



UNITE DE SOINS
ET DE **CARDIOLOGIE**
INTERVENTIONNELLE



NOUVELLES CLINIQUES NANTAISES



CRT in Heart Failure: New Frontiers

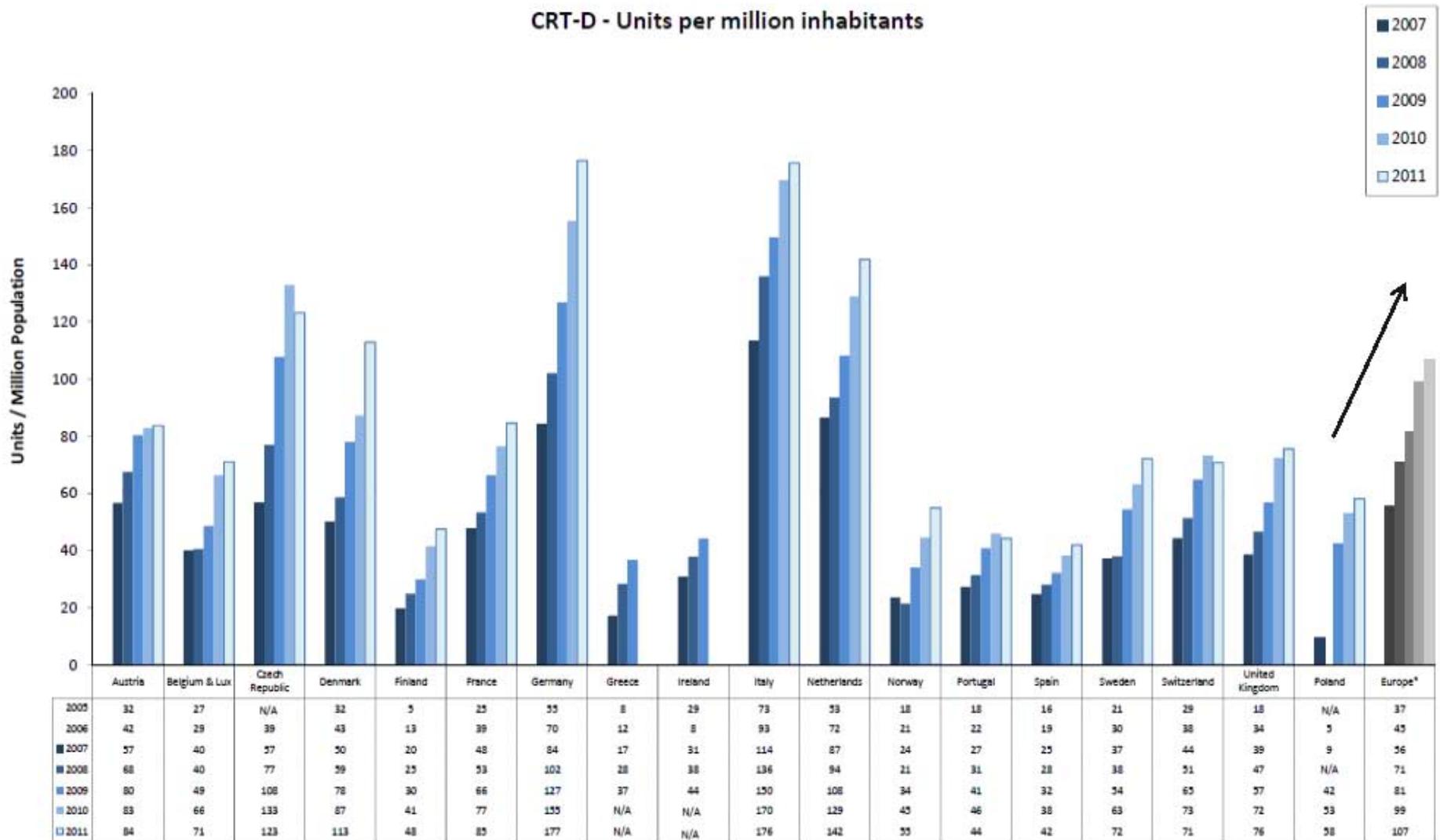
Davos, Feb 2013

D Gras, MD, Nantes, France

CRT in Heart Failure: New Frontiers

- **Background**
- Dual-Site LV Pacing during CRT
- Quadripolar LV Pacing approach
- LV Endocardial Pacing: LVEP
- Vagal Nerve stimulation in HF

CRT-D - Units per million inhabitants



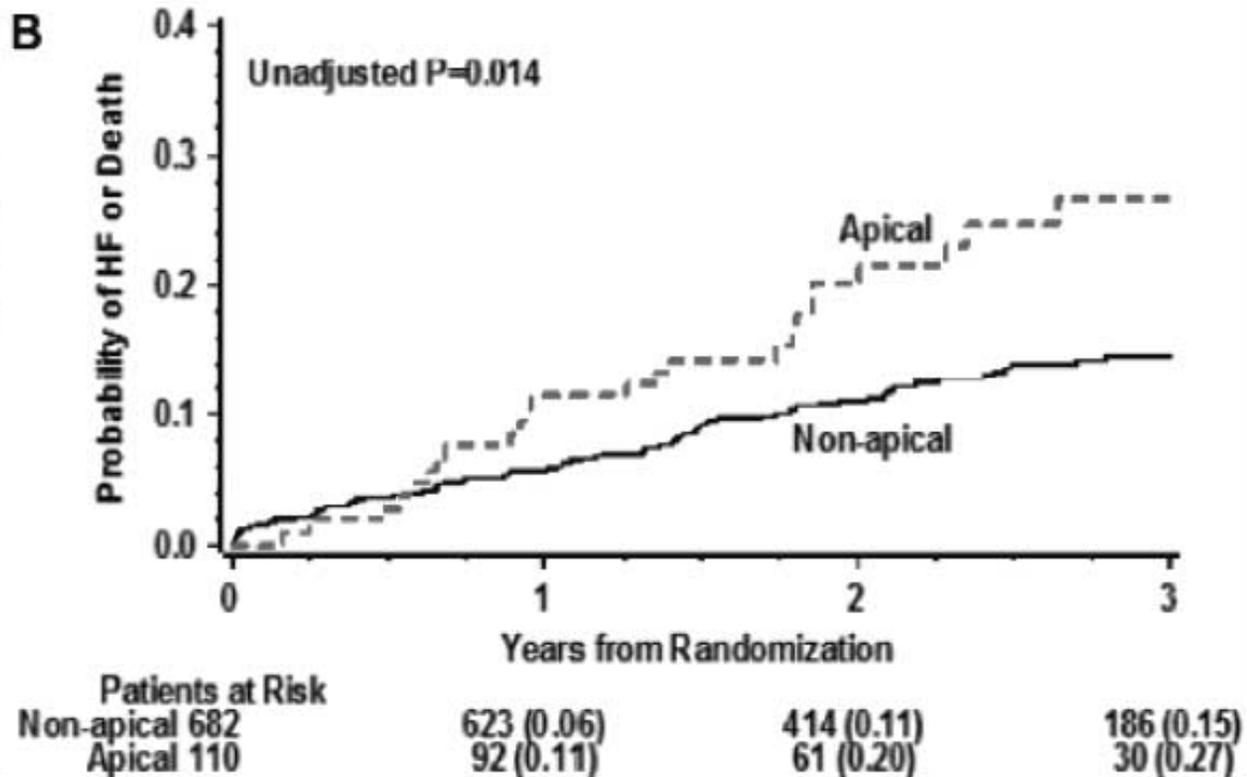
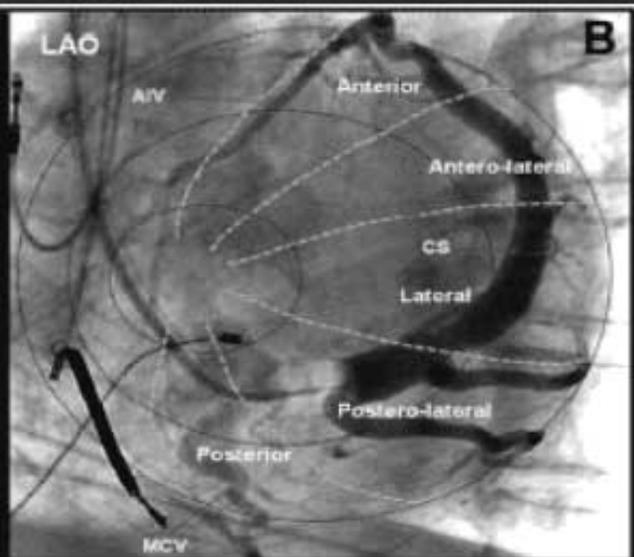
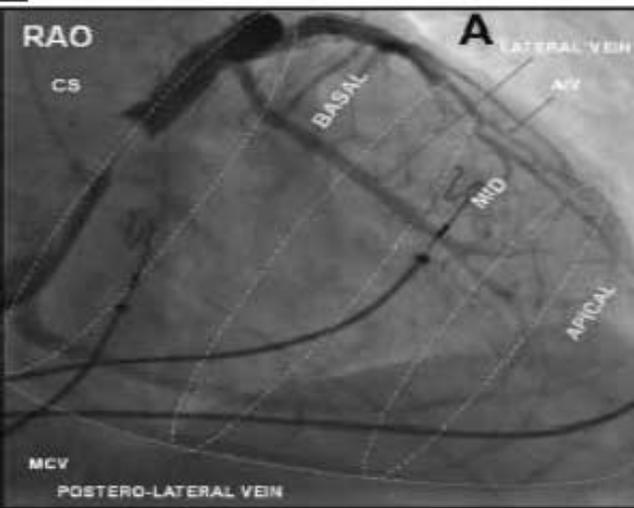
Source population data: OECD

Units - Eucomed based on reports from major manufacturers

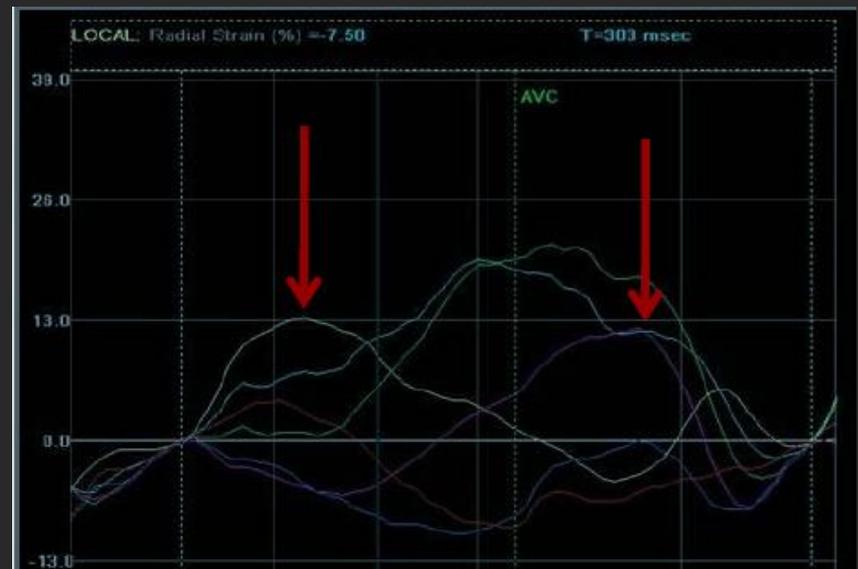
* Europe represents total of listed countries (N/A countries excluded)

Left Ventricular Lead Position and Clinical Outcome in the Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy (MADIT-CRT) Trial

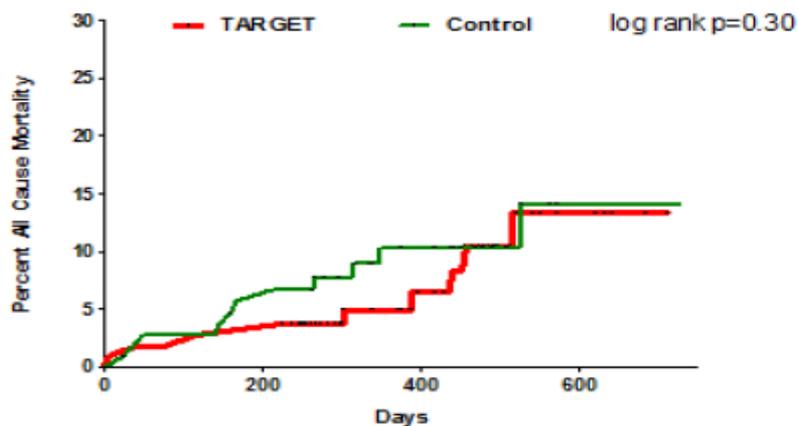
Jagmeet P. Singh, MD, DPhil*; Helmut U. Klein, MD*; David T. Huang, MD; Sven Reek, MD; Malte Kuniss, MD; Aurelio Quesada, MD; Alon Barsheshet, MD; David Cannom, MD; Ilan Goldenberg, MD; Scott McNitt, MS; James P. Daubert, MD; Wojciech Zareba, MD; Arthur J. Moss, MD



The Target Study



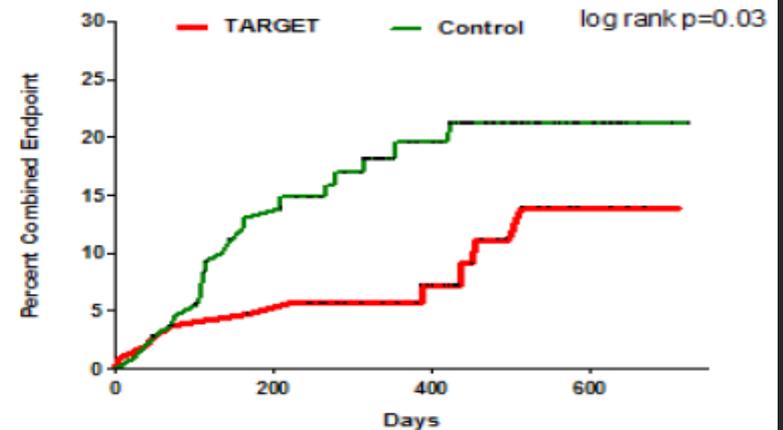
All Cause Mortality following CRT in the TARGET and Control Groups



No. At Risk
TARGET
CONTROL

110	103	61	19
110	105	62	17

Combined Endpoint of Death and Heart Failure Related Hospitalisation between the TARGET and Control Groups

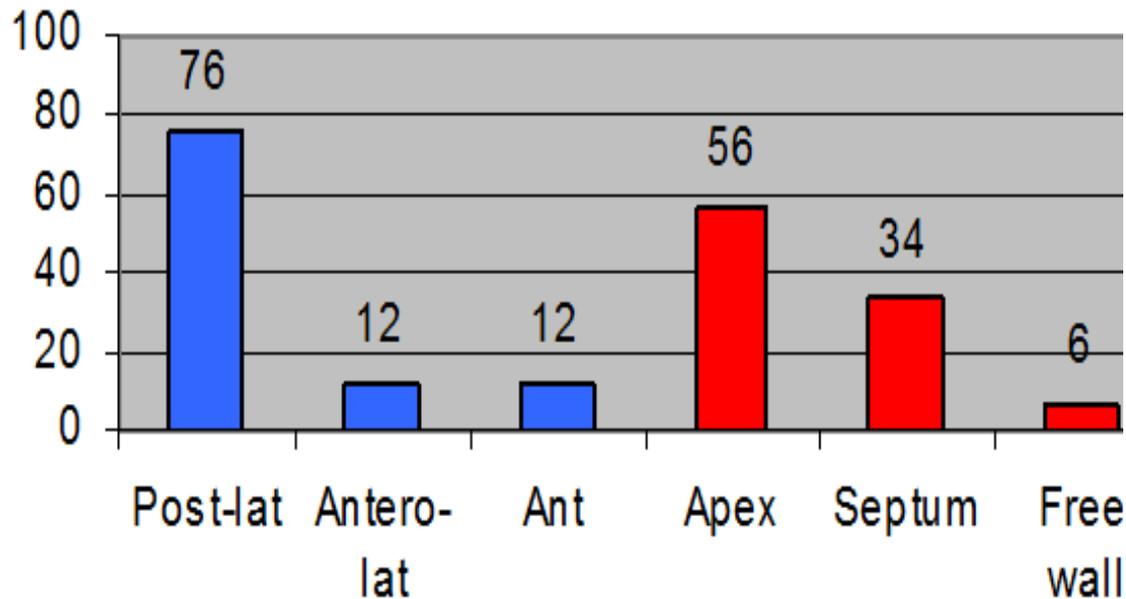


No. At Risk
TARGET
CONTROL

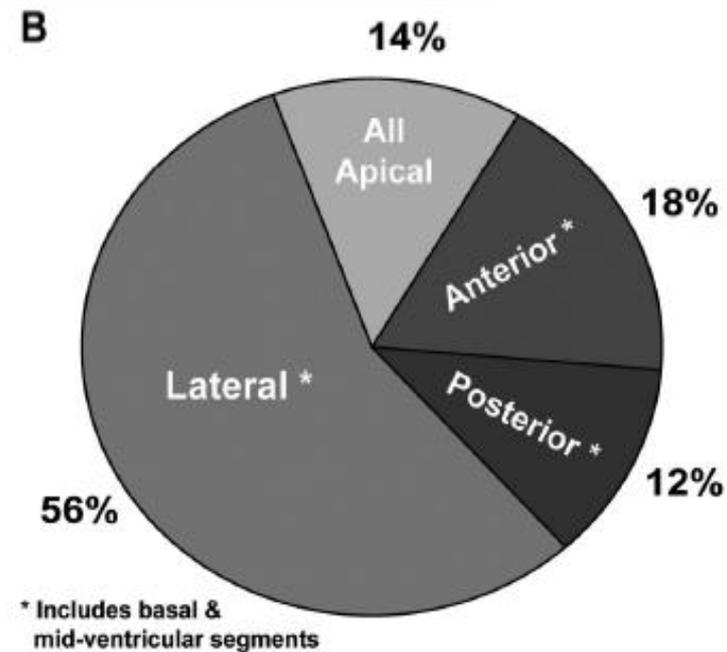
110	102	59	18
110	101	61	17

Care HF Implantation	Treatment Group (n=404 attempts)	Control Group (n=65 attempts)
1	349 (86.3)	58 (89.2)
2	36 (8.9)	2 (3.1)
3	5 (1.2)	0
Total	390 (96.4)	60 (92.3)

