UNITE DE SOINS ET DE CARDIOLOGIE INTERVENTIONNELLE

NOUVELLES CLINIQUES NANTAISES

Recent Advances in Electrical Therapies

Rythmo Sud

Nice, Oct 2013

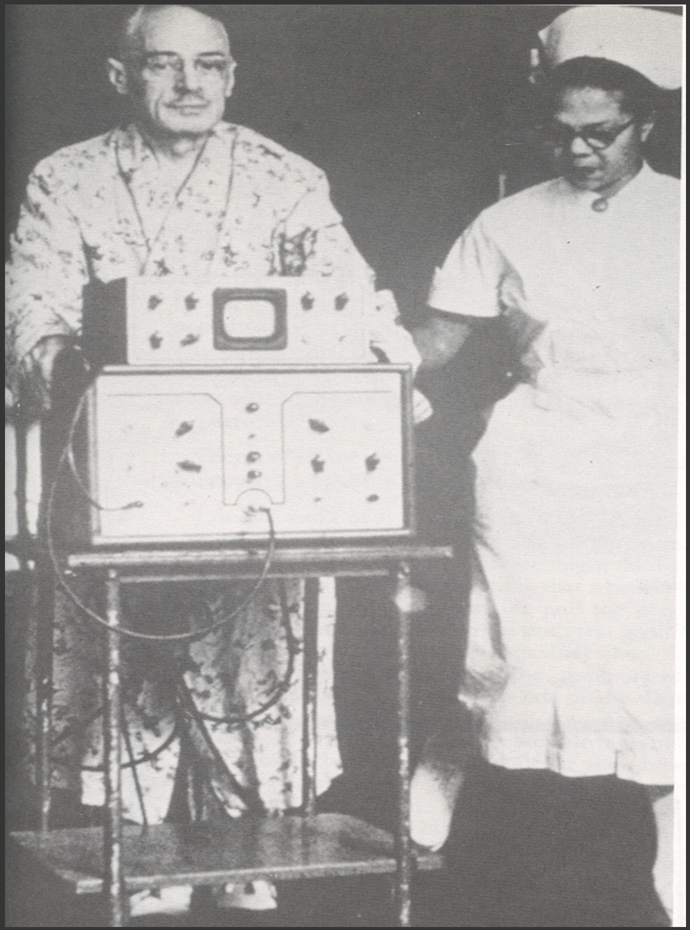
Gras, MD, Nantes, France

Recent Advances in Electrical Therapies

- **Leadless PM: LLP**
- Subcutaneous Lead ICD: S-ICD
- Recent CRT Recommendations
- Multisite, Quadripolar LV Pacing: MSP, 4P-LVP, MPP
- LV Endocardial Pacing: LVEP
- Vagal Nerve stimulation in HF: VNS
- Left Atrial Appendage Occlusion: LAAO

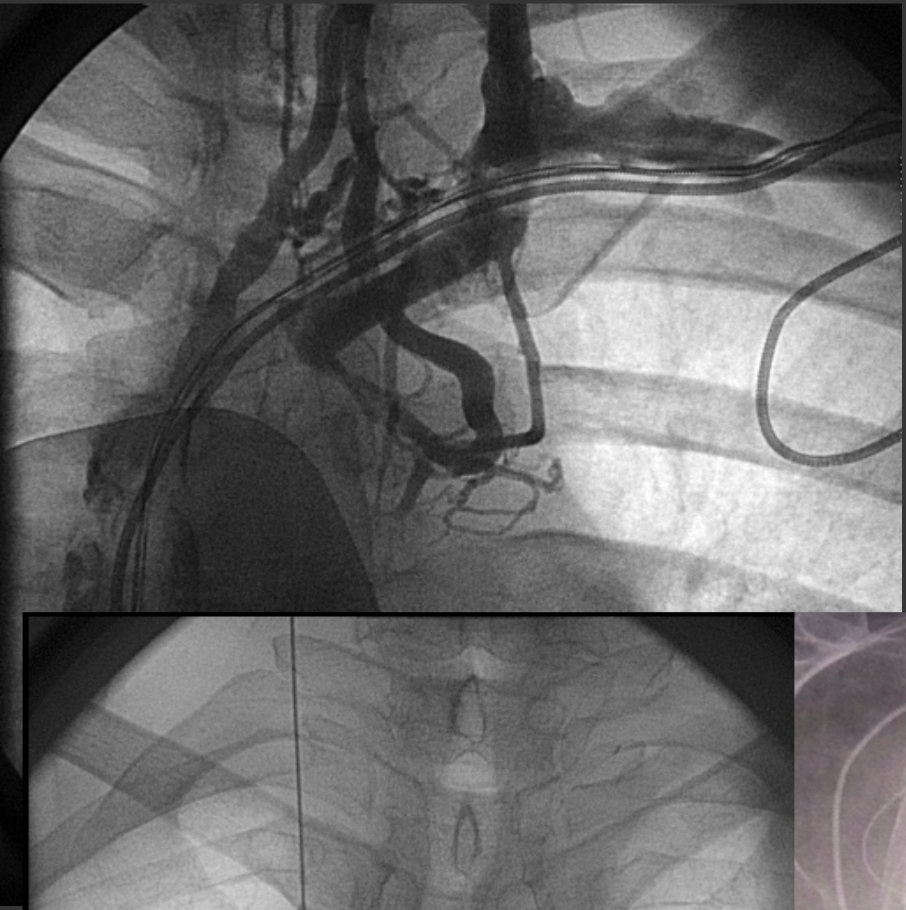
Unmet Needs in Cardiac Pacing & ICD

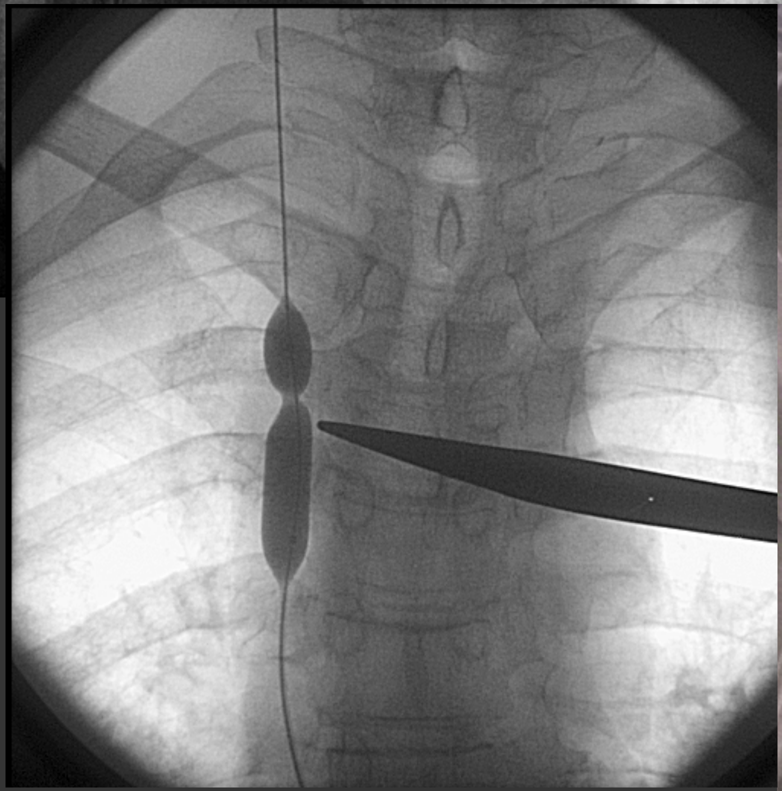
- **Pacing Lead failure**
  - *Up to 21% within 10 years after PM implantation*
- **ICD Lead failure**
  - *Lead replacement is mandatory in 38% within 8 years after ICD implantation*

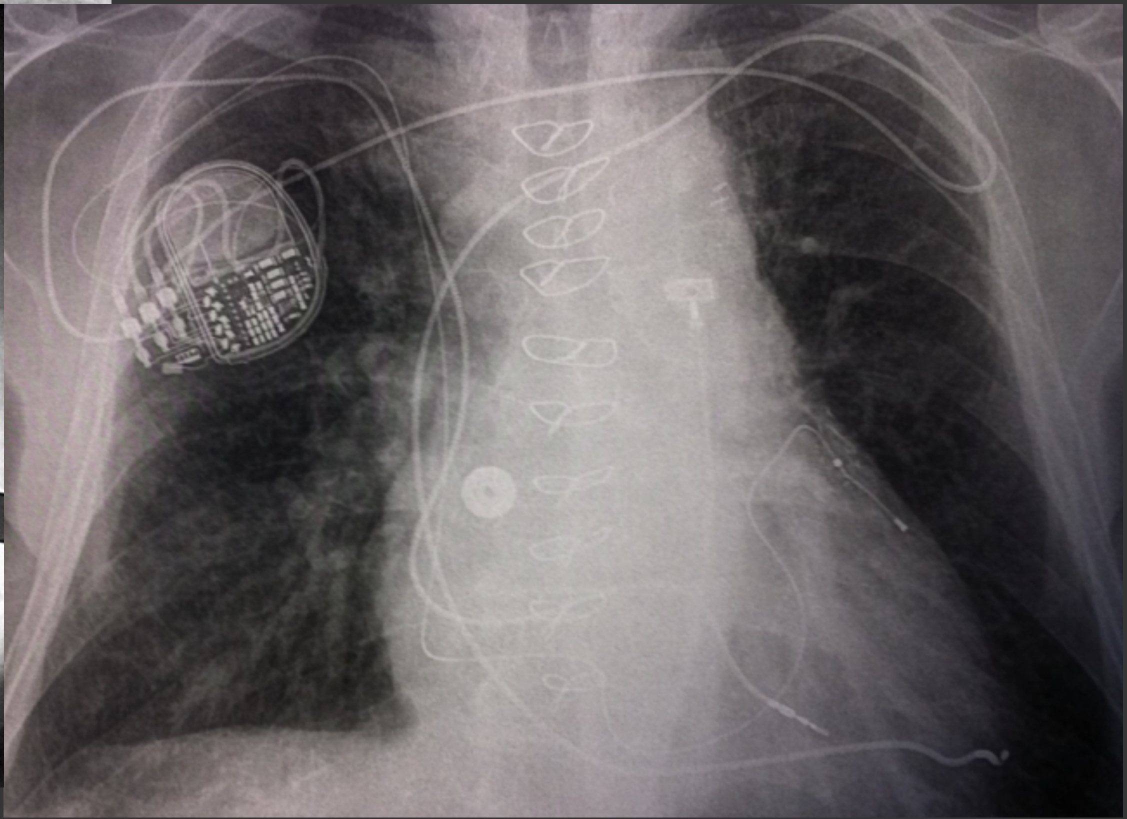


- Lead Fracture & Dislodgement
- Vasculatures and Cardiac Infections
- PNO Hemothorax, Cardiac Perforation
- Tricuspid Valve Injury
- Vascular Thrombosis

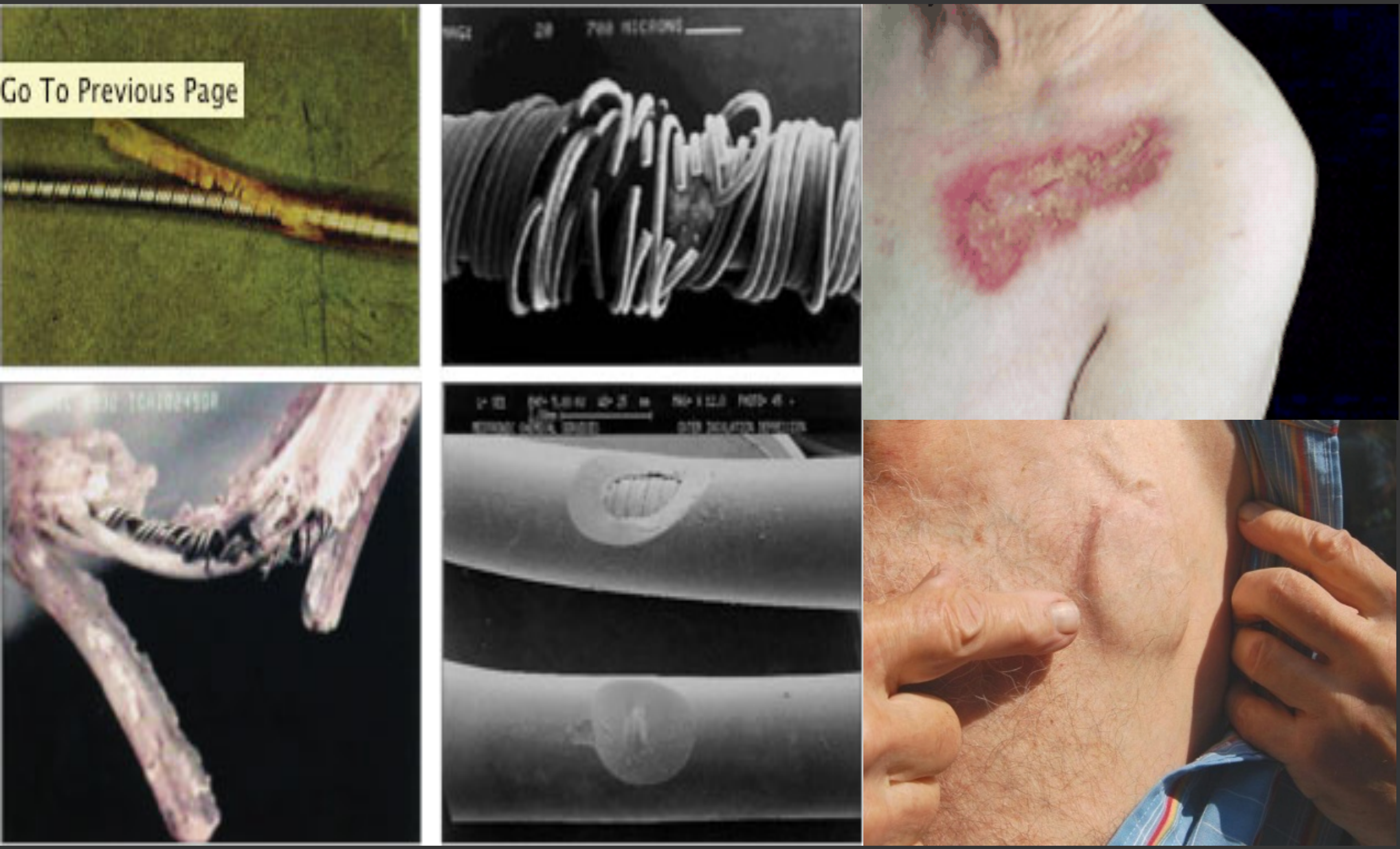
Subclavian Vein/IT Occlusion







PM Lead Issues in Clinical Practice



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J. ELECTROCARDIOLOGY, 3 (3-4) 325-331, 1970

Special Article

Totally Self-Contained Intracardiac Pacemaker*

J. WILLIAM SPICKLER, PH.D., NED S. RASOR, PH.D.†, PAUL KEZDI, M.D.
S. N. MISRA, M.D., K. E. ROBINS, P.E., AND CHARLES LeBOEUF, P.E.

SUMMARY

Recent developments in miniature long-life power sources and electronics, such as nuclear batteries and integrated circuits make feasible a new generation of pacemakers, the intracardiac pacemaker (IC), i.e., a completely self-contained pacemaker implanted inside the right ventricle by transvenous insertion. Since the IC pacemaker eliminates all leads, problems associated with the leads such

circuits have been improved substantia
addition, the development of the endo
catheter electrode has broadened the
of operative procedures to include a
portion of the patient population. Two
problems that still exist with conver
pacemakers are perforation or dislocat
the transvenous electrode and the short
the batteries that are presently used. Ir
tion, there is a certain physical and p
logical discomfort involved

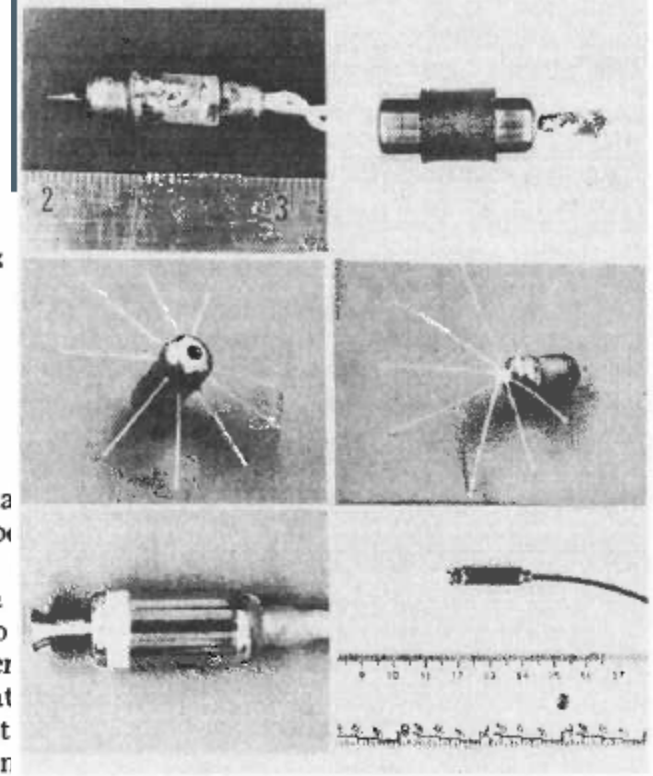


Fig. 2. Some early unsatisfactory dummy capsules

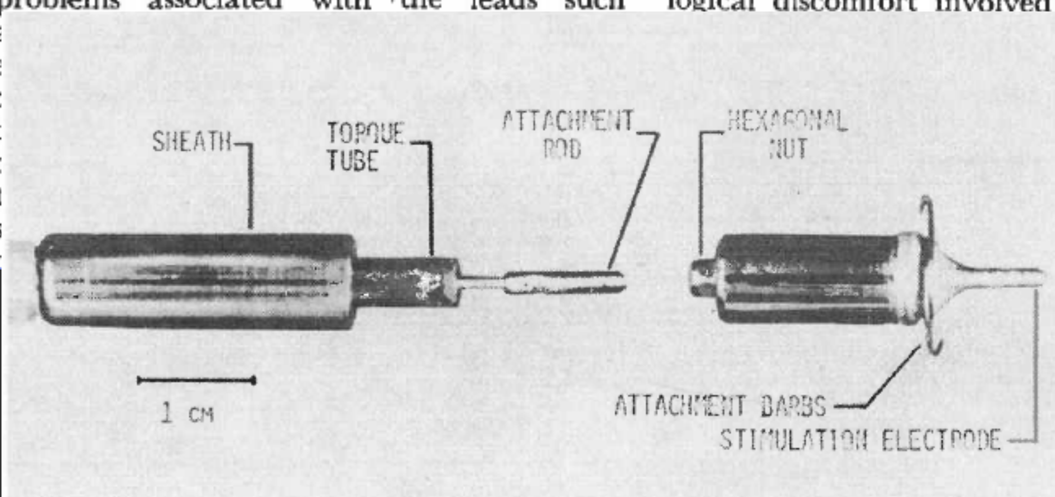


Fig. 4. Intracardiac pacemaker with catheter for transvenous insertion.

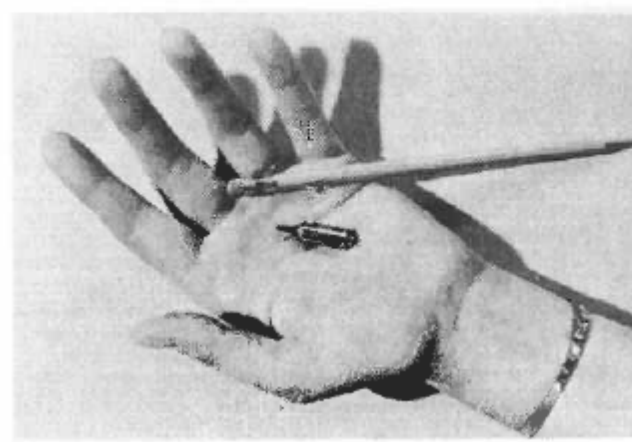
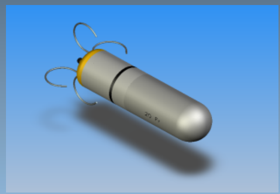


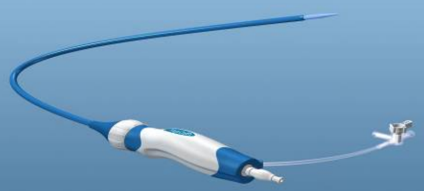
Fig. 8. Nuclear-powered intracardiac pacemaker.

Leadless Pacemaker Potential Benefits and Risks



Miniaturized, Leadless VVIR Pacer

Steerable Sheath/Catheter



Reduced Invasiveness

- *No surgery, Femoral venous access*
- *Less radiation exposure (femoral)*
- *More cosmetic for patient ("invisible")*

Improved Efficiency

- *Fewer complications (no lead or subQ device)*
- *MRI conditional*

More Cost-Effective Therapy

- *Reduced length of hospital stay*
- *Fewer acute and chronic complications*

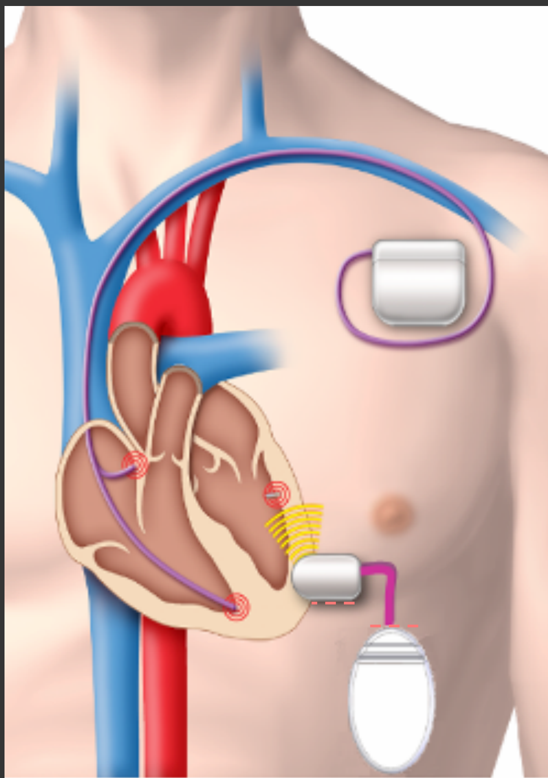
Risks (to be evaluated)

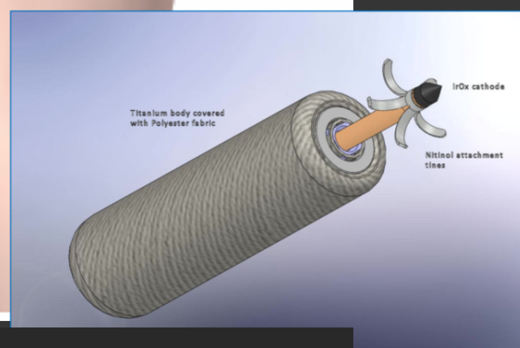
. *Device dislodgement, Migration*

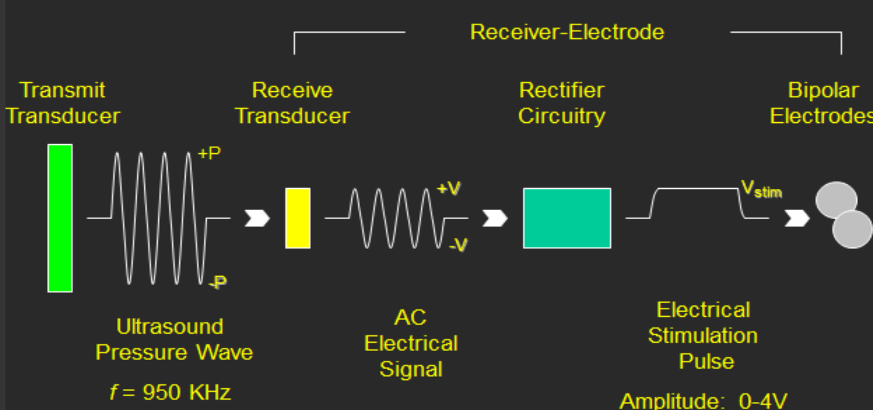
. *AV Dyssynchrony*

. *Explantation ??*

Leadless LV Pacing







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

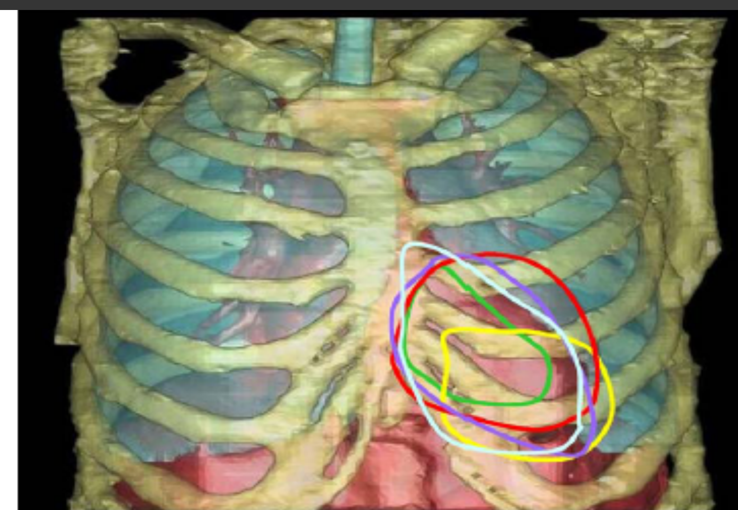


Figure 2 An example of clinically determined acoustic windows in 4 body positions (in red with the patient lying supine; in green with 30° right tilt; in yellow with 30° left tilt; in purple with 30° upright tilt) superimposed on the CT-determined acoustic window (in light blue with the patient lying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

Recent Advances in Electrical Therapies

- Leadless PM: LLP
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- Recent CRT Recommendations
- Multisite, Quadripolar LV Pacing: MSP, 4P-LVP, MPP
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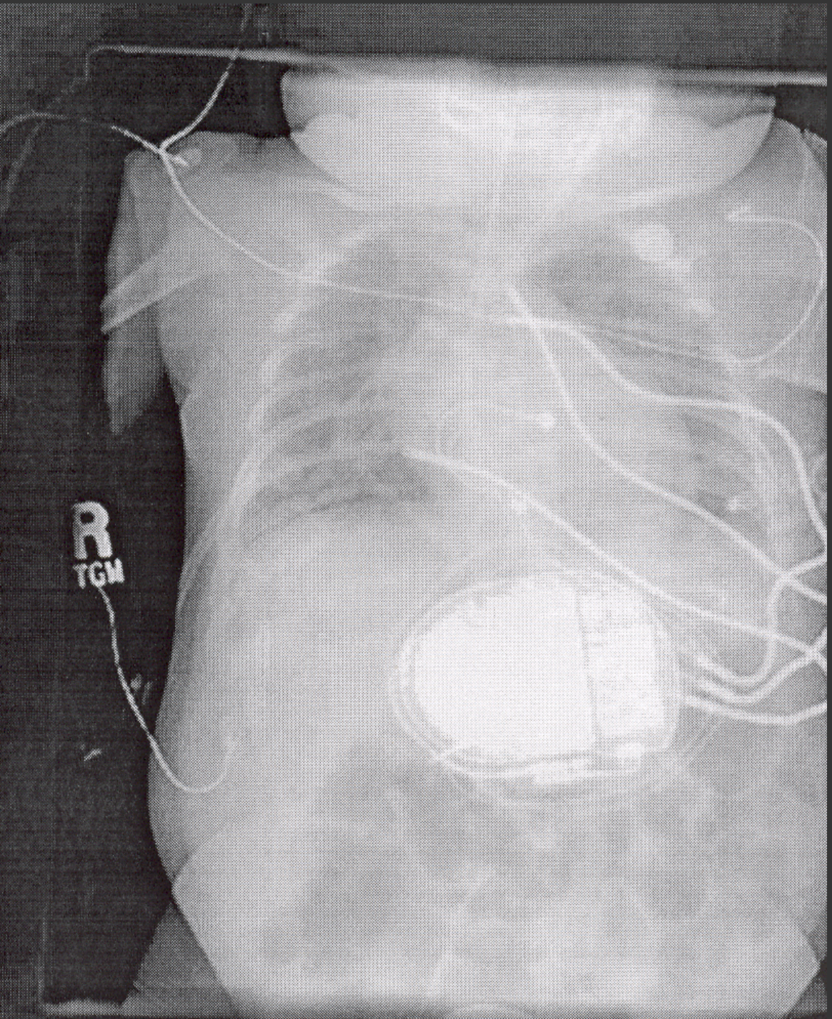
"Minimally Invasive ICD" – Pediatric Case Reports: Children with congenital heart disease

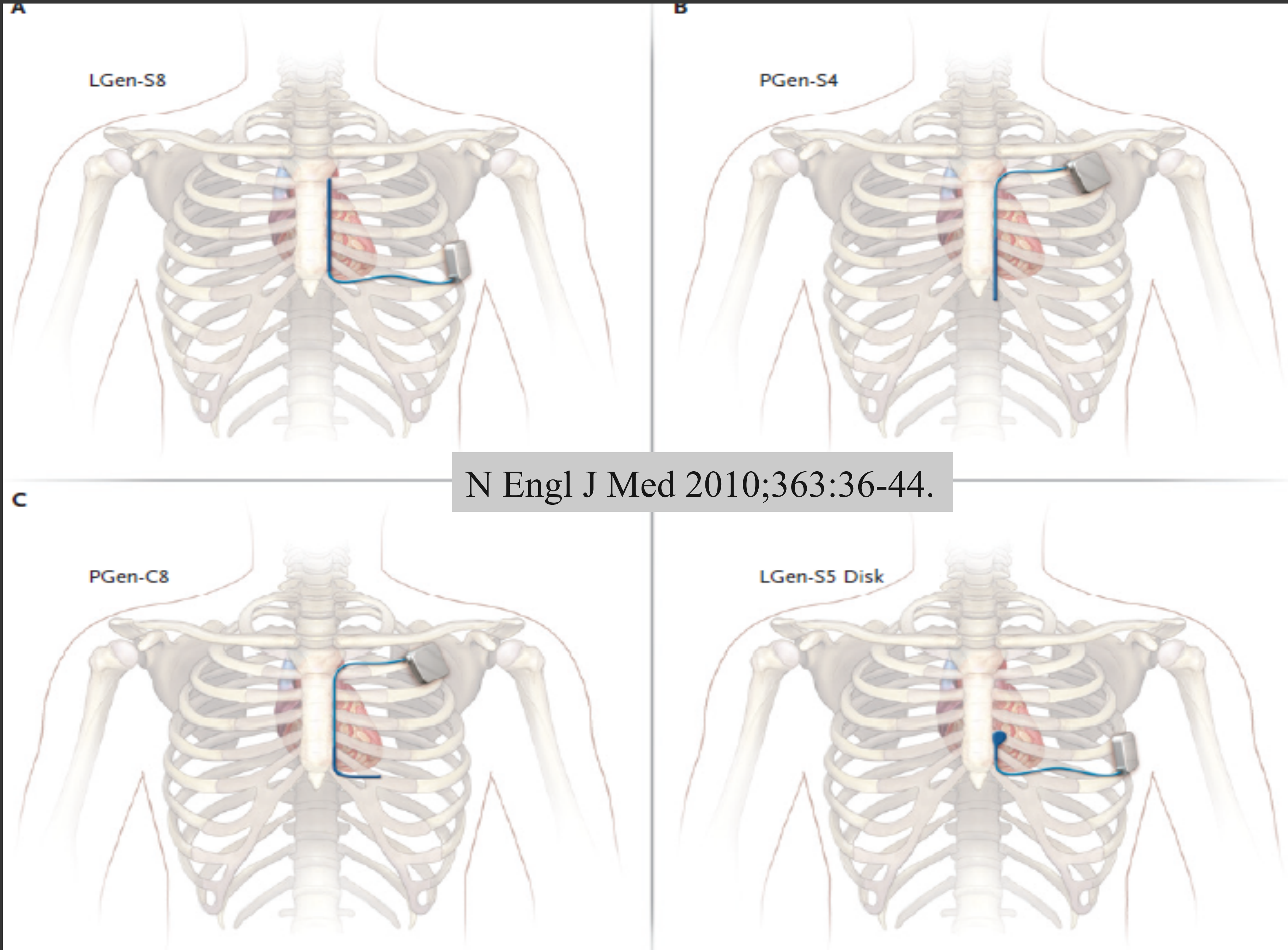


- SQ array around left thorax
- Abdominal active can generator
- Epicardial pace-sense lead

DFT ≤ 14 - 20 joules

Unique challenges of ICD implant in children due to size, growth, & frequent congenital heart disease with increased risk paradoxical embolism

Stephenson J CV EP 2006;17:41-6
Berul PACE 2001;24:1789-4;
Gradaus JCE 2001;12:356-60



N Engl J Med 2010;363:36-44.

