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Mayo Clinic Department of Cardiovascular Medicine

Pacing from 1 or 2 ventricles, His bundle or below?

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Faculty Disclosure

Relevant financial relationship(s) with industry

None

Off Label Usage

None

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Faculty Disclosure

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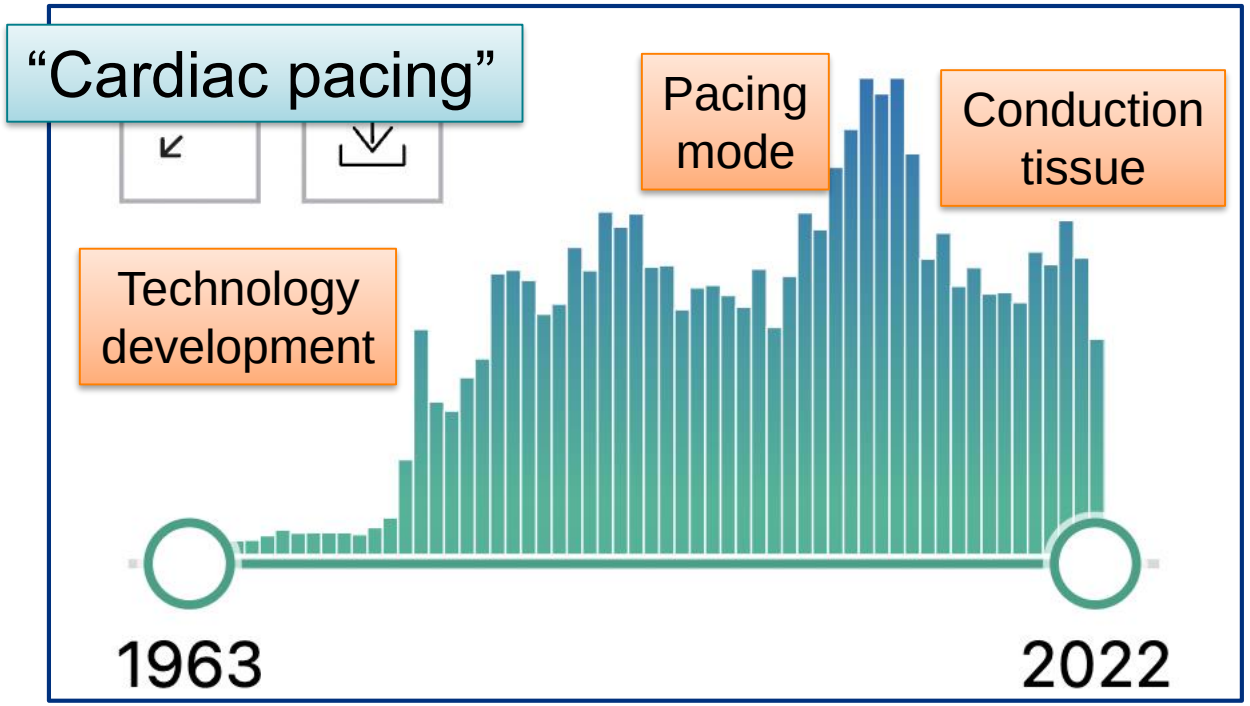
Ventricular depolarization:
Does it make a difference?

- Different methods for ventricular depolarization
- Evidence base
  - Bradycardia
  - Heart failure



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Ventricular depolarization:
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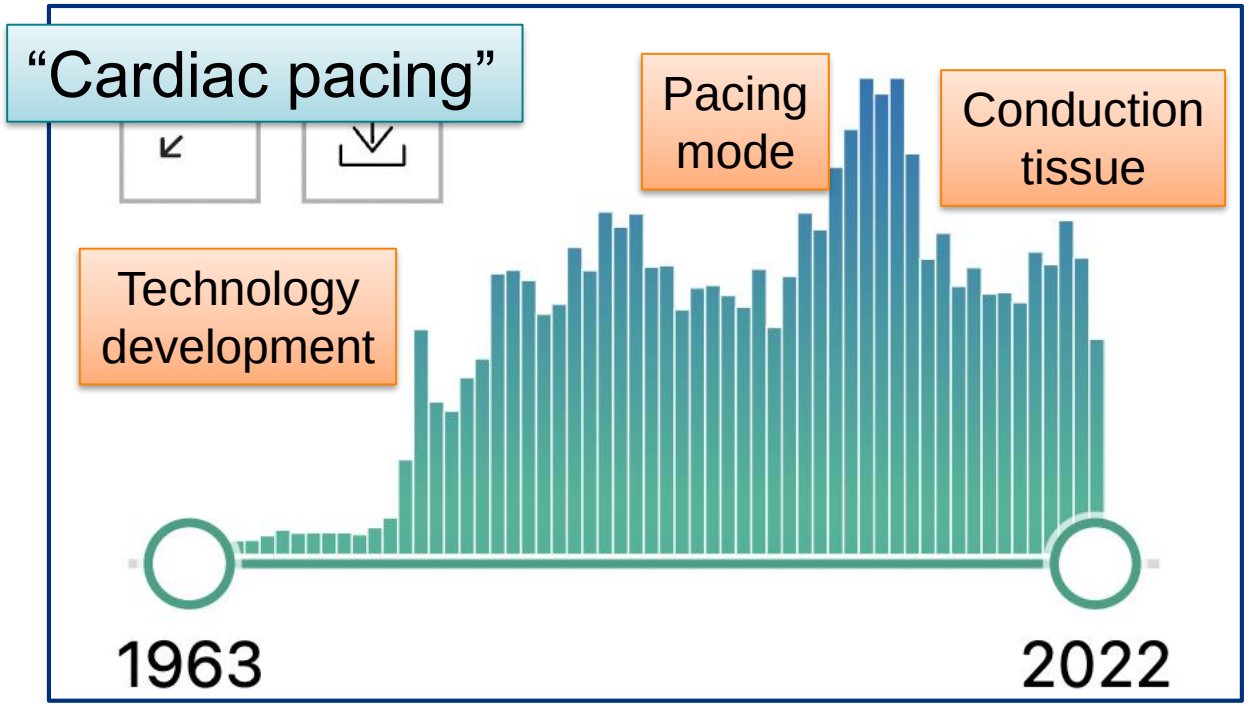

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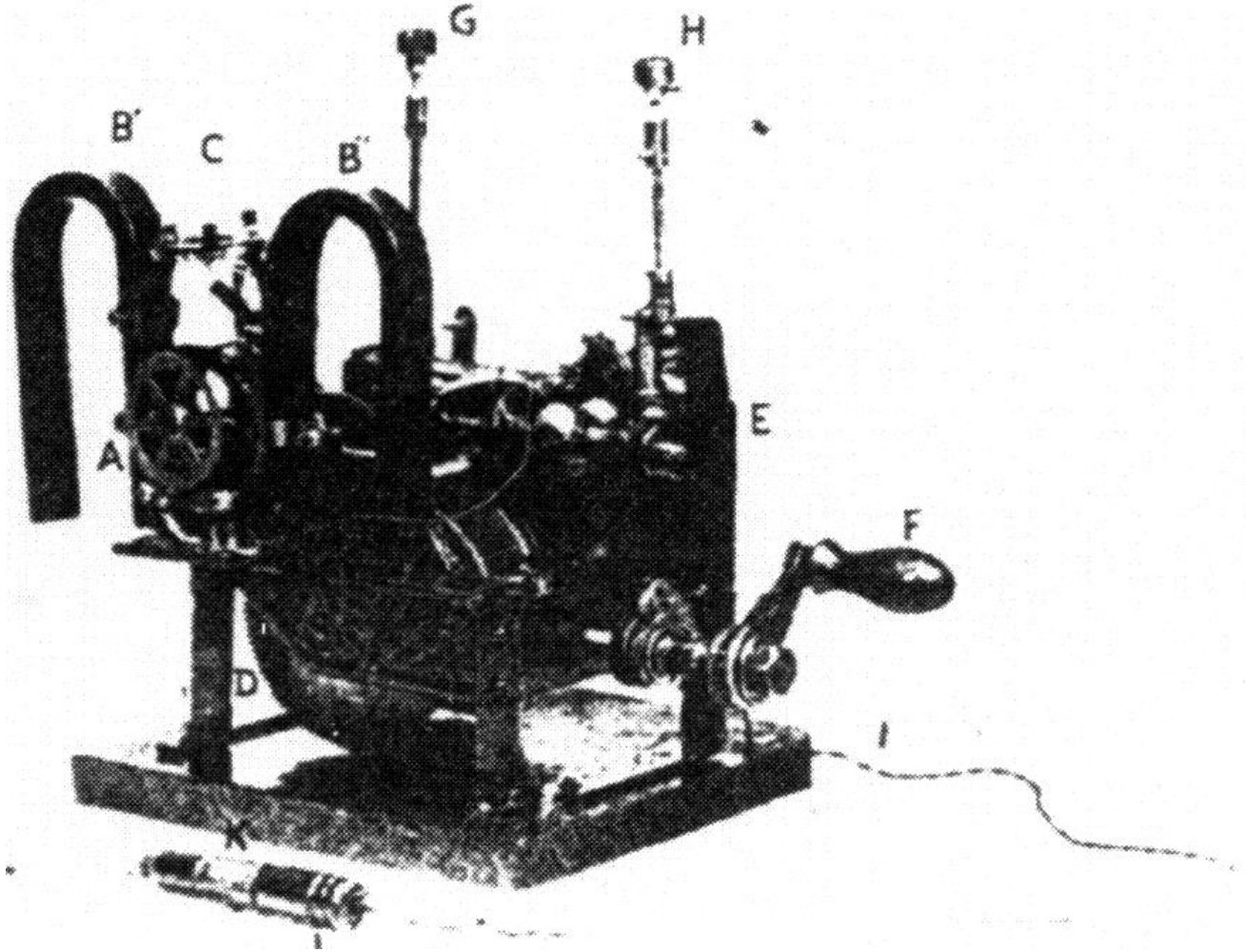

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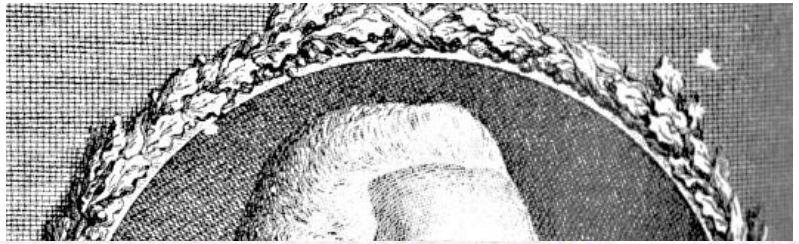

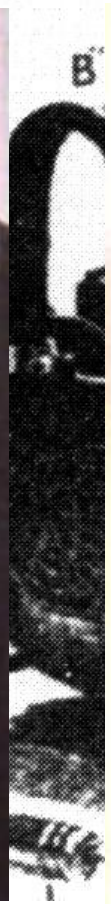

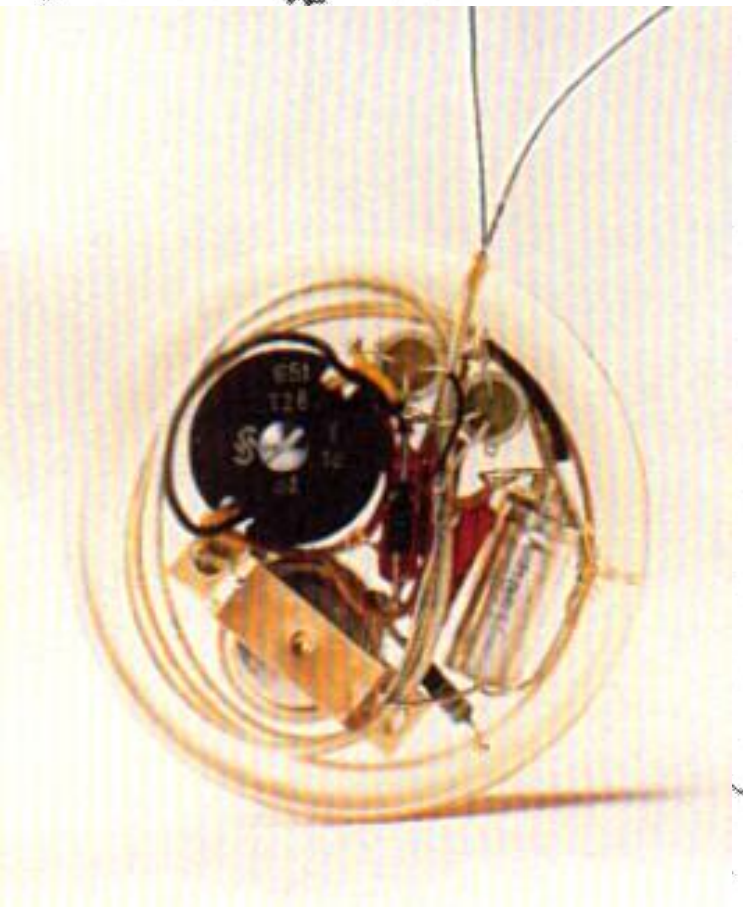

la Faculté de Médecine de Paris.

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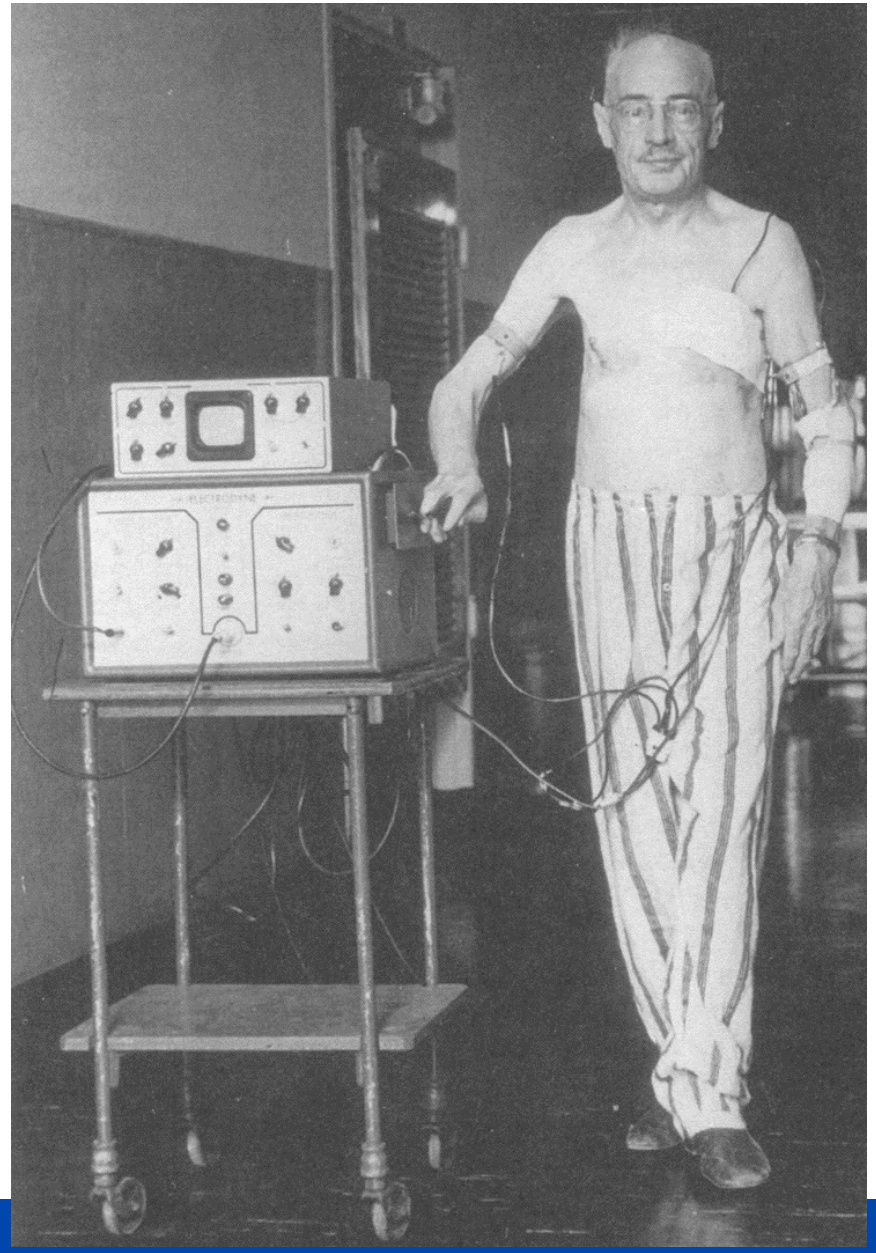