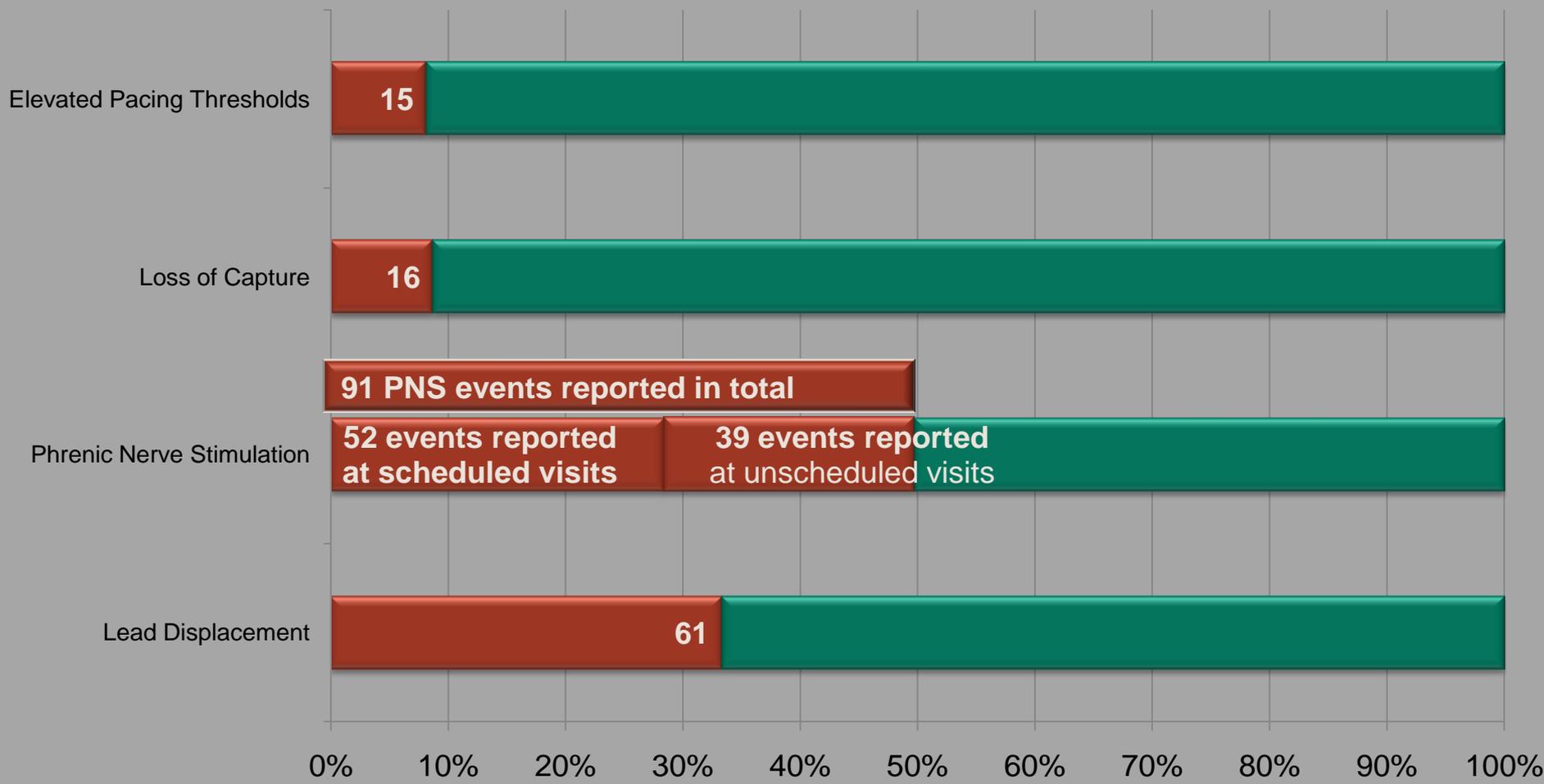
CARE HF



MADIT CRT



LV Lead Events frequency as percentage of total events over 12 months (164/1647 pts)

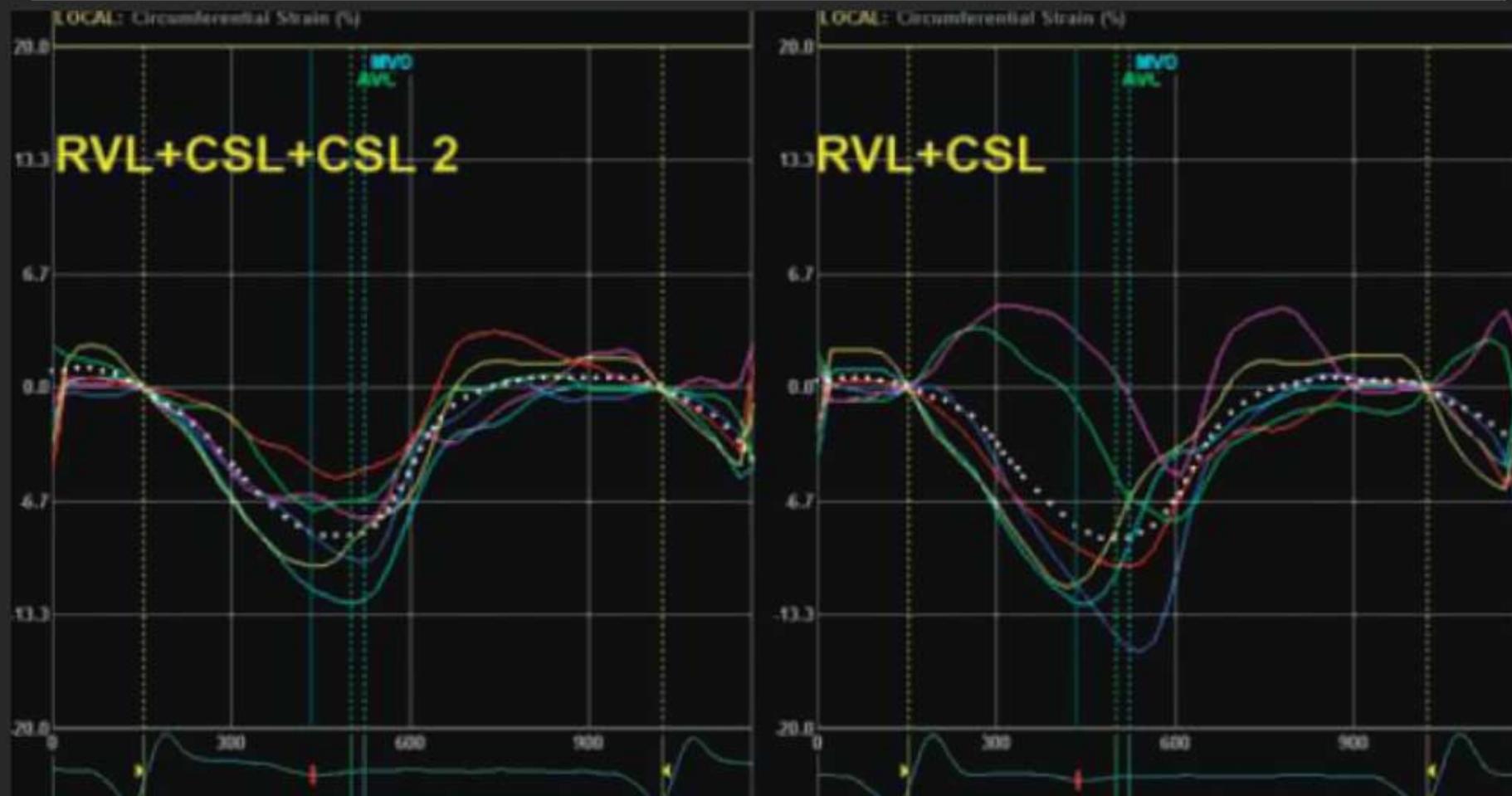


CRT in Heart Failure: New Frontiers

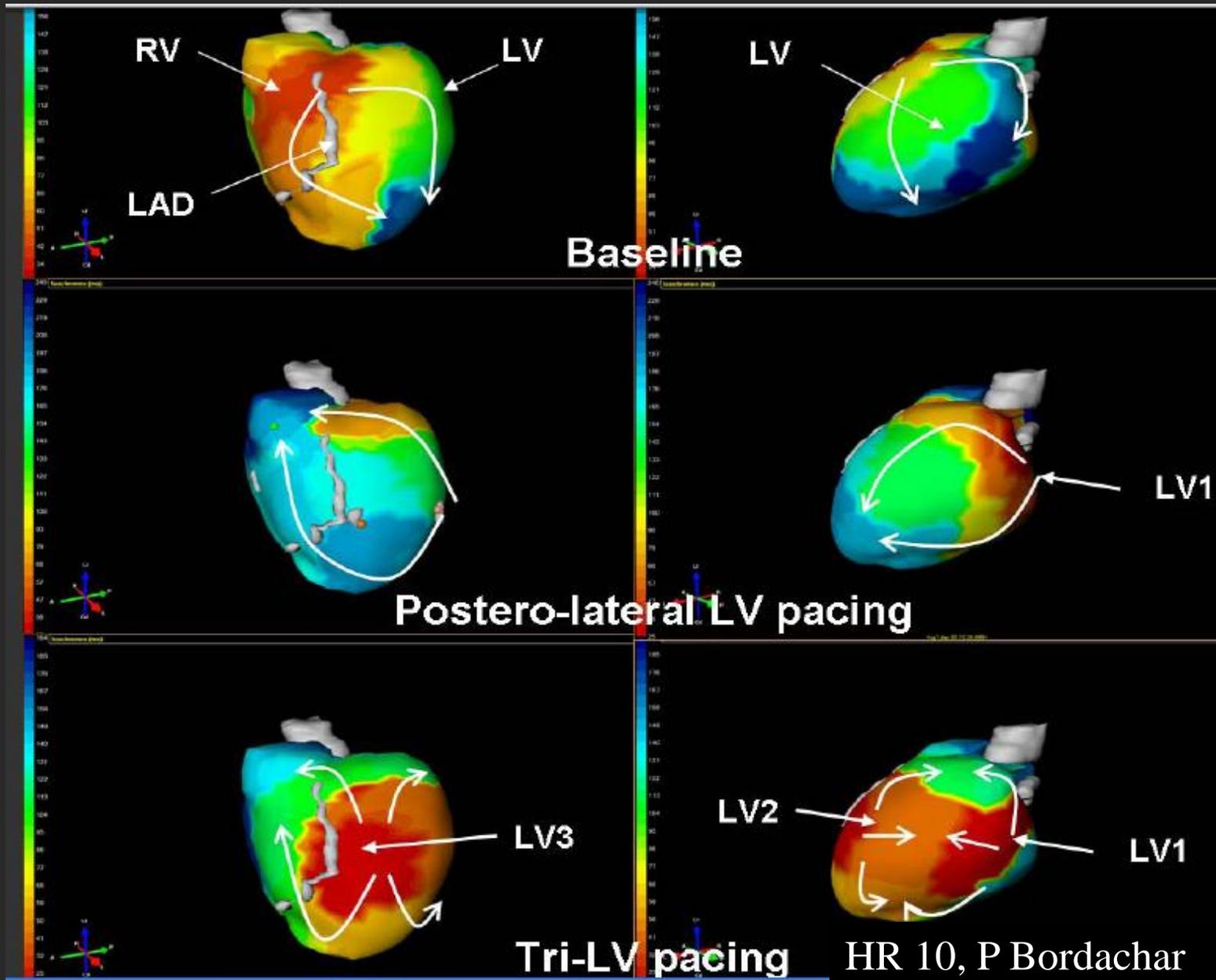
- Background
- **Dual-Site LV Pacing during CRT**
- Quadripolar LV Pacing approach
- LV Endocardial Pacing: LVEP
- Vagal Nerve stimulation in HF

A randomized comparison of triple versus dual site ventricular stimulation in patients with congestive heart failure

Christophe Leclercq¹, MD, PhD, Fredrik Gadler², MD, PhD, Wolfgang Kranig³, MD, Sue Ellery⁴, MD, Daniel Gras⁵, MD, Arnaud Lazarus⁶, MD, Jacques Clémenty⁷, MD, Eric Boulogne⁸, MSc, Jean-Claude Daubert¹, MD, for the Triple Resynchronization In Paced Heart Failure Patients (TRIP-HF) study group



Interest of Multisite LV Pacing

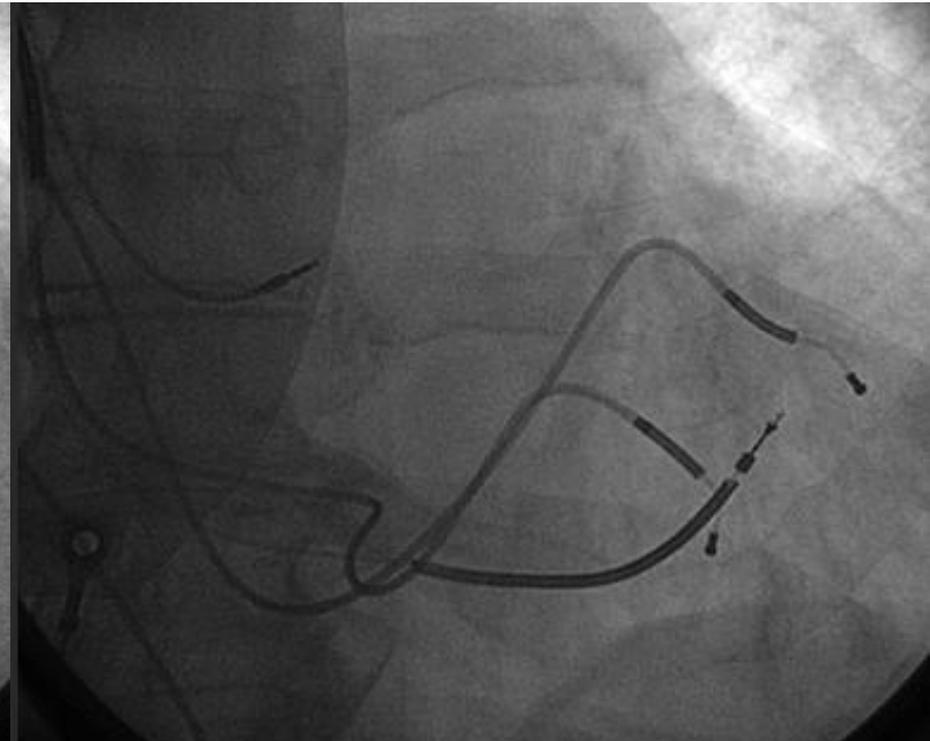
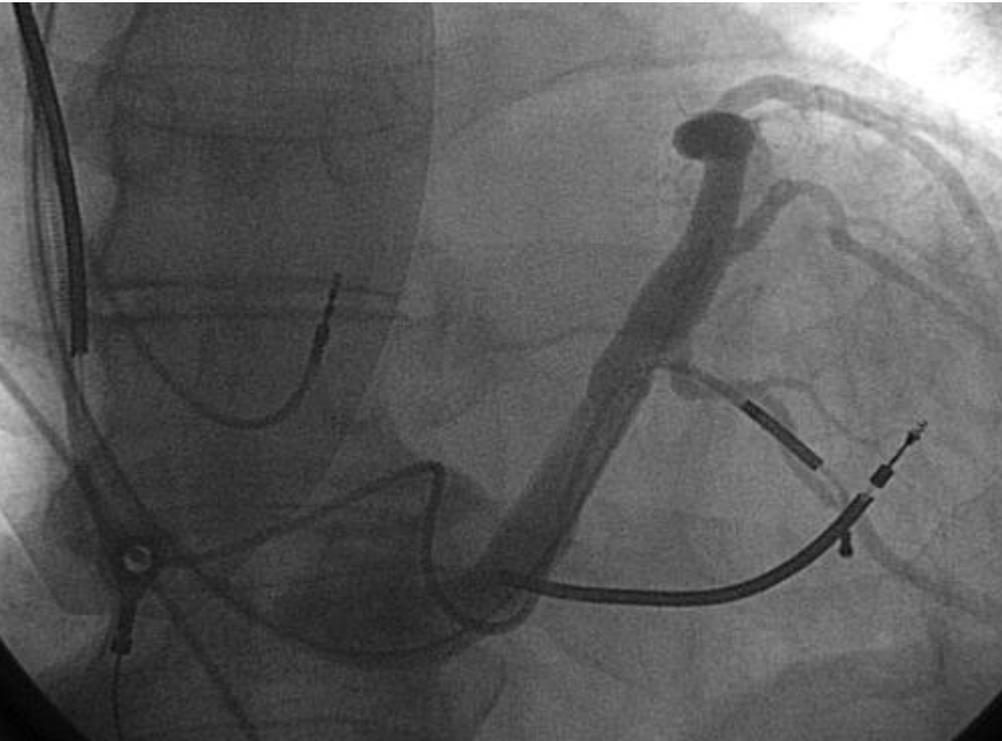


Atrial based, Dual Site LV, RV Pacing

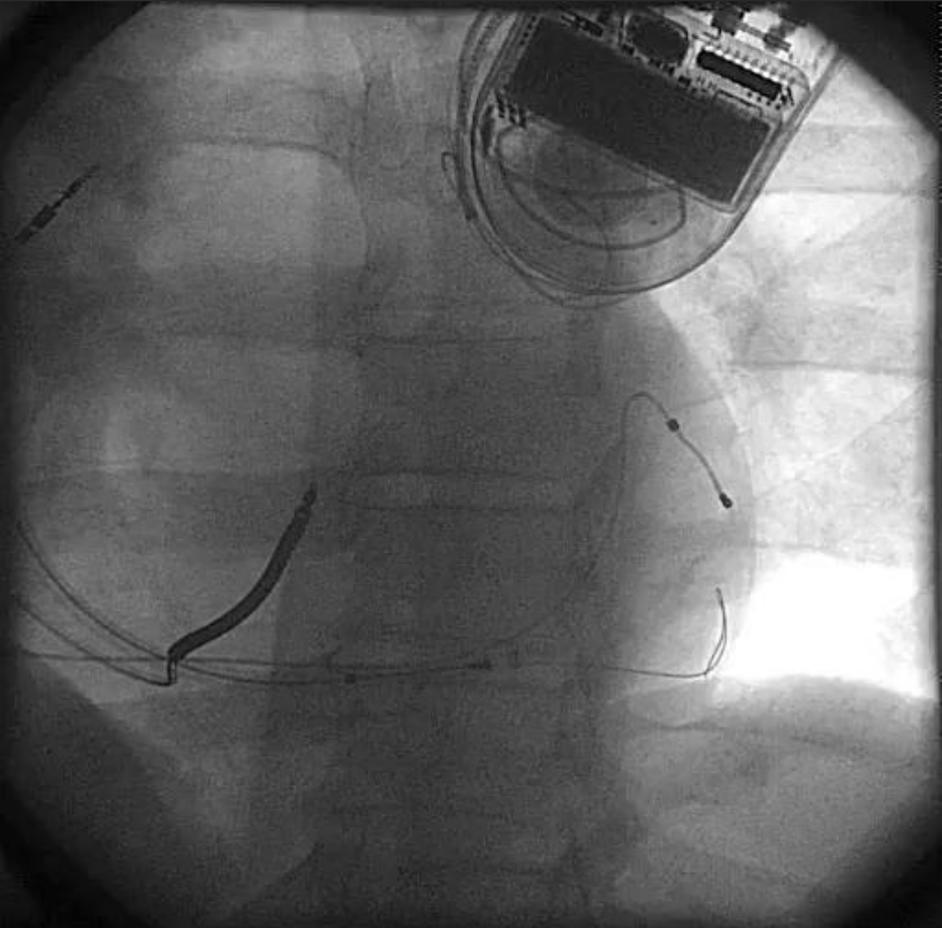
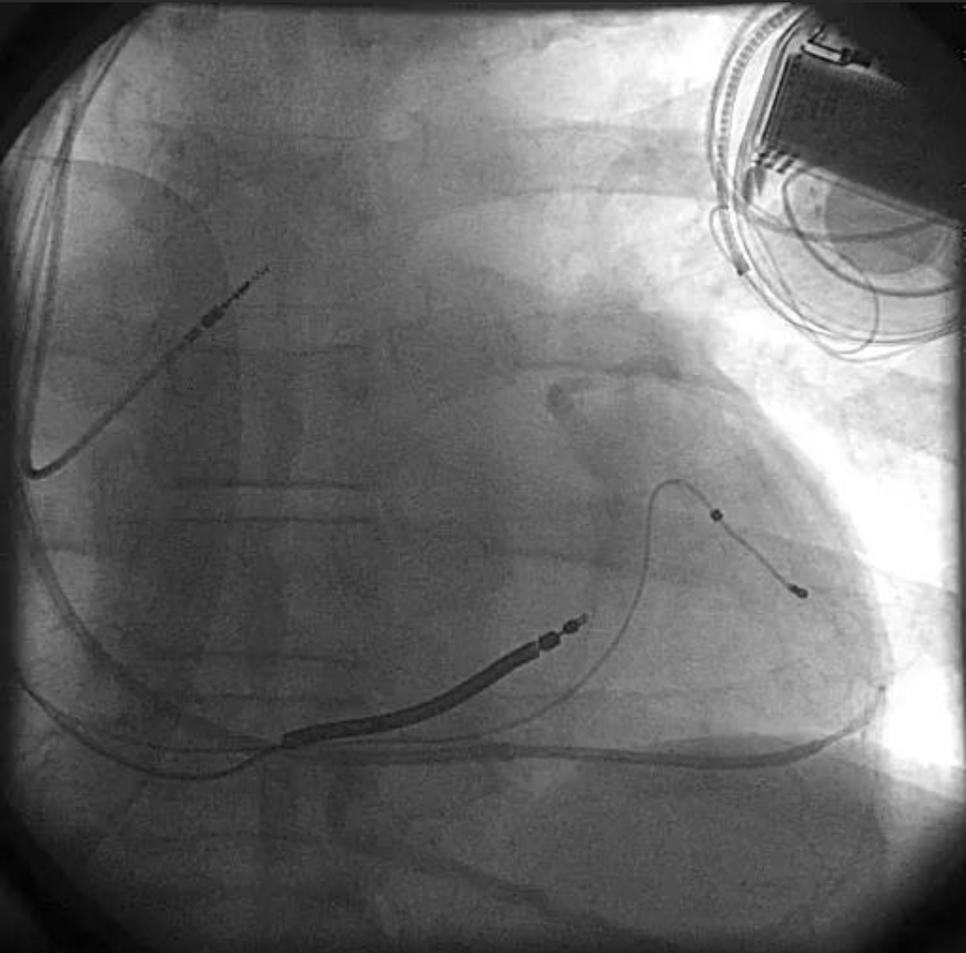
Clinical Trials

