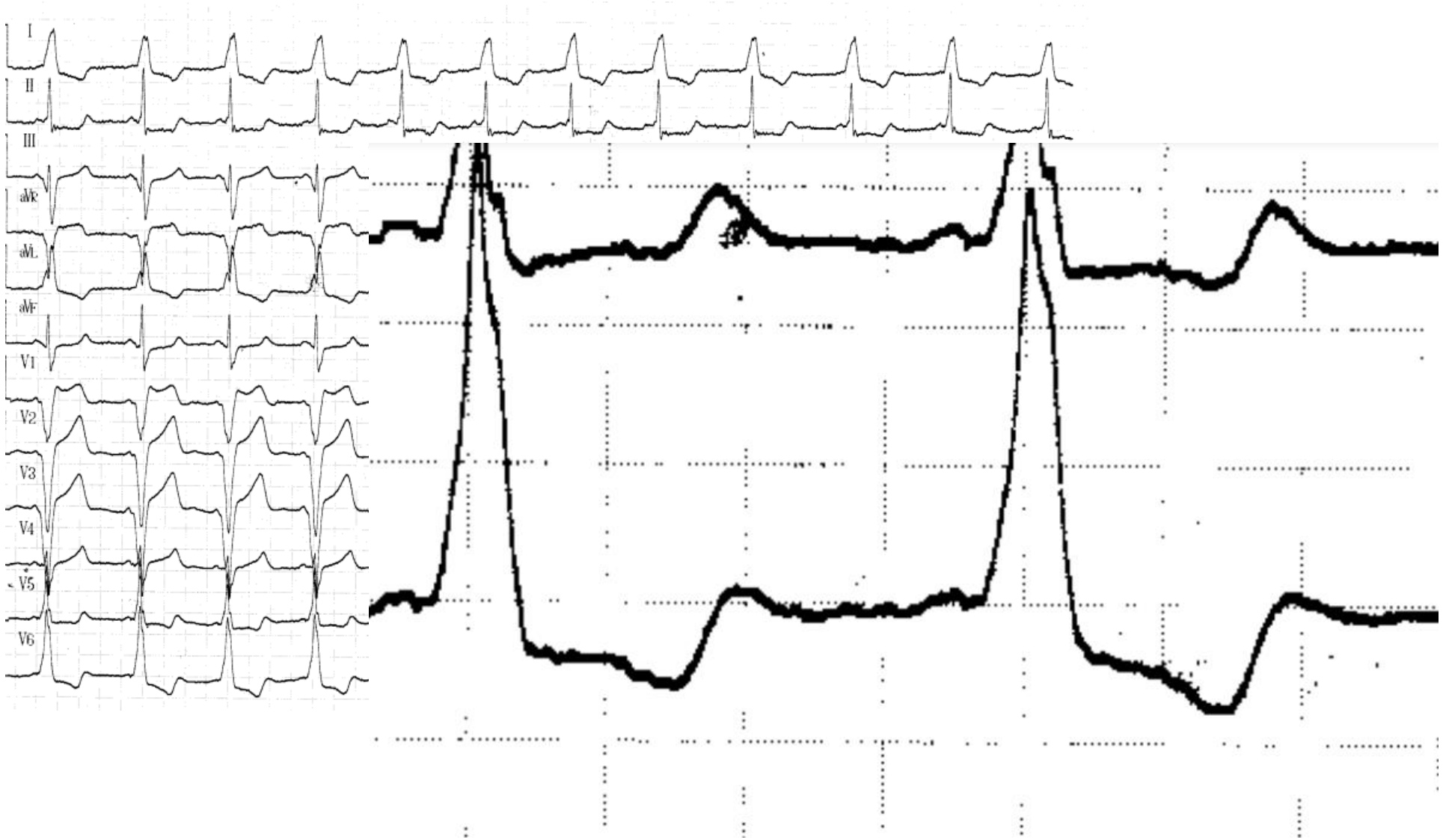
- His ventricular pacing
  - April 2019 – August 2021
  - Successful implantation: 35/42
  - Pacing characteristics:
    - 7/35 (20%) loss of his ventricular pacing
      - 1 loss of ventricular capture with ventricular pacing > 3.5V (at 3 months) (his selective pacing)
      - 6 loss of his pacing with persistent RV pacing
- LBB pacing
  - June 2021 – May 2022
  - Successful implantation: 42/45
  - Pacing characteristics:
    - No loss of ventricular capture

Primary outcome measure: Rate of effective physiological conduction system pacing, on 12 leads ECG at 6 months.