S-ICD Implantation Procedure

. Tripolar parasternal electrode is positioned parallel to and 1 to 2 cm to the left of the sternal midline

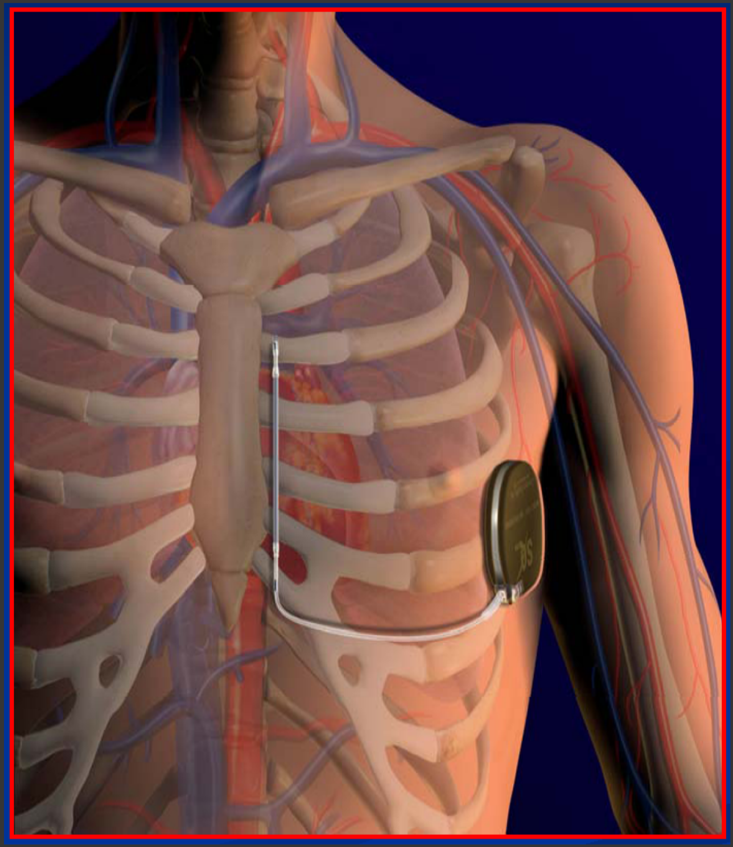
. Distal sensing electrode placed close to the manubriosternal junction

. Proximal sensing electrode placed adjacent to the xiphoid process

. PG is positioned over the sixth rib

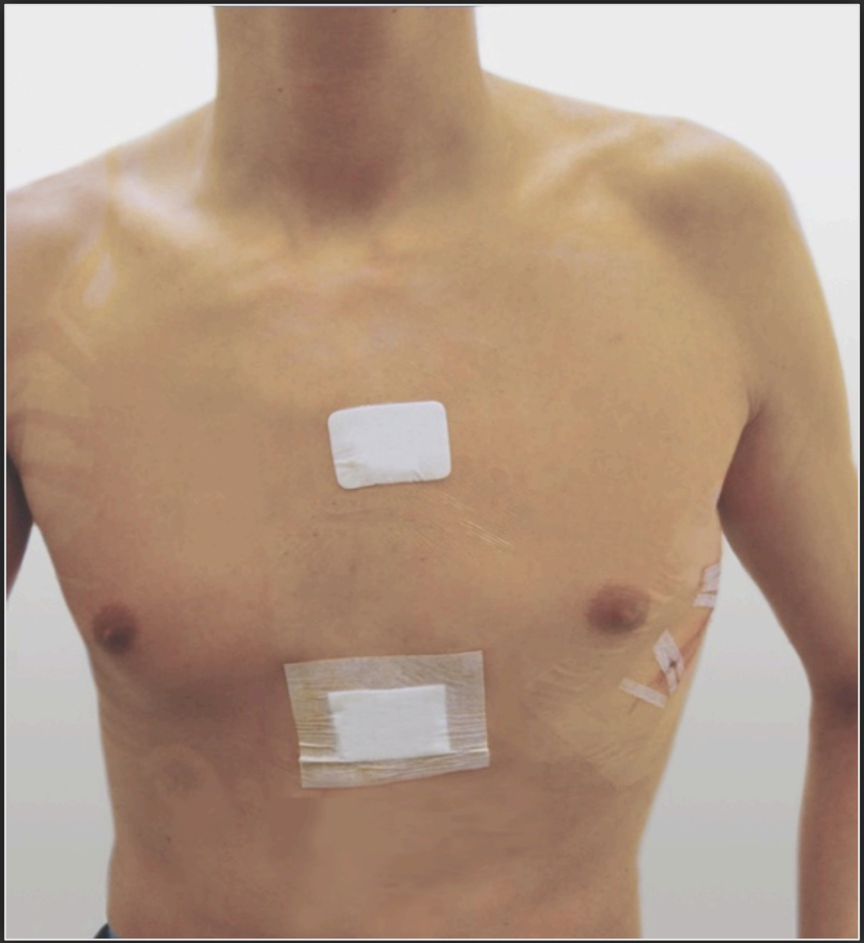
between the midaxillary line and the anterior axillary line.

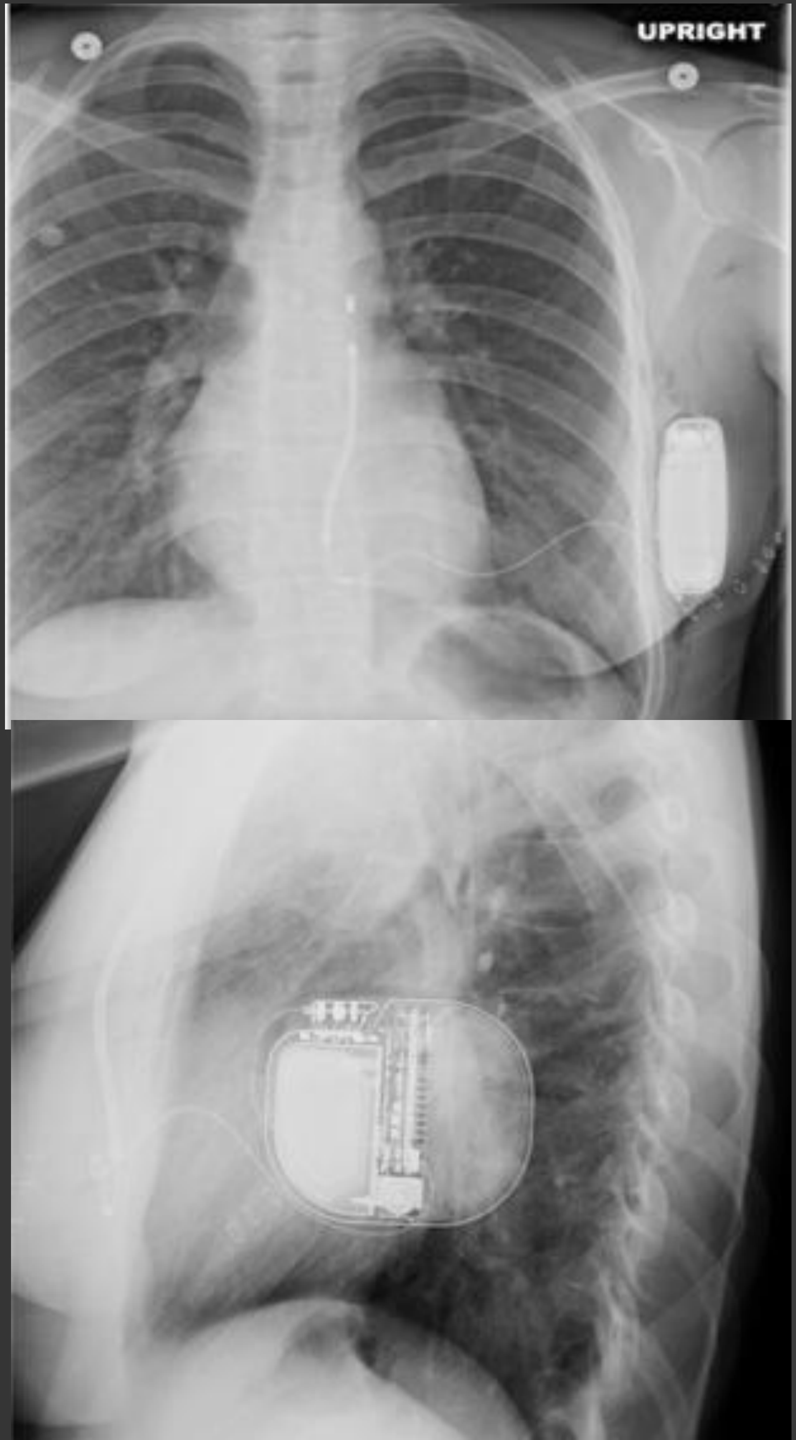
. No fluoroscopy is required



The electrode has an 8-cm shocking coil, flanked by 2 sensing electrodes.

S-ICD Implantation Procedure

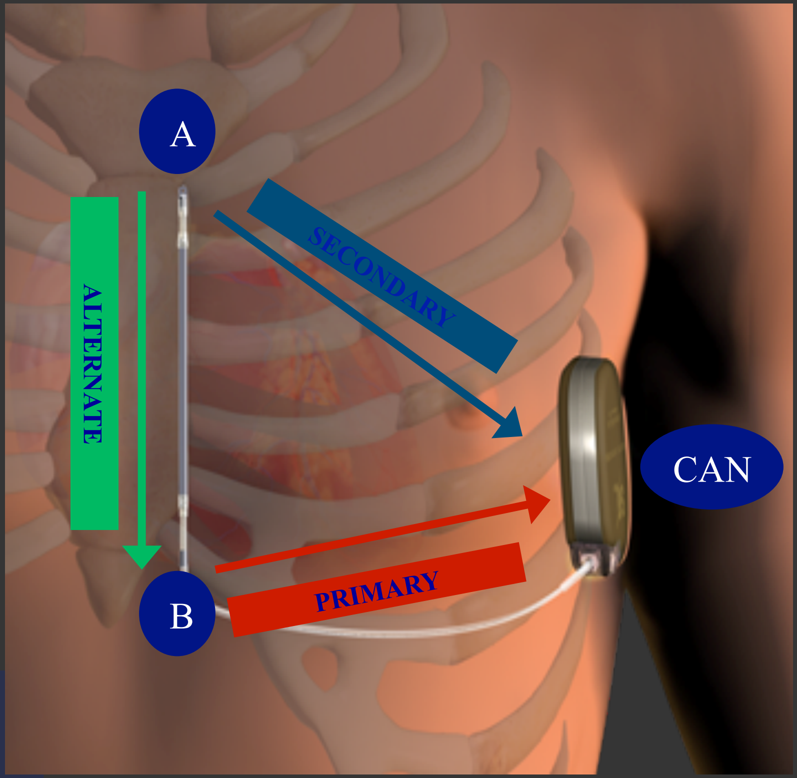




Sensing the Subcutaneous Signal

Automatic Setup Analyzes:

- QRS and T-wave amplitudes
- QRS:T-wave ratios (amplitude and timing)
- Patient posture
- QRS morphology and width



SELECT SENSE CONFIGURATION

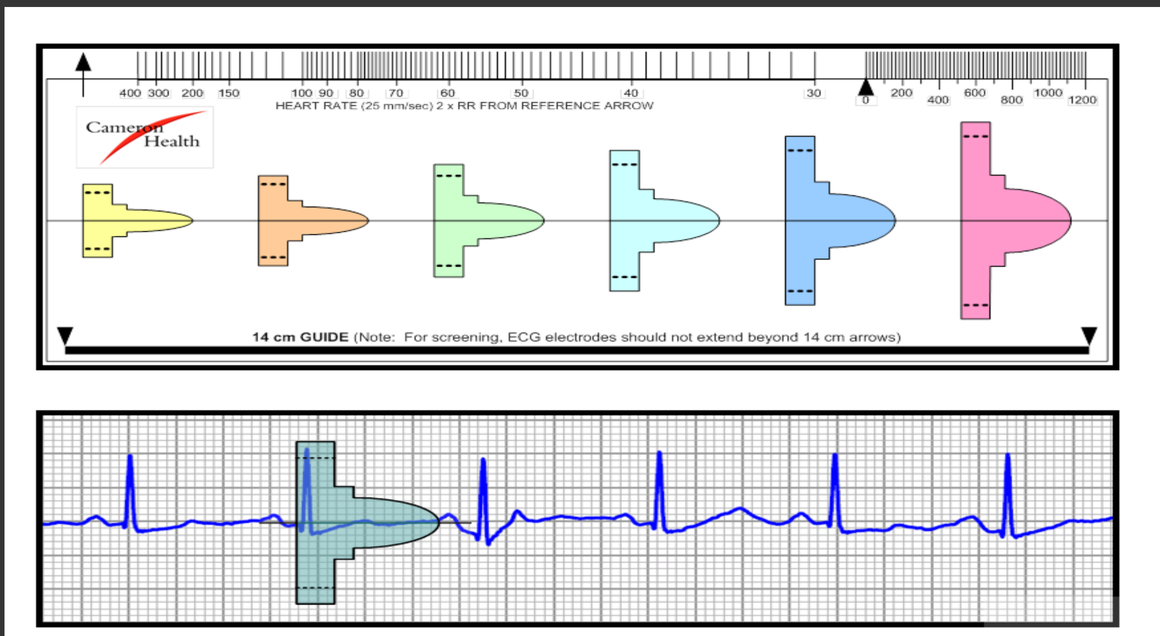
↓

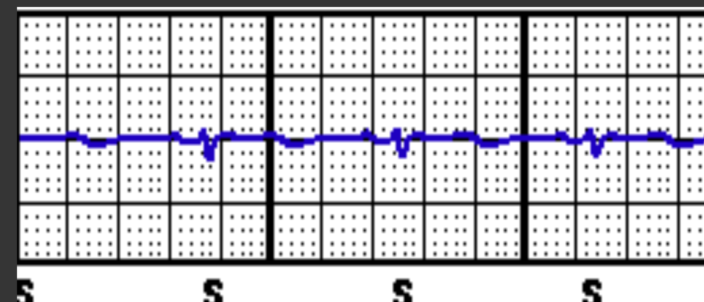
ANALYZE IMPACT OF POSTURE

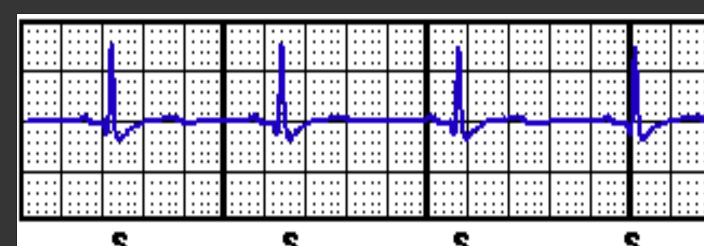
↓

FORM QRS TEMPLATE

Screening prior to and post S-ICD implantation







Variant Patient Posture

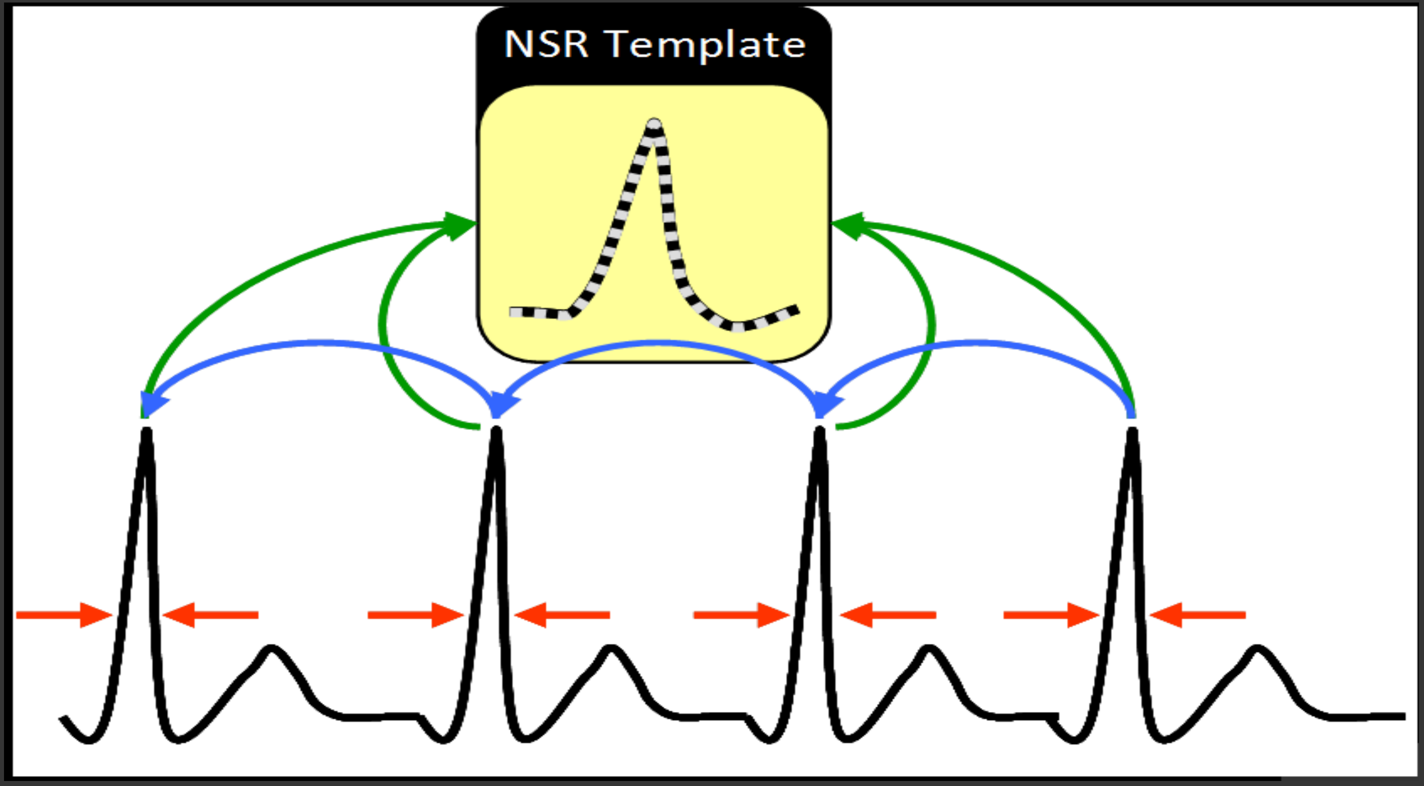
What About Acceptance of S-ICD?

- Inappropriate shocks due to oversensing (80 J output)
- Potential erosion/migration issues (large device 145 g; 58 cc)
- Tunnelling along rib margin and parasternally
- No painless therapies (ATP)
- No bradycardia support
  - ~5-10% of prophylactic ICD pts will develop concomittant bradycardia
  - Aggressive use of BB could exacerbate this condition (HF population)
- No heart failure monitors
- No remote patient follow up

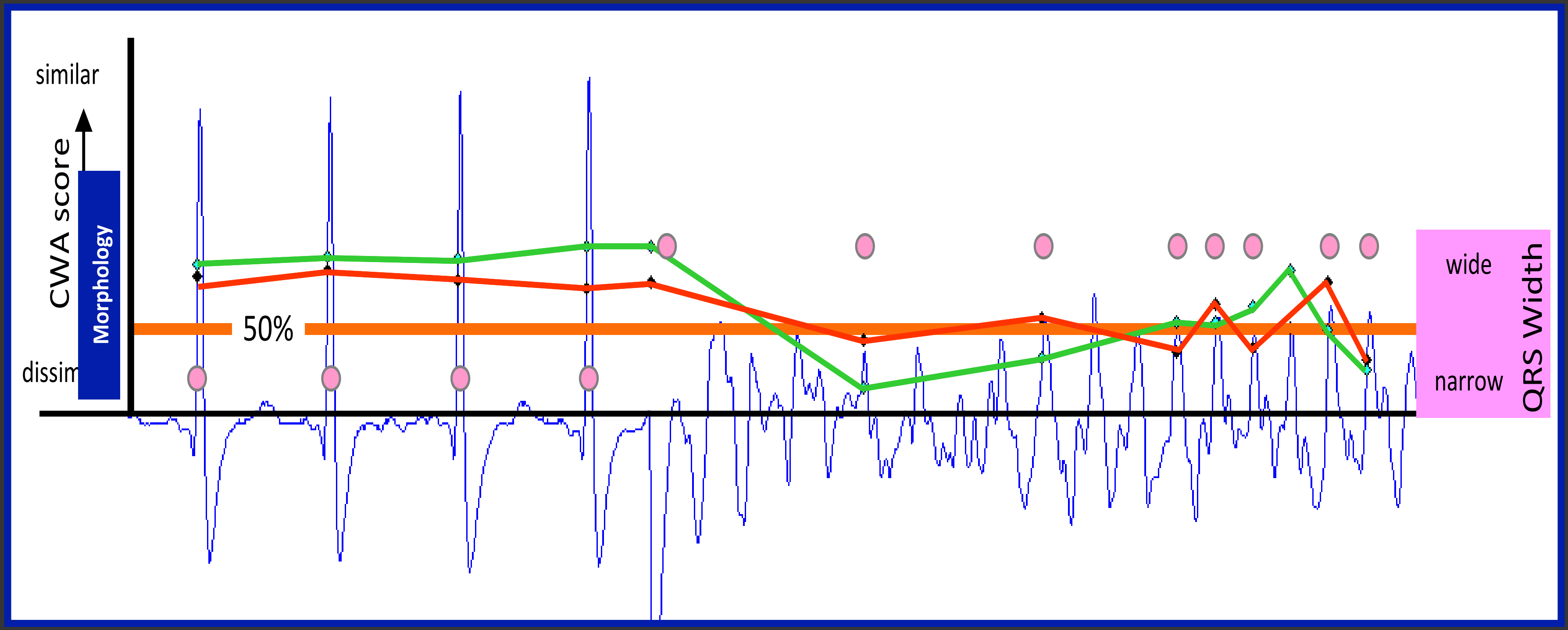
INSIGHT™ Rhythm Discrimination

3 methods to correctly identify & classify the S-ECG rhythm:

1. Static Morphology Analysis
2. Dynamic Morphology Analysis
3. QRS Width Analysis

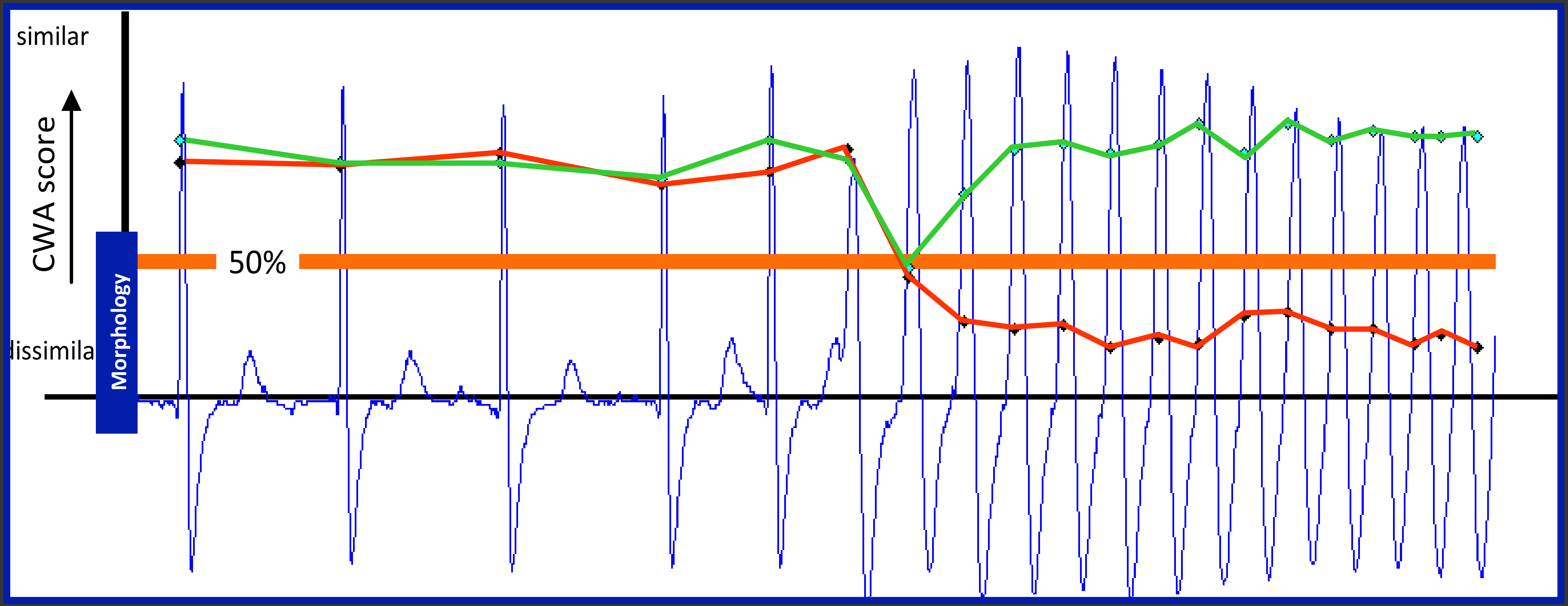


INSIGHT™ Rhythm Discrimination: PVT/VF



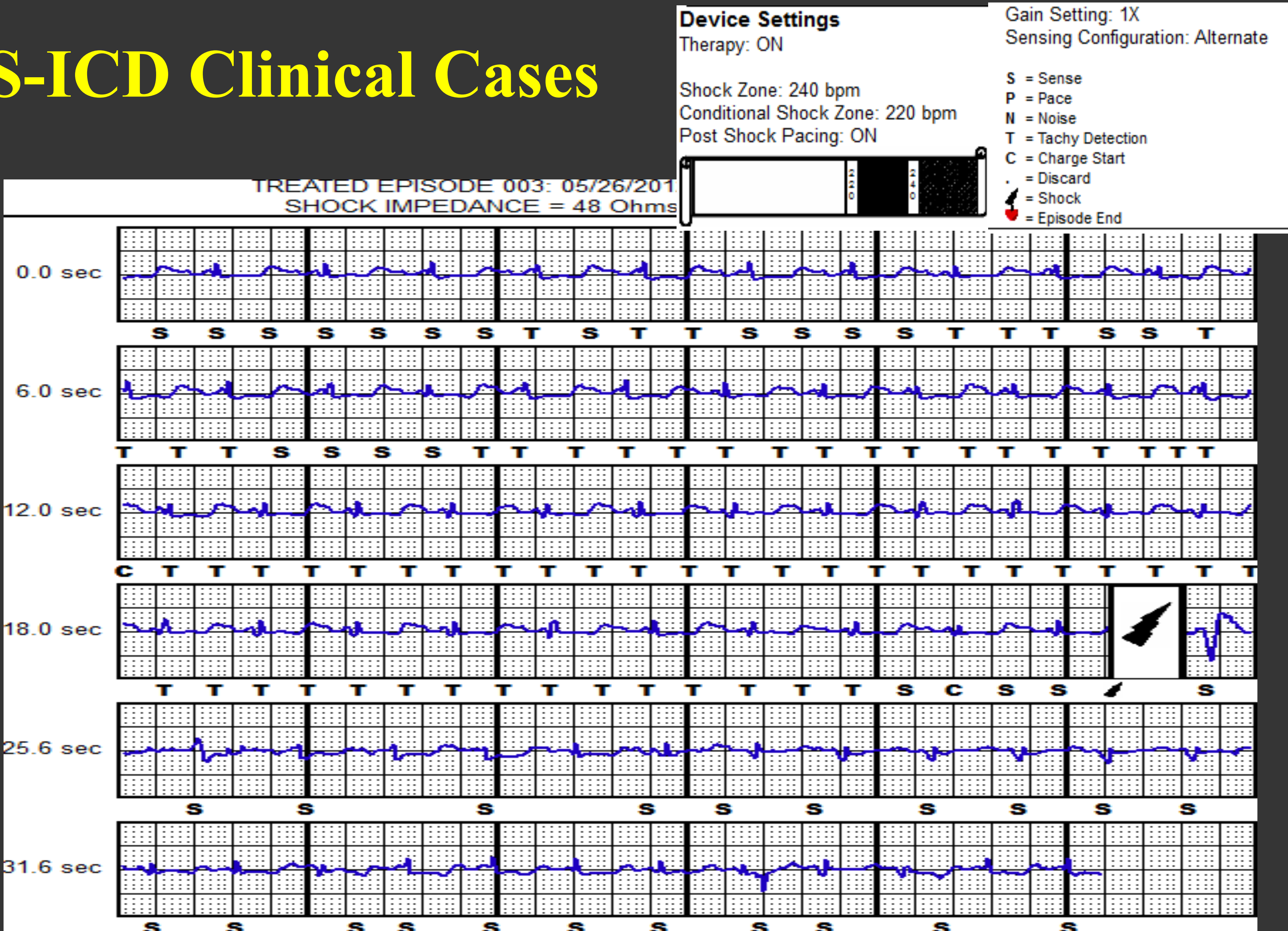
1. Static morphology (red line) and
2. Dynamic morphology (green line) fall during PVT/VF.
3. QRS Width (pink) increases during Vent tachyarrhythmias

INSIGHT™ Rhythm Discrimination: VT



1. Static morphology (red line) drops during VT while
2. Dynamic morphology (green line) remains high due to beat-to-beat similarity.