Addition of a Second LV Pacing Site in CRT Nonresponders Rationale and Design of the Multicenter Randomized V³ Trial

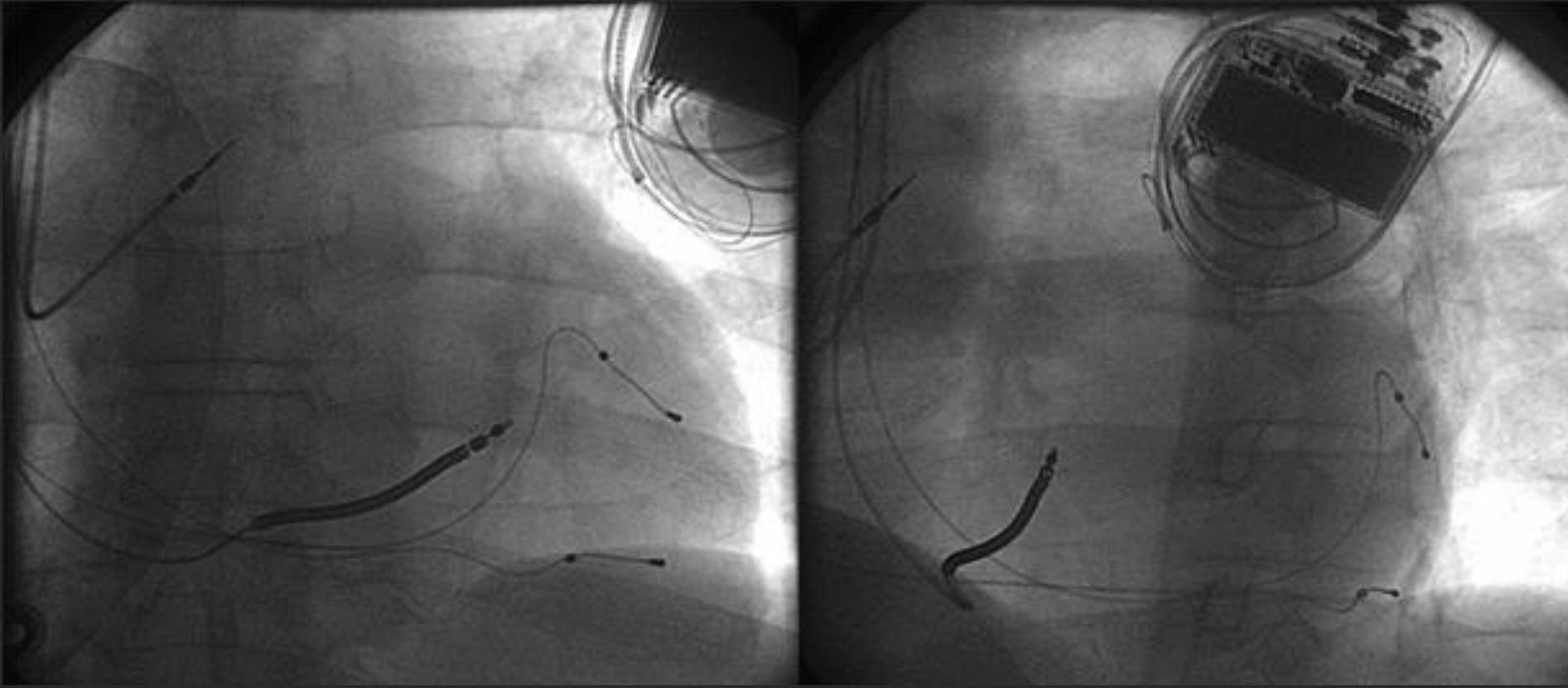
PIERRE BORDACHAR, MD,¹ CHRISTINE ALONSO, MD,² FREDERIC ANSELME, MD,³ SERGE BOVEDA, MD,⁴
PASCAL DEFAYE, MD,⁵ STEPHANE GARRIGUE, MD,⁶ DANIEL GRAS, MD,⁷ DIDIER KLUG, MD,⁸ OLIVIER PIOT, MD,⁹
NICOLAS SADOUL, MD,¹⁰ AND CHRISTOPHE LECLERCQ, MD¹¹



Atrial based, Dual Site LV, RV Pacing (ongoing V3 Trial)



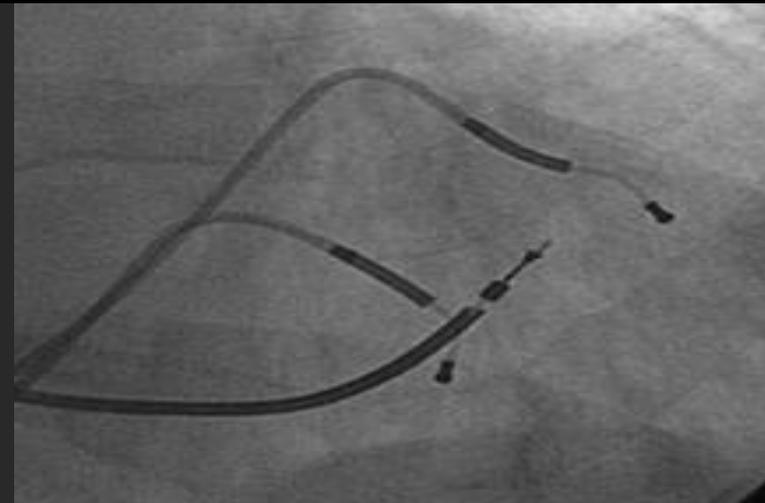
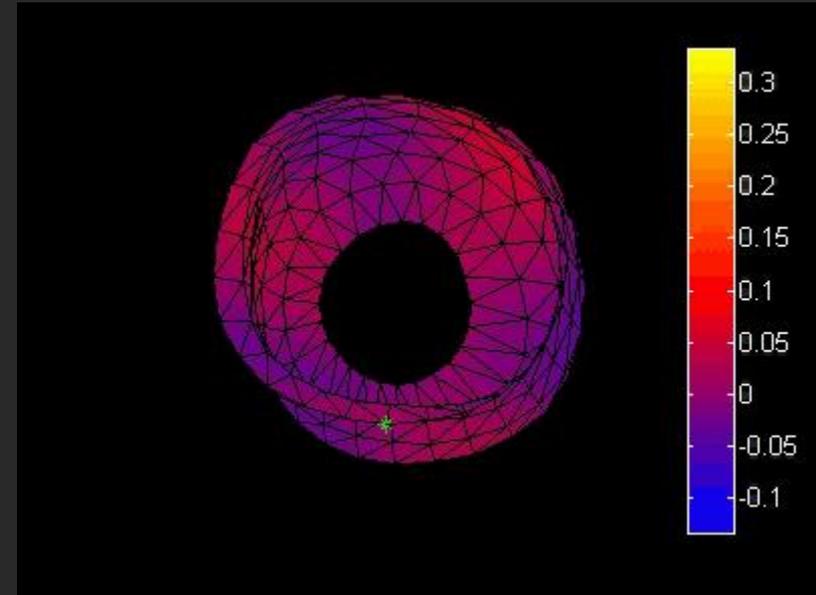
Interest of Additional LV Lead during CRT



Non-Traditional CRT: Novel Implant Techniques

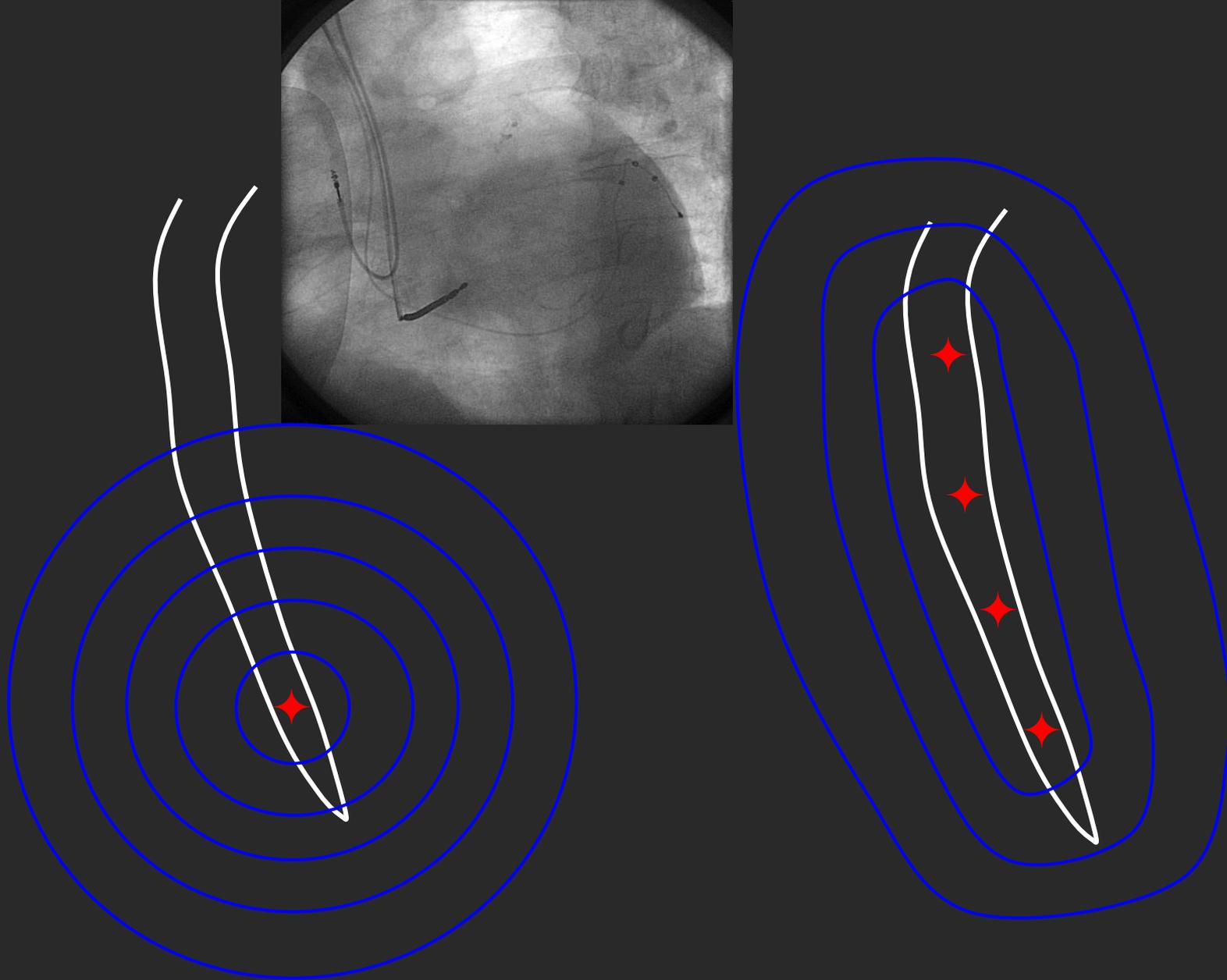
Atrial based, Dual Site LV, RV P

- Goal:
 - To Improve Ventricular activation & CRT Impact
 - Ongoing V3 Trial
- Potential Difficulties
 - Subclavian Vein Occlusion
 - Y Adaptor & Electrical csqces
 - Higher Risks of PNS
 - CS Anatomical Limitations