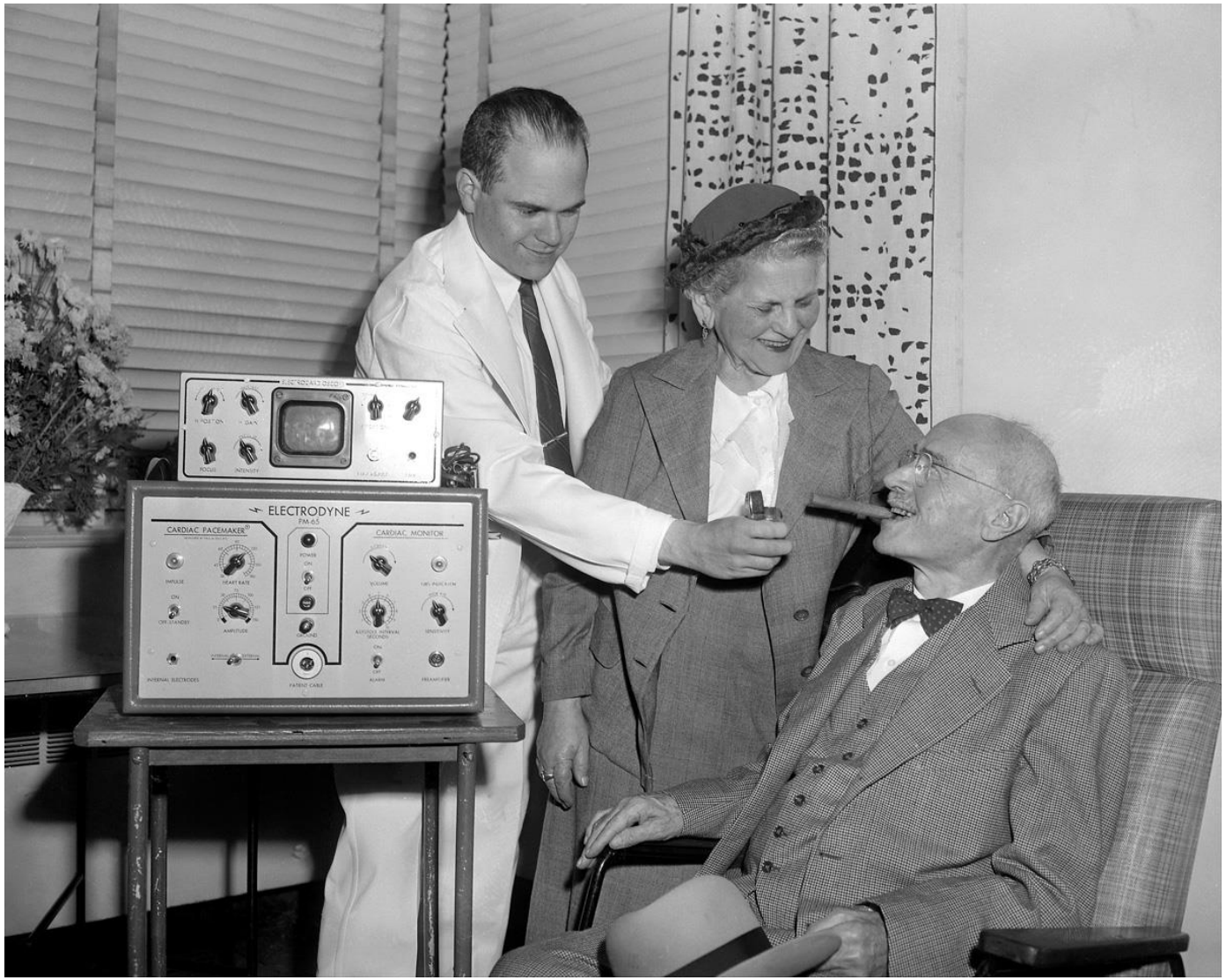

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Different anatomic locations for ventricular pacing

- Right ventricle
- Right and left ventricle (left ventricle)
- Conduction system

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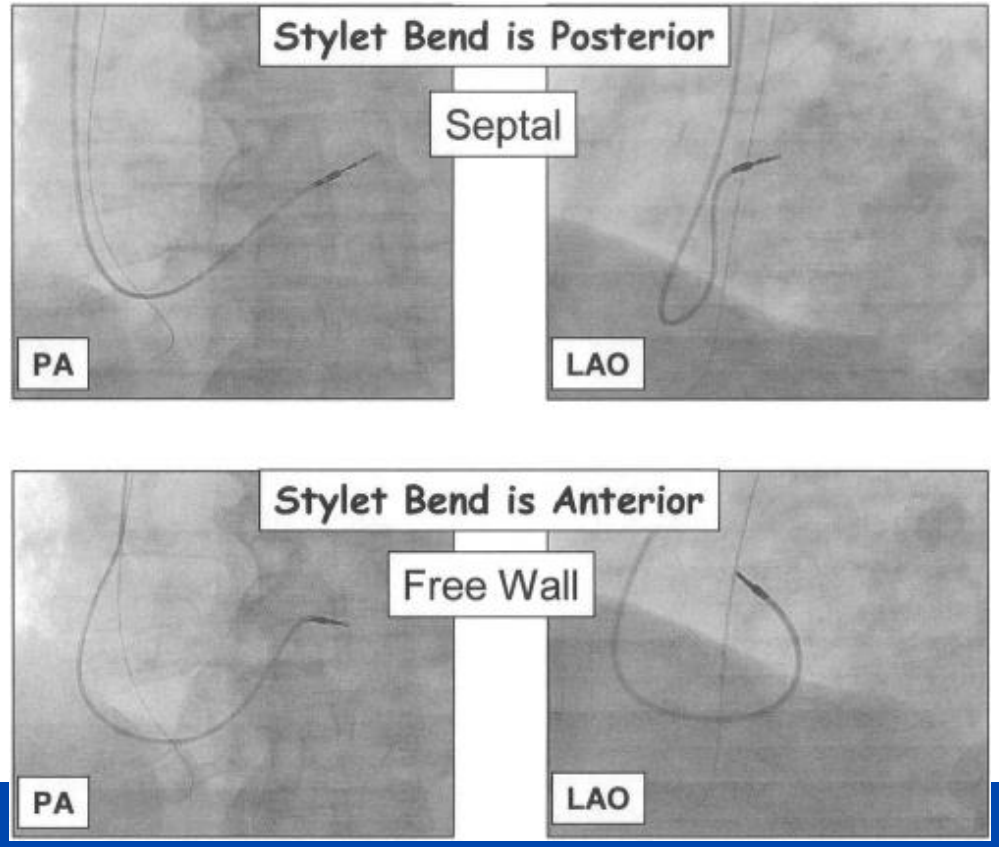
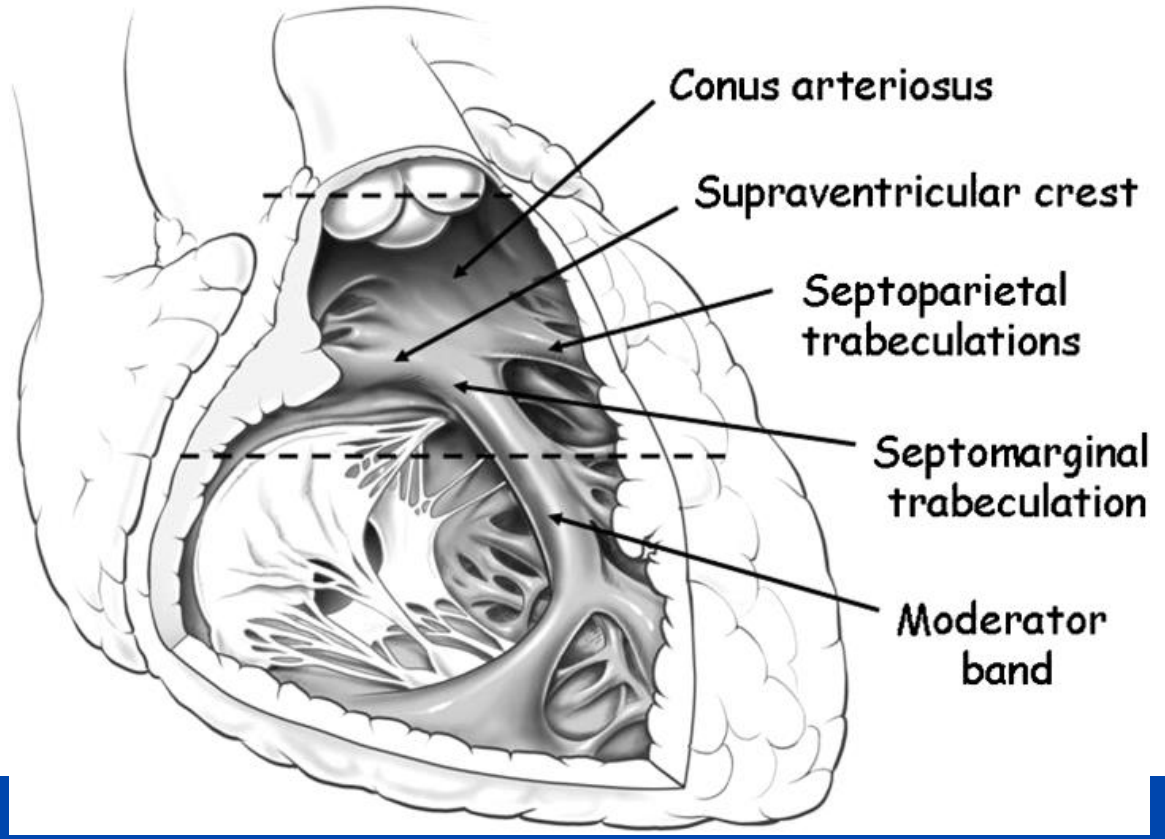
Right ventricular pacing

- Initially right ventricular apex and with the development of active fixation leads different sites were evaluated: *RVOT and RV septum*





Mond et al PACE 2007

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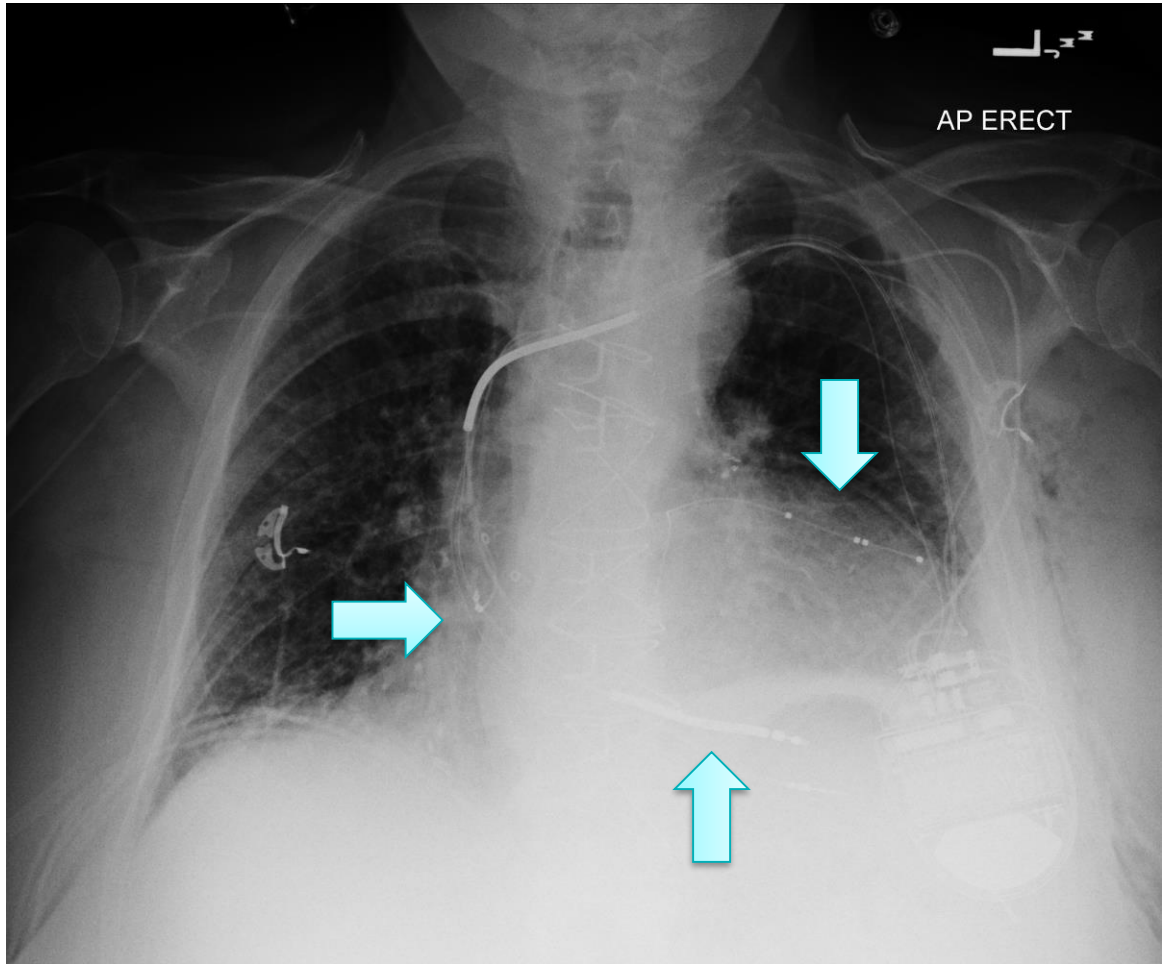
Cardiac resynchronization Therapy
RV and LV pacing

- In the1980's LV pacing identified to be more beneficial than RV pacing in acute hemodynamic studies, but difficult to implement with existing technology
- In 1987 Morton Mower applied for the patent for biventricular pacing
- First case series in 1994



Grines et al Circ 1990, Prinzen et alk AJP 1990, DeTeresa 7th World Symposium on Cardiac Pacing 1983, Befeler et al EJC 1979, Mower 1987, Bakker et al PACE 1994, Cazeau et al PACE 1994,