S-ICD Clinical Cases



Inappropriate shocks due to T wave oversensing

The Entirely Subcutaneous Implantable Cardioverter-Defibrillator

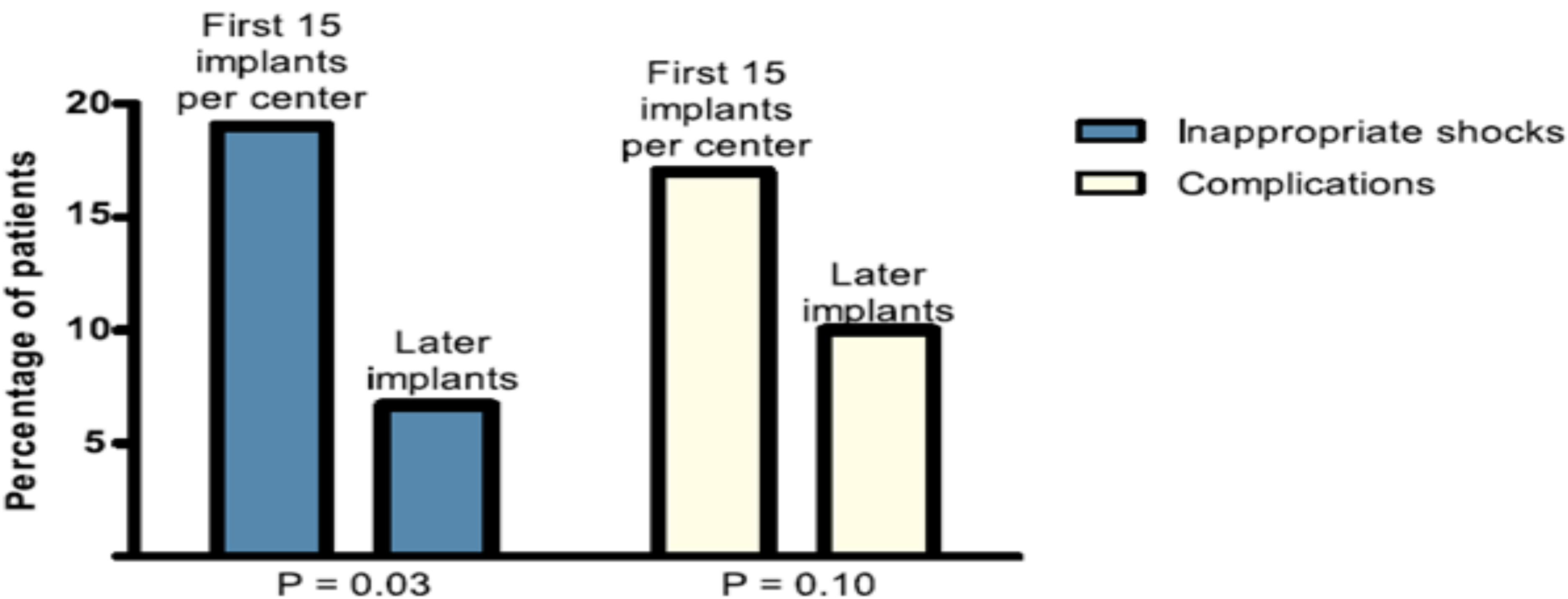
118 patients, FU 18 Months

8 pts: 45 successfull appropriate shocks

15 pts (13%) inappropriate shocks:

T Wave oversensing, myopotentials, double counting, AF

16 (14%) Complications:



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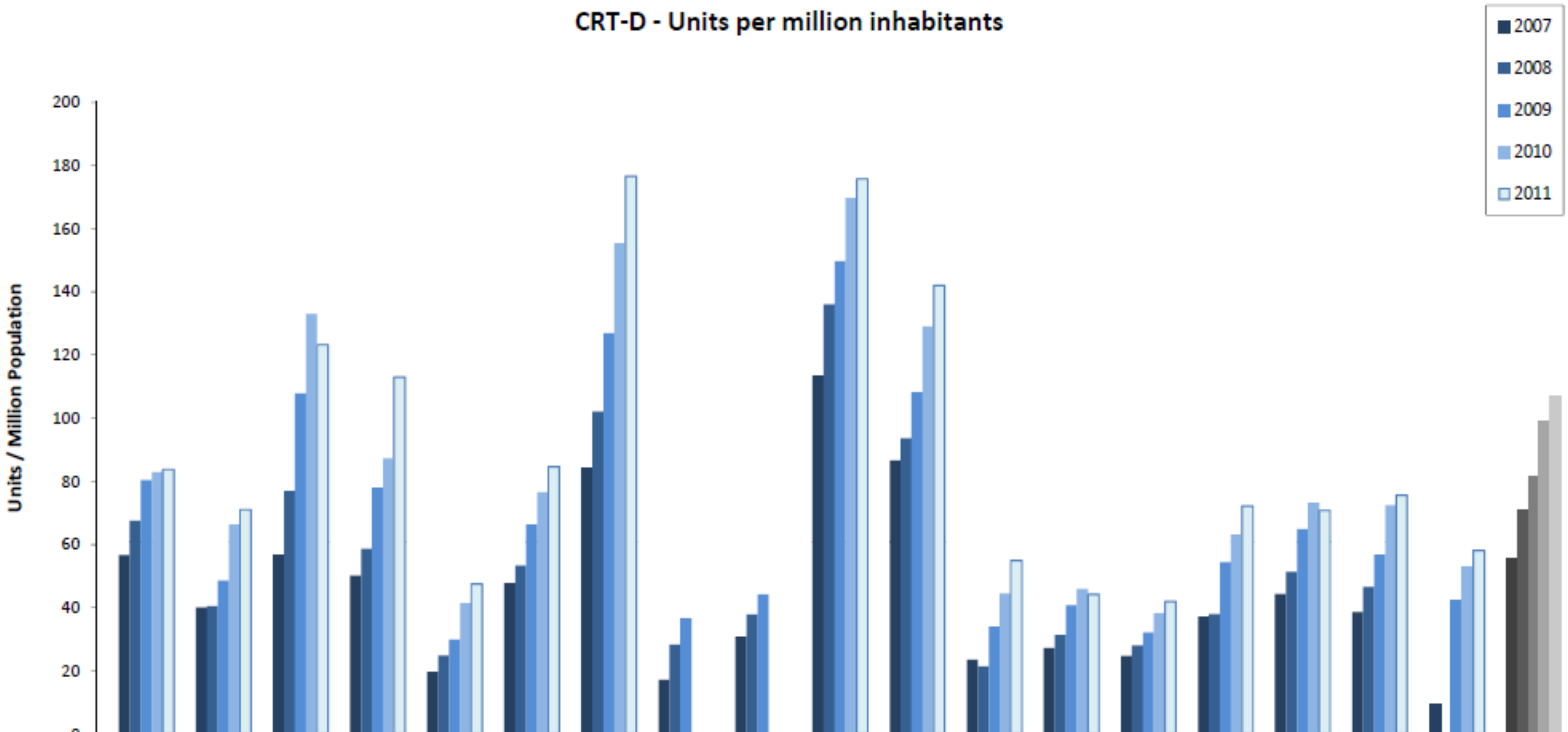
CRT-D - Units per million inhabitants



	Austria	Belgium & Lux	Czech Republic	Denmark	Finland	France	Germany	Greece	Ireland	Italy	Netherlands	Norway	Portugal	Spain	Sweden	Switzerland	United Kingdom	Poland	Europe*
2005	32	27	N/A	32	5	25	55	8	29	73	53	18	18	16	21	29	18	N/A	37
2006	42	29	39	43	13	39	70	12	8	93	72	21	22	19	30	38	34	5	45
2007	57	40	57	50	20	48	84	17	31	114	87	24	27	25	37	44	39	9	56
2008	68	40	77	59	25	53	102	28	38	136	94	21	31	28	38	51	47	N/A	71
2009	80	49	108	78	30	66	127	37	44	150	108	34	41	32	54	65	57	42	81
2010	83	66	133	87	41	77	155	N/A	N/A	170	129	45	46	38	63	73	72	53	99
2011	84	71	123	113	48	85	177	N/A	N/A	176	142	55	44	42	72	71	76	58	107

Source population data: OECD
Units - Eucomed based on reports from major manufacturers
* Europe represents total of listed countries (N/A countries excluded)

European Heart Journal (2013) 34, 2281–2329
doi:10.1093/eurheartj/eht150

ESC GUIDELINES

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

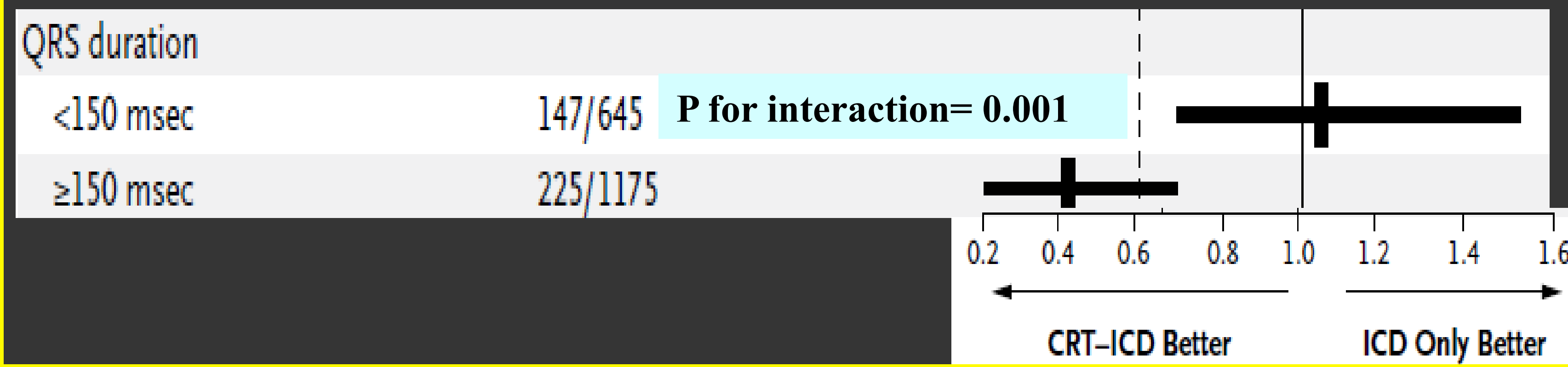
The Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA).

Authors/Task Force Members: Michele Brignole (Chairperson) (Italy)*, Angelo Auricchio (Switzerland), Gonzalo Baron-Esquivias (Spain), Pierre Bordachar (France), Giuseppe Boriani (Italy), Ole-A Breithardt (Germany), John Cleland (UK), Jean-Claude Deharo (France), Victoria Delgado (Netherlands), Perry M. Elliott (UK), Bulent Gorenek (Turkey), Carsten W. Israel (Germany), Christophe Leclercq (France), Cecilia Linde (Sweden), Lluís Mont (Spain), Luigi Padeletti (Italy), Richard Sutton (UK), Panos E. Vardas (Greece)

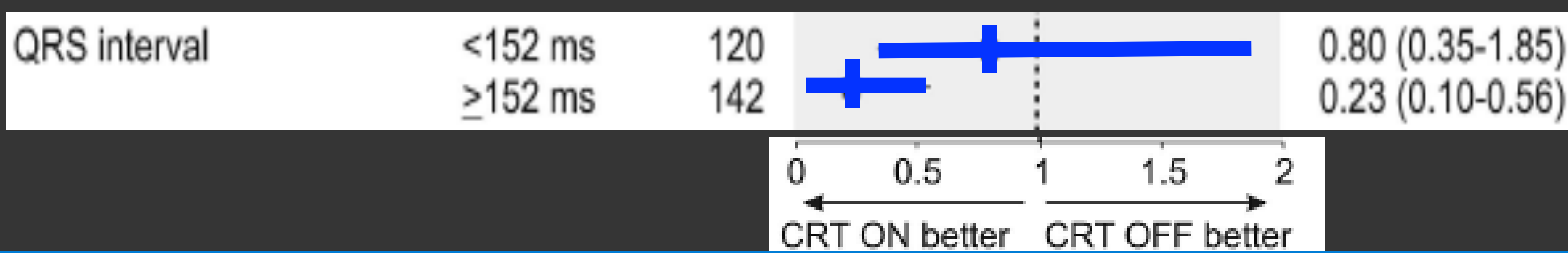
ESC Committee for Practice Guidelines (CPG): Jose Luis Zamorano (Chairperson) (Spain), Stephan Achenbach (Germany), Helmut Baumgartner (Germany), Jeroen J. Bax (Netherlands), Héctor Bueno (Spain), Veronica Dean (France), Christi Deaton (UK), Cetin Erol (Turkey), Robert Fagard (Belgium), Roberto Ferrari (Italy), David Hasdai (Israel), Arno W. Hoes (Netherlands), Paulus Kirchhof (Germany/UK), Juhani Knuuti (Finland), Philippe Kolh (Belgium), Patrizio Lancellotti (Belgium), Ales Linhart (Czech Republic), Petros Nihoyannopoulos (UK), Massimo F. Piepoli (Italy), Piotr Ponikowski (Poland), Per Anton Sirnes (Norway), Juan Luis Tamargo (Spain), Michal Tendera (Poland), Adam Torbicki (Poland), William Wijns (Belgium), Stephan Windecker (Switzerland).

Predictive value of QRS duration in NYHA class I-II patients

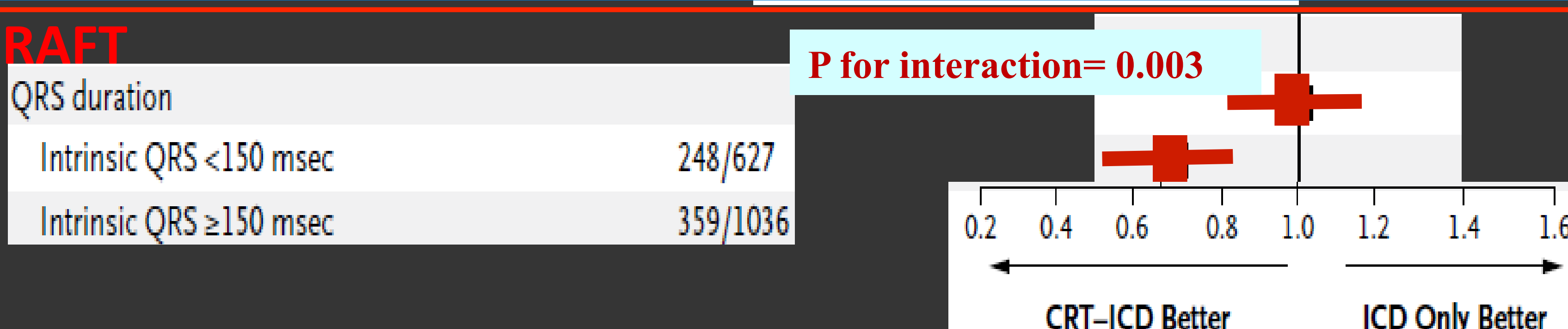
MADIT CRT



REVERSE 24-months



RAFT



Effectiveness of Cardiac Resynchronization Therapy by QRS Morphology in the Multicenter Automatic Defibrillator Implantation Trial Cardiac Resynchronization Therapy (MADIT-CRT)

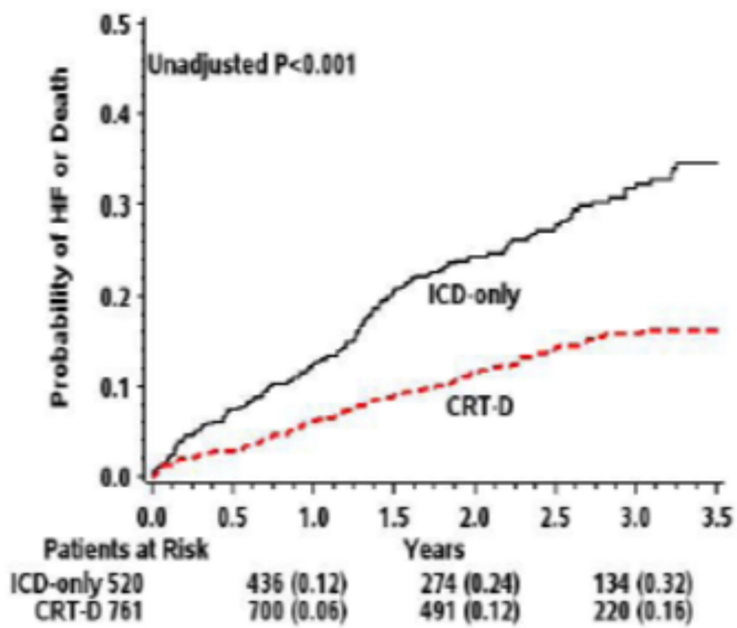
Wojciech Zareba, Helmut Klein, Iwona Cygankiewicz, W. Jackson Hall, Scott McNitt, Mary Brown, David Cannom, James P. Daubert, Michael Eldar, Michael R. Gold, Jeffrey J. Goldberger, Ilan Goldenberg, Edgar Lichstein, Heinz Pitschner, Mayer Rashtian, Scott Solomon, Sami Viskin, Paul Wang, Arthur J. Moss and on behalf of the MADIT-CRT Investigators

Circulation 2011;123;1061-1072; originally published online Feb 28, 2011;

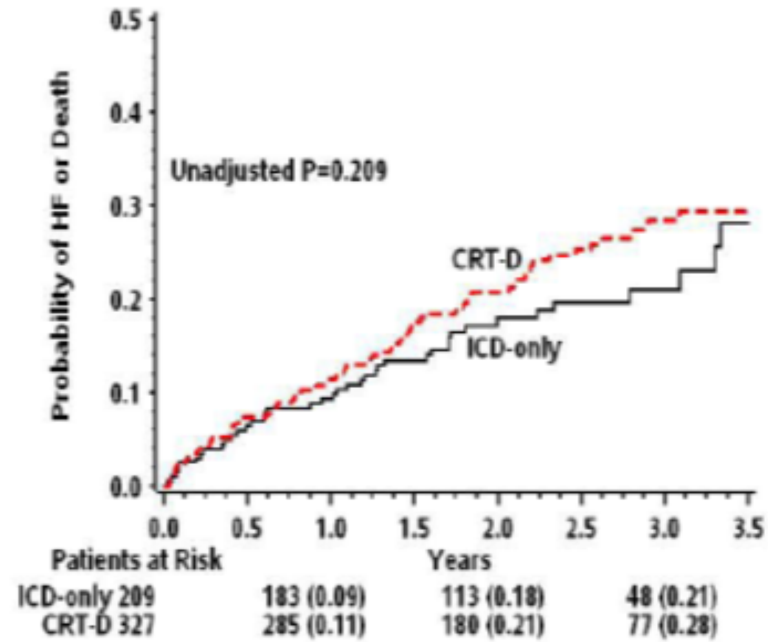
MADIT CRT *Primary endpoint: All-cause death or Heart Failure event*

Predictive value of QRS morphology in NYHA class I-II pts

LBBB

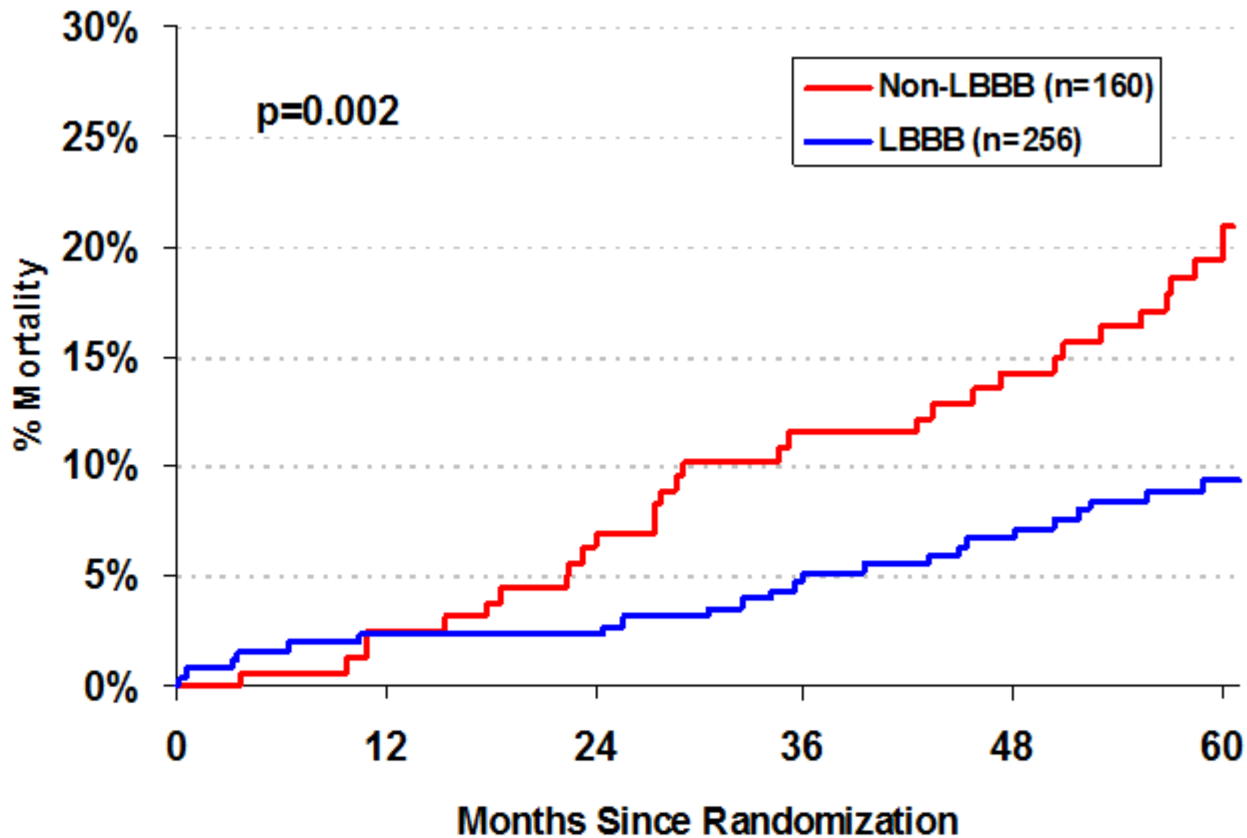


Non-LBBB



W Zareba et Al *Circulation*.2011;123: 1061-1072

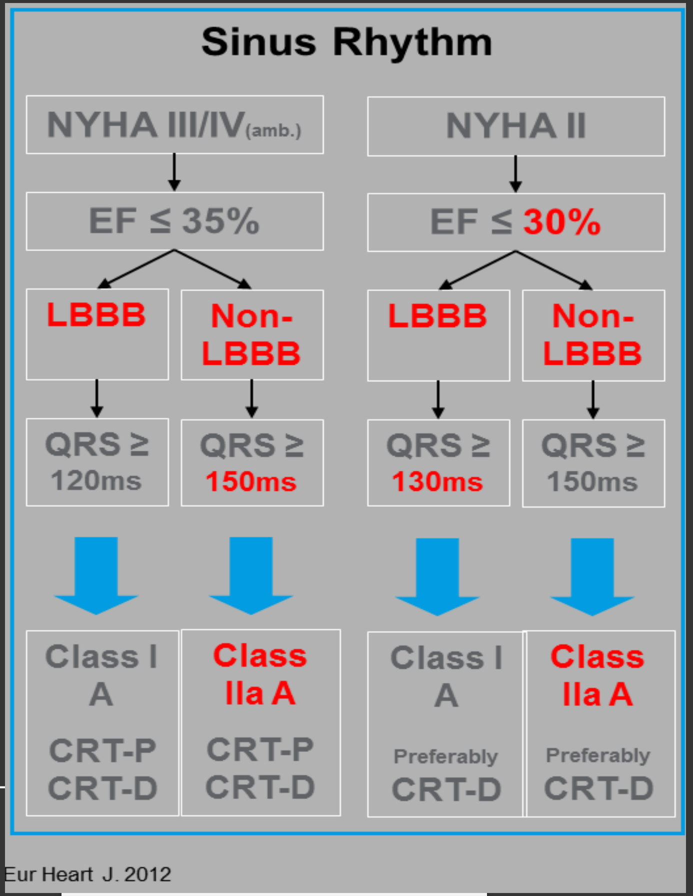
REVERSE 5-years: Mortality by QRS Morphology



C Linde et Al ESC Meeting, Munich 2012

Patients in SR + LBBB

NYHA-II, III et IV (ambulatory), OMT, EF ≤ 35%



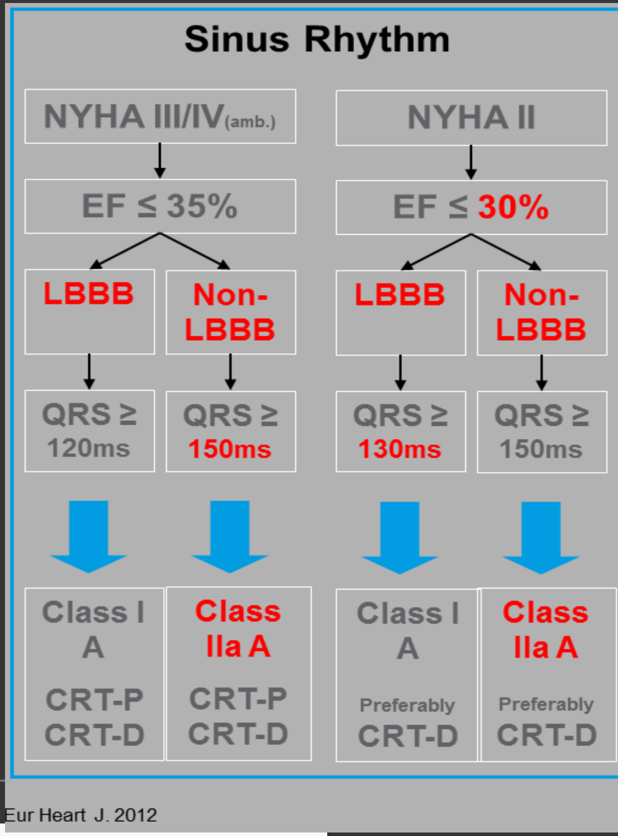
LBBB

- QRS < 120 ms → **No CRT**
- 120 ≤ QRS ≤ 150 ms → **CRT indication, Classe I, Level B**
- QRS > 150 ms → **CRT indication, Classe I, Level A**

ESC Guidelines, European Heart Journal, 2013, vol. 34, pp 2281-2329

Patients in SR + no LBBB

NYHA-II, III et IV (ambulatory), OMT, EF ≤ 35%



No LBBB

- QRS < 120 ms
  - No CRT
- 120 ≤QRS ≤150 ms
  - CRT indication, Classe IIb, Level B
- QRS > 150 ms
  - CRT indication, Classe IIa, Level B