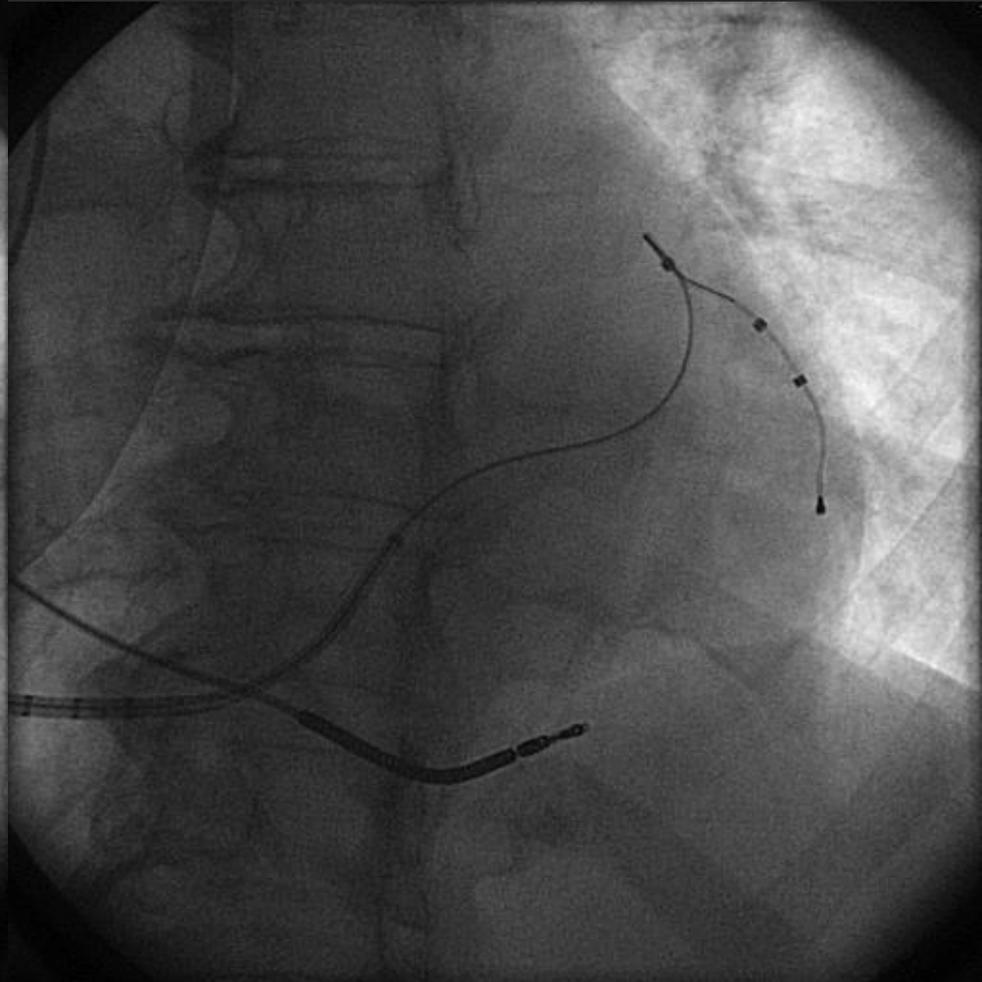
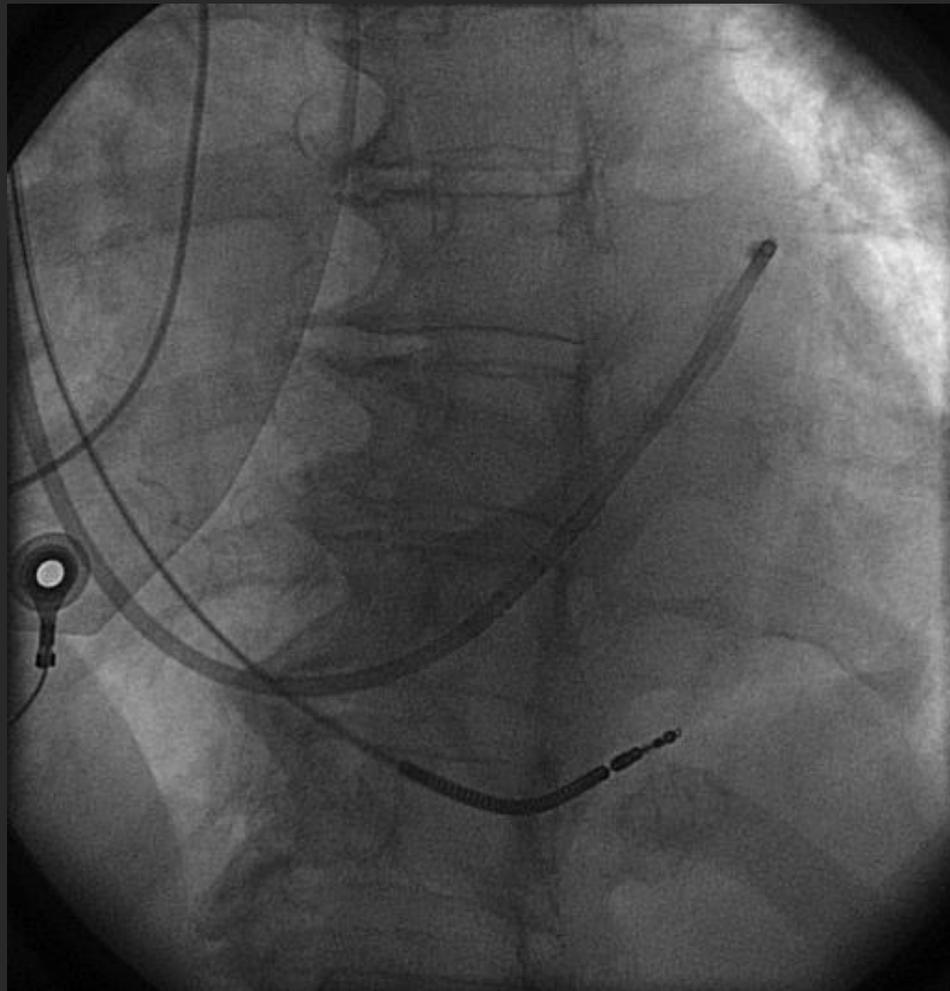
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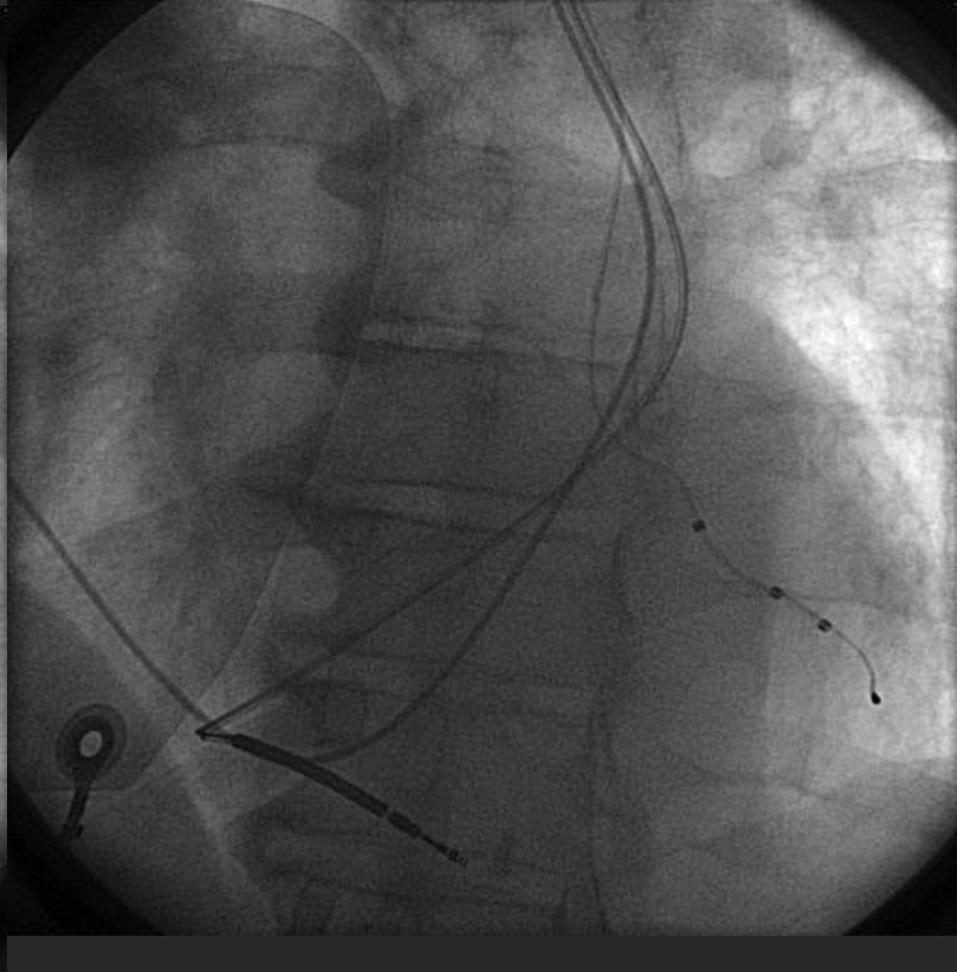
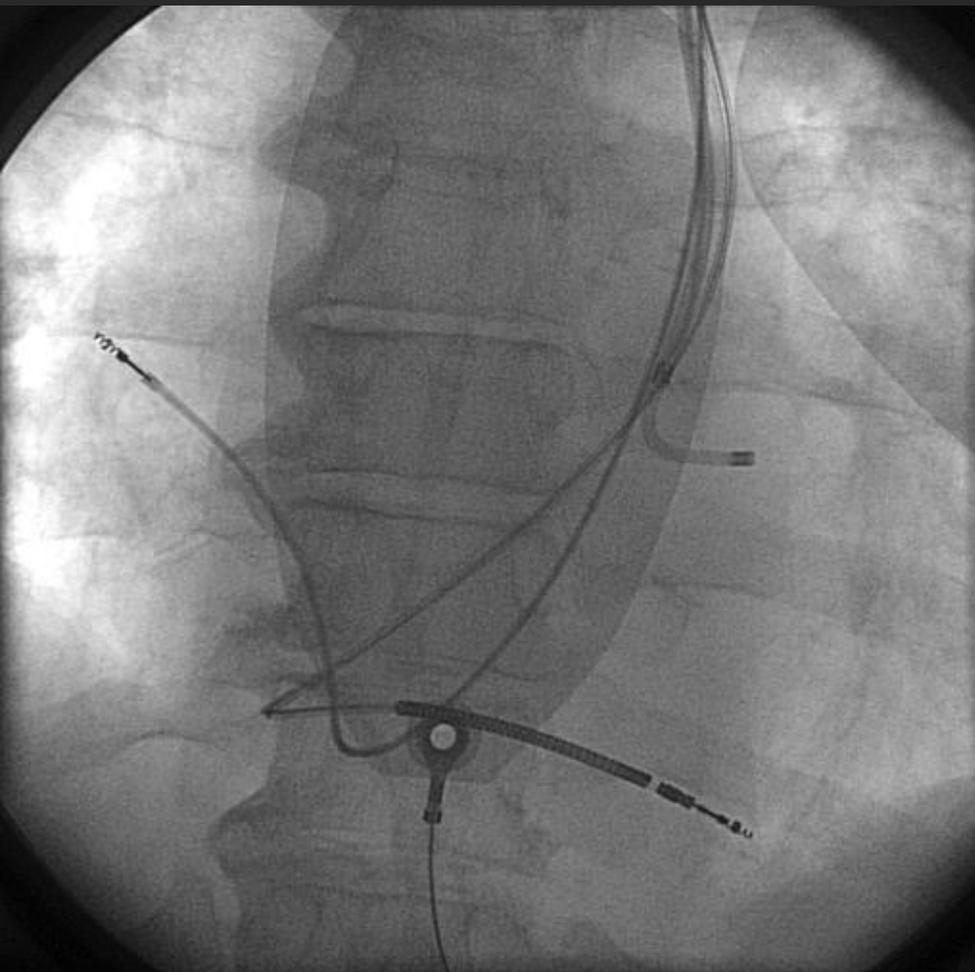


Single Site vs. MSLV in Healthy Heart

Subselection of Lateral Cardiac Vein during Quadripolar LV Lead Implant



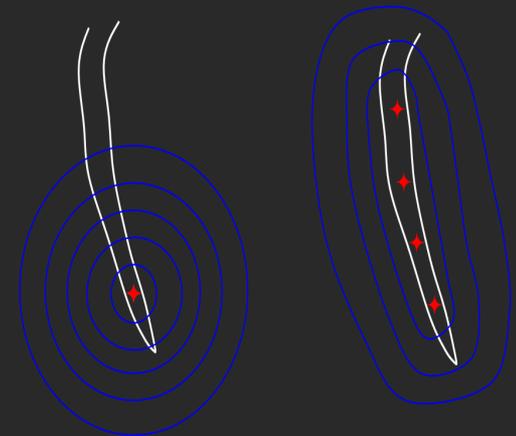
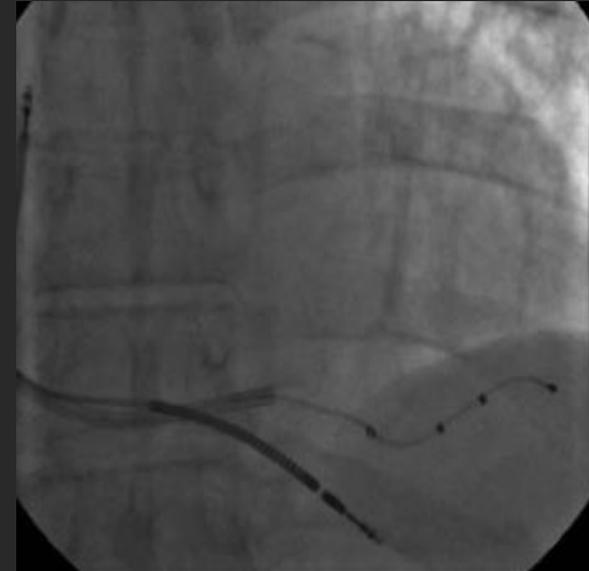
Quadripolar LV Lead in case of LSVC



Non-Traditional CRT: Novel Implant Techniques

Benefits of Quadri vs Bipolar LV Lead

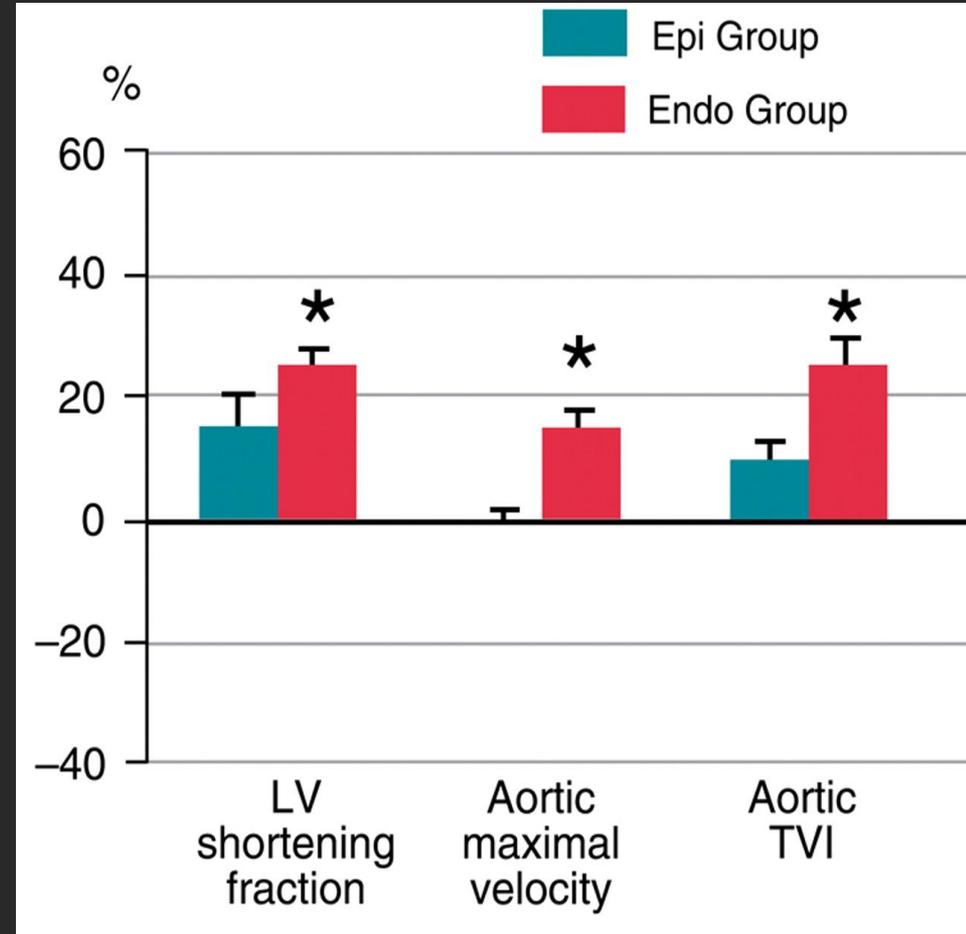
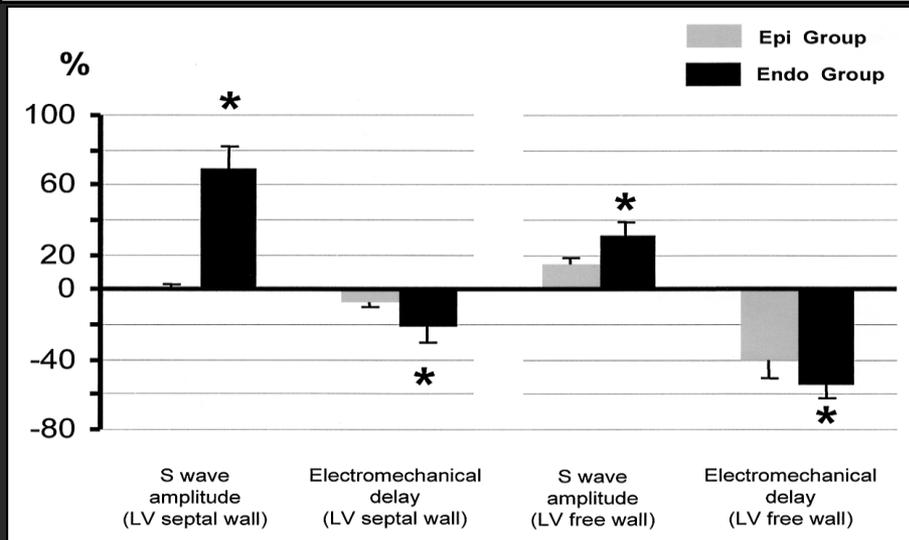
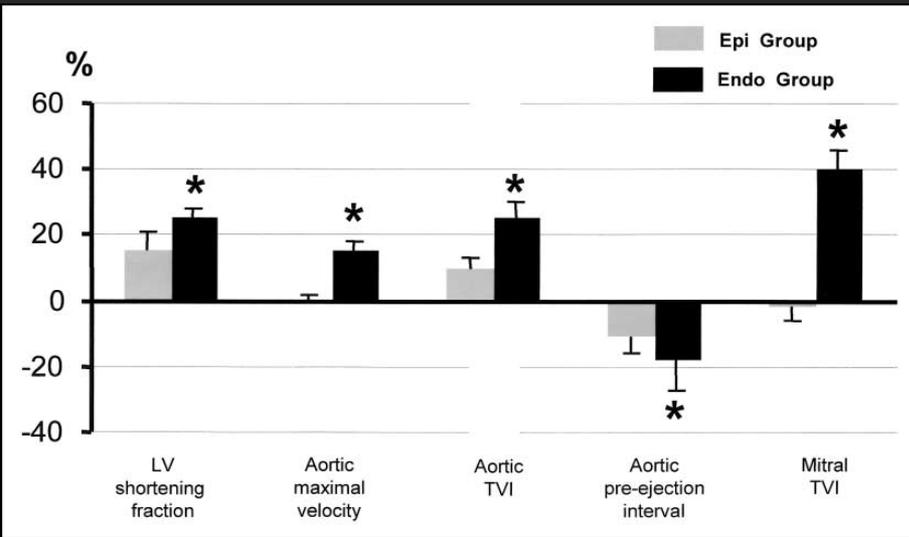
- Management of PN Stimulation
- Pacing Vector offering
 - The Best Hemodynamics
 - The Best Pacing Thresholds
- Lower Need for LV Lead Revision
- Similar Lead Implant procedure
- Simultaneous 4 P Pacing for a better CRT impact to be investigated



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Endocardial vs. Epicardial Biventricular Pacing.



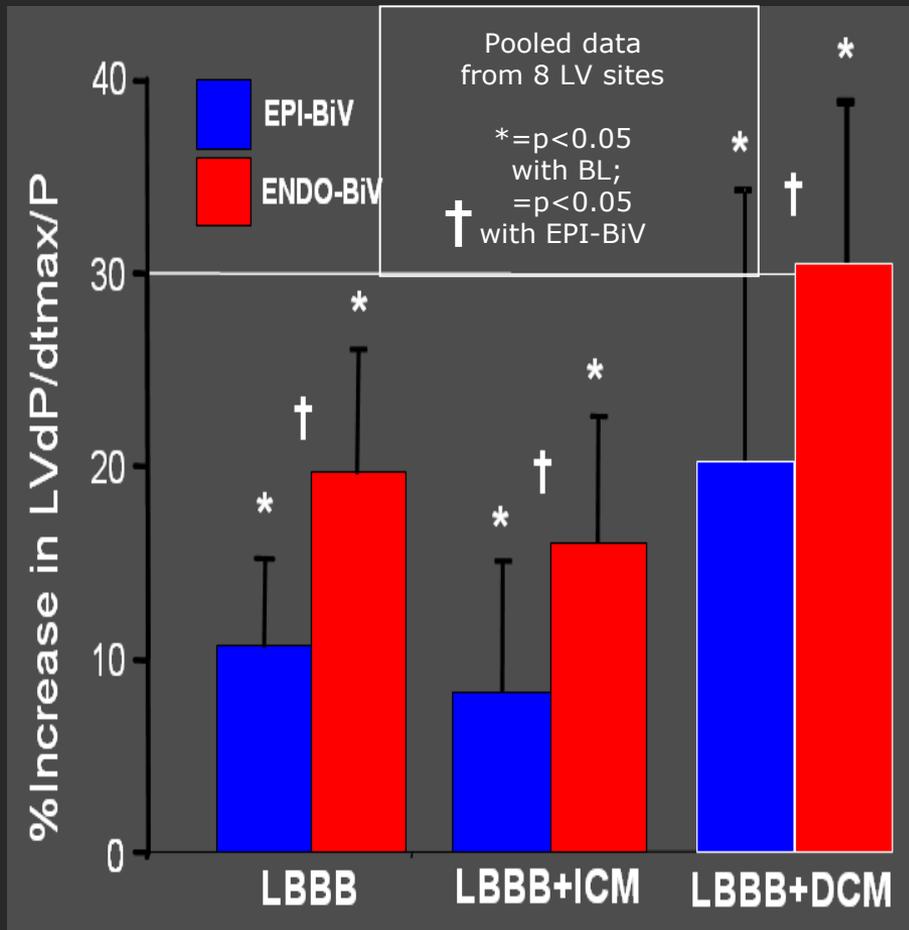
Garrigue S., Jais P, et. al.
AJC, 2001 88:858-862