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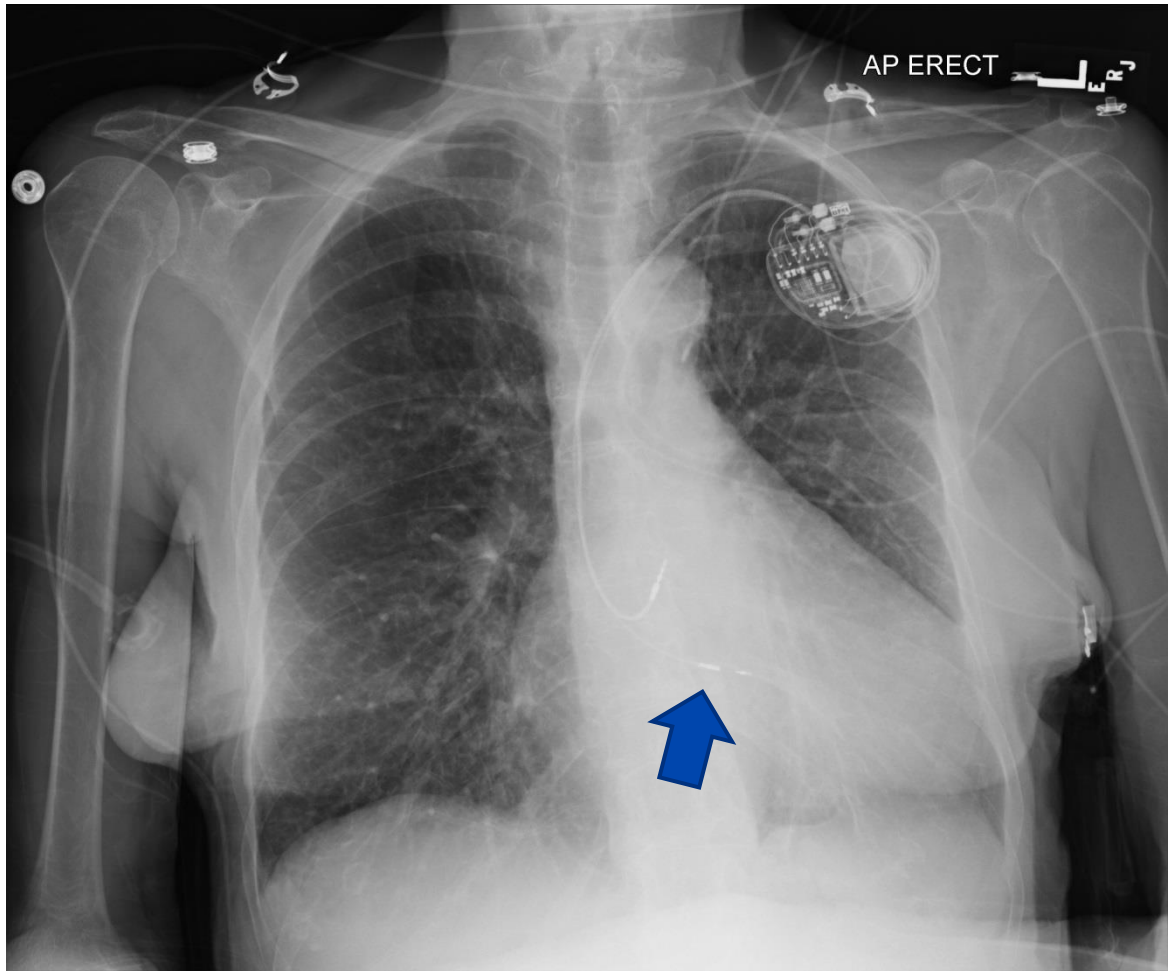
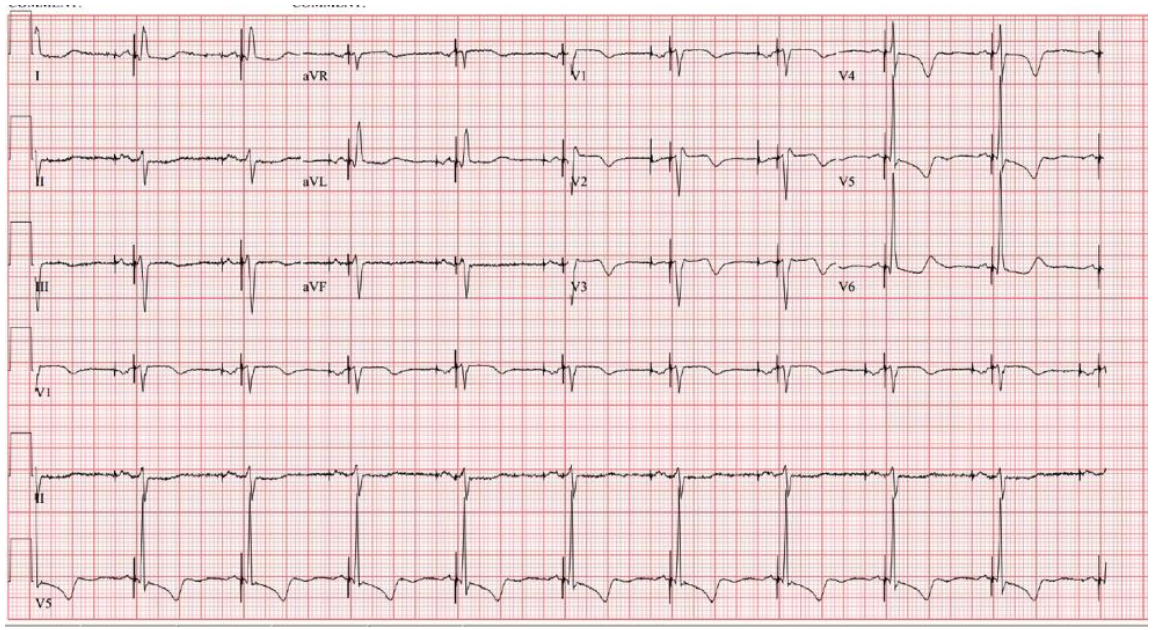
His bundle pacing





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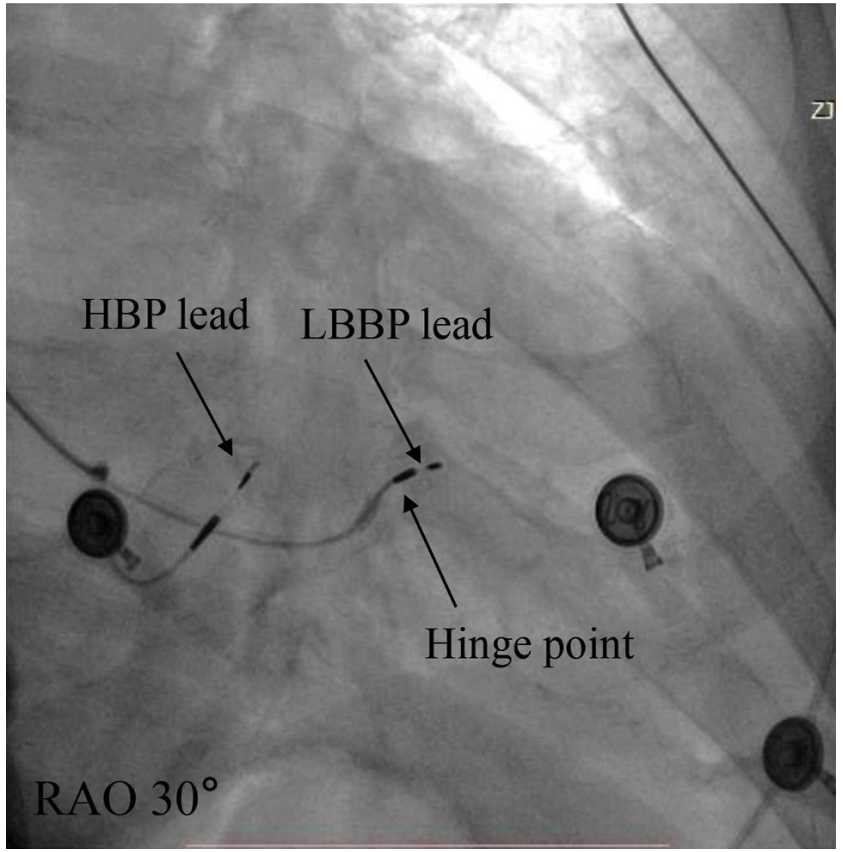
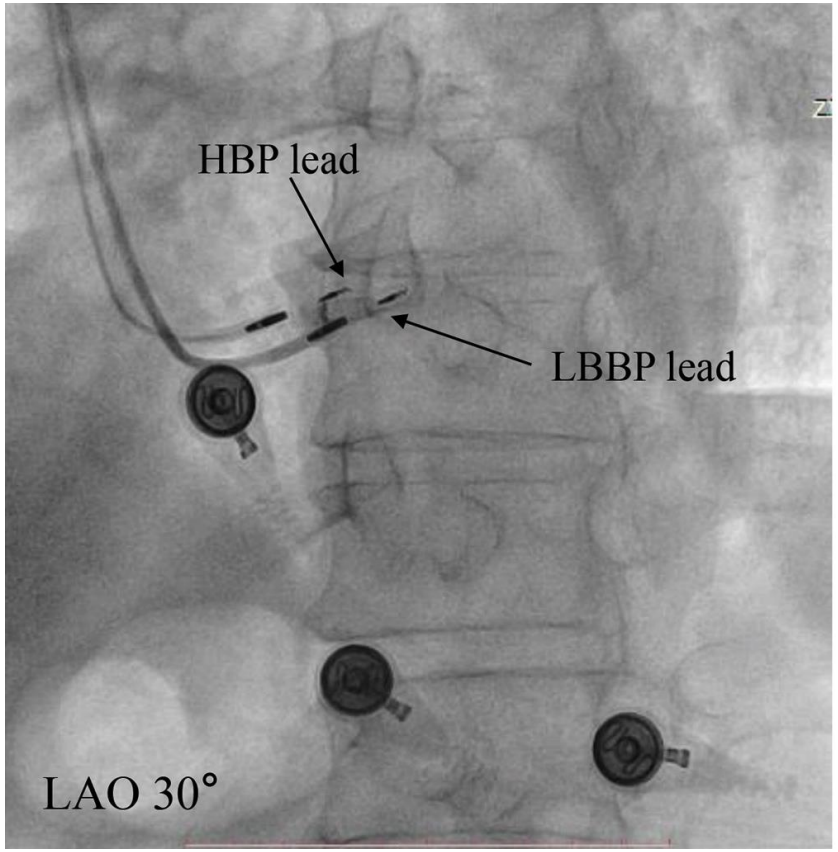
Left bundle pacing

Possible Advantages:

- Lower thresholds
- Larger R waves
- Less likely to be affected by distal block





Huang et al HR 2019; Huang et al CJC 2017

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Lef

Permanent, Direct His-Bundle Pacing

A Novel Approach to Cardiac Pacing in Patients With Normal His-Purkinje Activation

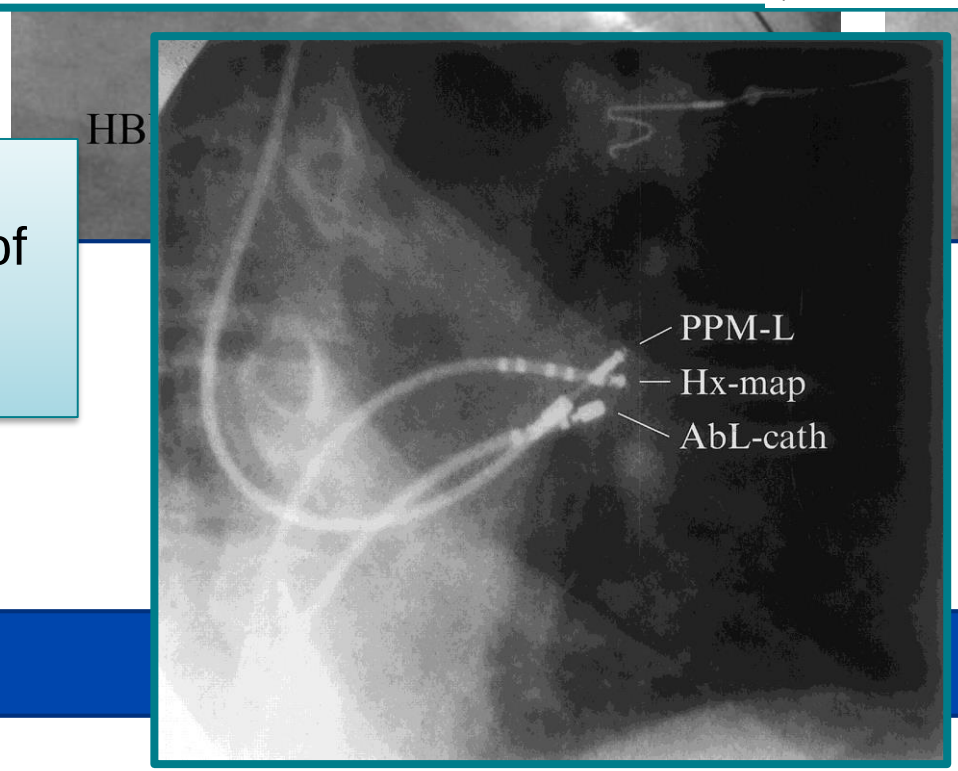
Pramod Deshmukh, MD; David A. Casavant, MS;
Mary Romanyshyn, CRNP; Kathleen Anderson, BSN

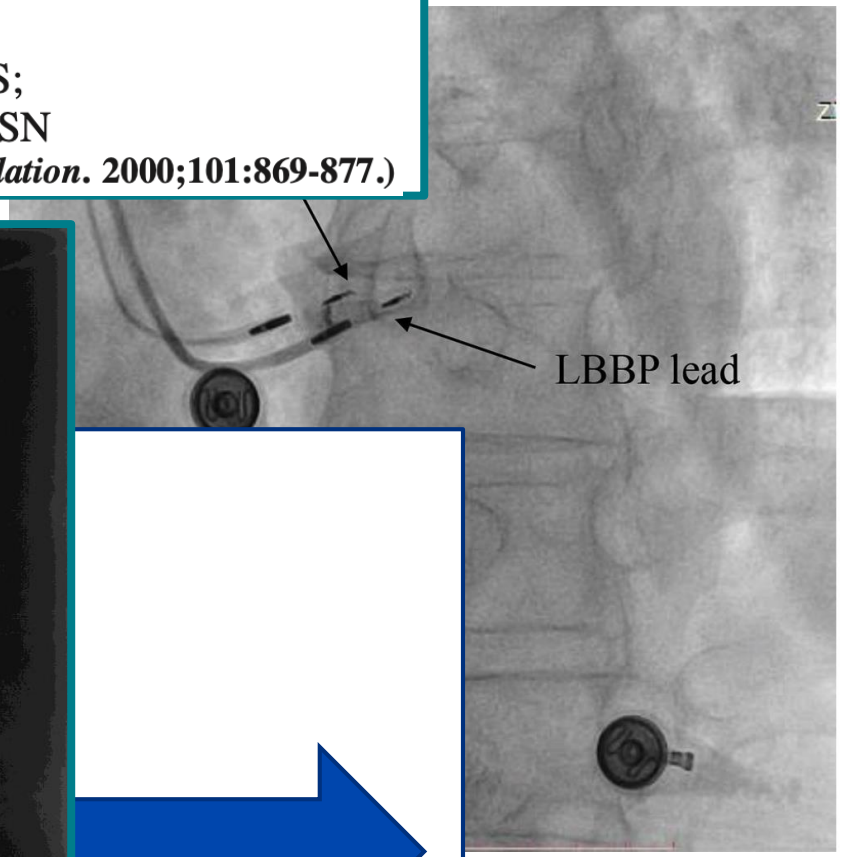
(*Circulation*. 2000;101:869-877.)

Possible Advantages:

- Lower th
- Larger P
- Less like affected b block

Initial description of His bundle pacing





2000

Huang et al HR 2019; Huang et al CJC 2017

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Left bundle

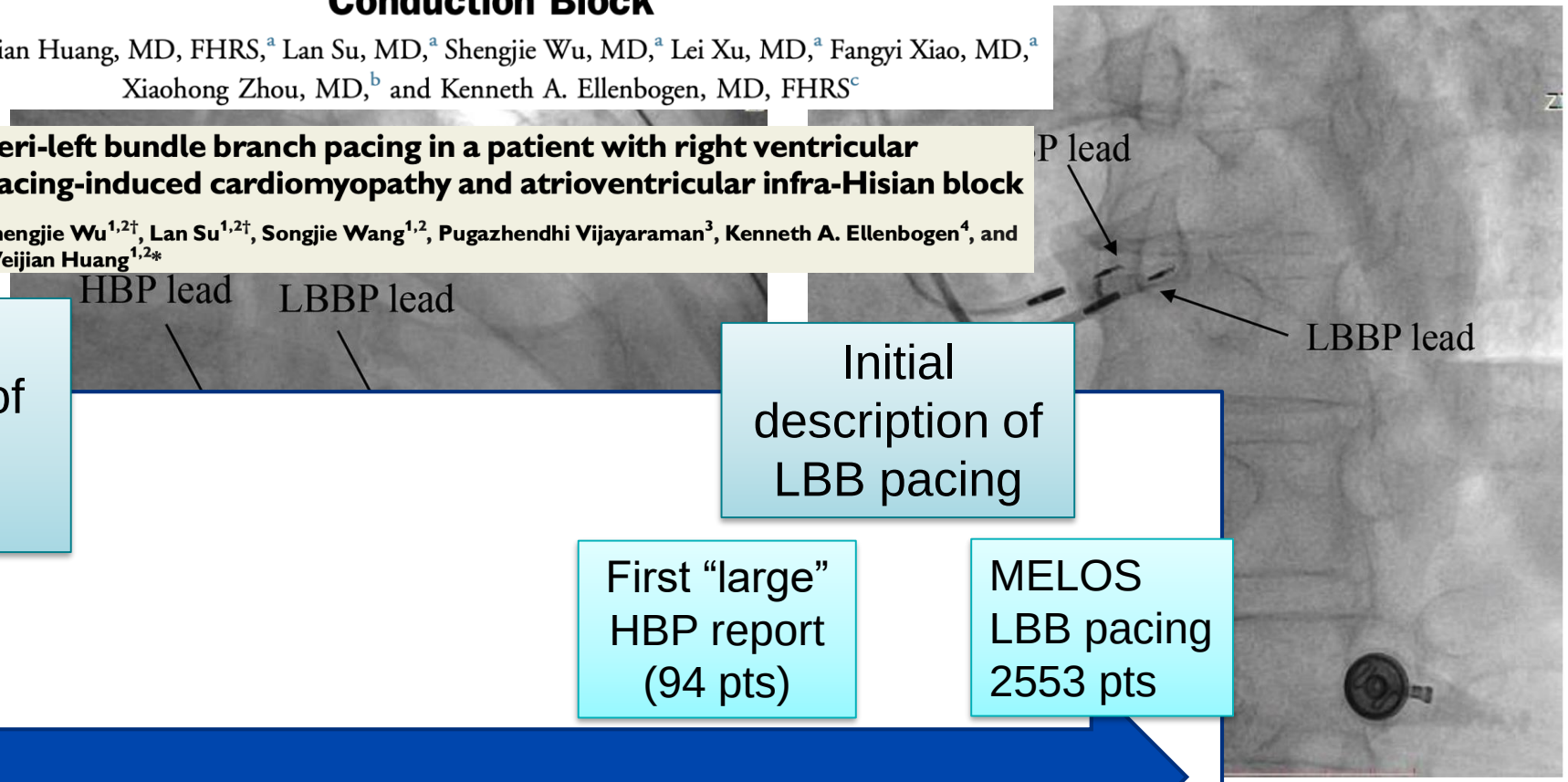
Case Report

A Novel Pacing Strategy With Low and Stable Output: Pacing the Left Bundle Branch Immediately Beyond the Conduction Block