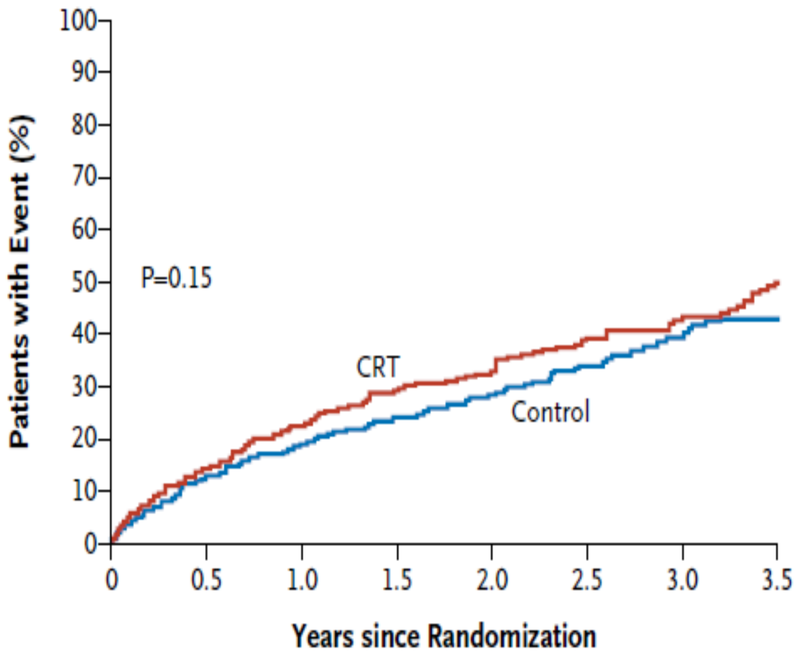
ESC Guidelines, European Heart Journal, 2013, vol. 34, pp 2281-2329

Cardiac-Resynchronization Therapy in Heart Failure with a Narrow QRS Complex

Frank Ruschitzka, M.D., William T. Abraham, M.D., Jagmeet P. Singh, M.D., Ph.D., Jeroen J. Bax, M.D., Ph.D., Jeffrey S. Borer, M.D., Josep Brugada, M.D., Ph.D., Kenneth Dickstein, M.D., Ph.D., Ian Ford, M.D., Ph.D., John Gorcsan III, M.D., Daniel Gras, M.D., Henry Krum, M.B., B.S., Ph.D., Peter Sogaard, M.D., D.M.Sc., and Johannes Holzmeister, M.D., for the EchoCRT Study Group*

The NEW ENGLAND JOURNAL *of* MEDICINE

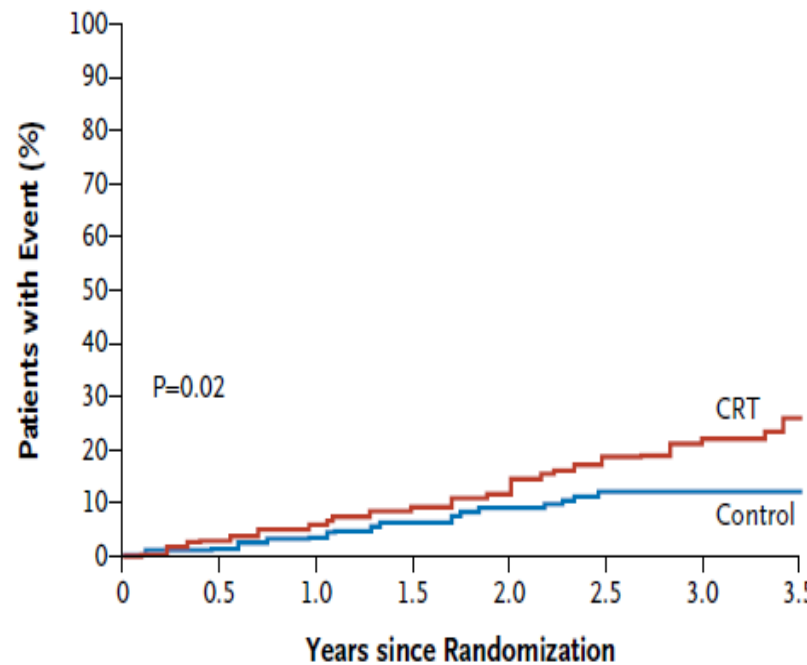
A Primary Composite Outcome



No. at Risk

CRT	404	297	223	155	103	65	42	19
Control	405	302	236	166	119	71	44	15

B Death from Any Cause



No. at Risk

CRT	404	334	267	199	132	84	56	25
Control	405	335	269	195	141	87	62	27

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

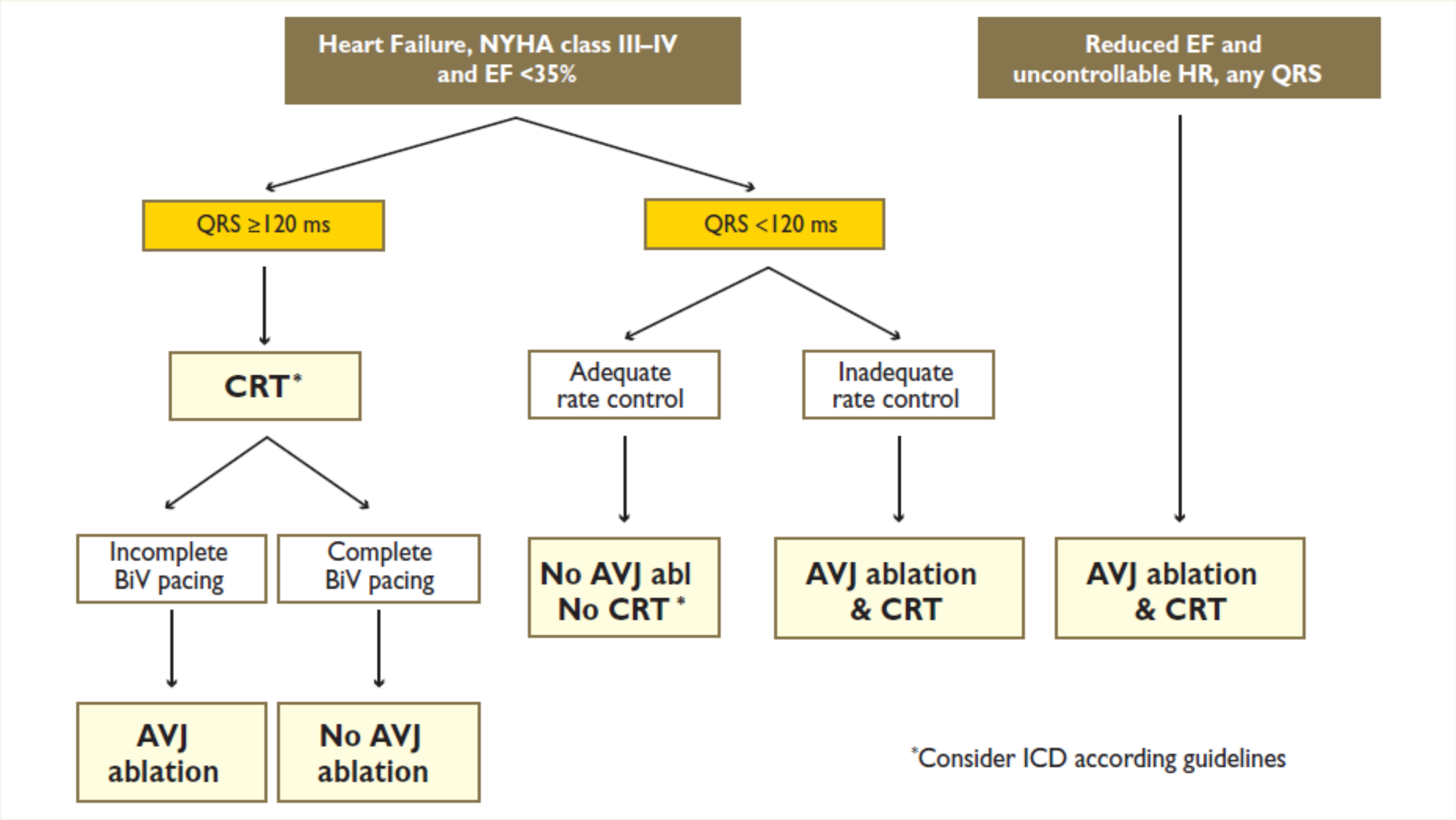


Figure 10 Indication for atrioventricular junction (AVJ) ablation in patients with symptomatic permanent atrial fibrillation (AF) and optimal pharmacological therapy. BiV = biventricular; CRT = cardiac resynchronization therapy; EF = ejection fraction; HR = heart rate; ICD = implantable cardioverter defibrillator; NYHA = New York Heart Association.

HF Patients with conventional indication for Cardiac Pacing

Upgrade from conventional PM or ICD

Indicated in case of
- EF < 35%, OMT
- classe NYHA-III- IV (ambulatory)
- High % of VP

Classe I, Level B

De Novo CRT

Indicated in case of:
- Reduced EF (<50%)
- Expected high % of VP

Classe IIa, Level B

Need for Pacing

NYHA III/IV	NYHA II
EF ≤ 35%	EF≤35%
any QRS	any QRS
Class IIa C CRT-P CRT-D	Class IIb C CRT-P CRT-D

ESC Guidelines, European Heart Journal, 2013, vol. 34, pp 2281-2329

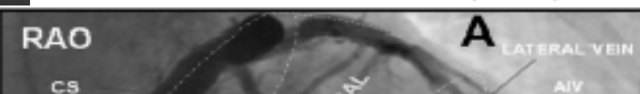
Choice of pacing mode (and cardiac resynchronization therapy optimization)

Recommendations	Class [a]	Level [b]	Ref. [c]
1) The goal of CRT should be to achieve BiV pacing as close to 100% as possible since the survival benefit and reduction in hospitalization are strongly associated with an increasing percentage of BiV pacing.	IIa	B	67–69
2) Apical position of the LV lead should be avoided when possible.	IIa	B	70–72
3) LV lead placement may be targeted at the latest activated LV segment.	IIb	B	73

ESC Guidelines, European Heart Journal, 2013, vol. 34, pp 2281-2329

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



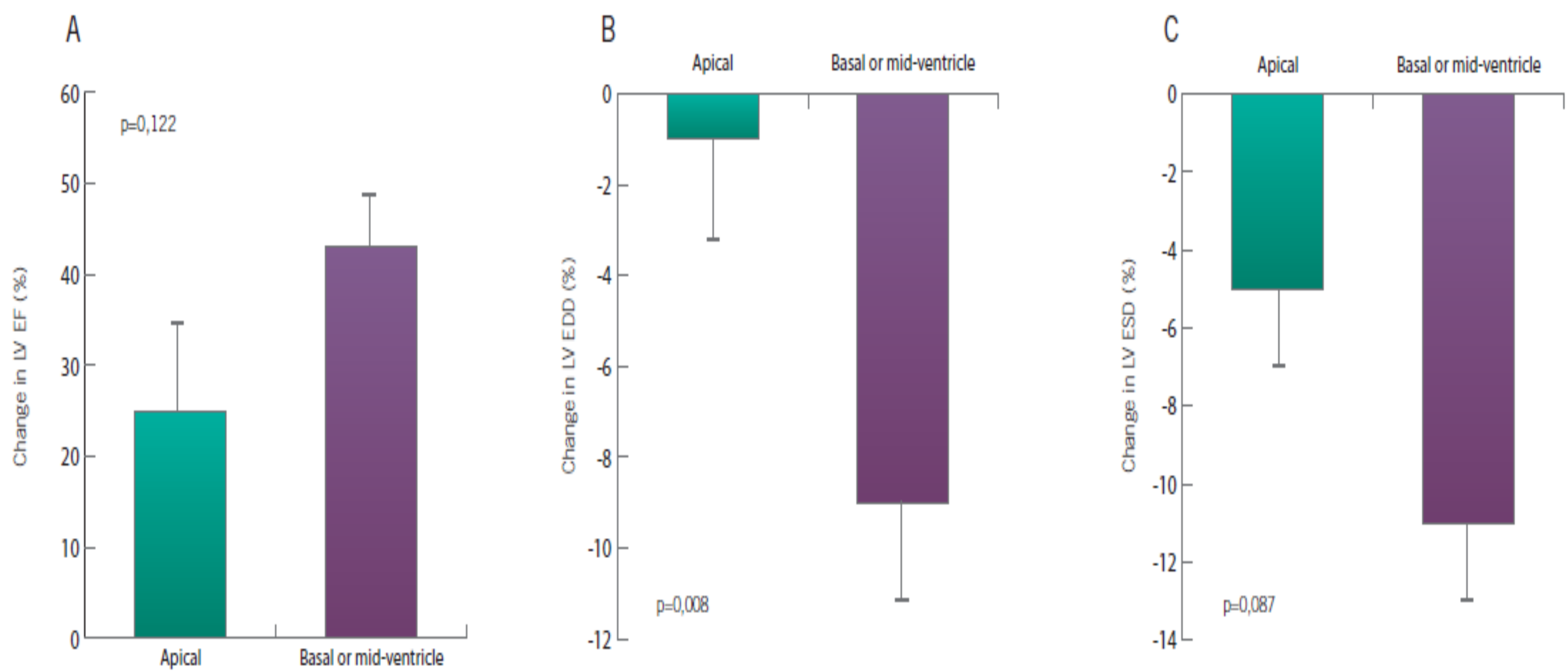
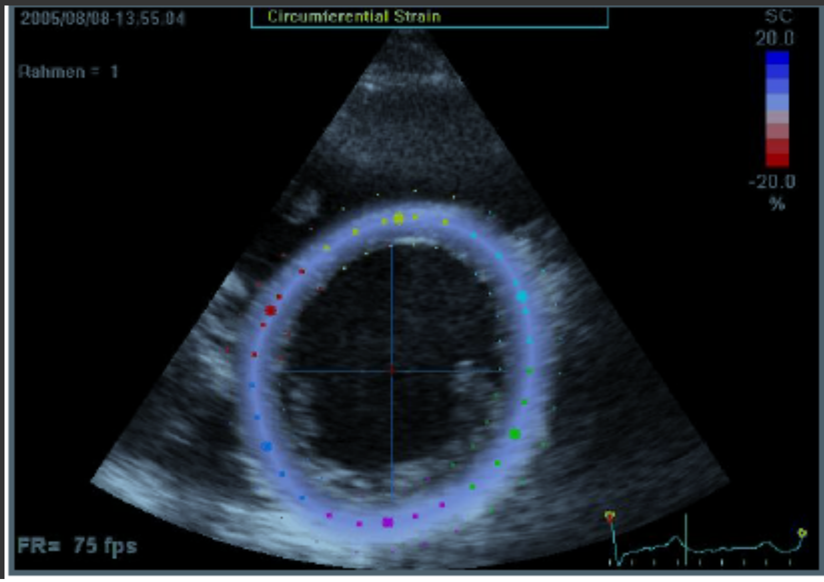
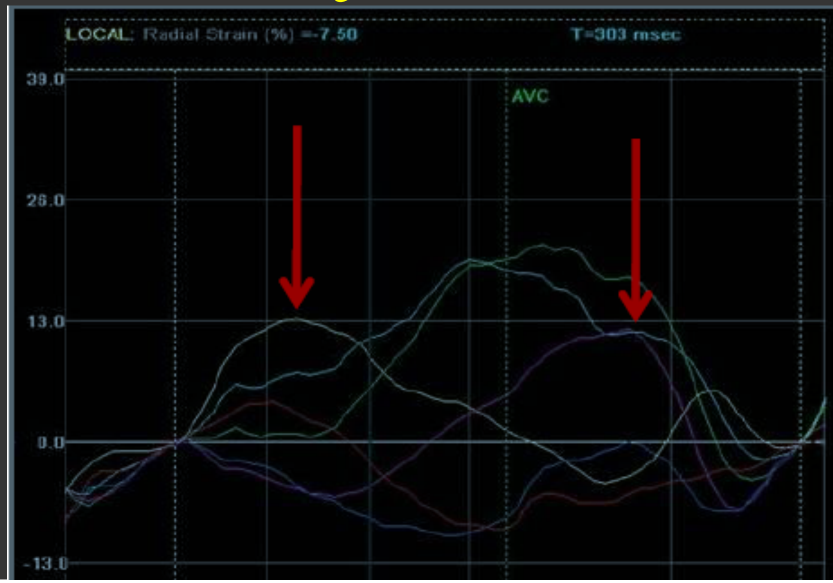


Figure 3: Percent change in reverse LV remodelling parameters at 6-month follow-up: LVEF (A), LV EDD (B), and LV ESD (C). Data are presented as mean and standard error of the mean.

The Target Study





All Cause Mortality following CRT in the TARGET and Control Groups

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

Echocardiography-Guided Left Ventricular Lead Placement for Cardiac Resynchronization Therapy: Results of the Speckle Tracking Assisted Resynchronization Therapy for Electrode Region (STARTER) Trial

Samir Saba MD, Josef Marek MD, David Schwartzman MD, Sandeep Jain MD, Evan Adelstein MD, Pamela White RN, Olusegun A. Oyenuga MD, Tetsuari Onishi MD, Prem Soman MD, John Gorcsan III MD University of Pittsburgh Medical Center, Pittsburgh, PA
Address correspondence to: Samir Saba, MD University of Pittsburgh Medical Center 200 Lothrop Street, Suite B-535 Pittsburgh, PA 15213-2582 sabas@upmc.edu

In Press: Circulation Heart Failure 2013

Recent Advances in Electrical Therapies

- Leadless PM: LLP
- Subcutaneous Lead ICD: S-ICD
- Recent CRT Recommendations
- Multisite, Quadripolar LV Pacing: MSP, 4P-LVP, MPP
- LV Endocardial Pacing: LVEP
- Vagal Nerve stimulation in HF: VNS
- Left Atrial Appendage Occlusion: LAAO

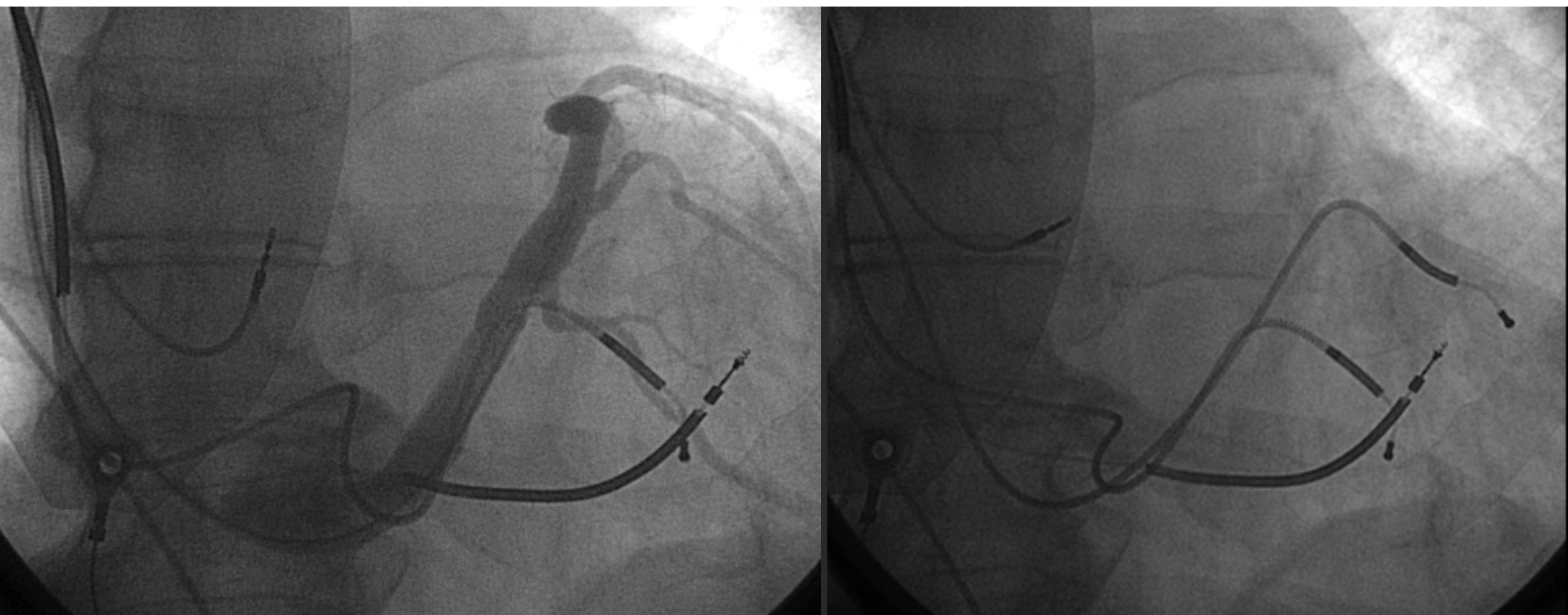
Journal of Cardiac Failure Vol. ■ No. ■ 2010

Atrial based, Dual Site LV, RV Pacing

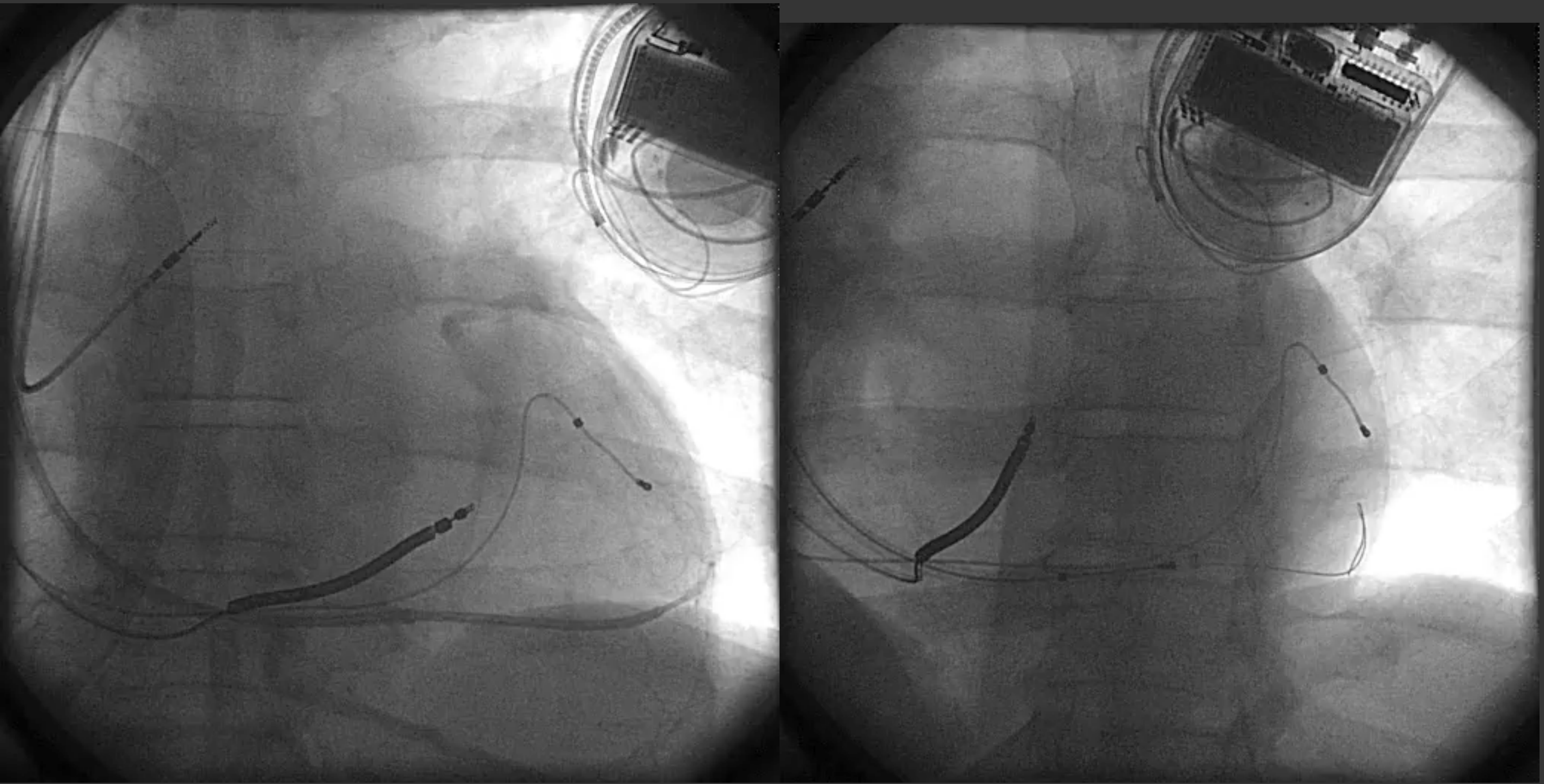
Clinical Trials

Addition of a Second LV Pacing Site in CRT Nonresponders Rationale and Design of the Multicenter Randomized V^3 Trial

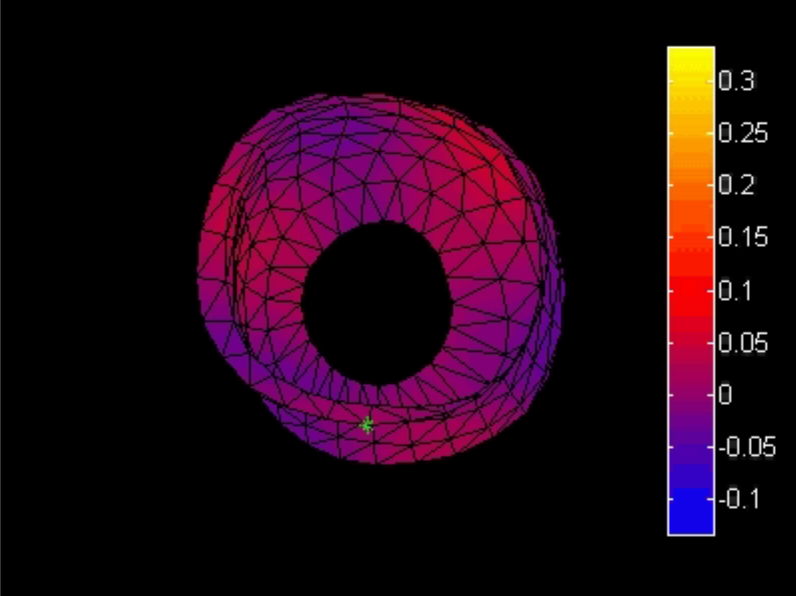
PIERRE BORDACHAR, MD,[1] CHRISTINE ALONSO, MD,[2] FREDERIC ANSELME, MD,[3] SERGE BOVEDA, MD,[4]
PASCAL DEFAYE, MD,[5] STEPHANE GARRIGUE, MD,[6] DANIEL GRAS, MD,[7] DIDIER KLUG, MD,[8] OLIVIER PIOT, MD,[9]
NICOLAS SADOUL, MD,[10] AND CHRISTOPHE LECLERCQ, MD[11]

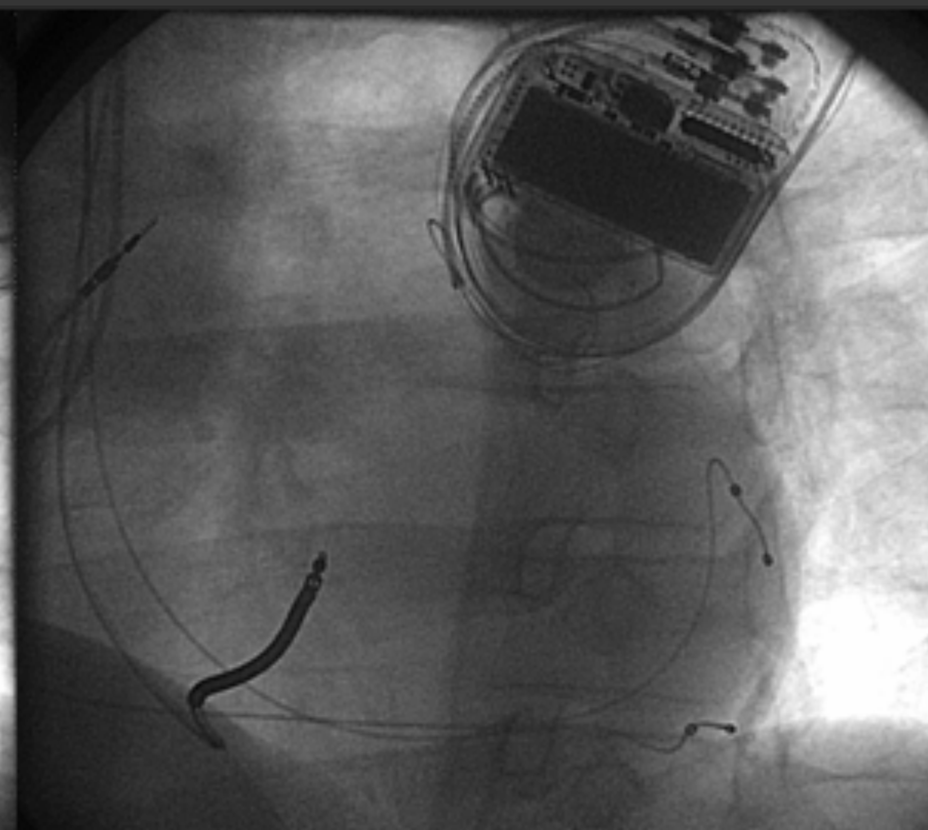


Atrial based, Dual Site LV, RV Pacing
(ongoing V3 Trial)