Morgan J M , Delgado V
Europace 2009;11:v22-v28

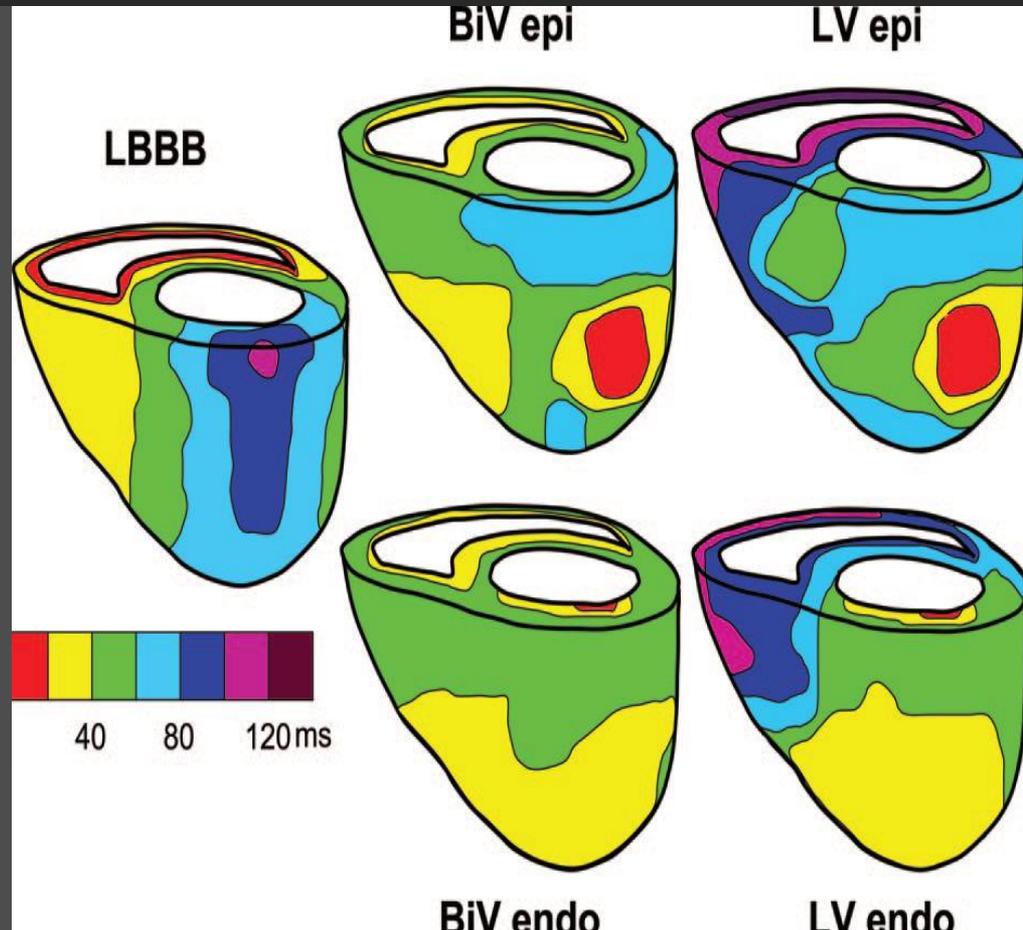
Endocardial vs Epicardial CRT provides:

Better LV Filling and Systolic Performance

More Homogenous Resynchronization

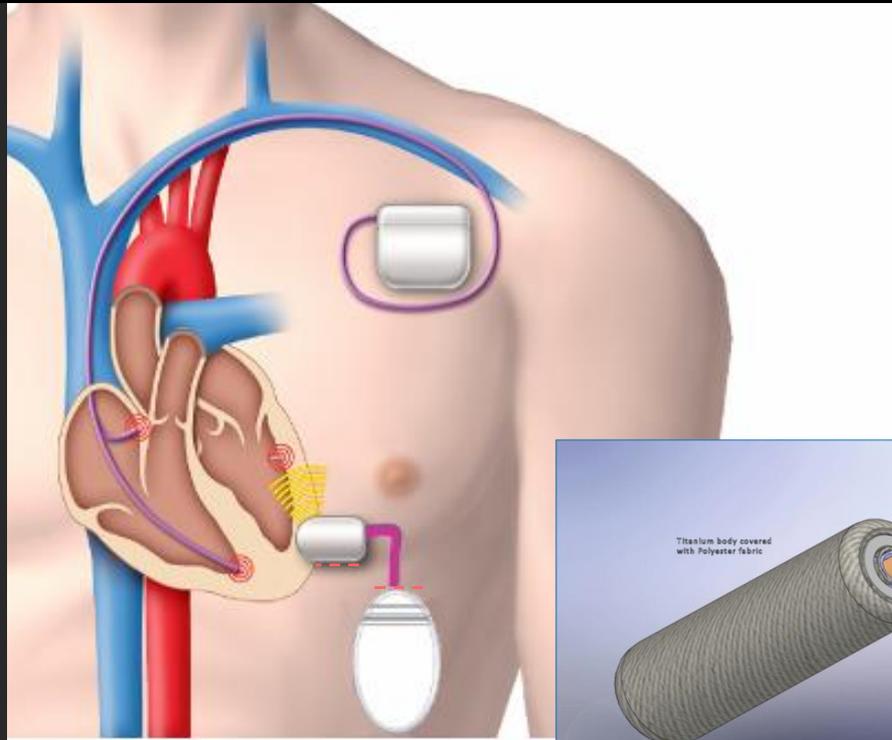


Prinzen et al



Van Deursen, Circ Arrhythmia
Electrophysiol. 2009;2:580-587

WISE-CRT: Wireless Stimulation Endocardially for CRT



- Works with any PM or ICD
- Simple co-implant
 - Transvenous right side system
 - Wireless left side system

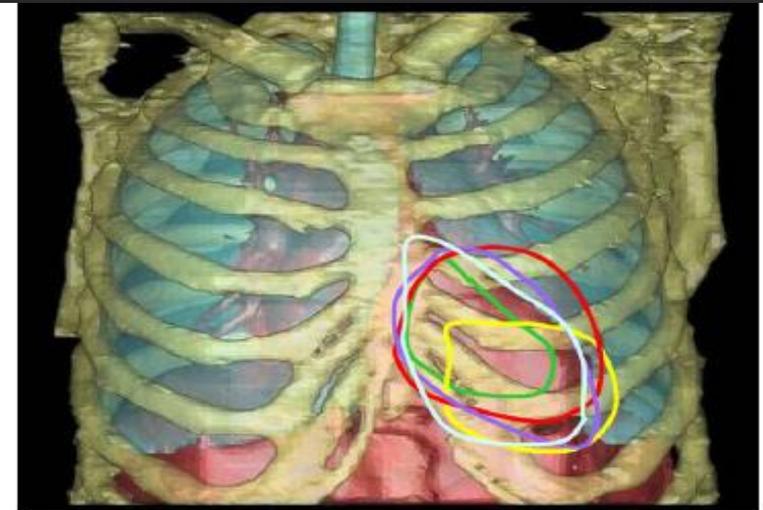
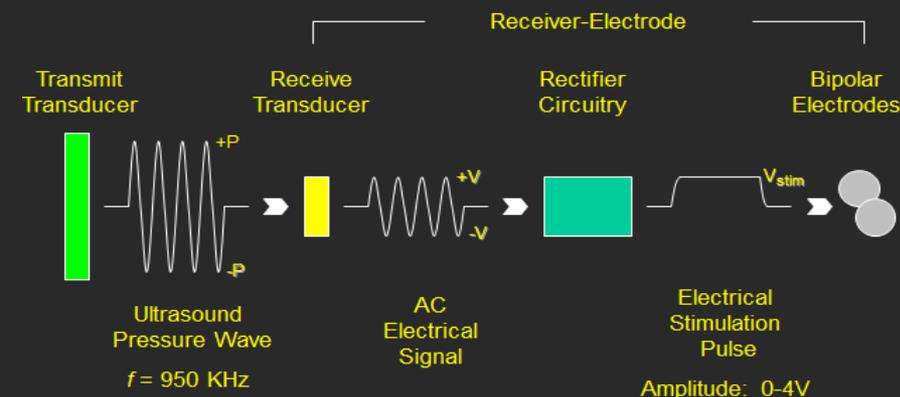
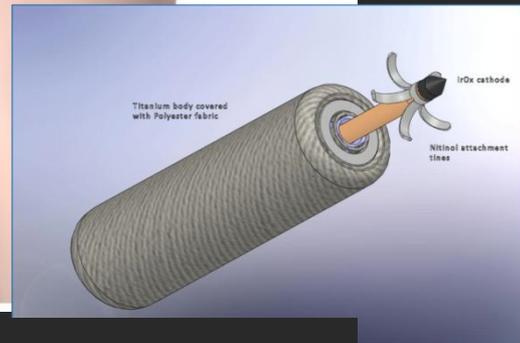
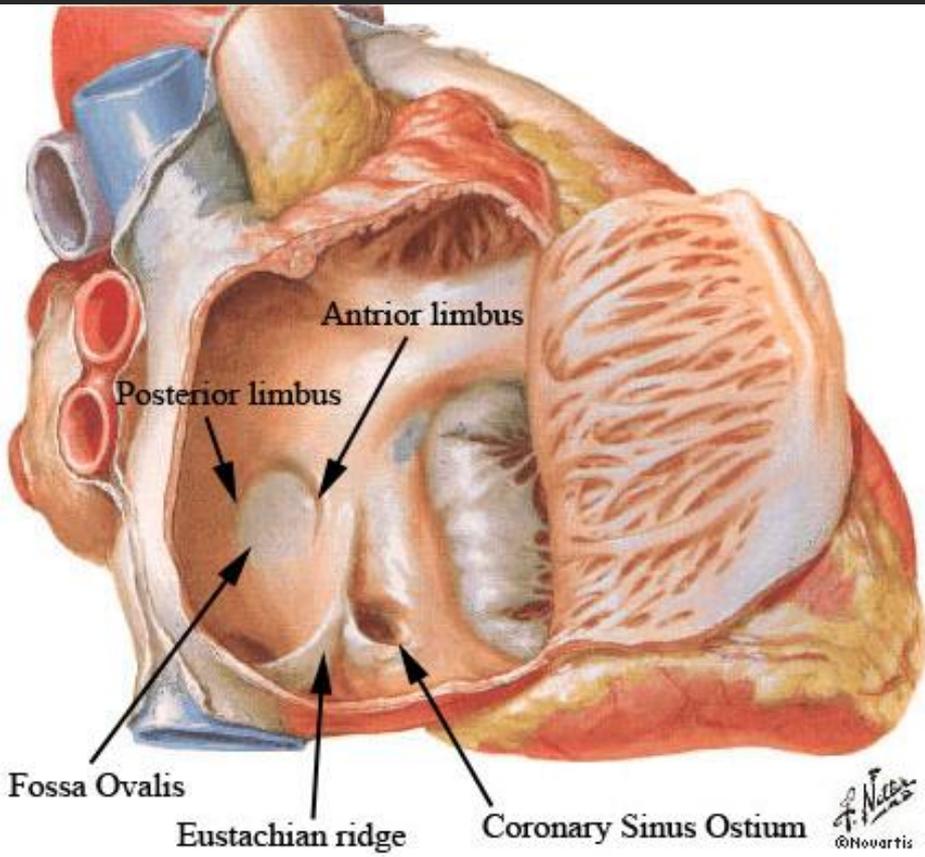


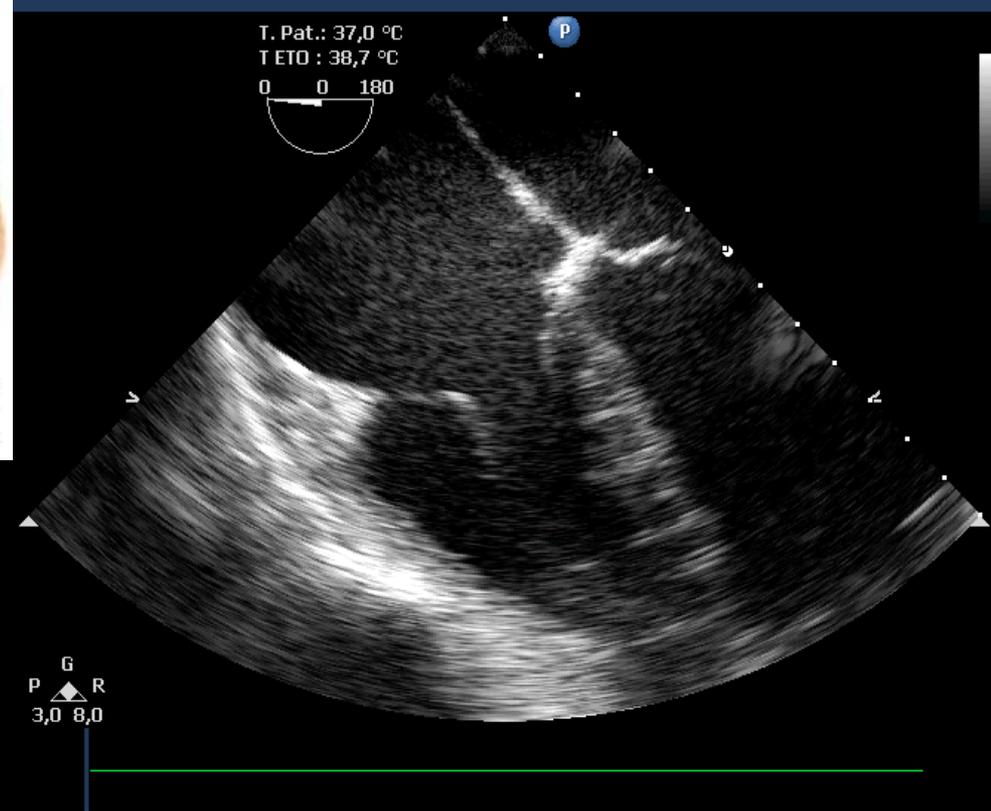
Figure 2 An example of clinically determined acoustic windows in 4 body positions (in red with the patient lying supine; in green with 30° right tilt; in yellow with 30° left tilt; in purple with 30° upright tilt) superimposed on the CT-determined acoustic window (in light blue with the patient lying supine and during end inspiration) on 3D reconstruction CT of the thorax. 3D = three-dimensional; CT = computed tomography.

TEE Evaluation before Transseptal Puncture

Location of Fossa Ovalis



VE IM 0,5 26/04/2011
04-26-110414 N.C.N. CARDIOLOGIE ITm 0,0 11:12:49



Ongoing Evaluation

LV Endo Pacing in Non CRT Responder

LV Lead placement
under TEE guidance

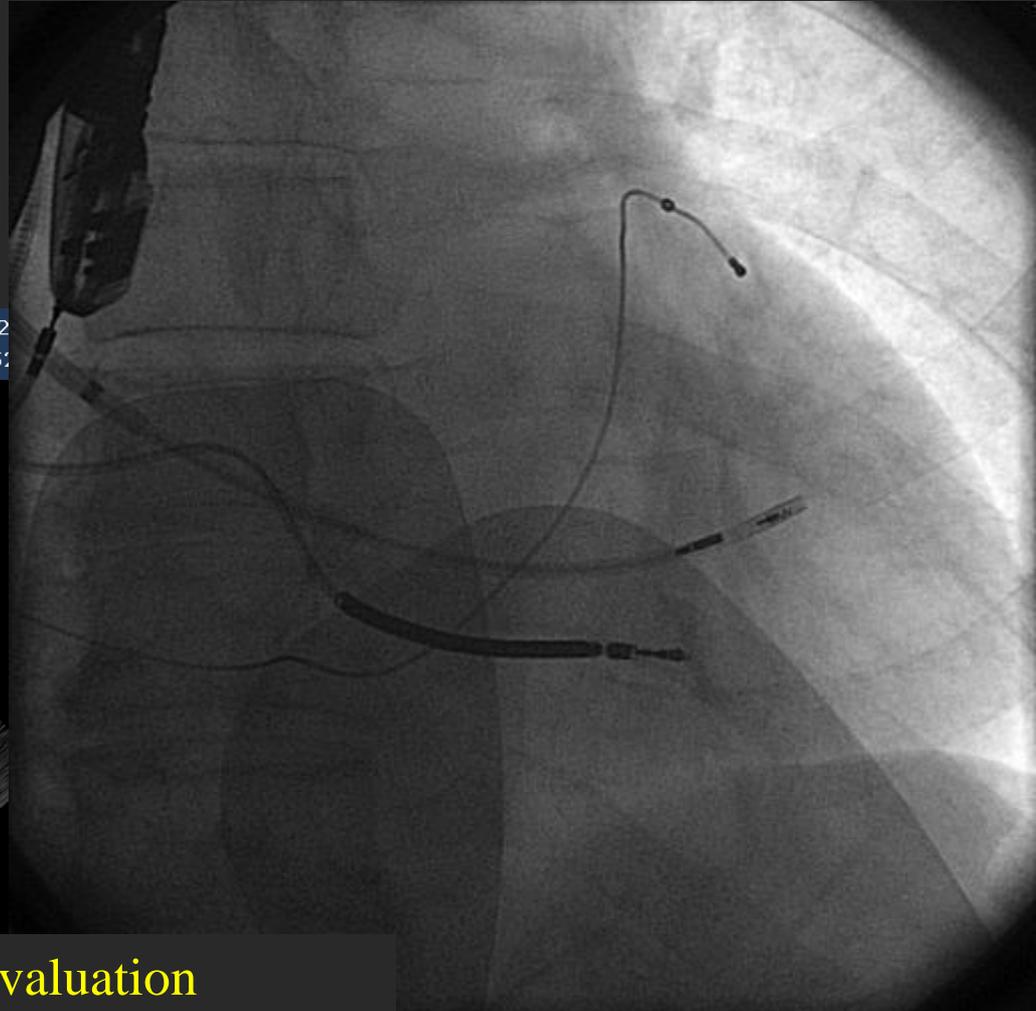
PHILIPS HERVE IM 0,5 26/04/2
11-04-26-110414 N.C.N. CARDIOLOGIE ITm 0,0 13:09:5