Weijian Huang, MD, FHRS,[a] Lan Su, MD,[a] Shengjie Wu, MD,[a] Lei Xu, MD,[a] Fangyi Xiao, MD,[a] Xiaohong Zhou, MD,[b] and Kenneth A. Ellenbogen, MD, FHRS[c]

Peri-left bundle branch pacing in a patient with right ventricular pacing-induced cardiomyopathy and atrioventricular infra-Hisian block

Shengjie Wu[1,2†], Lan Su[1,2†], Songjie Wang[1,2], Pugazhendhi Vijayaraman[3], Kenneth A. Ellenbogen[4], and Weijian Huang[1,2*]



Possible Advantages:

- Lower th
- Larger F
- Less like affected b block

Initial description of His bundle pacing

Initial description of LBB pacing

First "large" HBP report (94 pts)

MELOS LBB pacing 2553 pts

2000 2015 2017/2019 2022

Huang et al HR 2019; Huang et al CJC 2017

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Ventricular depolarization:
Does it make a difference?

- Different methods for ventricular depolarization
  - *Rapidly evolving field of physiologic pacing*
  - *More rapid adoption of LBB pacing when compared to His bundle pacing?*
- Evidence base
  - Bradycardia
  - Heart failure

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Ventricular depolarization:
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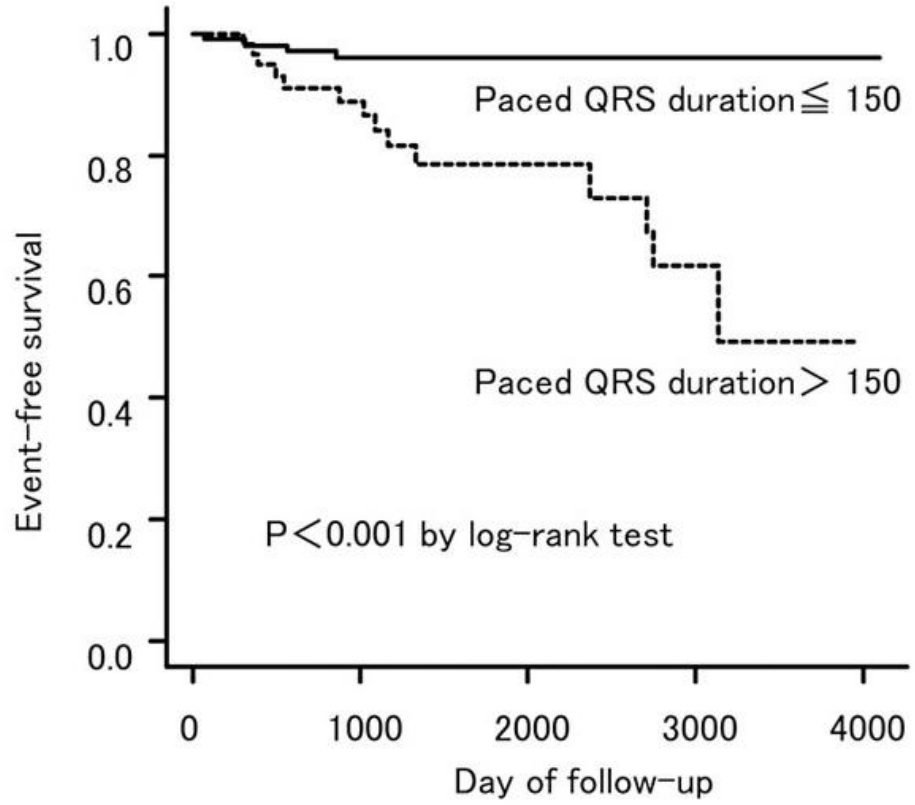
Right ventricular pacing induced LV dysfunction
Impact on LVEF

- Abnormal hemodynamics with RV pacing known for years
- Incidence has been identified as 7-11% in studies designed to evaluate incidence
- Perhaps lower with leadless pacing vs TVP (3% vs. 14%): tricuspid regurgitation?
- Incidence depends in part on definition
- Mixed results with RV pacing sites, but wide paced QRS duration appears to be a consistent predictor of higher likelihood of PICM



Patients at risk

Paced QRS ≦ 150	107	72	30	12	2
Paced QRS > 150	62	38	17	6	0

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Mittal , Yoshiyama et al J Arr 2022, Sanchez et al JCE 2020, Khursid et al HR 2014, Kaye et al Heart Lung Circ 2018, Lee MA et al JACC 1994,

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Bradycardia due to AVB
RCT for different right ventricular pacing sites in AVB

Septal vs. Apical

- 141 patients with high degree AVB randomized to septal or apical placed RV leads

LVEF

	Baseline	F/U (18 m)
Apical	57 ± 12%	57 ± 13%
Septal	58 ± 11%	57 ± 11%

RVOT vs. Apical

- 96 patients with high degree AVB randomized RVOT or apical placed RV leads

LVEF

	Baseline	F/U (12 m)
Apical	68 ± 6%	68 ± 5%
Septal	68 ± 6%	66 ± 7%

No patient developed Pacing induced CM

Gong et al Clin Card 2009, Galand et al Arch CV Dis 2022

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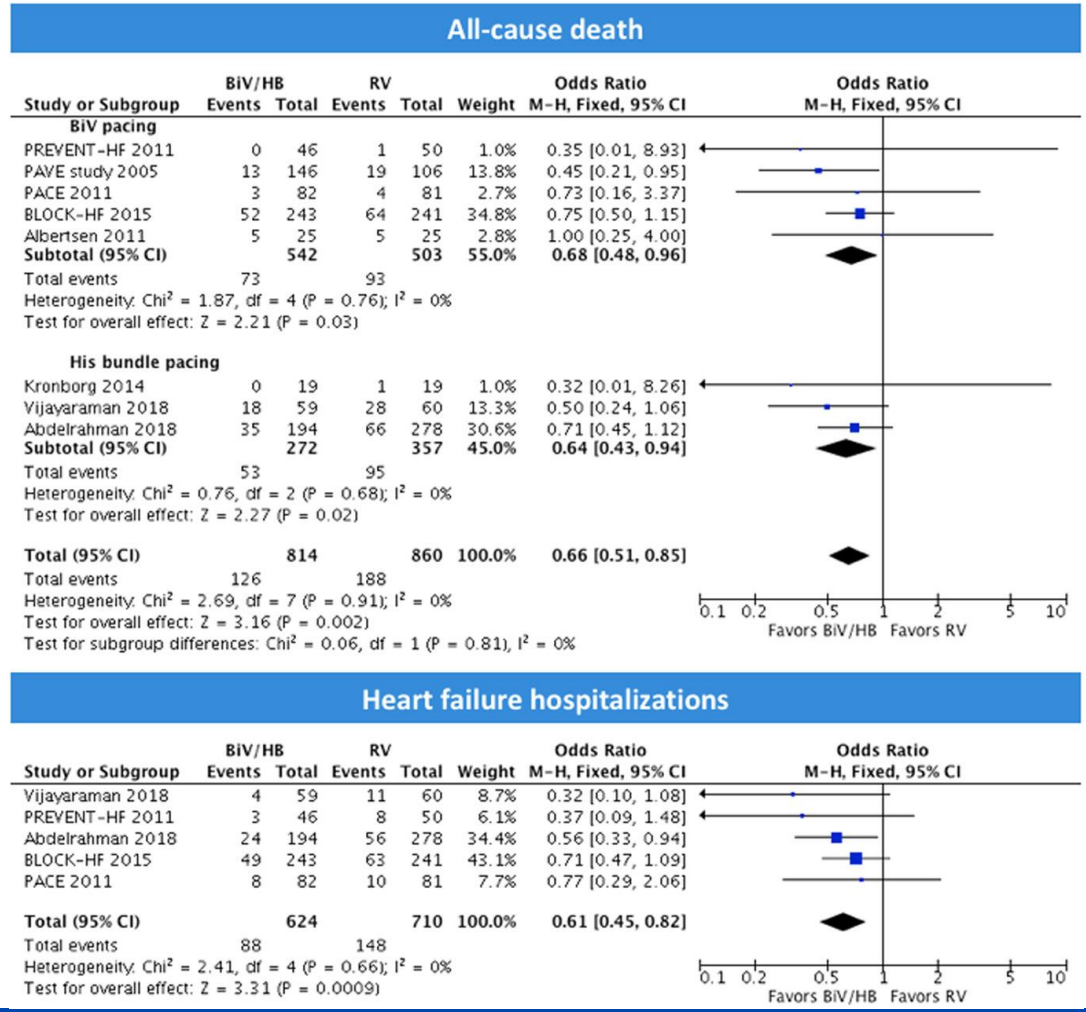
Meta-analysis for physiologic ventricular activation

Forest plot ("blobogram"): Study selection

"All cause death and heart failure hospitalizations reduced with CRT/HBP vs. RV pacing"



Fernandes GC JCE 2020

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Meta-analysis for physiologic ventricular activation

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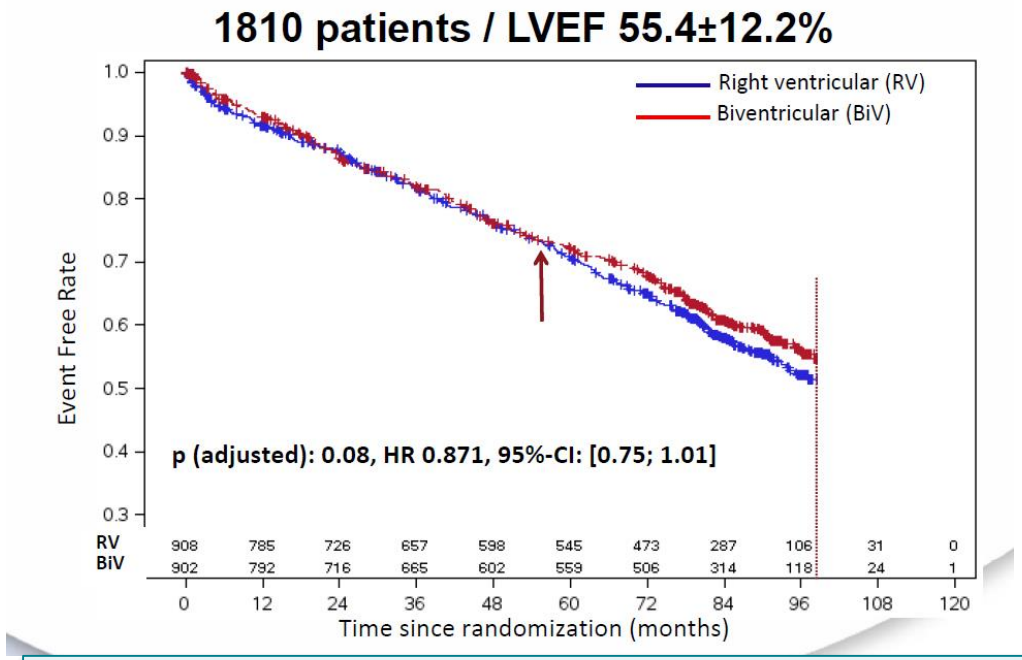
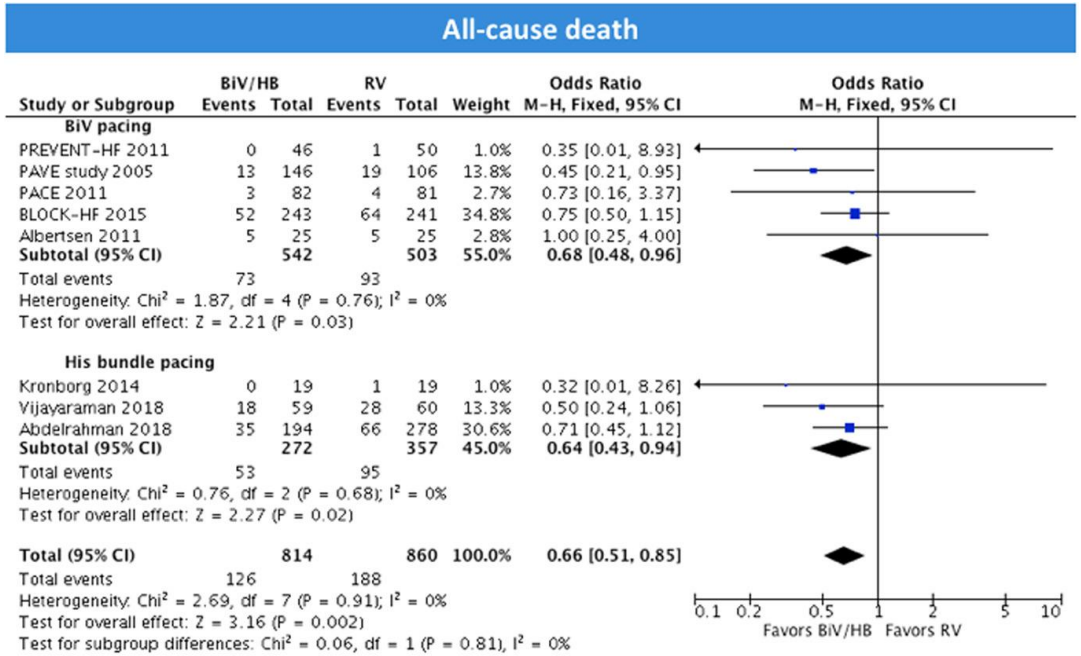
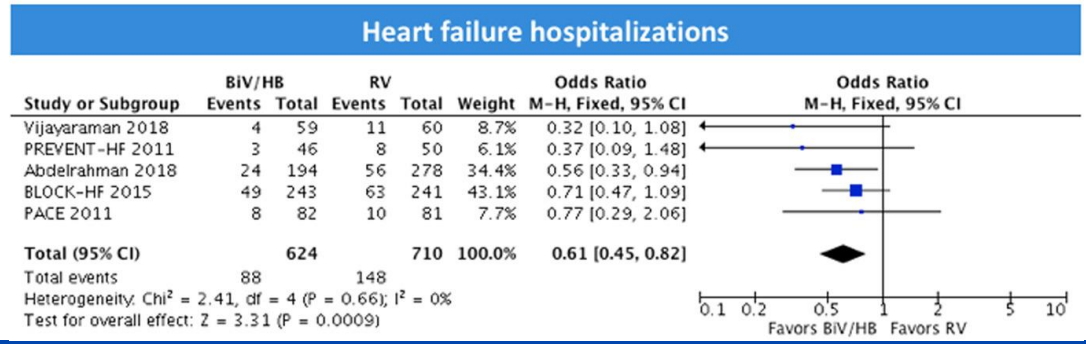


BioPace: Unpublished and not included
"More patients than all other studies combined"