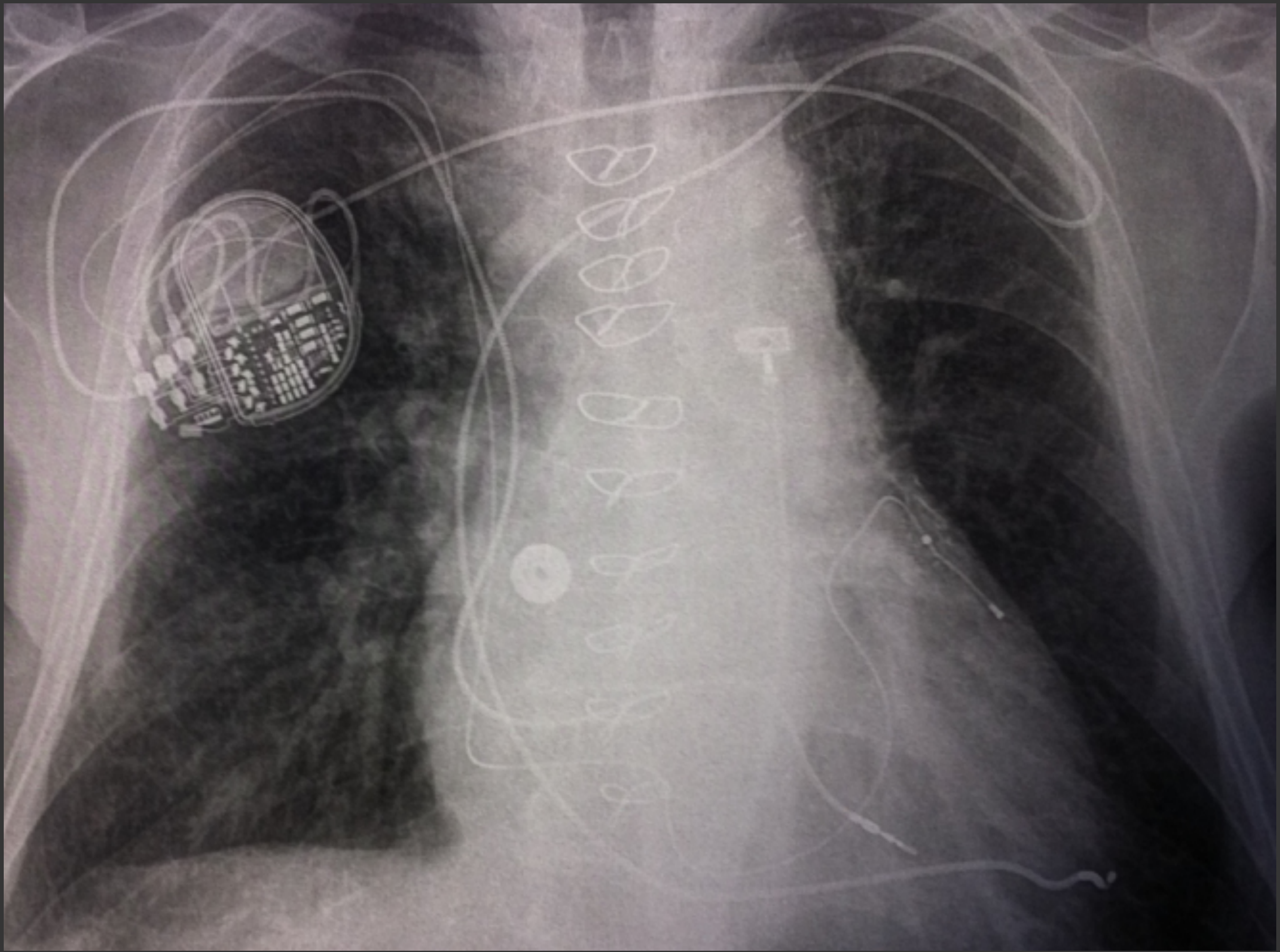


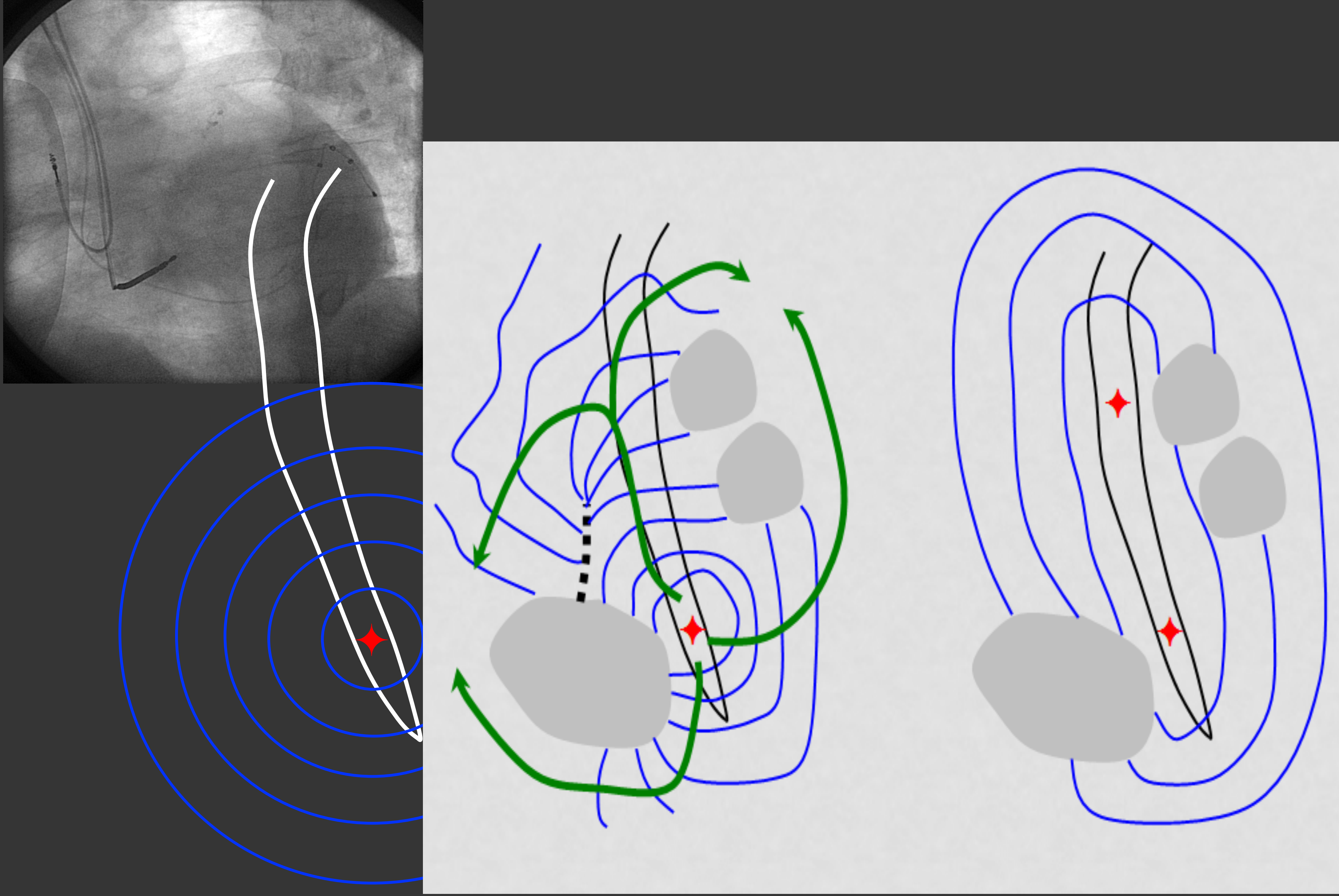
Interest of Additional LV Lead during CRT





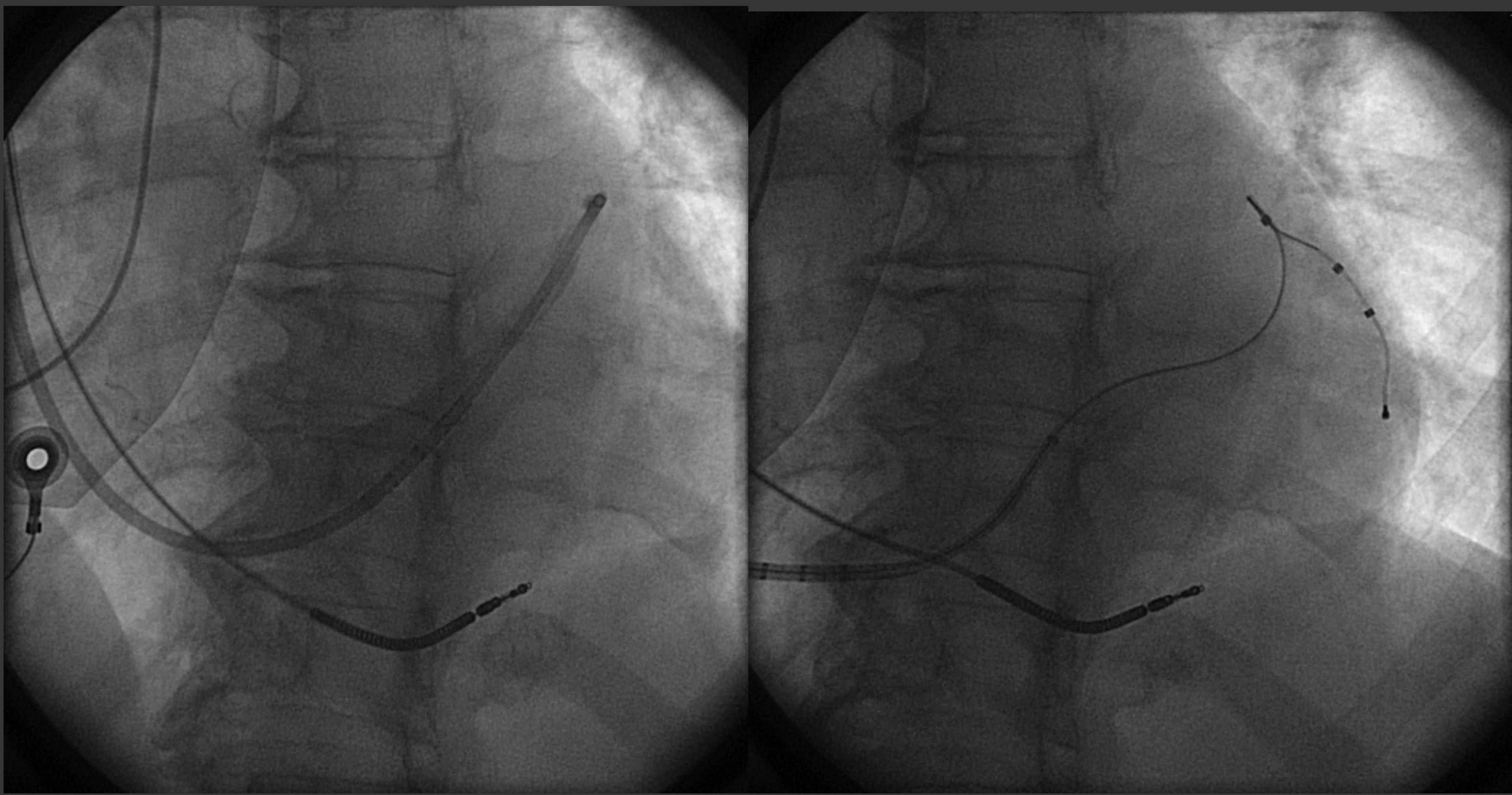
Right Subclavian vein Occlusion
DDD-PM Upgrade



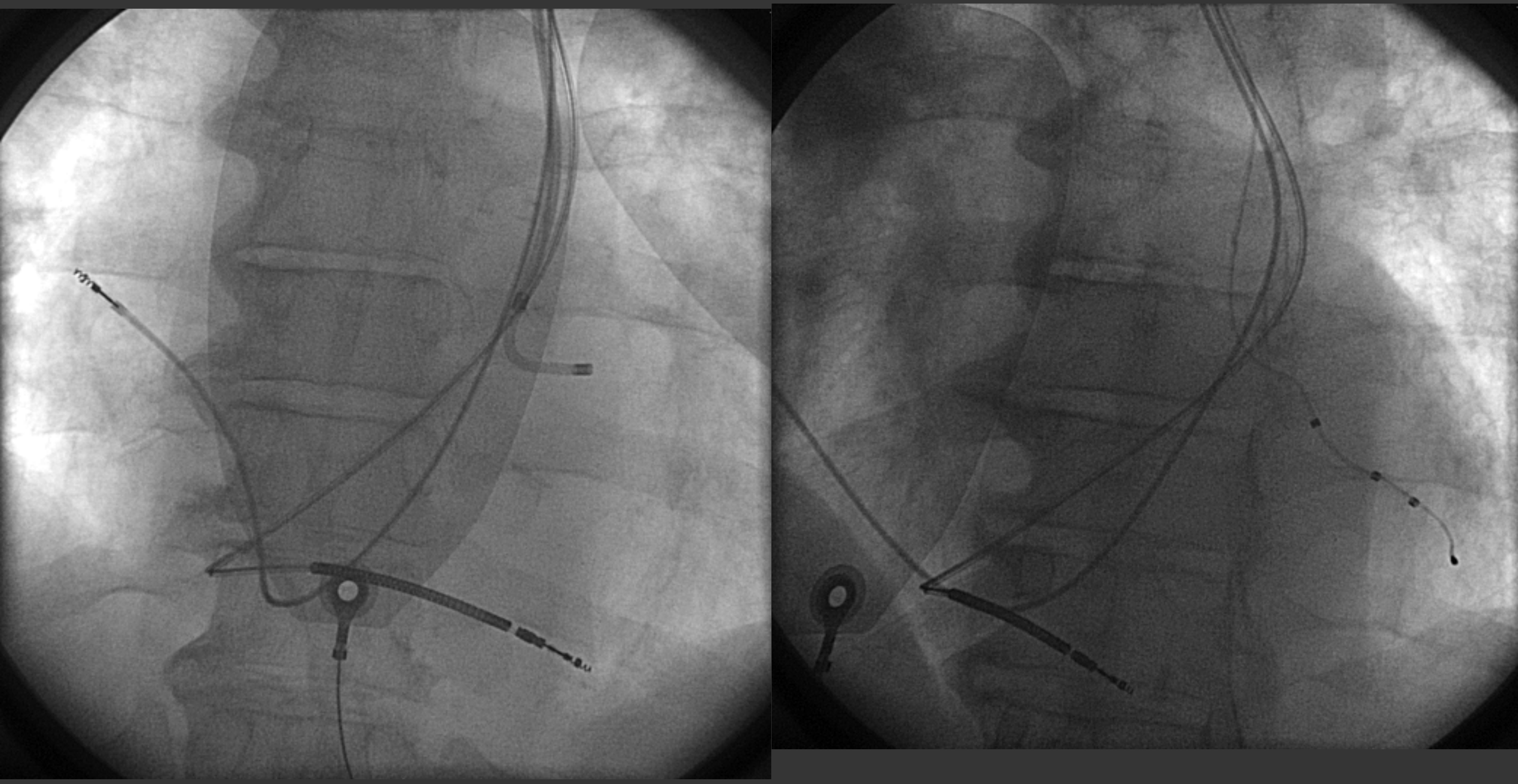


Additional Hemodynamic Impact of MPP

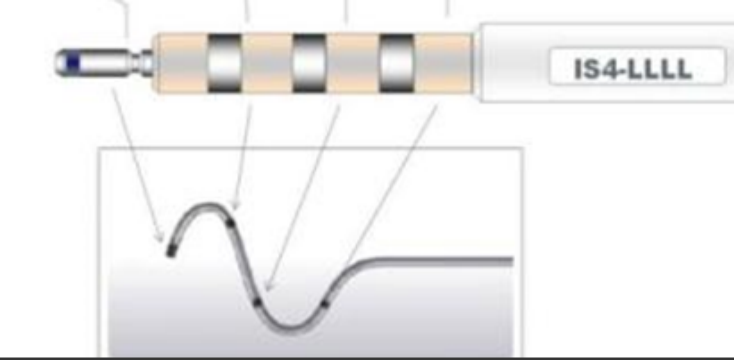
Subselection of Lateral Cardiac Vein during Quadripolar LV Lead Implant



Quadripolar LV Lead in case of LSVC



Goals of Quadripolar vs Bipolar LV Pacing



- Offering Multiple Pacing Vectors to individually adjust LV Pacing in Long-Term
  - Less Phrenic Nerve Stimulation
  - Optimal Pacing Thresholds (multiple vectors)
  - Pacing Vectors to Optimize Hemodynamics
  - Better Lead Stability, Less Lead revision
  - Similar LV Lead Implantation

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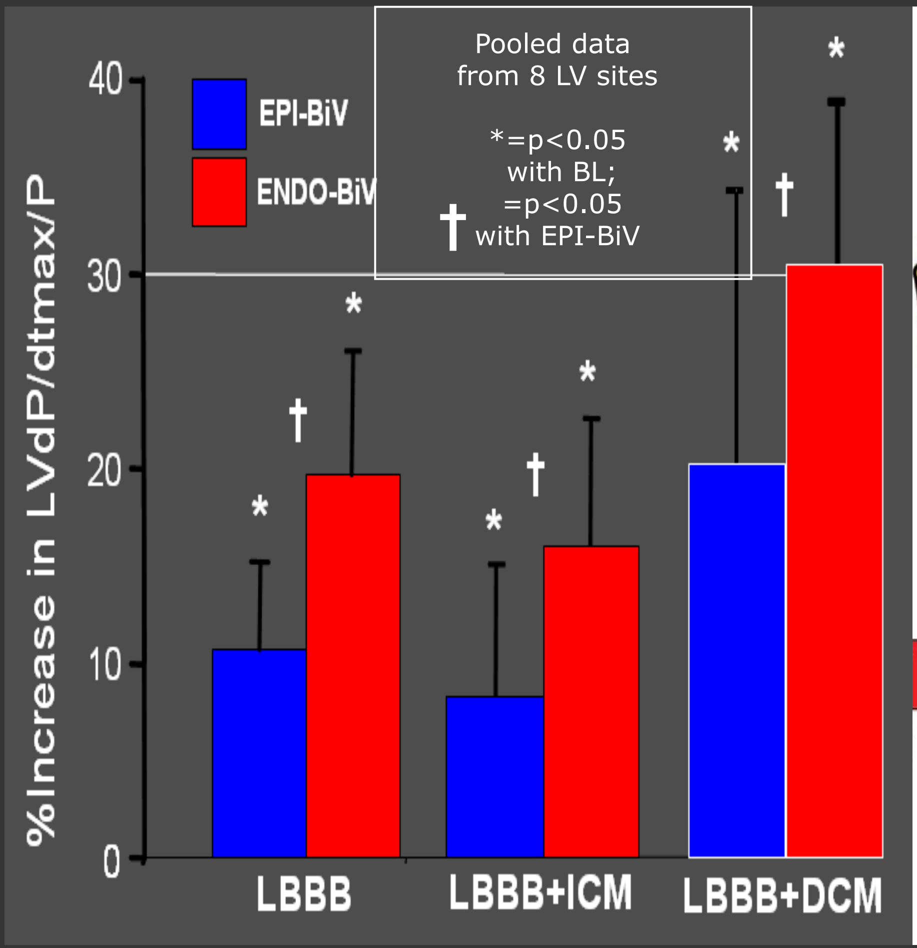
- **LV Endocardial Pacing: LVEP**
- Vagal Nerve stimulation in HF: VNS
- Left Atrial Appendage Occlusion: LAAO

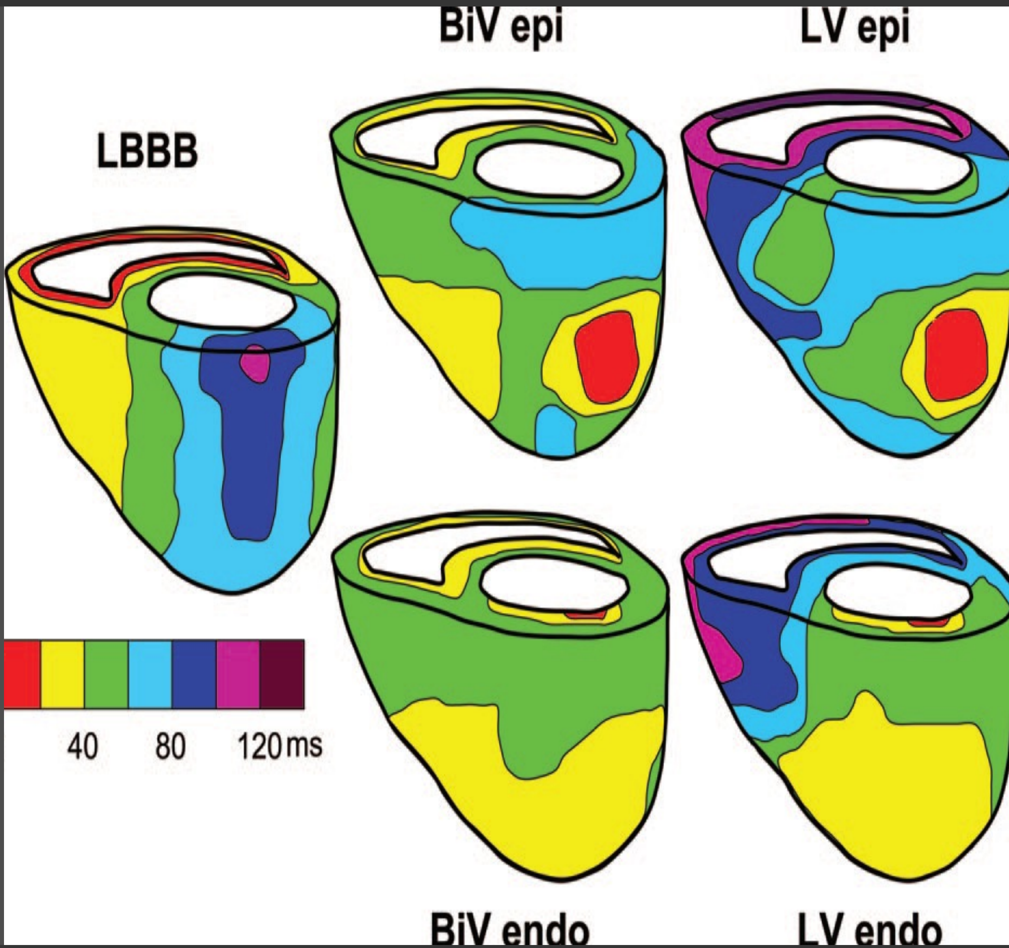
Endocardial vs Epicardial CRT provides:

Better LV Filling and Systolic Performance

More Homogenous Resynchronization



Prinzen et al



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

LV Endocardial or Triventricular Pacing to Optimize CRT in a Chronic Canine Model of Ischemic HF

Bordachar Am J Physiol Heart Circ Physiol 2012.

Table 1. Comparison of Hemodynamics during LV and BiV pacing (n=8)

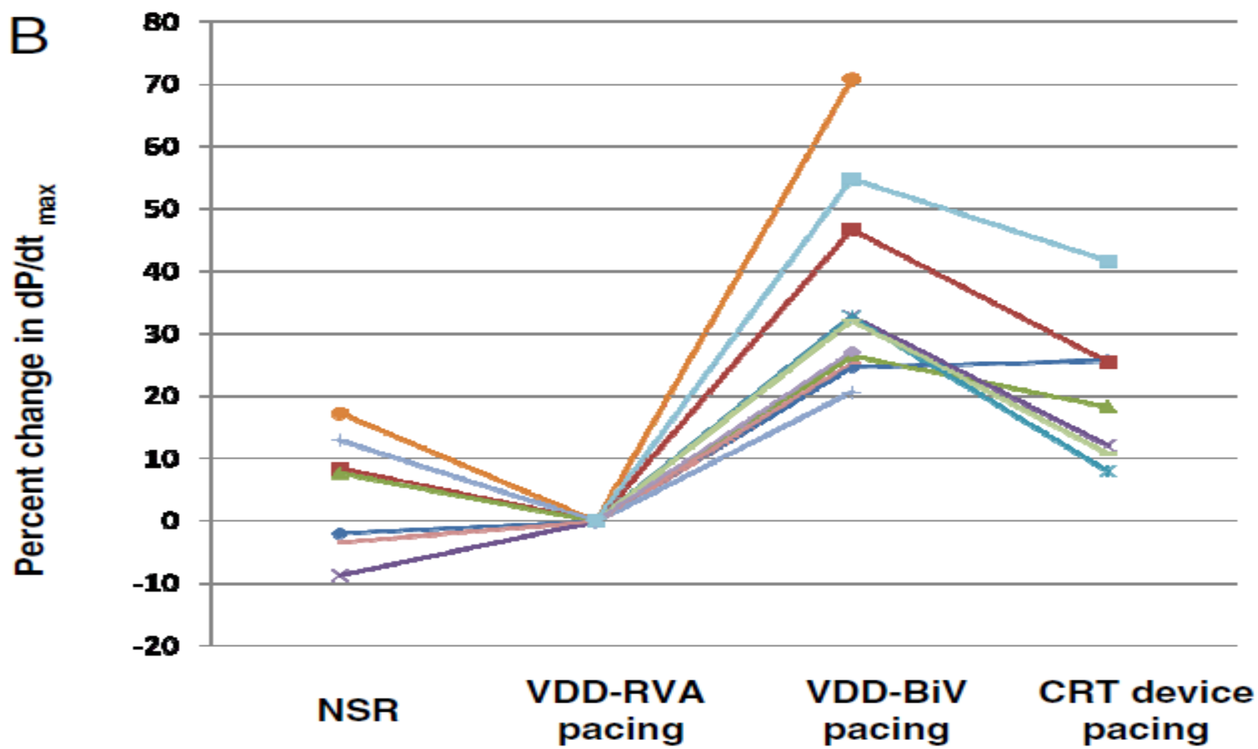
Table 3. Distribution of optimal sites during epicardial and endocardial pacing

Site \ Pacing	LV EPI	LV ENDO	BiV EPI	BiV ENDO
LVA	0%	38%	12%	12%
LVL	50%	12%	13%	25%
LVB	25%	38%	50%	63%
LVPOST	25%	12%	25%	0%

LVA: LV apex; LVL: LV lateral; LVB: LV basal; LVPOST: LV posterior

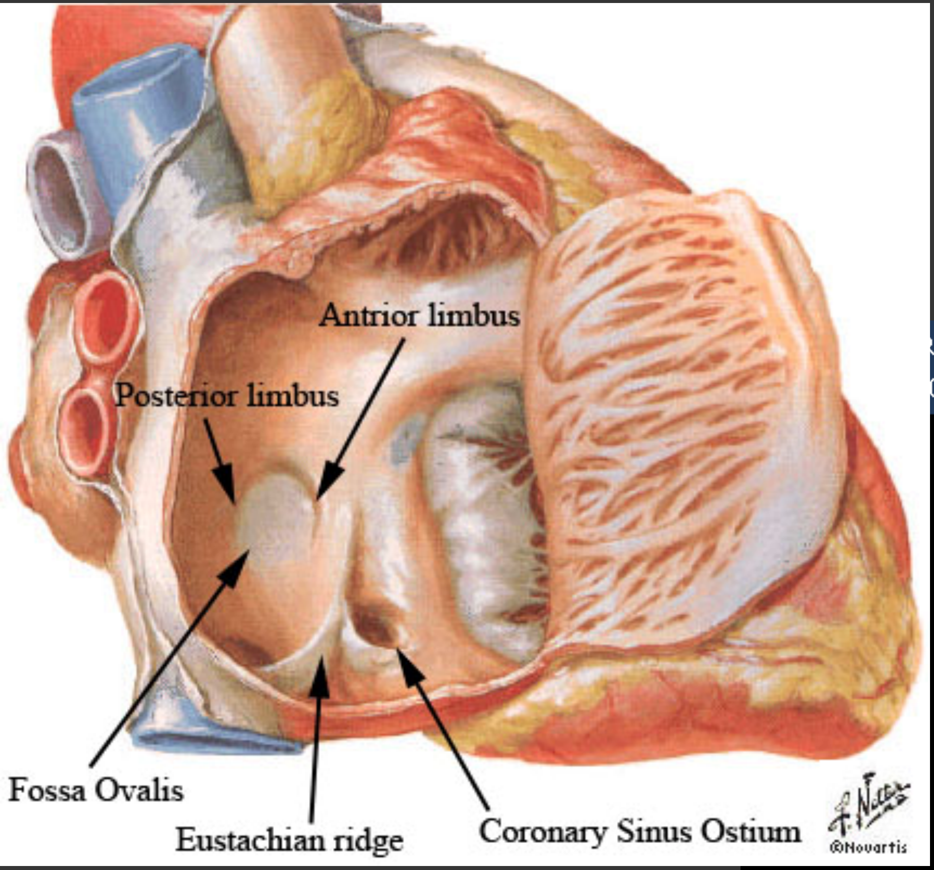
Optimal Left Ventricular Endocardial Pacing Sites for Cardiac Resynchronization Therapy in Patients With Ischemic Cardiomyopathy

David D. Spragg, MD,* Jun Dong, MD, PHD,*† Barry J. Fetics, MS,* Robert Helm, MD,* Joseph E. Marine, MD,* Alan Cheng, MD,* Charles A. Henrikson, MD,* David A. Kass, MD,* Ronald D. Berger, MD, PHD*