ETO
X7-2t
44HZ
14cm

T. Pat.: 37,0 °C
T ETO : 38,3 °C
0 84 180

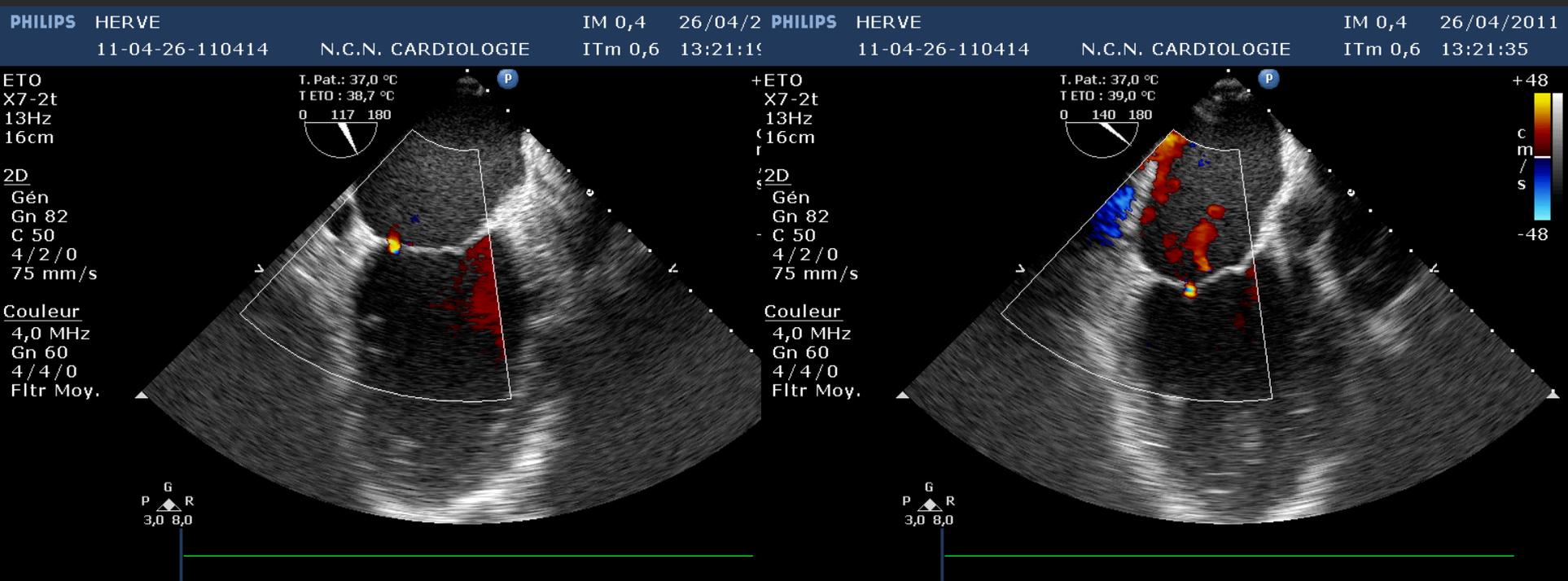
2D
Gén
Gn 70
C 50
4 / 2 / 0
75 mm/s

G
P R
3,0 8,0

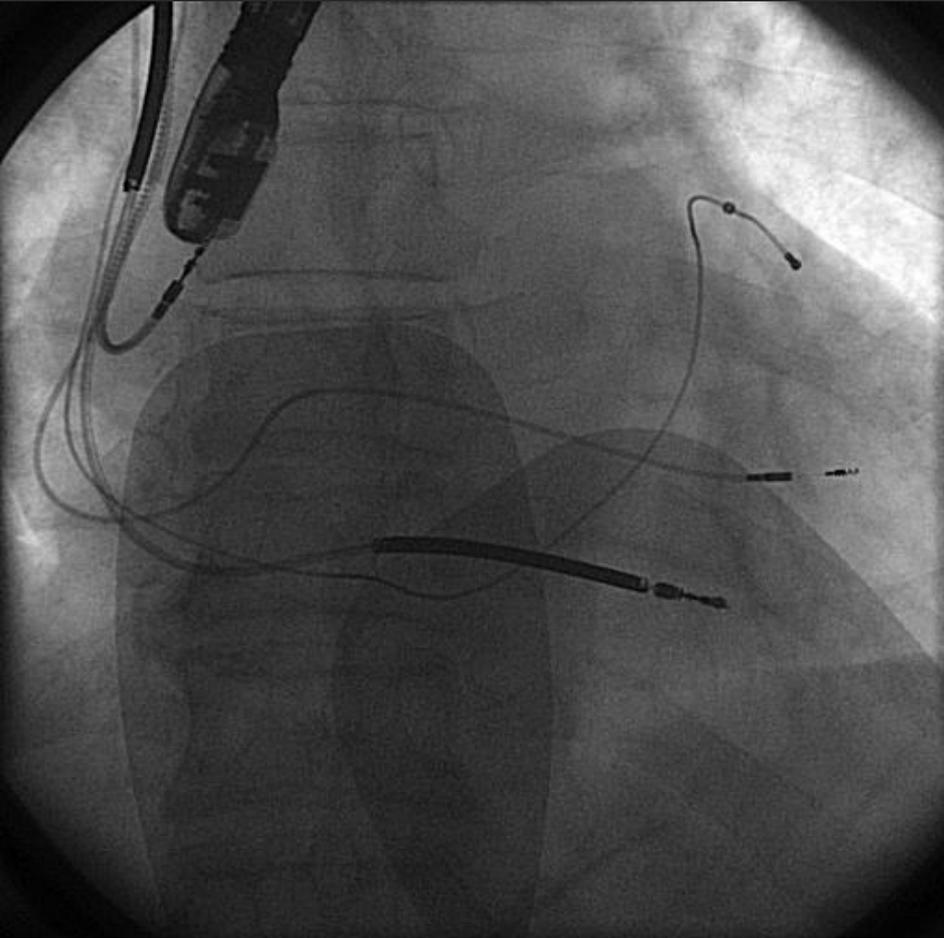


Ongoing Evaluation

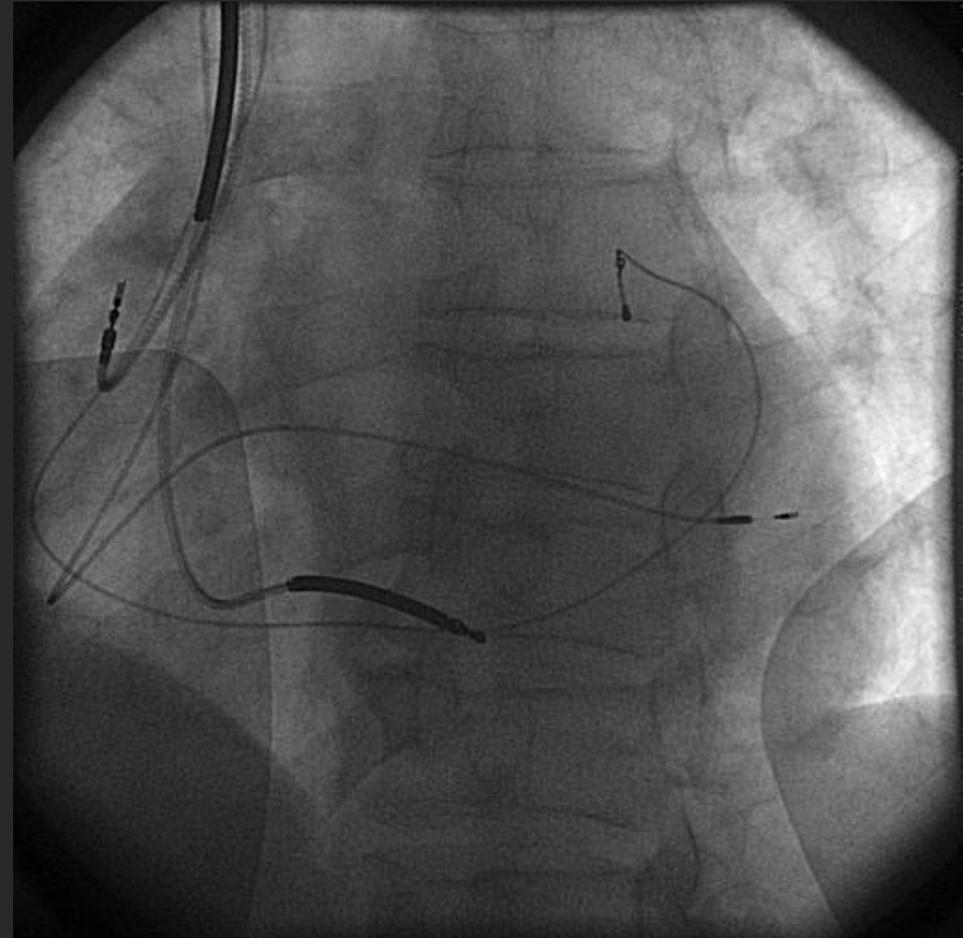
LV Lead Position post Implant, No Change in MR



LV Endo Pacing in Non CRT Responder

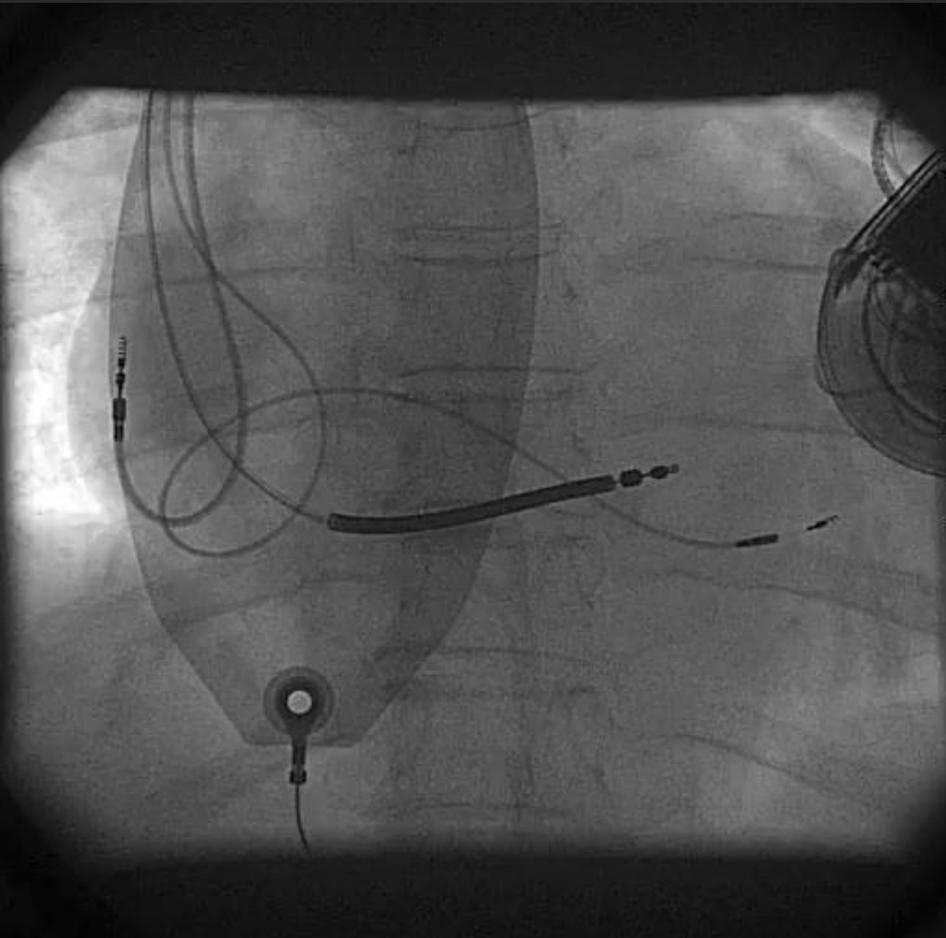


AP View

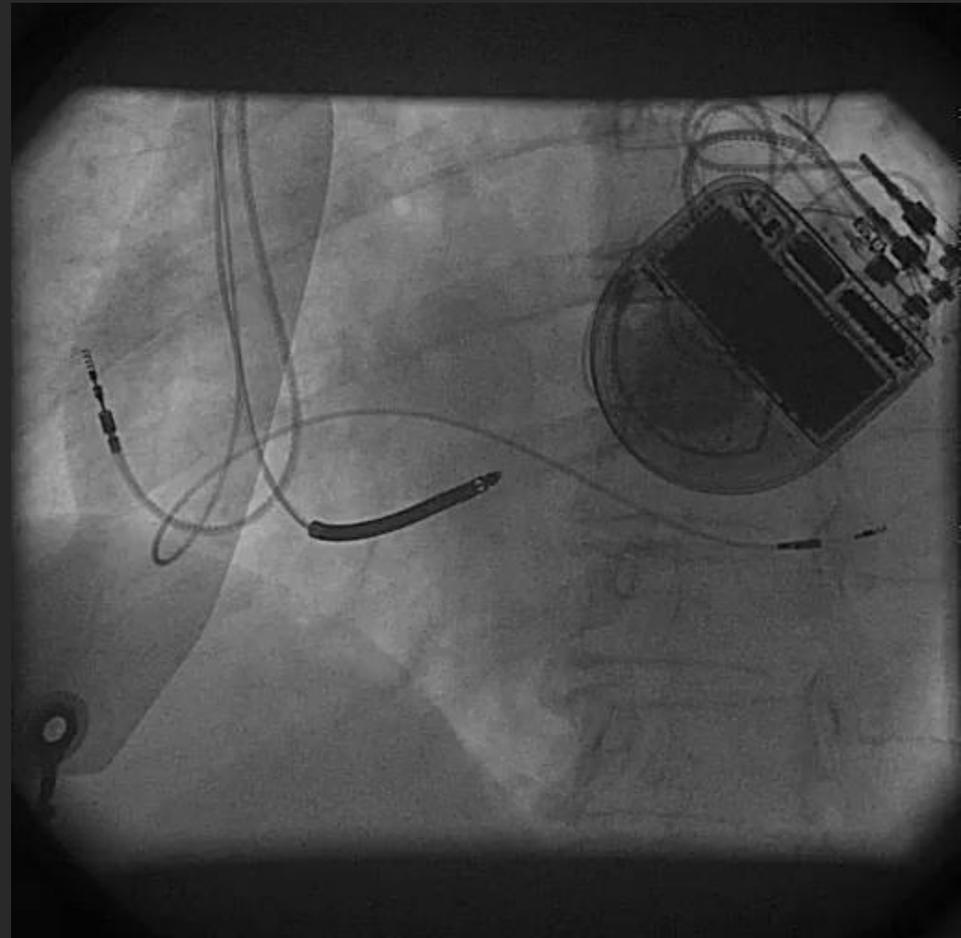


LAO View

LV endocardial Pacing during CRT

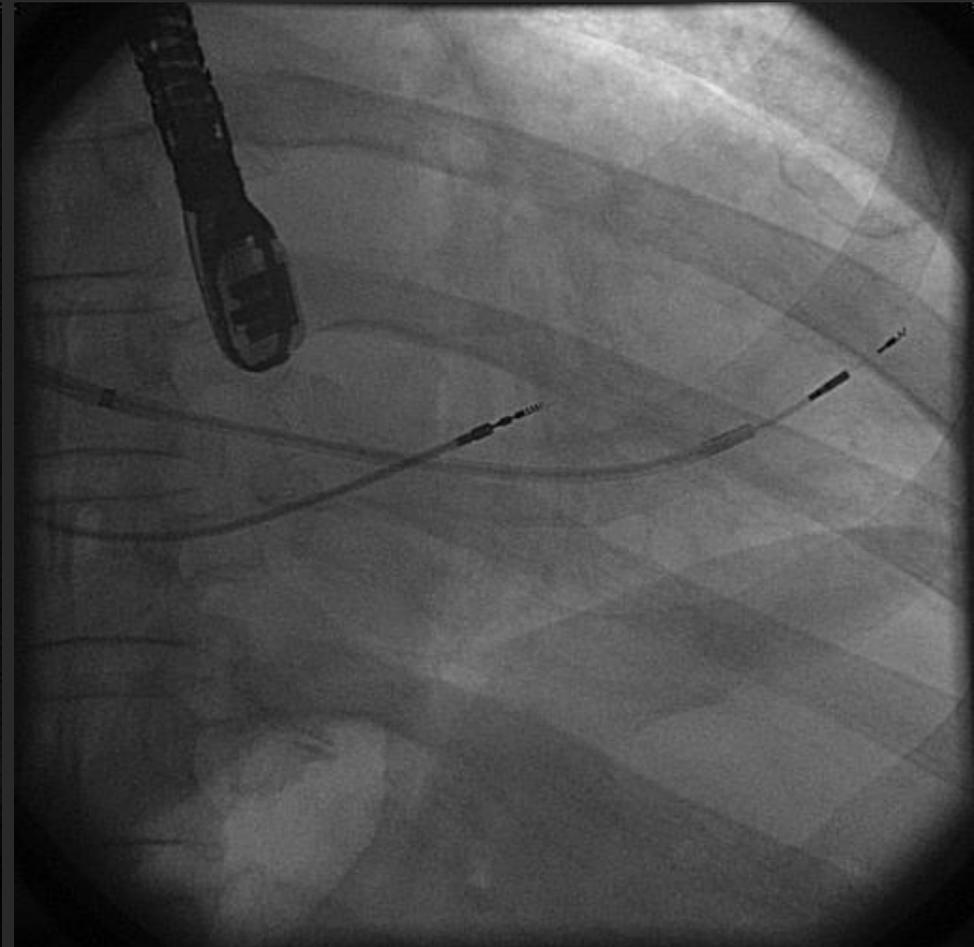
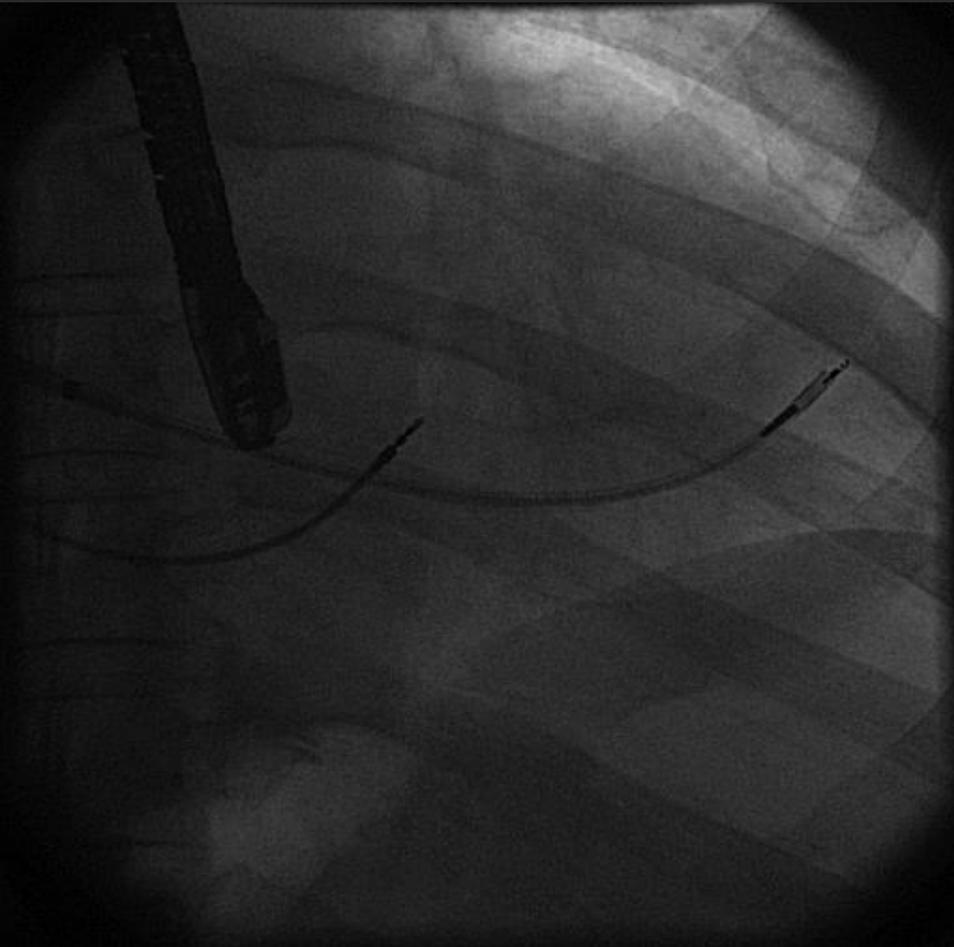


AP View



LAO View

PNS still happens during LV endo Pacing !!