Fernandes GC JCE 2020

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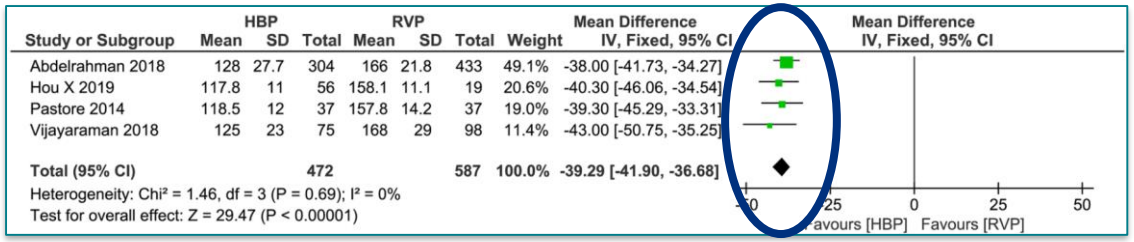
His bundle vs RV pacing

Meta-analysis of observational studies

QRS duration



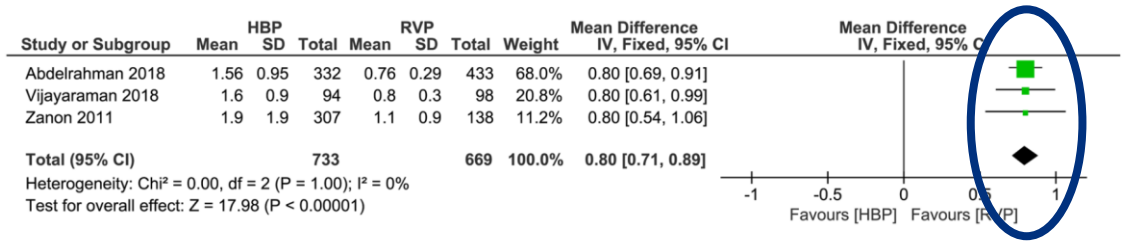
Study or Subgroup	HBP Mean	HBP SD	HBP Total	RVP Mean	RVP SD	RVP Total	Weight	Mean Difference IV, Fixed, 95% CI
Abdelrahman 2018	128	27.7	304	166	21.8	433	49.1%	-38.00 [-41.73, -34.27]
Hou X 2019	117.8	11	56	158.1	11.1	19	20.6%	-40.30 [-46.06, -34.54]
Pastore 2014	118.5	12	37	157.8	14.2	37	19.0%	-39.30 [-45.29, -33.31]
Vijayaraman 2018	125	23	75	168	29	98	11.4%	-43.00 [-50.75, -35.25]
Total (95% CI)			**472**			**587**	**100.0%**	**-39.29 [-41.90, -36.68]**

Heterogeneity: Chi² = 1.46, df = 3 (P = 0.69); I² = 0%
Test for overall effect: Z = 29.47 (P < 0.00001)

Mean Difference IV, Fixed, 95% CI

-50 -25 0 25 50
Favours [HBP] Favours [RVP]

Threshold



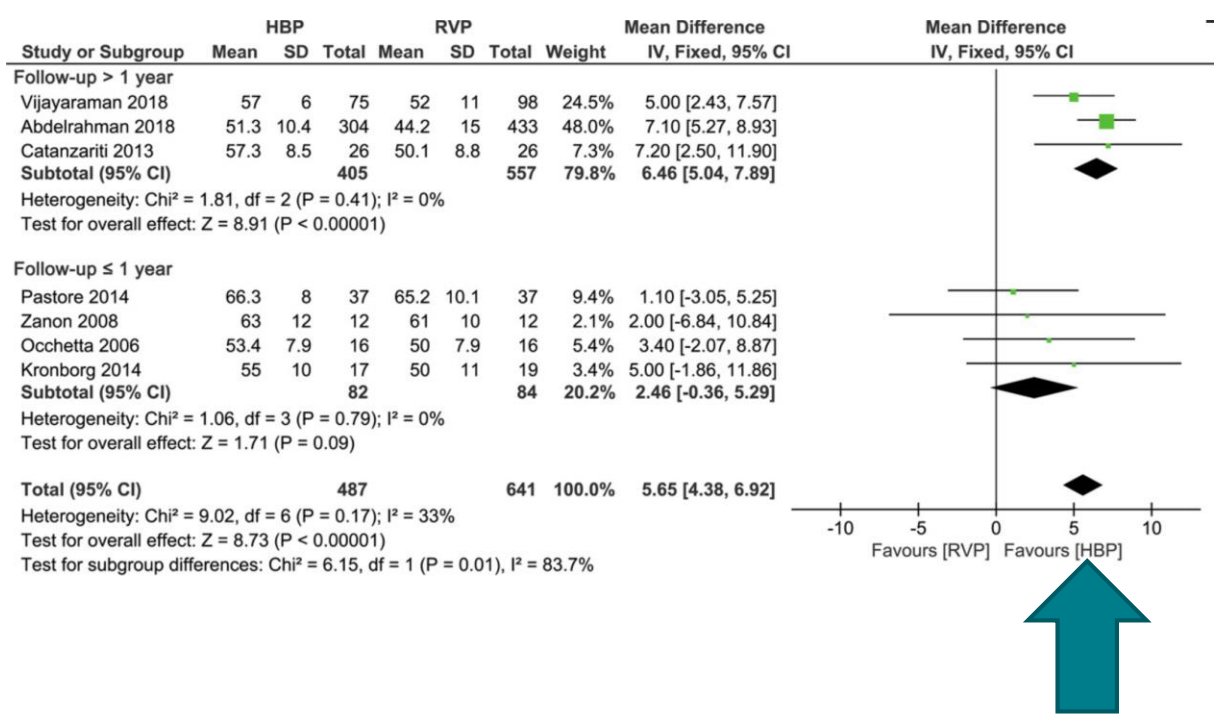
Study or Subgroup	HBP Mean	HBP SD	HBP Total	RVP Mean	RVP SD	RVP Total	Weight	Mean Difference IV, Fixed, 95% CI
Abdelrahman 2018	1.56	0.95	332	0.76	0.29	433	68.0%	0.80 [0.69, 0.91]
Vijayaraman 2018	1.6	0.9	94	0.8	0.3	98	20.8%	0.80 [0.61, 0.99]
Zanon 2011	1.9	1.9	307	1.1	0.9	138	11.2%	0.80 [0.54, 1.06]
Total (95% CI)			**733**			**669**	**100.0%**	**0.80 [0.71, 0.89]**

Heterogeneity: Chi² = 0.00, df = 2 (P = 1.00); I² = 0%
Test for overall effect: Z = 17.98 (P < 0.00001)

Mean Difference IV, Fixed, 95% CI

-1 -0.5 0 0.5 1
Favours [HBP] Favours [RVP]

LVEF



Study or Subgroup	HBP Mean	HBP SD	HBP Total	RVP Mean	RVP SD	RVP Total	Weight	Mean Difference IV, Fixed, 95% CI
Follow-up > 1 year								
Vijayaraman 2018	57	6	75	52	11	98	24.5%	5.00 [2.43, 7.57]
Abdelrahman 2018	51.3	10.4	304	44.2	15	433	48.0%	7.10 [5.27, 8.93]
Catanzariti 2013	57.3	8.5	26	50.1	8.8	26	7.3%	7.20 [2.50, 11.90]
Subtotal (95% CI)			**405**			**557**	**79.8%**	**6.46 [5.04, 7.89]**
Heterogeneity: Chi² = 1.81, df = 2 (P = 0.41); I² = 0%								
Test for overall effect: Z = 8.91 (P < 0.00001)								
Follow-up ≤ 1 year								
Pastore 2014	66.3	8	37	65.2	10.1	37	9.4%	1.10 [-3.05, 5.25]
Zanon 2008	63	12	12	61	10	12	2.1%	2.00 [-6.84, 10.84]
Occhetta 2006	53.4	7.9	16	50	7.9	16	5.4%	3.40 [-2.07, 8.87]
Kronborg 2014	55	10	17	50	11	19	3.4%	5.00 [-1.86, 11.86]
Subtotal (95% CI)			**82**			**84**	**20.2%**	**2.46 [-0.36, 5.29]**
Heterogeneity: Chi² = 1.06, df = 3 (P = 0.79); I² = 0%								
Test for overall effect: Z = 1.71 (P = 0.09)								
Total (95% CI)			**487**			**641**	**100.0%**	**5.65 [4.38, 6.92]**
Heterogeneity: Chi² = 9.02, df = 6 (P = 0.17); I² = 33%								
Test for overall effect: Z = 8.73 (P < 0.00001)								
Test for subgroup differences: Chi² = 6.15, df = 1 (P = 0.01), I² = 83.7%								

Mean Difference IV, Fixed, 95% CI

-10 -5 0 5 10
Favours [RVP] Favours [HBP]

Sun et al JCE 2020

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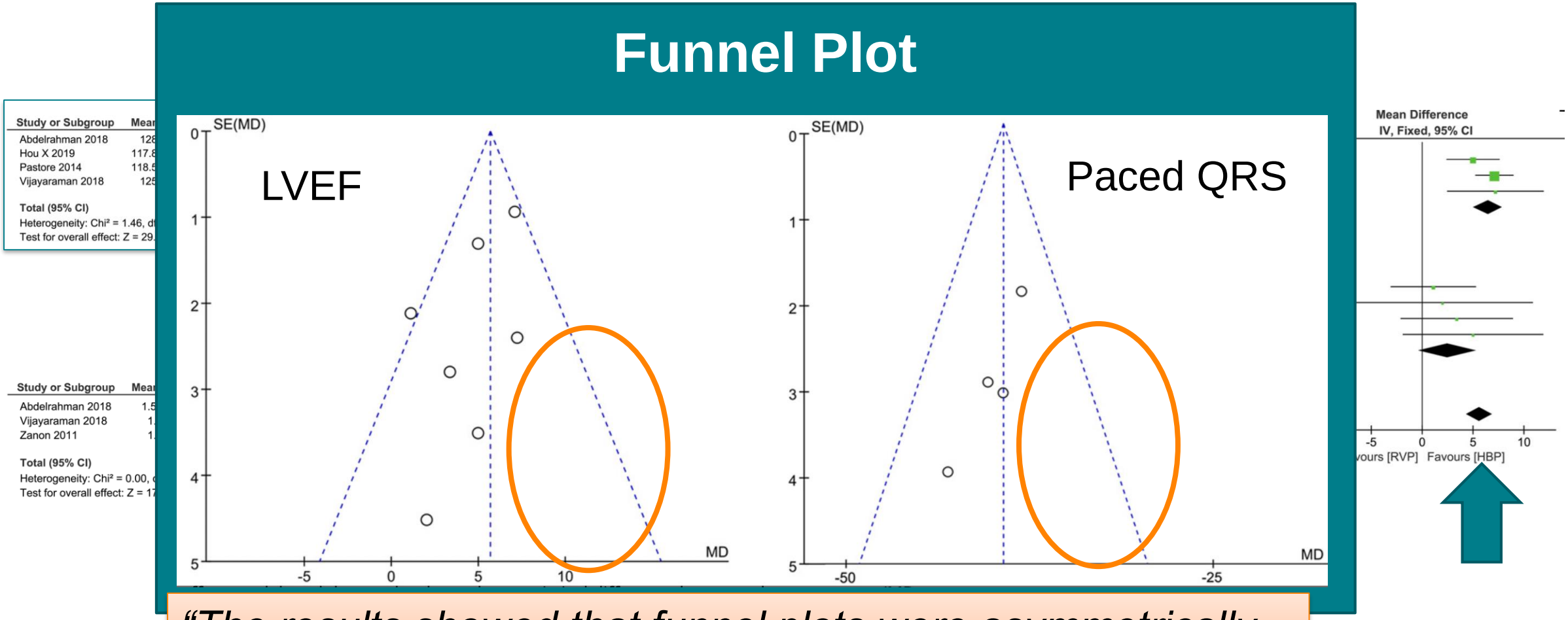
His bundle vs RV pacing

Meta-analysis of observational studies



"The results showed that funnel plots were asymmetrically distributed, and publication bias existed among studies."

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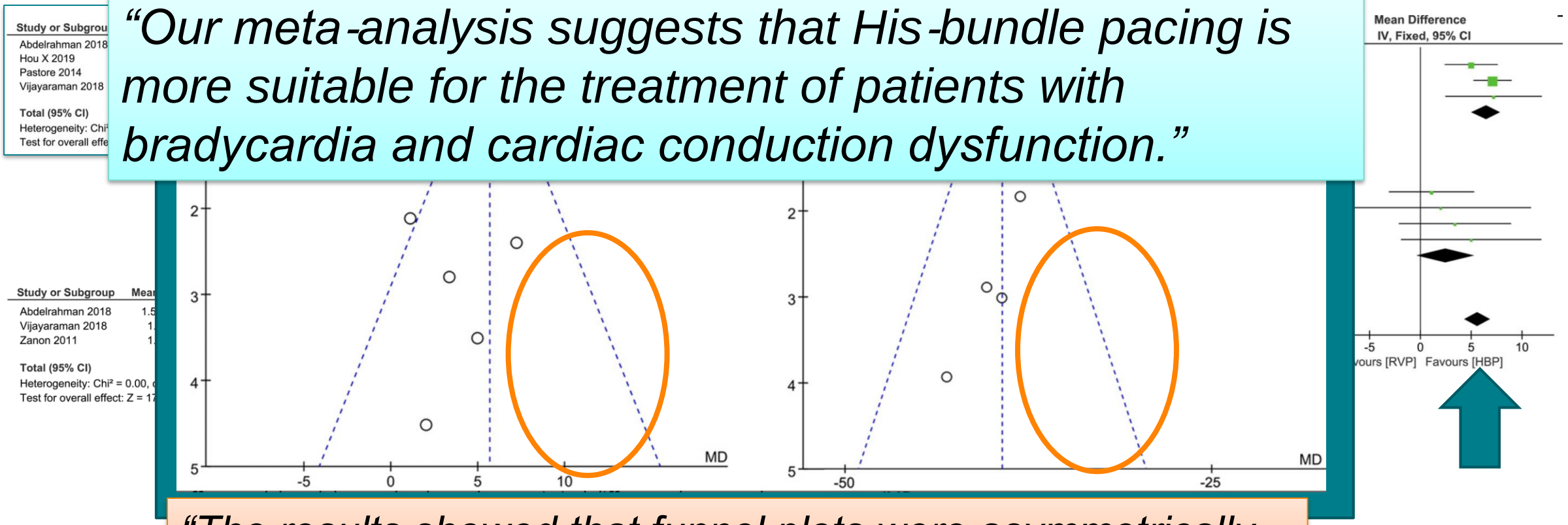
His bundle vs RV pacing
Meta-analysis of observational studies

Funnel Plot

"Our meta-analysis suggests that His-bundle pacing is more suitable for the treatment of patients with bradycardia and cardiac conduction dysfunction."



"The results showed that funnel plots were asymmetrically distributed, and publication bias existed among studies."