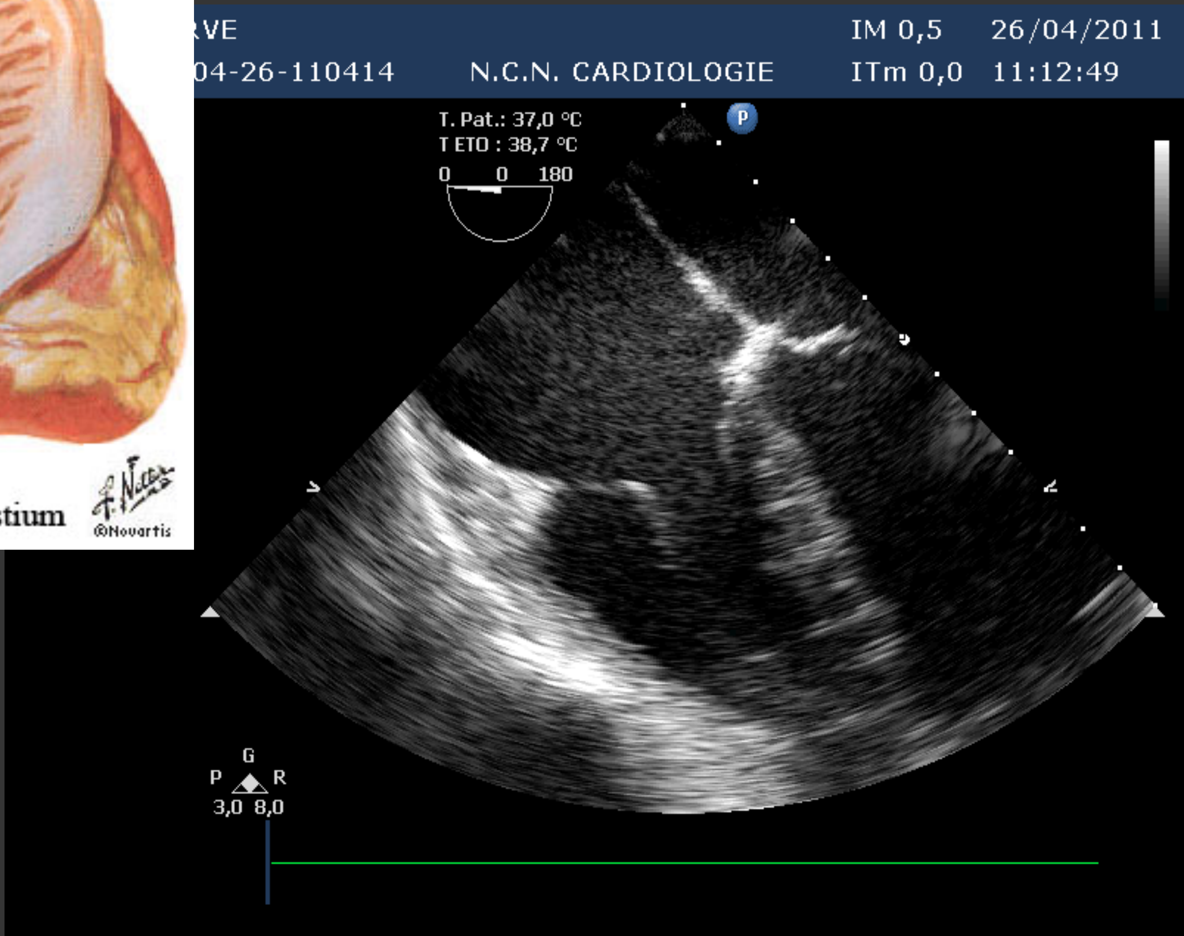


CRT delivered at best LV endocardial sites is more effective than via pre-implanted coronary sinus lead pacing. The location of optimal LV endocardial pacing varies among patients with ICM, and individual tailoring may improve CRT efficacy in such patients. (J Am Coll Cardiol 2010;56:774–81) © 2010 by the American College of

TEE Evaluation before Transseptal Puncture



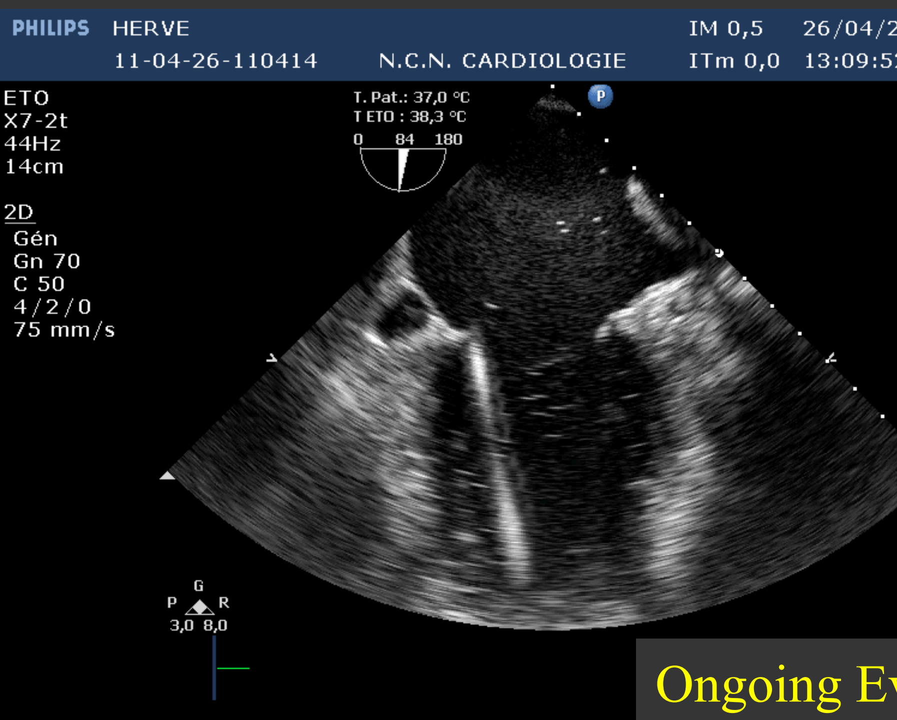
Location of Fossa Ovalis

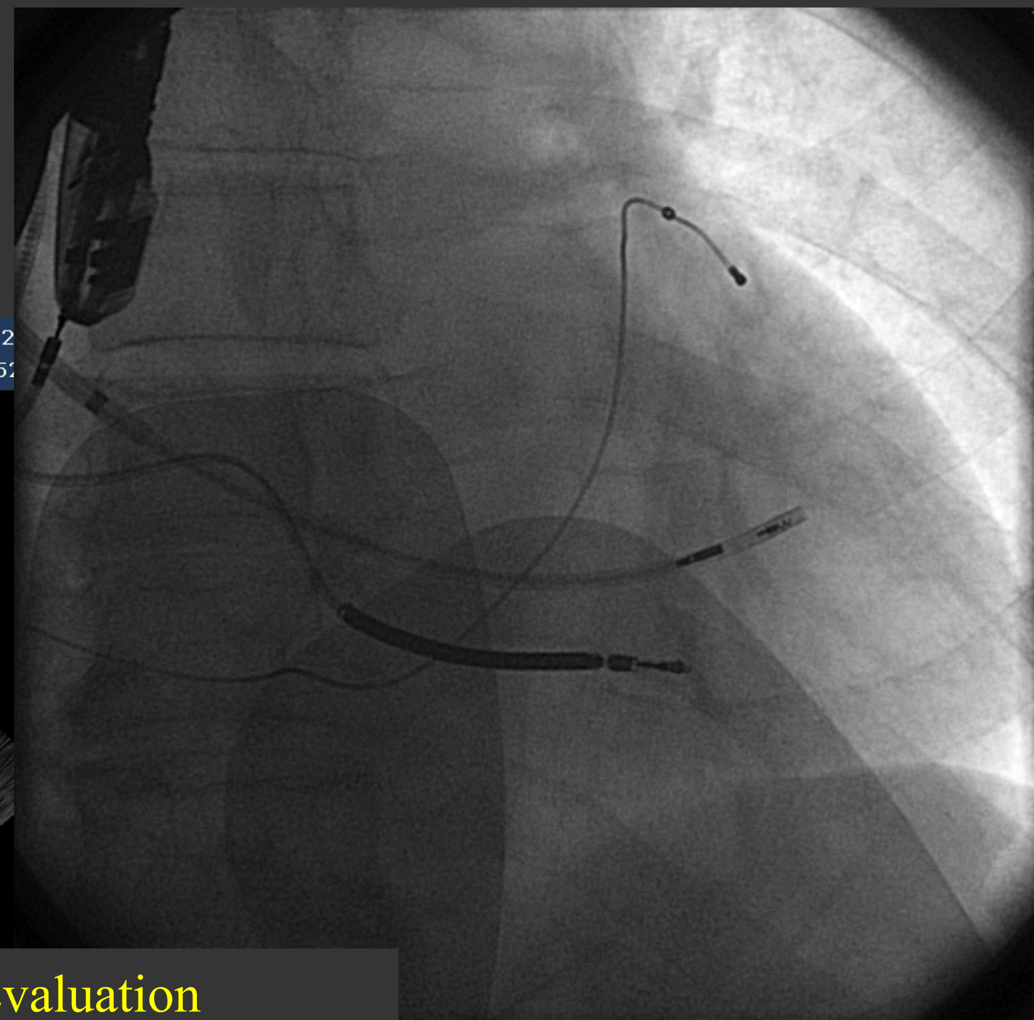


Ongoing Evaluation

LV Endo Pacing in Non CRT Responder

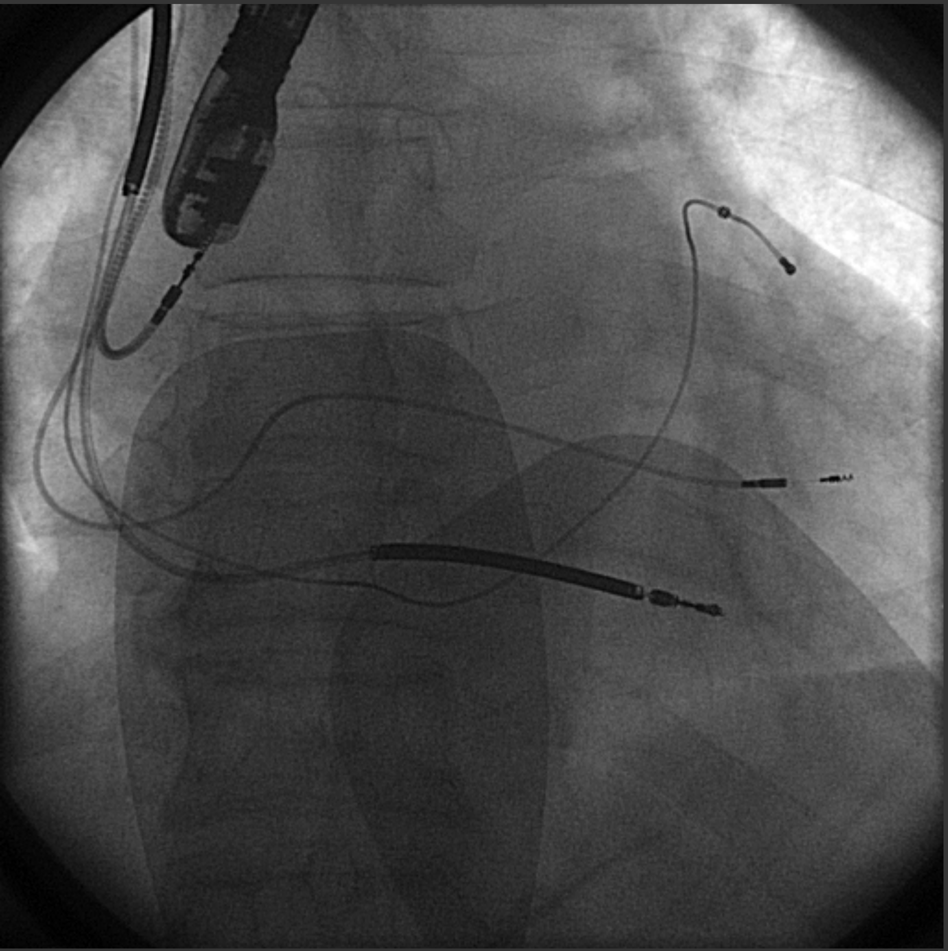
LV Lead placement
under TEE guidance



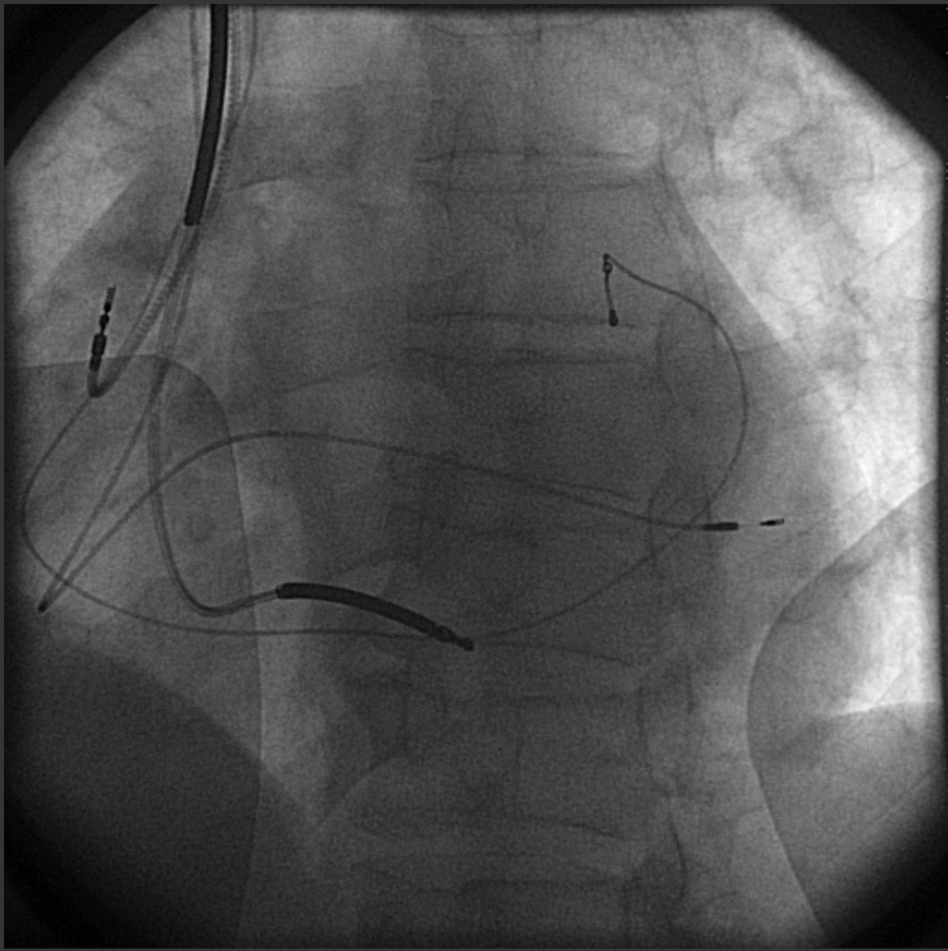


Ongoing Evaluation

LV Endo Pacing in Non CRT Responder



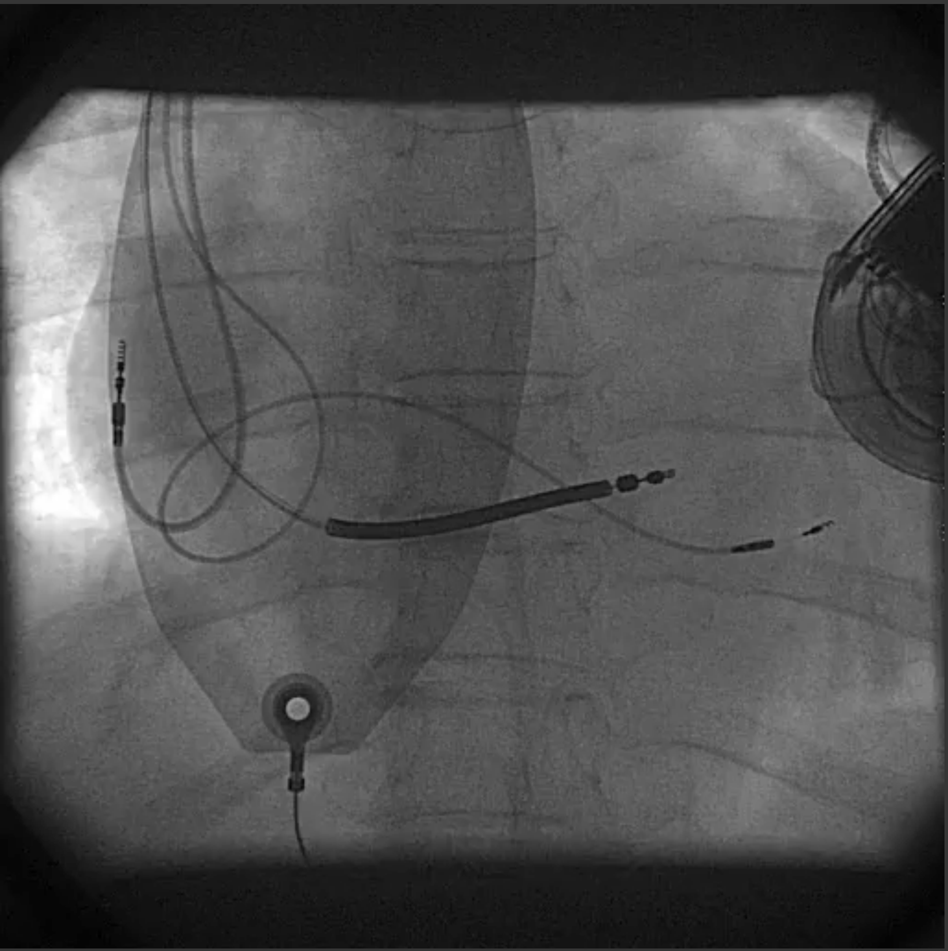
AP View



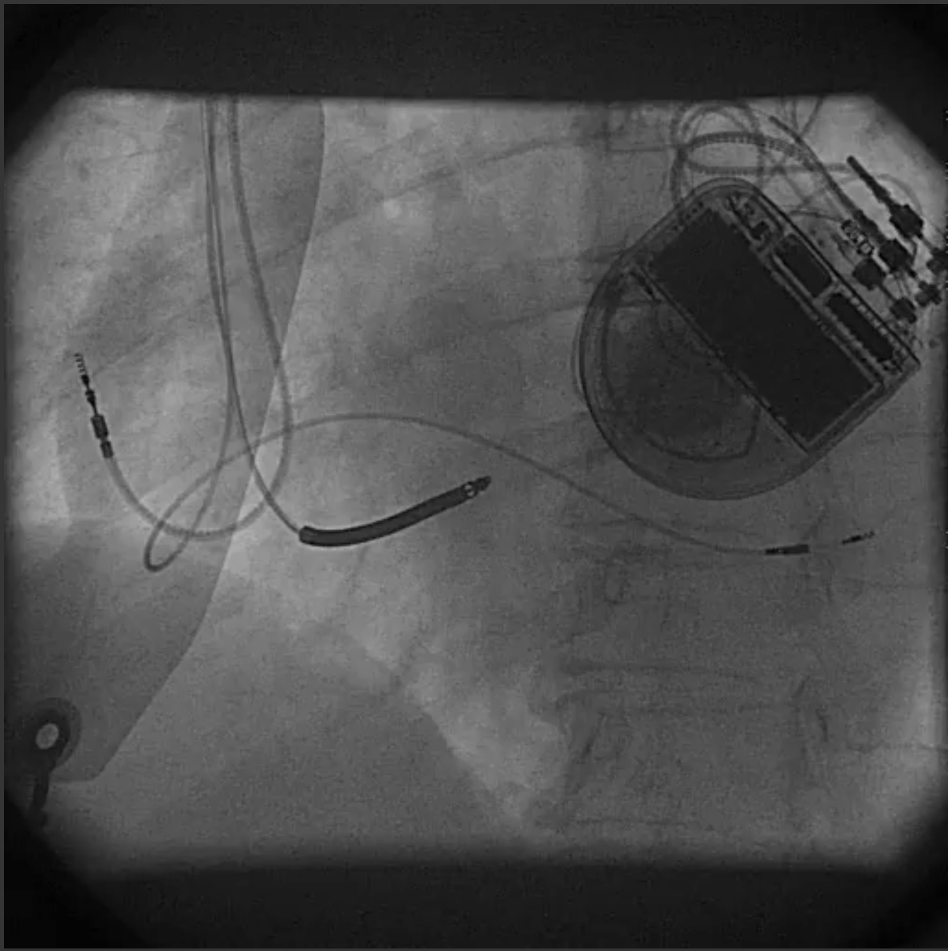
LAO View

Ongoing Evaluation

LV endocardial Pacing during CRT

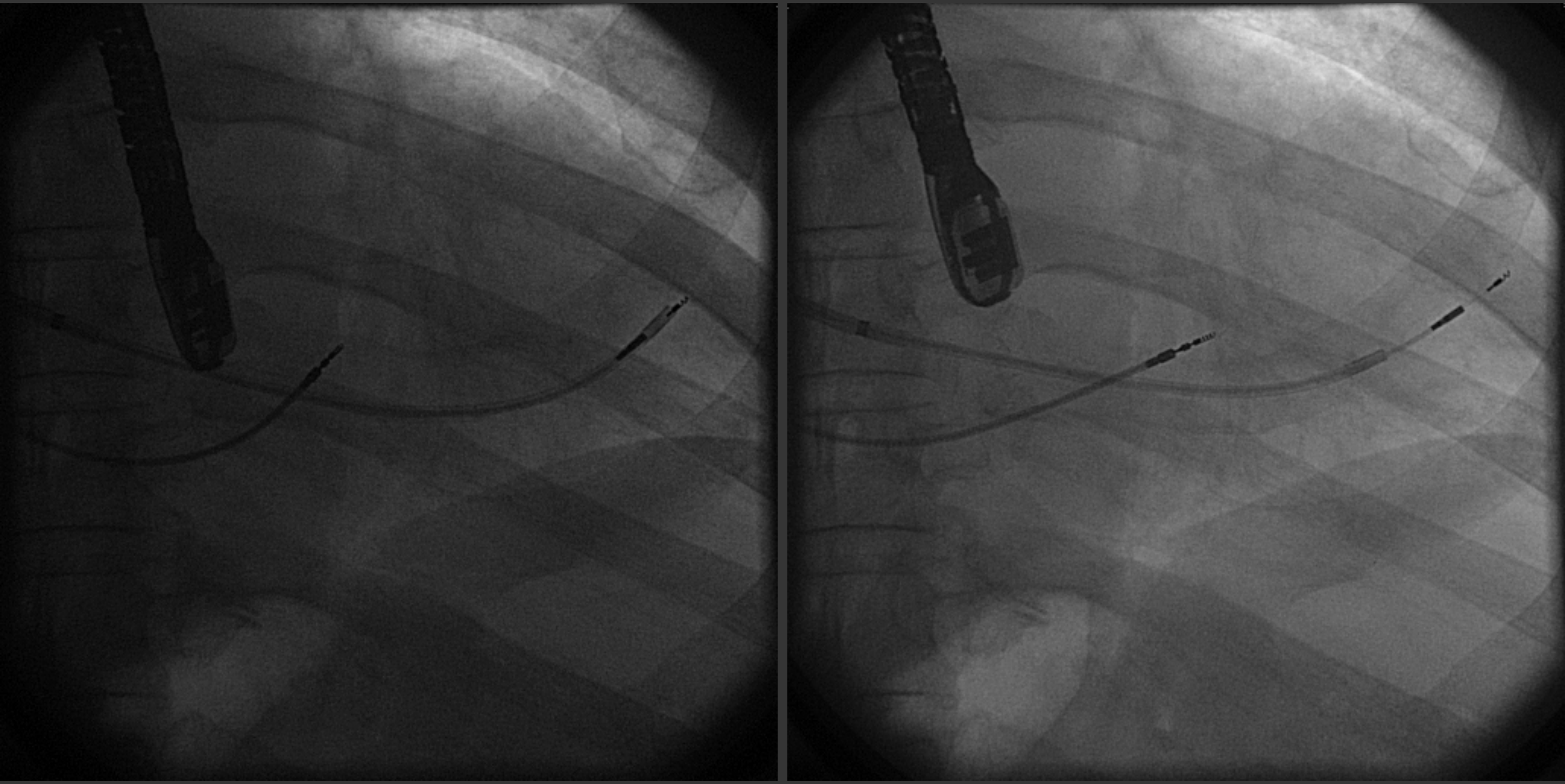


AP View

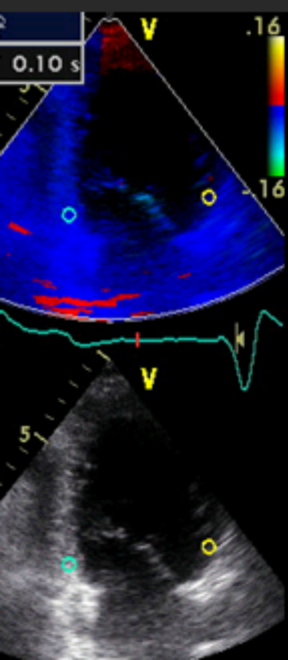


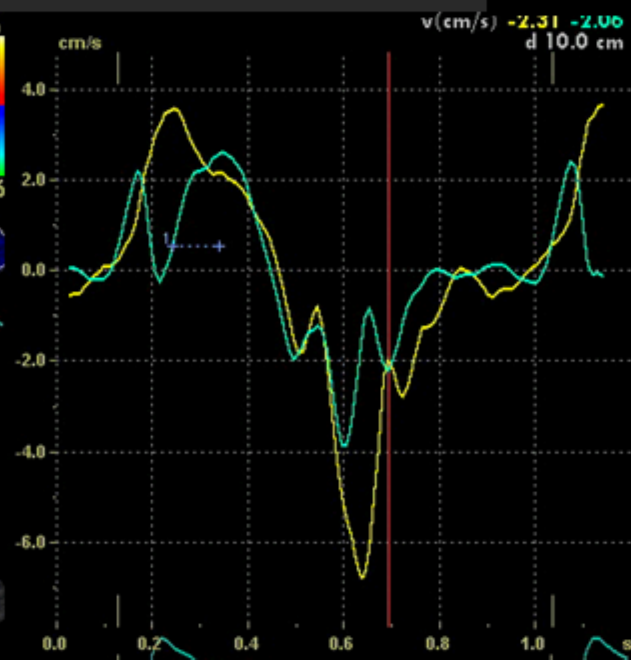
LAO View

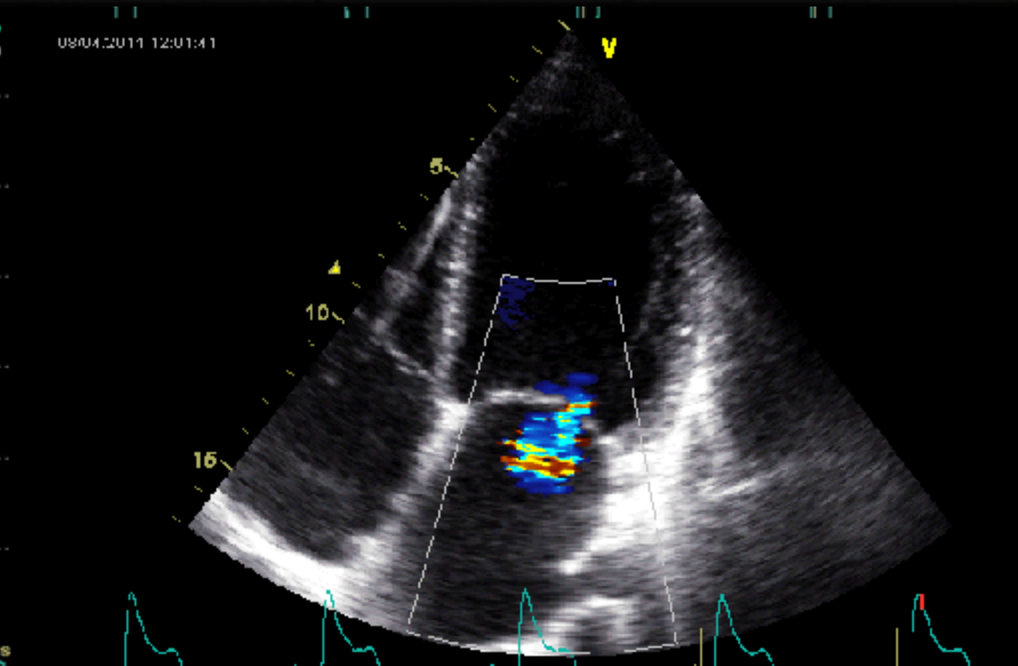
PNS still hapens during LV endo Pacing !!