Echo prior to Transseptal LV Lead implant

FE VG (sim.A4C) 19 %

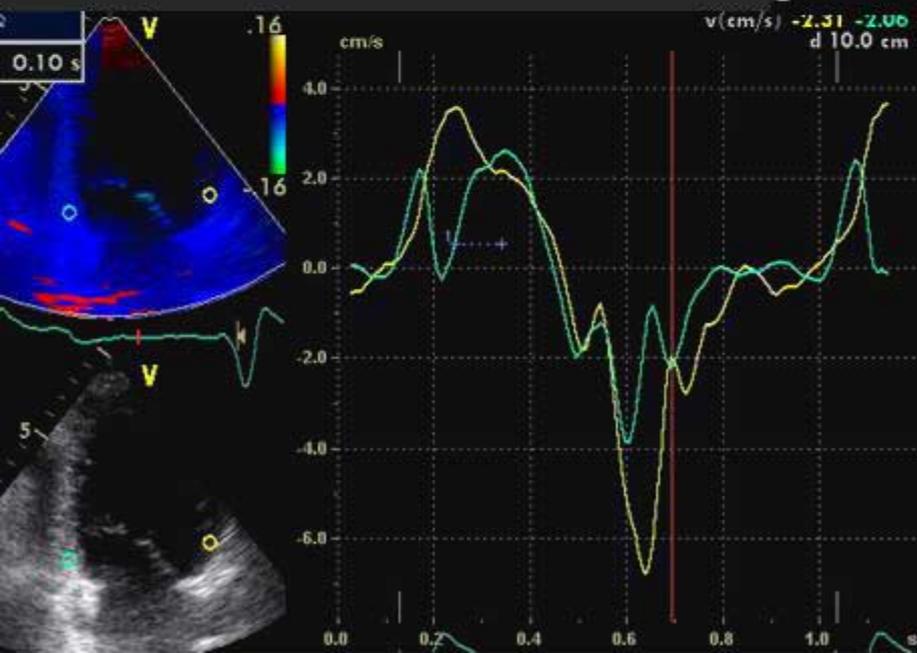
Vol. Eject.(simpson A4C) 25 ml

2 VGs Long(A4C) 8.5 cm

Vol.VG.tS(sim.4cav) 106 ml

1 VGd Long(4cav) 9.2 cm

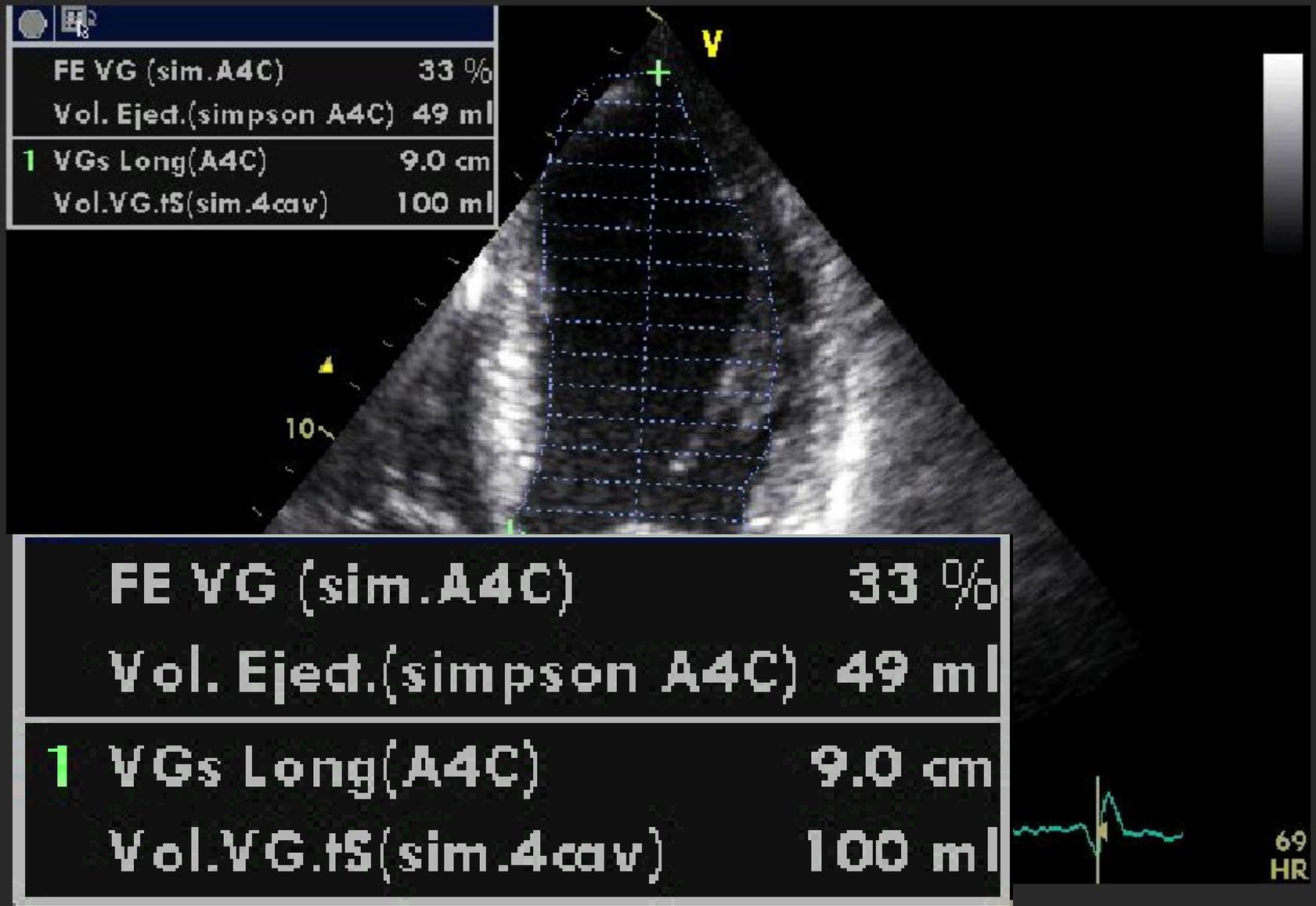
Vol.VG.tD(sim.4cav) 131 ml



08/04/2011 12:01:41

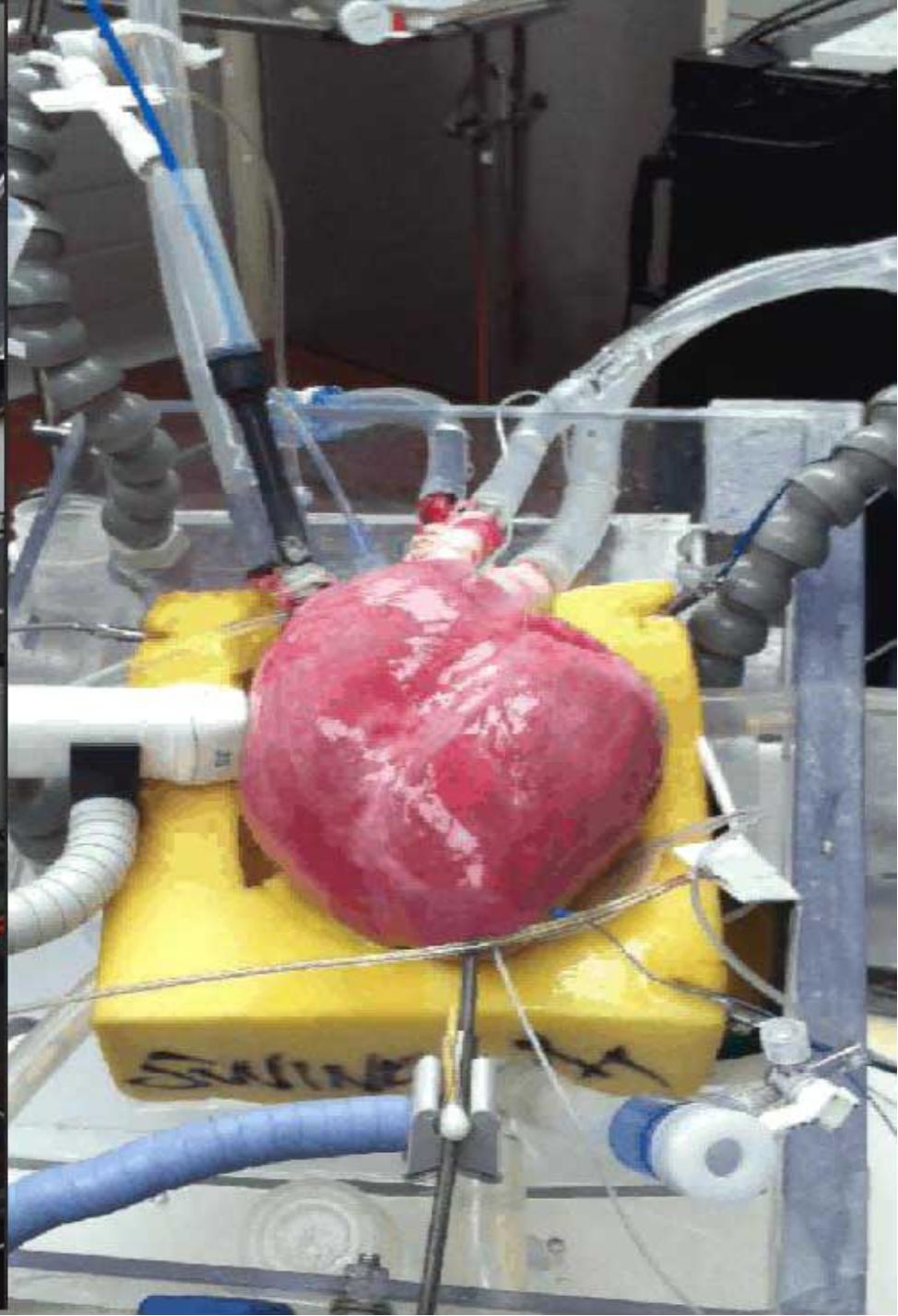


LV EF Echo Evaluation (Simson)



Permanent LV Endocardial Pacing in Clinical Practice

Avantages	Disavantages
<p>Easier access to LV Ventricle</p> <p>Better Hemodynamics</p> <ul style="list-style-type: none">Faster DepolarizationFaster Vent activation <p>Low risk of PNS</p> <p>Better short & long term PT</p>	<p>Transeptal Approach</p> <p>Embolic risk</p> <p>X Ray exposure</p> <p>Anticoagulation</p> <p>Mitral Regurgitation</p> <p>Lead Extraction ??</p>



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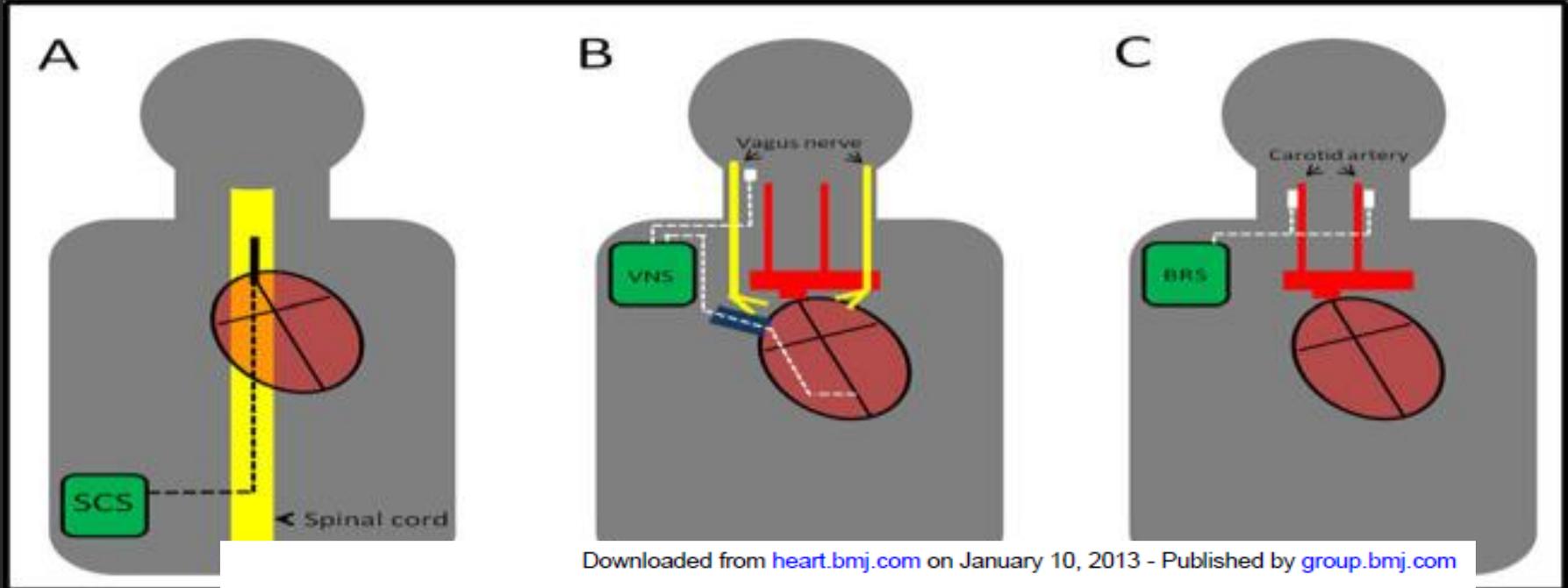
Device-based Neuromodulation Therapy for HF

Current Investigational Approaches

SCS

VNS

BRS



Spinal Cord Stimulation (SCS): SCS generators are implanted in the abdomen or paraspinal region. Leads are placed in dorsal columns between T1-T4

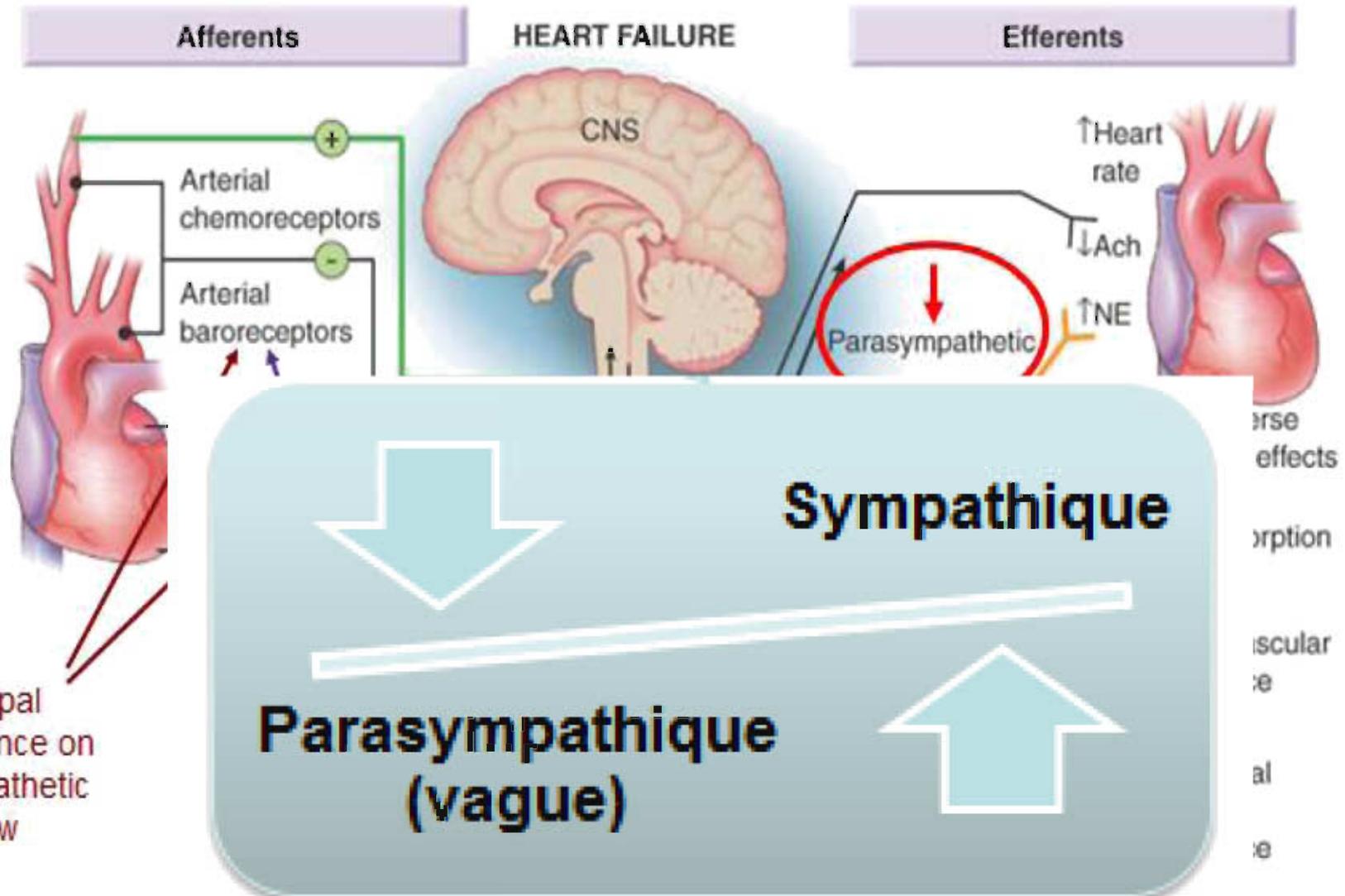
Vagal stimulation for the treatment of heart failure: a translational success story