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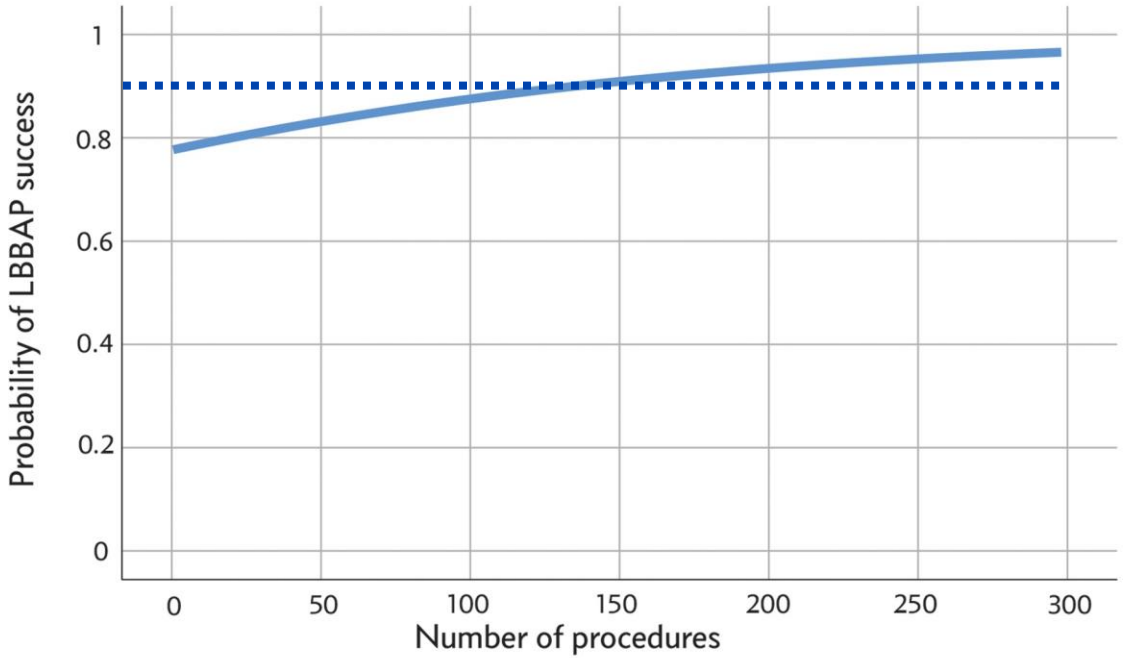
LBB area pacing

Multicentre European Left Bundle Branch Area Pacing Outcomes Study (MELOS)

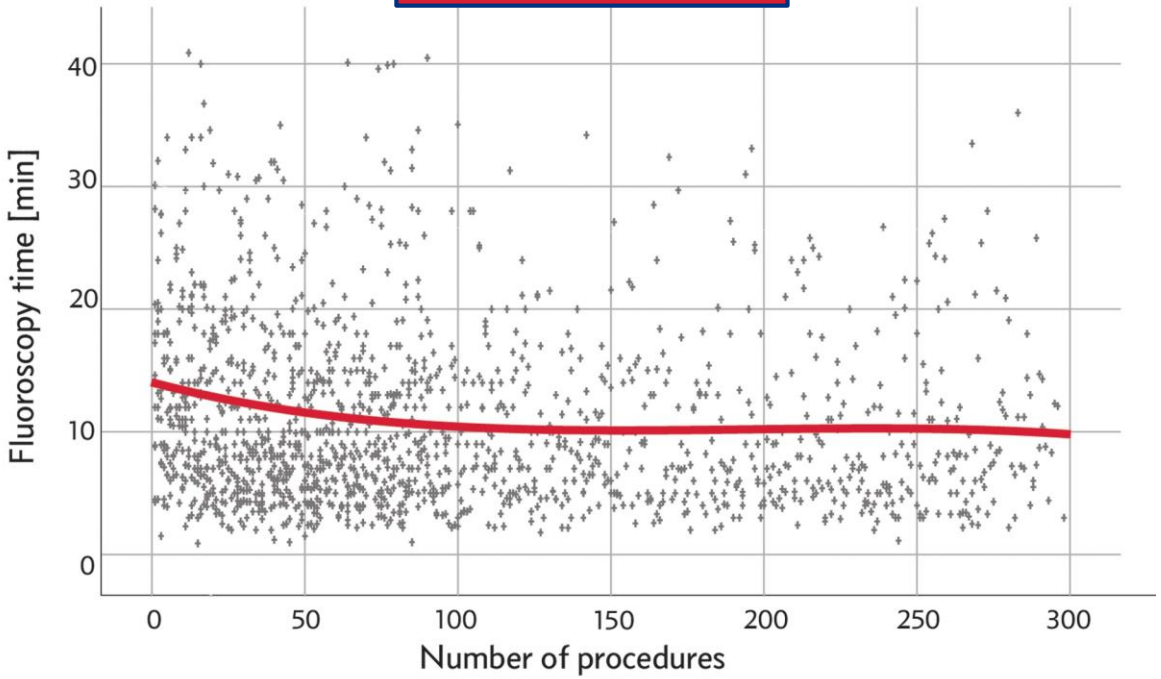
- 2,553 patients for any indication (28% HF, AVB 52%, SND 15%)

Learning curves

Probability of success



Fluoroscopy



Jastrzębski et al EHJ 2022

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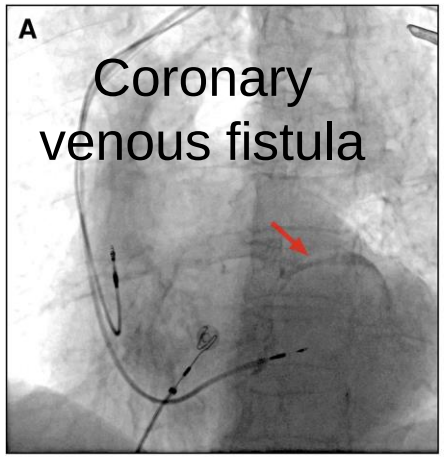

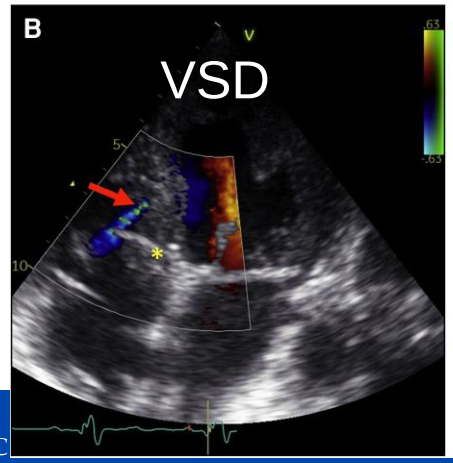

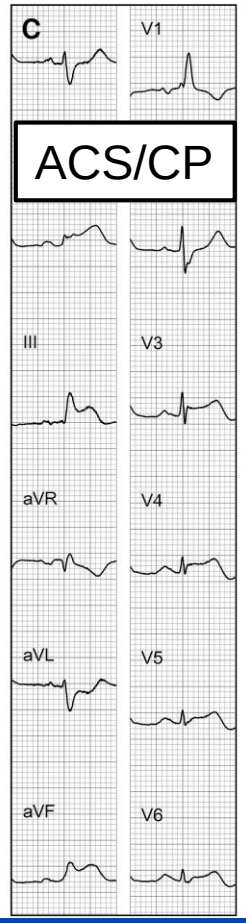

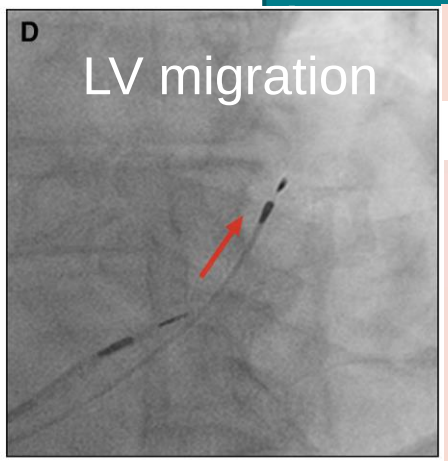

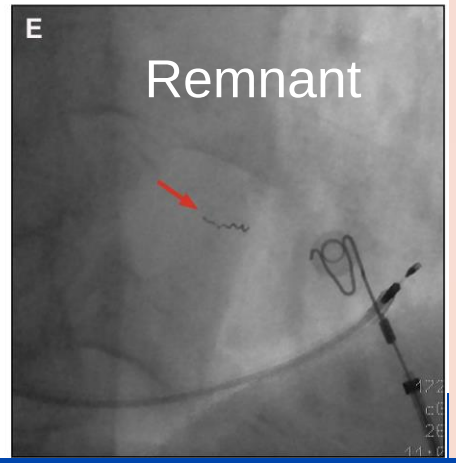

"Generic" complications	3.43%

Fluoroscopy

LBBAP lead complications	**8.3%**
• Acute perforation to LV	3.7%
• Lead dislodgement	1.5%
• Acute chest pain	1.0%
• Capture threshold rise	0.7%
• Acute coronary syndrome	0.4%
• Trapped/damaged helix	0.4%
• Delayed perforation to LV	0.1%
• Other	0.7%

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Professional Society Recommendations that address site of pacing for patients with bradycardia

2018 AHA/ACC/HRS Bradycardia Guidelines (2022 HF GL)

COR	LOE	Recommendation
IIa	B-R	Right ventricular pacing can be useful if LVEF 36-50% and ventricular pacing < 40%
IIa	B-R	Pacing to maintain physiologic left ventricular activation can be useful if LVEF 36-50% and ventricular pacing > 40% *(CRT in CHB, advanced AVB)*
IIb	B-R	Patients with AV block at the level of the AVN His bundle pacing may be useful

2021 ESC Device Guidelines

COR	LOE	Recommendation
I	A	CRT rather than RV pacing is recommended for patients with AVB and HFrEF (< 40%) regardless of NYHA Class
IIb	C	HBP may be considered as an alternative to RV pacing in patients with AVB and LVEF >40%, who are anticipated to have >20% ventricular pacing.

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Kusumoto et al JACC 2018, Glickson et al EHJ 2021, Heidenreich JACC 2022

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Ventricular depolarization:
Does it make a difference?

- Different methods for ventricular depolarization
- Evidence base
  - Bradycardia
    - *Maybe? Inconsistencies in the data?*
    - *Additional risk?*
  - Heart failure

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Ventricular depolarization:
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    - *Maybe? Inconsistencies in the data?*
    - *Additional risk?*
  - Heart failure

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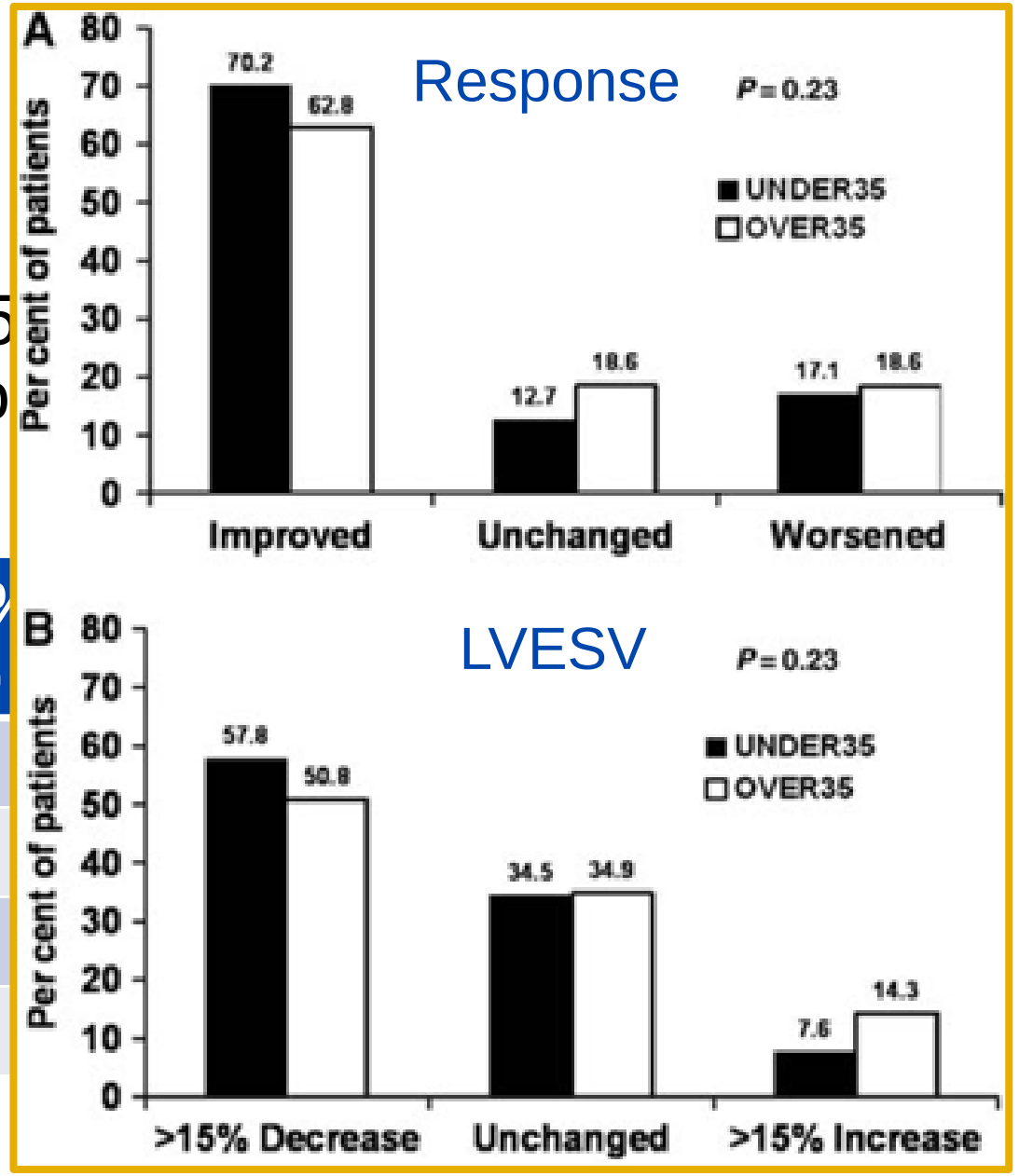
PROSPECT

- 426 patients enrolled with: LVEF ≤ 35
  Class III, IV Sx, QRS ≥ 130 ms and o
  GDMT

	All (361)	< 35% (275)	> 35% (86)
Age (y)	68	67	69
LVEF (%)	29	25	43
Ischemic (%)	54	49	69
DM (%)	31	28	38



Chung et al EJHF 2010

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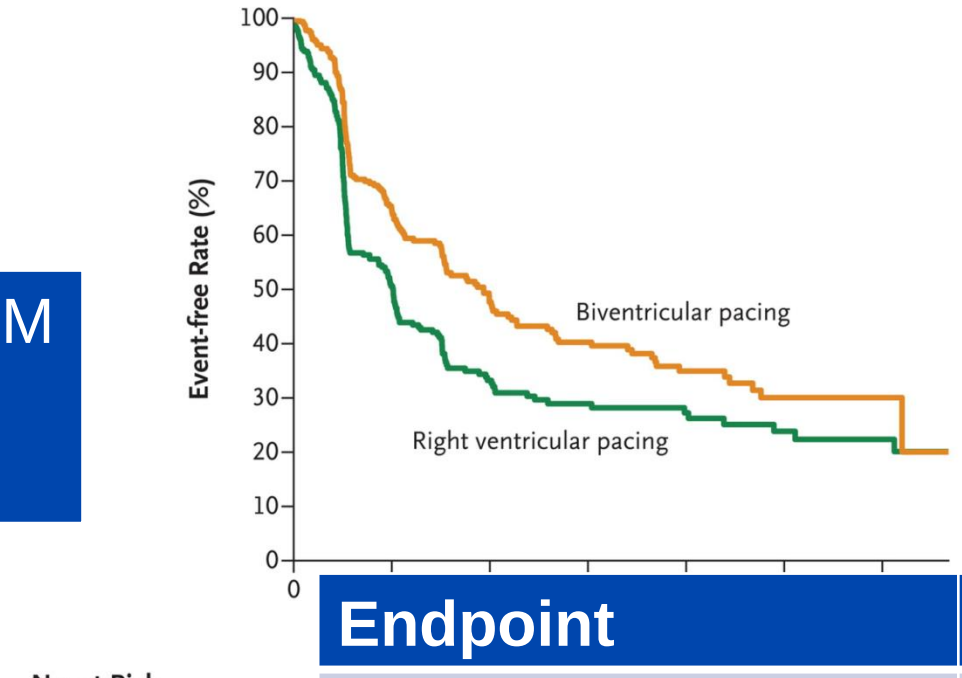
Biventricular pacing vs. right ventricular pacing: Block HF Trial

- 691 patients with HF Sx, EF < 50% randomized to

484 patients received a PPM
- 55% Class II
- LVEF: 43%

- Death
- HF event
- LV dilation



Endpoint	HR (95% CI)
Primary	0.73 (0.58-0.91)
Death	0.83 (0.59-1.17)
HF hospitalization	0.68 (0.49-0.94)