LBBAP
Larger target area than with HBP
Higher success rate in case of proximal block and potential to correct more distal conduction disease
Low capture thresholds
Good sensing parameters
Consistent myocardial capture (in addition by anodal capture with the ring electrode) to avoid asystole in case of loss of left bundle capture
No requirement for backup pacing leads
AV nodal ablation without risk of compromising lead function (due to distant position of the pacing lead)
Successful conduction tissue capture may be more difficult to demonstrate
Results in paced QRS with incomplete RBBB pattern (and possibly less electrical synchrony compared with HBP, especially in patients with normal baseline QRS)
Electrophysiological recording system useful for mapping the left bundle branch or Purkinje potential and confirming left bundle branch capture with measurement of stimulus to R-wave peak duration (although

Continued

LBBAP
lso possible using a pacing system analyser and 12-ead ECG recorder)
Currently only performed with a single lead model
Risk of transseptal perforation (during and after mplantation)
May be challenging in patients with septal scar or sep-al hypertrophy
Limited (but growing) evidence for safety and efficacy.
No experience with respect to lead performance dur-ng long-term follow-up
Long-term extractability needs to be demonstrated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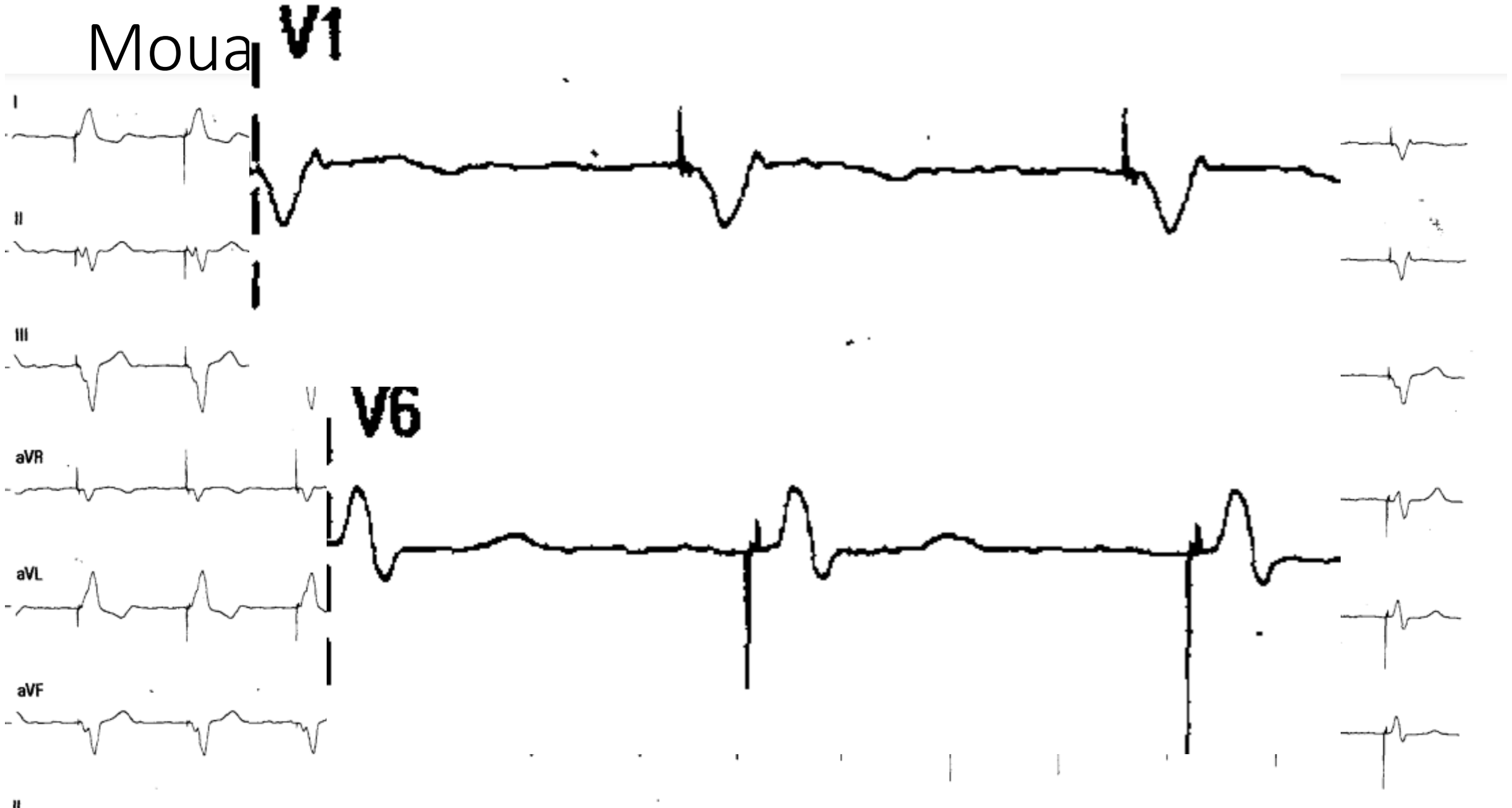