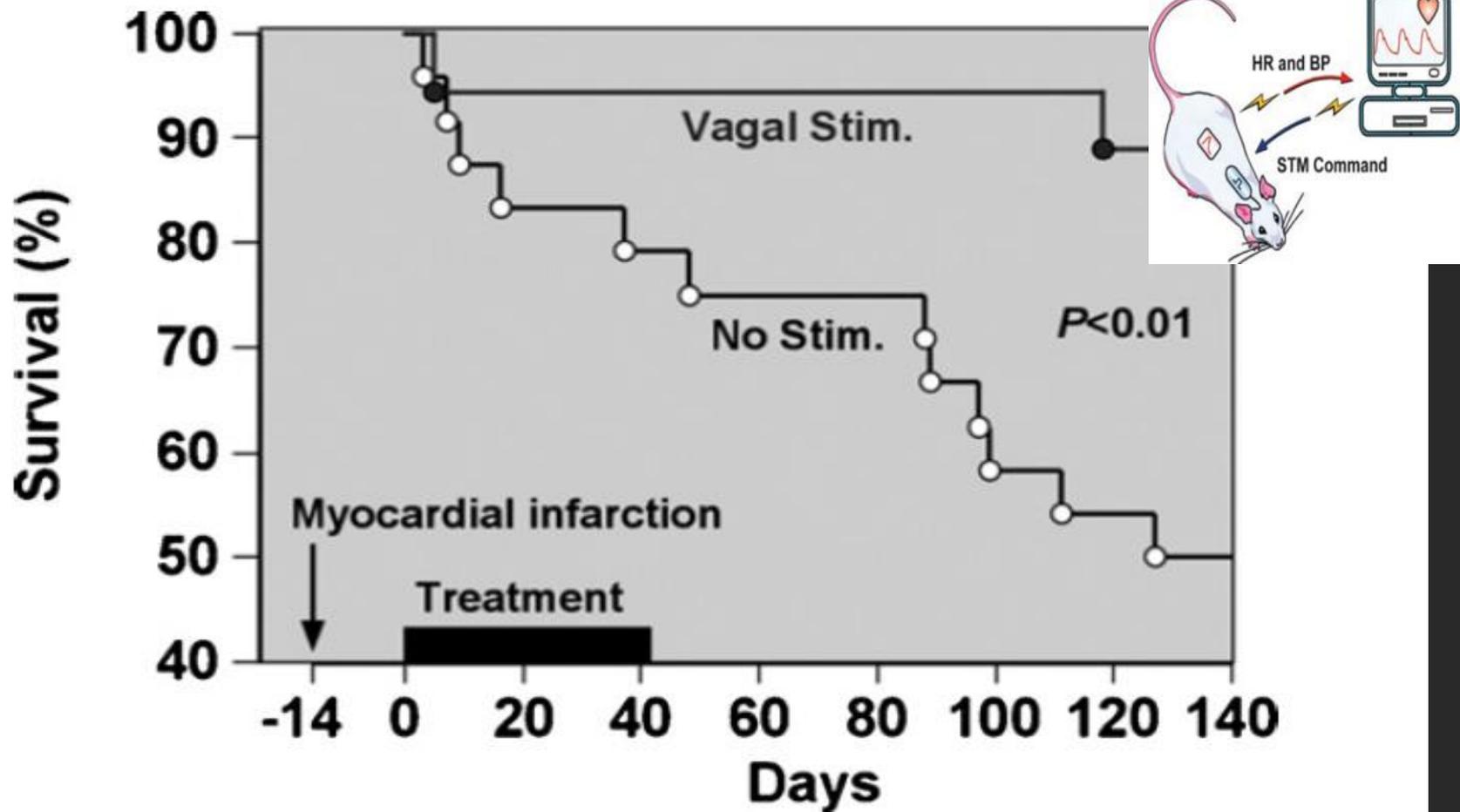
Peter J Schwartz^{1,2,3,4}

inhibition of cardiac activity (ie, low stimulation) the heart from sympathetic modulation home message stimulates—as bilateral studies—the in- ed to the also and sig- ion cardiac-bound s- ion synergistic effec- ion a significant wa-

Heart failure as an autonomic nervous system dysfunction

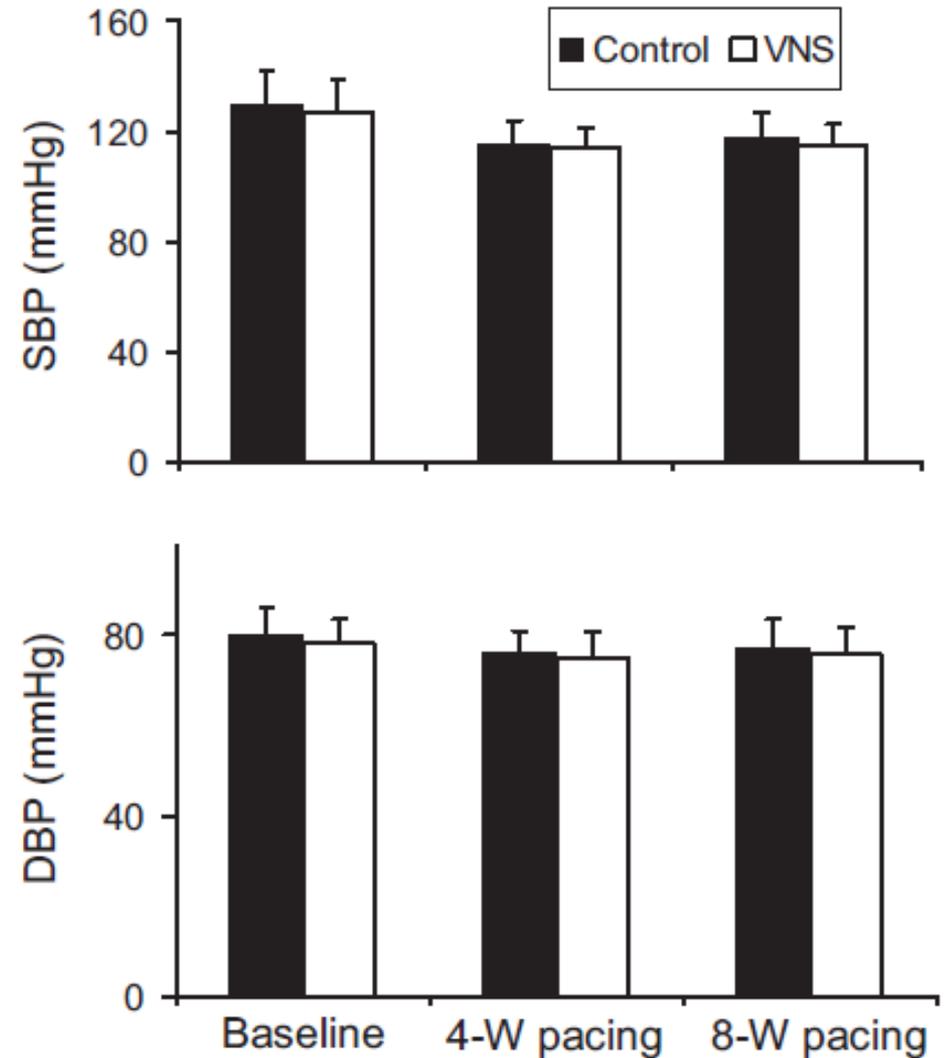
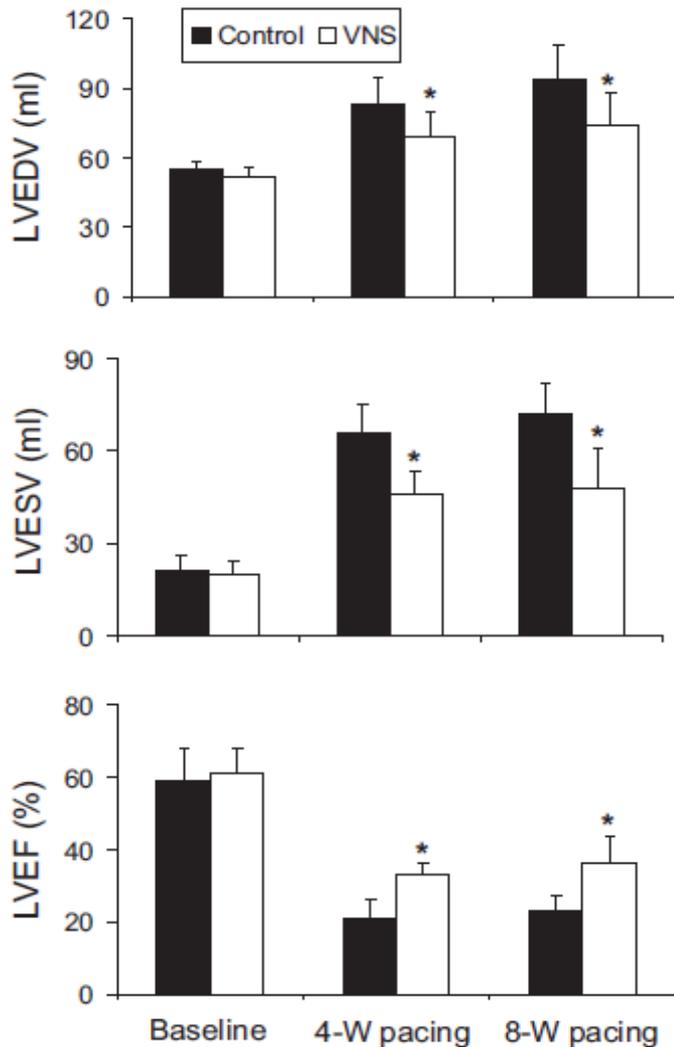
Takuya Kishi (MD, PhD)*





Vagal stimulation therapy achieved a 73% reduction in a relative risk ratio of death.

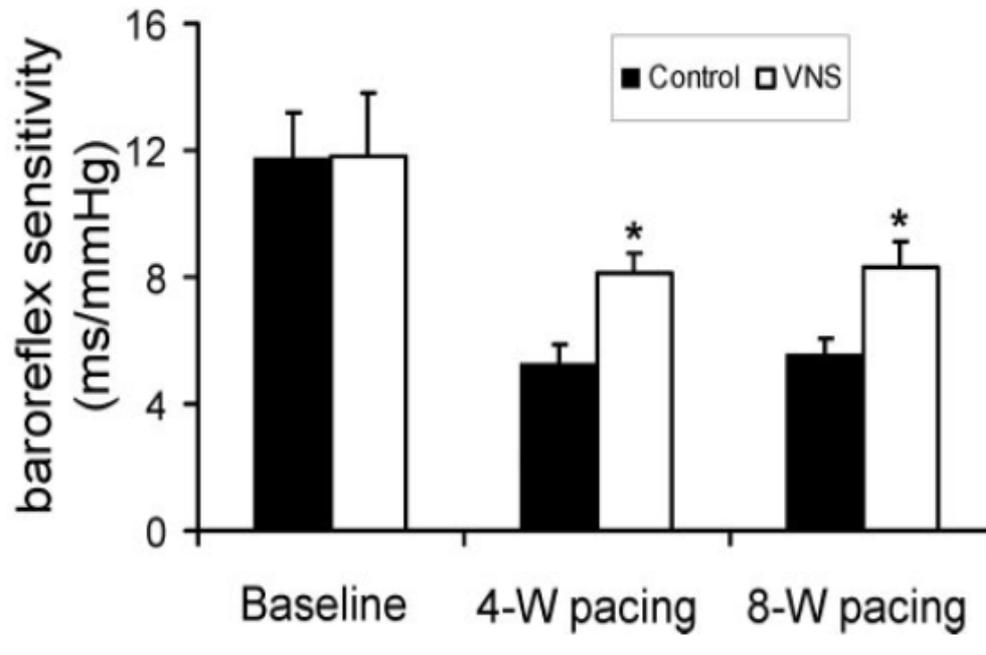
VNS in HF Canine High Rate Pacing Model



Adapted from Zhang Y, Circ Heart Fail 2009; 2:692-699

VNS in HF Canine High Rate Pacing Model

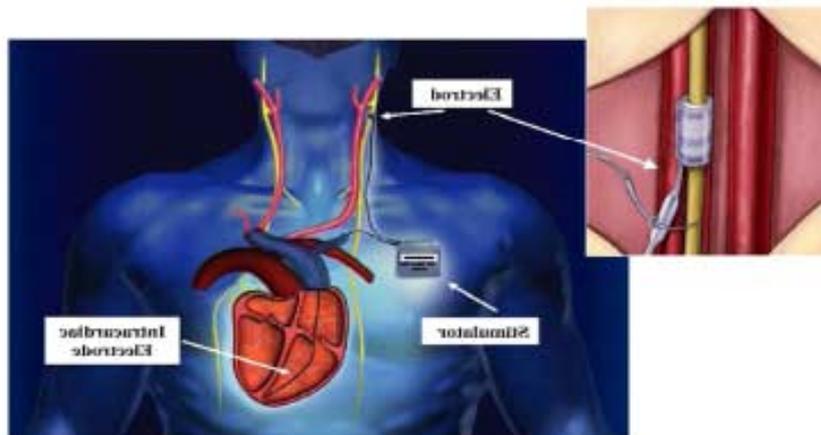
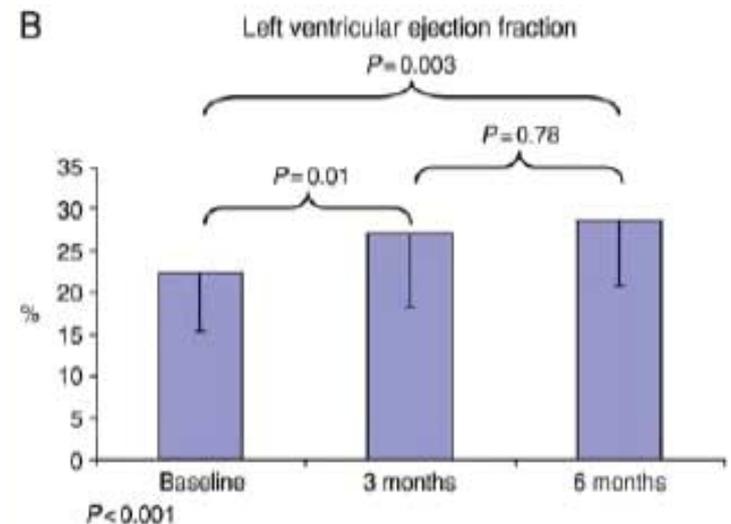
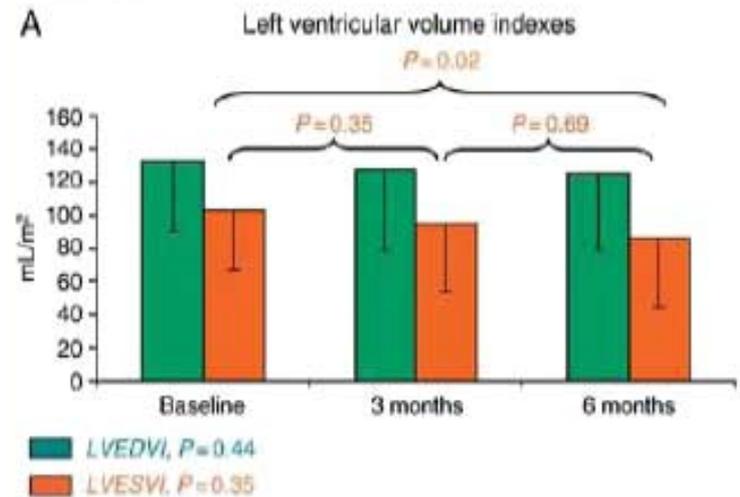
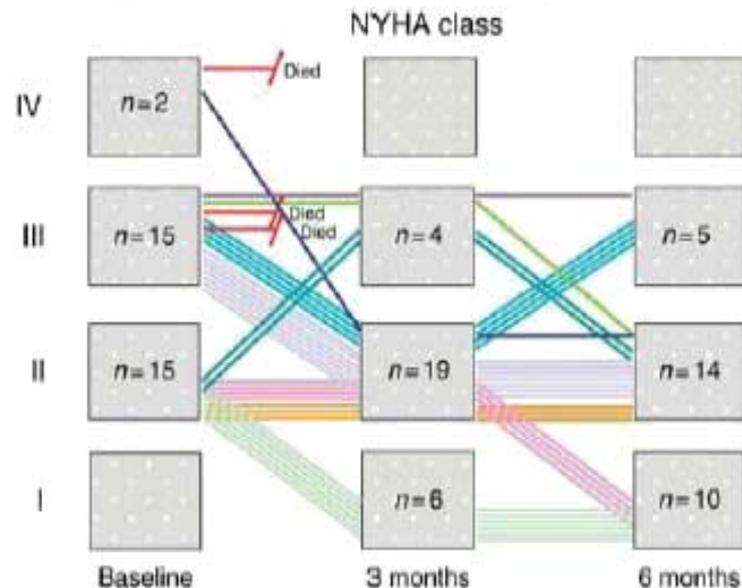
	Baseline		4-wk Pacing		8-wk Pacing	
	Control	VNS	Control	VNS	Control	VNS
RR, ms	510.7±77.0	514.5±61.5	394.8±36.7	428.8±55.7	407.1±47.2	451.0±76.1
SDNN, ms	84.2±21.7	86.6±21.8	23.2±5.9	36.6±5.1*	28.7±8.0	42.2±7.4*
RMSSD, ms	68.9±10.6	69.3±17.2	17.0±4.6	31.0±6.1*	22.1±5.3	37.2±7.1*
LF, norm	35.2±12.5	36.2±12.3	72.1±8.6	55.6±6.1*	65.3±10.3	53.2±9.6*
HF, norm	64.8±12.5	63.8±12.3	27.9±8.6	44.4±6.1*	34.7±10.3	46.8±9.6*
LF/HF	0.70±0.33	0.63±0.34	3.03±1.79	1.29±0.33*	2.23±1.46	1.22±0.75



Adapted from Zhang Y, Circ Heart Fail 2009; 2:692-699

Chronic vagus nerve stimulation: a new and promising therapeutic approach for chronic heart failure

Gaetano M. De Ferrari^{1*}, Harry J.G.M. Crijns², Martin Borggrefe³, Goran Milasinovic⁴, Jan Smid⁵, Markus Zabel⁶, Antonello Gavazzi⁷, Antonio Sanzo¹, Robert Dennert³, Juergen Kuschyk⁴, Srdjan Raspopovic⁵, Helmut Klein^{6,8}, Karl Swedberg⁹, and Peter J. Schwartz^{1,10,11,12,13}, for the CardioFit Multicenter Trial Investigators



NECTAR-HF Study: Protocol Overview

- **Study Design**

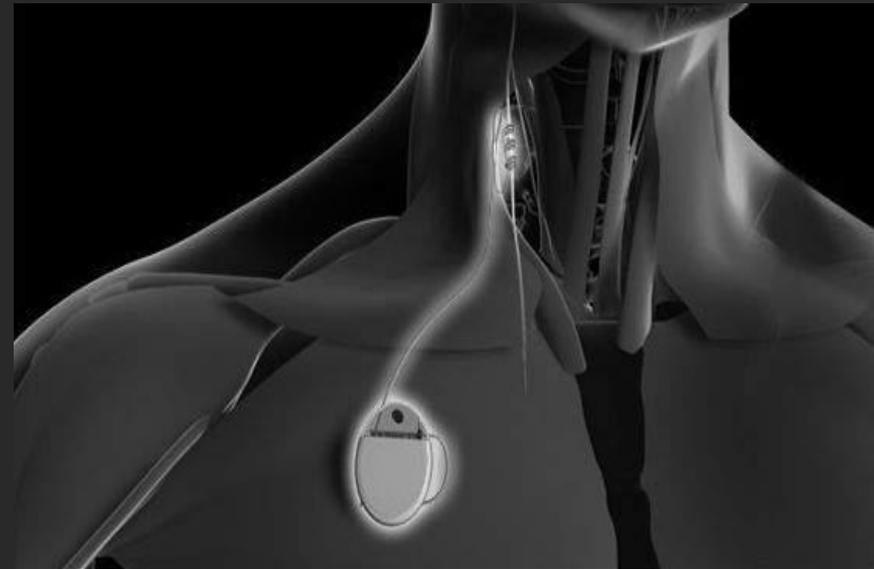
- Single-blind, placebo controlled, randomized 2:1 (therapy/control)
- Multicentre (European sites)
- Control patients crossed over to therapy at 6M follow-up & followed for safety through 18 months

- **Sample Size**

- 250 pts screened for eligibility
- 96 pts implanted with the system

- **Patient Population:**

- NYHA class III HF pts
- Ejection fraction of $\leq 35\%$
- Not CRT candidate, QRS ≤ 130 ms



CRT in Heart Failure: New Frontiers

Summary

- **Increasing Consideration for CRT**
- **Dual-Site LV Pacing during CRT: The V3 Trial**
- **Quadripolar LV Pacing approach: MPP Study**
- **LV Endocardial Pacing: The AISync Study**
- **Vagal Nerve stimulation in HF: Nectar Trial ...**