Curtis et al NEJM 2013

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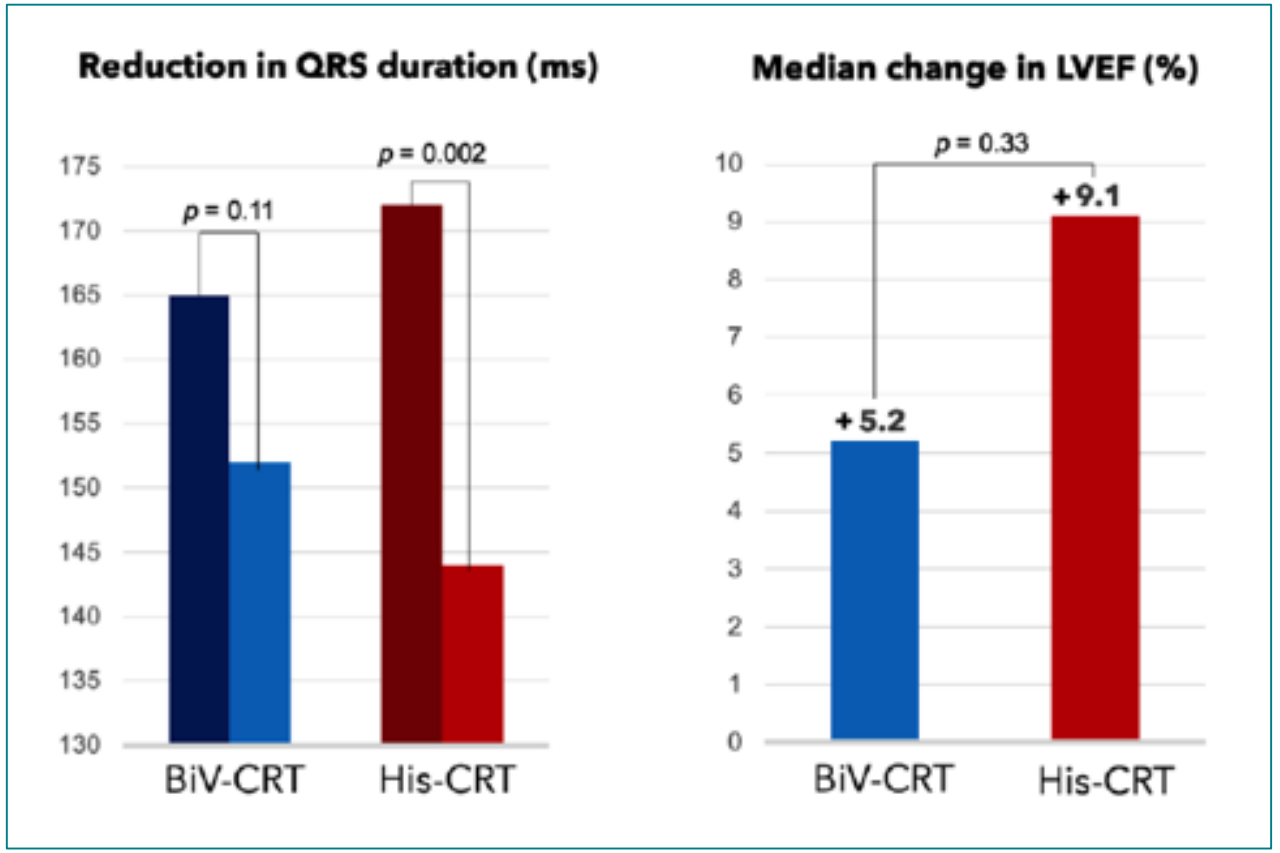
CRT vs. His bundle pacing in heart failure
His –Synch Trial

His-SYNCH Trial

- 41 patients randomized to His-CRT or BiV-CRT
- Crossover in 48% of His-CRT and 26% BiV-CRT
- Higher pacing thresholds in His-CRT



Upadyhay et al JACC 2019, HRS 2019

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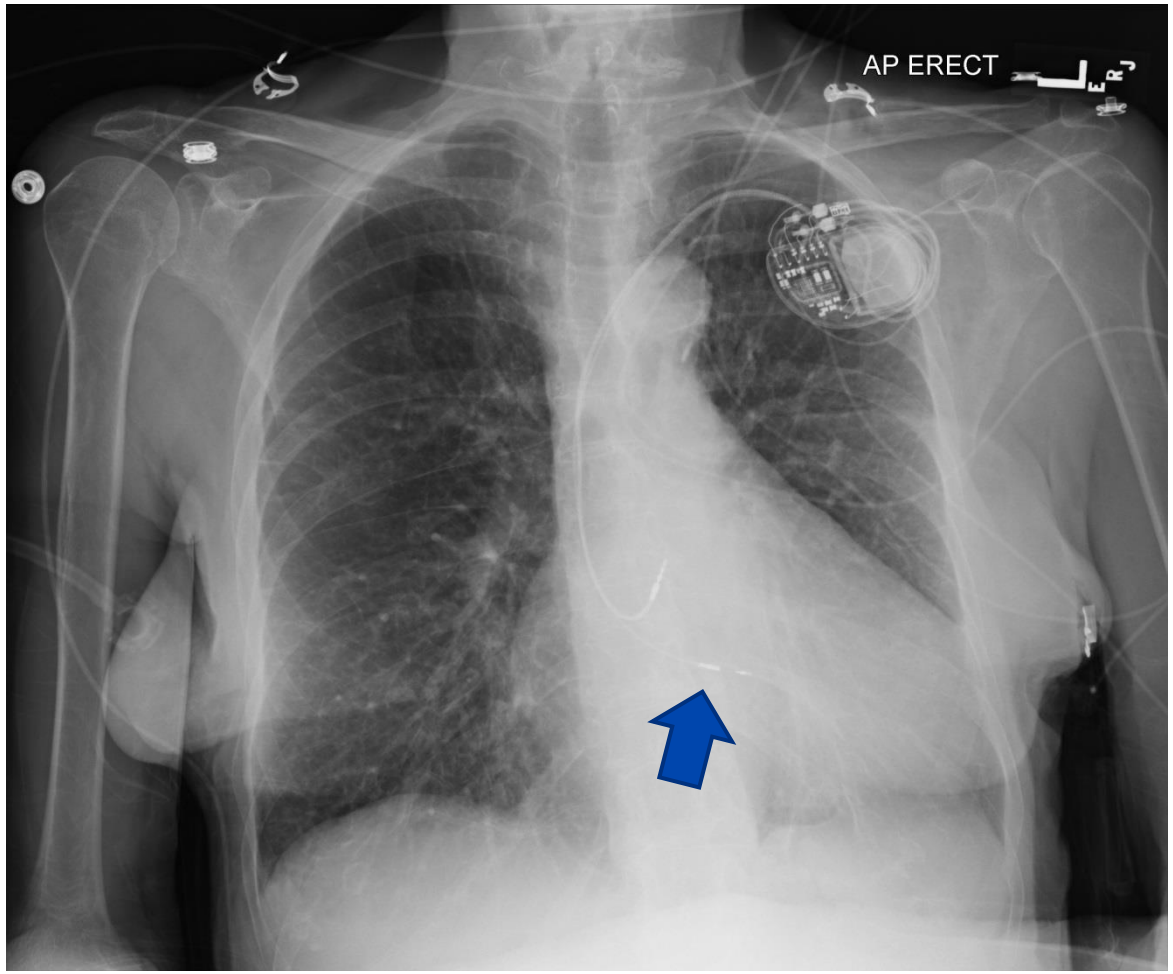
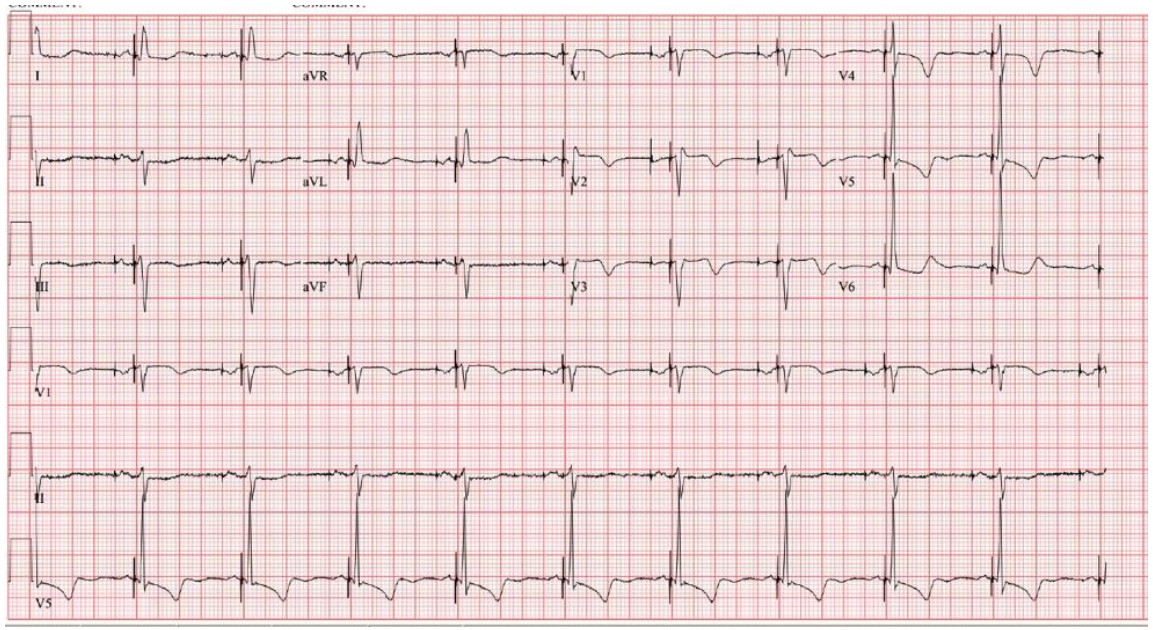
His bundle pacing





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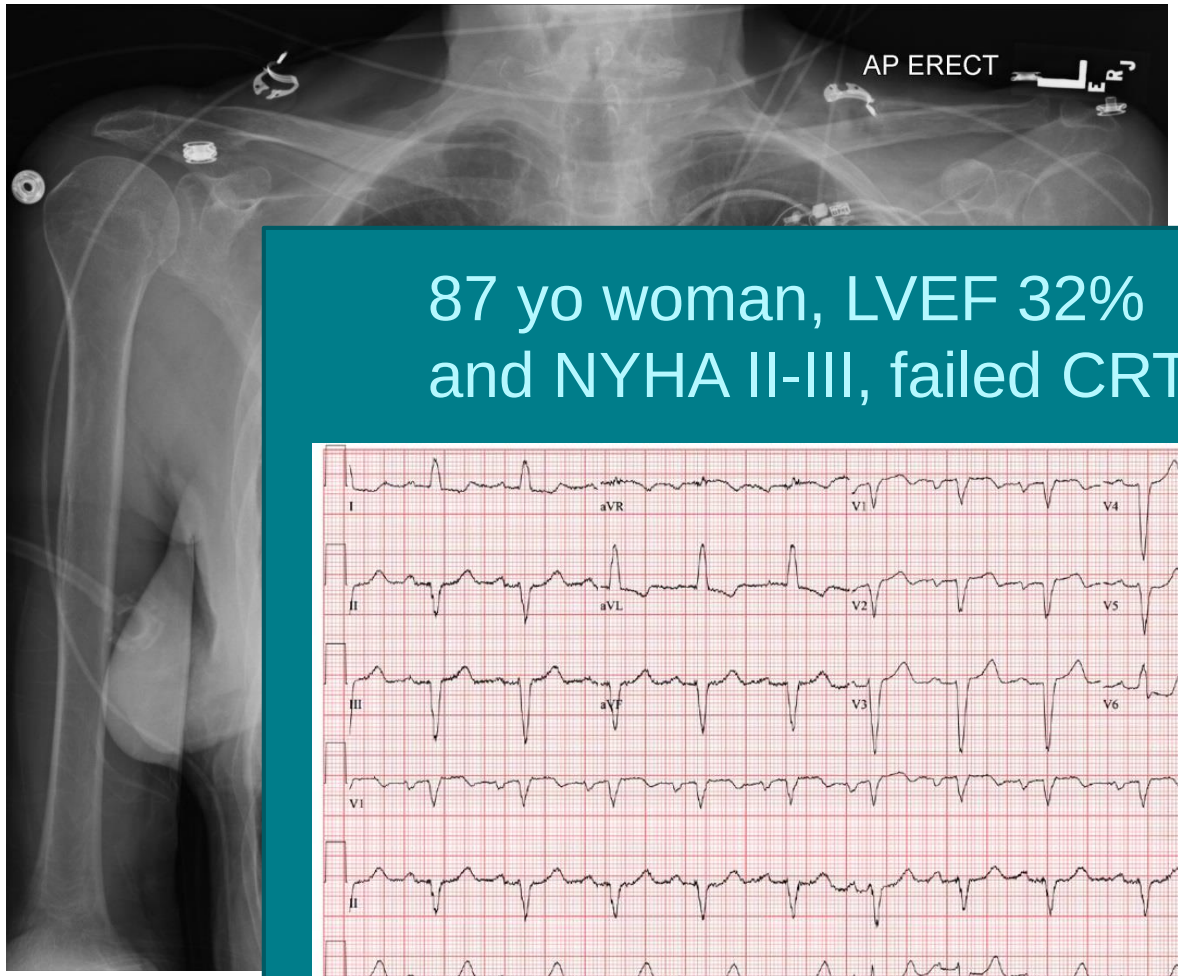
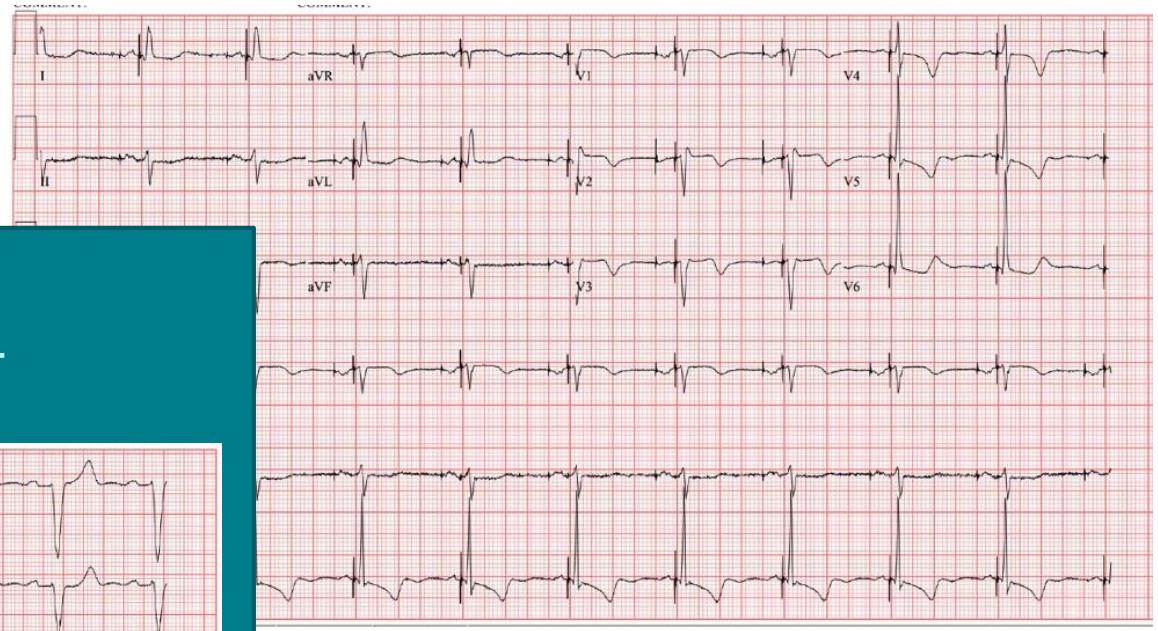
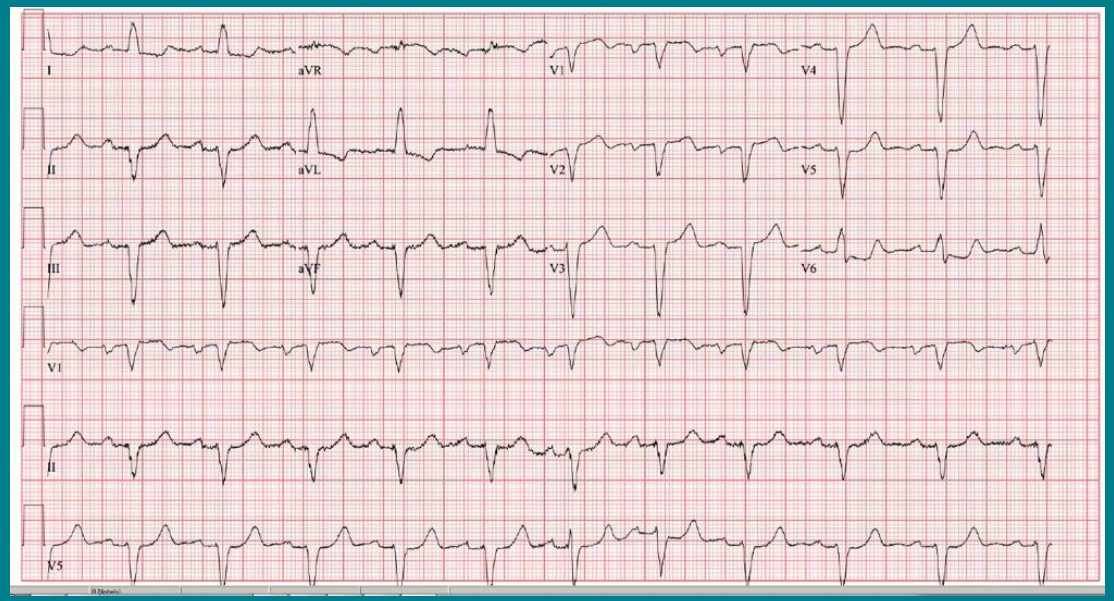
His bundle pacing