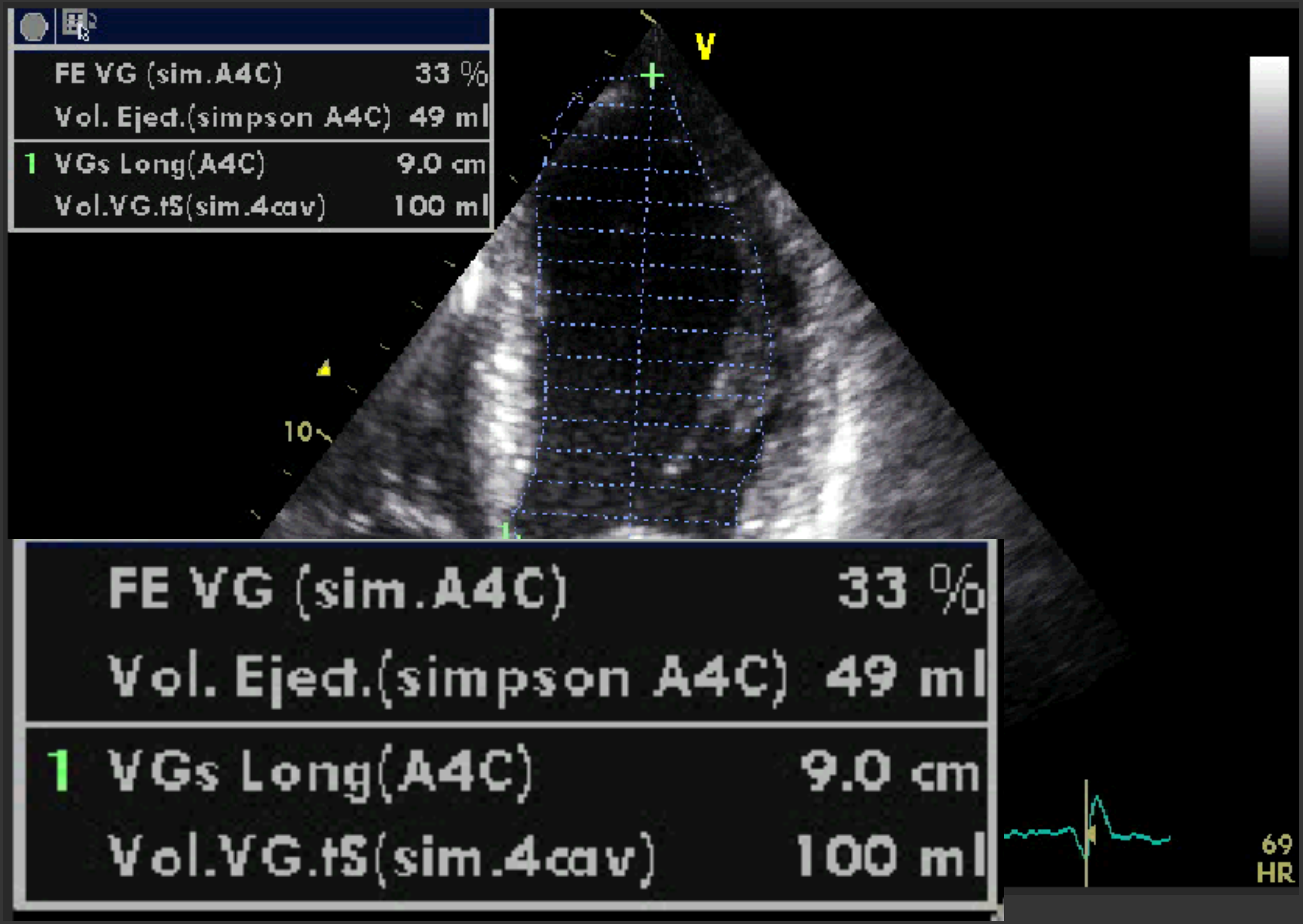
Echo prior to Transseptal LV Lead implant





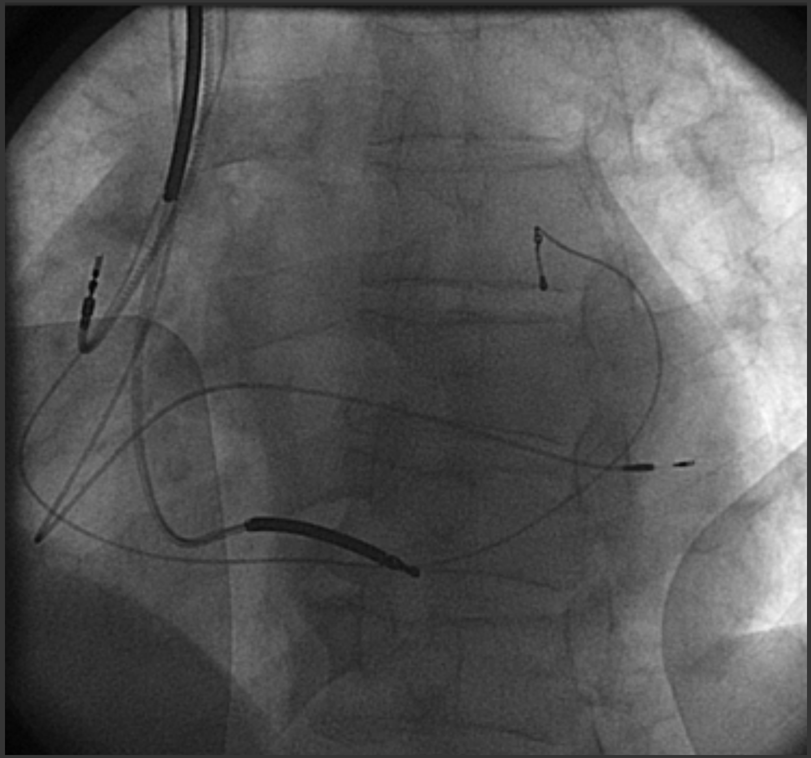


LV EF Echo Evaluation (Simson)



Permanent LV Endocardial Pacing in Clinical Practice

- Expected Benefits of LVEP:
  - Local Recruitment, V propagation
  - Optimized LV Pacing Location
  - Lower risk of PNS, Better PT



- Potential Side Effects:
  - TE events
  - Impact on MR
  - Lead Extraction, arrhythmias ..

- Indications:
  - Non Responders
  - Failure to Classical Approach
  - First Line option ?

- Next Steps
  - Clinical Studies
  - Improved Implant Tools
  - New LVEP Lead Design

Recent Advances in Electrical Therapies

- Leadless PM: LLP
- Subcutaneous Lead ICD: S-ICD
- Multisite, Quadripolar LV Pacing: MSP, 4P-LVP, MPP
- LV Endocardial Pacing: LVEP
- **Vagal Nerve stimulation in HF: VNS**
- 

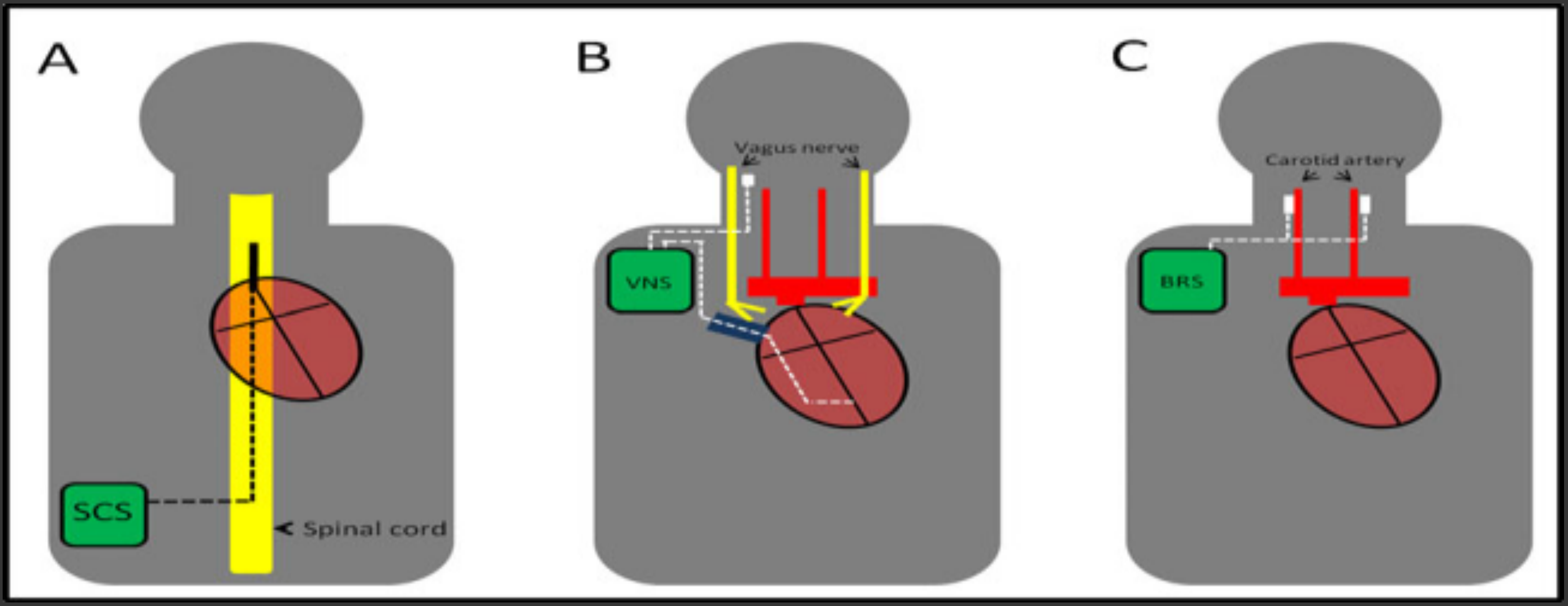
Vagal stimulation for the treatment of heart failure: a translational success story

Peter J Schwartz[1,2,3,4]

inhibition of ca
activity (ie, low
the heart from
sympathetic ne
home message
stimulates—as
studies—the in
also and si
cardiac-bound s
synergistic effec

Device-based Neuromodulation Therapy for HF
Current Investigational Approaches

SCS VNS BRS



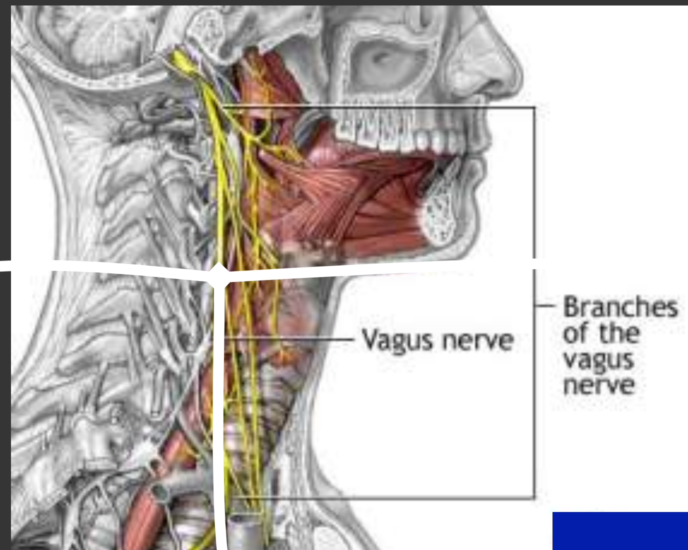
Spinal Cord Stimulation (SCS): SCS generator implant in abdomen or paraspinous region with a lead placed in dorsal epidural space between T1-T4

Vagal Nerve Stimulation (VNS): VN stimulator placed in right subpectoral region with a lead placed in RV and VN stimulating lead tunneled to cervical vagus region

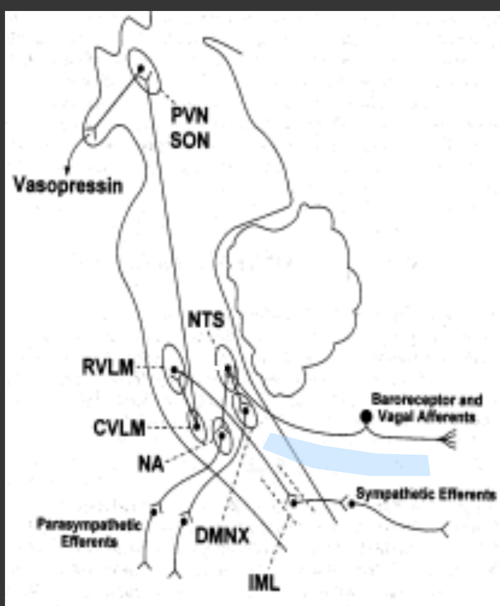
Baroreflex Stimulation (BRS): Baroreflex stimulation generator placed in right subpectoral region with bilateral stimulation leads tunneled to the carotid baroreceptor region

JC Lopshire and DP Zipes. Curr Cardiol Rep (2012) 14:593–600

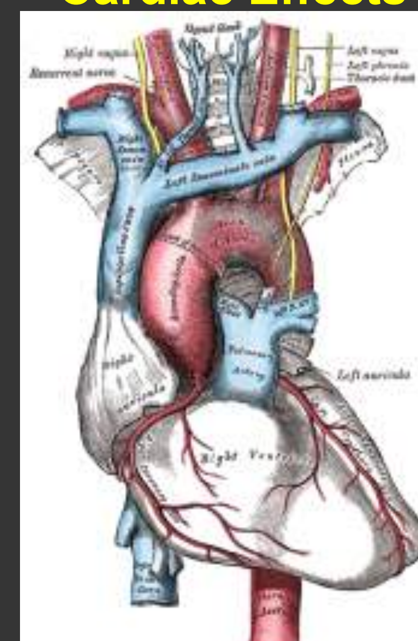
Impact of Vagal Stimulation



Central Effects

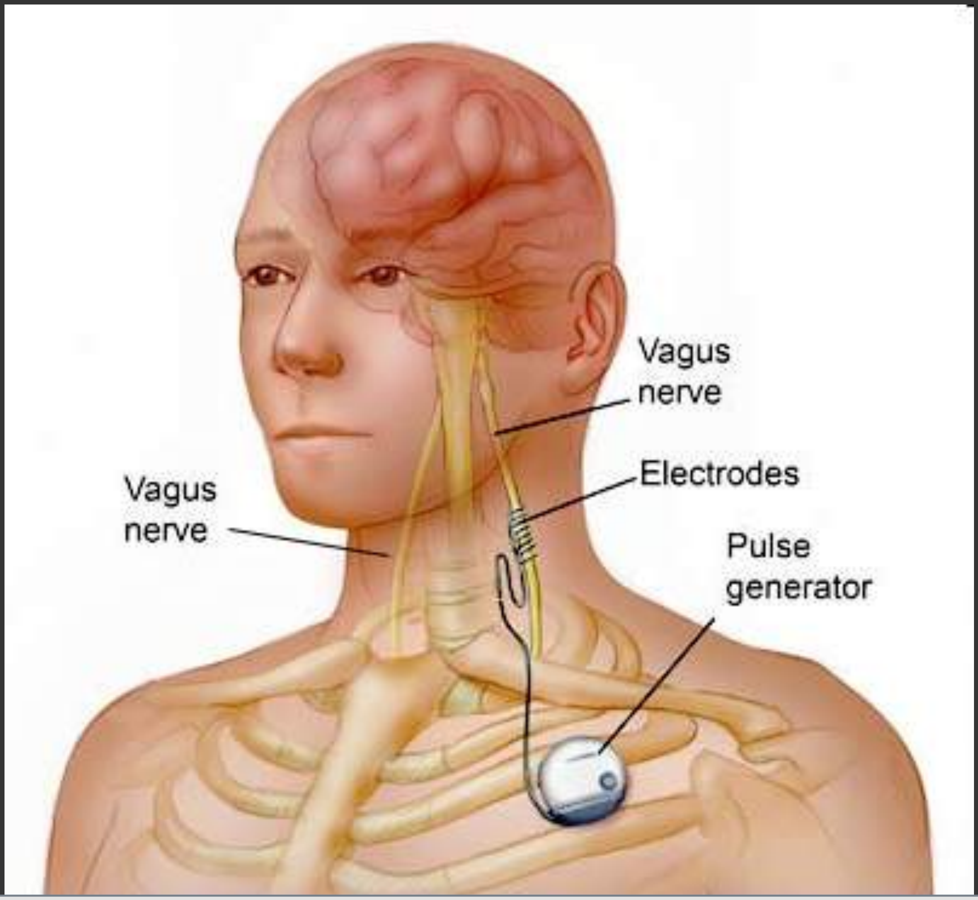


Cardiac Effects



Stimulating the cervical vagus nerve activates regions in the brain and in the heart

Vagal stimulation is indicated for epilepsy.



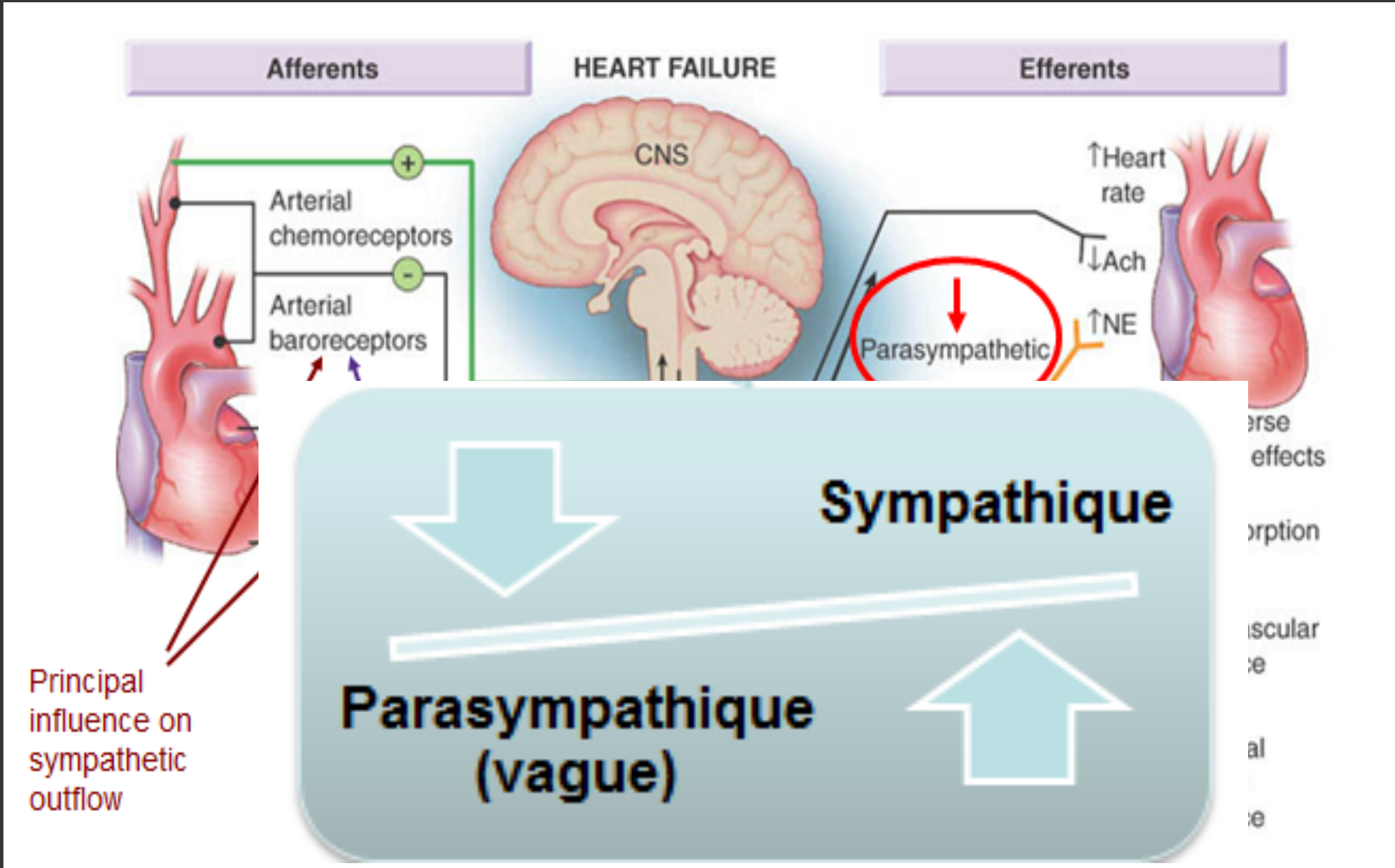
Please note:

Epilepsy treatment uses mainly left side vagus stimulation

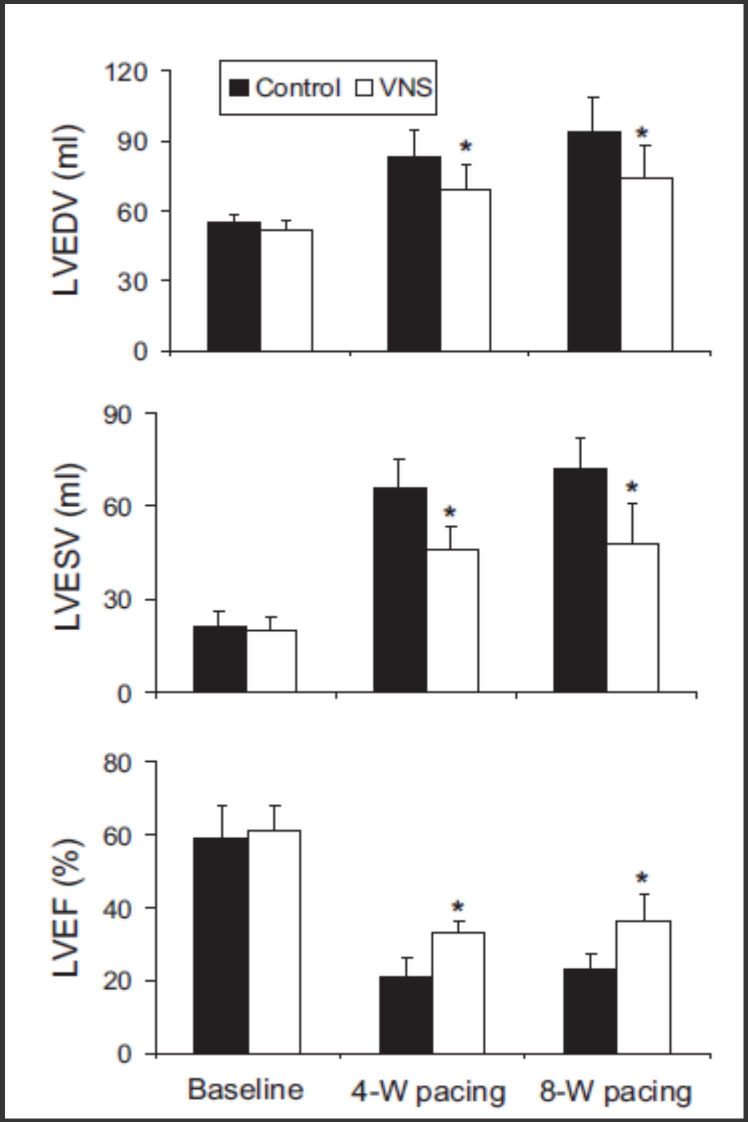
Cyberonics has implanted >60,000 devices. Safety profile established.

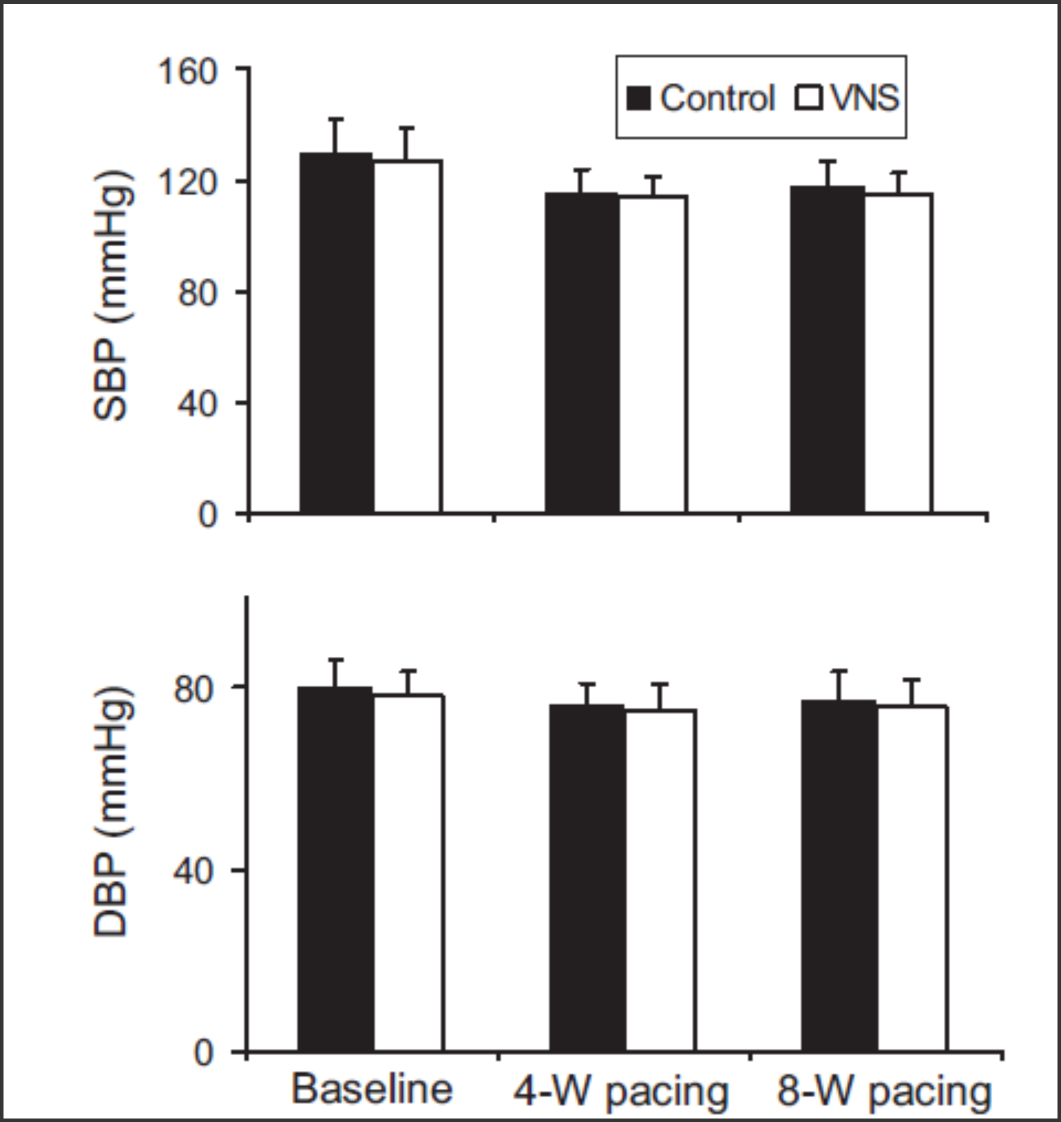
Heart failure as an autonomic nervous system dysfunction

Takuya Kishi (MD, PhD)*



VNS in HF Canine High Rate Pacing Model

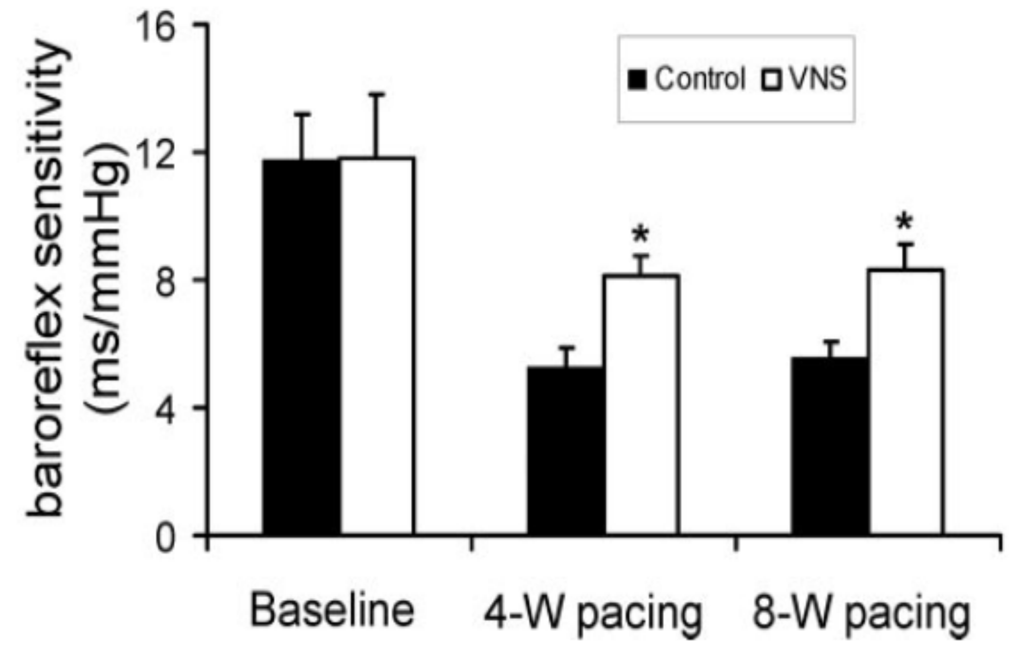




Adapted from Zhang Y, Circ Heart Fail 2009; 2:692-699

VNS in HF Canine High Rate Pacing Model

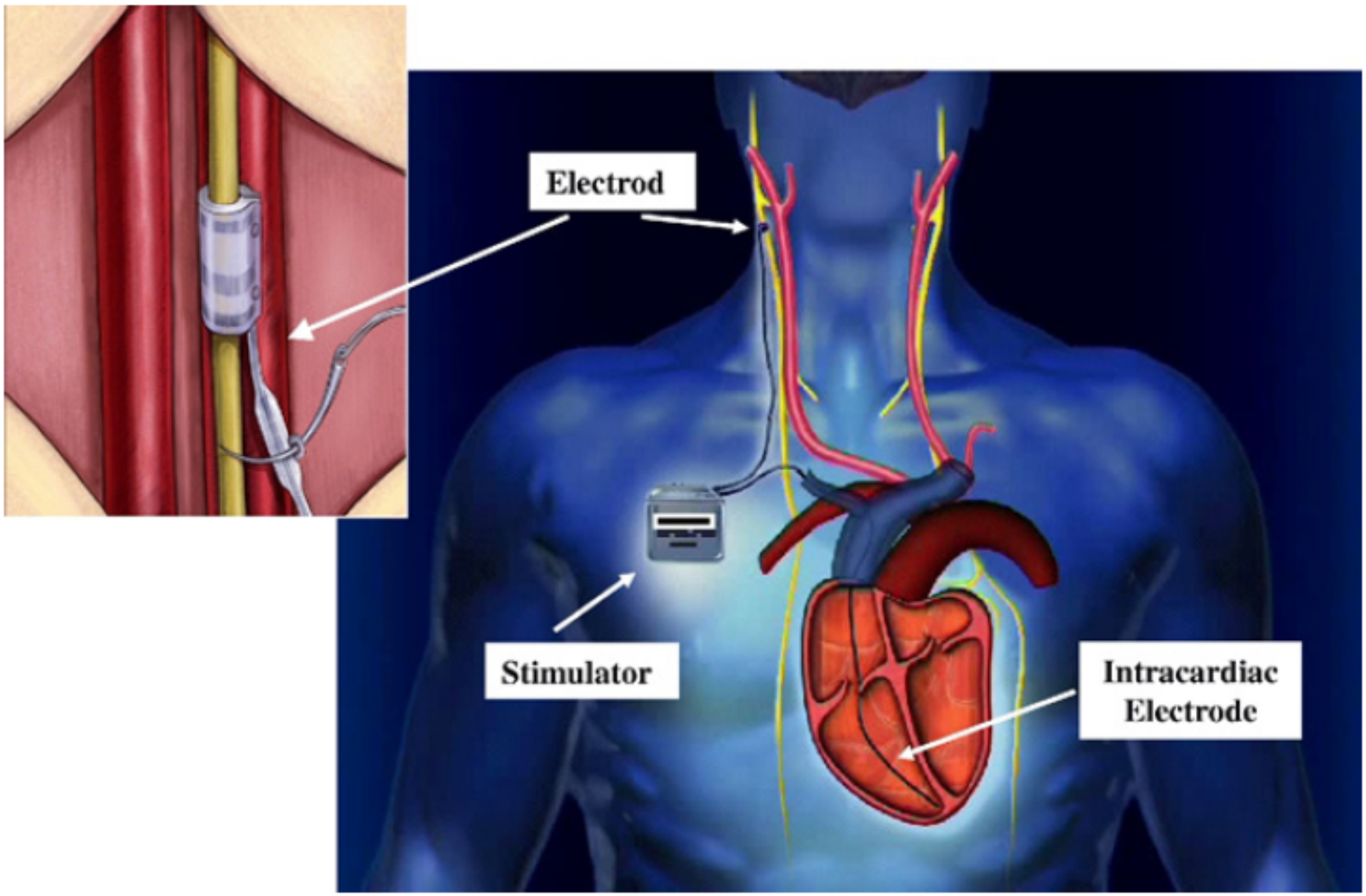
	Baseline		4-wk Pacing		8-wk Pacing	
	Control	VNS	Control	VNS	Control	VNS
RR, ms	510.7±77.0	514.5±61.5	394.8±36.7	428.8±55.7	407.1±47.2	451.0±76.1
SDNN, ms	84.2±21.7	86.6±21.8	23.2±5.9	36.6±5.1*	28.7±8.0	42.2±7.4*
RMSSD, ms	68.9±10.6	69.3±17.2	17.0±4.6	31.0±6.1*	22.1±5.3	37.2±7.1*
LF, norm	35.2±12.5	36.2±12.3	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. Crijns[2], Martin Borggrefe[3], Goran Milasinovic[4], Jan Smid[5], Markus Zabel[6], Antonello Gavazzi[7], Antonio Sanzo[1], Robert Dennert[3], Juergen Kuschyk[4], Srdjan Raspopovic[5], Helmut Klein[6,8], Karl Swedberg[9], and Peter J. Schwartz[1,10,11,12,13], for the CardioFit Multicenter Trial Investigators



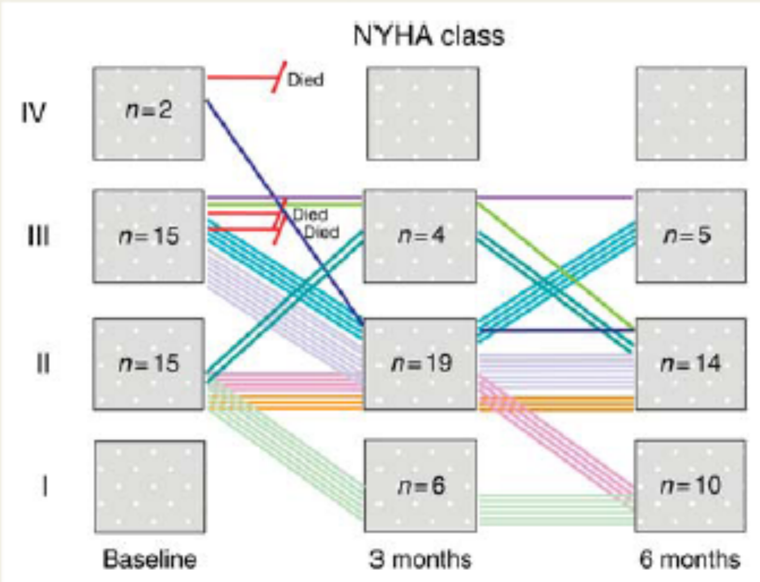


Figure 1 New York Heart Association class. Individual New York Heart Association class behaviour of each patient throughout the study. Red broken lines correspond to dead patients. Each patient is characterized by a single line.