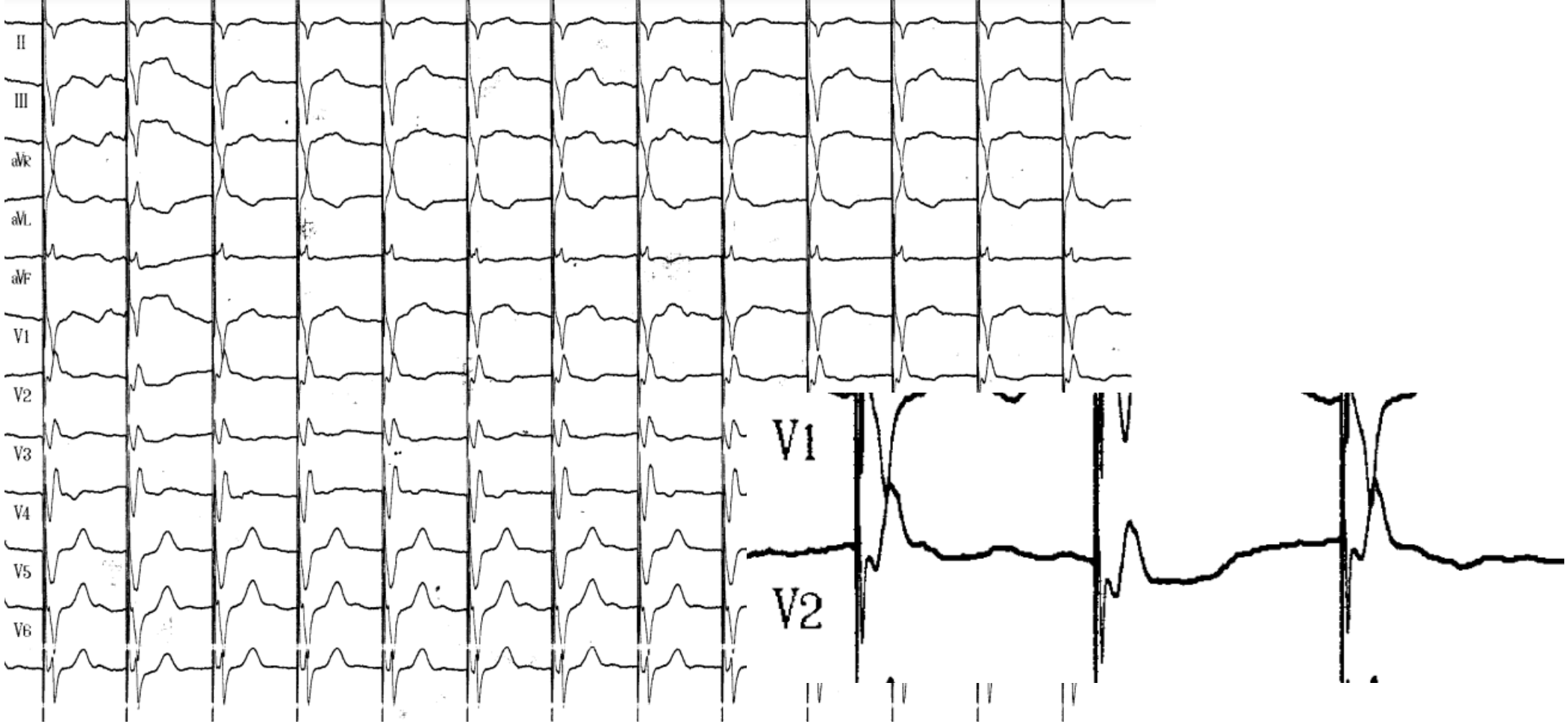
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V3
V4
V5
V6

V1
V2