87 yo woman, LVEF 32%
and NYHA II-III, failed CRT



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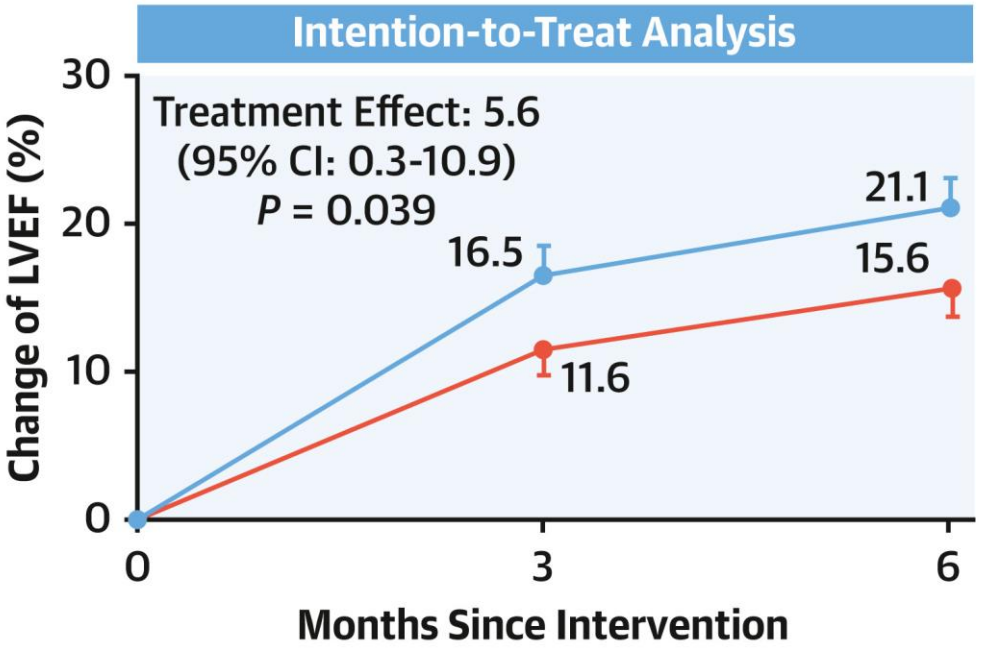
CRT v LBB pacing in heart failure

LBBB-RESYNC (Left Bundle Branch Pacing Versus Biventricular Pacing for Cardiac Resynchronization Therapy) Study

- 40 patients with NICM (LVEF < 40%) and LBBB randomized to LBB pacing or CRT
- 1° endpoint: LVEF



LVEF (%) (Mean ± SD)	Baseline	3-Month	6-Month
LBBP	28.3 ± 5.3	44.9 ± 13.1	49.4 ± 13.2
BiVP	31.1 ± 5.6	42.7 ± 10.1	46.5 ± 9.4

Wang et al JACC 2022

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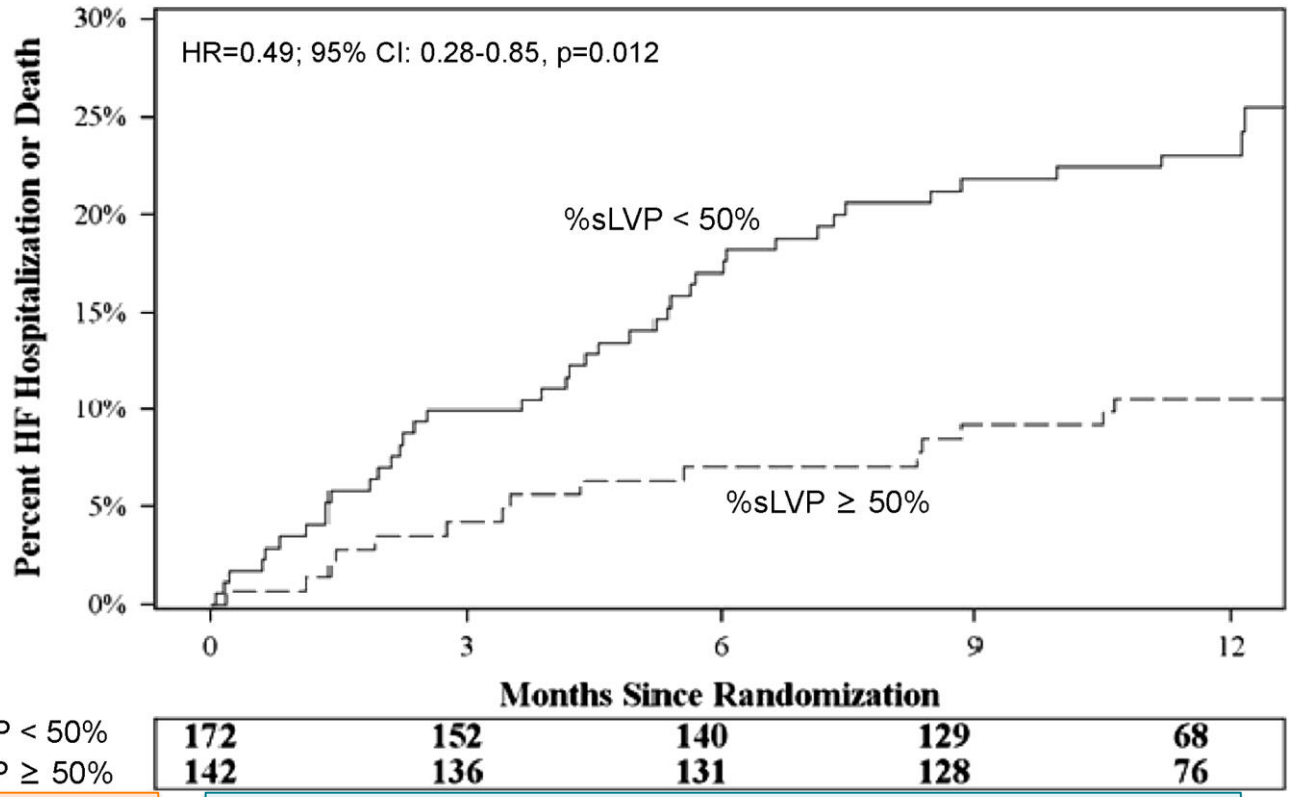
All CRT the same?
Adaptive CRT trial

- aCRT algorithm: In the setting of normal AV conduction and heart rates, algorithm provides synchronized LV pacing
- 318 in the aCRT arm and 160 patients with standard CRT



Less heart failure with LV only

And other data for less AF

Birnie et al HR 2013

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Professional society guideline recommendations for His/LBB pacing in HF

2018 AHA/ACC/HRS Bradycardia Guidelines

COR	LOE	Recommendation
IIa	B-R	Pacing to maintain physiologic left ventricular activation can be useful if LVEF 36-50% and ventricular pacing > 40%

2021 ESC Cardiac Device Guidelines
2022 AHA/ACC/HFSA HF Guidelines

None for HBP

Kusumoto et al JACC 2018, Glickson et al EHJ 2021, Heidenreich JACC 2022

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Professional society guideline recommendations for His/LBB pacing *or CRT* in HF

2018 AHA/ACC/HRS Bradycardia Guidelines

COR	LOE	Recommendation
IIa	B-R	Pacing to maintain physiologic left ventricular activation can be useful if LVEF 36-50% and ventricular pacing > 40% *(CRT in CHB, advanced AVB)*

2022 AHA/ACC/HFSA HF Guidelines

COR	LOE	Recommendation
IIa	B-NR	CRT if new/replacement PPM can be useful if LVEF ≤ 35% and ventricular pacing > 40%

2021 ESC Device Guidelines

COR	LOE	Recommendation
I	A	CRT rather than RV pacing is recommended for patients with AVB and HFrEF (< 40%) regardless of NYHA Class

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Kusumoto et al JACC 2018, Glickson et al EHJ 2021, Heidenreich JACC 2022

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Ventricular depolarization:
Does it make a difference?

- Different methods for ventricular depolarization
- Evidence base
  - Bradycardia
  - Heart failure
    - *Maintain physiologic left ventricular activation (CRT or HBP) for LVEF < 50% and significant pacing (IIa in the US GLs)*
    - *CRT Class I for LVEF < 40% in European GLs*

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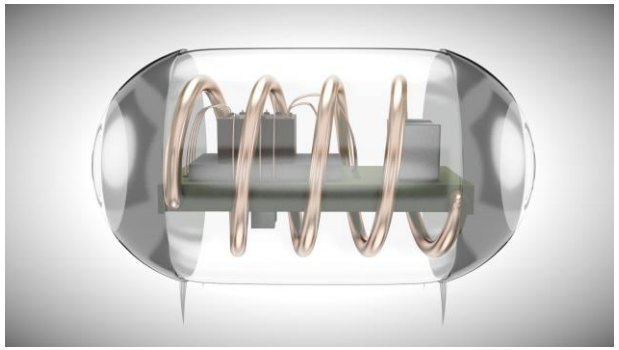
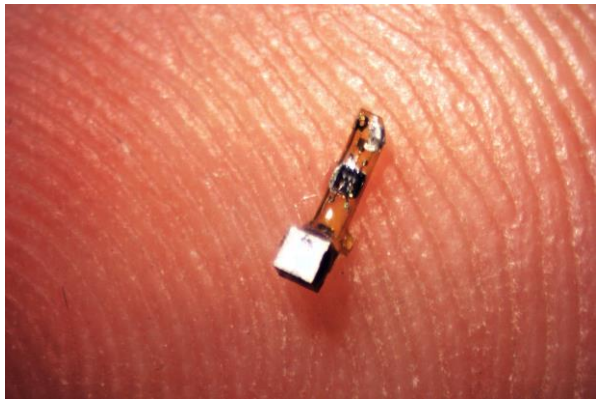
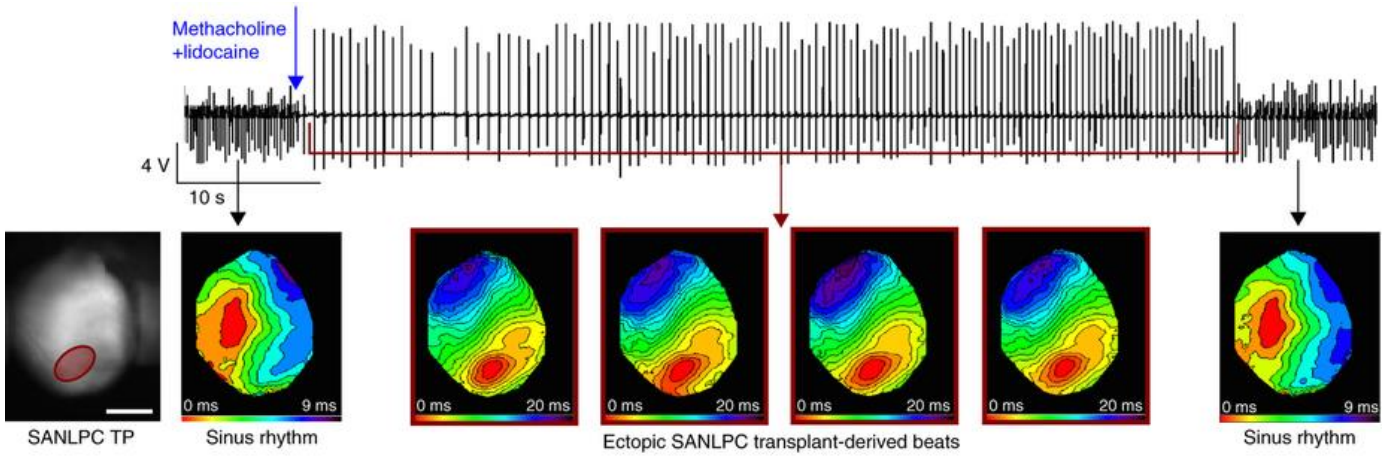
Future?

- Blue light
- Biological (hybrid)
- Self-powered/rechargeable
- Beyond pacing (bioink)







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Bradycardia

- Different methods for ventricular depolarization
- Evidence base
  - Bradycardia
  - Heart failure

- *Rapidly evolving field of physiologic pacing*
- *More rapid adoption of LBB pacing when compared to His bundle pacing?*

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Bradycardia

- Different methods for ventricular depolarization
- Evidence base
  - Bradycardia
  - Heart failure

- *Rapidly evolving field of physiologic pacing*
- *More rapid adoption of LBB pacing when compared to His bundle pacing?*

Conduction tissue pacing

- *Maybe? Inconsistencies in the data?*
- *Additional risk?*

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Bradycardia

- Different methods for ventricular depolarization
- Evidence base
  - Bradycardia
  - Heart failure

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- *More rapid adoption of LBB pacing when compared to His bundle pacing?*

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- *CRT Class I for LVEF < 40% in European GLs*

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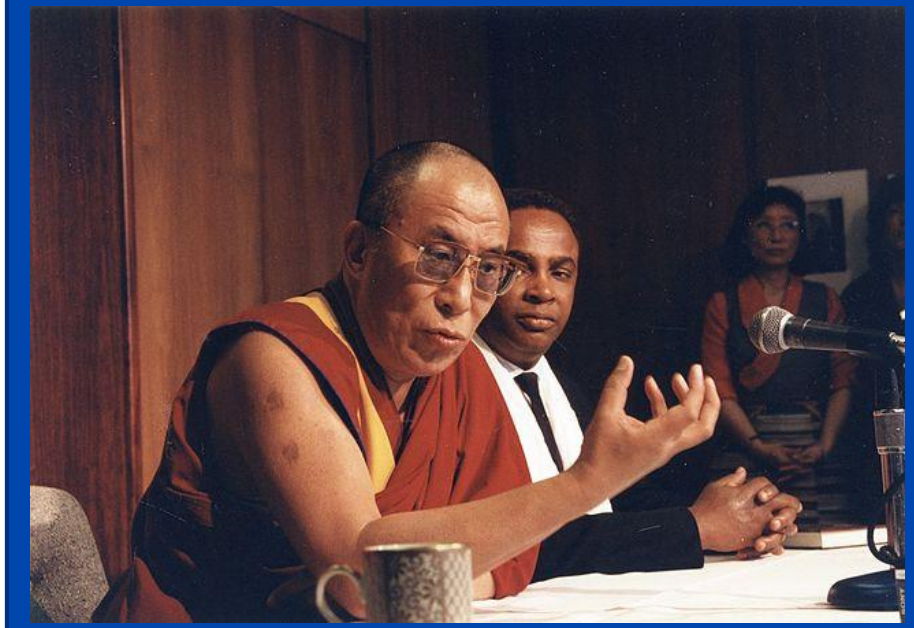
Bradycardia

- Different methods for ventricular depolarization
- Evidence base
  - Bradycardia

- *Rapidly evolving field of physiologic pacing*
- *More rapid adoption of LBB pacing when*



Know the rules well,
so you can break them effectively

Dalai Lama and Seattle Mayor Norm Rice, 1993.jpg

Tenzin Gyatso, 14th Dalai Lama and Seattle Mayor Norm Rice, 1993

Seattle Municipal Archives from Seattle, WA

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We love a “shiny and unique” penny, but a penny is a penny

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