Data limited to the 21 patients of the second phase of the study show a behaviour identical to the total cohort, but a non-significant decrease in LV systolic volume (see Supplementary material online, *Table S1*). Comparing baseline with 1-year evaluation in the 23 patients who completed this follow-up revealed maintenance and even magnification of the favourable effects of vagal stimulation (especially LVEF from 21 to 34%, *Table 5*).

Heart rate variability tended to increase during the study and the change in pNN50 was statistically significant (*Table 4*).

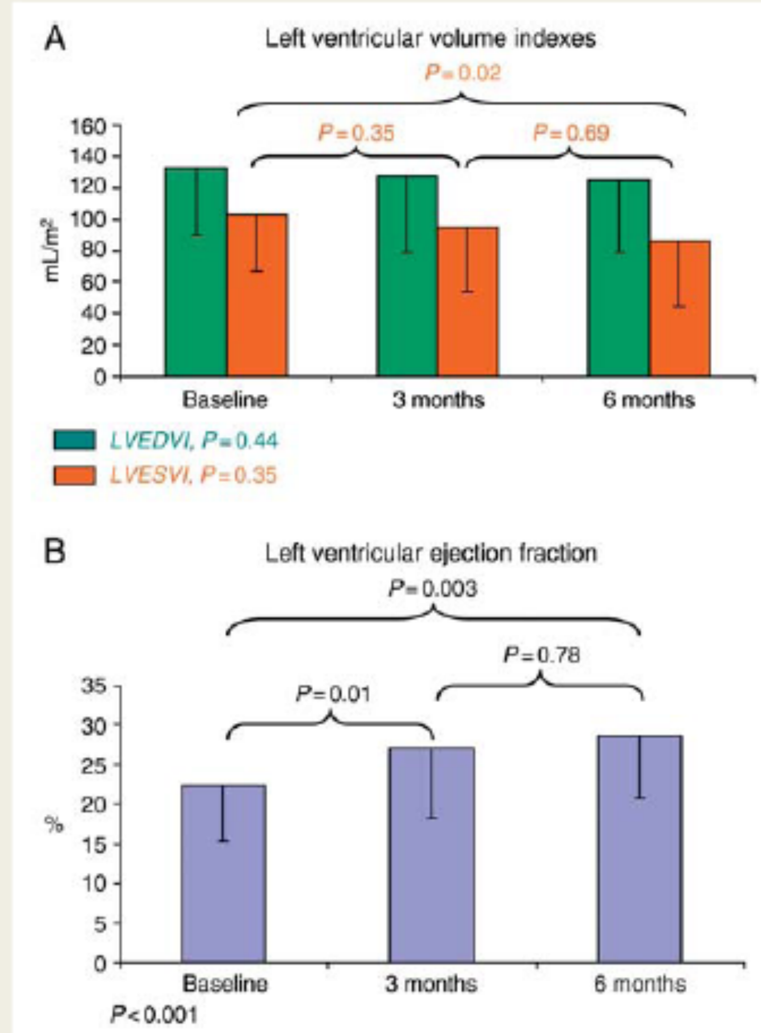


Figure 2 Echocardiographic evaluation. Left ventricular volume indexes (*A*) and ejection fraction (*B*) throughout the study. LVEDVI: left ventricular end-diastolic volume index. LVESVI: left ventricular end-systolic volume index.

CardioFit Multicenter Trial - Safety

- Non SAEs related to the device: n = 19

  Pain at stimulation site: 6

  Cough: 5

  Dysphonia: 4

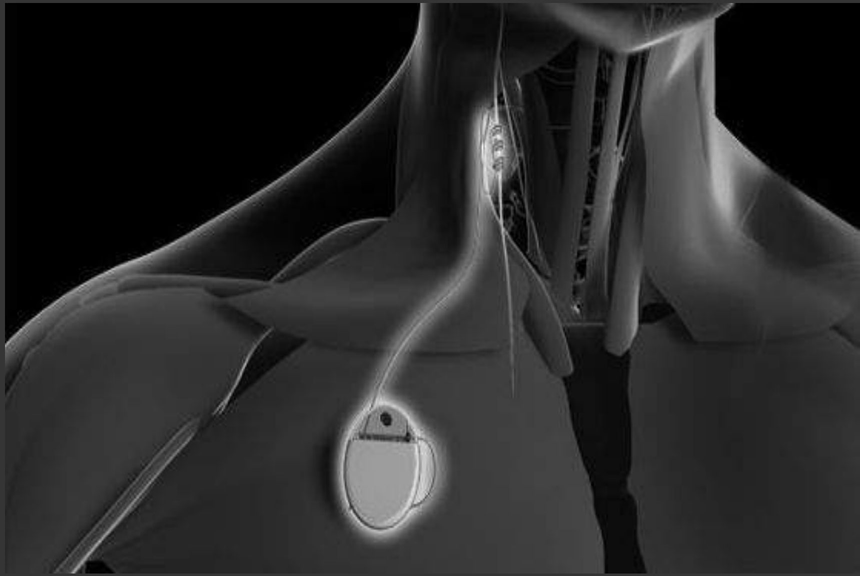
  Mandibular pain: 3

  Stimulus artefact on ECG: 1

- Non SAEs not related to the device: n = 11

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 ≤35%
  - Not CRT candidate, QRS ≤ 130 ms



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- **Left Atrial Appendage Occlusion: LAAO**

New Entries in the ESC Guidelines for the Management of Atrial Fibrillation (AF)[1]

Recommendation for Left Atrial Appendage Occlusion (LAAO)

The European Society of Cardiology has released the 2012 focused update on the guidelines for the management of atrial fibrillation. This update includes for the first time a recommendation for the use of left atrial appendage occlusion.

The update was developed with contribution from the European Heart Rhythm Association (EHRA).

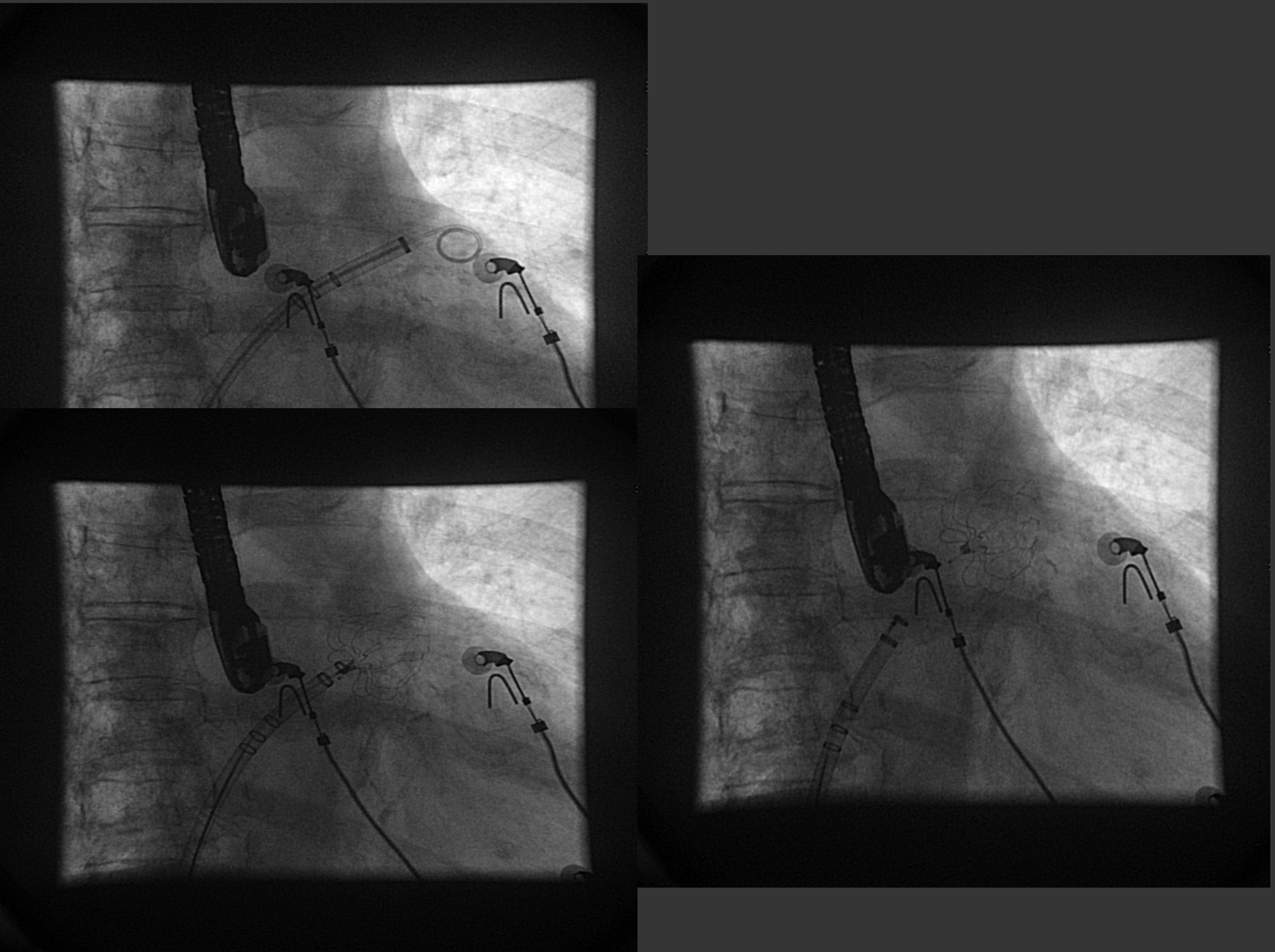
Recommendations for LAA closure/occlusion/excision

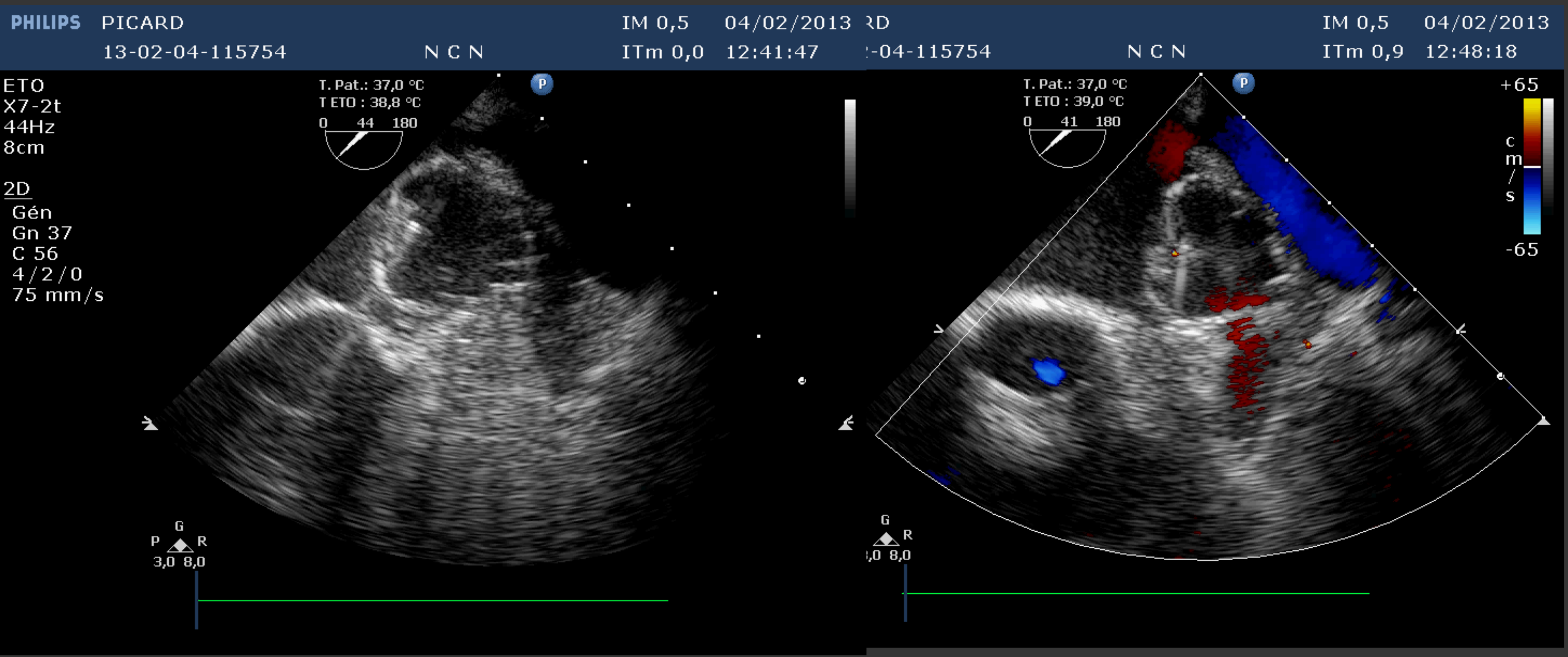
Recommendations	Class[a]	Level[b]	Ref[c]
Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.	IIb	B	115, 118
Surgical excision of the LAA may be considered in patients undergoing open heart surgery.	IIb	C	

LAA = left atrial appendage.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.

- "Interventional percutaneous occlusion/closure of the LAA has a role in patients with thromboembolic risk who cannot be managed in the long-term using any form of OAC."[1]

Source: Camm A, Lip G, De Caterina R, et al. "2012 focused update of the ESC Guidelines for the management of atrial fibrillation." *Eur Heart J.* Presented ahead of publication European Society of Cardiology Congress; 2012 August 25-29; Munich, Germany.

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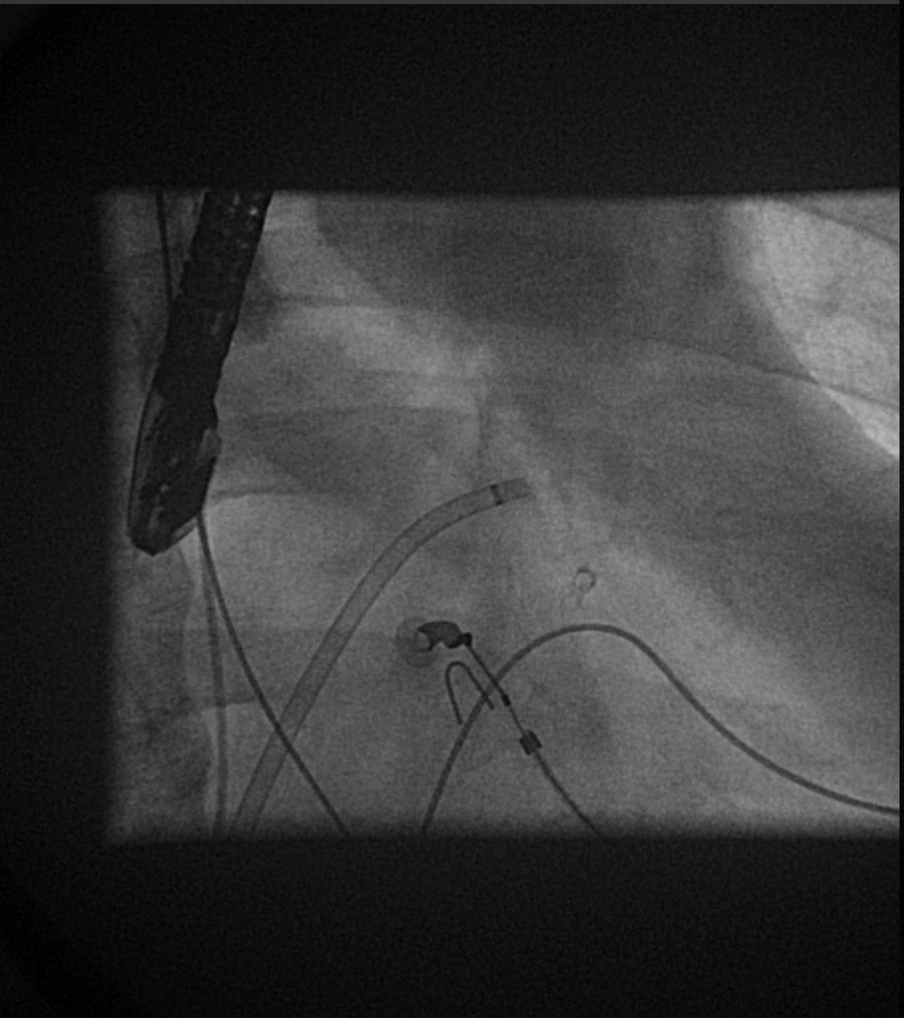
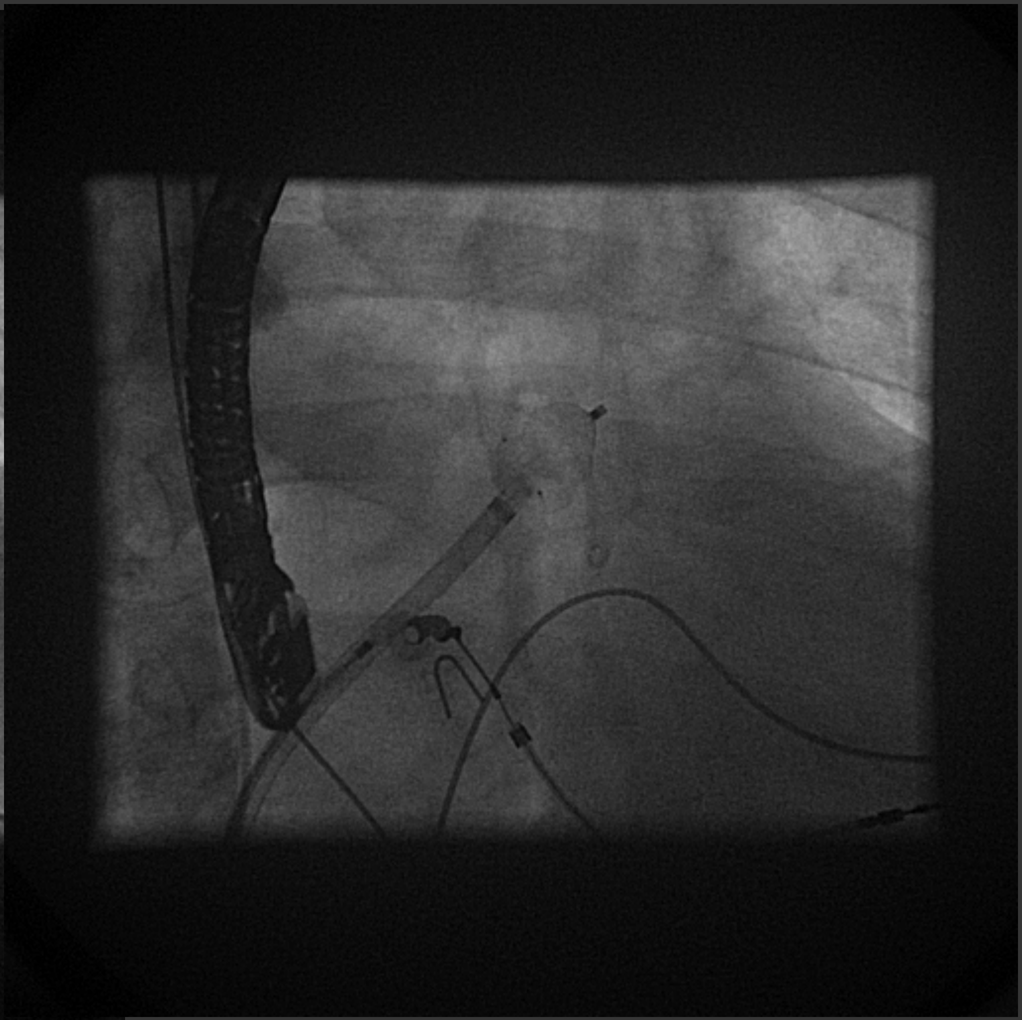

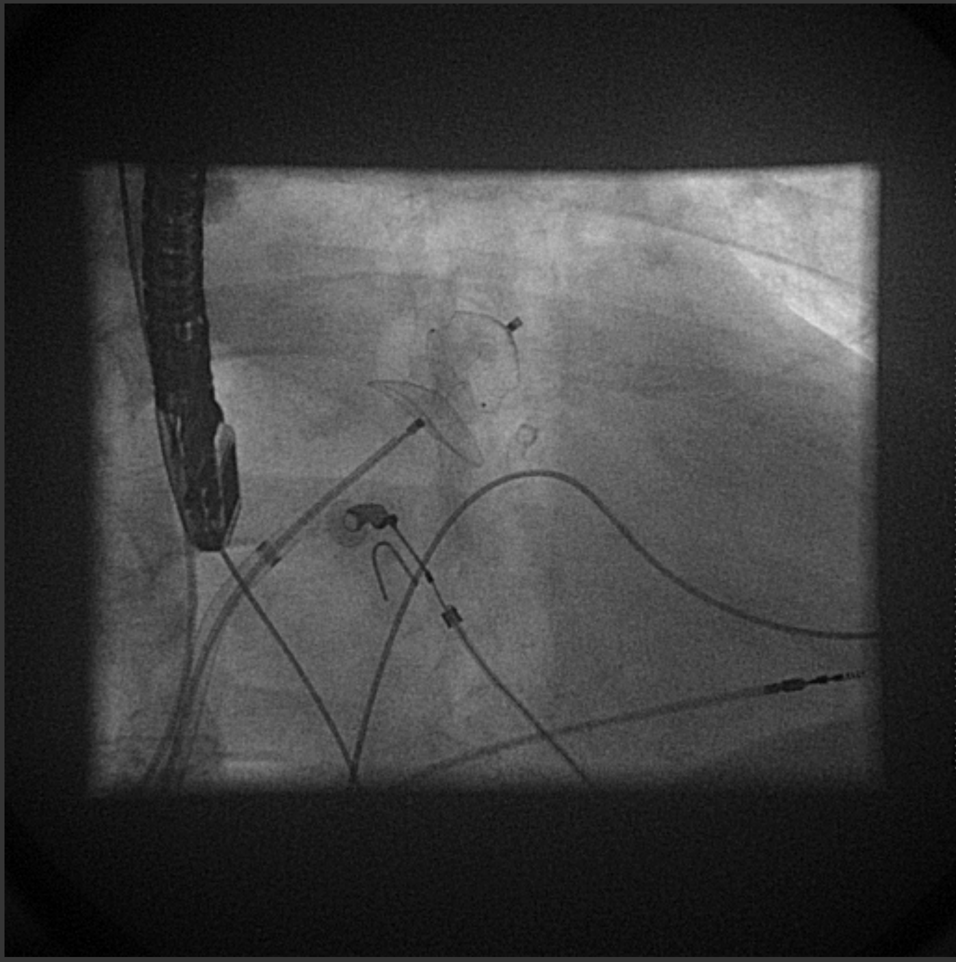
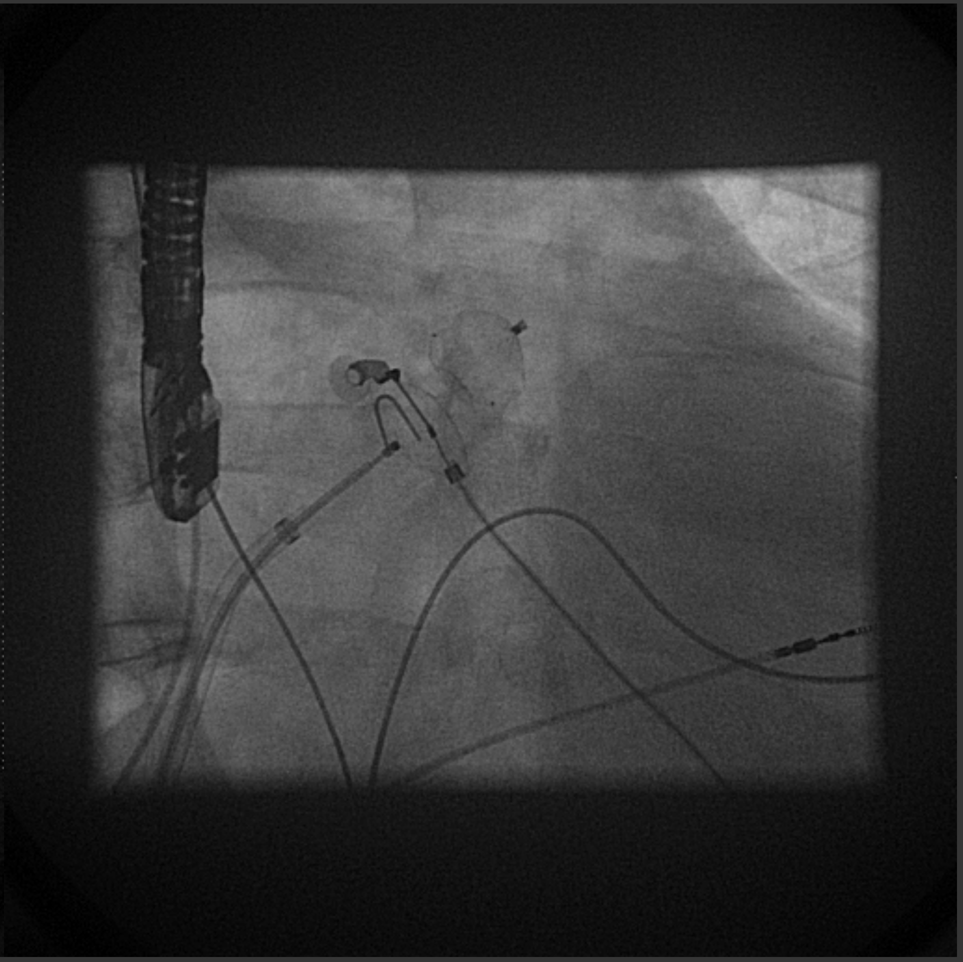

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   . Multisite Ventricular Pacing
   . Vagal Nerve stimulation in HF